

Table 2 (Continued)

|                      |   |   |  |
|----------------------|---|---|--|
| Numbers analyzed     | Per therapy intervention ( $n = 33$ ) or an exercise intervention ( $n = 25$ )  | Intervention group with therapy dog ( $n = 12$ ) and control group without a dog ( $n = 9$ )  | Animal assisted treatment group ( $n = 10$ ) and control group ( $n = 10$ )  |
| Outcome              | No significant differences in the Multidimensional Observation Scale for Elderly Subjects (MOSES) scores were found between or within groups before and after the interventions. There was a nonsignificant tendency for subjects who received the pet intervention to have less irritable behavior after treatment. However, women with dementia who received either pet therapy or exercise intervention had improved irritable behavior scores after treatment   | Patients in the IG + D group showed significant improvements in the LSP social contact score, in the positive and negative symptom dimension and total score of the PANSS, and in quality of life related with social relationships. Patients in the IG group showed significant positive changes in positive and general symptoms and total PANSS score. No differences were found between the two groups before and after the application of the intervention | The Social Adaptive Functioning Evaluation scores at termination showed significant improvement compared with baseline scores and were significantly more positive for the AAT group on both Total SAFE score and on the Social Functions subscale   |
| Harm                 | No description  | Nothing   | No description   |
| Conclusion           | This pilot study demonstrates the need for further research on animal-assisted interventions with hospitalized elderly persons. Differential improvement in women with dementia also requires further investigation   | Introducing a dog into the psychosocial intervention for patients with schizophrenia produced some positive outcomes. However, the results of the study are not conclusive and must be interpreted cautiously   | AAT proved a successful tool for enhancing socialization, ADLs, and general well-being   |
| Trial registration   | No description  | No description  | No description   |
| Fund                 | A grant from Sandoz/Jeffs Companion Animal Center   | The financial help of the La Caixa Foundation and was supported by the Spanish Ministry of Health, Instituto de Salud Carlos III, CIBERSAM. The authors declare that no competing interests exist   | No description   |
| Cost of intervention | No description  | No description  | No description   |
| Reference no.        | 21  |   | 22   |
| Author               | Pedersen I, et al.  |   | Carolyn AM, et al.   |
| Citation             | <i>Anthrozoos</i> 2012;25:149–160   |   | <i>Anthrozoos</i> 2000;13:43–47  |
| Title                | Farm animal-assisted intervention for people with clinical depression: a randomized controlled trial  |   | Animal-assisted therapy in psychiatric rehabilitation  |
| Aim/objective        | To examine potential changes in mental health in people with clinical depression, while working with farm animals as the only task on the farm  |   | To evaluate whether patients in the animal-assisted therapy group would show a greater increase in observed appropriate social behaviors than the control group patients who did not receive animal-assisted therapy   |
| Setting/place        | Eleven dairy farms from six different counties in Norway  |   | Terrell State Hospital, Terrell, Texas   |
| Participants         | 28 adult patients with clinical depression  |   | 69 inpatient participants at a large state psychiatric facility  |
| Intervention         | The intervention consisted of work and interaction with farm animals twice a week for 12 weeks. The time for each session spent on the farm per day varied from 1.5 to 3.0h due to differences in farm size, degree of mechanization, and the amount of work. A first introductory visit was used by the participants to get familiar with the farm and farmer. On the following visit, the participants worked together with the farmer in the cowshed. The participants were allowed to choose work such as grooming, mucking, feeding, taking care of the calves, and milking. They could also choose to spend their time in physical contact with the animals. The participants did not take part in any other work at the farm |   | The experimental AAT group had animals visit the class each day. The animals included dogs, rabbits, ferrets, and guinea pigs. The animals remained for the entire class period and were moved from patient to patient. Patients in the group were allowed to observe the animals or interact with the animals – hold them, pet them, and/or play with them as long as they did not disrupt the group. Patients were not required to participate directly with any animals; such participation was voluntary and the patients determined the level of individual involvement. However, there was only one female patient out of all of the AAT subjects that elected to not interact directly with the animals |

|                             |  |  |
|-----------------------------|--|--|
| Main and secondary outcomes | Depression anxiety, and self-efficacy  | Social Behavior Scale  |
| Randomization               | The randomization was conducted by a researcher blinded to farm and participants   | No description   |
| Blinding/masking            | No description   | It was not possible to keep the rater blind to condition since the behavior observations were made daily while the group was being conducted. However, neither those conducting the class nor the rater was privy to the design or intent of the study, and hence they remained essentially "blind". Data entry was by an individual who was also blind to the treatment conditions  |
| Numbers randomized          | The intervention group ( $n = 16$ ) and the control group ( $n = 13$ )   | Animal-assisted therapy group ( $n = 18$ ) and control group ( $n = 19$ )  |
| Recruitment                 | Thirty-five participants were recruited through advertisements, invitation letters from the Norwegian Labour and Welfare Service, and contact with health personnel. Potential participants received a letter describing the intervention, and the possibility to be allocated to either a control or an intervention group was stated   | There were 69 inpatient participants (70% male and 30% female) at a large state psychiatric facility   |
| Numbers analyzed            | The intervention group ( $n = 16$ ) and the control group ( $n = 13$ )   | Animal-assisted therapy group ( $n = 18$ ) and control group ( $n = 19$ )  |
| Outcome                     | A significant decline in depression and a significant increase in self-efficacy were seen in the intervention group between recruitment and of intervention. In the control group, no significant changes were found. No significant differences were found when comparing change in mental health measures in the intervention and control groups. However, more subjects in the intervention group (6) than in the control group (1) had clinically significant change, indicating that animal-assisted intervention in Green care could be beneficial for subgroups of clients and act as a useful supplement within mental health care | Animal-assisted therapy patients interacted more with other patients. Similarly, there was a main effect for weeks, with improvement in scores over time but no interaction between weeks and groups. There was a similar finding for the AAT group; patients smiled and showed pleasure significantly more often than the control group patients and thus improved over the four weeks with no interaction between weeks and groups |
| Harm                        | No description   | No description   |
| Conclusion                  | Those who participated in animal-assisted therapy experienced statistically significant changes in depression and generalized self-efficacy. Although the changes were not significantly different from those in the control group, more participants in the intervention could be beneficial for subgroups of clients and act as a useful supplement within mental health care  | These data suggest that AAT plays an important role in enhancing the benefits of conventional therapy and demonstrates the benefit of including a non-AAT group for comparison. The study also demonstrates the importance of using longitudinal, repeated measure designs. Previous studies may have failed to find significant effects because they were restricted to shorter intervals for measuring outcomes                    |
| Trial registration          | No description   | No description   |
| Fund                        | A grant from the Research Council of Norway, and Agricultural Agreement  | No description   |
| Cost of intervention        | No description   | No description   |

**Table 3** International classification of target diseases in each article.

| Chapter | ICD code     | Classification  | Reference no. (detail ICD code)   |
|---------|--------------|---|---|
| 1       | A00-B99      | Certain infectious and parasitic diseases   |   |
| 2       | C00-D48      | Neoplasms   | 13 (the unidentified due to many site of cancer)  |
| 3       | D50-D89      | Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism |   |
| 4       | E00-E90      | Endocrine, nutritional and metabolic diseases   |   |
| 5       | F00-F99      | Mental and behavioral disorders   | 12,19–20 (F20), 15,21 (F30-33), 18 (the unidentified due to including many geriatric diseases), 22 (F10-19) |
| 6       | G00-G99      | Diseases of the nervous system  |   |
| 7       | H00-H59      | Diseases of the eye and adnexa  |   |
| 8       | H60-H95      | Diseases of the ear and mastoid process   |   |
| 9       | I00-I99      | Diseases of the circulatory system  | 14 (I50.1)  |
| 10      | J00-J99      | Diseases of the respiratory system  |   |
| 11      | K00-K93      | Diseases of the digestive system  |   |
| 12      | L00-L99      | Diseases of the skin and subcutaneous tissue  |   |
| 13      | M00-M99      | Diseases of the musculoskeletal system and connective tissue  |   |
| 14      | N00-N99      | Diseases of the genitourinary system  |   |
| 15      | O00-O99      | Pregnancy, childbirth and the puerperium  |   |
| 16      | P00-P96      | Certain conditions originating in the perinatal period  |   |
| 17      | Q00-Q99      | Congenital malformations, deformations and chromosomal abnormalities                                |   |
| 18      | R00-R99      | Symptoms, signs and abnormal clinical and laboratory finding not elsewhere classified               |   |
| 19      | S00-T98      | Injury, poisoning and certain other consequences of external causes                                 | 16 (T90-93)   |
| 20      | V00-Y98      | External causes of morbidity and mortality  |   |
| 21      | Z00-Z99      | Factors influencing health status and contact with health services                                  |   |
| 22      | U00-U99      | Code for special purpose  |   |
| —       | Unidentified | Because many illnesses were mixed, we could not identify it.  | 17  |

A unique study was performed to examine potential changes in mental health in people with clinical depression who were working with farm animals as the only task on a farm.<sup>21</sup> The intervention consisted of work and interaction with farm animals twice a week for 12 weeks. Those who participated in animal-assisted therapy experienced statistically significant changes in depression and generalized self-efficacy. Additionally, more participants in the intervention could have been beneficial for the subgroups of clients and served as a useful supplement within mental health care, although these changes were not significantly different from those in the control group.

A study evaluated whether patients such as those with a mental illness diagnosis as well as a history of alcohol/drug abuse or other addictive behaviors in the AAT group would show a greater increase in observed appropriate social behaviors than patients in the control group.<sup>22</sup> AAT patients interacted more with other patients. Similarly, there was a main effect that lasted for weeks, with improvement in scores over time but no interaction between weeks and groups. There was a similar finding for

the AAT group; patients smiled and showed pleasure significantly more often than the control group and thus improved over four weeks, with no interaction between weeks and groups.

### Quality assessment

We evaluated 11 items from the Cochrane's criteria list in more detail (Table 4). Inter-rater reliability metrics for the quality assessment indicated substantial agreement for all 121 items (percentage agreement 97% and  $k=0.939$ ).

This assessment evaluated the quality of how the main findings of the study were summarized in the written report. In general, there was a remarkable lack of execution and/or description in the concealment, blinding, and intention-to-treatment (ITT) analysis. The items for which the description was lacking (very poor; <50%) in many studies were as follows (present ratio; %): "Was the treatment allocation concealed?" (45%); "Was the patient blinded to the intervention?" (40%); "Was the care provider blinded to the intervention?" (27%); "Was the outcome assessor blinded



**Table 4** Evaluation of the quality of methodology for each article.

| No                        | Criteria list   | Reference no. |     |     |     |     |     |     |     |     |     |     | Present description |          |
|---------------------------|---|---------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---------------------|----------|
|                           |   | 12            | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  | 21  | 22  | No/11               | Rate (%) |
| 1                         | Was the method of randomization adequate?   | ?             | y   | y   | y   | y   | y   | ?   | y   | n   | y   | ?   | 7                   | 64%      |
| 2                         | Was the treatment allocation concealed?   | ?             | n   | ?   | y   | y   | y   | y   | y   | ?   | n   | ?   | 5                   | 45%      |
| 3                         | Were the groups similar at baseline regarding the most important prognostic indicators? | y             | y   | y   | y   | y   | y   | y   | y   | y   | y   | y   | 11                  | 100%     |
| 4                         | Was the patient blinded to the intervention?  | ?             | n   | ?   | y   | y   | y   | n   | n   | n   | n   | y   | 4                   | 40%      |
| 5                         | Was the care provider blinded to the intervention?                                      | ?             | n   | n   | y   | ?   | ?   | y   | n   | n   | n   | y   | 3                   | 27%      |
| 6                         | Was the outcome assessor blinded to the intervention?                                   | ?             | ?   | ?   | n   | ?   | n   | ?   | y   | y   | n   | y   | 3                   | 27%      |
| 7                         | Were cointerventions avoided or similar?  | y             | n   | y   | y   | y   | y   | y   | ?   | ?   | y   | y   | 8                   | 73%      |
| 8                         | Was the compliance acceptable in all groups?  | y             | y   | y   | y   | y   | y   | y   | y   | ?   | y   | y   | 10                  | 91%      |
| 9                         | Was the drop-out rate described and acceptable?   | y             | y   | y   | y   | n   | n   | y   | y   | y   | n   | y   | 8                   | 73%      |
| 10                        | Was the timing of the outcome assessment in all groups similar?                         | y             | y   | y   | y   | y   | y   | y   | y   | y   | y   | y   | 11                  | 100%     |
| 11                        | Did the analysis include an intention-to-treat analysis?                                | n             | n   | y   | y   | y   | n   | n   | ?   | n   | y   | y   | 5                   | 45%      |
| Present description no/11 |   | 5             | 5   | 7   | 10  | 8   | 7   | 7   | 7   | 4   | 6   | 9   | —                   | —        |
| Rate (%)                  |   | 45%           | 45% | 64% | 91% | 73% | 64% | 64% | 64% | 36% | 55% | 82% | —                   | —        |

y, yes; n, no; ?, do not know or unclear; n/a, not applicable.

to the intervention?" (27%); and "Did the analysis include an ITT analysis?" (36%).

### Meta-analysis

There were three RCTs on schizophrenia and two RCTs on depression. We could not perform a meta-analysis because of heterogeneity by difference of outcome measurement and intervention method (e.g., in dog, and in dog or cat).

### Adverse events

Two studies reported no adverse events,<sup>13,19</sup> and one study described three patients who were afraid of dogs and did not participate in the intervention.<sup>12</sup> There were no descriptions about adverse events in the other eight studies<sup>14–18,20–22</sup> (Table 2).

### Costs of intervention

Two studies<sup>13,16</sup> described information about the cost of intervention (Table 2). Johnson et al. showed that dog visits

were no more costly than human visits because all organizations provide dog visits on a volunteer basis.<sup>13</sup> Allen et al. showed that the total calculated costs of initial canine training was \$10,000, lost investment income on initial training costs was 5% per annum compounded quarterly, animal maintenance was \$1000 per year, the expected canine service period was 8 years, and paid human assistance ranged from \$8 to \$12 per hour.

### Discussion

This is the first SR of the cure effectiveness of ATT based on RCTs. Our study is unique because it summarized the evidence for each target disease according to ICD-10 classification. We assume that this study will be helpful to researchers who want to understand the effect of ATT comprehensively, and it could provide indispensable information for the organization that is going to make the guidelines according to each disease.

Among the 11 RCTs that were identified, target diseases and/or symptoms included schizophrenia, depression, cancer, advanced heart failure, severe ambulatory

disability, older adults admitted to skilled rehabilitation units, elderly persons with chronic psychiatric, medical, and neurologic conditions, and a mental illness diagnosis, as well as a history of alcohol/drug abuse or other addictive behaviors, and intervention methods included various approaches such as dog, dolphin, bird, cat, cow, rabbit, ferret, and guinea pig.

### Tendency of target disease and outcome

The most commonly reported target diseases were "Mental and behavioral disorders (F10-20, 30-33, and unclear)",<sup>12,15,17-22</sup> and the effect of AAT on these diseases was improved mental health (e.g., anxiety and mood), QoL, and social behavior. The main reason given in these articles for improved mental health was that the feeling and memory of an animal allowed the patient to be comfortable, pleasant, and happy. For example, Le Roux and Kemp<sup>23</sup> reported the following narrative comments by participants: "we talked to each other about the dog", "visits from the dog made me think about my own dog when I was young", and "at night I think about Pietie (the dog) and I smile". In studies about the effects of AAT on anxiety, discomfort, fear, and pain, AAT has been variably applied as an accessory treatment for persons with addictions such as alcohol/drug abuses<sup>22</sup> and as evasion of direct discomfort for undergoing medical treatment for cancer.<sup>13</sup>

The other reported target diseases were "Diseases of the circulatory system (I50.1)"<sup>14</sup> and "Injury, positioning, and certain other consequences of external causes (T90-93)".<sup>16</sup> The former evaluated hemodynamic parameters, cardiac index, and neurohormone levels as primary outcomes. The latter assessed psychological variables such as well-being, internal locus of control, and community integration. Improvements seen in these studies were mainly due to effects of buffering a person's reactivity to mental stressor<sup>24,25</sup> and providing a sense of comfort and safety, and diverting attention away from the immediate stressors to a more pleasurable and calming interaction.<sup>26</sup>

### Validity of overall evidence based on quality assessment

#### Overall evidence and quality assessment

The Cochrane's list is the most important tool related to the internal validity of trials. In this SR, there were serious problems with the conduct and reporting of the target studies. Our review especially detected omissions of the following descriptions: method used to generate concealment, blinding, and ITT analysis. Descriptions of these items were lacking (very poor; <50%) in many studies.

In the Cochrane Review,<sup>27</sup> the eligibility criteria for a meta-analysis are strict, and for each article, heterogeneity and low quality of reporting must first be excluded. We could not perform a meta-analysis. Due to poor methodological and reporting quality and heterogeneity, there was insufficient evidence in the studies of AAT, and we are therefore unable to offer clearly any conclusions about the effects of AAT based on RCTs.

Moreover, the CONSORT 2010<sup>28</sup> and the CONSORT for non-pharmacological trials checklists<sup>29</sup> are relatively new, but it

was shown that the study protocol description and implementation for AAT studies should be subjected to these checklists.

#### Overall evidence

Most importantly, a specific adverse effect or harmful phenomenon such as allergy or fear for animals was not clearly observed overall, although we should consider the limitations and biases of these findings in the context of AAT patients/participants who are likely to enjoy animals. In other words, a person who dislikes animals will refuse intervention from the beginning.

The results of this study suggested that the RCTs conducted have been of relatively low quality. Only two RCTs were evaluated as "good description (80-100%)".<sup>15,22</sup> AAT with dolphins is an effective treatment for mild to moderate depression, and is based on a holistic approach through interaction with animals in nature.<sup>15</sup> AAT also plays an important role in enhancing the benefits of conventional therapy in psychiatric rehabilitation.<sup>22</sup> Furthermore, AAT may have positive effects on schizophrenia and/or serious mental disorders. We assume that the direct effects of AAT are generally improvement of mental health, elimination of the sense of isolation, and an improvement in QoL.

Although further accumulation of RCT data is necessary, AAT may be effective treatment for the following diseases and symptoms: cancer and/or advanced life-limiting illnesses that affect mental state and QoL, impaired circulatory function with mechanical assistance, autistic spectrum disorders involving communicative skills, and self-reported outcomes for hospitalized patients and other patients with various clinical conditions.

#### Future research agenda to build evidence

Table 5 shows the future research agenda for studies of the cure effect by AAT. Researchers should use the appropriate checklists for research design and intervention methods, which would lead to improvement in the quality of the study, and would contribute to the accumulation of evidence. Researchers should also present not only efficacy data, but also a description of any adverse events or harmful phenomena and the reasons for withdrawals and non-participation. Many studies in this review did not describe these factors.

As a gradual increase of intervention is necessary in cure and rehabilitation programs, it is easy to assign settings like "Stage" for the intervention, such as first stage and second stage. Therefore, we also expect to understand the results and detailed descriptions of "pragmatic trials"<sup>30</sup> as well as "explanatory trials" for the treatment effect by AAT.

Bowen et al.<sup>31</sup> suggested that public health is moving toward the goal of implementing evidence based intervention. But the feasibility of possible interventions, and whether comprehensive and multilevel evaluations are needed to justify them, must be determined. It is at least necessary to show the cost of such interventions. Introduction of an interventional method must be based on its cost-benefit, cost-effectiveness, and cost-utility.

In addition, AAT as an intervention is unique and completely different than pharmacological or traditional rehabilitation methods. Therefore, it may be necessary

**Table 5** Overall evidence and future research agenda to build evidence.

| Overall evidence in the present   | Research agenda   |
|---|---|
| After having premised study environment limited to the people who liked animals very much, AAT may be an effective treatment for mental and behavioral disorders such as depression, schizophrenia, and alcohol/drug addictions, and is based on a holistic approach, through interaction with animals in nature. | <ol style="list-style-type: none"> <li>1. Satisfactory description and methodology including the CONSORT 2010 and the CONSORT for nonpharmacological trials</li> <li>2. Description of the reason of participants refused (non-participation)</li> <li>3. Description of adverse effects (e.g., allergy, infection, bit, and fear) and withdrawals</li> <li>4. Description of intervention dose (if pragmatic intervention)</li> <li>5. Description of cost</li> <li>6. Development of the original check-list for AAT</li> </ol> |

to add some original items like herbal intervention,<sup>32</sup> acupuncture,<sup>33</sup> traditional Chinese medicine<sup>34</sup> and balneotherapy<sup>35</sup> to the CONSORT 2010 checklist as alternative and/or complementary medicines.

#### Strength and limitations

This review had several strengths: (1) the methods and implementation registered high on the PROSPERO database; (2) it was a comprehensive search strategy across multiple databases with no data restrictions; (3) there were high agreement levels for quality assessment of articles; and (4) it involved detailed data extraction to allow for collecting all articles' content into a recommended structured abstract. The conduct and reporting of this review also aligned with the PRISMA statement<sup>36</sup> for transparent reporting of SRs and meta-analyses.

This review had several limitations that should be acknowledged. Selection criteria were common across studies, as described above; however, bias remained due to differences in eligibility for participation in each study. Publication bias was a factor. Although there was no linguistic restriction in the eligibility criteria, we searched studies with only English and Japanese key words. In addition, this review reported on a relatively small and heterogeneous sample of studies. Moreover, we could not follow standard procedures for estimating the effects of moderating variables.

#### Conclusion

In a study environment limited to the people who like animals, AAT may be an effective treatment for mental and behavioral disorders such as depression, schizophrenia, and alcohol/drug addictions, and is based on a holistic approach through interaction with animals in nature.

To most effectively assess the potential benefits of AAT, it will be important for further research to utilize and describe (1) RCT methodology when appropriate, (2) the reasons for non-participation, (3) intervention dose, (4) adverse effects and withdrawals.

#### Contributors

TH, JK, SP, SO, HO, SH, HP, TO, and TA conceived the study and take responsibility for the summary of included studies and data extraction. KT and YM are the guarantors. HK and SO designed the study. HO, SP, TH and HK assessed the quality of articles. All authors critically described the manuscript for important intellectual content.

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#### Conflict of interest statement

None declared.

#### Ethical approval

Not required.

#### Data sharing

No additional data available.

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## Appendix. References to studies excluded in this review

| Exclusion no. | Author. Journal (year)   | Title   | Reason of exclusion             |
|---------------|--|---|---------------------------------|
| 1             | Nothing  | A study of animal-assisted therapy and weekday placement of a social therapy  | Not acceptable                  |
| 2             | Livingston G, et al. (nothing)   | The effectiveness and cost-effectiveness of sensory, psychological and behavioral interventions for managing agitation in older adults with dementia                      | Ongoing                         |
| 3             | Herrero P, et al. <i>Clinical Rehabilitation</i> (2013)                                | Study of the therapeutic effects of a hippotherapy simulator in children with cerebral palsy: a stratified single-blind randomized controlled trial                       | Not animal-assisted therapy     |
| 4             | Cano A. (2013)   | Randomized control trial of an animal-assisted intervention with adjudicated youth  | Not detected                    |
| 5             | Iammateo N, et al. (2013)  | Animal therapy in a pediatric setting   | Not detected                    |
| 6             | Beck CE, et al. <i>The Army Medical Department Journal</i> (2012)                      | The effects of animal-assisted therapy on wounded warriors in an occupational therapy life skills program   | Not randomized controlled trial |
| 7             | Rhodes RE, et al. <i>Preventive Medicine</i> (2012)                                    | Pilot study of a dog walking randomized intervention: Effects of a focus on canine exercise   | Not curative effect             |
| 8             | Berget B, et al. <i>Ann Ist Sanita</i> (2011)  | Animal-assisted therapy with farm animals for persons with psychiatric disorders  | Not randomized controlled trial |
| 9             | Moretti F, et al. <i>Psychogeriatrics</i> (2011)                                       | Pet therapy in elderly patients with mental illness   | Not randomized controlled trial |
| 10            | SilvaBorges, et al. <i>Arq Neuropsiquiatr</i> (2011)                                   | Therapeutic effects of a horse riding simulator in children with cerebral palsy   | Not animal therapy              |
| 11            | Kumasaka T, et al. <i>Journal of the Japanese Association of Rural Medicine</i> (2010) | Study of effectiveness of animal-assisted therapy for patients with mental illness in nursing support (in Japanese)   | Not curative effect             |
| 12            | Tsai CC, et al. <i>Anthrozoos</i> (2010)   | The effect of animal-assisted therapy on stress responses in hospitalized children  | Not curative effect             |
| 13            | Coakley AB, et al. <i>Complementary Therapies in Clinical Practice</i> (2009)          | Creating a therapeutic and healing environment with a pet therapy program   | Not randomized controlled trial |
| 14            | Martin C, et al. <i>Anthrozoos</i> (2009)  | Animal-assisted therapy in the treatment of substance dependence  | Not randomized controlled trial |
| 15            | Braun C, et al. <i>Complementary Therapies in Clinical Practice</i> (2009)             | Animal-assisted therapy as a pain relief intervention for children  | Not randomized controlled trial |
| 16            | LeRoux MC, et al. <i>Jornal compilation</i> (2009)                                     | Effect of a companion dog on depression and anxiety levels of elderly residents in a long-term care facility  | Not curative effect             |
| 17            | Berger AM, et al. (2009)   | Effects of pet therapy on pain in cancer patients   | Not published yet               |
| 18            | Toukhsati S, et al. (2009)   | The use of alternative therapies to treat geriatric depression  | Submit preparation at present   |
| 19            | Parish-Plass N. <i>Clin Child Psychology and Psychiatry</i> (2008)                     | Animal-assisted therapy with children suffering from insecure attachment due to abuse and neglect: a method to lower the risk of intergenerational transmission of abuse? | Not randomized controlled trial |
| 20            | Banks MR, et al. <i>J Am Med Dir Assoc</i> (2008)                                      | Animal-assisted therapy and loneliness in nursing homes: use of robotic versus living dogs  | Not curative effect             |
| 21            | Cole KM, et al. <i>American Journal of Critical Care</i> (2007)                        | Animal-assisted therapy in patients hospitalized with heart failure   | Reduplication                   |
| 22            | Prothmann A, et al. <i>Anthrozoos</i> (2006)   | Dogs in child psychotherapy: effects on state of mind   | Not randomized controlled trial |
| 23            | Motooka M, et al. <i>MJA</i> (2006)  | Effect of dog-walking on autonomic nervous activity in senior citizens  | Not curative effect             |

Appendix (*Continued*)

| Exclusion no. | Author. Journal (year)   | Title  | Reason of exclusion             |
|---------------|--|--|---------------------------------|
| 24            | Colombo G, et al. <i>Archives of Gerontology and Geriatrics</i> (2006)                       | Pet therapy and institutionalized elderly: A study on 144 cognitively unimpaired subjects                      | Not curative effect             |
| 25            | Anonymous (memo). <i>Harvard Men's Health Watch</i> (2006)                                   | Dolphins for the doldrums?   | Not original article            |
| 26            | Nathans-Barel I, et al. <i>Psychother Psychosom</i> (2005)                                   | Animal-assisted therapy ameliorates anhedonia in schizophrenia patients  | Not randomized controlled trial |
| 27            | Cole KM. <i>Circulation</i> (2005)   | Innovative interventions to improve management and outcomes in heart disease                                   | Not curative effect             |
| 28            | Stasi MF, et al. <i>Arch. Gerontol. Geriatr. Suppl.</i> (2004)                               | Pet-therapy: a trial for institutionalized frail elderly patients  | Not randomized controlled trial |
| 29            | Kovacs Z, et al. <i>Clinical Rehabilitation</i> (2004)                                       | Animal-assisted therapy for middle-aged schizophrenic patients living in a social institution. A pilot study   | Not randomized controlled trial |
| 30            | Bouchard F, et al. (2004)  | A magical dream: a pilot project in animal-assisted therapy in pediatric oncology                              | Not original article            |
| 31            | Richeson NE. <i>American Journal of Alzheimer's Disease and Other Dementias</i> (2003)       | Effects of animal-assisted therapy on agitated behaviors and social interactions of older adults with dementia | Not randomized controlled trial |
| 32            | Barker SB, et al. <i>The Journal of ECT</i> (2003)   | Effects of animal-assisted therapy on patients' anxiety, fear, and depression before ECT                       | Not randomized controlled trial |
| 33            | Johnson RA, et al. <i>American Behavioral Scientist</i> (2003)                               | Human-animal interaction: A complementary/Alternative medical (CAM) intervention for cancer patients           | Not curative effect             |
| 34            | Martin F, et al. <i>Western Journal of Nursing Research</i> (2002)                           | Animal-assisted therapy for children with pervasive developmental disorders                                    | Not randomized controlled trial |
| 35            | Banks MR, et al. <i>Medical sciences</i> (2002)  | The effects of animal-assisted therapy on loneliness in an elderly population in long-term care facilities     | Not curative effect             |
| 36            | Kaminski M, et al. <i>Children's Health Care</i> (2002)                                      | Play and pets: The physical and emotional impact of child-life and pet therapy on hospitalized children        | Not curative effect             |
| 37            | Kanamori M, et al. <i>American Journal of Alzheimer's Disease and Other Dementias</i> (2001) | A day care program and evaluation of animal-assisted therapy (ATT) for the elderly with senile dementia        | Not randomized controlled trial |
| 38            | Kingwell BA, et al. <i>Clinical Autonomic Research</i> (2001)                                | Presence of a pet dog and human cardiovascular responses to mild mental stress                                 | Not curative effect             |
| 39            | Hall PL, et al. <i>British Journal of Nursing</i> (2000)                                     | Pets as therapy: effects on social interaction in long-stay psychiatry   | Not randomized controlled trial |
| 40            | Bernstein PL, et al. <i>Anthrozoos</i> (2000)  | Animal-assisted therapy enhances resident social interaction and initiation in long-term care facilities       | Not curative effect             |
| 41            | Panzer-Koplow S, et al. <i>Bell and Howell Information and Learning</i> (2000)               | Effects of animal-assisted therapy on depression and morale among nursing home residents                       | Not curative effect             |
| 42            | Churchill M, et al. <i>Journal of Psychosocial Nursing</i> (1999)                            | Using a therapy dog to alleviate the agitation and desocialization of people with Alzheimer's disease          | Not randomized controlled trial |
| 43            | Hansen KM, et al. <i>Anthrozoos</i> (1999)   | Companion animals alleviating distress in children   | Not randomized controlled trial |
| 44            | Counsell CM. <i>Sc. In Nursing</i> (1997)  | Animal assisted therapy and the individual with spinal cord injury   | Not randomized controlled trial |
| 45            | Banman JK, et al. <i>The Journal of Pastoral Care</i> (1995)                                 | Animal-assisted therapy with adolescents in a psychiatric facility   | Not original article            |
| 46            | Folse EB, et al. <i>Anthrozoos</i> (1994)  | Animal-assisted therapy and depression in adult college students   | Not randomized controlled trial |



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# Effectiveness of music therapy: a summary of systematic reviews based on randomized controlled trials of music interventions

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**Objective:** The objective of this review was to summarize evidence for the effectiveness of music therapy (MT) and to assess the quality of systematic reviews (SRs) based on randomized controlled trials (RCTs).

**Study design:** An SR of SRs based on RCTs.

**Methods:** Studies were eligible if they were RCTs. Studies included were those with at least one treatment group in which MT was applied. We searched the following databases from 1995 to October 1, 2012: MEDLINE via PubMed, CINAHL (Cumulative Index of Nursing and Allied Health Literature), Web of Science, Global Health Library, and Ichushi-Web. We also searched all Cochrane Database and Campbell Systematic Reviews up to October 1, 2012. Based on the *International Classification of Diseases*, 10th revision, we identified a disease targeted for each article.

**Results:** Twenty-one studies met all inclusion criteria. This study included 16 Cochrane reviews. As a whole, the quality of the articles was very good. Eight studies were about “Mental and behavioural disorders (F00-99)”; there were two studies on “Diseases of the nervous system (G00-99)” and “Diseases of the respiratory system (J00-99)”; and there was one study each for “Endocrine, nutritional and metabolic diseases (E00-90)”, “Diseases of the circulatory system (I00-99)”, and “Pregnancy, childbirth and the puerperium (O60)”. MT treatment improved the following: global and social functioning in schizophrenia and/or serious mental disorders, gait and related activities in Parkinson’s disease, depressive symptoms, and sleep quality.

**Conclusion:** This comprehensive summary of SRs demonstrated that MT treatment improved the following: global and social functioning in schizophrenia and/or serious mental disorders, gait and related activities in Parkinson’s disease, depressive symptoms, and sleep quality. MT may have the potential for improving other diseases, but there is not enough evidence at present. Most importantly, no specific adverse effect or harmful phenomenon occurred in any of the studies, and MT was well tolerated by almost all patients.

**Keywords:** ICD-10, schizophrenia, mental disorders, Parkinson’s disease, depression, sleep

## Article focus

Although many studies have reported the effects of music therapy (MT), there is no review of systematic reviews (SRs) based on randomized controlled trials (RCTs).

## Key messages

The key messages of this paper are as follows.

1. This is the first SR of SRs of the effectiveness of cure based on music interventions in studies with RCT designs.

2. Our study is unique because it summarizes the evidence for each target disease according to the *International Classification of Diseases*, revision 10 (ICD-10).
3. We propose the future research agenda for studies on the treatment effect of MT.

## Strength and limitation of this study

The strengths of this study are as follows: 1) the methods and implementation registered high on the PROSPERO database; 2) it was a comprehensive search strategy across multiple databases with no data restrictions; and 3) there were high agreement levels for quality assessment of articles.

This study has three limitations. Firstly, some selection criteria were common across studies; however, the bias remained due to differences in eligibility for participation in each original RCT. Secondly, publication bias was a limitation. Lastly, since this review focused on summarizing the effects of MT for each disease, we did not describe all details on quality and quantity, such as type of MT, frequency of MT, and time on MT.

## Introduction

MT is widely utilized for treatment of and assistance in various diseases. In one literature review, the authors found seven case reports/series and seven studies on MT for multiple sclerosis patients. The results of these studies as well as the case reports demonstrated patients' improvements in the domains of self-acceptance, anxiety, and depression.<sup>1</sup> Another review examined the overall efficacy of MT in children and adolescents with psychopathology, and examined how the size of the effect of MT is influenced by the type of pathology, the subject's age, the MT approach, and the type of outcome.<sup>2</sup> The analysis revealed that MT had a medium to large positive effect (effect size =0.61) on clinically relevant outcomes that was statistically highly significant ( $P<0.001$ ) and statistically homogeneous. A more recent SR assessed the effects of musical elements in the treatment of individuals with acquired neurological disorder.<sup>3</sup> The results showed that mechanisms of recovery remained unclear: two of the three studies that examined mechanisms of recovery via neuro-imaging techniques supported the role of the right hemisphere, but reports were contradictory, and exact mechanisms of recovery remained indefinable. An interesting meta-analysis described results that justified strong consideration for the inclusion of neonatal intensive care unit (NICU) MT protocols in best practice standards for NICU treatment of preterm infants: examples of these therapies were listening to music for pacification, music reinforcement of sucking/

feeding ability, and music as a basis for pacification during multilayered, multimodal stimulation.<sup>4</sup>

Examining the curative effects of MT has unique challenges. A review article by Nilsson<sup>5</sup> described how nurses face many challenges as they care for the needs of hospitalized patients, and that they often have to prioritize physical care over the patient's emotional, spiritual, and psychological needs. In clinical practice, music intervention can be a tool to support these needs by creating an environment that stimulates and maintains relaxation, wellbeing, and comfort. Furthermore, the Nilsson article<sup>5</sup> presented a concrete recommendation for music interventions in clinical practice, such as "slow and flowing music, approximately 60 to 80 beats per minute", "nonlyrical", "maximum volume level at 60 dB", "patient's own choice, with guidance", "suitable equipment chosen for the specific situation", "a minimum duration of 30 minutes in length", and "measurement, follow up, and documentation of the effects". In addition, MT has been variably applied as both a primary and accessory treatment for persons with addictions to alcohol, tobacco, and other drugs of abuse. However, an SR<sup>6</sup> described that no consensus exists regarding the efficacy of MT as treatment for patients with addictions.

On the other hand, music may be considered an adjunctive therapy in clinical situations. Music is effective in reducing anxiety and pain in children undergoing medical and dental procedures.<sup>7</sup> A meta-analysis confirmed that patients listening to music during colonoscopy, which is now the recommended method for screening colon cancer, was an effective method for reducing procedure time, anxiety, and the amount of sedation. More importantly, no harmful effects were observed for all the target studies.<sup>8</sup> The usual practice following a cervical cancer abnormal cervical smear is to perform a colposcopy. However, women experience high levels of anxiety and negative emotional responses at all stages of cervical screening. An SR of RCTs evaluated interventions designed to reduce anxiety levels during colposcopic examination. Psychosexual dysfunction (ie, anxiety) was reduced by playing music during colposcopy.<sup>9</sup>

The definition of musical intervention is complex, but the literature describes two broad categories of music interventions: music medicine and MT.<sup>10</sup> Music medicine is the use of passive listening (usually involving prerecorded music) as implemented by medical personnel. In music medicine studies, the subject's preference for the music used may be considered by having him or her select from a variety of tapes. Alternately, some studies use predefined

music stimuli that do not take the subject's preferences into account. Furthermore, there is generally no attempt by the researcher to form a therapeutic relationship with the subject, and there is no process involved in the music treatment. In essence, music medicine studies usually allow one to assess the effects of music alone as a therapeutic intervention. In contrast, MT interventions most often involve a relationship between the therapist and the subject, the use of live music (performed or created by the therapist and/or patient), and a process that includes assessment, treatment, and evaluation. Patient preference for the music is usually a consideration in MT studies.

We were interested in evaluating the curative effect of MT according to diseases because many of the primary studies and review articles of much MT have reported results in this way. In particular, we wanted to focus on all cure and rehabilitation effects using the ICD-10. It is well known in research design that evidence grading is highest for an SR with meta-analysis of RCTs. Although many studies have reported the effects of MT, there is no review of SRs based on RCTs. The objective of this review was to summarize evidence for the effectiveness of MT and to assess the quality of SRs based on RCTs of these therapies.

## Methods

### Criteria for considering studies included in this review

#### Types of studies

Studies were eligible if they were SRs (with or without a meta-analysis) based on RCTs.

#### Types of participants

There was no restriction on patients.

#### Types of intervention and language

Studies included were those with at least one treatment group in which MT was applied. The definition of MT is complex, but in this study, any kind of MT (not only music appreciation but also musical instrument performance and singing, for example) was permitted and defined as an intervention. Studies had to include information on the use of medication, alternative therapies, and lifestyle changes, and these had to be comparable among groups. There was no restriction on the basis of language.

#### Types of outcome measures

We focused on all cure and rehabilitation effects using the ICD-10.

## Search methods for studies identification

### Bibliographic database

We searched the following databases from 1995 to October 1, 2012: MEDLINE via PubMed, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Web of Science, Ichushi Web (in Japanese), the Global Health Library (GHL), and the Western Pacific Region Index Medicus (WPRIM). The International Committee of Medical Journal Editors (ICMJE) recommended uniform requirements for manuscripts submitted to biomedical journals in 1993. We selected articles published (that included a protocol) since 1995, because it appeared that the ICMJE recommendation had been adopted by the relevant researchers and had strengthened the quality of the reports.

We also searched the Cochrane Database of Systematic Reviews (Cochrane Reviews), the Database of Abstracts of Reviews of Effects (Other Reviews), the Cochrane Central Register of Controlled Trials (Clinical Trials or CENTRAL), the Cochrane Methodology Register (Methods Studies), the Health Technology Assessment Database (Technology Assessments), the NHS Economic Evaluation Database (Economic Evaluations), About The Cochrane Collaboration databases (Cochrane Groups), the Campbell Systematic Reviews (the Campbell Collaboration), and the All Cochrane, up to October 1, 2012.

All searches were performed by two specific searchers (hospital librarians) who were qualified in medical information handling, and who were experienced in searches of clinical trials.

### Search strategies

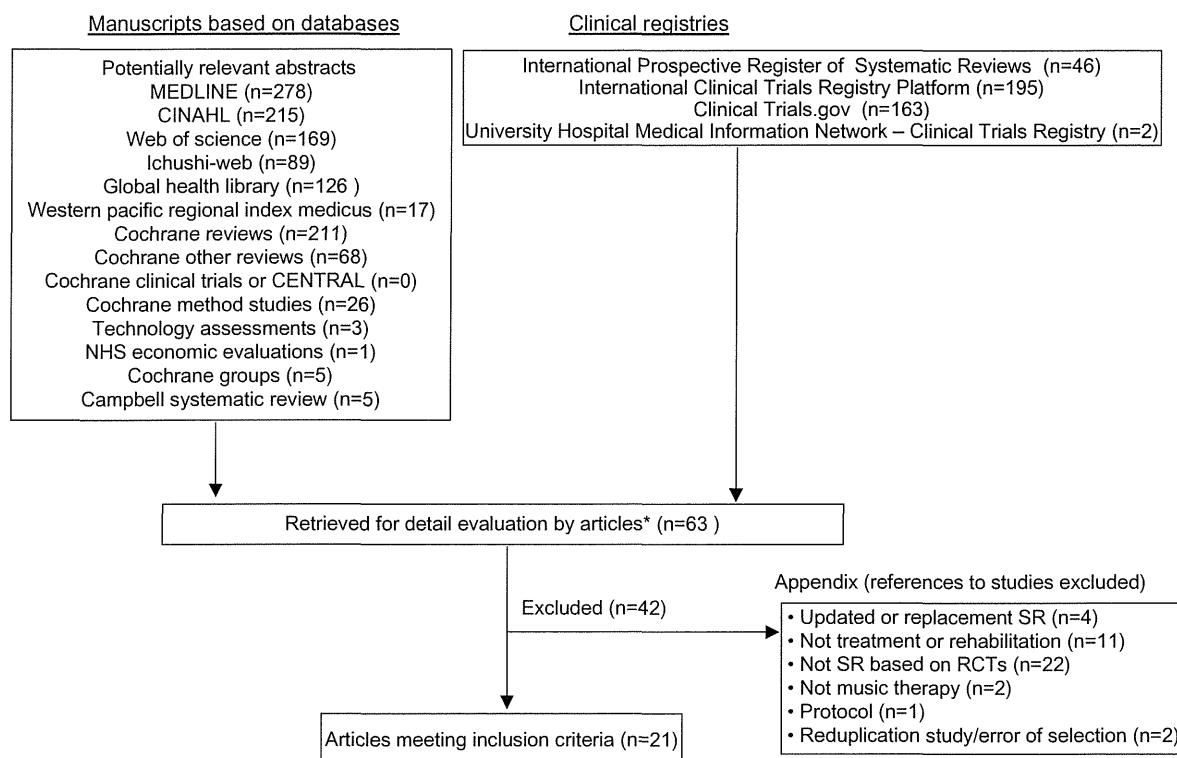
The special search strategies contained the elements and terms for MEDLINE, CINAHL, Web of Science, Ichushi Web, GHL, WPRIM, and All Cochrane databases (Figure 1 and Table 1). Only keywords about intervention were used for the searches. First, titles and abstracts of identified published articles were reviewed in order to determine the relevance of the articles. Next, references in relevant studies and identified SRs were screened.

### Registry checking

We searched the International Clinical Trials Registry Platform (ICTRP), Clinical Trials.gov, and the University Hospital Medical Information Network – Clinical Trials Registry (UMIN-CTR), up to October 1, 2012.

ICTRP in the WHO Registry Network meet specific criteria for content, quality and validity, accessibility, unique





**Figure 1** Flowchart of trial process.

**Note:** \*Reduplication.

**Abbreviations:** CINAHL, Cumulative Index of Nursing and Allied Health Literature; CENTRAL, Cochrane Central Register of Controlled Trials; RCT, randomized controlled trial; SR, systematic review.

identification, technical capacity, and administration. Primary registries meet the requirements of the ICMJE. Clinical Trials.gov is a registry of federally and privately supported clinical trials conducted in the US and around the world. UMIN-CTR is a registry of clinical trials conducted in Japan and around the world.

### Handsearching and reference checking

We handsearched abstracts published on MT in relevant journals in Japan. We checked the references of included studies for further relevant literature.

## Review methods

### Selection of trials

To make the final selection of studies for the review, all criteria were applied independently by four authors (ie, TH, JK, SJP, and TA) to the full text of articles that had passed the first eligibility screening (Figure 1). Disagreements and uncertainties were resolved by discussion with other authors (ie, HK, KT, and YM).

Studies were selected when 1) the design was an SR based on RCTs and 2) one of the interventions was a form of MT. Protocols without results were excluded, and we included

only completed studies. Cure and rehabilitation effects were used as a primary outcome measure. Trials that were excluded are presented with reasons for exclusion (Table S1).

### Quality assessment of included studies

To ensure that variation was not caused by systematic errors in the study design or execution, eleven review authors (HP, MY, HO, SO, SJP, TO, KT, TH, SH, JK, and HK) independently assessed the quality of the articles. A full quality appraisal of these papers was made using the combined tool based on the AMSTAR checklist<sup>11</sup> developed to assess the methodological quality of SRs.

Each item was scored as “present” (Yes), “absent” (No), “unclear or inadequately described” (Can not answer), or “not applicable” (n/a). Depending on the study design, some items were not applicable. The “n/a” was excluded from calculation for quality assessment. We displayed the percentage of descriptions that were present on all items for the quality assessment of articles. Then, based on the percentage of risk of poor methodology and/or bias, each item was assigned to one of the following categories: good description (80%–100%), poor description (50%–79%), or very poor description (0%–49%).

**Table 1** The special search strategies**1. MEDLINE**

- #1 Search music[all]
- #2 Search musical[all]
- #3 Search music[MeSH]
- #4 Search "Music Therapy"[Mesh]
- #5 Search song[Text Word]
- #6 Search songs[Text Word]
- #7 Search singing[Text Word]
- #8 Search (((((#1) OR #2) OR #3) OR #4) OR #5) OR #6) OR #7
- #9 Search systematic[sb]
- #10 Search Meta-Analysis[Publication type]
- #11 Search "Meta-Analysis as Topic"[MeSH Terms]
- #12 Search Meta-analysis\*[all]
- #13 Search Metaanalysis\*[all]
- #14 Search systematic review\*[all]
- #15 Search (((((#9) OR #10) OR #11) OR #12) OR #13) OR #14
- #16 Search (#8) AND #15
- #17 Search (#8) AND #15 Filters: Publication date from 1995/01/01

**2. CINHAL**

- #1 (TI music OR AB music) OR (TI musical OR AB musical) OR TX "music therap\*" OR MH music OR MH "music therapy"
- #2 (TI "song" OR AB "song") OR (TI "songs" OR AB "songs") OR (TI "singing" OR AB "singing") OR MH "singing"
- #3 MH "meta analysis" OR PT "meta analysis" OR TI "meta analy\*" OR AB "meta analysis"
- #4 MH "systematic review" OR PT "systematic review" OR TI "systematic review\*" OR AB "systematic review"
- #5 #1 or #2
- #6 #3 or #4
- #7 #5 and #6

**3. Web of Science**

- #1 (music\*) OR (music therap\*)
- #2 (song\*) OR (singing) NOT (song\*)
- #3 (meta analys\*) OR (systematic review\*)
- #4 #2 OR #1
- #5 #4 AND #3
- #6 #5 Article time span=1995-2012

**4. Ichushi Web**

- #1 (音楽療法/TH or 音楽療法/AL) or (音楽療法士/TH or 音楽療法士/AL) or 音楽/TH or 音楽/AL or ミュージック/AL or 歌唱/AL or (楽器/TH or 楽器/AL) or 演奏/AL
- #2 メタアナリシス/TH or メタアナリシス/AL or メタ分析/AL or (RD=メタアナリシス)
- #3 システマティックレビュー/TH or システマティックレビュー/AL or "systematic review"/AL
- #4 総説文献/TH or (文献研究/TH or 文献/AL) or レビュー/AL or (EBM/TH or EBM/AL)
- #5 #2 or #3 or #4
- #6 #1 and #5
- #7 (#6) and (DT=1995:2012 PT=会議録除く)

**5. GHL**

- (music or musical or singing) AND ("meta analysis" or meta-analysis or #systematic and review\*##)

**6. WPRIM**

- #1 All:music or music% or "music therap%"
- #2 Mesh Heading:Music/All Categories/All Subheadings
- #3 Mesh Heading:Music Therapy/All Categories/All Subheadings
- #4 Abstract:song? or singing

**Table 1 (Continued)**

- #5 Keywords:song? or singing
- #6 #5 or #4 or #3 or #2 or #1
- #7 MeSH Heading:Meta-Analysis/All Categories/All Subheadings
- #8 MeSH Heading:Meta-Analysis as Topic/All Categories/All Subheadings
- #9 All:meta-analy% or "meta analy%" or metaanaly%
- #10 All:"sistematic review" or "systematic review"
- #11 All:review%
- #12 #11 or #10 or #9 or #8 or #7
- #13 #12 and #6
- #14 #12 and #6 -Limits:1995-2012

**7. All Cochrane**

- #1 MeSH descriptor: [Music] explode all trees
- #2 MeSH descriptor: [Music Therapy] explode all trees
- #3 music\* (Word variations have been searched)
- #4 song\* or singing:ti,ab,kw (Word variations have been searched)
- #5 #1 or #2 or #3 or #4
- #6 MeSH descriptor: [Meta-Analysis] explode all trees
- #7 MeSH descriptor: [Meta-Analysis as Topic] explode all trees
- #8 "meta-analysis":pt (Word variations have been searched)
- #9 meta next analy\* (Word variations have been searched)
- #10 systematic next review\* (Word variations have been searched)
- #11 #6 or #7 or #8 or #9 or #10
- #12 #5 and #11 from 1995 (Word variations have been searched)

**8. Campbell Collaboration**

- music\* in "ALL text"

**9. ICTRP**

- music therapy\* OR music\* OR singing

**10. International Prospective Register of Systematic Review**

- music

**11. Clinical Trials. Gov**

- #1 music OR musical

**12. UMIN-CTR**

- 音楽 in 「自由記載語」

Disagreements and uncertainties were resolved by discussion with other authors (ie, KT and HK). Inter-rater reliability was calculated on a dichotomous scale using percentage agreement and Cohen's kappa coefficient ( $\kappa$ ).

**Summary of studies and data extraction**

Eleven review authors (HP, MY, HO, SO, SJP, TH, TO, SH, JK, KT, and HK) described the summary from each article based on the structured abstracts.<sup>12,13</sup>

**Benefit and harm**

The GRADE Working Group<sup>14</sup> reported that the balance between benefit and harm, quality of evidence, applicability, and the certainty of the baseline risk were all considered in judgments about the strength of recommendations. Adverse events for intervention were especially important information for researchers and users of clinical practice guidelines, and we presented this information with the description of each article.

(Continued)

**Table 2** A structured abstract of 21 systematic reviews

| Study                       | Title   | Aim/objective   | Data source/search strategy  | Study selection/selection criteria  |
|-----------------------------|---|---|--|---|
| Sinha et al <sup>17</sup>   | Auditory integration training and other sound therapies for autism spectrum disorders (ASD) | To determine the effectiveness of auditory integration therapy or other methods of sound therapy in individuals with autism spectrum disorders.   | For this update, we searched the following databases in September 2010: CENTRAL (2010, Issue 2), MEDLINE (1950 to September week 2, 2010), EMBASE (1980 to week 38, 2010), CINAHL (1937 to current), PsycINFO (1887 to current), ERIC (1966 to current), LILACS (September 2010) and the reference lists of published papers. One new study was found for inclusion. | Randomized controlled trials involving adults or children with autism spectrum disorders. Treatment was auditory integration therapy or other sound therapies involving listening to music modified by filtering and modulation. Control groups could involve no treatment, a waiting list, usual therapy, or a placebo equivalent. The outcomes were changes in core and associated features of autism spectrum disorders, auditory processing, QoL, and adverse events. |
| Mossler et al <sup>18</sup> | Music therapy for people with schizophrenia and schizophrenia-like disorders                | To review the effects of music therapy, or music therapy added to standard care, compared with “placebo” therapy, standard care or no treatment for people with serious mental disorders such as schizophrenia. | We searched the Cochrane Schizophrenia Group Trials Register (December 2010) and supplemented this by contacting relevant study authors, handsearching of music therapy journals, and manual searches of reference lists.  | All RCTs that compared music therapy with standard care, placebo therapy, or no treatment.  |

**Table 2** (Continued)

| Data extraction/data collection and analysis  | Main results   | The authors' conclusions   |
|---|--|--|
| <p>Two independent review authors performed data extraction. All outcome data in the included papers were continuous. We calculated point estimates and standard errors from paired <i>t</i>-test scores and post-intervention means. Meta-analysis was inappropriate for the available data.</p> <p>Studies were reliably selected, quality assessed, and data extracted. We excluded data where more than 30% of participants in any group were lost to follow-up. We synthesized non-skewed continuous endpoint data from valid scales using an SMD. If statistical heterogeneity was found, we examined treatment "dosage" and treatment approach as possible sources of heterogeneity.</p> | <p>We identified six RCTs of auditory integration therapy and one of Tomatis therapy, involving a total of 182 individuals aged 3–39 years. Two were cross-over trials. Five trials had fewer than 20 participants. Allocation concealment was inadequate for all studies. Twenty different outcome measures were used, and only two outcomes were used by three or more studies. Meta-analysis was not possible due to very high heterogeneity or the presentation of data in unusable forms. Three studies did not demonstrate any benefit of auditory integration therapy over control conditions. Three studies reported improvements at 3 months for the auditory integration therapy group based on the Aberrant Behavior Checklist, but they used a total score rather than subgroup scores, which is of questionable validity, and Veale's results did not reach statistical significance. Rimland 1995 also reported improvements at 3 months in the auditory integration therapy group for the Aberrant Behavior Checklist subgroup scores. The study addressing Tomatis therapy described an improvement in language with no difference between treatment and control conditions and did not report on the behavioral outcomes that were used in the auditory integration therapy trials.</p> <p>We included eight studies (total 483 participants). These examined effects of music therapy over the short-to medium-term (1–4 months), with treatment "dosage" varying from seven to 78 sessions. Music therapy added to standard care was superior to standard care for global state (medium-term, one RCT, <math>n=72</math>, RR 0.10, 95% CI 0.03–0.31; NN2, 95% CI 1.2–2.2). Continuous data identified good effects on negative symptoms (four RCTs, <math>n=240</math>, SMD average endpoint SANS <math>-0.74</math>, 95% CI <math>-1.00</math> to <math>-0.47</math>); general mental state (one RCT, <math>n=69</math>, SMD average endpoint PANSS <math>-0.36</math>, 95% CI <math>-0.85</math> to <math>0.12</math>; two RCTs, <math>n=100</math>, SMD average endpoint BPRS <math>-0.73</math>, 95% CI <math>-1.16</math> to <math>-0.31</math>); depression (two RCTs, <math>n=90</math>, SMD average endpoint SDS <math>-0.63</math>, 95% CI <math>-1.06</math> to <math>-0.21</math>; one RCT, <math>n=30</math>, SMD average endpoint Ham-D <math>-0.52</math>, 95% CI <math>-1.25</math> to <math>-0.12</math>); and anxiety (one RCT, <math>n=60</math>, SMD average endpoint SAS <math>-0.61</math>, 95% CI <math>-1.13</math> to <math>-0.09</math>). Positive effects were also found for social functioning (one RCT, <math>n=70</math>, SMD average endpoint SDSI score <math>-0.78</math>, 95% CI <math>-1.27</math> to <math>-0.28</math>). Furthermore, some aspects of cognitive functioning and behavior seem to develop positively through music therapy. Effects, however, were inconsistent across studies and depended on the number of music therapy sessions as well as the quality of music therapy provided.</p> | <p>There is no evidence that auditory integration therapy or other sound therapies are effective as treatments for autism spectrum disorders. As synthesis of existing data has been limited by the disparate outcome measures used between studies, there is not sufficient evidence to prove that this treatment is not effective. However, of the seven studies including 182 participants that have been reported to date, only two (with an author in common), involving a total of 35 participants, report statistically significant improvements in the auditory integration therapy group and for only two outcome measures (Aberrant Behavior Checklist and Fisher's Auditory Problems Checklist). As such, there is no evidence to support the use of auditory integration therapy at this time.</p> <p>Music therapy as an addition to standard care helps people with schizophrenia to improve their global state, mental state (including negative symptoms), and social functioning if a sufficient number of music therapy sessions are provided by qualified music therapists. Further research should especially address the long-term effects of music therapy, dose–response relationships, as well as the relevance of outcomes measures in relation to music therapy.</p> |

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| Study                         | Title  | Aim/objective   | Data source/search strategy  | Study selection/<br>selection criteria   |
|-------------------------------|--|---|--|--|
| Bradt et al <sup>19</sup>     | Music interventions for improving psychological and physical outcomes in cancer patients | To compare the effects of music therapy or music medicine interventions and standard care with standard care alone, or standard care and other interventions in patients with cancer.                       | We searched CENTRAL (The Cochrane Library 2010, Issue 10), MEDLINE, EMBASE, CINAHL, PsycINFO, LILACS, Science Citation Index, CancerLit, <a href="http://www.musictherapyworld.net">http://www.musictherapyworld.net</a> , CAIRSS, Pro Quest Digital Dissertations, ClinicalTrials.gov, Current Controlled Trials, and the National Research Register. All databases were searched from their start date to September 2010. We handsearched music therapy journals and reference lists and contacted experts. There was no language restriction. | We included all RCTs and quasi-RCTs of music interventions for improving psychological and physical outcomes in patients with cancer. Participants undergoing biopsy and aspiration for diagnostic purposes were excluded.   |
| Bradt and Dileo <sup>20</sup> | Music therapy for end-of-life care   | To examine effects of music therapy with standard care versus standard care alone or standard care combined with other therapies on psychological, physiological, and social responses in end-of-life care. | We searched CENTRAL, MEDLINE, CINAHL, EMBASE, PsycINFO, LILACS, CancerLit, Science Citation Index, <a href="http://www.musictherapyworld.de">http://www.musictherapyworld.de</a> , CAIRSS for Music, Pro Quest Digital Dissertations, ClinicalTrials.gov, Current Controlled Trials, and the National Research Register to September 2009. We handsearched music therapy journals and reference lists, and contacted experts to identify unpublished manuscripts. There was no language restriction.   | We included all RCTs and quasi-RCTs that compared music interventions and standard care with standard care alone or combined with other therapies in any care setting with a diagnosis of advanced life-limiting illness being treated with palliative intent and with a life expectancy of less than 2 years. |
| Vink et al <sup>21</sup>      | Music therapy for people with dementia   | To assess the effects of music therapy in the treatment of behavioral, social, cognitive and emotional problems of older people with dementia, in relation to the type of music therapy intervention.       | ALOIS, the specialized Register of the CDCIG was searched on April 14, 2010 using the terms: music therapy, music singing, sing, and auditory stimulation. Additional searches were also carried out on April 14, 2010 in the major health care databases MEDLINE, EMBASE, PsycINFO, CINAHL, and LILACS, trial registers and grey literature sources to ensure the search was as up-to-date and as comprehensive as possible.  | Randomized controlled trials that reported clinically relevant outcomes associated with music therapy in treatment of behavioral, social, cognitive, and emotional problems of older people with dementia.   |

| Data extraction/data collection and analysis  | Main results  | The authors' conclusions  |
|---|---|---|
| <p>Two review authors independently extracted the data and assessed the risk of bias. Where possible, results were presented in meta-analyses using MDs and SMDs. Post-test scores were used. In cases of significant baseline difference, we used change scores.</p> <p>Data were extracted, and methodological quality was assessed, independently by review authors. Additional information was sought from study authors when necessary. Results are presented using weighted MDs for outcomes measured by the same scale and SMDs for outcomes measured by different scales. Post-test scores were used. In cases of statistically significant baseline difference, we used change scores.</p> <p>Two reviewers screened the retrieved studies independently for methodological quality. Data from accepted studies were independently extracted by the reviewers.</p> | <p>We included 30 trials with a total of 1,891 participants. We included music therapy interventions offered by trained music therapists, as well as listening to prerecorded music offered by medical staff. The results suggest that music interventions may have a beneficial effect on anxiety in people with cancer, with a reported average anxiety reduction of 11.20 units (95% CI -19.59 to -2.82, <math>P=0.009</math>) on the STAI-S scale and -0.61 standardized units, (95% CI -0.97 to -0.26, <math>P=0.0007</math>) on other anxiety scales. Results also suggested a positive impact on mood (SMD =0.42, 95% CI 0.03-0.81, <math>P=0.03</math>), but no support was found for depression. Music interventions may lead to small reductions in heart rate, respiratory rate, and blood pressure. A moderate pain-reducing effect was found (SMD =-0.59, 95% CI -0.92 to -0.27, <math>P=0.0003</math>), but no strong evidence was found for enhancement of fatigue or physical status. The pooled estimate of two trials suggested a beneficial effect of music therapy on patients' QoL (SMD =1.02, 95% CI 0.58-1.47, <math>P=0.00001</math>). No conclusions could be drawn regarding the effect of music interventions on distress, body image, oxygen saturation level, immunologic functioning, spirituality, and communication outcomes. Seventeen trials used listening to prerecorded music, and 13 trials used music therapy interventions that actively engaged the patients. Not all studies included the same outcomes, and due to the small number of studies per outcome, we could not compare the effectiveness of music medicine interventions with that of music therapy interventions.</p> <p>Five studies (175 participants) were included. There is insufficient evidence of high quality to support the effect of music therapy on QoL of people in end-of-life care. Given the limited number of studies and small sample sizes, more research is needed. No strong evidence was found for the effect of music therapy on pain or anxiety. These results were based on two small studies. There were insufficient data to examine the effect of music therapy on other physical, psychological, or social outcomes.</p> <p>Ten studies were included. The methodological quality of the studies was generally poor, and the study results could not be validated or pooled for further analyses.</p> | <p>This systematic review indicates that music interventions may have beneficial effects on anxiety, pain, mood, and QoL in people with cancer. Furthermore, music may have a small effect on heart rate, respiratory rate, and blood pressure. Most trials were at high risk of bias, and therefore, these results need to be interpreted with caution.</p> <p>A limited number of studies suggest there may be a benefit of music therapy on the QoL of people in end-of-life care. However, the results stem from studies with a high risk of bias. More research is needed.</p> <p>The methodological quality and the reporting of the included studies were too poor to draw any useful conclusions.</p> |

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| Study                      | Title  | Aim/objective   | Data source/search strategy  | Study selection/selection criteria  |
|----------------------------|--|---|--|---|
| Bradt et al <sup>22</sup>  | Music interventions for mechanically ventilated patients | To examine the effects of music interventions with standard care versus standard care alone on anxiety and physiological responses in mechanically ventilated patients.   | We searched CENTRAL (The Cochrane Library 2010, Issue 1) MEDLINE, CINAHL, AMED, EMBASE, PsycINFO, LILACS, Science Citation Index, <a href="http://www.musictherapyworld.net">http://www.musictherapyworld.net</a> , CAIRSS for Music, Pro Quest Digital Dissertations, ClinicalTrials.gov, Current Controlled Trials, the National Research Register, and NIH RePORTer (formerly CRISP) (all to January 2010). We handsearched music therapy journals and reference lists and contacted relevant experts to identify unpublished manuscripts. There was no language restriction.               | We included all RCTs and quasi-RCTs that compared music interventions and standard care with standard care alone for mechanically ventilated patients.  |
| Cepeda et al <sup>23</sup> | Music for pain relief                                    | To evaluate the effects of music on acute, chronic, or cancer pain intensity, pain relief, and analgesic requirements.  | We searched the Cochrane Library, MEDLINE, EMBASE, PsycINFO, LILACS, and the references in retrieved manuscripts. There was no language restriction.   | We included RCTs that evaluated the effect of music on any type of pain in children or adults. We excluded trials that reported results of concurrent non-pharmacological therapies.  |
| Bradt et al <sup>24</sup>  | Music therapy for acquired brain injury                  | To examine the effects of music therapy with standard care versus standard care alone or standard care combined with other therapies on gait, upper extremity function, communication, mood and emotions, social skills, pain, behavioral outcomes, activities of daily living, and adverse events. | We searched the Cochrane Stroke Group Trials Register (February 2010), the Cochrane Central Register of Controlled Trials (the Cochrane Library Issue 2, 2009), MEDLINE (July 2009), EMBASE (August 2009), CINAHL (July 2010) PsycINFO (July 2009), LILACS (August 2009), AMED (August 2009), and Science Citation Index (August 2009). We handsearched music therapy journals and conference proceedings, searched dissertation and specialist music databases, trials and research reference lists, and contacted experts and music therapy associations. There was no language restriction. | RCTs and quasi-RCTs that compared music therapy interventions and standard care with standard care alone or combined with other therapies for people older than 16 years of age who had acquired brain damage of a non-degenerative nature and were participating in treatment programs offered in hospital, outpatient, or community settings. |

| Data extraction/data collection and analysis   | Main results   | The authors' conclusions  |
|--|--|---|
| <p>Two authors independently extracted the data and assessed the methodological quality. Additional information was sought from the trial researchers, when necessary. Results were presented using MDs for outcomes measured by the same scale and SMDs for outcomes measured by different scales. Post-test scores were used. In cases of significant baseline difference, we used change scores.</p>  | <p>We included eight trials (213 participants). Listening to music was the main intervention used, and seven of the studies did not include a trained music therapist. Results indicated that listening to music may be beneficial for anxiety reduction in mechanically ventilated patients; however, these results need to be interpreted with caution due to the small sample size. Findings indicated that listening to music consistently reduced heart rate and respiratory rate, suggesting a relaxation response. No strong evidence was found for blood pressure reduction. Listening to music did not improve oxygen saturation level. No studies could be found that examined the effects of music interventions on QoL, patient satisfaction, post-discharge outcomes, mortality, or cost-effectiveness.</p>   | <p>Listening to music may have a beneficial effect on heart rate, respiratory rate, and anxiety in mechanically ventilated patients. However, the quality of the evidence is not strong. Most studies examined the effects of listening to prerecorded music. More research is needed on the effects of music offered by a trained music therapist.</p> |
| <p>Data was extracted by two independent review authors. We calculated the MD in pain intensity levels, percentage of patients with at least 50% pain relief, and opioid requirements. We converted opioid consumption to morphine equivalents. To explore heterogeneity, studies that evaluated adults, children, acute, chronic, malignant, labor, procedural, or experimental pain were evaluated separately, as well as those studies in which patients chose the type of music.</p> | <p>Fifty-one studies involving 1,867 subjects exposed to music and 1,796 controls met inclusion criteria. In the 31 studies evaluating mean pain intensity there was a considerable variation in the effect of music, indicating statistical heterogeneity (<math>I^2 = 85.3\%</math>). After grouping the studies according to the pain model, this heterogeneity remained, with the exception of the studies that evaluated acute postoperative pain. In this last group, patients exposed to music had pain intensity that was 0.5 units lower on a 0–10 scale than unexposed subjects (95% CI <math>-0.9</math> to <math>-0.2</math>). Studies that permitted patients to select the music did not reveal a benefit from music; the decline in pain intensity was 0.2 units, 95% CI <math>(-0.7</math> to <math>0.2)</math>. Four studies reported the proportion of subjects with at least 50% pain relief; subjects exposed to music had a 70% higher likelihood of having pain relief than unexposed subjects (95% CI <math>1.21</math>–<math>2.37</math>). NNT = 5 (95% CI <math>4</math>–<math>13</math>). Three studies evaluated opioid requirements two hours after surgery: subjects exposed to music required 1.0 mg (18.4%) less morphine (95% CI <math>-2.0</math> to <math>-0.2</math>) than unexposed subjects. Five studies assessed requirements 24 hours after surgery: the music group required 5.7 mg (15.4%) less morphine than the unexposed group (95% CI <math>-8.8</math> to <math>-2.6</math>). Five studies evaluated requirements during painful procedures: the difference in requirements showed a trend towards favoring the music group (<math>-0.7</math> mg, 95% CI <math>-1.8</math> to <math>0.4</math>).</p> | <p>Listening to music reduces pain intensity levels and opioid requirements, but the magnitude of these benefits is small and, therefore, its clinical importance unclear.</p>  |
| <p>Two review authors independently assessed methodological quality and extracted data. We present results using MDs (using post-test scores), as all outcomes were measured with the same scale.</p>  | <p>We included seven studies (184 participants). The results suggest that RAS may be beneficial for improving gait parameters in stroke patients, including gait velocity, cadence, stride length, and gait symmetry. These results were based on two studies that received a low risk of bias score. There were insufficient data to examine the effect of music therapy on other outcomes.</p>   | <p>RAS may be beneficial for gait improvement in people with stroke. These results are encouraging, but more RCTs are needed before recommendations can be made for clinical practice. More research is needed to examine the effects of music therapy on other outcomes in people with acquired brain injury.</p>                                      |

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