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This supplementary material has been provided by the authors to give readers additional information about their work.
eMethods. Detailed Methods

eMethods 1. Search strategy and selection criteria

The meta-analysis was carried out complying with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (www.prisma-statement.org) (eTable 2). The protocol (registration number: CRD42021253875) was registered in the international prospective register of systematic reviews (www.crd.york.ac.uk/PROSPERO/). We conducted a systematic comprehensive literature search in PubMed, Embase, Web of Science, and Science Direct for studies on CTh published before June 15, 2021, using keywords such as “psychosis” or “psychotic” or “schizophrenia” or “schizoaffective” or “schizoaffective disorder” plus “cortical thickness” or “thickness”.

Additional publications were identified by manual search in the reference lists. Two authors (Y.J.Z, and Q.Z) independently conducted the literature search to ensure comprehensiveness. Any inconsistencies during the literature search were discussed and a consensus decision was reached about the appropriateness of the study for this meta-analysis.

Inclusion criteria were as follows: (a) studies published in English in a peer-reviewed journal; (b) included individuals with CHR for psychosis, or FEP, or long-term SCZ (which we defined studies where participants had illness duration greater than five years); (c) analyzed whole-brain CTh; and (d) provided the coordinates of significant clusters in Montreal Neurological Institute (MNI) or Talairach space. We excluded: (a) theoretical papers, case reports, reviews, and meta-analyses; (b) studies of individuals at genetic high risk for psychosis; (c) limited to region of interest analysis; (d) no statistical comparisons of CTh between individuals with CHR/FEP/long-term SCZ and HCs; and (e) peak coordinates of effects were not available even after contacting the authors. For longitudinal studies, only baseline data were included to avoid bias towards the effects of interventions or illness progression. For studies with multiple publications from overlapping samples, the one with the largest sample was included. For studies where multiple independent subgroups match criteria for one or more of the three illness stages of interest, the appropriate coordinates were included as separate datasets; if the coordinates of findings between subgroups and HCs were not available, we included the coordinates between the combined patient group (if they were within the range of one of our three illness stages) and HCs as one dataset. Eligible studies that reported no group differences were also included and estimated conservatively to have a null effect size in SDM.

eMethods 2. Quality assessment and data recording

A 12-parameter protocol was used to record average demographic and clinical characteristics of participants (sample size, gender, age, age of onset, illness duration, symptom severity, and medication status) and basic methodological information (statistical threshold of main findings and the method used to correct whole-brain results for multiple comparisons) (eTable 3). In the 12-point checklist, each point was scored 1 as fully met, 0.5 as partially met, or 0 as unfulfilled, respectively. Any study scoring >6.0 was included in the present meta-analysis. The checklist was not designed to critique the investigators or the work itself, but to provide an objective indication of the rigor of the individual studies. We also extracted the coordinates of significant findings and statistical values related to effect size (e.g., t statistics, Z score, or P value) for SDM calculations.

eMethods 3. SDM method of meta-analysis

Meta-analyses of CTh abnormalities were conducted using SDM software (version 5.15). The details of the SDM method have been described elsewhere, but we summarize the approach here. First, SDM uses the coordinates of cluster peaks and the effect sizes of significant differences between participants and controls to create an effect-size signed map for each study utilizing an anisotropic Gaussian kernel. When selecting coordinates, the same threshold was used throughout the whole brain in each study to avoid bias towards regions with liberal thresholds. Eligible studies that reported no group differences were also included and estimated conservatively to have a null effect size in SDM. We used the “VBM (voxel-based morphometry) - gray matter” modality, “gray matter” correlation template, and “FreeSurfer” mask to increase the accuracy of effect size maps, which restricted maps to cortical gray matter. Next, SDM was used to perform a random-effects analysis to obtain the mean map, combining data of each included study with both positive and negative differences included in the same map. We used SDM’s default thresholds (voxel threshold P<0.005 with peak Z>1 and a cluster extent of ten voxels) to display results in MNI coordinates.

eMethods 4. Jackknife, heterogeneity, and publication bias analysis

To test the replicability of results, whole-brain jackknife sensitivity analysis was conducted by repeating the main analysis N times (N=number of datasets in the meta-analysis), discarding one dataset at a time to determine whether the results remained significant. Between-study heterogeneity was estimated using I² statistic. Publication bias was examined with Egger tests to assess the asymmetry of funnel plots for each significant cluster of patient-control comparisons, in which any result showing P<0.05 was judged to have significant publication bias.

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**eMethods 5. Meta-regression analysis**

Meta-regression analyses were performed in the combined sample. In secondary exploratory studies, similar analyses were conducted in each group separately. The effect size values of each cluster were extracted from the SDM software and used for regression analyses with clinical and demographic variables. Clinical variables were not included in meta-regression analysis if data were available for fewer than nine studies, and thus only one variable (i.e., age) was explored in the CHR group and two variables (i.e., age and illness duration) were explored in FEP group and long-term SCZ group. Six variables (i.e., age, onset age, illness duration, positive, negative, and general scores of Positive and Negative Syndrome Scale [PANSS]) were explored in the combined group. Notably, since CHR group had no illness duration, meta-regression of this variable was performed only using data from the FEP and long-term SCZ groups. Aging effects on the human brain are believed to follow a nonlinear trajectory even through midlife in some brain regions, perhaps even more so in SCZ patients. Thus, nonlinear (i.e., a quadratic model) regression models were further examined when testing for age relationships. Bonferroni adjustments corrected for the number of variables examined and the number of clusters. Therefore, the corrected P threshold for the CHR group, FEP group, long-term SCZ group, and the combined group was 0.05, 0.0083, 0.0063, and 0.0017 for linear regression analysis; and 0.05, 0.017, 0.0125, and 0.01 for nonlinear regression analysis of age, respectively. If both linear and quadratic models for age effects were significant for a cluster, performance of the two regression models was evaluated by their root-mean-square error (RMSE) (i.e., the standard deviation of the residual) with a leave-one-dataset-out cross-validation strategy, then RMSE values of the two models were compared using a paired Wilcoxon signed-rank test (P<0.05).
eResults. Detailed Results

eResults 1. Results of quality assessments
The mean score of CHR studies was 9.7, 9.33 for FEP studies, and 9.95 for long-term SCZ studies (eTable 3). Quality assessment items that deducted the most scores of these studies were lack of desired information about medication status, comorbidity, coordinates availability, acquisition parameters, and subtype status.

eResults 2. Characteristics of studies included in the meta-analysis
Age did not differ between patients and controls in each included study, nor between studies in each of our three separate meta-analyses or in the pooled meta-analysis (all P>0.05). For FEP and long-term SCZ groups, there were no significant differences in sex ratio between patients and HCs in each included study (all P>0.05), nor in FEP (P=0.1702) or long-term SCZ (P=0.1156) meta-analyses. For the CHR group, three original studies showed significant between-group differences in sex ratio 11-13, as did our meta-analysis of CHR studies (P<0.001). Three subdirectories of eTable 4 summarize the demographic and clinical characteristics of each included study for CHR, FEP, and long-term SCZ groups, respectively.

1. Characteristics of ten studies in CHR individuals
Among the ten included studies in CHR individuals, seven were cross-sectional and three were longitudinal. For these three longitudinal studies 14-16, only baseline data were included. Two of the ten studies subdivided CHR samples into subgroups based on whether they converted to frank psychosis 14,15 and had psychotic symptoms 17. Notably, different diagnostic criteria were used to define the CHR participants. Five studies used the Structured Interview for Prodromal Syndromes (SIPS) criteria 14,15,17,19, three used the Comprehensive Assessment of At-Risk Mental States (CAARMS) criteria 10,20,21, one used Personal Assessment and Crisis Evaluation (PACE) criteria 11, and the remaining one used the Early Detection and Intervention in Psychosis (TIPS) 22.

CHR individuals of eight studies were medicated for the presentation of prodromal symptoms 11,14-17,19,21, of two were medication-naive 18,22. Four of the seven cross-sectional studies identified CTh alterations in CHR individuals compared with HCs 11,19,20,22, while the other three cross-sectional studies did not find significant between-group differences 17,18,21, nor did the three longitudinal studies at baseline 14-16. There were 13 datasets among the ten CHR studies included in the present meta-analysis.

2. Characteristics of 12 studies in individuals with FEP
Twelve studies were included in the FEP meta-analysis, in which eight were cross-sectional and four were longitudinally designed. Only baseline data of these four longitudinal studies were included 12,13,23,24. FEP individuals of nine studies were medicated (less than a year) 11-13,24-29, of two were medication-naive 30,31, and one study recruited individuals with FEP who were at a wash-out period 23. The illness duration of enrolled FEP individuals was specified in four studies 24,25,29,30 and unstated in two studies 11,13. While other six studies described it as the duration of untreated psychosis since the treatment time was quite short (i.e., less than a year) 12,23,26-28,31. Among the 12 FEP studies, three studies divided FEP individuals into subgroups based on drug class 23, cannabis use 24, and medication status 30, respectively. No significant case-control differences were reported in four of eight cross-sectional studies 26,28,30,31, nor in all four longitudinal studies at baseline 12,13,23,24. Thirteen datasets were eventually included in the present FEP meta-analysis.

3. Characteristics of ten studies in individuals with long-term SCZ
Ten included studies on CTh of long-term SCZ comprised nine cross-sectional and one longitudinal study. Only baseline data of the longitudinal studies were included 32. Eight studies enrolled all medicated individuals, among which six studies reported chlorpromazine equivalent dosages with a mean daily dose of 531.68 mg 33-38, one standardized the antipsychotic dosage using the defined daily dose with a mean unit of 1.53 39, and the remaining one did not report the medication dosage 40. One study recruited medication-naive individuals 18, and the remaining one used a mixture of antipsychotic-naive patients and some with previously treated but currently untreated individuals 32. Three studies recruited two subgroups depending on the treatment response 33,39 and homogeneous subtype 36. Significant CTh differences were reported between long-term SCZ individuals and HCs in all included studies except the longitudinal study at baseline 32. There were 12 datasets among the ten studies included in the final long-term SCZ meta-analysis.

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eResults 3. Results of jackknife, heterogeneity, and publication bias analysis

1. Results of the CHR group

In the CHR group, whole-brain jackknife sensitivity analysis showed that decreased CTh in bilateral mPFC was preserved in 11 of 13 combinations (eTable 9). This region showed very low heterogeneity ($I^2=3.59\%$) between studies. Egger test of funnel plot asymmetry was not statistically significant (eFigure 8).

2. Results of the FEP group

In the FEP group, whole-brain jackknife sensitivity analysis showed that decreased CTh in the right lateral STC, ACC, and insula were preserved in 12, 11, and 13 of 13 combinations, respectively (eTable 10). The right lateral STC and ACC showed low heterogeneity ($I^2=5.92\%, 11.17\%$, respectively) between studies, while the right insula showed high heterogeneity ($I^2=82.50\%$) between studies. Egger tests of funnel plot asymmetry were not statistically significant in the above three clusters (eFigure 9).

3. Results of the long-term SCZ group

In the long-term SCZ group, whole-brain jackknife sensitivity analysis showed that these CTh reductions were consistent, with effects in right insula and bilateral TP being preserved throughout all 12 combinations of datasets and those in the right pars orbitalis being significant in 12 combinations of 12 datasets (eTable 11). All findings showed low heterogeneity ($I^2=3.79\%, 3.82\%, 5.33\%, \text{ and } 8.4\%$ for right insula, right pars orbitalis, left temporal pole, and right temporal pole, respectively) between studies. Egger tests of funnel plot asymmetry were not statistically significant in any of the above four clusters (eFigure 10).

4. Results of the combined group

In the combined group with 38 datasets in total, whole-brain jackknife sensitivity analysis showed that decreased CTh in the right insula, left ACC, right pars orbitalis of IFC, left lateral MTC, and right lateral MTC were preserved in 38, 36, 36, 33, and 38 combinations of 38 datasets, respectively (eTable 12). The left ACC, right pars orbitalis, left lateral MTC, and right lateral MTC showed low heterogeneity ($I^2=3.26\%, 0.14\%, 8.25\%, \text{ and } 15.16\%$, respectively) between studies, while the right insula showed moderate heterogeneity ($I^2=45.00\%$) between studies. The Egger tests of funnel plot asymmetry were not statistically significant in the above five clusters (eFigure 11).
## eTable 1. Overview of published VBM and SBM meta-analyses on individuals at CHR, FEP, or long-term SCZ

| Stage | Study | methods | Sample size | Main results |
|-------|-------|---------|-------------|--------------|
| **CHR** | Fortea et al. 2021 | VBM & SBM | 1248 CHR vs 1122 HCs; 153 CV vs 547 NCV | 1. No significant differences in cortical GM were found in CHR individuals relative to HCs. 2. CV showed decreased cortical GM in right STC and MTC, ACC, and paracingulate gyrus than NCV. |
| | Liloia et al. 2021 | VBM | 580 CHR vs 6007 HCs | CHR individuals showed GMV reduction in right ACC than HCs. |
| | Hinney et al. 2020 | VBM | 94 CV vs 513 NCV | No statistically significant differences in hippocampal volume between CV and NCV at baseline, but a trend of reduction of right hippocampus volume associated with the transition was found. |
| | Saunders et al. 2019 | VBM | 191 CHR vs 134 HCs | 1. CHR individuals showed no significant differences in pituitary volume than HCs. 2. CV showed increased baseline pituitary volume than HCs. |
| | Smieskova et al. 2010 | VBM | 385 CHR vs 290 HCs | 1. CV showed reduced regional GMV in the insula, ACC, PFC, and cerebellum than NCV. 2. CV showed larger global volumes than NCV. |
| **FEP** | Wen et al. 2021 | SBM | 624 FEP vs 505 HCs | FEP individuals showed CTh reductions in the right MTC extending to STC, insula, and ACC than HCs. |
| | Liloia et al. 2021 | VBM | 1636 FEP vs 6007 HCs | FEP individuals showed GMV reduction in the left precentral gyrus, left IFC, bilateral STC, bilateral transverse temporal gyrus, right MTC, bilateral insula, bilateral ACC, left parahippocampal gyrus, and left amygdala than HCs. |
| | Shah et al. 2017 | VBM | 801 FEP (449 AN-FEP and 352 AT-FEP) vs 957 HCs | 1. AN-FEP individuals showed increased GM in the left inferior parietal gyri and left paracentral lobule, and decreased GM in the bilateral insula, right SFC, and left fusiform gyrus than HCs. 2. AT-FEP individuals showed increased GM in the right middle occipital gyrus, and right SFC and decreased GM in left ACC/paracingulate gyrus, left MTC, right postcentral gyrus, and left ITC than HCs. 3. GM in left supramarginal gyrus and left MTC were increased in AN-FEP but decreased in AT-FEP, whereas left MCC/paracingulate gyrus and right hippocampus GM was decreased in AN-FEP but increased in AT-FEP. |
| | Fraguas et al. 2014 | VBM | 156 FEP vs 163 HCs | FEP individuals showed progressive GMV changes in the frontal lobe than HCs. |
| | Olabi et al. 2012 | VBM | 555 FEP vs 621 HCs | FEP individuals showed GMV reductions in the bilateral caudate head, left insula, and bilateral uncus region. |
| | Vita et al. 2012 | VBM | 664 FEP vs 585 HCs | FEP individuals showed progressive GMV loss in the frontal, temporal and parietal lobes, and left Heschl gyrus than HCs. |
| | Chan et al. 2011 | VBM | 466 FEP vs 616 HCs | FEP individuals showed decreased GMV in the ACC and right insula than HCs. |

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| Study          | VBM   | Sample Description                                                                 | Key Findings                                                                                                                                 |
|---------------|-------|------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
| Leung et al. 2011 | VBM   | 162 AN-FEP vs 165 HCs; 336 AT-FEP vs 484 HCs                                        | 1. AN-FEP showed GMV reductions in the bilateral caudate, insula, uncus, STC, and ITC; left PCC, precentral and SFC, and culmen; and right cingulate, middle frontal cortex, IFC, claustrum, and cerebellar tonsil than HCs.  
2. AT-FEP showed GMV reductions in the bilateral insula, medial frontal cortex, IFC, and STC; left parahippocampal gyrus (amygdala), uncus, and ACC; and right thalamus, cingulate, precentral, and middle frontal gyrus than HCs.  
3. AN-FEP individuals showed less GMV deficits in the bilateral insula, medial frontal, and IFC; left parahippocampal gyrus (amygdala) and STC; and right precentral gyrus, but more extensive GMV deficits in the bilateral caudate and ITC; left PCC, precentral, SFC, and culmen; right cingulate, middle frontal, and STC and claustrum than AT-FEP individuals. |
| Ellison-Wright et al. 2008 | VBM   | 224 FEP vs 248 HCs                                                               | FEP individuals showed decreased GMV in the thalamus, left uncus/amygdala region, the insula bilaterally, and the ACC than HCs.                  |
| Liloia et al. 2021 | VBM   | 2120 long-term SCZ vs 6007 HCs                                                   | Long-term SCZ individuals showed GMV reduction in right medial frontal cortex, left IFC, left STC, bilateral anterior insula, bilateral ACC, bilateral amygdala, head of left caudal nucleus, and medial dorsal nucleus of left thalamus than HCs. |
| Chan et al. 2011 | VBM   | 808 long-term SCZ vs 856 HCs                                                     | Long-term SCZ individuals showed decreased GMV in the ACC, right insula, right parahippocampus, left amygdala, left frontal lobe, left insula, thalamus, and left PCC than HCs. |
| Ellison-Wright et al. 2008 | VBM   | 1332 long-term SCZ vs 1293 HCs                                                   | Long-term SCZ individuals showed decreased GMV in the thalamus, left uncus/amygdala region, the insula bilaterally, and the ACC than HCs. |

Abbreviations: CV, converters; NCV, nonconverters; CHR, clinical high-risk; SCZ, schizophrenia; VBM, voxel-based morphometry; GMV, gray matter volume; SBM, surface-based morphometry; CTh, cortical thickness; FEP, first-episode psychosis; AN-FEP, antipsychotic-naive FEP; AT-FEP, antipsychotic-treated FEP; STC, superior temporal cortex; SFC, superior frontal cortex; ACC, anterior cingulate cortex; PFC, prefrontal cortex; IFC, inferior frontal cortex; PCC, posterior cingulate cortex; MTC, middle temporal cortex; ITC, inferior temporal cortex; MCC, middle cingulate cortex; vs, versus; HCs, healthy controls.
**eTable 2. The checklist of methodology quality assessment for the included studies**

1. **The checklist of methodology quality assessment for the included studies in CHR individuals***

| 12-point checklist ² | Bakker ¹⁸ | Buechler ¹⁷ | Cannon ¹⁴ | Dukart ¹¹ | Gisselgård ²² | Jung ²⁰ | Klauser ²¹ | Kwak ¹⁹ | Tognin ¹⁶ | Ziermans ¹⁵ |
|----------------------|-----------|-----------|----------|---------|-----------|---------|---------|-------|-------|---------|
| **Category 1: Subjects** |           |           |          |         |           |         |         |       |       |         |
| 1 Patients were evaluated prospectively, specific diagnostic criteria were applied, and demographic data were reported | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2 Healthy comparison participants were evaluated prospectively; psychiatric and medical illnesses were excluded | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 3 Important variables (e.g., age, gender, drug status, illness duration, and symptom severity) were checked either via stratification or statistics | 1 | 1 | 1 | 0.5 | 1 | 0.5 | 0.5 | 1 | 1 | 1 |
| 4 All patients were comorbidity free | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| 5 All patients were medication naïve | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| 6 Sample size per group: ≥ 20, scores 1; ≥ 10, scores 0.5 | 0.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Category 2: Methods for image acquisition and analysis** |           |           |          |         |           |         |         |       |       |         |
| 7 Magnet strength: 3T, scores 1; 1.5T, scores 0.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0.5 | 1 | 1 | 0.5 |

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| Category | Criteria                                                                 | Score 1 | Score 0.5 | Score 0 | Total Score |
|----------|--------------------------------------------------------------------------|---------|-----------|---------|-------------|
| Category 3: Results and conclusions | | | | | |
| 11 | Statistical results were corrected for multiple comparison scores 1, uncorrected scores 0.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 9.5 |
| 12 | Conclusions were consistent with the results obtained, and the limitations were discussed | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | | 9.5 |

*Note: Each point was scored as 1, 0.5, or 0 if the criteria were fully met, partially met, or unfulfilled, respectively, and any study scoring >6.0 was included in the present meta-analysis.*
2. The checklist of methodology quality assessment for the included studies in FEP individuals*.

| 12-point checklist | Ansell 25 | Buchy 23 | Dukart 11 | Gutierrez-Galve 26 | Haukvik 12 | Lesh 30 | Lin 31 | Rais 24 | Reniers 13 | Scanlon 27 | Thormodsen 28 | Voets 29 |
|--------------------|-----------|----------|-----------|-------------------|------------|--------|--------|---------|-----------|-----------|-------------|----------|
| **Category 1: Subjects** |           |          |           |                   |            |        |        |         |           |           |             |          |
| 1 Patients were evaluated prospectively, specific diagnostic criteria were applied, and demographic data were reported | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2 Healthy comparison participants were evaluated prospectively; psychiatric and medical illnesses were excluded | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 3 Important variables (e.g., age, gender, drug status, illness duration, and symptom severity) were checked either via stratification or statistics | 1 | 1 | 0.5 | 1 | 1 | 1 | 1 | 1 | 0.5 | 1 | 0.5 | 1 |
| 4 All patients were comorbidity free | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 5 All patients were medication naïve | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| 6 Sample size per group: ≥ 20, scores 1; ≥ 10, scores 0.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

**Category 2: Methods for image acquisition and analysis**
|   | Magnet strength: 3T, scores 1; 1.5T, scores 0.5 | 0.5 | 0.5 | 1 | 0.5 | 0.5 | 1 | 0.5 | 1 | 0.5 | 0.5 | 0.5 |
|---|-----------------------------------------------|-----|-----|---|-----|-----|---|-----|---|-----|-----|-----|
| 8 | The imaging technique used was clearly described so that it could be reproduced | 1   | 1   | 1 | 1   | 1   | 1 | 1   | 1 | 1   | 1   | 1   |
| 9 | Whole brain analysis was automated without a previously defined region | 1   | 1   | 1 | 1   | 1   | 1 | 1   | 1 | 1   | 1   | 1   |
| 10| Spatial coordinates were reported in a standard space (e.g., Talairach or MNI coordinates) | 1   | 0   | 1 | 0   | 0   | 0 | 0   | 0 | 0   | 0   | 1   |

**Category 3: Results and conclusions**

|   | Statistical results were corrected for multiple comparison scores 1, uncorrected scores 0.5 | 1   | 1   | 1 | 1   | 1   | 1 | 1   | 1 | 1   | 1   | 1   |
|---|------------------------------------------------------------------------------------------|-----|-----|---|-----|-----|---|-----|---|-----|-----|-----|
| 12| Conclusions were consistent with the results obtained, and the limitations were discussed | 1   | 1   | 1 | 1   | 1   | 1 | 1   | 1 | 1   | 1   | 1   |

**Total score**

|   | 10.5 | 9.5 | 9.5 | 8.5 | 9.5 | 9.5 | 10 | 8.5 | 9.5 | 9.5 | 9   | 9.5 |

*Note: Each point was scored as 1, 0.5, or 0 if the criteria were fully met, partially met, or unfulfilled, respectively, and any study scoring >6.0 was included in the present meta-analysis.*
3. The checklist of methodology quality assessment for the included studies in long-term SCZ individuals*

| Category 1: Subjects | Barry | Green | Kong | Landin-Romero | Madre | Nelson | Quide | Xie | Zhang | Zugman |
|----------------------|-------|-------|------|---------------|-------|--------|-------|-----|-------|--------|
| 1 | Patients were evaluated prospectively, specific diagnostic criteria were applied, and demographic data were reported | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 2 | Healthy comparison participants were evaluated prospectively; psychiatric and medical illnesses were excluded | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 3 | Important variables (e.g., age, gender, drug status, illness duration, and symptom severity) were checked either via stratification or statistics | 1 | 1 | 0.5 | 0.5 | 1 | 1 | 1 | 1 | 1 | 0.5 |
| 4 | All patients were comorbidity free | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| 5 | All patients were medication naïve | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| 6 | Sample size per group: ≥ 20, scores 1; ≥ 10, scores 0.5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |

Category 2: Methods for image acquisition and analysis

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|   |   | Magnet strength: 3T, scores 1; 1.5T, scores 0.5 |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 7 |   |   |   |   |   |   |   |   |   |
| 8 |   | The imaging technique used was clearly described so that it could be reproduced |   |   |   |   |   |   |   |
| 9 |   | Whole brain analysis was automated without a previously defined region |   |   |   |   |   |   |   |
| 10|   | Spatial coordinates were reported in a standard space (e.g., Talairach or MNI coordinates) |   |   |   |   |   |   |   |

**Category 3: Results and conclusions**

|   |   | Statistical results were corrected for multiple comparison scores 1, uncorrected scores 0.5 |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 11|   |   |   |   |   |   |   |   |   |
| 12|   | Conclusions were consistent with the results obtained, and the limitations were discussed |   |   |   |   |   |   |   |

**Total score**

|   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 10.0 | 9.5 | 9.5 | 9.0 | 9.5 | 10.0 | 10.0 | 11.0 | 12.0 | 9.0 |

*Note: Each point was scored as 1, 0.5, or 0 if the criteria were fully met, partially met, or unfulfilled, respectively, and any study scoring >6.0 was included in the present meta-analysis.*

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### eTable 3. Demographic and clinical characteristics of studies included in the meta-analysis

#### 1. Demographic and clinical characteristics of the ten studies of individuals with CHR features of psychosis

| Study                     | Number (female) | Mean age, y | Symptom severity | Medication status (medicated number/CPZ equivalents (mg/day)) | Statistical threshold (correction) |
|---------------------------|-----------------|-------------|------------------|----------------------------------------------------------------|-----------------------------------|
| Bakker et al. 2016        | 18 (9) - 24 (10) | 22.7 - 23.4 | PANSS: 68.2 (Total), 11.3 (Pos), 11.8 (Neg), 45.1 (Gen)       | All naive                        | P < 0.05 (FDR)                    |
| Buechler et al. 2020 - NBS| 39 (14) - 34 (18) | 21.79 - 21.76 | SIPS: 38.24 (Total), 10.67 (Pos), 13.59 (Neg), 8.9 (Gen), 5.08 (Dis); GAF: 50.33 | 12/40.33                         | P < 0.05 (MCS)                    |
| Buechler et al. 2020 - BS | 46 (23) - 34 (18) | 22.7 - 21.76 | SIPS: 26.12 (Total), 4.67 (Pos), 11.24 (Neg), 7.28 (Gen), 2.93 (Dis); GAF: 57.98 | 8/21.66                          | P < 0.05 (MCS)                    |
| Cannon et al. 2015 - CV   | 35 (10) - 135 (62) | 18.8 - 20.5 | SIPS: NA (Total), 13.5 (Pos), NA (Neg), NA (Gen), NA (Dis)    | 35/93.3                           | P < 0.05 (FDR)                    |
| Cannon et al. 2015 - NCV  | 239 (93) - 135 (62) | 19.7 - 20.5 | SIPS: NA (Total), 11.9 (Pos), NA (Neg), NA (Gen), NA (Dis)    | 239/97.5                          | P < 0.05 (FDR)                    |
| Dukart et al. 2017        | 59 (16) - 26 (14) | 24.7 - 27.7 | BPRS: 39.4; SANS: 11                                         | 23/NA                            | P < 0.05 (alpha-sim)              |
| Gisselgård et al. 2018    | 41 (25) - 37 (18) | 16.7 - 16.9 | SIPS: 33.1 (Total), 10.1 (Pos), 10.9 (Neg), 8.8 (Gen), 3.3 (Dis); GAF: 49.9 | All naive                        | P < 0.005 (MCS)                   |
| Jung et al. 2011          | 29 (14) - 29 (14) | 22.24 - 23.24 | PANSS: 53.66 (Total), 12.72 (Pos), 11.72 (Neg), 29.17 (Gen); CAARMS: 37.41 | 10/NA                            | P < 0.01 (FDR)                    |
| Klauser et al. 2015       | 69 (22) - 32 (15) | 21.52 - 22.97 | CAARMS: 16.33                                               | 37/NA                            | P < 0.05 (FDR)                    |
| Kwak et al. 2019          | 74 (20) - 34 (14) | 20.61 - 20.29 | SOPS: 10.03 (Pos), 14.31 (Neg), 7.18 (Gen), 4.38 (Dis)       | 28/NA                            | P < 0.05 (MCS)                    |
| Tognin et al. 2014 - CV   | 50 (13) - 150 (51) | 22.9 - 23.4 | PANSS: 57.25 (Total), 12.06 (Pos), 15.44 (Neg), 29.75 (Gen); CAARMS: 8.37; GAF: 46.5; BPRS: 33.08; SANS: 21.26 | 5/NA                             | P < 0.05 (FWE)                    |
| Tognin et al. 2014 - NCV  | 117 (49) - 150 (51) | 23.3 - 23.4 | PANSS: 49.25 (Total), 10.27 (Pos), 12.02 (Neg), 26.95 (Gen); CAARMS: 6.82; GAF: 58.12; BPRS: 31.3; SANS: 19.48 | 21/NA                            | P < 0.05 (FWE)                    |
| Ziermans et al. 2012      | 43 (14) - 30 (15) | 15.6 - 15.9 | GAF: 59; BSABS: 20.5                                         | 21/NA                            | P < 0.05 (FDR)                    |

Abbreviations: BPRS, Brief Psychiatric Rating Scale; BS, basic symptoms; BSABS, Bonn Scale for the Assessment of Basic Symptoms; CAARMS, Comprehensive Assessment of At-Risk Mental States; CHR, clinical high-risk; CPZ, chlorpromazine; CV, converters; Dis, disorganization; FDR, False Discovery Rate; FWE, Family-Wise Error; GAF, global assessment of functioning; Gen, general; HCs, healthy controls; MCS, Monte Carlo simulation; NA, not available; NBS, not only basic symptoms; NCV, non-converters; Neg, negative; PANSS, Positive and
Negative Syndrome Scale; Pos, positive; SANS, Scale for Assessment of Negative Symptoms; SIPS, Structured interview for prodromal syndromes; SOPS, Scale of Prodromal Symptoms criteria.
### 2. Demographic and clinical characteristics of the 12 studies of individuals with FEP.

| Study                                      | Number (female) | Mean age, y | Age of onset, y | Illness duration, y | PANSS scores | Medication status (medicated number/CPZ equivalents (mg/day)) | Statistical threshold (correction) |
|--------------------------------------------|-----------------|-------------|-----------------|---------------------|--------------|-------------------------------------------------------------|-----------------------------------|
| Ansell et al. 2015 - FGA                  | 25 (8)          | 21.93       | 21.07           | 21.6                | 0.12         | 86/22.4/22/41.6                                            | P < 0.05 (FWE)                    |
| Ansell et al. 2015 - SGA                  | 27 (9)          | 21.95       | 21.07           | 21.4                | 0.25         | 88.6/22.4/21.9                                            | P < 0.05 (FWE)                    |
| Buchy et al. 2017                         | 130 (37)        | 24.1        | 24.3            | NA                  | 0.93         | NA/NA/NA/NA/NA                                             | P < 0.005 (RFT)                   |
| Dukart et al. 2017                        | 59 (17)         | 26.4        | 27.7            | NA                  | 0.87         | NA/NA/NA/NA/NA                                             | P < 0.05 (alpha-sim)              |
| Gutierrez-Galve et al. 2010               | 37 (12)         | 26.8        | 25              | NA                  | NA           | 37/NA                                                      | P < 0.05 (FDR)                    |
| Haukvik et al. 2016                       | 79 (27)         | 27.6        | 29.3            | 23.8                | 2.36         | 60.6/14.9/14/31.7                                         | P < 0.05 (FDR)                    |
| Lesh et al. 2015                          | 22 (3)          | 20.2        | 19.7            | NA                  | 0.58         | NA/NA/NA/NA/NA                                             | all naive                        | P < 0.05 (FDR)                    |
| Lin et al. 2019                           | 145 (76)        | 24.5        | 25.9            | 23.6                | 0.9          | 93.2/25.2/19.9/48.1                                        | all naive                        | P < 0.05 (FDR)                    |
| Rais et al. 2010                          | 32 (6)          | 23.28       | 24.72           | 21.54               | 1.07         | NA/17.23/18.18/NA/NA                                       | 51/NA                            | P < 0.1 (FDR)                     |
| Remiers et al. 2014                       | 22 (4)          | 20.64       | 22.48           | NA                  | NA           | NA/NA/NA/NA/NA                                             | 14/200                           | P < 0.002 (MCS)                   |
| Scanlon et al. 2014                       | 46 (14)         | 28.4        | 28.6            | NA                  | 1.17         | 65/17/15/33                                                | 46/224                           | P < 0.05 (FDR)                    |
| Thormodsen et al. 2013                    | 22 (12)         | 16.2        | 15.9            | NA                  | 0.41         | 57/14.4/12.7/29.9                                          | 17/1.47*                         | P < 0.05 (FDR)                    |
| Voets et al. 2008                         | 25 (7)          | 16          | 16              | 15                  | 1.4          | NA/NA/NA/NA/NA                                             | 25/340                           | P < 0.05 (FDR)                    |

*Defined Daily Dosages of antipsychotic medication use were calculated using the guidelines from the WHO (https://www.whocc.no/ate_ddd_index/).

Abbreviations: CPZ, chlorpromazine; FDR, False Discovery Rate; FEP, first-episode psychosis; FGA, first-generation antipsychotic; FWE, Family-Wise Error; Gen, general; HC, healthy controls; MCS, Monte Carlo simulation; NA, not available; Neg, negative; PANSS, Positive and Negative Syndrome Scale; Pos, positive; RFT, random field theory; SGA, second-generation antipsychotic.
### 3. Demographic and clinical characteristics of the ten studies of individuals with long-term SCZ.

| Study                        | Number (female) | Mean age, y | Age of onset, y | Illness duration, y | PANSS scores | Medication status (medicated number/CPZ equivalents (mg/day)) | Statistical threshold (correction) |
|------------------------------|-----------------|-------------|-----------------|--------------------|--------------|-------------------------------------------------------------|-----------------------------------|
| Barry et al. 2019           | 42 (6)          | 23 (6)      | 41.4            | 38.4               | 26.85        | 14.8                                                       | 61.55                             |
| Green et al. 2016            | 22 (12)         | 22 (12)     | 38.86           | 39.57              | 22.89        | 13.78                                                      | 73.9                             |
| Kong et al. 2015             | 22 (6)          | 20 (8)      | 53.95           | 52.75              | NA           | 31.54                                                      | NA                               |
| Landin-Romero et al. 2017    | 44 (18)         | 45 (19)     | 43.18           | 43.02              | NA           | 20.18                                                      | 32.86                            |
| Madre et al. 2020            | 128 (54)        | 127 (54)    | 41              | 39                 | 22           | 18                                                         | NA                               |
| Nelson et al. 2020           | 34 (9)          | 23 (4)      | 28.32           | 27.48              | 22.08        | 15                                                         | NA                               |
| Quide et al. 2019            | 60 (24)         | 61 (27)     | 41.16           | 35.98              | 22.53        | 18.33                                                      | 56.35                            |
| Xie et al. 2019 - DS         | 33 (0)          | 41 (0)      | 49.03           | 45.78              | 22.03        | 27                                                         | NA                               |
| Xie et al. 2019 - NDS        | 41 (0)          | 41 (0)      | 45.71           | 45.78              | 22.39        | 23.32                                                      | NA                               |
| Zhang et al. 2015            | 25 (11)         | 33 (15)     | 46.68           | 46.21              | 25.64        | 21.04                                                      | 88.71                            |
| Zugman et al. 2013 - NTR     | 67 (22)         | 80 (27)     | 35.81           | 33.46              | NA           | 12.21                                                      | 54.58                            |
| Zugman et al. 2013 - TR      | 61 (21)         | 80 (27)     | 33.8            | 33.46              | NA           | 12.9                                                       | 63.41                            |

*Defined Daily Dosages of antipsychotic medication use were calculated using the guidelines from the WHO ([https://www.whocc.no/atc_ddd_index/](https://www.whocc.no/atc_ddd_index/)).

Abbreviations: CPZ, chlorpromazine; CWC, cluster-wise correction; FDR, False Discovery Rate; FWE, Family-Wise Error; Gen, general; HC, healthy control; SCZ, schizophrenia; MCS, Monte Carlo simulation; NA, not available; NDS, nondeficit schizophrenia; Neg, negative; NTR, treatment response; PANSS, Positive and Negative Syndrome Scale; Pos, positive; RFT, random field theory; TR, treatment resistance.
**eTable 4. Results of the meta-regression analysis within each group, respectively**

| Clusters | Variables | Linear model | Quadratic model |
|----------|-----------|--------------|-----------------|
|          |           | R²  | P   | R²  | P   |
| CHR      |           |     |     |     |     |
| Left medial prefrontal cortex | age | 0.003 | 0.86 | 0.11 | 0.56 |
| FEP      |           |     |     |     |     |
| Right lateral superior temporal cortex | age | 0.001 | 0.93 | 0.43 | 0.06 |
| Right anterior cingulate cortex | age | 0.17 | 0.16 | 0.17 | 0.39 |
| Right insula | age | 0.01 | 0.75 | 0.09 | 0.64 |
| Right lateral superior temporal cortex | illness duration | 0.09 | 0.38 | -   | -   |
| Right anterior cingulate cortex | illness duration | 0.02 | 0.69 | -   | -   |
| Right insula | illness duration | 0.16 | 0.31 | -   | -   |
| Long-term SCZ |           |     |     |     |     |
| Right insula | age | 0.07 | 0.41 | 0.07 | 0.72 |
| Right inferior frontal cortex, orbital part | age | 0.22 | 0.13 | 0.22 | 0.33 |
| Right temporal pole, superior temporal cortex | age | 0.37 | 0.04 | 0.44 | 0.07 |
| Left temporal pole, middle temporal cortex | age | 0.43 | 0.02 | 0.59 | 0.02 |
| Right insula | illness duration | 0.04 | 0.52 | -   | -   |
| Right inferior frontal cortex, orbital part | illness duration | 0.26 | 0.09 | -   | -   |
| Right temporal pole, superior temporal cortex | illness duration | 0.49 | 0.01 | -   | -   |
| Left temporal pole, middle temporal cortex | illness duration | 0.60 | 0.003 | -   | -   |

Note: A region that survived Bonferroni correction for multiple comparisons (P<0.05) is shown in bold font. The corrected P threshold for the CHR group, FEP group, and long-term SCZ group was 0.05, 0.0083, and 0.0063 for linear regression analysis; and 0.05, 0.017, and 0.0125 for nonlinear regression analysis of age, respectively.

Abbreviations: CHR, clinical high-risk; FEP, first-episode psychosis; SCZ, schizophrenia.
eTable 5. Results of the comparison between CHR and long-term SCZ groups

| Region                                      | MNI coordinate | SDM | P, uncorrected | Voxel s | Cluster breakdown (voxels)                  |
|---------------------------------------------|----------------|-----|----------------|---------|--------------------------------------------|
|                                             |                |     |                |         |                                            |
| Long term-SCZ < CHR                         |                |     |                |         |                                            |
| Right insula                                | 40 4 2         | -2.95 | <0.001          | 1222    | Right insula (714)                          |
|                                             |                |     |                |         |                                            |
| Left inferior frontal cortex, orbital part  | 48 30 -1 2     | -2.41 | <0.001          | 368     | Left inferior frontal cortex, orbital part (350) |
|                                             |                |     |                |         | Left inferior frontal cortex, triangular part (18) |
| Left middle temporal cortex                 | -50 0 -2 0     | -2.02 | 0.002           | 344     | Left middle temporal cortex (231)           |
|                                             |                |     |                |         | Left superior temporal cortex (82)          |
|                                             |                |     |                |         | Left inferior temporal cortex (31)          |
| Right temporal pole, middle temporal cortex | 50 6 -1 3      | -1.92 | 0.002           | 143     | Right temporal pole, middle temporal cortex (108) |
|                                             |                |     |                |         | Right inferior temporal cortex (26)         |
|                                             |                |     |                |         | Right temporal pole, superior temporal cortex (9) |

Abbreviations: CHR, clinical high-risk; SCZ, schizophrenia; MNI, Montreal Neurological Institute.
### eTable 6. Results of the meta-regression analysis in the combined group

| Clusters                                | Variables | Linear model | Quadratic model |
|-----------------------------------------|-----------|--------------|-----------------|
|                                         |           | $R^2$        | $P$             | $R^2$        | $P$             |
| Right insula                            | age       | 0.07         | 0.12            | 0.16         | 0.05            |
| Left anterior cingulate cortex          |           | 0.02         | 0.42            | 0.03         | 0.64            |
| Right inferior frontal cortex, orbital part |         | 0.25         | 0.002           | 0.28         | 0.004           |
| Left lateral middle temporal cortex     |           | 0.47         | $<0.001$        | 0.64         | $<0.001$        |
| Right lateral middle temporal cortex    |           | 0.34         | $<0.001$        | 0.44         | $<0.001$        |
| Right insula                            | onset age | 0.07         | 0.38            | -            | -               |
| Left anterior cingulate cortex          |           | 0.51         | 0.004           | -            | -               |
| Right inferior frontal cortex, orbital part |         | 0.001        | 0.92            | -            | -               |
| Left lateral middle temporal cortex     |           | 0.02         | 0.66            | -            | -               |
| Right lateral middle temporal cortex    |           | 0.004        | 0.83            | -            | -               |
| Right insula                            | illness duration | 0.05       | 0.33            | -            | -               |
| Left anterior cingulate cortex          |           | 0.04         | 0.37            | -            | -               |
| Right inferior frontal cortex, orbital part |         | 0.26         | 0.01            | -            | -               |
| Left lateral middle temporal cortex     |           | 0.50         | $<0.001$        | -            | -               |
| Right lateral middle temporal cortex    |           | 0.36         | 0.002           | -            | -               |
| Right insula                            | positive symptom scores | 0.07       | 0.33            | -            | -               |
| Left anterior cingulate cortex          |           | 0.005        | 0.80            | -            | -               |
| Right inferior frontal cortex, orbital part |         | 0.001        | 0.89            | -            | -               |
| Left lateral middle temporal cortex     |           | 0.09         | 0.27            | -            | -               |
| Right lateral middle temporal cortex    |           | 0.000        | 0.98            | -            | -               |
| Right insula                            | negative symptom scores | 0.18       | 0.09            | -            | -               |
| Left anterior cingulate cortex          |           | 0.001        | 0.92            | -            | -               |
| Right inferior frontal cortex, orbital part |         | 0.07         | 0.30            | -            | -               |
| Left lateral middle temporal cortex     |           | 0.19         | 0.08            | -            | -               |
| Right lateral middle temporal cortex    |           | 0.01         | 0.68            | -            | -               |
| Right insula                            | general symptom scores | 0.03       | 0.56            | -            | -               |
| Left anterior cingulate cortex          |           | 0.000        | 1.00            | -            | -               |
| Right inferior frontal cortex, orbital part |         | 0.02         | 0.65            | -            | -               |
| Left lateral middle temporal cortex     |           | 0.02         | 0.68            | -            | -               |
| Right lateral middle temporal cortex    |           | 0.02         | 0.68            | -            | -               |

Note: Regions that survived Bonferroni correction for multiple comparisons ($P<0.05$) are shown in bold font. The corrected $P$ threshold for the combined group was 0.0017 for linear regression analysis; and 0.01 for nonlinear regression analysis of age, respectively.

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eTable 7. Comparison of mean root-mean-square error-based comparison between linear and quadratic models of age effects

| Clusters | Variables | Linear model | Quadratic model | paired Wilcoxon signed-rank test |
|----------|-----------|--------------|-----------------|---------------------------------|
|          |           | median | Range       | median | Range | Z value | P      |
| L MTC    | Age       | 0.14  | 0.12-0.14   | 0.12   | 0.09-0.12 | 5.37   | <0.001 |
| R MTC    | Age       | 0.14  | 0.11-0.14   | 0.13   | 0.09-0.13 | 5.37   | <0.001 |

Abbreviations: L, left; MTC, middle temporal cortex; R, right
### eTable 8. Results of the jackknife analysis in studies for CHR individuals

| Discarded study                  | Decreased cortical thickness |
|----------------------------------|------------------------------|
|                                  | Bilateral medial prefrontal cortex |
| Bakker et al. 2016               | Yes                          |
| Buechler et al. 2020 - BS        | Yes                          |
| Buechler et al. 2020 - NBS       | Yes                          |
| Cannon et al. 2015 - CV          | Yes                          |
| Cannon et al. 2015 - NCV         | Yes                          |
| Dukart et al. 2017               | Yes                          |
| Gisselgård et al. 2018           | Yes                          |
| Jung et al. 2011                 | No                           |
| Klauser et al. 2015              | Yes                          |
| Kwak et al. 2019                 | No                           |
| Tognin et al. 2014 - CV          | Yes                          |
| Tognin et al. 2014 - NCV         | Yes                          |
| Ziermans et al. 2012             | Yes                          |

|                                | 11/13                        |

Abbreviations: BS, basic symptoms; CHR, clinical high-risk; CV, converters; NBS, not only basic symptoms; NCV, non-converters.
**Table 9. Results of the jackknife analysis in studies for FEP individuals**

| Discarded study                | Decreased cortical thickness |   |   |
|--------------------------------|-----------------------------|---|---|
|                                | Right lateral superior temporal cortex | Right anterior cingulate cortex | Right insula |
| Ansell et al. 2015 - FGA       | Yes                         | Yes | Yes |
| Ansell et al. 2015 - SGA       | Yes                         | No  | Yes |
| Buchy et al. 2017              | Yes                         | Yes | Yes |
| Dukart et al. 2017             | Yes                         | Yes | Yes |
| Gutierrez-Galve et al. 2010    | Yes                         | Yes | Yes |
| Haukvik et al. 2016            | Yes                         | Yes | Yes |
| Lesh et al. 2015               | Yes                         | Yes | Yes |
| Lin et al. 2019                | Yes                         | Yes | Yes |
| Rais et al. 2010               | Yes                         | Yes | Yes |
| Reniers et al. 2014            | Yes                         | Yes | Yes |
| Scanlon et al. 2014            | No                          | Yes | Yes |
| Thormodsen et al. 2013         | Yes                         | Yes | Yes |
| Voets et al. 2008              | Yes                         | No  | Yes |
|                                | 12/13                       | 11/13 | 13/13 |

Abbreviations: FEP, first-episode psychosis; FGA, first-generation antipsychotic; SGA, second-generation antipsychotic
**eTable 10. Results of the jackknife analysis in studies for long-term SCZ individuals**

| Discarded study       | Decreased cortical thickness |
|-----------------------|------------------------------|
|                       | Right insula                |
|                       | Right pars orbitalis of inferior frontal cortex |
|                       | Left temporal pole, middle temporal cortex |
|                       | Right temporal pole, superior temporal cortex |
| Barry et al. 2019     | Yes                         |
| Green et al. 2016     | Yes                         |
| Kong et al. 2015      | Yes                         |
| Madre et al. 2020     | Yes                         |
| Nelson et al. 2020    | Yes                         |
| Quide et al. 2019     | Yes                         |
| Landin-Romero et al. 2017 | Yes             |
| Xie et al. 2019-DS    | Yes                         |
| Xie et al. 2019-NDS   | Yes                         |
| Zhang et al. 2015     | Yes                         |
| Zugman et al. 2013-NTR| Yes                         |
| Zugman et al. 2013-TR | Yes                         |
|                       | 12/12                        |
|                       | 11/12                        |
|                       | 12/12                        |
|                       | 12/12                        |

Abbreviations: DS, deficit schizophrenia; SCZ, schizophrenia; NDS, nondeficit schizophrenia; NTR, treatment response; TR, treatment resistance.
| Discarded study                        | Right insula | Decreased cortical thickness | Left anterior cingulate cortex | Right pars orbitalis of inferior frontal cortex | Left lateral middle temporal cortex | Right lateral middle temporal cortex |
|---------------------------------------|--------------|-----------------------------|--------------------------------|-----------------------------------------------|-----------------------------------|-----------------------------------|
| Ansell et al. 2015 - FGA             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Ansell et al. 2015 - SGA             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Bakker et al. 2016                    | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Barry et al. 2019                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Buchy et al. 2017                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Buechler et al. 2020 - BS            | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Buechler et al. 2020 - NBS           | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Cannon et al. 2015 - CV               | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Cannon et al. 2015 - NCV             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Dukart et al. 2017 - FEP             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Dukart et al. 2017 - CHR             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Gisselgård et al. 2018                | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Green et al. 2016                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Gutierrez-Galve et al. 2010           | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Hauvik et al. 2016                    | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Jung et al. 2011 - CHR                | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Klausner et al. 2015                  | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Kong et al. 2015                      | Yes          | Yes                         | Yes                            | No                                            | No                                | Yes                               |
| Kwak et al. 2019                      | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Landin-Romero et al. 2017             | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Lesh et al. 2015                      | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Lin et al. 2019                       | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Madre et al. 2020                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Nelson et al. 2020                    | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Quide et al. 2019                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Rais et al. 2010                      | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Reniers et al. 2014                   | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Scanlon et al. 2014                   | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Thormodsen et al. 2013                | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Tognin et al. 2014 - CV               | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Tognin et al. 2014 - NCV              | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Voets et al. 2008                     | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Xie et al. 2019 - DS                  | Yes          | Yes                         | No                             | No                                            | No                                | Yes                               |
| Xie et al. 2019 - NDS                 | Yes          | Yes                         | No                             | No                                            | No                                | Yes                               |
| Zhang et al. 2015                     | Yes          | Yes                         | Yes                            | No                                            | No                                | Yes                               |
| Ziemans et al. 2012                   | Yes          | Yes                         | Yes                            | Yes                                           | Yes                               | Yes                               |
| Zugman et al. 2013 - NTR              | Yes          | No                          | Yes                            | Yes                                           | Yes                               | Yes                               |
| Zugman et al. 2013 - TR               | Yes          | No                          | Yes                            | No                                            | No                                | Yes                               |

38/38  36/38  36/38  33/38  38/38

Abbreviations: CHR, clinical high-risk; FEP, first-episode psychosis; SGA, second-generation antipsychotic; NCV, non-converters; NTS, non-converters; OVA, olanzapine.
BS, basic symptoms; CV, converters; DS, deficit schizophrenia; FGA, first-generation antipsychotic; NBS, not only basic symptoms; NDS, nondeficit schizophrenia; NTR, treatment response; SCZ, schizophrenia; TR, treatment resistance.
# eTable 12. Proportion of individuals with affective psychosis included in the first-episode psychosis (FEP) group

| Studies            | Included samples of affective psychosis (number)                                      | Proportion of affective psychosis in all FEP individuals |
|--------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------|
| Buchy et al. 2017  | Bipolar I with psychotic features (14)                                               | 65/671=9.70%                                             |
|                    | Bipolar II with psychotic features (1)                                               |                                                          |
|                    | Major depression with psychotic features (8)                                         |                                                          |
| Haukvik et al. 2016| Bipolar I disorder with psychotic features (15)                                       |                                                          |
|                    | Bipolar II disorder with psychotic features (2)                                      |                                                          |
|                    | Bipolar unspecified (1)                                                              |                                                          |
|                    | Major depressive disorder with psychotic features (5)                                |                                                          |
| Reniers et al. 2014| Major depressive disorder with psychotic features (2)                                |                                                          |
|                    | Bipolar unspecified (1)                                                              |                                                          |
|                    | Bipolar disorder with psychotic features (1)                                         |                                                          |
| Scanlon et al. 2014 | Bipolar I disorder with psychotic features (9)                                       |                                                          |
|                    | Major depressive disorder with psychotic features (6)                                |                                                          |
eFigure 1. Differences in cortical thickness between CHR individuals and HCs
CTh reductions (cool color) in individuals with clinical high-risk (CHR) compared to healthy controls were found in the bilateral medial prefrontal cortex (mPFC). Color bar shows the SDM Z values. Abbreviations: L, left; R, right.
eFigure 2. Differences in cortical thickness between FEP individuals and HCs
CTh reductions (cool color) in individuals with first-episode psychosis (FEP) compared to healthy controls were found in the right lateral superior temporal cortex (STC), right anterior cingulate cortex (ACC), and right insula. Color bar shows the SDM Z values. Abbreviations: L, left; R, right.
eFigure 3. Differences in cortical thickness between long-term SCZ individuals and HCs

CTh reductions (cool color) in individuals with long-term schizophrenia (SCZ) compared to healthy controls were found in the right insula extending to frontal operculum, right pars orbitalis of inferior frontal cortex (IFC), bilateral temporal pole (TP) (including anterior part of middle temporal cortex, superior temporal cortex, and inferior temporal cortex). Color bar shows the SDM Z values. Abbreviations: L, left; R, right.
eFigure 4. Meta-regression results in the long-term SCZ group

Meta-regression results show that the illness duration of long-term schizophrenia (SCZ) is negatively correlated with cortical thickness in the left temporal pole (TP). The asterisk (*) indicates that the P value survived the Bonferroni correction.
eFigure 5. Differences in cortical thickness between CHR and long-term SCZ groups
Compared with clinical high-risk (CHR) individuals, individuals with long-term schizophrenia (SCZ) showed greater cortical thinning (cool color) in the right insula, right pars orbitalis of inferior frontal cortex (IFC), left lateral temporal cortex (LTC) (including superior temporal cortex (STC) and middle temporal cortex (MTC)), and right temporal pole (TP). Color bar shows the SDM Z values. Abbreviations: L, left; R, right.
eFigure 6. Differences in cortical thickness between combined group and HCs
CTh reductions (cool color) in the combined group (all studies pooled regardless of illness stage of participants) compared to healthy controls were found in the right insula extending to frontal operculum, left anterior cingulate cortex (ACC) extending to bilateral middle cingulate cortex, right pars orbitalis of inferior frontal cortex (IFC), and bilateral lateral middle temporal cortex (MTC). Abbreviations: Color bar shows the SDM Z values; L, left; R, right.
eFigure 7. Meta-regression results in the combined group

Meta-regression results show that the illness duration of the combined group is negatively correlated with cortical thickness in the left lateral middle temporal cortex (MTC). The asterisk (*) indicates that the P value survived the Bonferroni correction.

Left MTC

X=-50

Linear modal

$R^2=0.50, P<0.001^*$
eFigure 8. Results of funnel plot analysis for the meta-analysis of CHR studies

The Egger’s test and funnel plots revealed no significant publication bias in the bilateral medial prefrontal cortex ($Z=-0.84$, $t=-1.1$, df=11, $P=0.31$). Abbreviations: CHR, clinical high-risk; SE, standard error.
eFigure 9. Results of funnel plot analysis for the meta-analysis of FEP studies

The Egger’s test and funnel plots revealed no significant publication bias in the (A) right lateral superior temporal cortex ($Z= -0.87$, $t= -0.81$, df=11, $P=0.44$), (B) right anterior cingulate cortex ($Z= -1.96$, $t= -1.67$, df=11, $P=0.12$), and (C) right insula ($Z= -2.12$, $t= -1.41$, df=11, $P=0.19$). Abbreviations: FEP, first-episode psychosis; SE, standard error.
eFigure 10. Results of funnel plot analysis for the meta-analysis of long-term SCZ studies

The Egger’s test and funnel plots revealed no significant publication bias in the (A) right insula (Z=0.77, t=0.70, df=10, P=0.50), (B) right pars orbitalis of inferior frontal cortex (Z=1.43, t=1.17, df=10, P=0.27), (C) left temporal pole, middle temporal cortex (Z=1.72, t=1.45, df=10, P=0.18), and (D) right temporal pole, superior temporal cortex (Z=1.01, t=1.02, df=10, P=0.33).

Abbreviations: SCZ, schizophrenia; SE, standard error.
The Egger’s test and funnel plots revealed no significant publication bias in the (A) right insula (Z=-0.12, t=-0.22, df=36, P=0.83), (B) left anterior cingulate cortex (Z=-0.59, t=-1.52, df=36, P=0.14), (C) right pars orbitalis of inferior frontal cortex (Z=-0.56, t=-0.97, df=36, P=0.34), (D) left lateral middle temporal cortex (Z=-0.66, t=-1.51, df=36, P=0.14), and (E) right lateral middle temporal cortex (Z=-0.40, t=-0.97, df=36, P=0.34). Abbreviations: SE, standard error.
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