



## Case Management

### Introduction

Case management is a community-based program in which a nurse, social worker or other clinician oversees the treatment and wellbeing of assigned patients, and is responsible for assessing their treatment needs and implementing strategies to ensure these needs are met<sup>1</sup>.

Intensive case management is a variation on standard case management, and is used to care for people at high risk of hospital readmission<sup>1</sup>. In intensive case management, each person at risk of readmission is assigned a case manager who has a small caseload (less than 20 patients)<sup>2, 3</sup>, and is responsible for patient contact and assessing patient needs<sup>4, 5</sup>. Assertive community treatment is a form of intensive case management with a focus on service coordination, involving extensive integration, with multidisciplinary teams who share a small caseload<sup>1</sup>.

### 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 that describes a preferred way to

present a meta-analysis<sup>6</sup>. 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 or if there is a dose dependent response. We have also taken into account sample size and whether results are consistent, precise and direct with low associated risks (see end of table for an explanation of these terms)<sup>7</sup>. The resulting table represents an objective summary of the available evidence, although the conclusions are solely the opinion of staff of NeuRA (Neuroscience Research Australia).

### Results

We found six systematic reviews that met our inclusion criteria<sup>1, 3-5, 8, 9</sup>.

- Compared to standard care, high quality evidence shows intensive case management



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is associated with increased contact with psychiatric care, increased independent living, and a lower likelihood of being admitted to hospital or dropping out of treatment for up to 12 months. Moderate quality evidence suggests it may also improve quality of life and general functioning, and decrease homelessness for up to 6 months. By 7 to 12 months there is decreased unemployment and contact with police. After 12 months, there is an increased likelihood of living in stable accommodation, with better functioning, improved symptoms, and increased medication compliance.

- Moderate to high quality evidence suggests intensive case management reduces long-term dropout rates and medication non-adherence more than standard case management.
- For patients with a dual diagnosis (substance misuse and psychiatric disorder), moderate to low quality evidence suggests no significant benefit of intensive case management has over standard care for study retention, hospitalisation or service use, substance use, quality of life or functioning.



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*Burns T, Catty J, Dash M, Roberts C, Lockwood A, Marshall M*

**Use of intensive case management to reduce time in hospital in people with severe mental illness: Systematic review and meta-regression**

British Medical Journal 2007; 335(7615): 336-340

[View review abstract online](#)

<b>Comparison</b>	Intensive case management or assertive community treatment (caseload up to 20 patients) vs. standard care. The sample includes a majority of people with schizophrenia spectrum disorders.
<b>Summary of evidence</b>	Moderate to low quality evidence (large sample, inconsistent, imprecise, direct) suggests intensive case management showed benefit over standard care for fewer number of days in hospital, which was associated with greater team coherence for administering support.
<b>Number of days in hospital</b>	
<p><i>A significant, medium-sized effect favouring intensive case management for fewer days in hospital;</i>                  29 RCTs, N = 5,961, <math>d = -0.46</math>, 95%CI -0.84 to -0.08, <math>p = 0.019</math></p> <p>Meta-regression indicates that greater team organisation was associated with fewer days in hospital. Staffing levels, degree of case management in control groups, trial size and location did not show associations with number of days in hospital.</p>	
<b>Consistency in results<sup>†</sup></b>	Authors report that results are inconsistent.
<b>Precision in results<sup>§</sup></b>	Imprecise
<b>Directness of results<sup>  </sup></b>	Direct



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*Cleary M, Hunt GE, Matheson SL, Walter G*

**Psychosocial treatments for people with co-occurring severe mental illness and substance misuse: systematic review**

**Journal of Advanced Nursing 2009; 65(2): 238-258**

[View review abstract online](#)

<b>Comparison</b>	<p><b>Intensive case management or non-integrated models of care (including substance abuse treatments, family psychoeducation, crisis intervention and skills training) vs. standard care.</b></p> <p><b>Results are reported here for samples containing a majority of people with schizophrenia.</b></p>
<b>Summary of evidence</b>	<p><b>Moderate to low quality evidence (direct, unable to assess consistency or precision) suggests no benefit of intensive case management for reducing substance use or improving mental state.</b></p>
<b>Substance use</b>	
<p><i>Five randomised trials and 3 quasi-randomised trials (total N = 1,114) assessed intensive case management, with treatment duration varying from 4 weeks to 18 months;</i></p> <p>Authors report that all of the randomised studies and two quasi-randomised studies found no significant differences between groups. One quasi-randomised study reported greater reductions in alcohol use in the intervention group (<math>p &lt; 0.05</math>).</p>	
<b>Mental state</b>	
<p>Authors report that all randomised studies and one quasi-randomised study found no significant differences between groups. Two quasi-randomised studies reported mental state improvements in the intervention group, including fewer hospitalisations and improved symptom severity (<math>p &lt; 0.01</math>).</p>	
<b>Treatment retention</b>	
<p>Authors report that all five randomised studies and two quasi-randomised studies reported no significant differences between groups. One quasi-randomised study reported increased retention by 18 months in the intervention group (<math>p &lt; 0.01</math>).</p>	
<b>Consistency in results</b>	No measure of consistency is reported.

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<b>Precision in results</b>	No measure of precision is reported.
<b>Directness of results</b>	Direct

*Dieterich M, Irving DB, Park B, Marshall M*

### **Intensive case management for severe mental illness**

**Cochrane Database of Systematic Reviews 2017; (11): CD007906**

[View review abstract online](#)

<b>Comparison 1</b>	<b>Intensive case management vs. standard care.</b>
<b>Summary of evidence</b>	<p><b>High quality evidence (direct, consistent, precise, large samples) shows people receiving intensive case management were more likely to stay in contact with psychiatric care, live independently, and were less likely to be admitted to hospital or to dropout of treatment for up to 6 to 12 months. Moderate quality evidence suggests the increased contact with psychiatric care and independent living may extend to over 12 months.</b></p> <p><b>Moderate quality evidence (some inconsistency or imprecision) also suggests people receiving intensive case management may have better quality of life, better functioning and less homelessness for up to 6 months. By 7-12 months they may have lower cost of psychiatric hospital care, less unemployment, and less contact with the police. After 12 months they may continue to have improved functioning as well as improved symptoms, better medication adherence, and fewer days in hospital per month.</b></p>
<b>Service use</b>	
<p><i>A significant small to medium-sized effect of increased contact with psychiatric care in the intensive case management group in the medium and long term, less hospitalisation in the medium term, and fewer days in hospital in the long term;</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p>Contact with psychiatric care: 1 RCT, N = 95, RR = 0.54, 95%CI 0.28 to 1.05, <math>p = 0.071</math>  Hospitalisation: 2 RCTs, N = 244, RR = 0.61, 95%CI 0.22 to 1.69, <math>p = 0.34</math>, <math>I^2 = 81%</math>, <math>p = 0.02</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p>	

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<p>Contact with psychiatric care: 3 RCTs, N = 1,063, RR = 0.51, 95%CI 0.36 to 0.71, <math>p &lt; 0.05</math>, <math>I^2 = 34%</math>, <math>p = 0.22</math></p> <p>Hospitalisation: 5 RCTs, N = 1,303, RR = 0.85, 95%CI 0.77 to 0.93, <math>p &lt; 0.05</math>, <math>I^2 = 0%</math>, <math>p = 0.81</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>Days in hospital per month: 24 RCTs, N = 3,595, MD = -0.86, 95%CI -1.37 to -0.34, <math>p = 0.0011</math>, <math>I^2 = 74%</math>, <math>p &lt; 0.00001</math></p> <p>Contact with psychiatric care: 5 RCTs, N = 475, RR = 0.27, 95%CI 0.11 to 0.66, <math>p = 0.0042</math>, <math>I^2 = 44%</math>, <math>p = 0.13</math></p> <p>Hospitalisation: Over 12 months: 11 RCTs, N = 1,516, RR = 0.96, 95%CI 0.74 to 1.23, <math>p = 0.72</math>, <math>I^2 = 70%</math>, <math>p = 0.00028</math></p> <p>Emergency room admissions: 1 RCT, N = 178, RR = 1.13, 95%CI 0.72 to 1.76, <math>p = 0.61</math></p>	
<b>Consistency in results</b>	Consistent for keeping in contact with psychiatric care (all time points) and likelihood of hospital admission (medium term only). Inconsistent for all other measures, apart from outcomes with one RCT where consistency is not applicable.
<b>Precision in results</b>	Precise for keeping in contact with psychiatric care (overall, medium, long term), likelihood of hospital admission (medium term), and imprecise for all other measures. Unable to assess precision for average number of days in hospital as standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Mortality</b>	
<i>No significant differences between groups for all-cause mortality or suicide;</i>	
<u>Short-term – by 6 months</u>	
All-cause mortality: 2 RCTs, N = 161, RR = 1.04, 95%CI 0.16 to 6.91, $p = 0.97$ , $I^2 = 0%$ , $p = 0.38$	
Suicide: 2 RCTs, N = 127, RR = 0.35, 95%CI 0.04 to 3.27, $p = 0.36$ , $I^2 = 0%$ , $p = 0.97$	
<u>Medium-term – 7 to 12 months</u>	
All-cause mortality: 6 RCTs, N = 901, RR = 0.78, 95%CI 0.23 to 2.62, $p = 0.69$ , $I^2 = 0%$ , $p = 0.54$	
Suicide: 4 RCTs, N = 819, RR = 0.98, 95%CI 0.17 to 5.60, $p = 0.98$ , $I^2 = 0%$ , $p = 0.64$	
<u>Long-term – over 12 months</u>	
All-cause mortality: 9 RCTs, N = 1,456, RR = 0.84, 95%CI 0.48 to 1.47, $p = 0.53$ , $I^2 = 0%$ , $p = 0.61$	
Suicide: 9 RCTs, N = 1,456, RR = 0.68, 95%CI 0.31 to 1.51, $p = 0.35$ , $I^2 = 0%$ , $p = 0.91$	
<b>Consistency in results</b>	Consistent for all measures.





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<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Medication adherence and dropout rates</b>	
<p><i>A significant, small effect of fewer dropouts in the medium and long term, and a medium-sized effect of greater medication adherence in the long term in the intensive case management group, with no other differences between groups;</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p>Dropouts: 5 RCTs, N = 598, RR = 0.79, 95%CI 0.44 to 1.41, <math>p = 0.43</math>, <math>I^2 = 95%</math>, <math>p &lt; 0.00001</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p>Dropouts: 8 RCTs, N = 1,699, RR = 0.60, 95%CI 0.51 to 0.70, <math>p &lt; 0.05</math>, <math>I^2 = 0%</math>, <math>p = 0.51</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>Dropouts: 13 RCTs, N = 1,798, RR = 0.68, 95%CI 0.58 to 0.79, <math>p &lt; 0.05</math>, <math>I^2 = 2%</math>, <math>p = 0.42</math></p> <p>Medication adherence: 1 RCT, N = 71, RR = 0.35, 95%CI 0.15 to 0.81, <math>p = 0.014</math></p>	
<b>Consistency in results</b>	Inconsistent for short-term dropout rates, consistent for medium and long-term dropout rates, not applicable for medication (1 RCT).
<b>Precision in results</b>	Precise for medium and long-term dropout rates, imprecise for all other measures.
<b>Directness of results</b>	Direct
<b>Functioning</b>	
<p><i>Significant, medium-sized effects of better short-term functioning (GAF scores), and long-term functioning (GAF, ISSI, RFS scores) in the intensive case management group, with no significant medium-term effects;</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p>GAF: 4 RCTs, N = 797, RR = 2.07, 95%CI 0.28 to 3.86, <math>p = 0.024</math>, <math>I^2 = 0%</math>, <math>p = 0.65</math></p> <p>RFS: 1 RCT, N = 80, MD = -0.62, 95%CI -2.23 to 0.99, <math>p = 0.45</math></p> <p>SAS: 1 RCT, N = 80, MD = -3.34, 95%CI -7.55 to 0.87, <math>p = 0.12</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p>GAF: 3 RCTs, N = 722, RR = 0.09, 95%CI -3.11 to 3.28, <math>p = 0.96</math>, <math>I^2 = 55%</math>, <math>p = 0.11</math></p> <p>DAS: 1 RCT, N = 55, MD = 0.10, 95%CI -0.40 to 0.60, <math>p = 0.70</math></p> <p>RFS: 1 RCT, N = 80, MD = -0.86, 95%CI -2.72 to 1.00, <math>p = 0.36</math></p>	



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<p>SAS: 1 RCT, N = 80, MD = -3.30, 95%CI -7.83 to 1.23, <math>p = 0.15</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>GAF: 5 RCTs, N = 818, RR = 3.41, 95%CI 1.66 to 5.16, <math>p = 0.00013</math>, <math>I^2 = 0\%</math>, <math>p = 0.60</math></p> <p>ISSI: 1 RCT, N = 62, MD = 3.20, 95%CI 0.11 to 6.29, <math>p = 0.0042</math></p> <p>RFS: 1 RCT, N = 80, MD = -2.35, 95%CI -4.05 to -0.65, <math>p = 0.0069</math></p> <p>DAS: 1 RCT, N = 58, MD = -0.20, 95%CI -0.67 to 0.27, <math>p = 0.41</math></p> <p>SAS: 1 RCT, N = 80, MD = -2.75, 95%CI -7.13 to 1.63, <math>p = 0.22</math></p> <p>Strauss-Carpenter Scale: 1 RCT, N = 60, MD = 0.10, 95%CI -1.17 to 1.37, <math>p = 0.88</math></p>	
<b>Consistency in results</b>	Consistent for arrests (medium term), imprisonment (medium and long term), living independently (medium and long term), and homelessness (long term), Inconsistent for unemployment (medium and long term).
<b>Precision in results</b>	Precise for unemployment (medium term), competitive employment (medium term), independent accommodation (medium, long term), and stable accommodation (long term). Imprecise for all other measures. Unable to assess functioning scores as standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Contact with the legal system</b>	
<p><i>A significant, medium-sized effect of less contact with police in the intensive case management group in the medium term, with no other differences between groups;</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p>Contact with police: 1 RCT, N = 61, RR = 2.57, 95%CI 0.73 to 9.04, <math>p = 0.14</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p>Contact with police: 1 RCT, N = 88, RR = 0.23, 95%CI 0.09 to 0.55, <math>p &lt; 0.05</math></p> <p>Arrested: 3 RCTs, N = 604, RR = 1.08, 95%CI 0.61 to 1.90, <math>p = 0.80</math>, <math>I^2 = 0\%</math>, <math>p = 0.71</math></p> <p>Imprisoned: 4 RCTs, N = 804, RR = 0.80, 95%CI 0.39 to 1.64, <math>p = 0.54</math>, <math>I^2 = 52\%</math>, <math>p = 0.10</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>Arrested: 1 RCT, N = 178, RR = 0.66, 95%CI 0.32 to 1.37, <math>p = 0.27</math></p> <p>Imprisoned: 5 RCTs, N = 908, RR = 0.86, 95%CI 0.45 to 1.65, <math>p = 0.65</math>, <math>I^2 = 9\%</math>, <math>p = 0.33</math></p>	
<b>Consistency in results</b>	Consistent where applicable (> 1 RCT).



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<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Employment</b>	
<p><i>A significant, small effect of lower rates of unemployment in the intensive case management group in the medium term only, with no other differences between groups;</i></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p>Unemployment: 4 RCTs, N = 1,136, RR = 0.89, 95%CI 0.79 to 1.00, <math>p = 0.042</math>, <math>I^2 = 75%</math>, <math>p = 0.01</math></p> <p>Competitive employment: 1 RCT, N = 88, RR = 1.0, 95%CI 0.91 to 1.10, <math>p = 0.96</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>Unemployment: 4 RCTs, N = 1,129, RR = 0.70, 95%CI 0.49 to 1.00, <math>p = 0.051</math>, <math>I^2 = 94%</math>, <math>p &lt; 0.00001</math></p>	
<b>Consistency in results</b>	Inconsistent where applicable (> 1 RCT).
<b>Precision in results</b>	Precise for medium-term measures, imprecise for long-term measures.
<b>Directness of results</b>	Direct
<b>Accommodation status</b>	
<p><i>A significant, large effect of lower rates of homelessness in the intensive case management group in the short term, a small effect of higher likelihood of living independently and in stable accommodation in the medium term, and a small effect of living independently in the long term, with no other differences between groups;</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p>Homelessness: 1 RCT, N = 95, RR = 0.04, 95%CI 0.00 to 0.70, <math>p = 0.027</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p>Living independently: 5 RCTs, N = 1303, RR = 0.80, 95%CI 0.66 to 0.97, <math>p = 0.024</math>, <math>I^2 = 31%</math>, <math>p = 0.21</math></p> <p>Homelessness: 1 RCT, N = 88, RR = 0.32, 95%CI 0.03 to 2.95, <math>p = 0.31</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p>Living independently: 4 RCTs, N = 1185, RR = 0.65, 95%CI 0.49 to 0.88, <math>p = 0.0045</math>, <math>I^2 = 44%</math>, <math>p = 0.15</math></p> <p>Living in stable accommodation: 1 RCT, N = 168, RR = 0.80, 95%CI 0.65 to 0.98, <math>p = 0.035</math></p>	



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Homelessness: 3 RCTs, N = 418, RR = 0.78, 95%CI 0.34 to 1.82, $p = 0.57$ , $I^2 = 39%$ , $p = 0.19$	
<b>Consistency in results</b>	Consistent where applicable (> 1 RCT).
<b>Precision in results</b>	Precise for independent accommodation (medium, long term), and stable accommodation (long term). Imprecise for all other measures.
<b>Directness of results</b>	Direct
<b>Substance use</b>	
<i>No significant differences between groups;</i>	
Alcohol abuse: 1 RCT, N = 547, RR = 0.55, 95%CI 0.26 to 1.17, $p = 0.12$	
Illicit drug use: 1 RCT, N = 547, RR = 0.96, 95%CI 0.63 to 1.47, $p = 0.86$	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Mental state</b>	
<i>A significant effect of more improved symptoms in the intensive case management group in the short term (CSI scores), in the medium term (CSI scores), and in the long term (BSI scores), with no other differences between groups apart from more improved symptoms in the control group in the long term (CSI scores):</i>	
<u>Short-term – by 6 months</u>	
CSI: 1 RCT, N = 125, MD = -0.56, 95%CI -0.84 to -0.28, $p < 0.05$	
BPRS: 2 RCTs, N = 668, MD = -1.56, 95%CI -6.85 to 3.73, $p = 0.56$ , $I^2 = 92%$ , $p = 0.00039$	
BSI: 2 RCTs, N = 668, MD = - 0.06, 95%CI -0.19 to 0.06, $p = 0.34$ , $I^2 = 0%$ , $p = 0.88$	
<u>Medium-term – 7 to 12 months</u>	
CSI: 1 RCT, N = 125, MD = -0.35, 95%CI -0.65 to -0.05, $p = 0.024$	
BPRS: 2 RCTs, N = 662, MD = -0.96, 95%CI -2.42 to 0.51, $p = 0.20$ , $I^2 = 0%$ , $p = 0.35$	
BSI: 2 RCTs, N = 662, MD = -0.02, 95%CI -0.15 to 0.10, $p = 0.71$ , $I^2 = 0%$ , $p = 0.81$	
Depression: 1 RCT, N = 547, RR = 0.77, 95%CI 0.56 to 1.04, $p = 0.092$	
<u>Long-term – over 12 months</u>	
BPRS: 3 RCTs, N = 777, MD = -1.48, 95%CI -3.69 to 0.74, $p = 0.19$ , $I^2 = 85%$ , $p = 0.001$	
BSI: 2 RCTs, N = 647, MD = -0.18, 95%CI -0.31 to -0.06, $p = 0.004$ , $I^2 = 0%$ , $p = 0.43$	



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<p>CSI: 1 RCT, N = 168, MD = -0.32, 95%CI -0.53 to -0.11, <math>p = 0.0034</math>                  Depression: 1 RCT, N = 574, RR = 0.83, 95%CI 0.57 to 1.21, <math>p = 0.33</math></p>	
<b>Consistency in results</b>	Consistent for all measures except BPRS scores.
<b>Precision in results</b>	Imprecise, unable to assess general symptoms as standardised measures are not reported.
<b>Directness of results</b>	Direct
<b>Self-harm</b>	
<p><i>No differences between groups:</i>  <u>Medium-term – 7 to 12 months</u>                  2 RCTs, N = 620, RR = 0.99, 95%CI 0.61 to 1.59, <math>p = 0.96</math>, <math>I^2 = 0\%</math>, <math>p = 1.00</math>  <u>Long-term – over 12 months</u>                  1 RCT, N = 547, RR = 0.95, 95%CI 0.56 to 1.62, <math>p = 0.85</math></p>	
<b>Consistency in results</b>	Consistent where applicable
<b>Precision in results</b>	Imprecise for all measures
<b>Directness of results</b>	Direct
<b>Quality of Life</b>	
<p><i>A significant effect of improved quality of life in the short term in the intensive case management group, with no significant differences in the medium or long term:</i>  <u>Short-term – by 6 months</u>                  QOLI: 1 RCT, N = 125, MD = 0.53, 95%CI 0.09 to 0.97, <math>p = 0.019</math>  <u>Medium-term – 7 to 12 months</u>                  LQoLP: 1 RCT, N = 52, MD = 0.09, 95%CI -0.60 to 0.78, <math>p = 0.80</math>                  MANSA: 1 RCT, N = 81, MD = 0.20, 95%CI -0.29 to 0.69, <math>p = 0.42</math>  <u>Long-term – over 12 months</u>                  LQoLP: 3 RCTs, N = 274, MD = -0.13, 95%CI -0.38 to 0.12, <math>p = 0.29</math>, <math>I^2 = 0\%</math>, <math>p = 0.40</math>                  QOLI: 2 RCTs, N = 132, MD = 0.09, 95%CI -0.24 to 0.42, <math>p = 0.58</math>, <math>I^2 = 0\%</math>, <math>p = 0.46</math></p>	
<b>Consistency in results</b>	Consistent where applicable.
<b>Precision in results</b>	Unable to assess as standardised measures are not reported.



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<b>Directness of results</b>	Direct
<b>Client satisfaction</b>	
<p><i>A significant effect of greater client satisfaction in the control group in the short, medium and long term:</i></p> <p style="text-align: center;"><u>Short-term – by 6 months</u></p> <p style="text-align: center;">1 RCT, N = 61, MD = 6.20, 95%CI 2.60 to 9.80, <math>p = 0.00074</math></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p style="text-align: center;">2 RCTs, N = 500, MD = 1.93, 95%CI 0.86 to 3.01, <math>p = 0.00044</math>, <math>I^2 = 0\%</math>, <math>p = 0.89</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p style="text-align: center;">2 RCTs, N = 423, MD = 3.23, 95%CI 2.31 to 4.14, <math>p &lt; 0.05</math>, <math>I^2 = 0\%</math>, <math>p = 0.80</math></p>	
<b>Consistency in results</b>	Consistent where applicable
<b>Precision in results</b>	Unable to assess as standardized measures not reported
<b>Directness of results</b>	Direct
<b>Cost</b>	
<p><i>A significant effect of lower psychiatric hospital costs in the intensive case management group in the medium term, with no differences in long-term general health care costs;</i></p> <p style="text-align: center;"><u>Medium-term – 7 to 12 months</u></p> <p style="text-align: center;">Psychiatric hospital costs: 2 RCTs, N = 426, MD = -143.74, 95%CI -272.40 to -15.08, <math>p = 0.029</math>, <math>I^2 = 0\%</math>, <math>p = 0.67</math></p> <p style="text-align: center;"><u>Long-term – over 12 months</u></p> <p style="text-align: center;">General health care costs: 2 RCTs, N = 873, MD = -529.24, 95%CI -2143.59 to 1085.10, <math>p = 0.52</math>, <math>I^2 = 94\%</math>, <math>p &lt; 0.05</math></p>	
<b>Consistency in results</b>	Consistent for psychiatric hospital cost, inconsistent for health care cost.
<b>Precision in results</b>	Unable to assess as standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Comparison 2</b>	<b>Intensive case management vs. standard (non-intensive) case management.</b>
<b>Summary of evidence</b>	<b>High quality evidence (direct, consistent, precise, large sample) shows that people with schizophrenia receiving intensive case</b>

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	<p>management showed a decrease in dropout rates after 12 months compared to people with schizophrenia receiving standard case management.</p> <p><b>Moderate to high quality evidence (direct, mostly consistent, some imprecision, large sample) suggests no differences in medication compliance or death at 6 – 12 months, or contact with the legal system, employment, substance abuse, average endpoint scores on outcomes (HoNOS), substance use (SATS) and life skills (LSP). There were also no differences in behaviour, service use, accommodation status, mental states, quality of life, participant satisfaction or cost.</b></p>
<b>Service use</b>	
<p><i>No differences between groups;</i></p> <p><u>Long-term – over 12 months</u></p> <p>Days in hospital per month: 21 RCTs, N = 2,220, MD = -0.08, 95%CI -0.37 to 0.21, <math>p = 0.61</math>, <math>I^2 = 0%</math>, <math>p = 0.49</math></p> <p>Hospitalisations: 3 RCTs, N = 1,132, RR = 0.91, 95%CI 0.75 to 1.12, <math>p = 0.38</math>, <math>I^2 = 62%</math>, <math>p = 0.07</math></p>	
<b>Consistency in results</b>	Consistent for hospital admissions, inconsistent for number of days in hospital per month.
<b>Precision in results</b>	Precise for hospital admissions. Unable to assess average number of days in hospital per month as standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Mortality</b>	
<p><i>No differences between groups;</i></p> <p><u>Medium-term – 7 to 12 months</u></p> <p>All-cause mortality: 3 RCTs, N = 294, RR = 2.92, 95%CI 0.12 to 69.43, <math>p = 0.51</math>, <math>I^2 = 0%</math>, <math>p = 1</math></p> <p>Suicide: 6 RCTs, N = 929, RR = 1.61, 95%CI 0.26 to 9.85, <math>p = 0.61</math>, <math>I^2 = 24%</math>, <math>p = 0.27</math></p> <p><u>Long-term – over 12 months</u></p> <p>All-cause mortality: 5 RCTs, N = 1637, RR = 0.90, 95%CI 0.46 to 1.75, <math>p = 0.75</math>, <math>I^2 = 0%</math>, <math>p = 0.98</math></p> <p>Suicide: 3 RCTs, N = 1152, RR = 0.88, 95%CI 0.27 to 2.84, <math>p = 0.83</math>, <math>I^2 = 4%</math>, <math>p = 0.31</math></p>	
<b>Consistency in results</b>	Consistent for all measures.
<b>Precision in results</b>	Imprecise



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<b>Directness of results</b>	Direct
<b>Medication adherence and dropout rates</b>	
<i>A significant medium effect of lower dropout rates on the intensive case management group in the long term, with no differences between groups on all other measures;</i>	
<u>Medium-term – 7 to 12 months</u>	
Dropouts: 2 RCTs, N = 225, RR = 0.64, 95%CI 0.13 to 3.07, $p = 0.58$ , $I^2 = 84%$ , $p = 0.01$	
Medication adherence: 1 RCT, N = 73, RR = 1.14, 95%CI 0.42 to 3.05, $p = 0.80$	
<u>Long-term – over 12 months</u>	
Dropout: 7 RCTs, N = 1,970, RR = 0.70, 95%CI 0.52 to 0.95, $p = 0.021$ , $I^2 = 39%$ , $p = 0.13$	
Medication adherence (compliance sub-scale): 1 RCT, N = 239, MD = 0.60, 95%CI -0.05 to 1.25, $p = 0.069$	
Medication adherence (non-compliance subscale): 1 RCT, N = 239, MD = -0.60, 95%CI -1.63 to 0.43, $p = 0.25$	
<b>Consistency in results</b>	Consistent for long-term dropout rates only. Not applicable for outcomes with 1 RCT.
<b>Precision in results</b>	Precise for long-term dropout rates only. Unable to assess medication compliance as standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Functioning</b>	
<i>No differences between groups;</i>	
HoNOS: 1 RCT, N = 239, RR = -0.40, 95%CI -1.77 to 0.97, $p = 0.57$	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Contact with the legal system</b>	
<i>No differences between groups;</i>	
<u>Medium-term – 7 to 12 months</u>	
Contact with police: 1 RCT, N = 73, RR = 0.32, 95%CI 0.04 to 2.97, $p = 0.32$	





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<u>Long-term – over 12 months</u>	
Imprisoned: 2 RCTs, N = 959, RR = 1.15, 95%CI 0.64 to 2.08, $p = 0.63$ , $I^2 = 0\%$ , $p = 0.51$ Arrested: 1 RCT, N = 251, RR = 0.87, 95%CI 0.53 to 1.42, $p = 0.57$	
<b>Consistency in results</b>	Consistent where applicable.
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Employment</b>	
<i>No differences between groups;</i> <u>Medium-term – 7 to 12 months</u> Spent > 1 day employed: 1 RCT, N = 73, RR = 1.46, 95%CI 0.45 to 4.74, $p = 0.53$ Any paid employment: 1 RCT, N = 73, RR = 0.97, 95%CI 0.14 to 6.54, $p = 0.98$	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Accommodation status</b>	
<i>No differences between groups;</i> <u>Short-term – by 6 months</u> Average number of days per month in stable accommodation: 1 RCT, N = 203, MD = -0.20, 95%CI -2.48 to 2.08, $p = 0.86$ <u>Medium-term – 7 to 12 months</u> Living in supported accommodation: 1 RCT, N = 73, RR = 2.59, 95%CI 0.75 to 9.01, $p = 0.13$ Average number of days per month in stable accommodation: 1 RCT, N = 203, MD = 0.10, 95%CI -2.15 to 2.35, $p = 0.93$ <u>Long-term – over 12 months</u> Homelessness: 1 RCT, N = 251, RR = 0.69, 95%CI 0.34 to 1.38, $p = 0.29$ Average number of days per month in stable accommodation: 2 RCT, N = 901, MD = -0.19, 95%CI -1.37 to 1.00, $p = 0.76$ , $I^2 = 0\%$ , $p = 0.50$	

<b>Consistency in results</b>	Consistent where applicable.
<b>Precision in results</b>	Imprecise for RRs, unable to assess MDs.
<b>Directness of results</b>	Direct
<b>Substance use</b>	
<p><i>No differences between groups;</i></p> <p><u>Short-term – by 6 months</u></p> <p>SATS: 1 RCT, N = 203, MD = 0.07, 95%CI -0.28 to 0.42, <math>p = 0.69</math></p> <p><u>Medium-term – 7 to 12 months</u></p> <p>SATS: 1 RCT, N = 203, MD = -0.11, 95%CI -0.55 to 0.33, <math>p = 0.62</math></p> <p><u>Long-term – over 12 months</u></p> <p>SATS: 1 RCT, N = 203, MD = 0.11, 95%CI -0.41 to 0.63, <math>p = 0.68</math></p> <p>LSP: 1 RCT, N = 239, MD = 4.00, 95%CI -0.61 to 8.61, <math>p = 0.089</math></p> <p>Alcohol abuse: 1 RCT, N = 251, RR = 1.10, 95%CI 0.67 to 1.83, <math>p = 0.70</math></p> <p>Illicit drug use: 1 RCT, N = 251, RR = 1.08, 95%CI 0.69 to 1.71, <math>p = 0.73</math></p> <p>Remission from alcohol use disorder (AUS score &lt; 3): 1 RCT, N = 223, RR = 0.86, 95%CI 0.65 to 1.14, <math>p = 0.31</math></p>	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Imprecise for RRs, unable to assess MDs.
<b>Directness of results</b>	Direct
<b>Mental state</b>	
<p><i>No differences between groups;</i></p> <p><u>Short-term – by 6 months</u></p> <p>BPRS: 1 RCT, N = 203, MD = -0.65, 95%CI -3.99 to 2.69, <math>p = 0.70</math></p> <p><u>Medium-term – 7 to 12 months</u></p> <p>BPRS: 1 RCT, N = 203, MD = 1.62, 95%CI -4.76 to 1.52, <math>p = 0.31</math></p> <p><u>Long-term – over 12 months</u></p> <p>BPRS: 1 RCT, N = 203, MD = -0.22, 95%CI -3.32 to 2.88, <math>p = 0.89</math></p>	



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<p>CPRS: 1 RCT, N = 595, MD = 0.40, 95%CI -1.83 to 2.63, <math>p = 0.72</math>                  SANS: 1 RCT, N = 593, MD = 0.20, 95%CI -2.32 to 2.72, <math>p = 0.88</math></p>	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Unable to assess, standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Self-harm or harm to others</b>	
<p><i>No differences between groups;</i>  <u>Medium-term – 7 to 12 months</u>                  1 RCT, N = 73, RR = 0.88, 95%CI 0.40 to 1.90, <math>p = 0.74</math>  <u>Long-term – over 12 months</u>                  1 RCT, N = 708, RR = 1.06, RR = 0.70 to 1.61, <math>p = 0.79</math>                  2 RCTs, N = 959, RR = 1.00, 95%CI 0.69 to 1.46, <math>p = 0.99</math>, <math>I^2 = 0\%</math>, <math>p = 0.56</math></p>	
<b>Consistency in results</b>	Consistent where applicable (> 1 RCT).
<b>Precision in results</b>	Imprecise
<b>Directness of results</b>	Direct
<b>Quality of Life</b>	
<p><i>No differences between groups;</i>  <u>Short-term – by 6 months</u>                  QOLI: 1 RCT, N = 203, MD = -0.02, 95%CI -0.43 to 0.39, <math>p = 0.92</math>  <u>Medium-term – 7 to 12 months</u>                  QOLI: 1 RCT, N = 203, MD = -0.04, 95%CI -0.43 to 0.35, <math>p = 0.84</math>  <u>Long-term – over 12 months</u>                  LQoL: 1 RCT, N = 526, MD = 0.03, 95%CI -0.10 to 0.16, <math>p = 0.64</math>                  MANSA :1 RCT, N = 166, MD = 0.10, 95%CI -0.19 to 0.39, <math>p = 0.57</math></p>	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Unable to assess, standardised values are not reported.
<b>Directness of results</b>	Direct



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<b>Client satisfaction</b>	
<p><i>No differences between groups;</i> <u>Long-term – over 12 months</u></p> <p>Satisfaction with health services: 1 RCT, N = 490, MD = -0.40, 95%CI -1.25 to 0.45, <i>p</i> = 0.36 Patient needs (CAN): 1 RCT, N = 585, MD = -0.29, 95%CI -0.69 to 0.11, <i>p</i> = 0.15</p>	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Unable to assess, standardised values are not reported.
<b>Directness of results</b>	Direct
<b>Cost</b>	
<p><i>No differences between groups;</i> <u>Long-term – over 12 months</u></p> <p>General health care costs: 1 RCT, N = 667, MD = 77.0, 95%CI -66.63 to 220.63, <i>p</i> = 0.29</p>	
<b>Consistency in results</b>	Not applicable (1 RCT).
<b>Precision in results</b>	Unable to assess, standardised values are not reported.
<b>Directness of results</b>	Direct

*Drake RE, O'Neal EL, Wallach MA*

**A systematic review of psychosocial research on psychosocial interventions for people with co-occurring severe mental and substance use disorders**

**Journal of Substance Abuse Treatment 2008; 34(1): 123-138**

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<b>Comparison</b>	<p><b>Integrated case management and assertive community treatment for substance abuse vs. standard care.</b></p> <p><b>Only samples with schizophrenia spectrum disorders are reported.</b></p>
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**Case Management**

<b>Summary of evidence</b>	<b>Moderate to low quality evidence (direct, small to moderate sample size, unable to assess consistency or precision) suggests little benefit of integrated case management for reducing substance use, or improving mental state or global function.</b>
<b>Global outcomes</b>	
<p>One trial, N = 223, compared assertive community treatment (ACT, integrated paradigm) with standard case management, and reported no difference in mental health outcomes, but some improvement in drug and alcohol use as well as improved global function by 3 years in the ACT group.</p> <p>One trial, N = 198, compared ACT with treatment as usual, and reported no difference in mental health outcomes, drug and alcohol use, life satisfaction or global function by 3 years.</p> <p>One trial, N = 54, compared integrated treatment (incorporating standard case management with substance abuse therapy) with treatment as usual, and reported no difference in mental health outcomes, drug and alcohol use, life satisfaction or hospitalisation rate by 12 months.</p>	
<b>Consistency in results</b>	No measure of consistency is reported.
<b>Precision in results</b>	No measure of precision is reported.
<b>Directness of results</b>	Direct

*Hunt GE, Morley K, Sitharthan T, Siegfried N, Cleary M*

**Psychosocial interventions for people with both severe mental illness and substance misuse**

Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD001088. DOI: 10.1002/14651858.CD001088.pub3

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<b>Comparison</b>	<b>Intensive case management (ICM) or non-integrated models of care (including substance abuse treatments, family psychoeducation, crisis intervention and skills training) vs. treatment as usual (TAU).</b>
<b>Summary of evidence</b>	<b>Moderate to low quality evidence (small to medium samples, consistent where applicable, imprecise, direct,) suggests</b>

	<b>intensive case management has no significant benefit over treatment as usual for study retention, hospitalisation or service use, substance use, quality of life or functioning.</b>
<b>Study retention: lost to treatment</b>	
<i>No significant effect of ICM on retention rates;</i>	
By 6 months, N = 134, 3 RCTs, RR = 1.23, 95%CI 0.73 to 2.06, $p = 0.44$ , $I^2 = 0\%$ , $p = 0.62$	
By 12 months, N = 134, 3 RCTs, RR = 1.21, 95%CI 0.73 to 1.99, $p = 0.46$ , $I^2 = 0\%$ , $p = 0.59$	
By 18 months, N = 134, 3 RCTs, RR = 1.35, 95%CI 0.83 to 2.19, $p = 0.22$ , $I^2 = 32\%$ , $p = 0.23$	
<b>Study retention: lost to evaluation</b>	
<i>No significant effect of ICM on evaluation rates;</i>	
By 6 months, N = 121, 3 RCTs, RR = 1.00, 95%CI 0.38 to 2.60, $p = 1.00$ , $I^2 = 0\%$ , $p = 1.00$	
By 12 months, N = 121, 3 RCTs, RR = 1.00, 95%CI 0.43 to 2.35, $p = 1.00$ , $I^2 = 0\%$ , $p = 1.00$	
By 18 months, N = 92, 2 RCTs, RR = 1.26, 95%CI 0.48 to 3.30, $p = 0.63$ , $I^2 = 66\%$ , $p = 0.09$	
<b>Functioning</b>	
<i>No significant effect of ICM on functioning (significant 18 month RFS score favours control);</i>	
By 6 months, N = 50, 1 RCT, WMD = -0.78, 95%CI -2.91 to 1.35, $p = 0.47$	
By 12 months, N = 50, 1 RCT, WMD = 0.70, 95%CI -1.56 to 2.96, $p = 0.54$	
By 18 months, N = 29, 1 RCT, WMD = -2.67, 95%CI -5.28 to 0.06, $p = 0.045$	
<i>No significant effect of ICM on social adjustment by 18 months;</i>	
By 6 months, N = 50, 1 RCT, WMD = -0.93, 95%CI -6.34 to 4.48, $p = 0.74$	
By 12 months, N = 50, 1 RCT, WMD = 3.09, 95%CI -2.71 to 8.89, $p = 0.30$	
By 18 months, N = 29, 1 RCT, WMD = -3.75, 95%CI -10.12 to 2.62, $p = 0.25$	
<b>Consistency in results</b>	Not applicable for outcomes with 1 RCT, consistent for all other outcomes.
<b>Precision in results</b>	Imprecise for dichotomous outcomes (RR), unable to assess continuous outcomes (MD, not standardised).
<b>Directness of results</b>	Direct





## Case Management

Zygmunt A, Olfson M, Boyer CA, Mechanic D

### **Interventions to improve medication adherence in schizophrenia.**

American Journal of Psychiatry 2002; 159(10): 1653-64

[View review abstract online](#)

<b>Comparison</b>	<b>Community-based care (up to 24 months, including intensive case management or assertive community treatment) vs. standard case management.</b>
<b>Summary of evidence</b>	<b>Moderate quality evidence (direct, large sample, unable to assess consistency or precision) suggests community-based care (including intensive case management or assertive community treatment) may provide some benefit for treatment adherence over standard case management.</b>
<b>Medication adherence</b>	
<p>Community care programs were broadly defined to require a social network, monitoring of clinical status, stable housing and supportive services. Specific interventions in 10 studies (6 randomised, N = 2509) included assertive community treatment, intensive case management, educational support.</p> <p>Only 4 of the 10 studies (3 randomised), reported better medication adherence in the community care group over the comparison condition. One study reported assertive community treatment was more effective than intensive case management for increasing adherence.</p>	
<b>Consistency in results</b>	No measure of consistency is reported.
<b>Precision in results</b>	No measure of precision is reported.
<b>Directness of results</b>	Direct

## Explanation of acronyms

ACT = Assertive Community Treatment, AUS = Alcohol Use Scale, BPRS = Brief Psychiatric Rating



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Scale, BSI = Brief Symptom Inventory, CAN = Camberwell Assessment of Needs Interview, CI = Confidence Interval, CPRS = Comprehensive Psychopathological Rating Scale, CSI = Colorado Symptom Inventory, CSQ = Client Satisfaction Questionnaire,  $d$  = Cohen's  $d$ , DAS = Disability Assessment Scale, ER = Emergency Room,  $g$  = Hedges'  $g$  = standardized mean differences (see below for interpretation of effect size), GAF = Global Assessment of Functioning Scale, HoNOS = Health of the National Outcome Scale,  $I^2$  = the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance), ICM = intensive case management, ISSI = Interview Schedule for Social Interactions, LQoLP = Lancashire Quality of Life Profile, LSP = Life Skills Profile, MANSA = Manchester Short Assessment of Quality of Life, MD = mean difference,  $N$  = number of participants,  $p$  = statistical probability of obtaining that result ( $p < 0.05$  generally regarded as significant),  $Q$  =  $Q$  statistic for the test of heterogeneity,  $Q_w$  = test for within group differences (heterogeneity in study results within a group of studies – measure of study consistency),  $Q_B$  = test for between group differences (heterogeneity between groups of studies for an outcome of interest), QOLI = Lehman's Quality of Life Interview, RCT = randomised controlled trial, RFS = Role Functioning Score, ROMI = Rating of Medication Influences, RR = relative risk, SANS = Schedule for the Assessment of Negative Symptoms, SAS = Social Adjustment Scale, SATS = Substance Abuse Treatment Scale, TAU = treatment as usual, 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<sup>10</sup>.

† Different effect measures are reported by different reviews.

Prevalence refers to how many existing cases there are at a particular point in time. Incidence refers to how many new cases there are per population in a specified time period. Incidence is usually reported as the number of new cases per 100,000 people per year. Alternatively some studies present the number of new cases that have accumulated over several years against a person-years denominator. This denominator is the sum of individual units of time that the persons in the population are at risk of becoming a case. It takes into account the size of the underlying population sample and its age structure over the duration of observation.

Reliability and validity refers to how accurate the instrument is. Sensitivity is the proportion of actual positives that are correctly identified (100% sensitivity = correct identification of all actual positives) and specificity is the proportion of negatives that are correctly identified (100% specificity = not identifying anyone as positive if they are truly not).

Weighted mean difference scores refer to mean differences between treatment and comparison groups after treatment (or occasionally pre to post treatment) and in a randomised trial there is an assumption that both groups are comparable on this measure prior to treatment. Standardised mean differences are divided by the pooled standard deviation (or the standard deviation of one group when groups are homogenous) that allows results from different scales to be combined and compared. Each study's mean difference is then given a weighting depending on the size of the sample and the variability in the data. Less than 0.4 represents a small effect, around 0.5 a medium effect, and over 0.8 represents a large effect<sup>10</sup>.

Odds ratio (OR) or relative risk (RR) refers to the probability of a reduction ( $< 1$ ) or an increase ( $> 1$ ) in a particular outcome in a treatment group, or a group exposed to a risk factor, relative to the comparison group. For example, a RR of 0.75 translates to a reduction in risk of an outcome of 25% relative to those not receiving the treatment or not exposed to the risk factor. Conversely, a RR of 1.25 translates to an increased risk of 25% relative to those not receiving treatment or not having been exposed to a risk factor. A RR or OR of 1.00 means there is no difference between groups. A medium effect is considered if  $RR > 2$  or  $< 0.5$  and a large effect if  $RR > 5$  or  $< 0.2$ <sup>11</sup>. InOR stands for logarithmic OR where a InOR of 0 shows no difference between groups. Hazard ratios



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

Correlation coefficients (eg,  $r$ ) indicate the strength of association or relationship between variables. They can provide an indirect indication of prediction, but do not confirm causality due to possible and often unforeseen 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.

‡ Inconsistency refers to differing estimates of effect across studies (i.e. heterogeneity or variability in results) that is not explained by subgroup analyses and therefore reduces confidence in the effect estimate.  $I^2$  is the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance) - 0% to 40%: heterogeneity might not be important, 30% to 60%: may represent moderate heterogeneity, 50% to 90%: may represent considerable heterogeneity and over this is considerable heterogeneity.  $I^2$  can be calculated from  $Q$  (chi-square) for the test of heterogeneity with the following formula<sup>10</sup>;

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

§ Imprecision refers to wide confidence intervals indicating a lack of confidence in the effect estimate. Based on GRADE recommendations, a result for continuous data (standardised mean differences, not weighted mean differences) is considered imprecise if the upper or lower confidence limit crosses an effect size of 0.5 in either direction, and for binary and correlation data, an effect size of 0.25. GRADE also recommends downgrading the evidence when sample size is smaller than 300 (for binary data) and 400 (for continuous data), although for some topics, these criteria should be relaxed<sup>12</sup>.

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



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