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Original Research

The effectiveness of cognitive behavioural therapy versus antidepressants for treatment of post-stroke depression in adults

ORIGINAL RESEARCH

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ABSTRACT

Stroke is a common disorder with profound lasting effects and the UK's fourth leading cause of morbidity. One important after-effect is post-stroke depression (PSD). PSD can impact overall recovery, however treatment guidelines remain unclear. Usual care generally consists of antidepressants despite cognitive behavioural therapy (CBT) being a first-line treatment for depression. This evidence review aims to assess the effectiveness of CBT compared with antidepressants for treating PSD in adult stroke patients. Evidence searches of MEDLINE, PUBMED, The Cochrane Library, PsycINFO and NICE Evidence Search were conducted using strict search terms. The results were screened and appraised. A reference list search was carried out and included reviews with these results also screened and appraised. Appraisals used the AGREE II tool for guidelines and the CASP systematic review and randomised controlled trial (RCT) frameworks. Each stage was carried out by two independent reviewers, with disagreements resolved by a third reviewer. After applying inclusion and exclusion criteria, two guidelines, four reviews and one RCT were included in the synthesis. One review found CBT effective for treating PSD. Two reviews found CBT combined with antidepressants more effective than antidepressants alone. One review concluded CBT was ineffective for treating PSD. A single RCT found CBT more effective than antidepressants if PSD onset was nine months post-stroke, but PSD onset six months post-stroke was most effectively treated by antidepressants. Results for less than six months post-stroke were inconclusive. In conclusion, the findings of this evidence review suggest it is not possible to definitively conclude whether CBT is more or less effective than antidepressants. A combination of both is likely to be most effective. Lack of research means conclusions for clinical practice are difficult to draw. More research is needed before specific guidelines can be compiled.

INTRODUCTION

The World Health Organisation (WHO) defines stroke as a clinical syndrome characterised by "rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause apart from that of vascular origin". (1) Stroke is the fourth leading cause of death in the UK. (2) The long-term burden of stroke on survivors is just as significant: in 2016, stroke accounted for close to 20,000 age-specific years with lived disability per 100,000 in England. (3)

It is well-acknowledged that stroke can result in functional and physical decline. (4) Advances in the multidisciplinary team (MDT) approach to stroke aftercare, particularly physiotherapy, go some way towards addressing this issue. (5) However, the psychological effects of stroke, despite being seen in 30% of stroke patients, do not have such a recognised approach. (6)

An example of this is post-stroke depression (PSD). PSD can occur immediately or even years after a stroke and can be more debilitating for patients than the physical effects of stroke. (7) Additionally, PSD has the potential to seriously impede physical recovery due to its impact on motivation. (7)

The mechanism of PSD development is currently unclear, but it appears to be a combination of the direct physical effects of stroke on the brain and a psychological reaction to sudden and marked functional decline. (8) This ambiguity may account for the lack of recognised interventions for PSD, with the National Institute for Health and Care Excellence (NICE) stroke guidelines suggesting no clear pathway, stating instead to "Manage depression or anxiety in people after stroke who have no cognitive impairment in line with recommendations in depression in adults with a chronic physical health problem". (9)

In practice, lack of psychological practitioners within the stroke MDT often means specialised psychological treatment is not available, and the condition is poorly managed in the inpatient setting. (10)

Stroke patients still suffering from PSD after discharge are sometimes able to access general psychological support and cognitive behavioural therapy (CBT) through their general practitioner. CBT is the first-line treatment for depression in adults (11) and it is therefore thought that it may have some merit in treating PSD.

Evidently, PSD is an area in stroke rehabilitation which is underfunded and poorly understood. (8) There is limited knowledge into the best way to manage this condition, whether antidepressants, CBT, or a combination is most effective. The positive consequences for post-stroke patients of developing a clear and effective strategy for treating PSD could be extensive in both physical and psychological recovery.

Therefore, the aim of this evidence review is to assess the effectiveness of CBT compared with antidepressants for the treatment of PSD in adult stroke patients.

METHODS

Review Question

A population, intervention, comparator and outcome (PICO) framework was generated. This formed the basis of the review question: What is the effectiveness of cognitive behavioural therapy compared with antidepressants for the treatment of post-stroke depression in adult stroke patients?

The PICO framework was as follows:

Population: Adults who have had a stroke (according to the WHO definition) (1) and suffer from post-stroke depression, defined as depressive disorder due to another medical condition (i.e., stroke) (4, 12)
Intervention: CBT, defined as talking therapy to help change a patient's thinking and behaviour (13)
Comparator: Antidepressants
Outcome: Primary Outcome: Amelioration in depression (assessed by any validated depression rating scale)
Secondary Outcomes: Improvement in quality of life, improved functional ability

Literature Searches

A thorough literature search for guidelines, reviews and primary research studies was subsequently undertaken. Each of the steps outlined below were carried out by two independent reviewers with any disagreements resolved by a third reviewer.
Guidelines were searched for using NICE Evidence Search (Figure 1). Broad search terms (Table 1) were used because a scoping search revealed limited guidance on PSD. The search strategy is summarised in Figure 1. First, title/summary screening was undertaken, followed by a screen of full texts. Those meeting the inclusion criteria (Table 2) were then appraised using the AGREE II tool. (14)

Next, a review search was conducted using specific search terms (Table 1) using the following databases: MEDLINE, PUBMED, the Cochrane Library, and PsycINFO. Scoping searches revealed that including the search term 'antidepressant' would detrimentally limit the results as some papers used specific antidepressant names. It was therefore decided that to capture all relevant research, the use of antidepressants would form part of the inclusion criteria, instead of search terminology. More filters were added when searching PUBMED, such as 'meta-analysis' in addition to 'review', as the database uses filters and not limits. The search strategy used is demonstrated in Figure 2. Identified reviews were collated and duplicates were removed. Titles and abstracts were then screened to ensure the papers met inclusion and exclusion criteria. Next, a full text screen was undertaken. A reference list search was carried out on all included reviews. The Critical Appraisal Skills Programme (CASP) checklist for systematic reviews was used to critically appraise all included reviews. (15)

Finally, a search for primary research studies was completed using specific search terms (Table 1). The search was carried out on the following databases: MEDLINE, PUBMED, the Cochrane Library, and PsycINFO. A similar search strategy to the review search was carried out (Figure 2), with suitable papers being critically appraised using the CASP checklist for randomised controlled trials (RCTs). (16) One relevant RCT was identified through the search. (17) Despite being appraised in an included meta-analysis, (18) this study was re-evaluated by the current authors and is included in the results section below as it was the only paper to make a direct comparison between CBT alone and antidepressants alone, thus addressing the central review question.

Search Terms

Evidence searches on the databases listed above were carried out with the search terms and limits summarised in Table 1. The British English spellings of search terms were used, except for MeSH terms as the databases used the American English spelling. All PUBMED MeSH terms were automatically searched as both MeSH terms and keywords. See Appendix 1 for specific search terms used and results from each database.

Inclusion and Exclusion Criteria

The inclusion criteria applied to the guideline search were: English language guidelines, guidelines relevant to clinical practice, and guidelines that include recommendations for the treatment of PSD.

The inclusion criteria applied to the searches for reviews and primary research studies were: studies including patients who meet the review definition of stroke and the review definition of PSD, studies which evaluate CBT (according to this review's definition), and studies including an antidepressant comparator.

The exclusion criteria applied to the searches for reviews and primary research studies were: studies including patients under the age of 18.

RESULTS

Search Results

The search identified 2 guidelines, (19, 20) 3 narrative reviews, (21-23) 1 meta-analysis (18) and 1 RCT (17) meeting the inclusion criteria (see Figures 1 and 2). A reference list search returned no new papers. The results of identified papers are summarised in Table 2. Sample sizes were available for two out of the seven included literatures and were as follows: Wang et al (23 studies, 1972 participants), (18) Gao et al (2113 participants). (17)

Guidelines

There were no NICE guidelines identified. Two guideline documents were appraised using the AGREE-II tool: (14) the American Heart Association guidelines (19) for PSD and the Scottish Intercollegiate Guidelines Network (SIGN) (20) for stroke management.

The American Heart Association guidelines (19) stated that seven trials, (24-28) which investigated 775 individuals with PSD, suggested that "brief psychosocial interventions" may be useful in treating PSD. These seven trials were published in five research papers. (24-28) However, the guidelines did not comment on the concurrent use of antidepressants and there were few details about appraisal. Limitations recognised by the authors included small sample sizes and single-centre recruitment, so the trials were unlikely to be representative of a wider population. Due to the similar pattern of results demonstrated by the included studies, the authors concluded that psychosocial interventions show promise, but did not make any concrete recommendations.

The SIGN guideline published in 2010, (20) which addresses the management of patients after a stroke, stated that patients should be given antidepressants to treat their PSD. However, if the antidepressants did not work, the guidelines advised that patients should be considered for a talking-based therapy such as CBT. The SIGN guidelines relied on a Cochrane review of antidepressant and psychotherapy treatment for PSD to support their findings, (29) however, the studies included in this review had a high level of heterogeneity and the study types were not stated. As there was very little robust evidence of whether psychological therapies (including CBT) have efficacy in PSD treatment, the guidelines struggled to determine its usefulness.

Meta-analysis

One meta-analysis, Wang et al (18) was identified and appraised. A meta-analysis containing RCTs is the best available evidence according to the hierarchy of evidence; (30) therefore, this paper was appraised using the CASP systematic review checklist. (15) Wang et al evaluated whether CBT was more effective than standard care (seven RCTs), or whether CBT combined with an antidepressant was more effective than the antidepressant alone (14 RCTs) in treating PSD. (18) The results of the review demonstrated that both CBT alone and CBT combined with antidepressants were significantly more effective at reducing PSD than in the control groups (placebo, or antidepressant without CBT).

However, two other RCTs in this review had subjects in both the intervention (CBT) and control (placebo) groups who received antidepressants. There was no significant difference between the intervention and control groups, however these results may be swayed by some participants using antidepressants in the intervention/control groups. It would have been useful to see a baseline characteristics table to assess whether this would have had an effect. These results are shown in Table 3.

CBT was also shown to have a positive impact on anxiety, activities of daily living and neurological functional deficient as secondary outcomes.

Wang et al had a clearly defined PICO (P = patients with PSD according to any criteria, I = CBT alone or CBT with

Table 1

Search terms used to generate search results for guidelines, systematic reviews and primary research studies

Search	Database	Search Terms (MeSH terms underlined, keywords = normal type)	Limits/Filters Applied
Guidelines	NICE Evidence Search	Post-stroke Depression	Guidance
Reviews	MEDLINE (1946 – current day)	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy or Counseling or Cognitive Behaviour Therapy or CBT)	Limits Review English language
	PUBMED	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Filters Review Meta-analysis Systematic reviews English language
	Cochrane Library	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Limits Reviews
	PsycINFO (1967 – current day)	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accidents) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Limits Systematic reviews Literature reviews Meta-analysis English language
Primary research studies	MEDLINE (1946 – current day)	(Stroke OR Brain Ischemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioral Therapy or Counseling or Cognitive Behaviour Therapy or CBT)	Limits Randomized controlled trial English language
	PUBMED	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Filters Randomized controlled trial English language
	Cochrane library	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accident) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Limits Trials
	PsycINFO (1967 – current day)	(Stroke OR Brain Ischaemia OR Cerebral Haemorrhage OR Cerebrovascular Event OR Cerebrovascular Accidents) AND (Depression OR Post-stroke depression) AND (Cognitive Behavioural Therapy OR Counseling OR Cognitive Behaviour Therapy OR CBT)	Limits Clinical trial English language

Figure 1

Flowchart demonstrating the search strategy for guidelines

Flowchart includes the number of guidelines included and excluded at each

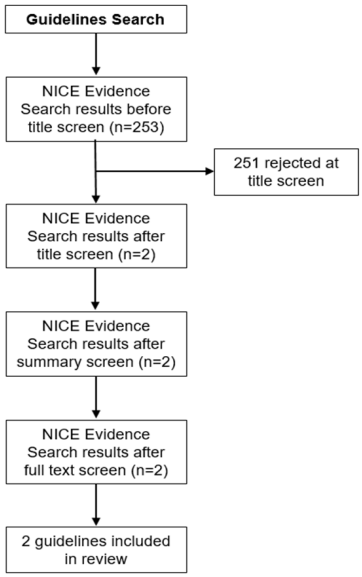

Figure 2

Flowchart demonstrating the search strategy for reviews and primary research

Flowchart includes the number of primary research studies and reviews included and excluded at each stage. Abbreviations: n = number of articles, PRS = primary research study, R = review

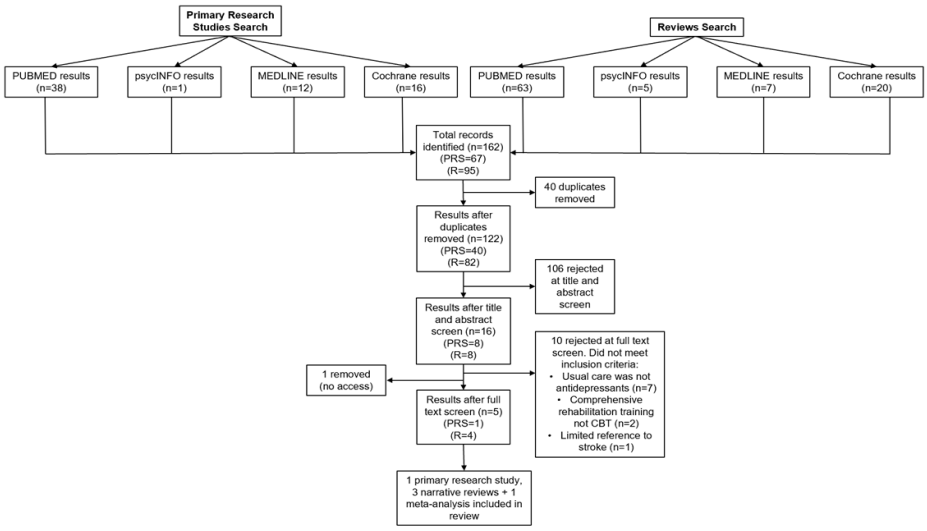

Table 2

Summary of Results of Included Literature

Authors	Study type	Setting	Year of publication	Results
Towfighi et al.	Guideline	American guidelines	2017	Brief psychological interventions may be useful in PSD treatment
Scottish Intercollegiate Guidelines Network	Guideline	Scottish guidelines	2010	Antidepressants were first-line PSD treatment and talking based therapy was second-line
Wang et al.	Meta-analysis	British and Chinese databases searched	2018	Both CBT alone and CBT combined with antidepressants were significantly more effective than placebo or antidepressants alone
Kneebone et al.	Narrative review	British review of international literature	2000	RCTs investigating CBT or other forms of psychotherapy found CBT was either not effective or showed "borderline statistical significance"
Robinson et al.	Narrative review	American review of international literature	2016	CBT alone was found to be ineffective
Hadidi et al.	Narrative review	American review of international literature	2017	CBT alone was found to be ineffective. A combination of antidepressants and problem based therapy was better than antidepressants alone
Gao et al.	Randomised controlled trial	Chinese RCT conducted in the outpatient setting	2017	Antidepressants were effective for PSD when it develops 6-9 months post-stroke, and CBT was effective >9 months post-stroke

Table 3

Results of the Wang et al meta-analysis (18)

Subgroup	Standardized Mean Difference [95% confidence intervals]	P-value	Number of RCTs
CBT alone	-0.76 [-1.22 to -0.29]	0.001	7
CBT with antidepressant	-0.95 [-1.20 to –0.71]	<0.0001	14
CBT with some participants on antidepressants	-0.20 [-0.53 to 0.13]	Not given but authors state there was no significant difference	2
Overall	-0.83 [-1.05 to -0.60]	<0.001	23

antidepressants, C = placebo or the same antidepressant as with the CBT group, O = efficacy) and comprehensive search strategy including English and Chinese databases. (18) The search was carried out by three independent investigators. The inclusion of non-English language papers from the Chinese databases reduces the risk of publication bias, as demonstrated by the Egger's regression test that found no statistically significant evidence of publication bias for the overall effect of CBT on PSD.

The search identified 23 applicable RCTs, which were then divided into the three subgroups shown in Table 3. They included a total sample size of 1,972 participants, with 21 of the studies (sample size 1,829) carried out on a Chinese population.

The quality of the studies was assessed using both the Cochrane Risk of Bias Tool and the Jadad scale. A study with a Jadad score of 3 or more was said to be of high quality; less than 3 indicated low quality. Only nine of the studies were found to be of high quality according to this scale. Reasons for the low quality of studies were secondary to the methods of randomisation being unclear in 15 studies, and poor reporting of compliance rates for the intervention. The authors also used I2 statistics to measure heterogeneity, with an I2 of 82% indicating significant heterogeneity between the studies. Although the results were statistically significant, the heterogeneity could mean that it was inappropriate to combine the different studies' results, as the different studies used varied methods and sample sizes. This was a common theme in the literature found.

Narrative Reviews

Kneebone et al, (21) Robinson et al, (22) and Hadidi et al (23) carried out literature reviews to collate information on psychological interventions in PSD. Most of the research included in these papers were RCTs, the highest quality primary research for interventions, according to the hierarchy of evidence. (21, 30) Despite RCTs being included, meta-analysis was not possible, due to the heterogeneity of the studies. For example, many different types of psychological interventions were assessed in each review, such as ecosystem-focussed therapy or problem-solving therapy. Therefore, despite these reviews containing high-quality primary research, the Wang et al meta-analysis is the highest quality evidence included in this evidence review. (18, 30)

Kneebone et al concluded that although CBT represented a promising area of future research, more investigations and high-quality RCTs were needed to fully establish its effect on PSD. (21) More recent reviews from Robinson et al and Hadidi et al concluded that CBT alone was ineffective. (22, 23) However, Hadidi et al found that a combination of problem-solving therapy (falling under this review's definition of CBT) and antidepressants was more likely to be effective than antidepressants alone. (23) These three reviews did not have specific PICO frameworks or focused questions, (21-23) but they all had clear aims: to gather all relevant information on psychological interventions (Kneebone et al) (21) and "nonpharmacological interventions" (Hadidi et al). (23) The purpose of the Robinson et al paper was to investigate antidepressants. (22) However due to their non-specific search terms, including "post stroke depression AND trial", (22) it also included studies on psychological interventions, which were discussed by the authors, hence its inclusion in this review. All reviews searched medical databases such as MEDLINE and psychology databases such as PsycINFO. They carried out reference searches and Hadidi et al reported their appropriate inclusion and exclusion criteria, for example, qualitative studies were excluded, and the patients included were required to have depressive symptoms. (23. However, there was no universal scale used by Hadidi et al to assess these symptoms. (23)

All three reviews included papers relevant to their aim. Kneebone et al included case studies and uncontrolled trials, (21) making it more likely that results could have been affected by confounders and bias, such as selection bias. The inclusion of such studies was recognised as a limitation by the authors. However, as this review was published in 2000 when there was less information available regarding the mental health of stroke survivors, these preliminary papers provide a useful introduction to this topic.

None of the reviews demonstrated a consistent appraisal of the quality of papers included, and full information on some of the studies, such as setting and the demographics of the population, was not available, therefore it was difficult to fully assess the quality of the paper.

The quality of case studies on CBT, featured in Kneebone et al. (21) were not evaluated and it was simply stated they resulted in an improvement in mood. The authors assessed the quality of the uncontrolled studies and concluded they were poor quality preliminary studies due to the lack of a control group. The quality of the few RCTs included was not formally assessed, there was no detail of randomisation or blinding given and most had small sample sizes. The RCT results showed that CBT or other forms of psychotherapy were not effective or demonstrated "borderline statistical significance", (21) however the authors emphasised the poor quality of these papers and therefore concluded that more RCTs were needed.

Incomplete details were given on the RCTs featured in Robinson et al. (22) but it was made clear that RCTs evaluating problem-solving therapy had small sample sizes and high dropout rates, increasing the chance of confounding factors and attrition bias affecting results. It was not stated if intention-to-treat analysis was used. Out of these three reviews, Hadidi et al. had considered most thoroughly the quality of papers included. (23) Although there was limited information about how this was carried out, the authors did discuss how the rigour of the studies varied, considering sample size (ranging from 14-411), time after stroke (48 hours to 5 years) and differences in baseline characteristics (for example variation in depression scores between groups). Hadidi et al., (23) similarly to the other reviews, did not present results as a meta-analysis. This was not justified by the authors, but as mentioned previously, was likely due to the heterogeneity between studies. Only one RCT explicitly stating CBT as the intervention was included. (31) The authors recognised the limitations of using this study, for example the CBT practitioner was not fully trained, and possible cognitive impairment was not considered by the RCT researchers.

Considering all three narrative reviews, it is difficult to evaluate whether the results are applicable to the local population, due to the poor quality and lack of information on the participant characteristics. All three reviews concluded that CBT is a promising area of research.

Primary Study (RCT)

One primary study, an RCT by Gao et al., (17) was found and appraised using the CASP RCT checklist. (16) As stated previously, this is the only relevant RCT that was found in the literature search that directly compared CBT alone to antidepressants alone, thus making it the most suitable study found for the review question. For this reason, it was covered in this review despite already being included in the Wang et al. meta-analysis (18). RCTs are not considered as robust as "filtered information" (30) such as meta-analyses and guidelines, therefore it is important to reflect on these results in combination with the literature appraised above. Gao et al. examined the effectiveness of CBT treatment stratified by time taken for PSD to develop after stroke. (17) This was not quantified in the Wang et al. meta-analysis. (18)

Gao et al. took patient groups at discharge and at 3, 6 and 9 months post-discharge following a stroke, and then split these groups into A, B and C as follows: Group A had placebo tablets and placebo psychological intervention, Group B had active citalopram antidepressant tablets and placebo psychological intervention, and Group C had placebo tablets and active CBT. (17)

It was a single-blind trial - the patients were blinded to the treatment they were receiving. They then followed these patients up for 3 months and used the Hamilton Depression Rating Scale (HAM-D) and the Bech-Rafaelsen Melancholia Scale (MES) to measure depressive symptoms.

The results of the study, when time stratification was not considered, showed no significant differences in the HAM-D scores between groups A, B and C. The only significant difference in MES scores was a lower score (fewer depressive symptoms) in Group B compared to Group A ($p=0.02$). This suggests antidepressants could be more effective than placebo tablets, whereas CBT is not significantly different to placebo psychological intervention at reducing depressive symptoms. These results contrast with Wang et al., (18) which showed that CBT alone was significantly more effective compared to placebo. It could be said that the results from Wang et al. are more valid as systematic reviews are higher in the hierarchy of evidence than RCTs. (18, 30) Furthermore, Gao et al. was not significantly highly weighted within the meta-analysis. (17, 18) However, Gao et al. was only one of two studies included in the meta-analysis with the highest possible Jadad score of 5, (17) and therefore is deemed to be of higher quality than the other RCTs in Wang et al. (18). This could mean that the meta-analysis results may be produced from RCTs with a higher risk of bias, and the Gao et al. results are more likely to be reliable.

Importantly for this review question, Gao et al. demonstrated that, without stratification by time, there was no significant difference in the depression rating scores between the groups receiving CBT alone (Group C) and the antidepressant alone (Group B). (17) However, when time stratification was considered, there was a different picture of results. At 6 months post-discharge, Group B had significantly lower HAM-D/MES scores when compared to Group A, and Group C showed no significant decrease in score in comparison to Group A. This could suggest that antidepressants (Group B) are more effective at reducing depressive symptoms than CBT (Group C) when treatment is initiated 6 months post-discharge. Furthermore, at 9 months post-discharge, Group C showed significantly lower MES scores compared to Group A, and Group B showed no significant decrease in comparison to Group A. These results demonstrate that CBT (Group C) may be more effective than antidepressants (Group B) when these symptoms develop later, when CBT treatment is initiated at 9 months post-discharge.

Gao et al. had a clearly focused PICO, appropriate randomisation with all groups having similar baseline characteristics and detailed follow-up of patients and drop-outs, with reasons provided. (17) However, some limitations included that there was no mention of whether participants were analysed with an intention-to-treat analysis. If not, this could lead to attrition bias and selection bias, due to loss of randomisation. Also, sample sizes were small, especially when split into time-stratified groups, therefore reducing the power of detecting significant differences between the subgroups.

DISCUSSION

The aim of this review was to assess the effectiveness of CBT compared to the effectiveness of antidepressants for the treatment of adults with PSD. The main findings suggest a mixture of results regarding the effectiveness of CBT, however there is evidence that this therapy could have a larger role in PSD treatment than it currently does. The available evidence varies considerably in methodological quality and so further research into the treatment for PSD is needed.

It should be considered that one of the reasons for lack of research into the treatment of PSD is a lack of understanding of the development of PSD. (8) The question remains over whether PSD results from the direct physical effects of stroke on the brain, a psychological reaction to the patient's own sudden and marked functional decline, or, perhaps more likely, a combination of both causes. Should this important question be answered, our understanding of PSD will improve and therefore this may lead to more research into PSD treatment. For example, it is not yet understood why CBT appears to be more effective in some studies than antidepressants. A theory for this could be that the possible biological mechanism of PSD does not align with the mechanism of action of antidepressants. However, we will not know if this is the case until future research on the development of PSD becomes available.

Furthermore, considering evidence around treating depression thought to be a consequence of other chronic illnesses may enable us to identify further treatment options to explore.

However, the possible direct biological mechanism of PSD means that a direct comparison to depression in other chronic illnesses may be unhelpful. This further emphasises the need for research into PSD development.

It has been identified that if a patient was to be given CBT as a PSD treatment, then this CBT should be individually adapted to suit different patient needs. (8) This is because PSD affects individuals differently such as effects on motivation and sleep, and a universal CBT protocol would not consider these differences. Qualitative research could help to understand the impact these aspects have on patients as individuals, where current scoring systems may fail to grasp the range of emotions patients feel in such a hard time.

This review has highlighted that there are prominent gaps in the research of treating PSD. One possible reason for this lack research could be societal attitudes towards mental ill-health. As mental illness is not defined by physical attributes, it is said that society in general finds it harder to accept that mental health is as important as physical health. (32) A 2011 NHS report about attitudes to mental illness found that 23% of the participants did not agree that mental illness was akin to physical illness. (32) These beliefs are reflected in funding differences between physical and mental illness. (33) This could explain the lack of research on the topic of PSD treatment, particular in the context of the sometimes-life-changing physical difficulties stroke can cause.

To address gaps in the knowledge of PSD, future RCTs should be conducted with a culturally diverse study population, mirroring that of the UK. This is of particular importance because most current evidence on this topic area was conducted on mainly Chinese populations. (17, 18) CBT as a treatment focuses on innate beliefs meaning participants from different cultures with different attitudes towards mental health are likely to respond differently to it. Hence it may not be appropriate for such studies to form the basis of UK national treatment guidelines. Understanding the issue within the context of the UK population to form relevant guidelines could provide public health benefit, given that the disability burden post-stroke is so high in the UK.

Changes in the methodology of current studies could help produce results more applicable to medical practice. High-quality RCTs directly comparing antidepressants to individually tailored CBT would be particularly useful for compiling new NICE guidelines. Continuing to research the effect of treatments started at different time periods post-stroke would be more reflective of clinical practice as patients are likely to present with depression at various times after their stroke. The emergence of such research would allow future clinicians to fully evaluate whether CBT is a worthwhile and possibly more effective treatment for PSD than antidepressants for certain patients.

Furthermore, changes in methodology could address challenges in conducting RCTs in this population group. Patients struggling with the most severe effects of stroke and post-stroke depression may be less likely to consent to participating in a study. The potential participation bias resulting from this could be reduced in future studies by controlling for severity of stroke and expected rehabilitation time. Attrition rates in those most affected by their stroke may also be higher and this is something to explore in the future, to ensure validity of results. In terms of impact on current practice, despite this review finding that there is not enough evidence for making definitive clinical guidelines, it should allow clinicians to feel more confident in suggesting CBT as a treatment option for PSD if they feel it is right for their patient. This may encourage more doctor-patient discussion and allow patients to be more involved in treatment decisions.

Beyond the boundaries of this review lies the question of how the availability, cost and patient acceptability of antidepressants and CBT influence a clinician's treatment decision, consequently affecting a patient's overall functional recovery from PSD. This influence on recovery has implications on the financial aspect of managing PSD. Improvements in both the psychological and physical effects of PSD are likely to decrease burden of care, which is usually high in post-stroke patients, allowing NHS resources to be used more efficiently.

CONCLUSION

To conclude, the treatment of PSD is an important yet under-funded area of research despite being a common consequence of a stroke. The findings of this review suggest the evidence supporting the use of CBT versus antidepressants for the treatment of PSD is inconclusive, which may in part be due to low levels of methodological quality. In practice, a combination of pharmacological and CBT treatment is likely to be most effective and this warrants further research. Future high-quality RCTs that include culturally diverse patient populations and clinically relevant interventions, comparisons and outcomes are needed to address this research question.

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