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Citation for published version:

Hawkins, E, Hawkins, R, Dennis, M, Williams, J & Lawrie, SM 2019, 'Animal-assisted therapy, including animal-assisted activities and resident animals, for improving quality of life in people with stroke', *Cochrane Library*, no. 4, CD013314. <https://doi.org/10.1002/14651858.CD013314>

Digital Object Identifier (DOI):

[10.1002/14651858.CD013314](https://doi.org/10.1002/14651858.CD013314)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Cochrane Library

Publisher Rights Statement:

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Animal-assisted therapy, including animal-assisted activities and resident animals, for improving quality of life in people with stroke

Protocol information

Review type: Intervention

Review number: 02320001

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Citation example: Hawkins E, Hawkins R, Dennis M, Williams J, Lawrie SM. Animal-assisted therapy, including animal-assisted activities and resident animals, for improving quality of life in people with stroke. Cochrane Database of Systematic Reviews, Issue . Art. No.: . DOI: .

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Dates

Assessed as Up-to-date: Not provided

Date of Search: Not provided

Next Stage Expected: 1 April 2020

Protocol First Published: Not specified

Review First Published: Not specified

Last Citation Issue: Not specified

What's new

Date	Event	Description
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History

Date	Event	Description
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Abstract

Background

Objectives

Search methods

Selection criteria

Data collection and analysis

Main results

Authors' conclusions

Plain language summary

[Summary title]

[Summary text]

Background

Description of the condition

Stroke is the third-leading cause of disability worldwide ([Feigin 2017](#)), and has been estimated to cost the UK GBP

8900 million per year ([Saka 2009](#)). It is estimated that individuals who have had a stroke 13% to 16% more likely to suffer a secondary stroke within the first year and 4% more likely to suffer a recurring stroke each following year ([Bailey 2018](#)).

The risk of secondary stroke can be reduced by targeting a number of risk factors, including modifiable lifestyle risk factors, such as increased physical activity and exercise, [Billinger 2014](#), and reductions in blood pressure and weight ([Meschia 2014](#)). These are examples of modifiable risk factors that could be targeted through animal-assisted therapy (AAT) to reduce the risk of secondary stroke. Some risk factors for secondary stroke highlighted in the guidelines from the Royal College of Physicians include blood pressure, atrial fibrillation, and lifestyle measures (e.g. physical activity, nutrition). Animal-assisted therapy has been associated with decreases in systolic blood pressure in hospitalised children ([Tsai 2010](#)), lower systolic pulmonary artery pressure, and lower neurohormone levels in people with heart failure ([Cole 2007](#)). Animal-assisted therapy could further be useful for stroke rehabilitation and adjustment to life poststroke.

Stroke guidelines from the Royal College of Physicians highlight several key areas of rehabilitation following stroke, including: activities of daily living, cognition (e.g. attention and concentration, executive function, memory), communication (e.g. aphasia), hydration and nutrition, mental capacity, mobility (e.g. weakness and ataxia, balance, falls, walking), mood and well-being (e.g. anxiety, depression), and spasticity ([Intercollegiate Stroke Working Party 2016](#)). These areas have been targeted by animal-assisted therapies for a number of conditions. Hippotherapy has been shown to improve performance of activities of daily living in children with movement disorders ([Silkwood-Sherer 2012](#)). Equine-assisted therapies that promote physical activity have been shown to improve gross motor function, energy expenditure, gait, and balance in children with cerebral palsy ([Kwon 2011](#); [McGibbon 1998](#)); improve strength and balance in adolescents with intellectual disabilities ([Giagazoglou 2012](#)); reduce spasticity of the lower body in people with spinal cord injury ([Lechner 2003](#)); and improve balance in individuals with multiple sclerosis ([Silkwood-Sherer 2007](#)). Other animal-assisted therapies have been shown to reduce anxiety in people with schizophrenia ([Berget 2011](#)); improve non-verbal communication in people with schizophrenia ([Kovács 2006](#)); reduce depression in outpatients with depression ([Antonioli 2005](#)); and increase motor activity and nutritional intake in people with Alzheimer's disease ([Edwards 2002](#); [Mossello 2011](#)).

The Australian Clinical Guidelines for Stroke Management define rehabilitation as "a holistic process ... with the aim of maximising the participation of the person with stroke in the community". These guidelines state that interventions should focus on impairment, activity, and levels of participation ([Stroke Foundation 2017](#)). Many outcomes that have shown improvement following animal-assisted therapies relate to participation of individuals in the community, for example increased socialisation behaviours in people with Alzheimer's disease and residents in long-term care facilities ([Batson 1998](#); [Bernstein 2000](#)). Equine-assisted therapy is associated with increased autonomy and social integration for adults with intellectual disability ([Borioni 2012](#)). Animal-assisted therapy has also been shown to reduce loneliness in residents in long-term care facilities ([Banks 2002](#)). These are also factors that could improve adjustment to life poststroke.

According to the American Heart Association (AHA) Guidelines for Adult Stroke Rehabilitation and Recovery ([Winstein 2016](#)), "rehabilitation services are the primary mechanism by which functional recovery and the achievement of independence are promoted in patients with acute stroke". Rehabilitation services are delivered by multidisciplinary teams. For example, skilled nursing services are needed to manage dependence for activities of daily living (ADLs); physicians are needed to manage hypertension or complex rehabilitation issues such as spasticity; and multiple therapeutic interventions are needed to manage motor/sensory deficits, cognitive deficits, and communication deficits. Animal-assisted therapy may be a good candidate to form part of multidisciplinary teams for the same reasons provided above, for example improvements in ADLs, communication, cognition, and spasticity.

The outcomes of rehabilitation are associated with the level of engagement and motivation of the patient ([Langhorne 2011](#)). Animal-assisted therapy could improve motivation and has been shown to improve attendance and participation in treatment ([Banks 2002](#)), and improve adherence to therapy sessions ([Calvo 2016](#)).

A number of problems have been identified in poststroke populations, including social isolation, attachments, and stress, which may negatively impact on poststroke outcomes but could be improved with animal-assisted therapies. Social isolation has been associated with poorer outcomes poststroke ([Boden-Albala 2005](#)), the presence and severity of depression ([Morris 1991](#)), and lower levels of life satisfaction ([Boosman 2011](#)). Improvements have been found in social functioning and social interactions following animal-assisted therapy ([Barak 2001](#); [Richeson 2003](#)). Another important area of stroke recovery is the impact of stress on recovery. Increased cortisol levels following stroke have been associated with poorer outcomes related to recovery, such as lower Barthel Index scores ([Dávalos 1996](#)), poorer functional outcomes ([Olsson 1990](#)), longer hospital stays ([Weant 2008](#)), and higher mortality ([Anne 2007](#)). It is important that stress is managed adequately in poststroke patients to aid recovery. Animal-assisted interventions have a buffering effect on stress ([Barker 2010](#)), and studies have shown that animal-assisted therapies reduce pulse in psychiatric patients, [Nepps 2014](#), and reduce salivary cortisol levels in people with schizophrenia ([Calvo 2016](#)). Animal-assisted therapies could be a promising treatment to improve poststroke outcomes, particularly those related to social isolation and stress. It is also important that, in the long term, people with stroke be integrated back into the community (social integration and participation), given that community engagement is associated with improvements in quality of life ([Tse 2017](#)).

Description of the intervention

Animal-assisted therapy is part of the wider animal-assisted intervention umbrella, which also includes animal-assisted

activities and resident animals. The American Veterinary Medical Association (AVMA) defines animal-assisted therapy as "a goal-directed intervention in which an animal ... is an integral part of the treatment process ... is delivered and/or directed by health or human service providers ... designed to promote improvement in human physical, social, emotional, or cognitive function" ([AVMA 2018](#)). Animal-assisted activities "provide opportunities for motivation, education, or recreation to enhance quality of life" and are provided by "specially trained professionals, paraprofessionals, or volunteers ... with animals that meet specific criteria". Resident animals live in a facility and "may be formally included in facility activity and therapy schedules after proper screening and training. Others may participate in spontaneous or planned interactions with facility residents and staff". Animal-assisted therapy is a more structured intervention than animal-assisted activities and resident animals, with a greater focus on improvements in functioning, which are documented and evaluated throughout the process. While we will look at all of the described interventions for the sake of inclusivity, due to the sparse nature of this area of research, we will use the term 'animal-assisted therapy' throughout the review for ease and simplification of terms.

The involvement of animals in therapeutic settings was first popularised in the 1960s ([Levinson 1997](#)), and has since been incorporated into the treatment of a number of different mental and physical illnesses, including depression, schizophrenia, alcohol and drug abuse, multiple sclerosis, and dementia ([Charry-Sánchez 2018](#); [Kamioka 2014](#)). Animal-assisted interventions are typically used as an adjunct to standard care as opposed to a stand-alone treatment option. A wide range of animals have been involved in therapy including, but not limited to, dogs, cats, horses, farm animals, birds, hamsters, fish, and dolphins. Focuses of therapy sessions can include a wide selection of activities, such as developing emotional bonds with animals, walking animals, group interactions, or simply the presence of an animal.

How the intervention might work

Several theories have been put forward to explain how interactions with animals may impact positively on human health ([Serpell 2017](#)). One such theory is the attachment, bonding, and social support theory, whereby animals serve as attachment figures or provide social support. Oxytocin plays an important role in social bonding, attachment, and regulating social interactions, and may play an important role in buffering against stress ([Heinrichs 2003](#)). Interactions with animals have been shown to increase levels of oxytocin in humans ([Odendaal 2003](#)), particularly when interactions are initiated by a dog's gaze ([Nagasawa 2009](#)). Animals, or attachment to an animal, can also improve social support by providing a source of comfort and act as a catalyst for social interactions with others ([McNicholas 2006](#)). It is well known that social support influences mortality risk, with higher levels of social support being associated with lower mortality risk ([Holt-Lunstad 2010](#)). Social support can also protect against illness and accelerate recovery from illness, including stroke ([Cobb 1976](#); [Glass 1992](#)). Incorporating animals into the treatment process could serve as a buffer against stress for stroke patients or those at risk of stroke and improve social support. The presence of a dog alone can reduce subjective experiences of stress and anxiety ([Lass-Hennemann 2014](#)). Petting a dog may also have positive health benefits, for example improved immune system functioning as demonstrated in increases in secretory immunoglobulin A ([Charnetski 2004](#)).

Animal-assisted therapy may also work by increasing the motivation of patients to participate in therapy sessions ([Holcomb 1989](#)), and provide greater motivation within therapy sessions. For example, animal-assisted therapy may help individuals with aphasia by providing greater motivation to communicate ([Macauley 2006](#)). Macauley noted that patients had a greater tendency to initiate communication towards the dog rather than the speech-language pathologist. Patients also spoke with less effort towards the dog than the clinician. Motivation may also play a role in mobility-related outcomes. Animal-assisted therapy with a dog may help motivate, and provide an incentive for, individuals to work on gait training and their ability to walk. For example, one study found that incorporating a dog into a therapeutic setting with obese children increased physical behaviour and sportive activity and led to more time spent walking with dog ([Wohlfarth 2013](#)). Hippotherapy may work for mobility-related problems, particularly gait, and spasticity as the rider responds to the reciprocal movement of the horse. Hippotherapy has been used for a variety of neuromuscular disorders and utilises the movement of the horse to promote a dissociation between the pelvis and trunk, which promotes balance ([Heine 1997](#)). The gait of horses and humans are also similar, thus riding a horse at a walking speed provides stimulation and motor and sensory inputs similar to that generated by human walking ([Uchiyama 2011](#)).

Why it is important to do this review

The use of animal-assisted therapy for improving outcomes for clinical populations has grown rapidly but evidence for its effectiveness is severely lacking. It is important at this stage to synthesise the evidence to determine the effectiveness of animal-assisted therapy for stroke, which has yet to be systematically reviewed. The results from which could greatly help in determining potential impacts to practice and policy, development of animal-assisted programmes for people with stroke, as well as identifying future directions for research.

Objectives

To assess the effects of animal-assisted therapy for improving quality of life for people with stroke. A secondary objective is to assess outcomes relating to the feasibility and potential barriers of providing animal-assisted therapy for stroke patients, including recruitment, cost, adherence, and attrition.

Methods

Criteria for considering studies for this review

Types of studies

We will only include randomised controlled trials and exclude quasi-randomised trials.

Types of participants

We will include all participants that present with any clinical diagnosis of stroke regardless of age, sex, setting, or severity of illness. In cases where studies have included participants of mixed diagnoses, we will only include these if the data have been presented separately for each diagnosis or where such data are obtainable from the study authors.

Types of interventions

We will include trials comparing animal-assisted therapy, or other animal-assisted interventions (animal-assisted activities and resident animals), compared to standard care alone, regardless of length of treatment, place of treatment, or type of animal used for therapy. We will also include comparisons between animal-assisted therapy, or other animal-assisted intervention, and active control groups.

Types of outcome measures

Primary outcomes

- Quality of life and well-being at the end of the intervention (short term) and at the end of follow-up (long term): any relevant scale, such as Quality of Life Scale (QOLS), Stroke Specific Quality of Life Scale (SS-QOL), 36-item Short Form Health Survey Questionnaire (SF-36), or EuroQoL Five Dimensions Questionnaire (EQ-5D). We have selected quality of life as the primary outcome due to the multidimensional nature of the outcome, and the meaningfulness to stroke patients of the outcome measured, particularly when measured using the SS-QOL ([Teixeira-Salmela 2009](#)). We also feel that quality of life is a good target for animal-assisted therapies.

Secondary outcomes

- Activities of daily living (ADLs): any relevant scale, such as modified Rankin Scale, Barthel Index, Frenchay Activities Index, Functional Independence Measure, Rivermead ADL Assessment.
- Physical activity: any relevant scale or measure, such as step count, activity monitor, Bouchard Physical Activity Questionnaire, International Physical Activity Questionnaire (IPAQ), the Physical Activity Scale for Individuals with Physical Disabilities (PASIPD), physical activity monitors.
- Social functioning: any relevant scale, such as Index of Social Engagement (ISE), Social Functioning Scale (SFS), Assessment of Interpersonal Problem Solving Skills (AIPSS), Living Skills Profile (LSP), behavioural observation of social functioning.
- Blood pressure.
- Stress: any relevant scale or measure, such as salivary or hair cortisol levels, Perceived Stress Scale (PSS).
- Adverse events: e.g. phobias, allergies, injury, infection, any other adverse effects.
- Death or dependency at the end of follow-up: we will define dependency as a Barthel Index score of less than 60 or a modified Rankin Score of more than 3 ([Sulter 1999](#)).
- Recurrent stroke at any time during follow-up.
- Aphasia: any relevant scale, such as Boston Diagnostic Aphasia Examination (BDAE), Western Aphasia Battery (WAB), Amsterdam-Nijmegen Everyday Language Test (ANELT).
- Mood: any relevant scale, such as Hospital Anxiety and Depression Scale (HADS), General Health Questionnaire 12 Item (GHQ-12), Patient Health Questionnaire 9 Item (PHQ-9).
- Cost: costs involved with animal-assisted therapy.
- Adherence to animal-assisted therapy.

Search methods for identification of studies

See the 'Specialised register' information at the [Cochrane Stroke Group's](#) website. We will search for trials in all languages and arrange for the translation of relevant articles where necessary.

Electronic searches

We will search the Cochrane Stroke Group trials register and the following electronic databases:

- Cochrane Central Register of Controlled Trials (CENTRAL; latest issue) in the Cochrane Library;
- MEDLINE (Ovid) (from 1948) ([Appendix 1](#));
- Embase (Ovid) (from 1980);
- PsycINFO (Ovid) (from 1806);
- CINAHL (EBSCO) (Cumulative Index to Nursing and Allied Health Literature; from 1937);
- CAB Abstracts (Ovid) (from 1910);
- Science Citation Index Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI) Conference Proceedings Citation Index - Science (CPCI-S), Conference Proceedings Citation Index - Social Science & Humanities (CPCI-SSH) (Web of Science) (from 1900);
- Applied Social Sciences Index & Abstracts (ASSIA) (from 1987);
- ProQuest Dissertations & Theses (from 1972);
- HABRI Central (Resources for the Study of the Human-Animal Bond) ([habricentral.org](#)).

We developed the MEDLINE search strategy ([Appendix 1](#)) with the help of the Cochrane Stroke Group Information Specialist and will adapt it for the other databases.

We will also search the following ongoing trials registers:

- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictcp/en/);
- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov).

Searching other resources

We will screen the reference lists of included studies to identify additional studies for inclusion in the review. We will contact first authors of the included studies for information regarding unpublished trials. We will conduct citation tracking using both Science Citation Index Cited Reference Search and Google Scholar.

Data collection and analysis

Selection of studies

Two review authors (EH, RH) will independently screen titles and abstracts of the references obtained as a result of the search, excluding obviously irrelevant reports. We will retrieve the full-text articles for the remaining references, and two review authors (EH, RH) will independently screen the full-text articles and identify studies for inclusion, and identify and record reasons for exclusion of the ineligible studies. Any disagreements will be resolved through discussion or by consulting the other review authors if necessary. We will collate multiple reports of the same study so that each study, not each reference, is the unit of interest in the review. We will record the selection process and complete a PRISMA flow diagram.

Data extraction and management

Two review authors (EH, RH) will independently extract data from the included studies using a data extraction form. Any disagreements will be resolved through discussion or by consulting another review author (SL). We will first pilot the data extraction form on a small selection of studies before conducting the full data extraction. We will contact study authors in cases where data are missing from study reports. In cases where trials have multiple reports, we will collate data into one data extraction form.

We will extract data for the following: sample size, gender, age, type of intervention, control condition, duration of treatment, length and frequency of treatment, animal(s) used, outcomes and outcome measures, and key findings. We will extract data for all outcomes and outcome measures reported in trials regardless of whether the outcomes have been prespecified in this review. We will only include the primary and secondary outcomes of interest in this review in meta-analysis.

Assessment of risk of bias in included studies

Two review authors (EH, RH) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Any disagreements will be resolved by discussion or by involving another review author (SL). We will assess risk of bias according to the following domains.

- Random sequence generation (selection bias).
- Allocation concealment (selection bias).
- Blinding of participants and personnel (performance bias).
- Blinding of outcome assessment (detection bias).
- Incomplete outcome data (attrition bias).
- Selective outcome reporting (reporting bias).
- Other bias.

We will grade the risk of bias for each domain as high, low, or unclear and provide information from the study report together with a justification for our judgement in the 'Risk of bias' tables.

Measures of treatment effect

For dichotomous outcomes, we will calculate a standard estimation of the risk ratio (RR) with 95% confidence intervals (CIs).

For continuous outcomes, we will calculate mean difference (MD) with 95% CI. In cases where different scales are used to measure the same outcome, we will calculate standardised mean difference (SMD) with 95% CI.

Unit of analysis issues

Cluster trials

We do not anticipate identifying any cluster-randomised controlled trials. However, if we identify any such studies, we will handle the data according to the guidelines presented in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Cross-over trials

We will only use data from the first phase of cross-over studies to avoid the risk of carry-over effects.

Studies with multiple treatment groups

Where a study includes multiple intervention groups, we will combine groups to create a single pairwise comparison.

Repeated observations

Where a study includes repeated observations, we will consult Section 9.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Dealing with missing data

We will contact study authors to request missing data. In cases where we are unable to obtain missing data, we will only include the study after conducting a sensitivity analysis to assess the impact of including or excluding such studies. We will not impute missing data. We will present study-level data so that missing and unclear data are clearly indicated and to make available any unpublished data acquired from investigators.

Assessment of heterogeneity

We will use the I^2 statistic to measure heterogeneity among the trials in each analysis. We will consider an I^2 statistic above 50% as indicative of substantial heterogeneity.

Assessment of reporting biases

We will use funnel plots to investigate reporting biases if we identify 10 or more studies, as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)).

Data synthesis

Where we consider studies to be sufficiently similar, we will conduct a meta-analysis by pooling the appropriate data using Review Manager 5 ([RevMan 2014](#)).

If we are confident that trials are estimating the same underlying treatment effect, we will use a fixed-effect meta-analysis. If clinical heterogeneity is sufficient to expect that underlying treatment effects differ between trials, we will use a random-effects meta-analysis. If there is substantial clinical, methodological, or statistical heterogeneity across trials that prevents the pooling of data, we will use a narrative approach to data synthesis.

We will address our secondary objective using narrative summaries.

GRADE and 'Summary of findings' table

We will create a 'Summary of findings' table using the following outcomes: quality of life (QoL), activities of daily living (ADLs), physical activity, social functioning, blood pressure, cortisol, adverse events ([Table 1](#)). We will use the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness, and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data to the meta-analyses for the prespecified outcomes ([Atkins 2004](#)). We will use methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)), employing GRADEpro GDT software ([GRADEpro GDT 2015](#)). We will justify all decisions to downgrade the quality of studies using footnotes, and will make comments to aid the reader's understanding of the review where necessary.

Subgroup analysis and investigation of heterogeneity

We will conduct the following subgroup analyses.

- Dose of intervention (e.g. < 50 hours, 50 to 100 hours, 101 to 200 hours, and > 200 hours).
- Type of intervention used (e.g. animal-assisted therapy, animal-assisted activity, resident animal(s)).
- Type of animal involved in the intervention (e.g. canine versus feline, canine versus equine, feline versus equine).
- Severity of stroke.
- Setting of intervention (e.g. home setting versus hospital setting).

Sensitivity analysis

We will repeat analyses after removing studies judged as having a high risk of bias based on the results of the 'Risk of bias' assessment. Should we identify studies with missing data that are unobtainable, we will repeat analyses excluding these studies to determine their impact on the primary analyses. We will also repeat analyses including cluster-randomised controlled trials, should these be identified.

Results

Description of studies

Results of the search

Included studies

Excluded studies

Risk of bias in included studies

Allocation (selection bias)

Blinding (performance bias and detection bias)

Incomplete outcome data (attrition bias)

Selective reporting (reporting bias)

Other potential sources of bias

Effects of interventions

Discussion

Summary of main results

Overall completeness and applicability of evidence

Quality of the evidence

Potential biases in the review process

Agreements and disagreements with other studies or reviews

Authors' conclusions

Implications for practice

Implications for research

Acknowledgements

Contributions of authors

EH wrote the protocol with input from all authors.

All authors provided comments on drafts and approved the final draft of the protocol.

Declarations of interest

Emma Hawkins: none known

Roxanne Hawkins: none known

Martin Dennis: none known

Joanne Williams: none known

Stephen M Lawrie: none known

Differences between protocol and review

Published notes

Characteristics of studies

Characteristics of included studies

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of findings tables

Additional tables

1 Template 'Summary of findings' table

Animal-assisted therapy for stroke							
Participants or population: people with stroke							
Setting: any setting							
Intervention: animal-assisted therapy, or other animal-assisted intervention, such as animal-assisted activity or resident animal(s)							
Comparisons: standard care alone or active control group: animal-assisted therapy versus standard care alone, animal-assisted therapy versus active control group, animal-assisted activity versus standard care alone, animal-assisted activity versus active control group, resident animal(s) versus standard care alone, resident animal(s) versus active control group, any other animal-assisted intervention versus standard care alone, any other animal-assisted intervention versus active control group							
Outcomes	Anticipated absolute effects (95% CI)			Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Standard care alone	Active control	Animal-assisted therapy (or other animal-assisted intervention)				
Quality of life (QoL)							
Activities of daily living (ADLs)							
Physical activity							
Social functioning							
Blood pressure							
Cortisol							
Adverse events							
CI: confidence interval							
GRADE Working Group grades of evidence							
High quality: Further research is very unlikely to change our confidence in the estimate of effect.							
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.							
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.							
Very low quality: We are very uncertain about the estimate.							

Footnotes

References to studies

Included studies

Excluded studies

Studies awaiting classification

Ongoing studies

Other references

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Other published versions of this review

Classification pending references

Data and analyses

Figures

Sources of support

Internal sources

- University of Edinburgh, UK
Emma Hawkins is funded by a PhD studentship (2016 to 2022) from the Division of Psychiatry, University of Edinburgh.

External sources

- No sources of support provided

Feedback

Appendices

1 MEDLINE search strategy

1. exp Animal Assisted Therapy/
2. bonding, human-pet/
3. dogs/ or cats/ or horses/
4. ((pet or animal or dog\$ or canine or horse\$ or equine) adj3 (assist\$ or related or \$) adj3 (activit\$ or therap\$ or intervention\$)).tw.
5. ((support or companion or therap\$) adj5 (cat\$ or animal\$ or dog\$ or reptil\$ or bird)).tw.
6. (hippotherapy or horseback).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. cerebrovascular disorders/ or basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp cerebral small vessel diseases/ or exp intracranial arterial diseases/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/ or stroke, lacunar/ or vasospasm, intracranial/ or vertebral artery dissection/
9. (stroke\$ or poststroke or apoplex\$ or cerebral vasc\$ or brain vasc\$ or cerebrovasc\$ or cva\$ or SAH).tw.
10. ((brain\$ or cerebr\$ or cerebell\$ or vertebrobasil\$ or hemispher\$ or intracran\$ or intracerebral or infratentorial or supratentorial or middle cerebral artery or MCA\$ or anterior circulation or posterior circulation or basilar artery or vertebral artery or space-occupying) adj5 (isch?emi\$ or infarct\$ or thrombo\$ or emboli\$ or occlus\$ or hypoxi\$)).tw.
11. ((brain\$ or cerebr\$ or cerebell\$ or intracerebral or intracran\$ or parenchymal or intraparenchymal or intraventricular or infratentorial or supratentorial or basal gangli\$ or putaminal or putamen or posterior fossa or hemispher\$ or subarachnoid) adj5 (h?emorrhag\$ or h?ematoma\$ or bleed\$)).tw.
12. hemiplegia/ or exp paresis/
13. (hemipleg\$ or hemipar\$ or paresis or paraparesis or paretic).tw.
14. or/8-13
15. randomized controlled trial.pt.
16. controlled clinical trial.pt.
17. randomized.ab.
18. placebo.ab.
19. randomly.ab.
20. trial.ab.
21. groups.ab.
22. or/15-21
23. 7 and 14 and 22