Animal-assisted therapy for schizophrenia and related disorders

Hawkins, Emma L.; Hawkins, Roxanne D.; Dennis, Martin; Williams, Joanne M.; Lawrie, Stephen M.

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Title: Animal-assisted therapy for schizophrenia and related disorders: a systematic review

Authors:

Emma L Hawkins[1]
emma.hawkins@ed.ac.uk

Roxanne D Hawkins[2]
roxanne.hawkins@uws.ac.uk

Martin Dennis[3]
martin.dennis@ed.ac.uk

Joanne M Williams[4]
jo.williams@ed.ac.uk

Stephen M Lawrie[1]
s.lawrie@ed.ac.uk

[1]Division of Psychiatry, University of Edinburgh, Edinburgh, UK
[2]School of Media, Culture, and Society, University of West Scotland, Glasgow, UK
[3]Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
[4]School of Health in Social Science, University of Edinburgh, Edinburgh, UK

Correspondence: Emma L Hawkins, MRes, Doctoral Researcher, Division of Psychiatry, University of Edinburgh, Edinburgh, EH10 5HF, UK. Email: emma.hawkins@ed.ac.uk. Phone: 0131 537 6763

Abstract:
Animal-assisted therapy (AAT) is increasingly researched as a potential treatment for physical and mental illness, including schizophrenia. The aim of the current paper is to systematically review randomised controlled trials (RCTs) to assess the effectiveness of AAT for schizophrenia and related disorders. We searched PubMed, PsycINFO, CINAHL, EMBASE, The Cochrane Library, CAB Abstracts, and Web of Science for RCTs of AAT for schizophrenia and related disorders. Primary outcomes were mental state and behaviour, clinical global response, and quality of life and wellbeing. Studies were eligible if they were RCTs that had compared AAT, or other animal-assisted intervention, to any control group using any participants with a clinical diagnosis of schizophrenia (or related disorder), regardless of age, gender, setting, or severity and duration of illness. Seven studies were identified for the review. Meta-analysis was not possible due to heterogeneity of studies, including marked differences in outcome measures and interventions. Five out of seven studies included symptoms as an outcome measure, with one reporting improvements in negative symptoms and one study reporting improvements in positive and emotional symptoms. The remaining studies reported no significant effects of AAT. Three studies included quality of life as an outcome measure but did not find any significant effects. Two studies did, however, report improvements in various measures of self-view. The use of AAT for schizophrenia remains inconclusive and there is currently not enough evidence to draw any firm conclusions due to heterogeneity of studies, risk of bias, and small samples. Rigorous, large-scale RCTs are needed to assess the true impact of AAT on schizophrenia.

Key words:
AAT, animal-assisted intervention, randomised controlled trial, negative symptoms, self-view

Introduction

Schizophrenia is typically a severe illness that is treated with antipsychotic medication, but outcomes are often poor, with a meta-analysis finding a recovery rate of only 13.5% meaning that only approximately 1 in 7 individuals met the criteria for recovery (Jääskeläinen et al., 2012). Antipsychotic drugs are largely effective for positive symptoms, but they have lower efficacy for negative symptoms (Leucht & Davis, 2017). Psychotherapies are often used in conjunction with antipsychotic medication. Examples of psychotherapies for schizophrenia include cognitive behavioural therapy (CBT), family therapy, and arts therapies. Results from cognitive behavioural therapies have been mixed, particularly over time, with one meta-analysis finding that older studies found stronger treatment effects than more recent studies (Velthorst et al., 2014). A recent Cochrane review also failed to find any evidence for the effectiveness of CBT over other psychosocial therapies for schizophrenia, including family therapy, supportive therapy, and other talking therapies (Jones et al., 2018). There is limited evidence for the use of social skills training to improve social skills in schizophrenia patients (Almerie et al., 2015), limited evidence for the use of family therapies in reducing the number of relapse events and hospitalizations of schizophrenia patients (Pharoah et al., 2010), and limited evidence for the use of art therapies in reducing negative symptoms (as measured using the Scale for the Assessment of Negative Symptoms (SANS); Ruddy & Milnes, 2005). It is therefore important that other alternative treatments and adjuncts are developed to improve outcomes in the management of schizophrenia.

Recently, there has been a rapid increase in the use of animal-assisted therapies for a wide range of mental and physical illnesses, including schizophrenia. However, evidence for the effectiveness of animal-assisted therapies for schizophrenia remains unclear. Pet Partners (formerly Delta Society) defines animal-assisted therapy (AAT) as 'a goal-oriented, planned, structured, and documented therapeutic intervention directed by health and human service providers as part of their profession' (Pet Partners, 2018). This review will also include animal-assisted activities (AAA), which Pet Partners defines as 'opportunities for motivational, educational, and/or recreational benefits to enhance quality of life…delivered by a specially trained professional, paraprofessional, and/or volunteer,' with an animal that 'meets specific criteria for suitability.' Animal-assisted therapy is a more structured intervention than animal-assisted activities, with a greater focus on improvements in functioning, which are documented and evaluated throughout the process. Pet therapy is a broader term that includes AAT and AAA. The use of animals in therapy was first popularised during the 1960's (Levinson & Mallon, 1997). Animals have since been incorporated into treatments for a number of illnesses including heart disease, stroke, depression, cancer, and dementia and AAT is typically used to promote improvements in emotional, social support, cognitive, and physical functioning. Animal-assisted therapy is typically used as an adjunct to other treatments and interventions (Nimer & Lundahl, 2007). Studies evaluating AAT have shown mixed results. Some studies have shown promising results, including lower systolic pulmonary artery pressure, lower neurohormone levels, and lower anxiety in heart failure patients (Cole et al., 2007), improvements in quality of life and mental health in stroke patients (Beinotti et al. (2013), reduction in symptoms of depression (Antonioli & Reveley, 2005), and improved global functioning in adolescents with acute mental disorders (Stefanini et al., 2015). However, some studies have failed to find any significant effects of animal-

assisted therapy. For example, studies have found no improvement to quality of life, gross motor function, and health in children with cerebral palsy (Davis et al., 2009), no improvement in mood or perceived health in cancer patients (Johnson et al., 2008), and no improvement in self-care functioning, disoriented behaviour, depressed or anxious mood, irritable behaviour, or withdrawn behaviour in geriatric psychiatry patients (Zisselman et al., 1996).

Animal-assisted therapy may be useful in the treatment of schizophrenia and related disorders when used as an adjunct to standard treatment for a number of reasons. Schizophrenia is characterized by positive and negative symptoms. Positive symptoms are those that are added to normal human experience and negative symptoms are those that are taken away from normal human experience. Animal-assisted therapy may be particularly useful in targeting negative symptoms. Negative symptoms that could be targeted by AAT include blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, and lack of spontaneity and flow of conversation. Given that two of the targets of AAT are to improve social and emotional functioning, it could be a valuable tool in schizophrenia treatment. There are a number of mechanisms by which animals may improve symptoms and functioning in schizophrenia. Oxytocin is one such mechanism. Administration of intranasal oxytocin is associated with a reduction of symptoms (as measured by the Positive and Negative Symptoms Scale (PANSS)) and improvements in social cognition in schizophrenia patients (Pedersen et al., 2011). Interacting with an animal has been shown to increase oxytocin levels in humans (Odendaal & Mientjes, 2003), and so could improve symptoms and social functioning through oxytocin release. Another mechanism is the role of the animal as a social catalyst to increase social interactions with others (McNicholas & Collis, 2006). Animal-assisted therapy has been shown to increase verbal interactions between nursing home residents (Fick, 1993), and increase initiation and participation in longer conversations (Bernstein et al., 2000). Animal-assisted therapy could improve motivation in patients to attend and participate in therapy sessions (Holcomb & Meacham, 1989). This is particularly important given the high rates of disengagement (up to one third) from care among individuals with serious mental illness (Kreyenbuhl et al., 2009). Animals have further been shown to improve rapport between patients and professionals with substance abuse patients rating the therapeutic alliance with their therapist as more positive after taking part in animal-assisted therapy (Wesley et al., 2009). This may be because of the animal's role as a non-judgemental and accepting presence in therapy sessions (Friesen, 2007). Animal-assisted therapy has been associated with a number of improvements in emotional functioning. Animal-assisted therapy is associated with moderate improvements in emotional wellbeing (Nimer & Lundahl, 2007), increased expression of emotions in children with acute mental disorders (Stefanini et al., 2016), and animal-assisted activities have been associated with increases in positive emotions in patients with Alzheimer's (Mossello et al., 2011).

While the use of AAT in the treatment of schizophrenia has received increased attention, it is important at this stage to thoroughly review both published and non-published studies to assess the effectiveness of AAT for schizophrenia, to assess the quality of the methods used, and guide future research. We aimed to systematically review evidence from randomised controlled trials to assess the effectiveness of animal-assisted therapy, compared to any control, for the treatment of schizophrenia and related disorders.

A further aim of the current review was to assess outcomes relating to the feasibility and potential barriers of providing AAT for schizophrenia patients, and to make recommendations for future research.

Methods

The systematic review was conducted following PRISMA guidelines (Moher et al., 2009). Meta-analysis was not possible due to heterogeneity, with marked differences in outcome measures and interventions.

Search strategy and selection criteria

Searches were carried out in the following electronic databases covering all dates up to 27th September 2017: PubMed, PsycINFO, CINAHL, EMBASE, The Cochrane Library (trials database), CAB Abstracts, Web of Science. The search strategy for EMBASE is provided in Table 1. Search terms for animal-assisted therapy were formulated by adapting a comprehensive search strategy used in another systematic review of animal-assisted interventions (AAIs; O'Haire et al., 2015). Hand searches of reference lists and citation tracking, using Google Scholar and Web of Science, were conducted for the final list of studies. An updated search was carried out on 29th August 2018, but no additional studies were identified.

[Table 1]

Reference manager software (EndNote X8.2) was used to collate articles and to remove duplicates. Title and abstract screening was carried out by one reviewer (EH). Full text articles were then retrieved for the remaining list of studies and full-text screening was carried out independently by two reviewers (EH and RH), with disagreements being noted and resolved through discussion or were further discussed with SL where an agreement could not be reached.

Studies were eligible to be included in the review if they were randomised controlled trials that had compared animal-assisted therapy, or other animal-assisted intervention, to a control group using any participants with a clinical diagnosis of schizophrenia or related disorder, including schizophreniform disorder and schizo-affective disorder, regardless of age, gender, setting, or severity and duration of illness. Only studies reported in the English language were considered for the review.

We decided to include all schizophrenia-related disorders for the sake of inclusivity due to the limited amount of research in this area.

Outcomes

Primary outcomes were mental state and behaviour (particularly changes in positive and negative symptoms), clinical global response, and quality of life and wellbeing as measured using any relevant scale, such as the Quality of Life Scale (QLS; Heinrichs et al., 1984) or the EuroQol Five Dimensions Questionnaire (EQ-5D; EuroQol, 1990).

Secondary outcomes were service use (any relevant scale, such as the Service Engagement Scale (SES; Tait et al., 2002), social functioning (any relevant scale such as the Index of Social Engagement (ISE; Mor et al., 1995), Social Functioning Scale (SFS;

Birchwood et al., 1990), Assessment of Interpersonal Problem Solving Skills (AIPSS; Donahoe et al., 1990), Living Skills Profile (LSP; Rosen et al., 1989), or behavioural observation of social functioning), medication, general functioning, physical health/activity, activities of daily living (ADL), and adverse effects (such as phobias, allergies, injury, suicide, or other cause of mortality).

Data extraction and risk of bias assessment

Data were extracted independently by two reviewers (EH and RH) using data extraction forms that were piloted on a limited selection of articles prior to conducting the full data extraction. Data were extracted for the following: diagnosis and diagnostic criteria, severity of illness, current treatment, sample size, gender, age, type of intervention, control condition, duration of treatment, length and frequency of treatment, animal/s used, outcomes, and key findings. Data are presented in Table 2.

The final selection of articles were independently assessed for risk of bias by two reviewers (EH and RH) using the Cochrane risk of bias tool (Higgins et al., 2011). Consensus was reached through discussion or was further discussed with SL where an agreement could not be reached. Data from the risk of bias assessment were input into Review Manager (RevMan) 5.3 where the summary figure was generated.

Results

The initial search retrieved 3956 articles (Figure 1). After removing duplicates there were 2963 studies for screening. 2932 records were removed after title and abstract screening. At full-text screening, a total of 24 studies were excluded. Reference lists of the remaining articles were hand searched to identify any additional studies. Two further studies were identified during citation tracking, but both were excluded. This left seven studies for detailed review. Full-text articles were available for six studies. The remaining study was a conference abstract. One study had an additional report.

[Figure 1]

The total number of participants randomised was 390. Sample sizes ranged from 20 to 105 participants (mean 55.7, SD 40.2). Mean ages ranged from 34.7 years to 79.1 years (mean 50.9, SD 16.7). Of those that reported the gender or sex of participants, there were 166 females and 179 males. One study randomised 105 participants but only provided demographic information for the 90 participants that completed the study. Reporting of sex and gender were inconsistent across the studies. Two studies used the term ‘gender,’ (references), two studies used the term ‘sex,’ and one study only made reference to ‘males’ and ‘females.’ No definitions of terms were included in any of the studies.

Participants were recruited from hospital populations. Six studies included inpatients only and one study included both inpatients and outpatients. Five studies included only individuals with a diagnosis of schizophrenia. One study included multiple diagnoses with individuals with a diagnosis of schizophrenia and schizotypal disorders forming the largest diagnosis group (37.7%). The remaining study included patients with a diagnosis of schizophrenia or schizoaffective disorder (76%), and patients with an affective or other disorder (24%). Patients were diagnosed using DSM-IV criteria (n=4) or ICD criteria (n=1).

One study used chart diagnosis, and the remaining study did not report diagnostic criteria. Studies were conducted in Spain (n=2), Taiwan (n=2), Israel (n=1), Norway (n=1), and in the USA (n=1).

Interventions included animal-assisted therapy (n=5), animal-assisted activity (AAA; n=1), and pet therapy (n=1). Test conditions included AAT in addition to standard treatment (n= 4). Detailed information was not provided for three studies. Comparison conditions included standard treatment (n=2), standard treatment plus an activity from a functional program (n=1), reading and discussion of current news (n=1), and standard treatment plus a novel intervention without a therapy dog (n=1). One study included two comparison conditions, which were regular hospital care and an active control group involving social skills exercises. One study did not provide any information regarding the comparison condition. The most common animals used were dogs (n=5). Other animals included cats (n=1), horses (n=1), farm animals (n=1), and hamsters (n=1). One study used both dogs and cats, and another study used both dogs and horses. Of those that reported treatment lengths, treatments ranged from 10 weeks to 12 months. Sessions lasted between 40 minutes and 10 hours, with session frequency ranging from one session per week to seven sessions per week. Apart from the pet therapy study, sessions lasted up to 4 hours with a frequency of either one session per week (n=3) or two sessions per week (n=3). The pet therapy study was less structured with treatment being the presence of a hamster in the participant's room for 10 hours each day. One study included a follow-up assessment after the end of the treatment period, which was at 6 months. None of the studies were reviewed by an Institutional Animal Care and Use Committee (IACUC).

[TABLE 2]

For the primary outcomes, one study found a significant improvement in negative symptoms in the treatment group, as measured using the Scale for the Assessment of Negative Symptoms (SANS). Another study reported a significant improvement in positive and emotional symptoms in the treatment group, but no significant difference for negative symptoms. Two studies reported a significant improvement in negative symptoms within the treatment group but no significant differences in Positive and Negative Symptom Scale (PANSS) scores were found between the treatment and control group. One study found no significant differences in Brief Psychiatric Rating Scale (BPRS) scores. There were no significant differences between treatment and control groups for quality of life, as measured using the QOLS-N, EQ-5D, and the Brief World Health Organization Quality of Life Assessment (WHOQOL-BREF). One study reported a significantly lower score on the general health item of the EQ-5D within the treatment group at the end of the intervention.

For the secondary outcomes, two studies reported no significant differences in social functioning between treatment and control groups as measured using the LSP. One of these studies reported a significant improvement in social contact within the treatment group, which was not found within the control group. However, they also found a significant worsening of non-personal social behaviour. One study reported significant improvements in total Social Adaptive Functioning Evaluation (SAFE) scores and in scores on the social functioning subscale in the treatment group compared to control. Adverse effects were not reported in four of the included studies, and two studies reported no adverse effects.

Significant improvements were reported in treatment groups for self-esteem, self-determination, self-efficacy (GSE), and anxiety. A significant reduction in violent incident reports was found in an equine-assisted psychotherapy (EAP) treatment group. One study also reported a significant reduction in salivary cortisol following AAT sessions. No significant differences were found between treatment and control groups for social support, salivary alpha-amylase as a measure of stress-relief, coping strategies, depression, intrusiveness, or other aggression measures.

Other outcomes of interest included adherence, animal recruitment (where animals were sourced from, e.g. from a charity such as Pets as Therapy, and degree of training that the animal had received), matching (between patients and animals), attrition, cost, dosage (number, duration, and frequency of sessions), and any barriers to providing AAT for schizophrenia (such as ethical barriers, health and hygiene, or patient and professional attitudes towards AAT). No information was provided regarding matching, cost, and barriers by any of the studies. Information regarding dosage are described elsewhere and presented in Table 2. One study reported significantly higher adherence to AAT (92.2%) than control (61.2%). High dropout rates were reported in one of the studies, in which 68% of participants from the treatment group completed the study and 93% from the control group completed the study. Dropout rates in other studies were as follows: 14.3%, 12.4%, 10%, and 8.3%. The majority of dropouts were reported as participants withdrawing from the study prior to the end of sessions (61.9%), with the remaining dropouts being those who did not attend any sessions (38.1%). Of those that reported sufficient information, the majority of dropouts across studies were from the treatment groups (86.2%). Animals were recruited from trainers, farmers, counsellors from a Pet Enrichment Therapy (PET) program, and an animal welfare centre. Animals were specially certified in two studies. In one study, although there was no official certification for therapy dogs in the country of study, physical and behavioural examinations were carried out by certified specialists.

Risk of Bias

[Figure 2]

Risk of bias was assessed using the Cochrane risk of bias tool (Higgins et al., 2011), the results of which are presented in Figure 2. Risk of bias across studies is presented in Figure 3.

Six studies were judged to be of unclear risk of bias for random sequence generation due to insufficient information regarding method of randomization. The remaining study reported that participants were allocated using computer randomization and so was judged as low risk of bias.

There were no statements regarding allocation concealment in any of the included studies and so were all judged as unclear risk of bias.

Most studies were judged to be of high risk of bias for blinding of participants and personnel due to the inability to blind individuals to the presence of an animal. While this was the case for all studies, two studies included active control groups, which may reduce

the risk of bias, and so were judged to be of unclear risk of bias. One study was judged to be of unclear risk of bias due to insufficient information regarding the control condition.

Four studies used blind raters and so were judged as low risk of bias for blinding of outcome assessment. However, one of these studies was judged as high risk of bias for a separate outcome as staff were not blind at post-test. One study was judged as high risk of bias as only one neuropsychologist participated in the study and so could not be blinded. A low risk of bias judgement was made for a separate outcome as saliva samples were analysed by laboratory technicians who were blind to treatment. The remaining two studies were judged as unclear risk of bias due to insufficient information.

One study was judged as low risk of bias for incomplete outcome data as all participants completed the study. Four studies were judged as high risk of bias due to withdrawals and exclusions that may have imbalanced groups, and lack of intention-to-treat analysis and/or use of a per protocol analysis. The remaining two studies were judged as unclear risk of bias due to insufficient information.

Two studies were judged to be of high risk of bias for selective outcome reporting. One study stated that they would investigate physiological and psychological aspects of schizophrenia in their aims, but no physiological results were reported, nor was there any mention of physiological measures in the methods. The second study did not fully report the results for one measure, instead reporting two out of three items. The remaining studies were judged to be of unclear risk of bias as study protocols were not available to be able to make a clear judgement.

Other sources of bias included baseline imbalances, and funding from the Affinity Foundation, which promotes the benefits of pets for humans. Two studies were judged to be of unclear risk of bias for other sources due to insufficient information. Other sources of bias were not identified in the remaining three studies.

Overall, there were few low risk of bias judgements made across the studies (10 out of 51), with a larger number of high risk (15 out of 51) and unclear risk of bias judgements (26 out of 51). Nurenberg et al. (2014) and Calvo et al. (2016) had the most ‘high risk’ judgements (5 out of 8) while Barak et al. (2001) had the most ‘low risk’ judgements (3 out of 7).

[Figure 3]

Discussion

The primary aim of the current review was to synthesise the published research to determine whether animal-assisted therapy is an effective treatment for schizophrenia based on results from randomised controlled trials. Meta-analysis was not possible in the review due to heterogeneity, particularly marked differences in outcome measures and interventions. Evidence for the effectiveness of animal-assisted therapy for the treatment of schizophrenia remains inconclusive and not sufficiently robust. This review identified mixed findings for the effectiveness of animal-assisted therapy for schizophrenia. Improvements were found for negative symptoms, positive and emotional symptoms, and SAFE scores, particularly the social functioning subscale, and on a number of measures of positive self-view (self-esteem, self-efficacy, and self-determination). Some within-treatment group effects were found for improvements in negative symptoms, and social contact. There was

no evidence for any benefits to quality of life and some studies failed to find any improvements for symptoms from measurement using the PANSS or BPRS. There were also no improvements found on the Living Skills Profile (LSP), Coping Strategies Scale, or for social support. It is important to note that because of serious flaws in the included studies and the high risk of bias and unclear bias across the studies, makes the interpretation of results impossible. This review cannot make any conclusions based on the included studies.

The potential benefit of AAT for negative symptoms, social difficulties, and negative self-view evident in this review are also noted in a number of observational studies. These include reports of significant reductions in symptoms, particularly negative symptoms following therapeutic riding (Cerino et al., 2011), as well as significant improvements in hedonic tone following AAT with a dog (Nathans-Barel et al., 2004). Significantly increased use of leisure time following AAT (Nathans-Barel et al., 2004), increased nonverbal communication (Kovács et al., 2006), increased prosocial behaviours (Marr et al., 2000), and increased scores on the Independent Living Skills Survey (ILSS), particularly for domestic activities and health subscale scores (Kovács et al., 2004) have also been observed. Increases in measures of positive self-view have been found following therapeutic horseback riding, including increases in self-esteem (Bizub et al., 2003; Corring et al., 2013), sense of agency (Bizub et al., 2003), self-confidence, and self-efficacy (Corring et al., 2013).

Lack of apparent evidence for benefits to quality of life in the current review may be due to the nature of the interventions used. Longer, and more frequent, interventions may be required to have a measurable impact on quality of life but it may be that AAT is not an effective treatment for targeting quality of life in schizophrenia patients. Results from a recent systematic review of dog-assisted interventions in health care identified improvements in quality of life in two out of three studies that included this measure (Lundqvist et al., 2017). However, the two studies that identified improvements looked at dementia patients, and the study included in the current review (Calvo et al., 2016) that did not show improvements, looked at schizophrenia. The worsening of non-personal social behaviour found in one study was concerning (Villalta-Gil et al., 2009). The authors noted that they did not focus on non-personal social behaviours in their intervention program (e.g. disruptive behaviours towards public objects). It is important that future studies take this into account to minimise any potential adverse effects.

Another factor that may influence results is the types of treatment/s patients are receiving prior to enrolling in AAT. However, only one study (Calvo et al., 2016) provided detailed information regarding the medications that patients were taking prior to AAT and that all individuals were enrolled in a psychosocial rehabilitation programme. Berget et al. (2008, 2011) provided general information regarding medication (Table 2) but no information regarding other treatment/s. Due to the lack of information, it is not possible to determine whether current treatments had any effect on outcomes. Severity and duration of illness may also be an important factor in outcomes. However, there was heterogeneity in the reporting on duration and severity. Some studies reported years spent in long term care (Barak et al., 2001; Berget et al., 2008, 2011; Nurenberg et al., 2015; Villalta-Gil et al., 2009), while other reported years since onset of illness (Calvo et al., 2016; Chu et al., 2009). The remaining study only stated that cases of illness were chronic (Kung et al., 2005). Again, it is difficult to determine the impact of duration and severity of illness on

outcomes. Future studies should provide complete reporting so that conclusions can be reached.

The secondary aim of this review was to assess feasibility and potential barriers of providing AAT for schizophrenia patients, but little information was available in the included studies. No information was provided regarding costs of AAT, barriers faced by therapists or researchers, or matching of participants to animals. Without this information, it is not possible to adequately assess feasibility and future research should address these outcomes to improve replicability and expansion of the use of AAT. Adherence was reported by one study, which showed significantly higher adherence to AAT compared to control. The review highlights some concerns regarding dropout rates from interventions. Of the studies that reported dropout rates, the majority noted higher dropout rates for intervention groups compared to control groups. Reasons given for dropouts included fear of dogs, discharge from hospital, risk of harm to animals involved, and little interest in included species and work involved. Future research should address these issues and develop strategies to improve adherence, attrition, patients' experiences of AAT, and take steps to ensure animal welfare. It is concerning that only one study made any mention of animal welfare (Calvo et al, 2016) and none of the studies were reviewed by an Institutional Animal Care and Use Committee (IACUC). Calvo et al. taught participants the concepts of animal welfare, assessed the welfare of the dogs before, during, and after the program, and excluded participants that exhibited behaviours that may have compromised the welfare of the dogs. It is vital that more studies address animal welfare sufficiently. Compromised animal welfare not only risks the health and wellbeing of the animal involved, but could also lead to less effective treatment if the animal is unable to perform well as a therapy animal. Dogs that are rated as more stressed by their owners and veterinarians are less likely to participate in social contact with an unfamiliar person (Lind et al., 2017). Risks to animals taking part in animal-assisted interventions have been noted in some studies, including the potential for mistreatment (Hatch, 2007), deliberate attempts to injure the animal, lethargy, and symptoms of depression (Heimlich, 2001). Future studies and animal-assisted intervention programmes should place a greater emphasis on animal welfare, as well as human wellbeing, taking a 'One Welfare' approach to recognise the interconnectedness of animal welfare, human wellbeing, and the environment (Pinillos et al., 2016). There are several guidelines available that provide information on animal welfare during animal-assisted interventions. The International Association of Human-Animal Interaction Organisations (IAHAIO) published the White Paper: Definitions for Animal Assisted Intervention and Guidelines for Wellness of Animals Involved in 2014 (Jegatheesan et al., 2014).

Due to limitations in the included studies, there is still a lack of evidence for the effectiveness of AAT for schizophrenia and results should be treated with caution. The limitations of the included studies are common across much of the literature and have been discussed at length in previous reviews (May et al., 2016; Crossman, 2017; Kazdin, 2017). Limitations identified in this review are presented and discussed in Table 3 with recommendations for future research. The number of high risk and unclear risk of bias decisions are of particular concern. The study that identified improvements in negative symptoms had unclear risk of bias for 7 out of 7 decisions (Kung et al., 2005). The study that identified improvements in social functioning had unclear risk of bias for 4 out of 7 decisions (Barak et al., 2001). The study that identified improvements in self-efficacy had

unclear risk of bias for 3 out of 7 decisions and high risk of bias for 2 out of 7 decisions (Berget et al., 2008, 2011). The study that identified improvements in self-esteem and self-efficacy had unclear risk of bias for 2 out of 7 decisions and high risk of bias for 3 out of 7 decisions (Chu et al., 2009). Methodological issues (Table 3) combined with high and unclear risk of bias make the findings from the majority of studies included in this review uninterpretable. It is vital that future studies address these issues and follow the CONSORT guidelines to ensure accurate reporting of randomised controlled trials (Schulz et al., 2010). The poor state of the research field was first highlighted in a review in 1984 (Beck & Katcher, 1984). Thirty-four years later and some of the same common limitations are still being found across studies. Whilst some aspects of the research have improved over time (May et al., 2016), future research must address limitations to allow firm conclusions regarding the efficacy of AAT as a treatment for schizophrenia and to allow for changes to be made to current policy and practice. Rigorous, large-scale randomised controlled trials with long-term follow-up are needed to determine the true impacts of AAT for schizophrenia.

[Table 3]

This review had a number of limitations: 1) we included studies of lower quality in order to be inclusive, 2) studies were limited to those reported in the English language due to a lack of resources, 3) we were unable to conduct a meta-analysis due to heterogeneity of studies. Strengths of this review include: 1) restriction to randomised controlled trials to assess the best available evidence, 2) inclusion criteria were not restricted to published articles from peer-reviewed journals, 3) inclusive and comprehensive search strategy 4) use of the Cochrane Tool for Assessing Risk of Bias. We used the Cochrane tool as it has been argued to be more reliable than subjective quality assessments (Higgins et al., 2011). As far as we are aware, this tool has not been used in other systematic reviews of animal-assisted interventions, although one study did use the Cochrane's criteria list (Kamioka et al., 2014). Prior to this review, we identified only one other systematic review on AAT that included unpublished studies (Germain et al., 2018). Only one systematic review was identified that examined animal-assisted interventions and schizophrenia (Jormfeldt & Carlsson, 2018). However, this review was limited to equine-assisted interventions, peer-reviewed papers, papers published between 2000 and 2016, and studies that included participants aged 18-65 years.

In conclusion, based on the results from this review, it would be premature at this point to make any changes to patient care and policy to incorporate animals into therapy. Rigorous, large-scale randomised-controlled trials with long-term follow-up are first needed to determine the true impacts of AAT for schizophrenia. There is some promise for the treatment of negative symptoms and negative self-view but results remain inconclusive. It is important to highlight the methodological flaws and predominantly high and unclear risk of bias of the included studies. Because of this, it is not possible to confirm whether AAT is or is not effective in treating schizophrenia based on the included studies. Given this, the need for the further development of negative symptom interventions (Elis et al., 2013), and the substantial burden of disease (Charlson et al., 2018), further research is required to determine the true impact of AAT on schizophrenia.

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Contributors
All authors were involved in the design of the study and development of the protocol. EH and RH assessed the studies, extracted the data, and conducted the risk of bias assessment. EH wrote the first draft with input and comments from RH and SL. All authors provided comments on and approved the final draft.

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Figure legends

Figure 1: PRISMA flow diagram of the selection of studies for inclusion in the systematic review to assess the effectiveness of AAT for schizophrenia.

Figure 2: 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study. The risk of bias assessment was conducted by two independent reviews with agreements made through further discussion.

+ represents low risk of bias

- represents high risk of bias

? represents unclear risk of bias

Figure 3: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.