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**TVÆRFAGLIG SMERTEBEHANDLING**

**Modul 7**

**MUSiC AND PAIN**

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1. INTRODUCTION

Pain is defined as "an unpleasant sensory and emotional experience that is associated with current or threatening tissue damage or as described in terms similar to such damage" (1).

Due to the physiological mechanisms involved in the development of pain, pain is divided into four basic groups (87):

1. **Nociceptive Pain**: There is evidence of tissue damage outside the nervous system.

2. **Inflammatory pain**: There is evidence of inflammation / inflammation.

3. **Neuropathic Pain**: There is evidence of tissue damage in the sensory part of the nervous system.

4. **Dysfunctional / centralized pain:** Tissue injury cannot be detected.

Clinically, pain is divided into the following groups (1):

1. **acute pain**,

2. **chronic non-malignant pain** – pain is commonly considered to be chronic when they last for more than 6 months,

3. **cancer-related pain**.

The best treatment for pain is to eliminate the cause, for example tissue damage or inflammation. Unfortunately, it is not always realistic. This can be achieved, for example, by surgical stabilization of bone fracture or removal of inflammatory or dysfunctional tissues. Opportunities for removing the tissue damage are much less in patients with neutopathic pain and do not exist at all for dysfunctional pain.

When the cause of pain cannot be removed, two types of treatment are used:

1. Medication therapy,

2. Non-medicatin therapy.

The medication therapy works best against acute pain and against chronic cancer-related pain. It is less effective against chronic non-malignant pain. However, long-term use of painkillers can lead to serious side effects and iatrogenic diseases (3-6).

Non-medicated pain management includes physiotherapy, manual therapy, psychotherapy (including psycho-induction and cognitive behavioral therapy), and other therapeutic methods (for example, hypnosis, acupuncture and TENS - *Transcutaneous Electrical Nerve Stimulation*, as well as other forms of electrotherapy such as SCS - *spinal cord stimulation*) (7). Music therapy is also used in the treatment of patients with pain (8).

There are various physiotherapeutic interventions, exercise and exercise programs as well as psychotherapeutic and educational methods available in pain management. Many of them have been evaluated in randomized controlled trials (9-25). The most promising approach seems to be cognitive behavioral therapy (CBT). However, in most studies, only one or two approaches have been tested at the same time. There have been very few comparative but non-randomized studies aimed at evaluating true multimodal therapies covering all areas of the biopsychosocial model framework (9). In spite of many treatment options, there is still a need for new treatments with demonstrated efficacy, low risk of side effects and high potential for widespread availability, especially for patients with chronic non-malignant pain. The use of music in the treatment process is a promising approach because music is cheap, virtually without side effects and easily accessible. Therefore, it is relevant to investigate how music can be used for pain management, especially for patients with chronic non-malignant pain.

In the absence of a universal normative definition of music, this is appropriate to work with operational and descriptive definitions relevant to specified projects. For this dissertation, music is defined **as a human activity that is deliberately made of sounds produced with voice and / or with musical instruments and is structured in a certain way separating them from the language.** Thus, some musical phenomena are beyond the scope of this dissertation. This applies, for example, to the specific music in which, in addition to the sound of instruments or songs, real sounds are used - sounds of nature, factory sounds, sounds of street traffic, random human voices, etc. (26). It also applies to John Cage's famous 4'33 '' (27).

The use of music in therapy can be called music intervention (28). It is available in two forms:

1. Music therapy

2. Music activity.

With **music therapy**, the goal is to build a therapeutic relationship in a course over a certain amount of time, and to create safe frameworks as a basis for processing personal experiences and feelings. Music therapy is a long-standing course, conducted by a trained therapist, with a clearly defined goal that weighs communication and interaction. (28) With **music activity**, the purpose is to stimulate, entertain, and teach. Needs of each individual are taken into account, but without going as close to the individual as with music therapy (22). Listening to music and the use of background music are typical examples of music activities that can be used in treatment and care (28).

2. OBJECTIVES AND EXPLANATORY STATEMENT

The purpose of this project is to identify and evaluate evidence of the effectiveness of music as treatment for pain focusing on chronic non-malignant pain. The study is focused on the practical implications, i.e. current and potential consequences for pain treatment. The available scientific literature provides various informations about possible connections between music and pain. Exercising music can be painful, especially for professional musicians (29-31). Listening to music can relieve pain (32-34). There is also a Cochrane metaanalysis of randomized studies using music in pain management (35). In the updated version of this metaanalysis, 97 studies, published between 1995 and 2014, were included. The analysis shows that the use of music in pain management reduces pain intensity and emotional stress from pain. Music reduces consumption of both opioids and non-opioids. Physiological reactions to pain are also reduced: music reduces heart rate, blood pressure and respirations rate (36). **However, there is neither meta-analysis nor systematic review of literature that focuses on studies where music was used in the treatment of patients with chronic non-malignant pain.** Therefore, it is important to carry out such an analysis, focusing on the practical (applied) implications. Results of this analysis can be used for:

- Identification of new research and development areas, and

- Development of pain management for patients with chronic non-malignant pain.

The following questions are expected to be answered:

1. Is music an effective remedy for chronic non-malignant pain?

2. Is there a difference in the effect between listening to music and professionally practiced music therapy?

3. Is active music therapy better than passive listening to music?

4. Is patient’s choice music more effective than music chosen by the therapist?

5. Can music be integrated with cognitive behavioral therapy?

6. What kind of music works best for pain?

7. Should different genres and forms of music be used against different kinds of chronic non-malignant pain (neurogenic, dysfunctional, inflammatory, nociceptive)?

3. METHODS

3.1. Review Strategy.

The study is planned as a literary review and takes the form of an exploratory review. This type of review has been used to find out what has been published about a particular subject, as well as to identify which research questions are answered and which problems should be investigated in the future (37).

3.2. Inclusion criteria.

3.2.1. Types of studies.

This project is not a rigorous meta analysis that only involves randomized trials in accordance with, for example, Cochrane Methodology (http://www.cochrane.org/) or PRISMA Methodology (http://www.prisma-statement.org/Default.aspx). In addition to review of randomized prospective clinical studies, review and analysis of other types of studies will be conducted, including:

1) Non-randomized prospective studies

2) Case-control studies

3) Retrospective studies

4) Case reports and other anecdotal studies.

Both quantitative, qualitative and mixed-method studies are included, as well as systematic reviews with quantitative data analysis, while narrative reviews are excluded. Meta analyzes are also included. Such measures are important if the results of the study are to inspire further research. It is possible to identify results that can be used in clinical practice. Furthermore, it is possible to identify areas where more research is necessary..

The publication's language will be limited to English, Danish, Swedish, Norwegian, German and French.

3.2.2. Participants.

Studies with the participation of people with chronic non-malignant pain are included. There are no limitations in relation to the person's gender, age or ethnicity. Animal testing is excluded.

3.2.3. Intervention.

 The analysis includes studies where people have been exposed to music intervention in one of the forms mentioned in the introduction.

3.2.4. Outcomes.

Treatment results are assessed according to IMMPACT recommendation for clinical trials in pain management (38). According to IMMPACT recommendations, the 6 following core output should be considered in the design of clinical trials in pain management:

(1) Pain

(2) Physical function

(3) Emotional function

(4) Participants’ assessment of improvement and satisfaction with treatment

(5) Side effects and

(6) Participants’ disposition and compliance.

The analysis includes studies with at least one of the above outputs.

The study is aimed at to identify evidences. Evidences have different degrees of strength. The higher the degree of strength, the more relevant is the use of results in practice. High-grade evidences are used to develop new recommendations and clinical guidelines (39). To identify the strength of evidences, Oxford evidence levels and strengths are used (40).

3.2. Search process.

 3.2.1. Search strategy.

There are two search strategies used:

1. **manual search**, which includes review of literature lists in academic books and articles the name in the literature list, as well as review of content in journals *Danish Music Therapy* and *Ugeskrift for Læger*; the following websites are also checked:

- http://www.wfmt.info/ - World Federation of Music Therapy,

- www.musik.aau.dk - music education at Aalborg University,

- www.musikterapi.aau.dk - music therapy at Aalborg University

- www.danskmusikterapi.dk - Danish Music Therapist Association

2. **electronic search in databases**.

3.2.2. Databases and websites

Searching is conducted the following databases:

- MEDLINE / PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online, MEDLARS Online) is a bibliographic database for life sciences and biomedical information; PubMed is a free search engine that has primary access to the MEDLINE database - <https://www.ncbi.nlm.nih.gov/pubmed/>

- EMBASE - a biomedical and pharmacological database with slightly different content than MEDLINE - <https://www.elsevier.com/solutions/embase-biomedical-research>

- PsycINFO - a database of abstracts of literature in psychology - <http://www.apa.org/pubs/databases/psycinfo/>

- RILM (Repertoire International de Litterature Musicale) - an organization seeking to provide comprehensive and accurate representation of music science in all countries and languages ​​and across all disciplinary and cultural boundaries - <http://www.rilm.org/>

- Web of Science - A Scientific Citation Indexing - <https://clarivate.com/products/web-of-science/web-science-form/web-science-core-collection/>

- Scopus - A database containing scientific abstracts and citations - <https://www.elsevier.com/solutions/scopus>

- Pro Quest Central - a bibliographic database containing journals, books, dissertations, etc. - <http://www.proquest.com/>

3.2.3. Keywords.

The following keywords are used: pain, music, music therapy, dance, exercise with music, singing, playing music, listen to music, vibroacoustic therapy, vibrotactile stimulation, background music.

To combine keywords in different configurations, Boolean operators (<https://library.alliant.edu/screens/boolean.pdf>) are used.

3.3. Evaluation of publications.

Evaluation process is performed according to flow chart inspired by PRISMA flow chart for analysis of clinical studies (Figure 1). The process is also inspired by Delphi methodology (41), but subject to the fact that this stude has only one author. Thus, one can only talk about inspiration from Delphi methodology, but not about the full use of this method.

The process is divided into 4 rounds:

1. **Identification round**, where studies found in electronic search are compared to studies found in chain search and duplicates are excluded from further analysis.

2. **Screenings round**, where the titles and abstracts are screened to remove non-relevant studies.

3. **Evaluation round**, where the full texts of the remaining articles are reviewed to select studies that meet inclusion criteria. At this round, the level of evidence and the degree of strength for each study is also assigned and randomized studies are identified. Here are studies with results relevant for patients with chronic non-malignant pain identified.

4. **Synthesis**, where the studies results are reviewed. Quantitative and qualitative data are analyzed and conclusions are made regarding the practical recommendations and suggestions for further research.

4. ETHICAL CONSIDERATIONS AND DISSEMINATION OF RESULTS

Ethical approval is not required for this project because the project does not include the collection of data from individuals. It is assumed, that studies included in this project have been made in accordance with the applicable ethnic guidelines. If in doubt about this, the study will not be included in the analysis and the problem will be described in details.

This project is realized as a master's thesis in master education in interdisciplinary pain treatment at Aalborg University. In future, the results of the project can be conveyed as an article in a professional journal and as media reports, both in print and electronically.

5. RESULTS

5.1. Summary of searching round.

The searching process is summarized in figure 2. Searching was completed 31. March 2018. Totally, 7902 publications was identified in electronic searching in the following databases:

* MEDLINE / PubMed – 1217 publications
* EMBASE – 2097 publications
* PsycINFO – 849 publications
* RILM – 1253 publications
* Web of Science – 1181 publications
* Scopus – 1251 publications

Searching in Pro Quest Central using the same key words key words as in other databases identified 343.563 publications. This was not possible to study all of them. Thus, searching was limited to key words ‘chronic non-cancer pain’ combined with ‘music’ and other key words specified earlier. This limited searching identified 603 publications. All of them were identified in other databases, and they are not included in analysis.

In addition, manual searching identified 7 publications. Thus, 7909 publications were identified in the identification round.

After removing of duplicates, 1219 publications were identified to the further analysis.

5.2. Summary of screening round.

In the screening round, 1171 publications were excluded because either the aim of studies was not relevant for the purpose of this project or studies did not meet other inclusions criteria.

The 48 studies identified in the screening round as eligible to further analyses are presented in tab.1.

Table 1. Studies included in the evaluation round.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study** | **Language** | **Type of study** | **Intervention** | **Full text available** |
| Garza-Villarreal EA et al. (42) | English | Systematic review and meta-analysis | Various | Yes |
| Pongan E et al. (43) | English | Prospective, randomized, single-blind controlled trial | Singing in the choir | Yes |
| Johnson AJ et al. (44) | English | Prospective, non-randomized, non-controlled trial | Listening to music combined with hypnotic suggestions | Yes |
| Raglio A et al. (45) | English | Prospective randomized controlled trial | Active music therapy | No |
| Lee JH (36) | English | Meta-analysis | Various | Yes |
| Llovet AK et al. (46) | English | Meta-anlysis | Various | Yes |
| Espi-Lopez GV et al. (47) | English | Prospective randomized controlled pilot trial | Therapeutic aerobic exercise with music therapy | Yes |
| Hopper MJ et al. (48) | English | Qualitative, retrospective, semi-structured interviews | Choral singing | Yes |
| Bremner MN et al. (49) | English | Randomized, mixed-methods design | Music combined with Reiki. Ranomization to music alone or Reiki with music. | Yes |
| Bradt J et al. (50) | English | Prospective, randomized, mixed methods study | Vocal music therapy | Yes |
| Owens JE et al. (51) | English | Mixed-methods study, retrospective | Various | Yes |
| Linnemann A et al. (52) | English | Ecological momentary assessment study  | Listening to music | Yes |
| Garza-Villareal EA et al. (53) | English | Prospective, non-randomized trial | Listenig to music | Yes |
| Alparslan GB et al. (54) | English | Randomized controlled intervention study | Listening to music | Yes |
| Sherry DD et al. (55) | English | Prospective, non-randomized trial | Dance as part of multimodal non-pharmacologic intervention | Yes |
| Mercadie L et al. (56) | English | Prospective controlled trial | Listening to music | Yes |
| Weber A et al. (57) | English | Prospective, controlled, randonized trial | Listening to music combined with vibrostimulation in acupuncture points | Yes |
| Crawford C et al. (58) | English | Systematic review | Sensory Art Therapies | Yes |
| Garza-Villareal et al. (59) | English | Prospective, non-randomized trial | Listening to music | Yes |
| Picard LM et al. (60) | English | Prospective, non-randomized trial | Listening to music | Yes |
| Holden R et al. (61) | English | Qualitative cohort study  | Listening to music | Yes |
| Korhan EA et al. (62) | English | Prospective non-randomized trial | Listening to music | Yes |
| Matsota P et al. (63) | English | Systematic review | Various | Yes |
| Guetin S et al. (64) | English | Prospective randomized single-blind controlled study | Individual music therapy sessions | Yes |
| Knox D et al. (65) | English | Post hoc analysis of experimental data | Listening to music under pain stimulation (cold pressor) | Yes |
| Chi GC et al. (66) | English | Explorative review  | Various | Yes |
| Onieva-Zafra MD et al. (67) | English | Prospective randomized controlled trial | Listening to music | Yes |
| Park H (68) | English | A quasi experimental design and a nonprobability convenience sample | Listening to music | Yes |
| Skingley A et al. (69) | English | Systematic review | Various | Yes |
| Castillo-Bueno MD et al. (70) | English | Systematic review | Various | No |
| Sand-Jecklin K et al. (71) | English | Quasi-experimental methodology with a pre-post intervention design | Individual music therapy sessions | Yes |
| Siedlecki SL (72) | English | Prospective randomized controlled trial | Listening to music | Yes |
| Mu PF et al. (73) | English | Systematic review | Various | No |
| Nilsson U (74) | English | Systematic review | Various | No |
| Reid MC et al. (75) | English | Explorative review | Various | Yes |
| Richards T et al. (76) | English | Systematic review | Various | No |
| Lim PH (77) | English | Descriptive survey of studies  | Various | Yes |
| Siedliecki SL et al (78) | English | Prospective randonized controlled trial | Listening to music | Yes |
| Dileo C (79) | English | Meta-analysis | Various | No |
| Cepeda et al. (35) | English | Cochrane review | Various | Yes |
| Kenny DT et al. (80) | English | Prospective randomized controlled study | Group singing | Yes |
| McCaffrey R (81) | English | Prospective randomized controlled trial | Listening to music | Yes |
| Good M (82) | English | Narrative review | Various | Yes |
| Buchhaupt T (83) | German | Case report | Individual music therapy sessions | Yes |
| Hillecke T et al. (84) | German | Theoretical study | No intervention | Yes |
| Mariauzouls C et al. (85) | German | Prospective non-randomized pilot study | Vibration-assisted music therapy | No |
| Muller-Busch HC et al. (86) | German | Prospective non-randomized study | The Nordoff/Robbins method of active music therapy  | Yes |
| Schorr JA (87) | English | Prospective non-randomized study | Listening to music | No |

5.3. Summary of evaluation round

In the evaluation round the following studies were excluded from further analysis (reason for exclusion is given i parenthesis):

* Garza-Villarreal EA et al. (42, studies with both non-cancer and cancer pain patients are included)
* Raglio A et al. (45, full text is not available)
* Lee JH (36, studies with both acute and chronic pain patients are included)
* Llovet AK et al. (46, studies with various diseases, not only pain patients, are included)
* Bremner MN et al. (49, the aim of the study was to assess the effect of Reiki, not music)
* Garza-Villareal EA et al. (53, updated results from the earlier study: Garza-Villareal et al. - 136)
* Alparslan GB et al. (54, a CD with concret music (warter and wave sounds) was used. This in not in the scope of this rewiev - see music definition in the introduction)
* Crawford C et al. (58, studies with both non-cancer and cancer pain patients are included)
* Matsota P et al. (63, studies with both acute and chronic pain patients are included)
* Knox D et al. (65, experimental study with healthy volunteers)
* Chi GC et al. (66, explorative review)
* Skingley A et al. (69, studies with various diseases, not only pain patients, are included)
* Castillo-Bueno MD et al. (70, unpublished studies in Spanish are included)
* Siedlecki SL (72, updated results from the earlier study: Siedliecki SL et al. - 155)
* Mu PF et al. (73, full text is not available)
* Nilsson U (74, full text is not available)
* Reid MC et al. (75, explorative review)
* Richards T et al. (76, full text is not available)
* Lim PH (77, descriptive survy of studies)
* Dileo C (79, studies with various diseases, not only pain patients, are included)
* Cepeda et al. (35, studies with various diseases, not only pain patients, are included)
* Good M (82, narrative review)
* Hillecke T et al. (84, theoretical study, on therapeutic intervention tested)
* Mariauzouls C et al. (85, full text is not available)
* Schorr JA (87, full text is not available)

Thus, 23 studies are included in the synthesis round (tab. 2).

Table 2. Studies initially included in synthesis round.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study** | **Disease – type of pain** | **Number of patients included** | **Design** | **Type of music used** |
| Pongan E et al. 2017 (43) | Altzheimer’s disease (mild form) – chronic pain. | 59 | Patients were randomized to a 12-week singing (SG; *n* = 31) or painting group (PG; *n* = 28). | The choir conductor selected the songs according to the patients’ preferences.  |
| Johnson AJ et al. 2017 (44) | Chronic pain: musculoskeletal conditions, cancer, fibromyalgia, mood disorders, and inflammatory conditions. | 12 | One arm study. No control group. | 15 minutes of string orchestra music (*Fantasia on a Theme of Thomas Tallis* by Ralph Vaughn-Williams).  |
| Espi-Lopez GV et al. 2016 (47) | Fibromyalgia | 35 | Patients were randomized to one of the three groups: G1 - therapeutic aerobic exercise with music therapy (n = 13); G2 - therapeutic aerobic exercise at any rhythm (n = 13); CG – control, no music (n = 9) Excluded(n = 3) | Melodic music, adapted to the tastes of the participants and also adapted to the way the exercise was performed. For this, they were shown a list of 100 pieces of music in which participants chose a minimum of 20 preferences.  |
| Hopper MJ et al. 2016 (48) | Chronic pain (otherwise not specified) | 7 | Qualitative, retrospective, semi-structured interviews | Singing in the choir (duration of attendance: 2-18 months). |
| Bradt J et al. 2016 (50) | Chronic non-malignant pain - neuropathic and/or musculoskeletal | 55 | Paients were randomly allocated to either vocal music therapy (VMT, n=28) or wait-list control (WLC, n=27)  | The VMT treatment program consisted of eight 60-minute weekly group therapy sessions (6–8 participants in each group) administered by the lead investigator, a board-certified music therapist with expertise in chronic pain management.  |
| Owens JE et al. 2016 (51) | Chronic non-malignant pain -neuropathic and/or musculoskeletal | 18 | Retrospective study. Concurrent mixed methods design (semi-structured interviews). | Playing and/or listening to self-choosen music.  |
| Linnemann et al. 2015 (52) | Fibromyalgia | 30 | Ecological momentary assessment study, pre-post intervention design, no control group. | Music individualy choosen by patient. |
| Sherry DD et al. 2015 (55) | Fibromyalgia | 64 | One arm study (no control group), pre-post intervention design. | Dance as a part of an intensive physical and psychosocial program. |
| Mercadie L et al. 2015 (56) | Fibromyalgia | 22 | No randomization. The participants could self choose listening to either music (M) or environmental sounds (S), as well as they could choose either passive listening (PL; listening only) or active listening (AL; listening while carrying out another activity).  | Instrumental music was selected from a list provided by Music Care©: 20 pieces, each 20 minutes long, including world music (Andean, African, Indian, Irish, Jamaican, Asian, Oriental), classical music (with piano, violin, clarinet, or harp), or modern music (Jazz, New age, Rock, Lounge, Electro).  |
| Weber A et al. 2015 (57) | Fibromyalgia | 120 | Randomization to four groups (30 patients each): (1) listening to music, (2) vibratory stimuli on a combination of acupuncture points on the skin, (3) both procedures in a simultaneous and synchronized manner, with inclusion of binaural beats, (4) (control) received no stimulation  | The music program comprised a sequence of classical Bach compositions: (1) Brandenburg concerto no. 4 in G major—Presto; (2) Brandenburg concerto no. 6 in B-flat major—Allegro; (3) Jesu, Joy of Man’s Desiring in G—Moderato; (4) Violin concerto in A minor— Andante; (5) Air on the G string—Adagio.  |
| Garza-Villareal et al. 2014 (59) | Fibromyalgia | 22 | The participants listened to pink noise, followed by wash-out period and listening to music. Pre-post intervention design. No control group. | Semi self-chosen music: patients were asked for their favorite songs, musician, or band, taking into consideration that investigators wanted the songs to be pleasant and relaxing. The patients were asked for the names of at least three songs they wanted to listen to. The proposed songs were screened by the investigators in order to ensure all songs in the experiment would have low beats-per-minute.  |
| Picard LM et al. 2014 (60) | Fibromyalgia | 24 | One arm study (no control group), pre-post intervention design. | Participants were given a music program (‘Music to Promote Sleep’ on the Sonic Aid label by Somerset Entertainment) on an MP3 player.  |
| Holden R et al. 2013 (61) | Chronic pain non-cancer pain (not othervise specified) | 318 | Questionnaire send to patients. | Not specified. |
| Korhan EA et al 2014 (62) | Chronic neutopathic pain (probably no patients wiyh cancer-related pain) | 30 | No control group, quasi-experimental repeated measures within-subject design.  | Classical Turkish music (probably investigators choice) played to patients using a media player (MP3) and headphones during single 60 min therapeutic session.  |
| Guetin S et al. 2012 (64) | Mechanical, inflammatory, fibromyalgic, or neuropathic chronic pain. | 87 | Patients randomized to either intervention arm (n=44) or control arm (n=43). | Musical sequences provided by Music Care© (classical: piano, violin, flute, etc.; jazz: trumpet, saxophone, trom- bone, etc.; world music: India, Andes, Africa, etc.). The patients were asked to note the duration, frequency of listening and type of music chosen.  |
| Onieva-Zafra MD et al. 2013 (67) | Fibromyalgia | 60 | Randomization to either a music intervention group (n=30) or a control group (n=30).  | Two compact discs developed by the investigator. A selection of classical music mixed with salsa music. Patients listened to music at home In 8 weeks. |
| Park H et al. 2010 (68) | Dementia | 15 | Prospective one arm study (no control group), pre-post intervention design. | Participants listened to their preferred music for 30 minutes before peak agitation time, 2 days a week, for 2 weeks, followed by no music for 2 weeks. This 4-week cycle was repeated once.  |
| Sand-Jecklin K et al. 2010 (71) | Acute pain in hospitalized patients. | 31 | A quasi-experimental methodology with a pre-post intervention design  | Live music. |
| Siedliecki SL et al 2006 (78) | Chronic non-malignant pain (osteoarthritis,   herniated disc, rheumatoid arthritis, degenerative join disease, fibromyalgia)  | 60 | Patients were randomly assigned to a standard music group (SM, n = 22), patterning music group (PM, n = 18) or control group (n = 20).  | PM group were asked to select upbeat, familiar, instrumental or vocal music or sounds of nature. Participants in the SM group were offered a choice of one 60-minute relaxing instrumental music tape from a collec- tion of five tapes (piano, jazz, orchestra, harp and synthesizer). All participants kept a diary for 7 days.  |
| Kenny DT et al. 2004 (80) | Chronic pain (othervise not specified) | 60 | Block randomization (10 patients per block) to either singing og standard care (n=30) or standard care alone (n=30). Participants who failed to attend their singing sessions were examined as a separate comparison group (number of those patients is not clearly specified).  | Songs of lively tempo, syncopated rhythm, pitch range of no more than an octave, and simple structure and words. A trained singing teacher and a piano accompanist (first author) conducted the singing sessions of 30 min duration.  |
| McCaffrey R et al. 2003 (81) | Osteoarthritis | 66 | Randomization (women : men = 2 : 1) to either exeprimental group (listening to music, n=33) or control group (standard care, n=33). | The experimental group was given a cassette tape player and a cassette prepared by the primary investigator on which 20 minutes of relaxation music were recorded. The tape consisted of three musical selections by Mozart: (1) Andantino from Concerto for Flute, Harp, and Orchestra in C, K.299; (2) Overture A Le nozze di Figaro, K.492; and (3) Sonata Symphonie No. 40, first movement.  |
| Buchhaupt T 2000 (83) | Chronic headache | 1 | Case raport. | Active music therapy. |
| Muller-Busch HC et al. 1997 (86) | Chronic non-malignant pain (fibromyalgia, msculoskeletal pain,primary chronic polyarthralgia) | 22 | Non-randomized prospective study. Patients received either musictherapy (intervention group, n=12) or standard care (control group, n=10). Criteria for patients allocation are not clearly defined. | Patients were treated with music therapy sessions twice a week for 2 to 3 months on an outpatient basis by a music therapist using the Nordoff-Robbins method. |

The folowing studies were excluded from further anlaysis (reason for exclusion is given in parenthesis):

* Johnson AJ et al. (44, patients with cancer related pain were included)
* Sand-Jecklin K et al. (71, acute pain in hospitalized patients)
* Siedliecki SL et al (78, sounds of nature could be chosed by patients. This in not in the scope of this rewiev - see music definition in the introduction)
* Buchhaupt T (83, chronic headache)

Finally, 19 studies are identified to meet the scope of this project (tab.3).

Tab.3. Studies finally included in synthesis of results.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study** | **Level of evidence and grade of recommenda-tion** | **IMMPACT outputs** | **Results** | **Commentary** |
| Pongan E et al. 2017 (43) | 1bA | 1, 3, 4, 6 | Both singing and painting interventions led to significant pain reduction (*p* = 0,01), reduced anxiety (*p* < 0,0001), and improved Quality of Life (*p* = 0,002). Depression was reduced over time in painting group only (*p* = 0,01).  | Numeric Rating Scale (NRS), Simple Visual Scale (SVS), and Brief Pain Inventory (BPI) were used for chronic pain assessment. Another outcomes relevant for Altzheimer’s paients were analysed. It is out of the scope of this review.  |
| Espi-Lopez GV et al. 2016 (47) | 1bA | 1, 2, 3, 6 | At post-intervention, group G1 improved in all variables (depression - p = 0,002, quality of life - p = 0,017, general discomfort - p = 0,001, and balance - p = 0,000), while group G2 improved only in general discomfort (p = 0,002).  | Faces Pain Scale, Fibromyalgia impact Questionnaire, Beck Depression Inventory, and Berg Balance Scale were used.Effect of music on pain intensity is not clearly reported. |
| Hopper MJ et al. 2016 (48) | 4C | Not specified | Participants’ narratives provided support for participation in the choir in enhancing positive affect, self-worth, interpersonal relationships and overall wellbeing. The choir enabled continued progress towards accomplishing key pain management programme aims: self-management, coping and living well with pain.  | Thematic analysis of the data uncovered seven themes: physical improvements, emotional Impact, personal growth, interpersonal processes, relationship with the ‘self’, living well with pain and sharing the music and spreading the word.  |
| Bradt J et al. 2016 (50) | 1bA | 1, 2, 3, 4, 5, 6 | Large effect sizes in vocal therapy group were obtained for self-efficacy at weeks 8 (SMD = 1,09, 95% CI 0,45 to 1,73) and 12 (SMD = 0,77, 95% CI 0,13 to 1,42). Moderate effect size was found for pain interference at week 8 (SMD = 0,6, 95% CI 0,01 to 1,22). No improvements were found for general activities and emotional functioning. Moderate effect sizes were obtained for pain intensity (SMD = 0,6, 95% CI −0,01 to 1,2) and small effect sizes for coping (SMD = 0,26, 95% CI −0,36 to 0,88), albeit not statistically significant. Qualitative findings suggested that the treatment resulted in enhanced self-management, motivation, empowerment, a sense of belonging, and reduced isolation.  | Effect sizes: standardized mean difference (SMD) also known as Cohen’s *d*. Reported with and associated 95% confidence intervals (CI).After end of the study, vocal therapy was offered to patints from wait list.The following instruments were used: Westhaven-Yale Multidimensional Pain Inventory, Interference Scale, Pain Self-Efficacy Questionnaire, Hospital Anxiety and Depression Scale, Patient Global Impression of Change Scale. In addition, participants rated their average pain intensity as well as average pain coping during the past week using an 11-point (0–10) numeric rating scale.  |
| Owens JE et al. 2016 (51) | 3bB | Not specified | Some patients living well with pain use music for pain relief. | Study was not aimed to evaluate music as a therapeutic intervention. |
| Linnemann et al. 2015 (52) | 2bB | 1, 3 | Listening to the music increased perceived control over pain (p< 0,001), especially when the music was positive in valence and when it was listened to for the reason of ‘activation’ or ‘relaxation’. In contrast, no effects on perceived pain intensity were observed (p= 0,317).   | Perceived control over pain was measured using the item ‘I had the feeling that I was in control of the pain,’ which was rated on a 6-point Likert scale ranging from 0 to 5, with low values indicating low control over pain and high values indicating high control. Perceived pain intensity was measured using a VAS ranging from 0 (‘At the moment, I am in no pain’) to 100 (‘At the moment, I am in the most intense pain possible’).  |
| Sherry DD et al. 2015 (55) | 2bB | 1, 2, 3 | The mean pain score decreased significantly from program entry to the end of the pro- gram (from 66 of 100 to 25 of 100; *P* = 0,001). At the 1-year follow-up, 33% reported no pain. All measures of function improved significantly and remained at that level or continued to improve over the subsequent year. All Pain Stages of Change Questionnaire, adolescent version subset scores improved significantly initially and were stable or improved at 1 year, as did the Pediatric Quality of Life Inventory, Teen Report total score.  | Study was not aimed to evaluate dance as a therapeutic intervention.Only children (15-17 years old, median 16 years) were inrolled in the study. They received no medication agains pain. |
| Mercadie L et al. 2015 (56) | 2bB | 1, 2 | When patients listened to music or environmental sounds at rest, pain and fatigue levels were significantly reduced after 20 minutes of listening (p < 0,001), with no difference of effect magnitude between the two stimuli. This improvement persisted 10 minutes after the end of the listening session. In active situations, pain did not increase in presence of the two stimuli. Contrary to authors’ expectations, music and environmental sounds produced a similar relieving effect on pain and fatigue, with no benefit gained by listening to pleasant music over environmental sounds.  | Pain and fatigiue evaluated on the Visual Analogue Scale (VAS). |
| Weber A et al. 2015 (57) | 1bA | 2, 3 | Significant improvement in all groups. Group with both procedures (vibration and music) delivered in a simultaneous and synchronized manner achieved largest improvement (p<0,001). | The assessment was performed both before and after treatment by using following questionnaires: The Fibromyalgia Impact Questionnaire (FIQ), and The Health Assessment Questionnaire (HAQ).  |
| Garza-Villareal et al. 2014 (59) | 2bB | 1, 2 | Listening to relaxing, pleasant, self-chosen music reduced (pain p= 0,04 for pain intensity and p= 0,006 for pain unpleasantless), and increased functional mobility (p< 0,006). The music-induced analgesia was significantly correlated with the TUG scores, thereby suggesting that the reduction in pain unpleasantness increased functional mobility.  | TUG (“timed-up & go task”) was used to measure functional mobility after each auditory. Mobility improvement was obtained with music played prior to the motor task (not during), therefore the effect cannot be explained merely by motor entrainment to a fast rhythm. condition. The following instruments were also used: the Spanish version of the Pain Catastrophizing Scale, State- Trait Anxiety Inventory, and Center for Epidemiologic Studies Depression Questionnaire. Pain was measured using the Verbal Rating Scale.  |
| Picard LM et al. 2014 (60) | 2bB | 1, 2, 3, 4, 5, 6 | Both the FIQ median score (p = 0,004) and The Jenkins Sleep Scale median value (p = 0,001) improved significantly at study completion. The outcomes of the patient global impression of change ratings were mostly positive (P=0.001). Being tired on awakening declined significantly (p = 0,021). However, there was no significant improvement in pain level or tiredness. There were no serious adverse events.  | The primary outcome was sleep improvement.Fibromyalgia Impact Questionnaire (FIQ) and Jenkins Sleep Scale, as well as Patient Global Impression of Change Scale were used. |
| Holden R et al. 2013 (61) | 4C | Not specified | Music gives enjoyment, relaxation, and distraction and those who listened to music more frequently had a higher quality of life. | A questionnaire was sent to investigate the music listening behaviour and beliefs of patinets wih chronic pain in Glasgow.  |
| Korhan EA et al. 2014 (62) | 2bB | 1 | The patients’ mean pain intensity scores were reduced by music (p = 0,001), and that decrease was progressive over the 30th and 60th minutes of the intervention, indicating a cumulative dose effect.  | Patients were hospitalized in an algology clinic.Visual Analog Scale was used for pain intensity assessment.  |
| Guetin S et al. 2012 (64) | 1bA | 1, 3, 6 | At day 60 in the music intervention arm, this technique enabled a more significant reduction (p < 0,001) in pain when compared with the arm without music intervention. In addition, music intervention contributed to significantly reducing both anxiety/depression (p < 0,001) and the consumption of anxiolytic agents (p = .028). | Treatment started under hospitalization.Visual Analog Scale for pain intensity, and Hospital Anxiety and Depression scale were used.  |
| Onieva-Zafra MD et al. 2013 (67) | 1bA | 1, 3, 6 | The music group participants reported a significant reduction in pain in VAS (pain on movement: p = 0,002; pain on rest: p = 0,001), as well as in MPQ-LF (sensory categories: p = 0,039, affective categories: p = 0,096, and evaluative categories: p = 0,018), at week 4 compared with the baseline interview, The mean depression scores measured by the BDI from baseline to week 4 improved for the music group (p = 0,016). However, depression scores measured by VAS did not differ significantly.  | Visual Analog Scale (VAS) was used for both pain and depression. McGill Pain Questionnaire Long Form (MPQ- LF) was used for pain. Beck Depression Inventory (BDI) was used for depression. |
| Park H et al. 2010 (68) | 2bB | 1 | Pain levels after listening to music were significantly lower than before listening to the music (p < 0.05).  | Four instruments were used to collect data for this study: The Mini Mental State Exam (MMSE), Assessment of Personal Music Preference (APMP), Modified Cohen-Mansfield Agitation Inventory (M-CMAI), and Modified Pain Assessment in the Dementing Elderly (M-PADE).  |
| Kenny DT et al. 2004 (80) | 1bA | 2, 3 | Participants who attended the singing sessions showed evidence of postintervention improvements in active coping (p = 0,024), relative to those who failed to attend, when preintervention differences in active coping were controlled for. While the singing group showed marked improvements from pre- to postintervention on mood, coping, and perceived pain variables, these im- provements were also observed among comparison partici- pants.  | The following insturuments were used: Zung Depression Inventory, Pain Self-Efficacy Questionnaire, Pain Responses Self-Statements, Oswesn'y Low-Back Pain Disability Questionnaire, and Profile of Mood States.   |
| McCaffrey R et al. 2003 (81) | 1bA | 1 | Those who listened to music had less pain on both the Pain Rating Index on day 1 (p < 001), day 7 (p < 001) and day 14 (p < 001) and on the Visual Analogue Scale on day 1 (P < 001), day 7 (P < 001) and day 14 (P < 001), when compared with those who sat quietly and did not listen to music.  | Two sections in the Short Form McGill Pain Questionnaire (SF-MPQ) were used to measure the perceived level of pain in this study: The Pain Descriptor Scale section of the SF-MPQ measured the evaluative aspects of pain and the Visual Analog Scale (VAS) measured present pain intensity.  |
| Muller-Busch HC 1997 (86) | 3bB | 1, 2 | Significant reduction in pain intensity and an improvement in pain-related functional limitations after music therapy (p < 0.05). | Visual Analog Scale for pain intensity, as well as Pain-related Functional Impairment and Disability Scale were used. |

**IMMPACT outcomes**: 1 - pain; 2 - physical function; 3 - emotional function; 4 - participants' assessment of improvement and satisfaction with treatment; 5 - side effects; 6 - participants' disposition and compliance.

5.4. Synthesis of studiets’ results.

Studies finally identified in this review include only patients with chronic-non cancer pain. The main results are reported in tab.3.

Eight studies include only patients with fibromyalgia (47,52,55-57,59,60,67). In one study only patients with osteoarthritis were included (81). There are two studies with only inclusion of patients with dementia (43,68). The remaining studies include patients with different types of chronic non-cancer pain.

Adult persons were included in all but one study. Sherry et al. (55) investigated the effect of multimodal non-pharmacological treatment program for adolescents with juvenile fibromyalgia. Dance was included in the treatment program. This study seems to be important, because it does not show difficulties with to integrate music activity (dance) with another parts of multimodal treatment program.

In the terms of design, there are 8 prospective randomized controlled studies (43,47,50,57,64,67,80,81) and 8 prospective non-randomized cohort studies (52,55,56,59,60,62,68,86). There are both qualitative, quantitative and mixed-methods studies. The number of patients included in each study varies from 7 to 318. Number of IMMPACT outcoms in each study varies from one to six. All recommended IMMPACT outcomes are included in only two studies (50,60). IMMPACT outcomes are not specified in two studies (51,61).

In all identified studies music showed moderate to strong tendency to improve patient’s physical and emotional function, as well as coping against pain. No one study showed negative effect of music activity in patients with chronic non-cancer pain. However, not all studies showed reduction in pain intensity in response to music. Linnemann et al. (52) did not obtained reduction in perceived pain intensity in patients with fibromyalgia listening to music at home. However, patients in this study reported better perceived control over pain, when listening to music. This study was designed as one-arm prospective trial without control group. Espi-Lopez et al. (47) did not reported effect of music on pain intensity clearly.

Results obtained by Weber et al. (57) indicate, that combination of music with vibration (known as vibroacustic therapy) could give larger improvement than music alone in patients with fibromyalgia. After all, this study is the largest one identified in this review – 120 patients were included.

There were no side effects releated to music. In studies with music therapy some minor logistical and compliance problems were reported. For some patients this was problematic to come to therapeutic sessions because distance from home to treatment center (50).

Different forms of music therapy and music activity were used in the identified studies. In the terms of type of music, both classical, rhytmic and folk music were tested. In some studies music chosen by therapist was preferred In another studies the patient’s chosen music was used. However, the patient’s semi self-chosen music seems to be preferred It can be done in two ways: either patient chooses music from the list provided by therapist, or therapist chooses music from the list provided by patient (43,47,56,59,64).

In the terms of questions expected to be answered in this review (see section 2. OBJECTIVES AND EXPLANATORY STATEMENT), the results of identified studies indicate the following:

1. All studies showed that both music therapy and music activity has a positive effect on patients with chronic non-cancer pain.
2. There are no studies comparing listening to music and professionally practiced music therapy in patients with chronic non-cancer pain.
3. Based on available studies, it is not possible to compare the effect of active music therapy and passive listening to music.
4. Both patient’s choice music and music chosen by the therapist seem to be effective.
5. Music seems to be easy integrated with another non-pharmacological therapeutic approaches. However, they are not studies investigating, how either music therapy or music intervention can be combined with cognitive behavioral therapy (CBT).
6. Currently, it is not possible to determine what kind of music works best for chronic non-cancer pain.
7. There are not sufficient data to determine, whether different genres and forms of music should be used against different kinds of chronic non-malignant pain (neurogenic, dysfunctional, inflammatory, nociceptive).

6. DISCUSSION AND CONCLUSIONS

This explorative review suggests that music therapy and music activity in different forms (listening to music, singing, dance, playing music) can reduce self-reported pain, anxiety, and depression symptoms in a diverse range of patients with chronic non-cancer pain patients. Music showed strong tendency to improve patient’s physical and emotional function, as well as coping against pain.

All of the identified studies reported beneficial effects of music, and in general, these effects were significant. On the basis of results of identified studies, some practical recommendations can be given (level of evidence and grade of recommendation is shown in parenthesis):

1. Music should be recommended in the treatment of patients with fibromyalgia (1b, A)
2. Music should be recommended in the treatment of chronic pain in patients with dementia (1b, A)
3. Music should be recommended as pain remedy in patients with osteoarthritis (1b, A)
4. Music can be used as part of treatment in patients with different forms of chronic non-cancer pain (2a, B).

It is important to emphasize that music apparently does not have side effects, and music activity at patient’s home seems to be without logistical and compliance problems.

However, many questions remain unanswered. Future research should be focused on the following problems:

* Better defining of the role of music in the treatment of other forms of chronic non-cancer pain than fibromyalgia
* Lack of comparative studies of music therapy and music activity in the treatment of chronic non-cancer pain
* Validation of different attitudes to selection of different forms of music used in the treatment of chronic non-cancer pain
* Better defining of interactions between music and other forms of treatment
* Better understanding of the mechanisms responsible for the effectiveness of music as a means to treat the patients with chronic non-cancer pain.

This last question seems to be most intriguing. Mercadie et al. (133) show, that listening to either pleasant music or environmental sounds can produce a similar relieving effect on pain and fatigue in patients with fibromyalgia. Is it music or sound that works? Another possible direction could be to study music as mediator of emotional responses and how this infleunces pain experience.

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Fig.1. Flow diagram for literature search and review.

Publications initially included in synthesis
(n = )

Full text publications assessed for eligibility
(n = )

Publications in screening
(n = )

Publications after removing of duplicates
(n = )

Publications identified in manual searching
(n = )

Publications identified in electronic searching in databases

(n = )

## Identifikation

## Identification

## dentification

## Synthesis

## Screening

## Evaluation

Publications finally included in synthesis
(n = )

Excluded in screening

 (n = )

Excluded
(n = )

Full text publications excluded
(n = )

Fig.2. Flow diagram for literature search and review (see text for additional informations).

Publications initially included in synthesis
(n = 23)

Full text publications assessed for eligibility
(n = 48)

Publications in screening
(n = 1219)

Publications after removing of duplicates
(n = 1219)

Publications identified in manual searching
(n = 7)

Publications identified in electronic searching in databases

(n = 7902)

## Identifikation

## Identification

## dentification

## Synthesis

## Screening

## Evaluation

Full text publications excluded
(n = 4)

Publications finally included in synthesis
(n = 19)

Excluded in screening

 (n = 1171)

Full text publications excluded
(n = 25)