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Cost-effectiveness evaluations of psychological therapies for schizophrenia and bipolar disorder: a systematic review

Cost-effectiveness of psychological therapies

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Abstract

Objectives

This review aims to assess the cost-effectiveness of psychological interventions for schizophrenia/bipolar disorder (BD), to determine the robustness of current evidence and identify gaps in the available evidence.

Methods

Electronic searches (PsycINFO, MEDLINE, Embase) identified economic evaluations relating incremental cost to outcomes in the form of an Incremental Cost-Effectiveness Ratio (ICER) published in English since 2000. Searches were concluded in November 2018. Inclusion criteria were: adults with schizophrenia/BD; any psychological/psychosocial intervention (e.g. psychological therapy and integrated/collaborative care); probability of cost-effectiveness at explicitly-defined thresholds reported. Comparators could be routine practice, no intervention, or alternative psychological therapies. Screening, data extraction, and critical appraisal were performed using pre-specified criteria and forms. Results were summarised qualitatively. The protocol was registered on the PROSPERO database (CRD42017056579).

Results

Of 3,864 studies identified, 12 met the criteria for data extraction. All were integrated clinical and economic randomised controlled trials. The most common intervention was cognitive behavioural therapy (CBT, 6/12 studies). The most common measure of health benefit was the quality-adjusted life-year (QALY) (6/12). Follow-up ranged from 6-months to 5-years. Interventions were found to be cost-effective in most studies (9/12): the probability of cost-effectiveness ranged from 35-99.5%. All studies had limitations and demonstrated uncertainty (particularly related to incremental costs).

Conclusions

Most studies concluded psychological interventions for schizophrenia/BD are cost-effective, including CBT, though there was notable uncertainty. Heterogeneity across studies makes it difficult to reach strong conclusions. There is a particular need for more evidence in the population with BD and for longer-term evidence across both populations.

Key words: schizophrenia, bipolar disorder, cost-effectiveness, cost-utility, economic evaluation.
Background

Schizophrenia and bipolar disorder (BD) are among the top 20 causes of disability in the world, with an estimated 15.2 million years lived with disability (YLD) due to schizophrenia and 9.9 million YLD due to BD globally (2013 estimates) (1). The rate of all-cause mortality in schizophrenia and BD, over 15-year follow-up, is 2.08 and 1.77 times greater than the general population, respectively (2). Additionally, the premature mortality gap between individuals with schizophrenia and BD, and the general population is growing (2). The majority of premature deaths are linked to physical illness, such as cardiovascular and metabolic disease (2–8). Review evidence points to a link between premature mortality and morbidity and long-lasting negative health behaviours (7). A wide range of other factors also impact on quality of life, including cognitive impairment, discrimination, stigma, social exclusion, and reduced opportunities for employment and education (7,9,18,19,10–17). The impact on caregivers quality of life and time is also substantial (7).

As well as the humanistic burden, there is a large economic burden associated with schizophrenia and BD. Review evidence points to annual costs attributed to schizophrenia of between US$94 million and US$102 billion for different countries across the world (20). At least half (50-85%) of these were indirect costs, such as productivity loss (e.g. absenteeism from work) or informal care (20). Total costs for people with schizophrenia and BD are estimated to reach £14.7 billion by 2026, with 57% of these associated with lost earnings (21).

Typically, the first-line therapeutic option for schizophrenia or BD is pharmacological (e.g. antipsychotic medication and/or mood stabilisers). However, some individuals do not adhere to, or actively decline medication for a variety of reasons; and symptoms may be unresponsive to medication, or require further support (22). Psychological therapies, plus usual care (typically pharmacological treatments), can improve symptoms, and increase quality of life and functioning in people with schizophrenia and BD (23–26). Guidelines suggest that psychological therapies should be part of management strategies that are tailored to individual needs (27,28).

People with schizophrenia and BD comprise the majority of the population with severe mental illness; 94% of severe mental health service users in the UK have a diagnosis of either schizophrenia or BD (29). Available literature highlights the economic and patient burden of schizophrenia and BD, demonstrating the need for effective treatment in this patient group. Constraints on health and social care funding require that existing resources are allocated efficiently; economic evaluation provides a useful tool to support decision making for these patient groups.
Most systematic reviews of the cost-effectiveness of treatments for psychosis have focused on pharmacological therapies. Three previous reviews which included psychological therapies were identified for schizophrenia or BD (30–32). Amos et al. (2012) focused on early intervention (EI) for psychosis (30). Desmedt et al. (2016) evaluated the cost-effectiveness of integrated care models for people with chronic diseases, which included six studies on schizophrenia (31). Finally, Pari et al. (2014) focused on management strategies (including pharmacological management) for BD (32). While these reviews are valuable, they contain little recent evidence and are somewhat limited in scope, either by intervention or population group. Therefore, a more up-to-date literature search and comprehensive synthesis of the evidence is required to support evidence-based practice and research in the field.

The aim of this review was to determine the robustness of the current evidence base for economic evaluations of psychological interventions for schizophrenia or BD, and to identify any gaps in this evidence base.

**Methods**

The review protocol was published on the online PROSPERO international register of systematic reviews (CRD42017056579) (33).

**Search strategy**

Searches were initially performed in August 2015 and were updated in January 2017 and November 2018. Searches were restricted to publications from year 2000 onwards (to maximise relevance to current practice) in English language on the OVID Medline, EMBASE and PsychINFO databases. The NHS EED database was searched in the initial search; later searches excluded this database since new papers were not added after 2015. Search terms included terms specific to economic evaluation, the population of interest, and psychological therapy. Strategies and terms varied according to the database design. Free-text and standardised (MESH) subject terms were used. Strategies were pilot tested to ensure all studies already known to the authors were retrieved. The full search strategies are provided in the supplementary material (supplementary material, Table 1).

**Selection of studies**

Inclusion criteria are outlined in Table 1. Studies not meeting these criteria were excluded during the screening process.

[Table 1]
Independent screening was undertaken at two stages (firstly of abstracts and titles, then of full papers) by four reviewers (GES, DB, KPH, JE). A fifth reviewer was used to resolve disagreements (LMD). The primary reason for exclusion was recorded at both stages.

**Data extraction and quality appraisal**

The NHS EED quality checklist for data extraction and critical appraisal was adapted to develop a predefined data extraction form and the CHEERS checklist was used to support critical appraisal (34,35). Data extraction and quality assessment included information on study methodology, results, limitations, evidence gaps and risk of bias. Data extraction was completed by one reviewer (DB papers published until 2016; LMD papers published from 2016 onwards) with 20% of data extraction checked by a second reviewer (GES).

Review findings are presented via narrative synthesis. As expected, and typical of economic evaluations, included studies and interventions were highly heterogeneous, limiting the usefulness of any quantitative synthesis (e.g. meta-analysis).

Cost values were converted into 2017 US dollars, using the price index for each country and the purchasing power parity conversion factor, to facilitate comparison between studies set in different countries (36,37).

**Results**

In total 4,412 articles were identified through database searches; 3,864 remained after excluding duplicates. Primary screening of abstracts and titles reduced this to 232 papers for full text review. Twelve papers, specific to schizophrenia or BD, were identified and included in the review.

[Figure 1]

An overview of the key study characteristics is provided in Table 2.

[Table 2]
Critical appraisal

An overview of the quality of reporting (using the CHEERS checklist) of the economic evaluations is provided in the supplementary material (supplementary material, Table 2).

Population

According to trial recruitment criteria, the majority of study populations were predominantly made up of participants with schizophrenia (38,40–48). Two studies focused on participants with BD (39,49). Study participants were predominantly male and between 23-46 years old (Table 2). Note that this review included studies considering a population with an author reported diagnosis of schizophrenia or BD, exact diagnosis criteria could vary across studies.

There was inconsistency in how duration of illness was defined. Three studies did report duration of illness: Barton et al. (2009) reported a mean of 4.8 years, van der Gaag et al. (2011) 10.14 to 11.02 years, and Priebe et al. (2016) a median of 11 years (range 7 to 18) (40,43,47). Patel et al. (2010) reported that over a half of patients had been in contact with psychiatric services for at least 10 years (42). McCrone et al. (2010) reported the proportion of patients with a first episode of psychosis (86% in the intervention group versus 71% in the control group) (41). Two studies reported the duration of untreated illness: Karow et al. (2012) reported means of 167 and 182 weeks in the intervention and control arms, respectively, and Rosenheck et al. (2016) a median of 74 weeks (45,48). One study reported the age of onset (22 years) (44), while another focused on the mean number of previous hospitalisations (6.3 in the intervention arm, 5.1 in the control arm) (39). Camacho et al. (2017) reported that over a half of participants had 20 or more previous bipolar episodes (49). In two studies duration of illness was not reported at all (38,46). These differences in quantifying duration of illness demonstrate the challenges in comparing study populations and drawing conclusions related to subgroups or specific populations. The observed variation in study populations (some of which is unclear due to differences in reporting) means that we are unable to differentiate between subgroups. Therefore, we considered the 12 studies as a whole.

Intervention and comparator

The most common intervention was CBT (6/12 studies) (38–43). The inclusion of CBT is clearly associated with publication date; the 6 oldest studies evaluate CBT as an intervention whereas the 6 more recent studies consider alternative psychological interventions. Four studies considered interventions focusing on multidisciplinary provision of care (41,45,46,48). Three other intervention types were identified; Crawford et al. (2012) evaluated
art therapy, Priebe et al. (2016) evaluated body psychotherapy (which uses movement and the body as a form of treatment) and Camacho et al. (2017) evaluated group psychoeducation which aims to enhance people’s understanding of their condition (44,47,49). “Standard care” was the most common comparator (9/12) (38,39,41–46,48). Standard care definitions varied across studies, but common themes included usual access to secondary mental health services and pharmacological treatment. The exact components of standard care (e.g. specific medications and doses) were not typically reported however, these are likely to be reported in the trial publications. One study did not describe standard care at all (42). This variation reduces the generalisability of each study.

Measure of health benefit

Six of the included articles presented a CUA (40,44,45,47–49), typically using the generic EQ-5D questionnaire to derive utilities and estimate quality-adjusted life-years (QALYs) (40,44,45,47,49). Rosenheck et al. (2016) applied a published mapping algorithm to estimate utility weights from Positive and Negative Symptom Scale (PANSS) scores using standard gamble and visual analogue scales (48,50).

The 10 CEAs used eight different measures of health benefit. Three used the Global Assessment of Functioning (GAF), a scoring system for severity of illness in psychiatry (38,44,46). Other psychiatric measures included full vocational recovery (41), the Social Functioning Scale (43) and PANSS negative scale scores (47). One study used a subset of the Wechsler Adult Intelligence Scale-III (WAIS-III) focusing on working memory (42). Another used the generic Quality of Life Scale (48). The studies focusing on participants with BD conducted a CEA using the cost per days free of bipolar episodes (39) and the cost to avoid one relapse or to gain a relapse-free year (49). The heterogeneity in outcome measures used means that it is difficult to determine an overall, comparative, estimate of cost-effectiveness. This is a common issue with CEAs, as there are no agreed threshold levels of cost per disease-specific outcome (51–53).

Included costs

The most common perspective taken within included studies was that of the healthcare provider (7/12) (39,40,45,47–49). Types of costs differed across studies. One study considered costs of schizophrenia-related health care only, excluding assertive community treatment and all other costs. This was the most limited inclusion of costs in the identified studies (45). Other studies captured intervention, inpatient, outpatient, and residential day service costs. Most included primary and community care, medication and social workers (10/12). Less common costs included were: criminal justice services (3/12) (41,42,44), patient out of pocket costs (3/12)
(38,40,43), social security benefits (e.g. sick pay) (42), lost wages (43) and informal care (all 1/12) (43). Three studies discounted future costs. (38,44,46). However, this was not necessary in most studies due to the short time horizons (<1 or 2 years). Two studies appeared to collect certain costs but did not report them. The first described the inclusion of productivity losses; later excluding these because fewer than 5% of participants were employed at baseline (44). The second detailed that medication data were collected but not costed. It is unlikely that this omission has an important bearing on cost-effectiveness conclusions, as interventions are unlikely to affect medication use within the short study timeframe (47).

Risk of bias

All economic evaluations were conducted using data collected in trials. One trial was non-randomised, increasing the risk of selection bias (45). The remaining evaluations were part of randomised trials, generally regarded as robust evidence. Over half reported that assessors were blinded but blinding of clinicians and participants was not possible due to the intervention types (38,39,42,44,46,47,49). The remaining studies did not report blinding (40,41,43,45,48). While blinding is important in reducing study bias, it is accepted that blinding is more challenging in non-pharmacological trials (54). All studies showed that arms were similar at baseline, with no significant differences that may confound results. Six studies confirmed that they were not powered to detect differences in cost-effectiveness (42–44,46–48); the remainder did not report this information. Two studies applied a complete case analysis (41,46), two did not report how they handled missing data (42,48) and 8 imputed missing data using various techniques (38–40,43–45,47,49). Eight studies explicitly adjusted for a variety of baseline demographic data (38–42,44,47,49).

Follow-up ranged from 6-months to 5-years (median 18 months). Only two studies were over 2 years in duration.

Study results

The key results from included studies are presented in Table 3. It is important to note that these results reflect varying time horizons.

All included studies found empirical clinical improvements in the intervention arm. Six noted that this difference was statistically significant, including 5/6 CBT studies and half of all team-based interventions (2/4) (38,39,41–43,45,48). Barton et al. (2009) also considered a CBT intervention but did not describe whether the change was statistically significant (40). One of the team-based interventions (early interventions for first-episode psychosis) was found to cause no significant change in health (46). Two ‘experimental’ treatments (art therapy and body
psychotherapy) did not have a statistically significant impact on health (44,47). The third (psychoeducation) did not report statistical significance, however, the 95% CI for the trial analysis did not cross zero for QALYs, indicating a statistically significant result (49). Camacho et al. (2017) reported that the within trial economic analysis demonstrated a net benefit of group psycho-education (vs group peer support) on three health benefit measures (QALYs, relapse avoided and relapse free years). The authors used an economic model to explore the cost effectiveness of group psychotherapy compared to treatment as usual. This also found a net improvement in QALYs for group psychotherapy. However, the 95% confidence intervals crossed zero, suggesting this difference was not statistically significant (49).

Incremental costs were highly uncertain. All but two studies noted that the impact of the intervention on overall costs was not statistically significant (38,39,41–48). The two remaining studies did not report any statistical significance testing (30); one of these did show that the 95% CI crossed zero, indicating incremental costs were not statistically significant (49). The study by Hastrup et al. (2013) stands out as an outlier, reporting the highest intervention saving of $35,864 per patient, but with the longest follow-up period (5 years) (46). Six studies conducted some form of sensitivity analysis on costs including: omitting medication costs, varying discount rates, and assuming therapy groups were run by volunteers (38,40,44,46–48). None of these sensitivity analyses indicated statistically significant differences in incremental costs. Since they focused on costs only, key drivers of cost-effectiveness are unknown.

ICER results across studies are challenging to summarise due to differences in the chosen measure of health benefit. Seven studies reported cost savings due to the intervention (38,39,41,42,45–47), and therefore the intervention was dominant in cost-effectiveness terms (health improving and cost saving). Four studies reported the ICER using QALYs, ranging from dominant to $87,562 per QALY. Studies reported the likelihood of cost-effectiveness relative to a specified cost-per-outcome threshold, and this raises one of the key limitations of the studies: recommended thresholds only exist for QALYs (52,55,56). Three studies presented the percentage likelihood of cost-effectiveness conservatively, assuming that the decision maker would not be prepared to pay anything additional for an improvement in health (38,41,42). Given the lack of thresholds for the majority of health benefits, it is left to decision makers to consider how much they would be prepared to pay for specific health gains.

[Table 3]
Discussion

All included studies showed health benefits attributed to the respective intervention, generally to a significant degree, though incremental costs were much more uncertain, as no studies identified a significant impact on costs. The majority of studies therefore concluded that psychological interventions, including CBT, are cost-effective for the treatment of people with schizophrenia. Only two studies were identified for BD with different conclusions regarding cost-effectiveness. A key limitation of the identified literature is that many studies used arbitrary thresholds for cost-effectiveness and no study reported being powered to detect differences in costs so there is some subjectivity around these conclusions.

Heterogeneity across studies makes comparisons challenging, in particular, the use of different measures of health outcome. The variation in outcome measures is likely to be partly due to the lack of a recommended outcome measure. It has been argued that generic measures of health, such as the EQ-5D, may be insensitive to psychosis symptoms and that a symptom-based measure should be considered (57–59), though others refute this (60–62). One review noted that while there have been many patient-reported outcome measures (PROMs) developed in psychosis, methodological quality is limited and different measures focus on different aspects (e.g. treatment satisfaction, quality of life, quality of the therapeutic relationship) (63). This multi-faceted approach to PROMs makes it hard to identify which outcome is the most appropriate. In addition, the choice of outcome measure is likely to be affected by the specific objectives of the intervention, which may focus on one aspect of the illness. There is a continuing debate regarding whether clinical recovery is aligned with patient experience, and thus whether it is truly meaningful to the individual (64).

A further complication is that there are no clear decision-making thresholds for most measures used in studies. Where there is no agreed threshold, the percentage likelihoods of cost-effectiveness produced by studies cannot be meaningfully compared.

The review found limited evidence regarding long-term differences in health and cost outcomes with psychological interventions in this population. Longer-term trials, and modelling studies extrapolating trial data over longer durations, would be useful to resolve this evidence gap.

While the evidence generally supports the use of psychological therapies in this population, decision/policy makers wishing to use the evidence would need to consider whether the results can be generalised to their setting, such as the applicability of standard care in the trial and the age of the population within the trial. They would
also have to determine an acceptable willingness to pay for specific health gains. Additionally, there are psychological interventions that have not yet been evaluated for cost-effectiveness, such as mindfulness, for which clinical evidence is heterogeneous and of limited quality (65). No studies were identified that looked at varying medication and introducing psychological treatment concurrently, which would be interesting as these are likely to be used in combination with one another. As more evidence becomes available, this review will need to be updated.

Our findings are similar to previous reviews, suggesting that although the results are predominantly in favour of psychological therapies within this group, there are issues of generalisability, uncertainty and a paucity of long-term data (30–32).

This review is subject to a number of limitations. It was restricted to English language articles and did not include unpublished literature. Including the grey literature and unpublished reports may be more likely to identify studies with inconclusive or negative cost-effectiveness results (66). Additionally, studies have found that economic data are more susceptible to publication bias when compared to clinical data (67). However, a search of the grey literature was outside the scope and resources for this review. Nevertheless, our review did identify published studies with inconclusive results (e.g. demonstrated by the reporting of non-significant cost outcomes) and negative results, which may mitigate the impact of publication bias. Our setting type did not include online interventions; although no studies were screened out because of this. The growth of online therapies in mental health has so far focused on adults with depression and anxiety. However, it is likely that future studies will consider the role of technology in the treatment of severe mental illness meaning that the scope of future reviews will need to be expanded (68). Finally, the review included psychological therapies, as existing reviews typically focused on pharmaceuticals. However, it may be useful to view findings for each intervention type side by side.

The review highlights a number of important considerations for future research; longer-term evidence, from randomised controlled trials and/or economic modelling studies, is needed to assess all important differences in health and cost outcomes from psychological interventions for schizophrenia and BD. Future studies should consider the comparability and ease of interpretation of their cost-effectiveness results; decision makers are unlikely to be able to draw firm conclusions from an evidence base comprising such varied measures of health benefit. Generic measures of benefit, such as QALYs, can be easily compared across studies and even disease groups. Furthermore, QALYs have well-defined thresholds against which to base decisions regarding cost-effectiveness. Sensitivity analyses of clinical data, which can identify key drivers of cost-effectiveness, were
generally lacking in the included studies. This form of analysis can characterise decision uncertainty and also guide future data collection. Finally, most studies were conducted in the UK and Europe. Research findings from a wider range of geographical settings are needed to ensure that decision makers have evidence that is generalisable to their jurisdiction.
Acknowledgments

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Conflict of interest

The authors declare that they have no conflicts of interests.
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Figure 1. Identification of studies
Table 1: Inclusion criteria for systematic review of psychological interventions for schizophrenia and bipolar disorder

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Requirement for Inclusion</th>
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<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Adults with schizophrenia or bipolar disorder. Studies that included individuals with dual diagnosis and/or co-morbidity were eligible for inclusion.</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Psychological interventions, which include ‘psychological therapy’, IAPT (Improving Access to Psychological Therapies), integrated care, collaborative care, talking therapies, psychological well-being practitioners, and/or liaison workers.</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>Comparison with routine practice or no intervention, or with any of the above interventions.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Full economic evaluation relating costs and outcomes in an incremental cost-effectiveness ratio (ICER), or some measure of net benefit that incorporates health outcomes. Studies had to include a ‘cost-effectiveness acceptability curve’ (CEAC) or explicitly report probabilities of being cost-effective to allow for an assessment of uncertainty.</td>
</tr>
<tr>
<td><strong>Setting and study type</strong></td>
<td>Studies in a community, primary or outpatient setting.</td>
</tr>
<tr>
<td></td>
<td>Studies that include a full economic evaluation comparing both costs and outcomes.</td>
</tr>
<tr>
<td></td>
<td>Any study types/designs except case reports.</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Journal articles published in English language between January 2000 and November 2018.</td>
</tr>
<tr>
<td>Author (year)</td>
<td>Population</td>
</tr>
<tr>
<td>--------------</td>
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</tr>
</tbody>
</table>
| Haddock et al. (2003) (38) | Dual diagnosis of schizophrenia, schizoaffective disorder or delusional disorder, and substance dependence/misuse  
- Mean age: NR  
- Proportion male: NR  
- Sample size = 36 | Secondary and community care in the UK | Cognitive-behavioural therapy combined with motivational intervention plus standard care | Standard care | CEA (GAF) | 18 months |
| Lam et al. (2005) (39) | Bipolar I disorder  
- Mean age: intervention 46.4 (SD 12.1), control 41.5 (SD 10.8)  
- Proportion male: CTG 54%, SC 57%  
- Sample size = 103 | Secondary care in the UK | Cognitive therapy plus standard care | Standard care | CEA (days free of bipolar episodes) | 30 months |
| Barton et al. (2009) (40) | Early psychosis, including schizophrenia, schizoaffective disorder, bipolar disorder, and psychotic depression  
- Mean age: 28.9 (range: 18-52)  
- Proportion male: 71.4%  
- Sample size = 77 | Secondary and community care in the UK | Social recovery orientated cognitive-behavioural therapy | Case management | CUA (EQ-5D) | 9 months |
| McCrone et al. (2010) (41) | Confirmed diagnosis of non-affective psychosis (schizophrenia was the most common condition)  
- Mean age: intervention 26 (SD 6), control 27 (SD 6)  
- Proportion male: intervention 55%, control 74%  
- Sample size = 144 | Secondary and community care in the UK | Assertive outreach | Standard care | CEA (full vocational recovery) | 18 months |
| Patel et al. (2010) (42) | Schizophrenia (alongside cognitive and social functioning difficulties)  
- Mean age: 36 | Secondary care in the UK | Cognitive remediation therapy plus standard care | Standard care | CEA (Wechsler Adult Intelligence Scale-III) | 40 weeks |
<table>
<thead>
<tr>
<th>Study Authors and Year</th>
<th>Information</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Outcomes</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>van der Gaag et al. (2011) (43)</td>
<td>Schizophrenia or schizoaffective disorder with persistent symptoms despite antipsychotic medication</td>
<td>Secondary care in the Netherlands</td>
<td>Cognitive behavioural therapy plus standard care</td>
<td>CEA (Social Functioning Scale (SFS) days of normal functioning)</td>
<td>18 months</td>
</tr>
<tr>
<td>Crawford et al. (2012) (44)</td>
<td>Schizophrenia</td>
<td>Secondary and community care in the UK</td>
<td>Group art therapy plus standard care</td>
<td>CEA (GAF score) CUA (EQ-5D)</td>
<td>12 months</td>
</tr>
<tr>
<td>Karow et al. (2012) (45)</td>
<td>Schizophrenia, schizophrenic spectrum disorder, schizoaffective disorder, delusional disorder, or psychotic disorder not otherwise specified</td>
<td>Secondary care in Germany</td>
<td>Assertive community treatment (ACT) and integrated care</td>
<td>Standard care CUA (EQ-5D)</td>
<td>12 months</td>
</tr>
<tr>
<td>Hastrup et al. (2013) (46)</td>
<td>A clinical diagnosis within the schizophrenia spectrum</td>
<td>Secondary and community care in Denmark</td>
<td>Early interventions for first-episode psychosis</td>
<td>Standard care CEA (GAF)</td>
<td>5 years</td>
</tr>
<tr>
<td>Priebe et al. (2016) (47)</td>
<td>Schizophrenia</td>
<td>Community care in the UK</td>
<td>Body psychotherapy Pilates class</td>
<td>CUA (EQ-5D) CEA (PANSS negative score)</td>
<td>6 months</td>
</tr>
<tr>
<td>Study</td>
<td>Condition</td>
<td>Mean age</td>
<td>Proportion male</td>
<td>Sample size</td>
<td>Setting</td>
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<tr>
<td>Rosenheck et al. (2016) (48)</td>
<td>First-episode psychosis</td>
<td>23</td>
<td>Intervention 66%, control 78%</td>
<td>404</td>
<td>Community care in the USA</td>
</tr>
<tr>
<td>Camacho et al. (2017) (49)</td>
<td>Bipolar disorder</td>
<td>45</td>
<td>Proportion male: 42%</td>
<td>304</td>
<td>Primary care in England</td>
</tr>
</tbody>
</table>

**Key:** ACT, assertive community treatment; CEA, cost-effectiveness analysis; CBT, cognitive behavioural therapy; CUA, cost-utility analysis; EQ-5D, EuroQoL 5-Dimension questionnaire; GAF, global assessment of functioning; NR, not reported; IMT, integrated multidisciplinary team-based treatment approach; PANSS, positive and negative symptom scale; QLS, quality of life scale; SD, standard deviation; SFS, social functioning scale; WAIS-III, Wechsler Adult Intelligence Scale-III working memory.
Table 3: Key study outcomes

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Haddock et al. (2003) (38)</td>
<td>Cognitive-behavioural therapy combined with motivational intervention plus routine care vs routine care alone</td>
<td>9.91 improvement on GAF</td>
<td>-$2,452</td>
<td>Dominant</td>
<td>69% (any amount for an extra point on GAF)</td>
</tr>
<tr>
<td>Lam et al. (2005) (39)</td>
<td>Cognitive therapy plus standard care</td>
<td>110 fewer Bipolar episode days</td>
<td>-$2,530</td>
<td>Dominant</td>
<td>80% ($18 per day free from a bipolar episode)</td>
</tr>
<tr>
<td>Barton et al. (2009) (40)</td>
<td>Social recovery orientated cognitive-behavioural therapy vs case management</td>
<td>0.035 QALYs gained</td>
<td>$1,171</td>
<td>$33,007 per QALY</td>
<td>54% ($35,031 per QALY threshold)</td>
</tr>
<tr>
<td>McCrone et al. (2010) (41)</td>
<td>Assertive outreach vs standard care</td>
<td>6.0 improvement on MNSA 12% more with a vocational recovery</td>
<td>-$4,429</td>
<td>Dominant</td>
<td>76% (not willing to pay anything for a MNSA improvement)</td>
</tr>
<tr>
<td>Patel et al. (2010) (42)</td>
<td>Cognitive remediation therapy vs standard care</td>
<td>1.33 improvement on WAIS-III</td>
<td>-$241</td>
<td>Dominant</td>
<td>80% (anything for an improvement)</td>
</tr>
<tr>
<td>van der Gaag et al. (2011) (43)</td>
<td>Cognitive behavioural therapy vs standard care</td>
<td>77 additional days of normal functioning</td>
<td>$4,972</td>
<td>$66 per day with normal functioning</td>
<td>70% ($118 for an additional day of normal functioning)</td>
</tr>
<tr>
<td>Crawford et al. (2012) (44)</td>
<td>Group art therapy plus standard care</td>
<td>0.043 QALYs gained</td>
<td>-$2,072</td>
<td>$48,136 per QALY</td>
<td>50% (flat CEAC – between 0 and $17,128 willingness to pay per QALY)</td>
</tr>
<tr>
<td>Karow et al. (2012) (45)</td>
<td>Assertive community treatment and integrated care vs standard care</td>
<td>0.1 QALYs gained</td>
<td>-$3,502</td>
<td>Dominant</td>
<td>99.5% ($69,990 per QALY)</td>
</tr>
<tr>
<td>Study Authors and Year</td>
<td>Treatment Comparison</td>
<td>Effect on Outcomes</td>
<td>Cost</td>
<td>Dominant</td>
<td>Cost-Effectiveness</td>
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<tr>
<td>Hastrup et al. (2013) (46)</td>
<td>Early interventions for first-episode psychosis vs standard care</td>
<td>1.19 improvement on GAF</td>
<td>-$35,864</td>
<td>Dominant</td>
<td>80% ($69,737 per point increase in the GAF)</td>
</tr>
<tr>
<td>Priebe et al. (2016) (47)</td>
<td>Body psychotherapy vs pilates class</td>
<td>0.001 QALY gain 0.21 PANSS negative score reduction</td>
<td>-$37</td>
<td>Dominant</td>
<td>65% ($29,785 per QALY)</td>
</tr>
<tr>
<td>Rosenheck et al. (2016) (48)</td>
<td>An integrated, multidisciplinary, team-based treatment approach vs standard care</td>
<td>0.25 improvement on the QLS</td>
<td>$3,804</td>
<td>94% ($40,000 per QLS-SD) 90-95% ($210,000 per QALY)</td>
<td></td>
</tr>
<tr>
<td>Camacho et al. (2017) (49)</td>
<td>Group psychoeducation vs group peer support</td>
<td>0.023 QALYs 0.131 years relapse free 0.102 number of relapses avoided</td>
<td>$1,635</td>
<td>35% ($44,678 per QALY) 99% ($44,678 per relapse free year) 99% ($44,678 per relapse avoided)</td>
<td></td>
</tr>
</tbody>
</table>

**Key:** CEA, cost-effectiveness analysis; CUA, cost-utility analysis; GAF, global assessment of functioning; MANSA, Manchester Short Assessment of Quality of Life; NR, not reported; PANSS, positive and negative symptom scale; QLS, quality of life scale; SD, standard deviation; SFS, social functioning scale; WAIS-III, Wechsler Adult Intelligence Scale-III working memory.

**Note:** For the study by Camacho et al. 2017 the trial results are presented here as they reflect the primary analysis.
Figure 1: Identification of studies

Identification
- Records identified through databases (n=4412)
- Records screened (n=3864)
- Full-text articles assessed for eligibility (n=232)
- Number of studies included (n=12)

Screening
- Duplicates removed (n=548)
- Records excluded after abstract review (n=3632)
- Full-text articles excluded (n=220)
- Population (n=71)
- Intervention/comparator (n=28)
- Setting (n=5)
- No economic evaluation (n=13)
- Partial economic evaluations (n=45)
- No CEAC analysis (n=36)
- Study type (protocol, news, conference) (n=19)
- Duplicates (n=3)
### Supplementary material

#### Table 1 Search terms

**OVID Medline**

1. Collaborative care.mp.
2. integrat* care.mp.
3. "Delivery of Health Care, Integrated"/
4. Psychotherapy/ec
5. Mood Disorders/th
6. Depressive Disorder/th
7. Depressive Disorder, Major/th
8. talking therap*.mp.
9. liaison service*.mp.
10. liaison work*.mp.
11. IAPT.mp.
12. Improving access to psychological therap*.mp.
13. Community Mental Health Centers/ec
14. Cognitive Therapy/
15. Anxiety/th [Therapy]
16. Bipolar Disorder/rh [Rehabilitation]
17. Bipolar Disorder/th [Therapy]
18. Complementary Therapies/ec [Economics]
19. Depression/th [Therapy]
20. Depressive Disorder/rh [Rehabilitation]
21. Depressive Disorder, Treatment-Resistant/th [Therapy]
22. Mental Disorders/th [Therapy]
23. Primary Health Care/ec [Economics]
24. Psychotherapy/mt [Methods]
25. Psychotherapy, Brief/ec [Economics]
26. Psychotherapy, Group/ec [Economics]
27. Psychotic Disorders/th [Therapy]
28. Psychotic Disorders/rh [Rehabilitation]
29. Schizophrenia/rh [Rehabilitation]
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62. 57 not 61
63. or/1-42
64. or/43-45
65. 62 and 63 and 64
66. (letter or editorial or note or news or congresses or case reports).pt.
67. 65 not 66
68. limit 67 to (english language and humans and yr="2017 - 2019")

**EMBASE**

1. cognitive therapy/
2. community mental health team.mp.
3. family therapy/ and cost effectiveness analysis/
4. family work.mp.
5. *mental disease/dm [Disease Management]*
6. *patient counseling/
7. psychotherapy/ and cost effectiveness analysis/
8. telecare.mp.
9. peer support.mp.
10. *group therapy/
11. or/1-10
12. schizophrenia/
13. bipolar disorder/
14. Psychotic Disorders/
15. or/12-14
16. Health Economics/
17. exp Economic Evaluation/
18. exp Health Care Cost/
19. pharmacoeconomics/
20. or/16-19
21. (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab.
22. (expenditure$ not energy).ti,ab.
23. (value adj2 money).ti,ab.
24. budget$.ti,ab.
25. or/21-24

26. 20 or 25

27. (metabolic adj cost).ti,ab.

28. ((energy or oxygen) adj cost).ti,ab.

29. ((energy or oxygen) adj expenditure).ti,ab.

30. or/27-29

31. 26 not 30

32. 11 and 15 and 31

33. (letter or editorial or note or news or congresses or case reports).pt.

34. 32 not 33

34. limit 33 to (human and english language and yr="2017 - 2019")

**PsychINFO**

1. *Cognitive Behavior Therapy/

2. *family therapy/

3. Metacognitive group training.mp.

4. *Psychosocial Rehabilitation/

5. Collaborative care.mp.

6. integrat* care.mp.

7. talking therap*.mp.

8. liaison service*.mp.

9. liaison work*.mp.

10. IAPT.mp.

11. Improving access to psychological therap*.mp.

12. *Bipolar disorder/

13. *Schizophrenia/

14. exp Psychosis/

15. "costs and cost analysis"/

16. "Cost Containment"/

17. (economic adj2 evaluation$).ti,ab.

18. (economic adj2 analy$).ti,ab.

19. (economic adj2 (study or studies)).ti,ab.

20. (cost adj2 evaluation$).ti,ab.
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<td>(cost adj2 consequence$).ti,ab.</td>
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<td>41 not 44</td>
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<td>limit 45 to (human and english language and yr=&quot;2017 - 2019&quot;)</td>
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</table>
Table 2 CHEERS checklist

Key: 0 = Not reported, 1 = Partly reported, 2 = Well reported, - = Not applicable.

<table>
<thead>
<tr>
<th>Section/item</th>
<th>No</th>
<th>Recommendation</th>
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<tr>
<td><strong>Title and abstract</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.</td>
</tr>
<tr>
<td>Abstract</td>
<td>2</td>
<td>Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.</td>
</tr>
<tr>
<td><strong>Introduction</strong></td>
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</tr>
<tr>
<td>Background and objectives</td>
<td>3</td>
<td>Provide an explicit statement of the broader context for the study.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Present the study question and its relevance for health policy or practice decisions.</td>
</tr>
<tr>
<td><strong>Methods</strong></td>
<td></td>
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</tr>
<tr>
<td>Target population and subgroups</td>
<td>4</td>
<td>Describe characteristics of the base case population and subgroups analysed, including why they were chosen.</td>
</tr>
<tr>
<td>Setting and location</td>
<td>5</td>
<td>State relevant aspects of the system(s) in which the decision(s) need(s) to be made.</td>
</tr>
<tr>
<td>Study perspective</td>
<td>6</td>
<td>Describe the perspective of the study and relate this to the costs being evaluated.</td>
</tr>
<tr>
<td>Comparators</td>
<td>7</td>
<td>Describe the interventions or strategies being compared and state why they were chosen.</td>
</tr>
<tr>
<td>Time horizon</td>
<td>8</td>
<td>State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.</td>
</tr>
<tr>
<td>Discount rate</td>
<td>9</td>
<td>Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.</td>
</tr>
<tr>
<td>Choice of health outcomes</td>
<td>10</td>
<td>Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.</td>
</tr>
<tr>
<td>Measurement of effectiveness</td>
<td>11a</td>
<td>Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.</td>
</tr>
<tr>
<td></td>
<td>11b</td>
<td>Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.</td>
</tr>
<tr>
<td>Measurement and valuation of preference</td>
<td>12</td>
<td>If applicable, describe the population and methods used to elicit preferences for outcomes.</td>
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<td>Based outcomes</td>
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</tr>
<tr>
<td>Estimating resources and costs</td>
<td>13a</td>
<td>Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
</tr>
<tr>
<td>Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.</td>
<td>13b</td>
<td>- - - - - - - - - 2</td>
</tr>
<tr>
<td>Currency, price date, and conversion</td>
<td>14</td>
<td>Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.</td>
</tr>
<tr>
<td>Choice of model</td>
<td>15</td>
<td>Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.</td>
</tr>
<tr>
<td>Assumptions</td>
<td>16</td>
<td>Describe all structural or other assumptions underpinning the decision-analytical model.</td>
</tr>
<tr>
<td>Analytical methods</td>
<td>17</td>
<td>Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.</td>
</tr>
<tr>
<td>Results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study parameters</td>
<td>18</td>
<td>Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.</td>
</tr>
<tr>
<td>Incremental costs and outcomes</td>
<td>19</td>
<td>For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.</td>
</tr>
<tr>
<td>Characterising uncertainty</td>
<td>20a</td>
<td>Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).</td>
</tr>
<tr>
<td>Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.</td>
<td>20b</td>
<td>- - - - - - - - - 2</td>
</tr>
<tr>
<td>Characterising heterogeneity</td>
<td>21</td>
<td>If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.</td>
</tr>
</tbody>
</table>

Discussion
<table>
<thead>
<tr>
<th>Study findings, limitations, generalisability, and current knowledge</th>
<th>Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.</th>
<th>1</th>
<th>1</th>
<th>2</th>
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<tr>
<td>Source of funding</td>
<td>Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.</td>
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<tr>
<td>Conflicts of interest</td>
<td>Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.</td>
<td>0</td>
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<td>2</td>
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Note that study reporting will vary according to journal requirements. Additionally, all studies were conducted alongside randomised controlled trials and therefore items not reported may have been reported elsewhere.