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# Occipital lobe

## Introduction

The occipital lobe is located at the posterior section of the brain and primarily comprises the brain's visual cortices. There are two streams of visual information through the visual primary and association cortices, which deal separately with broad object details and motion, and fine detail and colours.

Schizophrenia has been associated with altered structure and function of the occipital cortex. Understanding of any brain alterations in people with schizophrenia may provide insight into changes in brain development associated with the illness onset or progression. Reviews contained in this technical summary reflect structural imaging (MRI, DTI), and functional imaging (fMRI, PET) investigations, as well as metabolic studies (MRS) of the occipital lobe in schizophrenia.

## Method

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

Review reporting assessment was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist, which describes a preferred way to present a meta-analysis[1]. Reviews rated as having less than 50% of items checked have been excluded from the library. The PRISMA flow diagram is a suggested way of providing information about studies included and excluded with reasons for exclusion. Where no flow diagram has been presented by individual reviews, but identified studies have been described in the text, reviews have been checked for this item. Note that early reviews may have been guided by less stringent reporting checklists than the PRISMA, and that some reviews may have been limited by journal guidelines.

Evidence was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group approach where high quality evidence such as that gained from randomised controlled trials (RCTs) may be downgraded to moderate or low if review and study quality is limited, if there is inconsistency in results, indirect comparisons, imprecise or sparse data and high probability of reporting bias. It may also be downgraded if risks associated with the intervention or other matter under review are high. Conversely, low quality evidence such as that gained from observational studies may be upgraded if effect sizes are large, there is a dose dependent response or if results are reasonably consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)[2]. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).



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## Results

We found twelve systematic reviews that met our inclusion criteria[3-14].

*Structural changes: MRI and DTI*

- Moderate quality evidence suggests reduced white matter integrity in the occipital cortex and fusiform gyrus in people with schizophrenia compared to controls.
- Moderate to low quality evidence suggest a higher frequency of abnormal (reversed) asymmetry in the occipital lobe in people with schizophrenia.

*Functional changes: fMRI, PET, MRS*

- Moderate quality evidence suggests reduced activity in the middle occipital gyrus during executive functioning tasks in people with schizophrenia.
- Moderate quality evidence suggests reduced functional activity in the right lingual gyrus during episodic memory encoding, and reduced activation of the right cuneus and fusiform gyrus during episodic memory retrieval in people with schizophrenia.
- Moderate quality evidence suggests decreased activation during emotion processing tasks in the fusiform, lentiform and middle occipital gyri of people with schizophrenia. During explicit emotion tasks, there is decreased activation in the fusiform gyrus, and during implicit emotion tasks, there is decreased activation in the middle occipital gyris.



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*Achim AM, Lepage M*

## Episodic memory-related activation in schizophrenia: meta-analysis

**British Journal of Psychiatry 2005; 187: 500-509**

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| | |
|---|---|
| **Comparison** | **Functional activation in people with schizophrenia vs. healthy controls during episodic memory tasks.** |
| **Summary of evidence** | **Moderate quality evidence (large sample sizes, direct, unable to assess precision and consistency) suggests decreases in functional activation during memory retrieval tasks in the right fusiform gyrus.** |
| **Functional activation** | |
| Meta-analysis results reported for 228 activation foci from either fMRI or PET.<br>11 studies, N = 298<br>*Reduced activation in people with schizophrenia compared to controls in;*<br>Right fusiform gyrus (medial temporo-occipital gyrus): Talairach coordinates (26, -74, -8), ALE: 0.0054, Voxel probability: 0.000004 | |
| **Consistency in results‡** | No measure of heterogeneity is provided. |
| **Precision in results§** | No confidence intervals are reported. |
| **Directness of results‖** | Direct |

*Fornito A, Yucel M, Patti J, Wood SJ, Pantelis C*

## Mapping grey matter reductions in schizophrenia: An anatomical likelihood estimation analysis of voxel-based morphometry studies

**Schizophrenia Research 2009; 108(1-3): 104-113**

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| **Comparison** | **Whole brain comparison of grey matter volume and grey matter concentration (grey matter as a proportion of the whole brain** |

| | |
|---|---|
| | **volume) in people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Moderate quality evidence (large samples, direct, unable to assess consistency or precision) suggests grey matter reductions in the occipito-temporal gyrus in people with schizophrenia.** |
| **Grey matter volume** | |
| Meta-analysis was performed using Anatomical Likelihood Estimate (ALE) analysis on Voxel-Based Morphometry MRI studies.<br>FWHM 12mm, FDR corrected at $p < 0.05$<br>37 studies, N = 3336<br>*Clusters where grey matter concentration reductions were significantly more frequent than volume reductions;*<br>Left occipito-temporal gyrus: Talairach coordinates (-52.58, -62.73, -7.35), Voxel cluster size 296mm$^3$, ALE 0.72 x $10^{-3}$<br><br>As GMC had fewer foci available for comparison, a random subset was initially selected for comparison with GMV. To increase validity of this comparison, four additional GMC/GMV contrasts were performed with different GMC subsets, and demonstrated high consistency between randomisations.<br>*Both cluster size and ALE statistic were larger for comparisons using concentration measures compared to volume measures;*<br>Cluster size $t = 2.54$, $p = 0.02$<br>ALE statistic $t = 2.82$, $p = 0.01$ | |
| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

*Fusar-Poli P, Perez J, Broome M, Borgwardt S, Placentino A, Caverzasi E, Cortesi M, Veggiotti P, Politi P, Barale F, McGuire P*

**Neurofunctional correlates of vulnerability to psychosis: A systematic review and meta-analysis**

**Neuroscience & Biobehavioral Reviews 2007; 31(4): 465-484**

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|---|---|
| **Comparison** | **Functional activation in individuals following their first episode of schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Low quality evidence (one small study) is unclear as to the direction of the changes in functional activity in the occipital cortex during cognitive tasks in individuals with first-episode schizophrenia.** |
| **Functional activation during Information processing task** | |
| 1 study, N = 23<br>Reduced activation of occipital lobe (*d* = 1.26) in medication-naïve patients compared to controls during information processing tasks. | |
| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

*Kanaan RA, Kim JS, Kaufmann WE, Pearlson GD, Barker GJ, McGuire PK*

**Diffusion tensor imaging in schizophrenia**

**Biological Psychiatry 2005; 58(12): 921-929**

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|---|---|
| **Comparison** | **White matter fractional anisotropy (FA) in people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Moderate quality evidence (large sample size, direct, unable to assess precision and consistency) suggests decreased FA in the occipital cortex of people with schizophrenia.** |
| **Functional activation** | |
| 19 studies, N = 640<br>Occipital lobe illustrated decreased FA in at least one study between people with schizophrenia and controls.<br>Parieto-occipital cortex reported no significant difference in FA between schizophrenia patients and controls. | |



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| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

*Kyriakopoulos M, Bargiotas T, Barker GJ, Frangou S*

**Diffusion tensor imaging in schizophrenia**

**European Psychiatry: the Journal of the Association of European Psychiatrists 2008; 23(4): 255-273**

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|---|---|
| **Comparison** | **White matter integrity, assessed by voxel-based analysis, in people with schizophrenia vs. healthy controls** |
| **Summary of evidence** | **Moderate to low quality evidence (sample size unclear, direct, unable to assess precision and consistency) suggests reduced FA in the occipital lobe.** |
| **Functional activity** | |
| 15 studies, N = unclear<br>Occipital lobe illustrated decreased FA in 5 studies between schizophrenia patients and controls. | |
| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct comparison of white matter integrity between schizophrenia patients and controls |

*Li H, Chan R, McAlonan G, Gong Q-Y*

**Facial emotion processing in schizophrenia: A meta-analysis of functional neuroimaging data**

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## Occipital lobe

| **Schizophrenia Bulletin 2010; 36(5): 1029-1039**<br>View review abstract online | |
|---|---|
| **Comparison** | **Functional activity in people with schizophrenia vs. controls during a facial emotion processing task.** |
| **Summary of evidence** | **Moderate quality evidence (direct, unable to assess consistency or precision) suggests that people with schizophrenia show decreased activation during emotion processing tasks in the fusiform, lentiform and middle occipital gyri. During explicit emotional tasks, people with schizophrenia showed decreased activation in the fusiform gyrus, while implicit emotion tasks were association with decreases in the middle occipital gyri.** |

**Functional activity during a facial emotion processing task**

Meta-analysis was performed using Anatomical Likelihood Estimate (ALE) analysis.

18 studies, N = 228

*Areas of activation that were significantly larger in controls than in people with schizophrenia;*

Left fusiform gyrus: Talairach coordinates (-38, -66, -13), 19 foci, 1768mm$^3$, 0.100 ALE

Right lentiform nucleus: Talairach coordinates (23, -4, -7), 7 foci, 424mm$^3$, 0.062 ALE

Right fusiform gyrus: Talairach coordinates (38, -64, -10), 6 foci, 408mm$^3$, 0.097 ALE

Right fusiform gyrus: Talairach coordinates (40, -50, -15), 5 foci, 408mm$^3$, 0.065 ALE

Direct between-group contrasts examined regions of differential activation between people with schizophrenia and controls.

*13 studies reported reduced activation in people with schizophrenia compared to controls during an emotion perception task in;*

Right middle occipital gyrus: Talairach coordinates (48, -72, 4), 2 foci, 208mm$^3$, 0.060 ALE

Subgroup analysis assessed the studies by task type: explicit emotion and implicit emotion.

*Subtraction meta-analysis of activation during an explicit emotional task found decreased activation in people with schizophrenia compared to controls in;*

Left fusiform gyrus: Talairach coordinates (-39, -65, -13), 18 foci, 1840mm$^3$, 0.082 ALE

Right fusiform gyrus: Talairach coordinates (40, -52, -14), 5 foci, 472mm$^3$, 0.068 ALE

Right fusiform gyrus: Talairach coordinates (38, -64, -10), 5 foci, 432mm$^3$, 0.097 ALE

Right lentiform nucleus: Talairach coordinates (22, -3, -5), 3 foci, 256mm$^3$, 0.060 ALE

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| *Subtraction meta-analysis of activation during an implicit emotional task suggesting decreased activation in people with schizophrenia compared to controls;*<br>Right middle occipital gyrus: Talairach coordinates (48, -72, 4), 2 foci, 216mm$^3$, 0.060 ALE |

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| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No measure of precision reported |
| **Directness of results** | Direct |

*Minzenberg MJ, Laird AR, Thelen S, Carter CS, Glahn DC*

**Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia**

**Archives of General Psychiatry 2009; 66(8): 811-822**

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|---|---|
| **Comparison** | **Functional activation in people with schizophrenia vs. healthy controls** |
| **Summary of evidence** | **Moderate quality evidence (observational, large sample) suggests people with schizophrenia show reduced activity in the middle occipital gyrus during executive function tasks.** |

| **Functional activation during executive function tasks** |
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| 41 studies, N = 1217<br>ALE analysis – FWHM 12mm, False Discovery Rate (FDR) corrected model<br>*Significantly reduced activity in people with schizophrenia compared to controls in;*<br>Left middle occipital gyrus: Talairach centre of mass (-42, -70, 6), cluster volume 416mm$^3$ |

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|---|---|
| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

# Occipital lobe

*Navari S, Dazzan P*

## Do antipsychotic drugs affect brain structure? A systematic and critical review of MRI findings.

**Psychological Medicine 2009; 39(11): 1763-1777**

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|---|---|
| **Comparison** | **Brain volume in medicated, drug-free and drug-naïve people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Low quality evidence (sample sizes unclear, indirect, unable to assess consistency or precision) is unclear as the effect of antipsychotic medications on brain structure.** |

**Grey matter volume**

*Drug-free or drug-naïve patients compared to treated patients and controls;*

1 study, N unclear

Both patient groups showed reduced cortical thickness in the occipital cortex compared to controls.

*Patients medicated for less than 12 weeks prior to the treatment period being investigated, compared to drug naïve and controls;*

1 study, N unclear

Patients medicated with typical antipsychotics showed reduced cortical thickness of occipital cortex.

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| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No measure of precision reported |
| **Directness of results** | Direct |

*Olabi B, Ellison-Wright I, McIntosh AM, Wood SJ, Bullmore E, Lawri, SM*

## Are There Progressive Brain Changes in Schizophrenia? A Meta-Analysis of Structural Magnetic Resonance Imaging Studies

**Biological Psychiatry 2011; 70(1): 88-96**

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# Occipital lobe

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|---|---|
| **Comparison** | **Grey matter volume in people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Moderate to high quality evidence (large sample sizes, inconsistent, precise, direct) suggests no difference in occipital lobe volume over time in schizophrenia compared to controls.** |
| **Grey matter volume** | |
| Progressive changes in grey matter volume reported across longitudinal MRI scans over 1-10 years.<br>31 studies, N = 1867<br>*No significant differences between groups;*<br>Occipital GM: N = 282, 6 studies, $d$ = -0.174, 95%CI -0.67 to 0.32, $p$ = 0.491, $I^2$ = 69.9%<br>Occipital WM: N = 227, 4 studies, $d$ = -0.327, 95%CI -0.74 to 0.08, $p$ = 0.117, $I^2$ = 45.9% | |
| **Consistency in results** | Inconsistent. |
| **Precision in results** | Precise |
| **Directness of results** | Direct |

*Ragland JD, Laird AR, Ranganath C, Blumenfeld RS, Gonzales SM, Glahn DC*

**Prefrontal activation deficits during episodic memory in schizophrenia**

**American Journal of Psychiatry 2009; 166(8): 863-874**

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| | |
|---|---|
| **Comparison** | **Functional activation during episodic memory tasks in people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Moderate quality evidence (large sample, direct, unable to assess precision or consistency) suggests activity during episodic encoding is reduced in the right lingual gyrus, and reduced in the right cuneus during episodic retrieval in people with schizophrenia.** |
| **Functional activity during episodic encoding** | |

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| ALE analysis – FWHM 12mm, False Discovery Rate (FDR) corrected model $p < 0.05$<br>*Significantly decreased activity in people with schizophrenia than controls;*<br>Right lingual gyrus: cluster volume 1192mm3, Talairach centre of mass (18, -86, 0) |
| **Functional activity during episodic retrieval** |
| ALE analysis – FWHM 12mm, False Discovery Rate (FDR) corrected model $p < 0.05$<br>*Significantly decreased activity in people with schizophrenia than controls;*<br>Right cuneus: cluster volume 2568mm$^3$, Talairach centre of mass (16, -86, 10) |

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|---|---|
| **Consistency in results** | No measure of heterogeneity is reported. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

*Sommer I, Aleman A, Ramsey N, Bouma A*

## Handedness, language lateralisation and anatomical asymmetry in schizophrenia: meta-analysis

**British Journal of Psychiatry 2001; 178: 344-351**

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|---|---|
| **Comparison** | **Anatomical asymmetry in people with schizophrenia vs. controls.** |
| **Summary of evidence** | **Moderate to low quality evidence (mostly inconsistent, imprecise, direct) suggest a higher frequency of abnormal (reversed) asymmetry in the occipital lobe in people with schizophrenia compared to controls.** |

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| **Anatomical asymmetry** |
| *Significantly higher frequency of absent or reversed occipital lobe asymmetry in people with schizophrenia compared to controls;*<br>5 studies, N = 579, weighted difference rate = 0.22, 95%CI 0.12 to 0.28, $p = 0.01$, Q = 87.55, $p = 0.003$ |

# Occipital lobe

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| **Consistency in results** | Inconsistent |
| **Precision in results** | Imprecise |
| **Directness of results** | Direct |

*Steen RG, Hamer RM, Lieberman JA*

**Measurement of brain metabolites by $^{1}$H magnetic resonance spectroscopy in patients with schizophrenia: a systematic review and meta-analysis**

**Neuropsychopharmacology 2005; 30(11): 1949-1962**

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|---|---|
| **Comparison** | **N-acetyl aspartate (NAA) activity (measured by $^{1}$H-MRS) in grey and white matter regions in people with schizophrenia vs. healthy controls.** |
| **Summary of evidence** | **Low quality evidence (sample size unclear, direct inconsistent, unable to assess precision) is unclear of occipital NAA levels in people with schizophrenia compared to controls.** |
| **NAA** | |
| Grey matter<br>8 studies, N unclear<br>Patient average 102.8% of control levels<br>White matter<br>1 study, N unclear<br>Patient average 96.0% of control levels | |
| **Consistency in results** | Significant heterogeneity reported, $p<0.0001$. |
| **Precision in results** | No confidence intervals are reported. |
| **Directness of results** | Direct |

# Occipital lobe

## Explanation of acronyms

ALE = activation likelihood estimate, CI = Confidence Interval, *d* = Cohen's *d* and *g* = Hedges' *g* = standardized mean differences (see below for interpretation of effect size), DTI = diffusion tensor imaging, FA = fractional anisotropy, FDR = false discovery rate correction for multiple comparisons, fMRI = functional magnetic resonance imaging, $I^2$ = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), MNI = Montreal Neurological Institute, N = number of participants, NAA = N-acetyl aspartate, *p* = statistical probability of obtaining that result ($p < 0.05$ generally regarded as significant), PET = positron emission tomography, Q = Q statistic (chi-square) for the test of heterogeneity, vs = versus

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## Explanation of technical terms

* Bias has the potential to affect reviews of both RCT and observational studies. Forms of bias include; reporting bias – selective reporting of results, publication bias - trials that are not formally published tend to show less effect than published trials, further if there are statistically significant differences between groups in a trial, these trial results tend to get published before those of trials without significant differences; language bias – only including English language reports; funding bias - source of funding for the primary research with selective reporting of results within primary studies; outcome variable selection bias; database bias - including reports from some databases and not others; citation bias - preferential citation of authors. Trials can also be subject to bias when evaluators are not blind to treatment condition and selection bias of participants if trial samples are small[15].

† Different effect measures are reported by different reviews.

ALE analysis (Anatomical Likelihood Estimate) refers to a voxel-based meta-analytic technique for structural imaging in which each point of statistically significant structural difference is spatially smoothed into Gaussian distribution space, and summed to create a statistical map estimating the likelihood of difference in each voxel, as determined by the entire set of included studies. Incorporated with the Genome Scan Meta-analysis (GSMA), the meta-analysis of coordinates from multiple studies can be weighted for sample size to create a random effect analysis. The ALE statistic (if reported) represents the probability of a group difference occurring at each voxel included in the analysis.

Fractional similarity network analysis refers to a network analysis technique in which secondary networks are identified within the larger framework of activity, creating a matrix for regional co-activity.

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) which allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect[15].

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction (< 1) or an increase (> 1) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if RR > 2 or < 0.5 and a large effect if RR > 5 or < 0.2[16]. lnOR stands for logarithmic OR where a lnOR of 0 shows no difference between groups. Hazard ratios



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measure the effect of an explanatory variable on the hazard or risk of an event.

Correlation coefficients (eg, *r*) indicate the strength of association or relationship between variables. They are an indication of prediction, but do not confirm causality due to possible and often unforseen confounding variables. An *r* of 0.10 represents a weak association, 0.25 a medium association and 0.40 and over represents a strong association. Unstandardised (*b*) regression coefficients indicate the average change in the dependent variable associated with a 1 unit change in the independent variable, statistically controlling for the other independent variables. Standardised regression coefficients represent the change being in units of standard deviations to allow comparison across different scales.Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

‡ Inconsistency refers to differing estimates of treatment effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate. $I^2$ is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent substantial heterogeneity and 75% to 100%: considerable heterogeneity. $I^2$ can be calculated from Q (chi-square) for the test of heterogeneity with the following formula;

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

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, this criteria should be relaxed[17].

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

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