Author’s response to reviews

Title: Effects of dog-assisted therapy in adults with dementia: a systematic review and meta-analysis

Authors:

Jessica Zafra-Tanaka (j.zafra.t@gmail.com)
Kevin Pacheco-Barrios (kevin.pacheco.barrios@gmail.com)
Walter Tellez (tellezwa94@gmail.com)
Alvaro Taype-Rondan (alvaro.taype.r@gmail.com)

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Author’s response to reviews:

We proceed to answer to each of the reviewer's comments:

Sverre Bergh (Reviewer 1): Thanks for the opportunity to read your manuscript and critical review the text. DAT is popular in nursing homes and other places of care for persons with dementia, and both theoretical and based on clinical experience it seems as a good idea for treating different symptoms of dementia. On the other side, it may have some side-effects, and its effect should be critical reviewed. I therefore appreciate your effort to present a meta-analysis of the effect of DAT. I enjoyed the manuscript. It is well written, easy to follow, and generally of good quality. Nevertheless, I have some comments for the authors, that I hope they can address:

1.1 I would like if you could include some information about publication bias. Have you been searching ClinicalTrials.gov and other databases for planned RCT on DAT that have not been publishing?

Publication bias has not been assessed because we only found six RCTs. Cochrane states that publication bias can be evaluated with 10 or more studies. In addition, we have not searched in ClinicalTrials.gov or other databases for planned RCT, which was not planned in our protocol.

1.2 There are other international databases for research papers as Embase, PsycINFO, CINAHL, AgeLine, and PROSPERO. Did you think about including some of these databases in
your search? It is not sure that expanding the databases searched in would increase the number of papers, but any thoughts about why you only searched PubMed, Scopus and CENTRAL?

With regards to the reasons why we only searched PubMed, Scopus and CENTRAL, we picked these datasets is that they are open-source. PubMed concentrates most of the medical literature published, while CENTRAL concentrates a great amount of clinical trials.

We are aware that there are other databases for research papers. However, only a small number of extra-articles are retrieved when adding other databases to Pubmed, and the conclusions of the systematic reviews almost never change. The reviewer can further explore the following papers on which we based our decision to look only on those datasets:


Moreover, to minimized the chances of not retrieving important articles located at other databases, we decided to look into the references of the articles we had selected.

1.3 Figure 1. Flow chart. I am a bit confused about the numbers. You assessed 37 full text papers, of whom 27 were excluded for different reasons. That should leave you with 10 papers, before you added two papers that cited the papers identified in step one. Please clarify.

As the reviewer states, when adding the eight papers we included from the databases search and the excluded studies we obtain 35 and not 37. We have double-checked our selection process and found that the numbers presented in the flow chart had a mistake. We have now corrected the flow chart so it presents the correct numbers.

Gary Christopher (Reviewer 2): BPSY-D-18-00812. Effects of dog-assisted therapy in adults with dementia: a systematic review and meta-analysis

ABSTRACT
2.1 The Background section is repetitive.

With regards to the background section, we believe that it is important to clearly state what we mean by “dog assisted therapy”, its use in patients with dementia, and to present the PICO question that we seek to answer. However, we do think it’s a repetitive. Thus, we have changed the paragraph as follows: “Dog-assisted therapy (DAT) is a non-pharmacological intervention based on the interaction between patients and dogs, which has been proposed to help adults with dementia. However, evidence to support it is lacking. Thus, we aim to evaluate the effects of DAT on this population and to assess the certainty of the evidence of the RCTs estimates.”

2.2 What does "published from inception" mean (Methods)?

With the terms “published from inception” we meant to say that we used no custom date range, we included all articles published until the date we performed the search. We have rephrased this sentence so it is more clearly understood: “We included randomized controlled trials (RCTs) and quasi-experimental (QE) controlled studies published up to March 2018”

INTRODUCTION

2.3 The opening paragraph could be more clearly written, with better definitions and less use of brackets.

With respect to the opening paragraph, we have taken into account the suggestions made by the reviewers and we have changed the definition of dog-assisted therapy to clearly state the definition. We have also changed the way the paragraph was written so as to reduce the number of brackets, as follows:

“Animal-assisted therapies (AAT) are interventions in which animals participate as an integral part to improve specific outcomes in the patient (1). Dog-assisted therapies (DAT) is a subtype of AAT in which patients interact with dogs (1). This interaction can include diverse activities such as petting, brushing, feeding, playing with, strolling with, or talking to the dog. DAT has been described as promising in helping people with diverse conditions, especially psychiatric conditions and cognitive disorders such as dementia (2).”

2.4 The paragraph beginning, "Two recent systematic reviews have assessed," is again not at all easy to read for similar reasons.

In order to make this paragraph easy to read, we have changed it as follows: “Regarding AAT and its effects on dementia, two systematic reviews have been recently published: one systematic review found 32 studies that addressed AAT, from which 27 used dogs and 8 of these were randomized controlled trials (RCTs); and concluded that AAT is effective in reducing the
behavioral and psychological symptoms of dementia (3). Another systematic review that evaluated the benefits of AAT for cognitive impairment found ten studies (five RCTs and five quasi-experimental [QE] studies) up to June 2017, all of which included dogs, either alone or accompanied by other animals. This systematic review found statistically significant effects of DAT in depression and agitation. However, this is based on a meta-analyses that combined RCTs and non-RCTs, which is not currently suggested (4).”

2.5 There is no explanation what GRADE methodology is and why it is relevant. Indeed, this section provided little rationale for the systematic review.

We have two main reasons to perform a new systematic review: 1) previous systematic reviews have mixed results from RCTs and cohort studies leading to possible confounding bias, and 2) a systematic evaluation of the certainty of the evidence is necessary to correctly assess the effects of DAT. To evaluate the certainty of the evidence we have decided to use GRADE given that it allows reproducibility of this evaluation.

We have re-written the paragraph as follows: “Although these systematic reviews suggest that DAT have some benefits in persons with dementia, they tend to mix results from RCTs and other study designs, which preclude an adequate evaluation of the role of confounding variables. Moreover, these reviews do not assess the certainty of evidence which is necessary when making health care decisions. To evaluate the certainty, we will use a systematic framework called Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology (5). GRADE has been increasingly used by different institutions devoted to clinical practice guidelines development and decision making given that it allows reproducibility in the assessment of certainty of evidence (6). Thus, using GRADE will help us to correctly assess the current confidence in the final estimates and therefore, it will help us formulate recommendations and future studies in the topic. Thus, the aim of this systematic review was to search for RCTs and QE controlled studies in order to evaluate the effects of DAT in adults with dementia and to assess the certainty of the evidence for RCTs estimates using the GRADE methodology.”

METHOD

2.6 There needed to be evidence of eligibility criteria here.

We agree that it is important to state the eligibility criteria (inclusion and exclusion criteria), this we have written a paragraph that clearly states them: “For this systematic review, we included all RCTs and QE controlled studies that directly evaluated any beneficial or adverse effect of DAT in adults with dementia. We excluded those studies for which full-text could not be accessed.”
2.7 What were the keywords used to search the databases?

The keywords we used were attached as supplementary materials, and are the following:

<table>
<thead>
<tr>
<th>Date</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scopus</td>
<td>TITLE-ABS-KEY ((dementia OR (Alzheimer* W/1 disease) OR “Cognitive Dysfunction” OR “cognitive impairment” OR &quot;Neurocognitive Disorders&quot; OR “cognitive decline”) AND (&quot;pet therapy&quot; OR &quot;Animal Assisted&quot; OR &quot;Bonding, Human-Pet&quot; OR “Animal Human Bonding” OR “canine-assisted” OR “dog-assisted” OR companion animal*[tiab] OR “pets as therapy” OR “pet as therapy” OR ((dog OR animal OR pet) AND visitation))) March 2018 160</td>
</tr>
<tr>
<td>CENTRAL</td>
<td>1. MeSH descriptor dementia, this term only</td>
</tr>
<tr>
<td></td>
<td>2. MeSH descriptor Alzheimer Disease, this term only</td>
</tr>
<tr>
<td></td>
<td>3. MeSH descriptor Cognitive Dysfunction, this term only</td>
</tr>
<tr>
<td></td>
<td>4. MeSH descriptor Neurocognitive Disorders, this term only</td>
</tr>
<tr>
<td></td>
<td>5. Dementia:ti,ab or (Alzheimer*:ti,ab and disease:ti,ab) or cognitive impairment:ti,ab or Neurocognitive Disorders:ti,ab or cognitively impaired:ti,ab or cognitive decline:ti,ab</td>
</tr>
<tr>
<td></td>
<td>6. MeSH descriptor Pets, this term only</td>
</tr>
<tr>
<td></td>
<td>7. MeSH descriptor Animal Assisted Therapy, this term only</td>
</tr>
<tr>
<td></td>
<td>8. MeSH descriptor Bonding, Human-Pet, this term only</td>
</tr>
<tr>
<td></td>
<td>9. pet therapy:ti,ab or animal assisted:ti,ab or animal-assisted:ti,ab or animal human bonding:ti,ab or canine-assisted:ti,ab or dog-assisted:ti,ab or companion animal*:ti,ab or pet as therapy:ti,ab or pets as therapy:ti,ab</td>
</tr>
<tr>
<td></td>
<td>10. dog:ti,ab or animal:ti,ab or pet:ti,ab and visitation:ti,ab</td>
</tr>
<tr>
<td></td>
<td>11. #1 or #2 or #3 or #4 or #5</td>
</tr>
</tbody>
</table>
2.8 More was needed on the data analysis, such as effect sizes, heterogeneity, and so on.

In our opinion, this section was detailed enough. For the methods section, we have followed the PRISMA checklist, and detailed the analysis used to calculate the global effect sizes, and to evaluate heterogeneity.

RESULTS

2.9 Remove bullet-points. Nice summary table. Figures were helpful.

As the reviewer suggested, we have removed the bullet-points.

DISCUSSION

2.10 The writing here is clearer than in some of the previous sections. However, I am sure some of the statements made in the 'Certainty of evidence and implications for clinical practice' sections can be substantiated. In particular, the statement, "Even though most of the studies did not report information on costs of DAT implementation, we believe it might be expensive for some health systems, due all the resources needed," seems rather speculative. It might be correct, but I am not sure there is evidence here to back it up.

We considered that the suggestion made by the reviewer is very important. Thus, we have looked for evidence regarding costs of housing, food and veterinary care for a dog and found that it is around 8000USD during the animal’s life. We have modified that sentence as follows: “Even though most of the studies did not report information on costs of DAT implementation, a previous study reported that around 8 000USD are needed to take care of a dog and provide it with adequate housing, food, and veterinary care (31). This can represent a huge amount of money for some health systems.”

2.11 Also, the statement, "DAT should not be used routinely as a therapy for patients with dementia," seems a little preemptive given the flaws indicated in all the studies under review.
One assumes a tighter-controlled study with better outcome measures might show some benefit, then again it might not. The conclusion seems a little strong given the current situation.

Given that there is currently no evidence to support the effects of DAT in patients with dementia, we consider that the most conservative approach is that DAT is not used. It is truth that further research with adequately design studies are needed, but this does not mean that DAT should be used while we wait to get evidence of it’s effects.

Mahbobeh Faramarzi (Reviewer 3): The authors designed a systematic review(SR) on DAT. There are two previous SRs Yakimicki (2018) and Hu (2018) on Animal-assisted intervention. The authors included 6 studies that seems that the same two previous RSs. The author claimed that previous SRs mixed RCT with other type studies and didn't use GRADE. I could see the Tables (Also, Table of six included studies) in the Supplementary section. I have some question about the SR:

3.1 Are your 6 included studies the same two previous SR (Yakimicki (2018) and Hu (2018))?  
The reviewer refers to the RCTs found and included in our SR. Yes, they are the same RCTs that the Yakimicki (2018) and Hu (2018) RS found.

3.2 If your answer is yes, why do not use more comprehensive database than two previous SRs for search?  
The reasons why we chose to use our search strategy have been stated in comment 1.2

3.3 This study concluded that 6 six included studies were low GRADE, therefore the results of Previous SRs was not confirmed. There is a main question: Is there needed to plan a SR for only assessment of DRADE of primary studies?  
We have two main reasons to have performed the current SR; 1) one previous SR did not performed a meta-analysis and the other SR mixed results from RCTs and observational studies (which is not methodologically adequate), and 2) the certainty of the evidence was not previously evaluated. Evaluating the certainty of evidence with GRADE provides a systematic evaluation of the evidence and allows policy makers to make an informed decision. Thus, we believe our study is valuable.

3.4 The Table of the "characteristics of included studies" is the essential Table that should be insert in the main text, not Supplementary material.

We considered that what the reviewer states is very important. Thus, we will contact the editor to ask if it possible to insert that table in the main text.
Martino Belvederi Murri (Reviewer 4): The present meta-analysis examines the effectiveness of dog-assisted interventions for patients with dementia. This area of research is extremely important, both for society and clinical settings. The review seems adequately conducted and reported. The authors employ the GRADE system to rate methodological quality.

In my view, however, the main problem of this study lies in terms of originality/timing. As the authors rightly point out, two other systematic reviews (one with meta-analysis) have been recently published on this topic, but with a slighter larger focus (not just dementia, not just dog-assisted). The first included over 30 studies, this one only ten.

The reviewer points out a concern that has previously been address in comments 2.5 and 3.3.

Another problematic issues are the following:

- since the number of existing studies is quite small, the authors have pooled results from both RCTs and quasi-experimental studies. Although this is a relatively common practice, it remains unclear how the results should be interpreted.

We totally agree with the reviewer, for that reason we decided not to pool results from RCTs and quasi-experimental studies. Thus, all of our forest plots present one pooled estimate for the RCTs and another polled estimate for the quasi-experimental studies.

- The authors state they excluded some studies based on the issue a ) they couldn’t get the full text of the article. I deeply sympathise with this problem (as any researcher I also had to face it at some point), but it remains an important source of bias b) I can't find any statement indicating the authors have tried to get access to data that wasn't published (e.g. data for the subgroup of patients with dementia). Failure to do so also results in an important source of bias

We are aware that it is important source of bias, for that reason we did contact the authors of those papers asking them to share the information. However, we couldn’t access to it.