**A systematic review of effectiveness of interventions applicable to**

**radiotherapy that are administered to improve patient comfort,**

**increase patient compliance, and reduce patient distress or anxiety**

Simon Goldsworthy MSc1,2,Shea Palmer PhD2, Jos M. Latour PhD, RN3, Helen McNair PhD4, Mary Cramp PhD2

1. Radiotherapy, Beacon Centre, Musgrove Park Hospital, Taunton and Somerset NHS Foundation Trust, Taunton, United Kingdom.
2. Faculty of Health and Applied Sciences, University of the West of England, Bristol, United Kingdom.
3. Faculty of Health and Human Sciences, University of Plymouth, Plymouth, United Kingdom
4. Royal Marsden NHS Foundation Trust and Institute of Cancer Research, Sutton, United Kingdom.

**Correspondence**: simon.goldsworthy@tst.nhs.uk

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**ABSTRACT**

**Objectives**

The aim of this review was to search existing literature to identify comfort interventions that can be used to assist an adult patient to undergo complex radiotherapy requiring positional stability for periods greater than 10 minutes. The objectives of this review were to; 1) identify comfort interventions used for clinical procedures that involve sustained inactivity similar to radiotherapy; 2) define characteristics of comfort interventions for future practice; and 3) determine the effectiveness of identified comfort interventions. The Preferred Reporting Items for Systematic Reviews and meta-analyses statement and the Template-for-Intervention-Description-and Replication guide were used.

**Key findings**

The literature search was performed using PICO criteria with five databases (AMED, CINAHL EMBASE, MEDLINE, PsycINFO) identifying 5,269 titles. After screening, 46 randomised controlled trials met the inclusion criteria. Thirteen interventions were reported and were grouped into four categories: Audio-visual, Psychological, Physical, and Other interventions (education/information and aromatherapy). The majority of aromatherapy, one audio-visual and one educational intervention were judged to be clinically significant for improving patient comfort based on anxiety outcome measures (effect size ≥0.4, mean change greater than the Minimal-Important-Difference and low-risk-of-bias). Medium to large effect sizes were reported in many interventions where differences did not exceed the Minimal-Important-Difference for the measure. These interventions were deemed worthy of further investigation.

**Conclusion**

Several interventions were identified that may improve comfort during radiotherapy assisting patients to sustain and endure the same position over time. This is crucial for the continual growth of complex radiotherapy requiring a need for comfort to ensure stability for targeted treatment.

**Implications for practice**

Further investigation of comfort interventions is warranted, including tailoring interventions to patient choice and determining if multiple interventions can be used concurrently to improve effectiveness.

**INTRODUCTION**

Positioning and immobilisation of patients are crucial for reproducible and accurate delivery of radiotherapy in both radical and palliative settings to ensure tumour control while avoiding healthy tissue toxicity1-2. Recent studies have shown that comfort in patients receiving radiotherapy for prostate cancer can be determined by treatment position3 and a strong association was observed between comfortable patient positioning and improved treatment accuracy in patients’ receiving radiotherapy for breast cancer4. As more complex treatment techniques like stereotactic ablative body radiotherapy (SABR) becomes standard, and treatment times are extended above 10 minutes, the comfort of patients is an important consideration5-6. It is also hypothesized that there is an association between patient comfort and radiotherapy treatment time7 and one limitation to technical radiotherapy advancements is managing the patient’s tolerability of immobilisation to complete the procedure while also achieving comfort8. Hypothetically, not providing a comfort intervention might increase the treatment time in radiotherapy.

To assist with identification and development of suitable comfort interventions, there is a need to consider what patient comfort is and means. Patient comfort is defined holistically as a state of having met the basic human needs for ease, relief, and transcendence in four contexts9-11. In radiotherapy procedures the role and purpose of holistic comfort interventions aim to make the procedure more tolerable to patients and ensure compliance reducing discomfort, anxiety, distress and claustrophobia. Comfort has been explored in a few studies including a focus group of patients with head and neck cancer receiving radiotherapy2. Their experiences reflected the definition of holistic comfort9-11 and indicated that therapeutic radiographers may not fully appreciate their level of discomfort. A survey of 100 head and neck cancer patients who had received radiotherapy found that a quarter were anxious and that interventions were required including better patient preparation/education12. In UK and European guidelines, recommendations on how to manage patient comfort during radiotherapy are limited2,13-14. Greater evidence of comfort intervention effectiveness is required to inform national radiotherapy practice and guidelines.

Interventions such as communication with professionals and music were reported to reduce distress in up to 86% of patients receiving radiotherapy for head and neck cancer15. A previous systematic review explored the efficacy of holistic comfort interventions during invasive paediatric nursing procedures such as venepuncture, port access and intramuscular injection16. The review grouped comfort interventions into four categories: music, amusement and entertainment, caregiver facilitation and a multifaceted approach and supported the use of various distraction methods to reduce anxiety, distress, fear and pain during procedures18. Further studies have investigated interventions ranging from music to self-hypnosis and deep breathing exercises17-18. Thus, there are promising procedural comfort interventions that may be applicable in radiotherapy. A limited number of interventions have been investigated to manage patient comfort during radiotherapy19-20.

The aim of this review was to search existing literature to identify comfort interventions that can be used to support an adult patient to undergo clinical procedures that requires a patient to sustain the same position over a period greater than 10 minutes. The current estimated time cut off set at 10 minutes was deployed to capture procedures that would replicate the radiotherapy phase after positioning when patients must remain still during pre-treatment verification and treatment delivery such as SABR or palliative radiotherapy. The focus above 10 minutes was set to ensure a breadth of clinical procedures were included that would be more representative of radiotherapy. The objectives of this review were to: 1) identify comfort interventions that are used for clinical procedures that involve sustained inactivity similar to radiotherapy; 2) record the characteristics of the comfort interventions for future practice; and 3) determine the effectiveness of the comfort interventions.

**METHODS**

**Protocol and registration**

A review protocol was developed and prospectively published in PROSPERO (CRD42017059688) in line with the Centre of Reviews and Dissemination21.

**Information sources**

The review was structured and reported according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement22 and the Template for Intervention Description and Replication (TIDieR)23 Guide.

**Search**

Five databases, AMED, CINAHL EMBASE, MEDLINE and PsycINFO, were searched to identify relevant text in titles, abstracts and key words to develop search terms. The literature search used the same databases and refined terms (electronic supplement A). The search was restricted to title and abstract fields to avoid retrieving non-related papers from the subject headings.

Selection criteria for eligible primary research was defined according to the Participant(P), Intervention(I), Control(C), Outcome(O) and Studies(S)24 framework:

1. Adult patients (≥18 years) undergoing a clinical procedure that required alignment, stabilisation, immobilisation and having to sustain, endure or tolerate the procedure while conscious over a period greater than 10 minutes. Clinical procedures included those where patients must remain stable and unwanted movement is critical. In the surgical and radiotherapy setting, unwanted movement could result in collateral damage such as the laceration or irradiation of surrounding normal tissue respectively and potentially poorer outcomes for patients.
2. Interventions to aid comfort; ease, relieve, relief, reduce distress/anxiety, relax, calm, alleviate, distract, or transcend a patient/service user immediately before or within a clinical procedure which requires alignment, stabilisation, or immobilised and has to sustain, endure or tolerate the procedure while conscious.

(C) Usual standard of care or comparator (another intervention)

(O) Assessments of patient comfort, psychological well-being, patient satisfaction and quality of life outcomes.

(S) Randomised controlled trials (RCTs) and controlled clinical trials (CCTs).

Studies published in English between 2000 and January 2019 were included to focus on contemporaneous practice. The searches were initially performed in August 2017 and updated in January 2019. Following removing of duplicates, two researchers independently reviewed the titles and abstracts initially and then full texts to identify papers that met the eligibility criteria. A consensus meeting was held, and concordance was achieved on 95% of the full texts. A third reviewer arbitrated on inclusion of the remaining 5% (n=4) of full texts.

**Data extraction**

Data was extracted from each paper by one researcher using a data extraction form based on the TIDieR checklist and guidelines23 and reviewed by a second researcher. The data extraction form included: authors, year of publication, study design, setting, participants, clinical procedures, outcome measures, main outcomes (measured before and after clinical procedure delivery, or as a mean change), and delivery characteristics of the comfort interventions.

**Risk of bias**

The Cochrane Risk of Bias Checklist (Version 5.1.0) was used to assess risk of bias (RoB) in RCTs25. Six areas of ROB were assessed (random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; and selective reporting) with each area given either “low,” “high,” or “unclear” risk of bias25. To reduce the effect of human factors in assessing RoB27-28 an online software RoBotReviewerTM which aims to semi-automate evidence synthesis using machine learning was used28-29 alongside review by the researchers. International clinical trials registers were accessed to determine selective reporting bias; if not registered then studies were judged unclear for RoB. For CCTs the RoB was assessed using Risk-of-Bias-In-Non-Randomised-Studies-of Interventions. For this review, studies were judged not acceptable if there was high risk for selection bias in both domains because randomisation is a crucial attribute of well-designed RCTs. Studies judged high risk in one area of selection bias, or another RoB component were deemed acceptable but treated with caution, and not included in the data synthesis.

**Data synthesis**

Only validated outcome measures were included in the synthesis and were reported separately for intervention and comparator groups. Where available, the change in outcome measures from before to after clinical procedures was calculated as mean differences, percentage change, Cohen’s D effect size (normalised distribution) or r-effect size (non-normalised distribution) with 95% confidence intervals (CI)30-31. Studies were selected for the Cohen’s D or r-effect size analysis dependant on whether the data followed a normal distribution32-33, confirmed by the reported use of Kolmogorov-Smirnov (KS) or Shapiro-Wilk (SW) test for normality or assumed based on the use of parametric tests37-38. Where mean and standard deviations (SD) were not reported, an estimation from either inter quartile range or p-value was calculated34-37. Meta-analysis was not conducted because of the clinical heterogeneity in the study populations, healthcare settings, interventions and comparator types.

To determine whether comfort interventions make an important difference to the patients, the clinical significance of studies was assessed to supplement statistical significance30-32. In this review, clinical significance was determined using effect size and the minimal importance difference (MID). Effect sizes were interpreted using the following criteria: small effect (≤ 0.4), medium effect (≥ 0.5 ≤ 0.7) or large effect (≥ 0.8)38. Minimal important differences (MID) of validated outcome measures were identified from the literature39-42. A comfort intervention was considered to demonstrate clinical significance when the effect size exceeded 0.4, mean differences were greater than the MID and RoB was acceptable.

**RESULTS**

**Study selection**

Database searches initially identified 5269 titles (Figure 1). After removing duplicates (n=191), 5078 titles and abstracts were screened, and 4994 papers were removed leaving 84 papers for full review. Of these, 38 papers were excluded for reasons listed in Figure 1. One CCT was excluded because it used a parallel cross over design with potential for cross contamination between intervention and comparator groups. In total 46 papers were included in the review43-88.

**Study characteristics** (electronic supplement B & C).

The studies included consisted of 46 RCTs with a total of 5782 patients 43-88. The age of participants ranged between 18 and 80 years. The study design of RCTs included; two-arm parallel, multiple arm parallel, and mixed factorial multiple/ parallel arm study designs.

*Clinical procedures*

Nineteen different clinical procedures were identified. The two most common clinical procedures were observational investigations such as bronchoscopy/hysteroscopy (n=14) and interventional radiology (n=13).

*Outcome measures*

Most studies reported an anxiety outcome measure (n=44) and 29 studies used the State-Trait Anxiety-Inventory (STAI) aligning to psychological wellbeing. The STAI examines feelings ‘at the present moment’ and gives a score between 20 and 80, with a higher score indicating greater anxiety levels89. One study used a 6-item short STAI which is stated to be more sensitive to fluctuations in anxiety90. One study used the anxiety Visual-Analogue-Scale (VAS-A)41-42, and another study used the Beck-Anxiety-Inventory (BAI) and Hamilton-Anxiety-Scale (HAS) and non-validated numeric rating scales for comfort, satisfaction, willingness to repeat and experience of the environment91. Only validated anxiety measures including the STAI, the VAS-A, the BAI and the HAS, reported before and after clinical procedures, were included in the data synthesis. For the STAI, the MID was set at 1039-40. The MID was set at 46 for the VAS-A41, 8.8 for the BAI and 8.2 for the HAS42.

**Comfort interventions** (electronic supplement B).

Thirteen comfort interventions were identified and grouped into the four categories (Table 1): Audio-visual, Psychological, Physical, and Other Interventions (education/information and aromatherapy). Comfort interventions were delivered before the clinical procedure in 10 studies, during the clinical procedure in 19 studies and both before and during the clinical procedure in 17 studies.

* Audio-visual technology interventions include audio only (n =20)43-48,55,60-61,64,66, 68,70-74,77,82,84,86, audio-visual (n= 6)50,51,53,60,69,88, virtual reality (n =2)67,85 and visual only (n=1)88. The interventions were used for the purpose of improving (dis)comfort, reducing anxiety, distraction, improving well-being and relaxation. A wide range of music genres were used ranging from classical to easy listening popular music, chants and nature sounds. The delivery features ranged from music or video players, loudspeakers or earphones to headsets and goggles for virtual reality. Interventions were delivered by professionals and/or self-administered by patients.
* Psychological interventions include breathing techniques (n=1)80, cognitive behavioural therapy (n=1)79, distraction (n=1)64, empathetic attention (n=4)49,60,65,76 and hypnosis (n=4)57,65,76,81. The interventions were used for the purpose of reducing discomfort, anxiety and pain, or improving satisfaction and relaxation. The delivery features ranged from face to face to audio players. Interventions were delivered by therapists or self-administered by patients via audio players.
* Physical interventions includes massage (n=2)75,80, therapeutic touch (n=1)54, reflexology (n=2)56,78 and stress balls (n=1)60. The interventions were used for the purpose of reducing discomfort, anxiety, distress and pain, or improving satisfaction. The delivery was face to face with professionals.
* Other interventions includes education/information (n=4)43,62-63,87 and aromatherapy (n=5)52, 58, 59,78,83. The interventions were used for the purpose of improving experience and satisfaction or reducing anxiety and psychophysiological arousal/parameters. Interventions were delivered by a range of personnel and methods.

Some studies with multiple arm parallel designs investigated interventions that crossed the above categories (n=5)45,64,73,75,80.

**Cochrane Risk of bias for included studies**

Each of the included RCTs had areas where the ROB was high, low, and unclear (Fig.2). 38% of RCTs had a low overall risk of bias. Low risk for random sequence generation and concealment was reported in 77% and 32% of studies respectively. Blinding of professionals or participants to the allocated comfort intervention was reported in 6% of studies, whilst blinding of outcome assessment was completed in 36%. 81% of RCTs were judged unclear for selective reporting because trials were not registered. 3 RCTs were deemed unacceptable due to high risk of selection bias and were not included in the data synthesis59, 67,69.

**Effectiveness of comfort interventions**

Only anxiety outcomes were synthesised as the outcome measures were validated and reported before and after clinical procedure (Table 2). This resulted to exclude another 17 RCTs45-46,49,54,58,61-62, 65,70,72,74,76,78-79, 84-86. 26 RCTs were included in the data synthesis.

Audio-visual technology interventions includes studies of audio alone44, 47-48, 50, 55, 60, 64, 66, 68, 71,73,77, 82, 88, ,audio-visual50-51, 53, 60 and visual88 interventions with data available for synthesis.

*Audio:* six out of eleven studies of audio interventions reported statistical significance favouring the intervention (p<0.05)44, 47, 55, 60, 73. The mean difference in anxiety exceeded the MID in one intervention and with a medium effect size was judged clinically significant71. Medium to large effect sizes were observed in all eleven studies.

*Audio-visual:* three out of four audio-visual interventions studies reported statistically significance favouring the intervention (p<0.05) 51, 53, 60. The mean difference in anxiety exceeded the MID in two studies50-51; one had a small effect size51 and one favoured the comparator group50. Medium to large effect sizes were observed in all other studies50, 51, 53, 60, 88.

*Visual:* one visual intervention study favoured the intervention statistically (p <0.05) 88. The mean difference in anxiety did not exceed the MID but had a large effect size88.

Only one study investigating music interventions was deemed clinically significant71.

Psychological interventions with data available for synthesis included distraction64, empathetic attention60 and hypnosis57, 81 interventions.

*Distraction:* one study did not show a statistically significant effect for distraction intervention64. The difference in mean anxiety did not exceed the MID64, and the effect size favoured the comparator group.

*Empathetic attention:* one study reported statistical significance favouring the intervention60 (p<0.05). The mean difference in anxiety did not exceed the MID, and while it had a large effect size, it was deemed not clinically significant.

*Hypnosis:* two studies reported statistical significance favouring hypnosis interventions57, 81(p<0.05). Both had large effect sizes but the mean difference in anxiety did not exceed the MID in either study 57, 81.

No intervention in this category was considered clinically significant.

Physical interventions were used in three studies with data available for synthesis and involved physical touch: reflexology56, massage75, and stress balls60.

Two out of three studies reported statistical significance favouring the intervention (p<0.05) 56, 60. The mean difference in anxiety exceeded the MID in one study75 with large effect sizes in the other two56, 60. None of the physical interventions were judged clinically significant56, 60, 75.

Other intervention studies with data available for synthesis involved education/information63, 83 and aromatherapy52, 83 interventions.

Education/ information: three studies evaluated the effects of education/information interventions 43, 63, 87. After the clinical procedure one studies reported statistical significance favouring the intervention (p<0.05)63.The mean difference in anxiety did not exceed the MID in two studies 43, 63,and small to large effects sizes favouring the comparator were observed. One study investigating a multi-media information and instruction intervention deemed to be clinically significant87.

*Aromatherapy:* two studies evaluated the effects of aromatherapy essential oil interventions with different methods of diffusion52, 83. One study reported statistical significance favouring the intervention (p<0.05)52 and the other did not83. The difference in mean anxiety exceeded the MID in both studies52, 83. Medium to large effect sizes were observed in both studies and were deemed clinically significant52, 83. These two studies investigating Lavandula angustifolia, Citrusaurantium L, Lavender-sandalwood, and Orange-peppermint aromatherapy were deemed clinically significant52, 83.

**DISCUSSION**

The aim of this review was to identify effective comfort interventions to support patients undergoing clinical procedures that require a patient to sustain the same position over a period greater than 10 minutes. Thirteen comfort interventions were identified which ranged from aromatherapy to virtual reality delivered before and during nineteen different clinical procedures in 46 studies. Anxiety outcomes were synthesised as the outcome measures were validated and reported before and after clinical procedure in 26 studies.

The findings of the review showed that many comfort interventions produced statistically significant improvement in anxiety outcomes but did not demonstrate clinical significance as defined for this study. Aromatherapy52, 59, 83 used in colonoscopy, interventional radiology and minor surgery demonstrated both statistical and clinical significance and could be used in radiotherapy with careful consideration of application. Aromatherapy using vaporising systems may be contraindicated because of the potential for skin irritation or allergies linked to radiation induced skin toxicity or for vapour damage to radiotherapy equipment. A clothing tab infused with aromatherapy oils, found to be favourable in previous clinical trials92, may be more appropriate in radiotherapy . Audio and audio-visual interventions demonstrated medium to large effect sizes44,47,48,51,53,55,60,67,68,71,73,77,82,88 with several showing clinical significance that warrant further investigation in radiotherapy. A number of radiotherapy departments have audio-visual technology available to support their patients and audio interventions have been successfully tested in radiotherapy. For example, Chen et al93 reported that music therapy reduced pre-radiotherapy anxiety only but did not examine the effect during the clinical procedure and for this reason, was not included in our synthesis. Audio interventions may be contraindicated in radiotherapy at times where constant communication between radiographers and patients is required such as verbal instructions to patients on performing deep inspiration breath hold or where an audio device such as earphones or audio pillows attenuates the radiation beam. Devices may be impractical due to an immobilisation mask. Visual interventions may not be so easily accommodated during some radiotherapy techniques but some interventions such as decorative wall colour or murals may be a pragmatic option.

Three psychological interventions and two physical interventions provided immediately before or during the clinical procedure demonstrated medium to large effect sizes57,60,81. Psychological interventions provided as part of the preparation for radiotherapy have been studied and cognitive behavioural therapy and hypnosis have been shown to significantly (*p =* .0035) improve breast cancer patient general experiences94. Similarly, massage provided during a course of radiotherapy treatment reduced anger anxiety and depression in patients with breast cancer receiving radiotherapy (*p* < 0.001)95. This review focused on interventions that could be delivered within radiotherapy sessions. Psychological interventions could be readily adopted if self-administered using an audio player. Use of empathetic interventions encouraging social interaction could be challenging to deliver. However Gibbon et al96 found that patient orientated communications skills training for the radiotherapy multi-disciplinary team resulted in significantly more empathetic interaction (*p* = 0.037).

Distraction using physical devices such as stress balls could be implemented with care taken not to disrupt the desired position for accurate radiotherapy. One intervention providing educational information via DVD demonstrated clinical significance87 and could be implemented in a radiotherapy department. These interventions could also be applicable to clinical procedures including brachytherapy where there is need to develop non-pharmacological interventions97 and paediatric radiotherapy where general anaesthesia could be reduced98.

One gap observed from the studies is the effect of combining interventions as a ‘comfort package’ to enhance effectiveness. Simmons et al80 investigated four interventions to support patients undergo cataract surgery with favourable results for combined interventions. Similarly, a systematic review by Bice et al19 found statistically significant differences favouring multifaceted (more than one intervention) interventions in most studies included in their review. Further research investigating a comfort intervention package (multiple interventions) may provide greater effectiveness for patients during radiotherapy treatment.

Some methodological aspects of the systematic literature review and reviewed studies warrant further consideration. Firstly, anxiety outcome measures may not be the most suitable measure of comfort.The current review included studies with interventions that aimed to comfort, or to alleviate or reduce discomfort, anxiety and distress of clinical procedures. Comfort can be viewed holistically within physical, sociocultural, psychospiritual and environmental contexts that are not reflected in anxiety measures. There are limited comfort outcome measures, however the recently validated Radiotherapy-Experience-Questionnaire could be considered for measuring comfort in radiotherapy99. Going forward, use of comfort outcome measureswithin all specialties is required for generating new evidence and confirming treatment effects of comfort interventions.

For the purposes of this review, clinical significance of the anxiety measures was demonstrated with a medium or above effect size (≥ 0.4) and mean differences greater than the MID. However, the availability of information about MID specific to the outcome measures reported in this review was limited. The MID level of 10 for the STAI was based on a population of smokers; in a non-smoking population the MID maybe higher or lower40. Similarly, the MID for the BAI and HAS was based on a sample of patients with Parkinson’s 42. Further work is required for MID development in appropriate populations to assist with determining clinically effective interventions.

The research quality of the reviewed studies was an issue and a meta-analysis was not conducted due to this factor and because of the challenges of defining the nuances of comfort, clinical procedures and interventions. 8 RCTs were deemed unacceptable due to a high risk of selection bias and were not included in the data synthesis. Many studies did not register with an international clinical trial register which affected the assessment of selective reporting; these studies were therefore judged as having unclear RoB. Although there were some methodological challenges, a rigorous review process was followed and a semi-automated machine learning programme, RoBotReviewerTM 28-29, was used for Cochrane RoB to increase the rigour of this review by reducing the impact of human factors during data extraction. Combining the use of semi-automated extraction with manual assessment was useful and future reviews should consider using machine or deep learning systems to improve the rigour and quality of data extraction100.

To our knowledge, this is the first systematic review that could support the further investigation of comfort interventions in radiotherapy. Given the limited recommendation of how to manage patient comfort during radiotherapy from national and European guidelines2,9, the findings of this review and further investigation of comfort interventions will provide the evidence required for future guidelines. Given the perpetual increase in new effective treatment options and technology available in radiotherapy, it is essential that the community embraces and implements comfort interventions ensuring the best outcomes for patients.

**CONCLUSION**

The majority of aromatherapy interventions were clinically significant and they can be potentially considered for radiotherapy that require patients to sustain and endure the same position over time similar to these clinical procedures. There was limited evidence for other comfort interventions, although most effect sizes favoured the intervention, suggesting important benefit to patients. Further investigation of these comfort interventions is warranted, including tailoring interventions to patient choice and determining if multiple interventions could be used concurrently to improve their effectiveness. This is crucial for complex radiotherapy that necessitates more demand and attention to patient comfort to ensure stability for targeted treatment.

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## Identification

## Included

## Eligibility

Full-text articles assessed for eligibility   
(n = 84)

## Screening

Records excluded after reading titles & abstracts (n = 4994)

Records screened   
(n = 5078)

Records identified through database searching   
(n = 5269)

Records after duplicates removed   
(n = 191)

Full-text articles excluded (n = 38)

Reasons by frequency (some had more than one exclusion):

1 - Written in Arabic

8 - Participants under 18yrs

4 - General anaesthetic used

7 – Clinical procedure does not require stabilisation/ alignment

1 – Focus on side effects

13 – Non eligible outcome measure

1 – Clinical procedure less than 10 minutes

1 – Study protocol

1 – qualitative study

1 – Intervention does not comfort, relax, or ease patients

1 – Not focused on clinical procedure

Studies included in review   
(n = 46)

Studies included in data synthesis   
(n = 26)

**Figure 1. Flow diagram of the strategy search.**

**Table 1 – Intervention delivery characteristics**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Comfort intervention** | **Rationale** | **Materials** | **Delivery features** | **Delivered by** |
|
| **AUDIO-VISUAL TECHNOLOGY INTERVENTIONS** | | | | |
| **Audio 🡪** | Reduce anxiety 43-48,55, 60, 64, 66, 71-73, 77, 84, 86, 88, discomfort48, stress61, pain42, 60, 64, 71-72, 77, heart rate68, analgesics/ anxiolytics71  Improve satisfaction48, 60, 74, compliance48, 82, 92, relaxation42, 70-71, comfort70-71, wellbeing59, reactive hyperaemia index74 | A range of music genres. 42, 44-48, 55, 60-61, 64, 68, 70-73, 77, 82  Vedic chants73  Nature sounds  Music therapy (meditative, relaxing)66, 68, 74, 86 | Music player (e.g. CD player/computer)44-48, 60-61, 64, 68, 70-73, 77, 82, 86,  Loudspeaker70-72, 82  Earphones45-48, 60-61, 64, 68, 73, 77 Cushion with speaker74, 86 Not specified42,55, 68  🞟Most at 50-80bpm42, 44-48, 55, 60-61, 64, 68, 70-73, 77, 82 | Technician42  Music therapist45  Research nurse44  Student nurses46  Nurses46-47,55,60, 70  Investigators48, 55  Physicians42, 46  CT technologists68  Study personnel86  Not specified50, 61 , 64, 66, 68, 72-74, 77, 82, 84, 88 |
| **Audio- visual 🡪** | Reduce anxiety50-53, 60  Reduce pain50-52,60  Improve experience52-53  Improve satisfaction52  Tolerate procedure69 | Nature sounds such as a waterfall50-51, 88 Nature scene such as a mountain stream, tropical beach, general landscape scenery and animation50-51,69, 88   Videos included documentaries and movies,60, 88   Comedies, documentaries and panel-based quiz shows Iranian music69 | Music player (e.g. CD player/computer)50-51, 69  loudspeaker  Earphones50-52, 69  Wall or ceiling mounted murals of nature scenes with/without lighting50-51,53,69, 80.  Video goggles connected to DVD52-53  Wall mounted monitor connected to DVD  Projector connected to DVD60 | Standard clinic staff51  Nurse52,60  Not specified50, 52-53, 69 |
| **Visual 🡪** | Distraction from pain,  anxiety, and tolerate procedure88 | Scenery, animation, to film88 | Monitor with DVD player  (no sound)88 | Not specified88 |
| **Virtual  reality (VR) 🡪** | Reduce pain85  Reduce anxiety85  Reduce opioid use67 |  Throwing/shooting snowballs at objects by clicking a computer mouse button67, 85 | Headset goggles, earphones, DVD player, VR system67  VR group donned a VR helmet and track ball hand controller85 | Nurses67  Not specified85 |
| **Comfort interventions** | **Rationale** | **Materials** | **Delivery features** | **Delivered by** |
|
| **PSYCHOLOGICAL INTERVENTIONS** | | | | |
| **Breathing techniques 🡪** | Reduce discomfort, pain & anxiety80 | Verbal coaching  and slow breathing instructed80 | Face to face80 | Nurses80 |
| **Cognitive behavioural therapy 🡪** | Improve relaxation79 |  Live guided imagery79  Recorded guided imagery79 |  Face to face79   CD player79 | Trained therapist79 |
| **Distraction 🡪** | Reduce pain & anxiety64 |  Participant reads a book64 |  A book64 | Research nurses64 |
| **Empathic attention 🡪** | Reduce pain60, 76  Reduce anxiety49, 60, 76  Improve satisfaction60  Reduce discomfort65  Reduce adverse effects65 |  Verbal empathy49,65,76 & touch49  Non-verbal attention76 Engage in conversation60, 76 Attentive listening, Perception of control, Emotionally neutral, Avoid negative suggestion76 |  Face to face 49, 60, 65, 76 | Nurse60  Medical student65, 76  Psychology graduate65, 76  Therapist49 |
| **Hypnosis 🡪** | Reduce pain76, 81  Reduce anxiety57, 76, 81  Reduce discomfort &Reduce adverse effects65 |  Progressive relaxation, visualisation, & deep trance57,65, 81 |  Face to face, 65, 81 Self hypnosis57,76 | Nurse65, 76  Medical student65, 76  Psychology graduate65, 76  Not specified57  Social worker81 |
| **Comfort interventions** | **Rationale** | **Materials** | **Delivery features** | **Delivered by** |
|
| **PHYSICAL INTERVENTIONS** | | | | |
| **Massage, therapeutic touch  & reflexology🡪** | Reduce pain75,80  Reduce anxiety56, 75, 78  Reduce diststress54  Reduce discomfort54,80 |  Massage75,80  “energy repatterning” hand movements over parts of the patient’s anatomy (often the torso) where energy field abnormalities are detected54  Three reflexology acupressure points for the pituitary gland, heart and solar plexus were stimulated by hand56,78 |  Face to face light finger80 & 20 minutes Effleurage strokes across different parts of the body Massage75  Face to face Kriegler and Kunz Therapeutic touch Massage54  Face to face foot reflexology (both feet) for 10 minutes56,78 | Nurse80  Four trained practitioners54  Massage therapist75  Reflexologist56,78 |
| **Distraction 🡪** | Reduce pain, anxiety and improve patient satisfaction60 | Stress balls60 |  Stress balls manipulated during clinical procedure by participant60 | self-directed by patientt60 |
| **Comfort interventions** | **Rationale** | **Materials** | **Delivery features** | **Delivered by** |
|
| **OTHER INTERVENTIONS** | | | | |
| **Education/ information 🡪** | Improve experience43  Reduce anxiety62, 87  Reduce psychophysiological arousal63  Increase satisfaction87 | Participant watches live examination63  Video education/ information43 Audio information about procedure62 Instructional Accessibility-enhanced multimedia informational education (AEMIE)87 |  Monitor screen of examination63  Monitor screen with DVD player43, 87 Music player & headphones62 Head mounted display with headphnes63 | Radiographer43  Research assistant62  Nurse63, 87 |
| **Aromatherapy 🡪** | Reduce anxiety 52, 58-59, 83  Reduce physiology parameters59, 78 | Lavandula angustifolia Miller, citrus aurantium L. essencses52  Lavender oil, grapefruit oil, and Osmanthus fragrans+B7 oil for diffusion58 Neroli essences were poured on gauze59  Essential oils lavender/sandalwood on tab or orange/peppermint on tab83 |  Participants inhaled aroma from the tissue paper for 20 minutes from a 20cm distance52  Diffuser used58  Delivered via handhold- nebulizer with oxygen mask which pneumatically pump the oil into the mask; the oxygen masks were placed on the participants nose to smell for five minutes59 Tabs placed on participant gown83 | Study researchers52 Endoscopist58 Nurse83 Not specified59,78 |



**Figure. 2. Cochrane risk of bias summary of randomised controlled trials (n=46)**

**Table 2 – Clinical significance of interventions before & after clinical procedures (based on anxiety outcome measures)**

| **Source** | **Comfort intervention**  **category** | **Outcome measure** | | **Mean difference Before-after clinical procedure** | | |  | **Mean difference between groups** | **% difference between groups** | **Effect size with CI (95%)** | **Intervention Clinically significant** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Type | Minimal important difference (MID) | **Intervention Group** | | **Comparator Group** | |
| Mean difference | ≥MID | Mean difference | ≥MID |
| Angioli R, et al 201444 | **Audio-visual technology interventions** | STAI | 10 | 3.4 | X | 1.1 | X | 2.2 | 66% | 4.2 (3.8 to 4.5) | No |
| Buffum MD, et al 200647 | STAI | 10 | 3.4 | X | 1.1 | X | 2.2 | 66% | 4.1 (3.5 to 4.6) | No |
| Chlan L, et al 200048 | STAI | 10 | 2.4 | X | -1.6 | X | 4.0 | 167% | 0.7 (0.2 to 1.2) \* | No |
| Hayes A, et al 200355 | STAI | 10 | 4.4 | X | 1.5 | X | 2.9 | 66% | 1.2 (0.9 to 1.5) | No |
| Hudson BF, et al 201560(music) | STAI | 10 | 0.0 | X | -2.3 | X | 2.3 | 102% | 1.3 (1.7 to 1.0) | No |
| Kwekkeboom KL, et al 200364 | STAI | 10 | 4.1 | X | 7.0 | X | -2.9 | -71% | -5.0 (-3.8 to -6.2) | No |
| LEE WL, et al 201766 | STAI | 10 | 5.3 | X | -0.7 | X | 5.9 | 88% | 5.6 (4.6 to 6.6) | No |
| Ng MY, Et al 201668 | STAI | 10 | 2.0 | X | 1.2 | X | 0.8 | 41% | 0.6 (0.3 to 0.9) | No |
| Nilsson U, et al 200971 | Short STAI | 10 | 14.7 | ✓ | 14.3 | ✓ | 0.4 | 2% | 0.5 (0.5 to 0.5) \* | Yes |
| Padam A, et al 201773 | STAI | 10 | 1.9 | - | 1.4 | X | 0.5 | 26% | 0.4 (0.0 to 0.7) | No |
| STAI | 10 | 3.8 | X | 1.4 | X | 2.4 | 63% | 2.6 (2.1 to 3.1) | No |
| Shabanloei R, et al 201077 | STAI | 10 | 9.7 | X | 5.8 | X | 3.9 | 40% | 3.6 (2.9 to 4.3) | No |
| Sobana R, et al 201582 | Short STAI | 10 | 6.1 | X | 0.1 | X | 6.1 | 99% | 2.0 (2.6 to 1.3) | No |
| Diette GB, et al 200350 | STAI | 10 | 13.5 | ✓ | 12.0 | ✓ | 1.5 | 11% | -1.8 (-1.3 to -2.4) | No |
| Drahota A, et al 200851 | STAI | 10 | 13.5 | ✓ | 12.0 | ✓ | 1.5 | 11% | 0.2 (-0.3 to 0.6) \* | No |
| Fang AS, et al 201653 | STAI | 10 | 6.1 | X | 0.1 | X | 6.1 | 99% | 2.0 (2.5 to 1.5) | No |
| Hudson BF, et al 201560 (DVD) | STAI | 10 | 2.3 | X | -2.3 | X | 4.6 | 199% | 3.3 (3.8 to 2.8) | No |
| Xiaolian J, et al 201588 | STAI | 10 | 5.0 | X | 4.1 | X | 0.8 | 17% | 0.7 (0.3 to 1.0) | No |
| STAI | 10 | 2.5 | X | -2.3 | X | 4.7 | 7% | 3.3 (3.8 to 2.8) | No |
| Hızlı F, et al 201557 | **Psychological interventions** | BAI | 8.8 | 3.0 | X | -1.9 | X | 4.8 | 38% | 0.9 (0.6 to 1.2) \* | No |
| HAS | 8.2 | 4.6 | X | -2.8 | X | 7.4 | 40% | 0.9 (0.6 to 1.3) \* | No |
| Snow A, et al 201281 | VAS-A (0-100mm) | 46 | 22.0 | X | 13.0 | X | 9.0 | 41% | 0.7 (1.2 to 0.3) | No |
| Kwekkeboom KL,  et al 200364 | STAI | 10 | 6.3 | X | 7.0 | X | 0.7 | 11% | -1.2 (-0.5 to -1.9) | No |
| Hudson BF, et al 201560 | STAI | 10 | 2.5 | X | -2.3 | X | 4.7 | 193% | 3.3 (3.8 to 2.8) | No |
| Heidaria F, et al 201756 | **Physical interventions** | STAI | 10 | 4.4 | X | 1.5 | X | 2.9 | 66% | 1.0 (0.9 to 1.0) \* | No |
| Rosen J, et al 201375 | STAI | 10 | 6.5 | X | 8.6 | X | -2.1 | -32% | -0.2 (0.5 to -0.9) | No |
| STAI | 10 | 12.1 | ✓ | 9.5 | X | 2.6 | 21% | 0.2 (0.9 to -0.4) | No |
| Hudson BF, et al 201560 | STAI | 10 | 3.0 | X | -2.3 | X | 5.3 | 176% | 2.4 (2.8 to 1.9) | No |
| Ahlander BM, et al 201843 | **Other: Education/  information** | STAI | 10 | 6.5 | X | 1.1 | X | 5.4 | 83% | -1.0 (-1.4 to-0.6) | No |
| Kola S, et al 201363 | STAI | 10 | -4.0 | X | 4.5 | X | -8.5 | 212% | 1.0 (-1.2 to -0.7)\* | No |
| 10 | 6.2 | X | 3.5 | X | 2.7 | 44% | 0.4 (-0.3 to 1.1)\* | No |
| 10 | -6.2 | X | 4.5 | X | -10.7 | -173% | -1.0 (-1.3 to-0.5)\* | No |
| 10 | 4.1 | X | 3.9 | X | 0.1 | 3% | 0.0 (-0.3 to 0.4) \* | No |
| Wu KL, et al 201487 | STAI | 10 | 16.3 | ✓ | 10.2 | ✓ | 6.2 | 38% | 0.9 (0.6 to 1.2) \* | Yes |
| 13.5 | ✓ | 10.2 | ✓ | 3.3 | 25% | 0.5 (0.0 to 1.0) \* | Yes |
| Eslami J, et al 201852 | **Other:  Aromatherapy** | STAI | 10 | 12.8 | ✓ | -1.0 | X | 13.8 | 92% | 5.9 (4.7 to 7.1) | Yes |
| STAI | 10 | 13.7 | ✓ | -1.0 | X | 14.7 | 93% | 9.0 (4.7 to 10.7) | Yes |
| Hu PH, et al 201059 | STAI | 10 | 11.0 | ✓ | 7.1 | X | 3.9 | 35% | 0.3 (-2.6 to 2.1) \* | No |
| Trambert T, et al 201483 | STAI | 10 | 14.2 | ✓ | 2.9 | X | 11.3 | 79% | 0.5 (-2.4 to 3.3) \* | Yes |
| STAI | 10 | 6.5 | X | 2.9 | X | 3.6 | 55% | 0.2 (-2.8 to 3.1) \* | No |

**Electronic Supplement A – Search and Mesh terms**

|  |  |  |  |
| --- | --- | --- | --- |
| **COMFORT** | **CLINICAL PROCEDURE** | **INTERVENTION** | **RESEARCH DESIGN** |
| ((((((uncomfortable).ti,ab OR  (discomfort\*).ti,ab OR (anxiety OR anxious).ti,ab OR exp ANXIETY/ OR (distress\*).ti,ab OR (stress\*).ti,ab OR exp "STRESS, PSYCHOLOGICAL"/ OR (fear\*).ti,ab OR exp FEAR/ OR (fright\*).ti,ab OR (scare\*).ti,ab OR (emotion\*).ti,ab OR (tension OR tense\*).ti,ab OR (misapprehen\*).ti,ab OR (apprehens\*).ti,ab OR (panic).ti,ab OR exp "PANIC DISORDER"/ OR (claustrophob\*).ti,ab OR exp "PHOBIC DISORDERS"/) | Radiotherapy\*  “radiation therap\*”  exp RADIOTHERAPY/ ((procedur\*).ti,ab OR exp  "SURGICAL PROCEDURES, OPERATIVE"/ OR ("local anaesthe\*").ti,ab OR ("regional anaesthe\*").ti,ab OR ("conscious surgery").ti,ab OR ("awake surgery").ti,ab OR (surgery).ti,ab OR (immobil\*).ti,ab OR (invasive).ti,ab OR exp "MINIMALLY INVASIVE SURGICAL PROCEDURES"/)) [DT 2000-2018]" NOT ((child\*).ti,ab OR (paediatric\* OR pediatric\*).ti,ab)) | AND (((ease\*).ti,ab OR  (comfort\*).ti,ab OR (transcend\*).ti,ab OR (relax\*).ti,ab OR exp RELAXATION/ OR (relieve OR relief).ti,ab OR (alleviat\*).ti,ab OR (distract\*).ti,ab OR (calm\*).ti,ab) AND ((intervention\*).ti,ab OR (treat OR treatment\*).ti,ab OR (therap\*).ti,ab OR (technique\*).ti,ab OR (hypnosis).ti,ab OR exp HYPNOSIS/ OR exp "MIND-BODY THERAPIES"/))) AND | (("randomised  control trial\*").ti,ab OR ("randomized control trial\*").ti,ab OR exp "CONTROLLED CLINICAL TRIALS AS TOPIC"/ OR exp "NON-RANDOMIZED CONTROLLED TRIALS AS TOPIC" |

**Electronic Supplement B – Characteristics of included studies**

| **Sources** | **Setting** | **Design** | **Study  participants** | **Comfort Intervention** | **Clinical procedure** | **Clinical procedure timings (minutes)** |
| --- | --- | --- | --- | --- | --- | --- |
| Ahlander  BM, et al 201843 | Outpatient: diagnostic imaging  department at 1 hospital | RCT -  two-arm parallel design | 49 video information  48 comparator | Education/ information; administered before procedure | Cardiovascular magnetic resonance imaging | 40 – 80 |
| Angioli R, et al 201444 | Outpatient: gynaecology day surgery at 1 hospital | RCT -  two-arm parallel design | 185 music  187 comparator | Audio: administered during procedure | Hysteroscopy | 10 – 30 |
| Argstatter H, et al 200645 | Outpatient: cardiology day surgery at 1 hospital | RCT -  multiple arm parallel design | 28 music  28 coaching  27 comparator | Audio & coaching; administered before & during procedure | Intracardiac catheterization | 30 – 40 |
| Björkman I, et al 201346 | Outpatient: endoscopy department at 1 hospital | RCT -  two-arm parallel design | 60 music  60 comparator | Audio; administered before & during procedure | Colonoscopy | 30 |
| Buffum MD, et al 200647 | Outpatient: interventional radiology department at 1 hospital | RCT -  two-arm parallel design | 89 music  81 comparator | Audio; administered before & during procedure | Vascular angiography | 30 – 60 |
| Chlan L, et al 200048 | Outpatient: endoscopy department at 1 hospital | RCT -  two-arm parallel design | 30 music  34 comparator | Audio; administered during procedure | Flexible sigmoidoscopy | 10 -20 |
| Choi SM, et al 201649 | Outpatient: bronchoscopy department at 1 hospital | RCT -  multiple arm parallel design | 89 verbal empathy  88 verbal empathy & touch  90 comparator | Empathic attention; administered before procedure | Impacted mandibular third molar removal | 20 |
| Diette GB,  et al 200350 | Outpatient: endoscopy department at 1 hospital | RCT -  two-arm parallel design | 41 audio-visual  39 comparator | Audio-visual; administered before & during procedure | Flexible bronchoscopy | 15 - 45 |
| Drahota A, et al 200851 | Outpatient: nail surgery clinics at 1 hospital & 1 community centre | RCT -  two-arm parallel design | 78 audio-visual  74 comparator | Audio-visual; administered before & during procedure | Minor surgery | 60 |
| Eslami J, et al 201852 | Outpatient: urology department at 1 hospital | RCT -  multiple arm parallel design | 30 aromatherapy: lavandula angustifolia miller essence  30 aromatherapy: citrus aurantium L.  30 comparator | Aromatherapy; administered before & during procedure | Laparoscopic cholecystectomy | 30 |
| Fang AS, et al 201653 | Outpatient: interventional radiology (IR) department at 1 hospital | RCT - two-arm parallel design | 39 video glasses 44 comparator | Audio-visual; administered during procedure | Interventional radiology | 20 - 30 |
| Frank LS et al 200754 | Outpatient: day surgery at 1 hospital | RCT -  two-arm parallel design | 42 therapeutic touch  40 comparator | Massage/ therapeutic touch & reflexology; administered before & during procedure | Stereotactic core breast biopsy | 30 - 60 |
| Hayes A, et al 200355 | Outpatient:  gastrointestinal diagnostic centre at 1 hospital | RCT -  two-arm parallel design | 100 music  98 comparator | Audio; administered before & during procedure | colonoscopy or esophagogastroduodenoscopy | 15 - 30 |
| Heidaria F, et al 201756 | Outpatient:  coronary angiography department at 1 hospital | RCT -  two-arm parallel design | 45 h& reflexology  45 comparator | Therapeutic touch; administered before procedure | Coronary angiography | 30 - 40 |
| Hızlı F, et al 201557 | Outpatient: urology day surgery at 1 hospital | RCT -  two-arm parallel design | 32 hypnotherapy  32 comparator | Hypnosis; administered before procedure | Transrectal ultrasound‑ guided prostate needle biopsy | 30 |
| Hozumi H, et al 201758 | Outpatient: colonoscopy department at 1 military hospital | RCT -  multiple arm parallel design | 72 vehicle (placebo)  71 lavender  71 grapefruit  74 osmanthus fragrans  73 comparator | Aromatherapy; administered during procedure | Colonoscopy | 30 |
| Hu PH, et al 201059 | Outpatient: colonoscopy at 1 hospital | RCT -  two-arm parallel design | 14 neroli aromatherapy  13 comparator | Aromatherapy; administered before procedure | Colonoscopy | 30 |
| Hudson BF, et al 201560 | Outpatient: private clinic specializing in minimally invasive treatment of venous conditions | RCT -  multiple arm parallel design | 84 music  80 DVD  78 interaction  80 stress ball  76 comparator | Audio,  audio-visual, interaction & stress ball; administered during procedure | Minimally invasive surgery of venous conditions | 60 |
| Jiménez-Jiménez M, et al 201361 | Outpatient:  angiography & vascular surgery department at 1 hospital | RCT -  two-arm parallel design | 40 music  40 comparator | Audio; administered during procedure | Varicose vein crossectomy with great saphenous vein versus Stripping | 20 - 30 |
| Kekecs Z,  et al 201462 | Outpatient: cataract surgery department in 1 hospital | RCT -  two-arm parallel design | 34 education & therapeutic suggestion  50 comparator | Education/ information; administered before procedure | Cataract surgery | 30 - 45 |
| Kola S, et al 201363 | Outpatient: colposcopy department at 1 hospital | RCT - mixed factorial & multiple parallel design | 40 high-information 39 low-information 38 comparator  Each group split between high & low monitors based on Miller Behavioural Style Scale | Education/information; administered during procedure | Colposcopy | 10 – 20 |
| Kwekkeboom KL, et al 200364 | Outpatient: oncology clinic at 1 hospital | RCT -  multiple arm parallel design | 24 music  14 distraction  20 comparator | Audio & distraction; administered before & during procedure | Tissue biopsy or vascular port placement | 20 - 40 |
| Lang EV, et al 200065 | Inpatient &  outpatient: interventional radiology department at 1 hospital | RCT -  multiple arm parallel design | 80 attention  82 hypnosis  79 comparator | Empathic attention & hypnosis; administered during procedure | Percutaneous transcatheter diagnostic & therapeutic peripheral vascular & renal interventions | 30 - 60 |
| LEE WL, et al 201766 | Outpatient: diagnostic imaging department at 1 hospital | RCT -  two-arm parallel design | 35 meditative music  37 comparator | Audio; administered during procedure | Positron emission tomography (PET) scans | 30 - 60 |
| McSherry T, et al 201867 | Inpatient: burns ward at 1 hospital | RCT -  two-arm parallel cross over design | 10 immersive virtual reality (IVR) with first dressing change  8 IVR with second dressing change | Virtual reality; administered during procedure | Painful wound care procedures | 10 - 20 |
| Ng MY, et al 201668 | Outpatient: diagnostic imaging department at 1 hospital | RCT -  two-arm parallel design | 100 music  97 comparator | Audio;  administered before & during procedure | cardiac computed tomography | 15 |
| Navidian A, et al 201869 | Outpatient: bronchoscopy department at 1 hospital | RCT -  two-arm parallel design | 30 audio-visual  30 comparator | Audio-visual; administered during procedure | Flexible bronchoscopy | 15 - 45 |
| Nilsson U, et al 200970 | Outpatient: percutaneous coronary intervention unit at 1 hospital | RCT -  two-arm parallel design | 121 music  117 comparator | Audio; administered during procedure | Coronary angiography | 30 - 40 |
| Nilsson U, et al 201271 | Outpatient: percutaneous coronary intervention unit at 1 hospital | RCT -  two-arm parallel design | 34 music  34 comparator | Audio; administered during procedure | Coronary angiography | 30 - 40 |
| Packiam VT,  et al 201872 | Outpatient: urology department at 1 hospital | RCT -  two-arm parallel design | 85 music  97 comparator | Audio; administered during procedure | Transrectal prostate biopsies | 10 |
| Padam A, et al 201773 | Outpatient: department of physiology & gastroenterology in 1 hospital | RCT - multiple arm parallel design | 67 vedic chants 66 classical music 66 comparator | Audio; administeredbefore procedure | Upper gastrointestinal endoscopy | 30 |
| Ripley L, et al 201474 | Outpatient:  cardiac catheterization laboratory in 1 hospital | RCT -  two-arm parallel design | 36 music intervention 34 comparator | Audio;  administered before & during procedure | Cardiac catheterization | 30 – 40 |
| Rosen J, et al 201375 | Outpatient: haematology/ oncology & multidisciplinary clinics at 1 hospital | RCT -  multiple arm parallel design | 40 massage  (7 did not receive) 20 structured attention  (6 did not receive) | Massage, therapeutic touch  & reflexology; administered before & during procedure | Placement of vascular access devices | 20 - 40 |
| Schupp CJ, et al 200576 | Outpatient: radiology department in 1 hospital | RCT -  mixed factorial & multiple parallel design | Low state anxiety group (<43) 37 attention  36 hypnosis  43 comparator   High state anxiety group (≥43) 43 attention  43 hypnosis  34 comparator | Empathic attention & hypnosis; administered before & during procedure | Interventional radiology | 20 - 30 |
| Shabanloei R, et al 201077 | Outpatient:  haematology & oncology research centre at 1 hospital | RCT -  two-arm parallel design | 40 music  40 comparator | Audio;  administered during procedure | Bone marrow biopsy & aspiration | 30 |
| Shahsavari H, et al 201778 | Outpatient: bronchoscopy department at 1 hospital | RCT -  two-arm parallel design | 40 reflexology  40 comparator | Reflexology; administered before procedure | Flexible bronchoscopy | 15 - 45 |
| Shenefelt PD, et al 201379 | Outpatient: dermatologic surgery clinic at 1 hospital | RCT -  multiple arm parallel design | 13 guided imagery live induction  13 guided imagery Recorded induction  13 comparator | Cognitive behavioural therapy; administered before & during procedure | Dermatologic procedures | 10 - 90 |
| Simmons D,  et al 200480 | Outpatient: ophthalmology department in 1 hospital | RCT -  multiple arm parallel design | 20 massage  20 verbal coaching & slow breathing  20 massage, verbal coaching & slow breathing  20 comparator | Massage, verbal coaching & breathing techniques; administered before & during procedure | Cataract surgery | 30 - 45 |
| Snow A,  et al 201281 | Outpatient: cancer treatment centre at 1 hospital | RCT -  two-arm parallel design | 41 hypnosis  39 comparator | Hypnosis; administered before & during procedure | Bone marrow aspiration/ biopsy procedure | 30 |
| Sobana R, et al 201582 | Outpatient: gastrointestinal endoscopy department at 1 hospital | RCT - two-arm parallel design | 30 music 30 comparator | Audio; administered before procedure | Upper gastrointestinal endoscopy | 30 |
| Trambert T, et al 201483 | Outpatient: breast care centre at 1 hospital | RCT -  multiple arm parallel design | 30 lavender-sandalwood  30 orange-peppermint  28 comparator | Aromatherapy; administered during procedure | Breast biopsy | 30 - 60 |
| Ugras GA, et al 201884 | Inpatient:  otorhinolaryngology surgery at 1 hospital | RCT -  multiple arm parallel design | 45 natural sounds  45 classical Turkish music  45 classical western music  45 comparator | Audio;  administered before procedure | Otorhinolaryngology surgery | 15 - 720 |
| Walker  MR, et al 201485 | Outpatient: urology department at 1 hospital | RCT -  two-arm parallel design | 22 virtual reality  23 comparator | Virtual reality; administered during procedure | Cystoscopy | 15 - 30 |
| Weeks BP,  et al 201186 | Outpatient: cardiac catheterization laboratory in 1 hospital | RCT -  multiple arm parallel design | 30 loudspeaker music intervention  34 focused music intervention 34 comparator | Audio; administered during procedure | Coronary angiography | 30 - 40 |
| Wu KL, et al 201487 | Outpatient: cardiac catheterization laboratory in 1 hospital | RCT -  multiple arm parallel design | 43 accessibility-enhanced multimedia informational education (AEMIE)  46 instructional DVD education  46 comparator | Education/ information; administered before & during procedure | Cardiac catheterisation | 30 – 40 |
| Xiaolian J,  et al 201588 | Outpatient: endoscopy centre at 1 hospital | RCT -  multiple arm parallel design | 60 visual  60 audio-visual  60 comparator | Visual & audio-visual; administered during procedure | Colonoscopy | 30 |

**Electronic Supplement C – Data extraction table**

| **Sources** | **Comfort Intervention** | **Outcome measures** | **Intervention/comparator** | **Main outcomes** | | | | | | | | |  |  | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Data reported before clinical procedure** | | | | | **Data reported after clinical procedure/ mean magnitude of reduction\*** | | | | | | |
| **Mean** | **Median** | **SD/SE‡** | **IQR/ range** | **P-value** | **Mean** | **Median** | **SD/**  **SE‡** | **IQR/ range** | **95% CI** | | **P-value** |
| Ahlander BM, et al 201843 | Education/ information |  | Video information: | - | 35 | - | 28, 43 | *p*=0.10 | - | 28 | - | 22.5, 36 | - | | *p*=0.20 |
| STAI | comparator: | - | 35 | - | 28, 43 | - | 30 | - | 24, 38 | - | |
| HAD | Video information: | - | 6 | - | 2, 9 | *p*= 0.01 | - | - | - | - | - | | - |
|  | comparator: | - | 6.6 | - | 3, 8.5 | - | - | - | - | - | | - |
| Angioli R, et al 201444 | Audio | STAI | Music: | 39.75 | - | 8.94 | - | *p*>0.05 | 27.59 | - | 6.3 | - | - | | *p*<.001 |
| Comparator: | 39.15 | - | 7.42 | - | 32.66 | - | 11.6 | - | - | |
| Argstatter H, et al 200645 | Audio & coaching | STAI | Music: | - | - | - | - | - | 7.3\* | - | 9.4 | - | - | | *p*=0.05 |
| Coaching: | - | - | - | - | - | 7.3\* | - | 9.4 | - | - | |
| Comparator: | - | - | - | - | - | 7.3\* | - | 9.4 | - | - | |
| Björkman I, et al 201346 | Audio | STAI | Music: | - | - | - | - | - | - | - | - | - | - | | *p*=0.007† |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Relaxation | Music: | - | - | - | - | - | - | - | - | - | - | | *p*=0.065† |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Wellbeing | Music: | - | - | - | - | - | - | - | - | - | - | | *p*=0.006† †favours music |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Buffum MD, et al 200647 | Audio | STAI | Music: | 38.57 | - | 10.5 | - | *p*=0.149 | 35.2 | - | 9.7 | - | - | | *p*=0.05 |
| Comparator: | 36.23 | - | 10.5 | - | 35.1 | - | 10.59 | - | - | |
| Chlan L, et al 200048 | Audio | STAI | Music: | 36.9 |  | 12.5 |  | *p*=0.28 | 34.5 | - | 10 | - | - | | *p*=0.002 |
| Comparator: | 40.2 |  | 11.9 |  | 41.8 | - | 13.5 | - | - | |
| Satisfaction | Music: | - | - | - | - | - | - | - | - | - | - | | *p*=0.11‡ †favours music |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Discomfort | Music: | - | - | - | - | - | 4.3 | - | 2.1 | - | - | | *p*=0.026 |
| Comparator: | - | - | - | - | - | 5.2 | - | 1.7 | - | - | |
| Choi SM, et al 201649 | Empathic attention | VAS-A (1-10mm) | Verbal empathy: | - | 30 | - | 10, 55 | *p*=0.682 | -1.2\* | - | - | - | -4.1,1.8 | | *p*<0.05 |
| Verbal empathy/ touch: | - | 30 | - | 10, 55 | -0.3\* | - | - | - | -5.7, 1.9 | |
| Comparator: | - | 37 | - | 20, 59 | -0.3\* | - | - | - | -2.9, 2.3 | |
| Satisfaction | Verbal empathy: | - | - | - | - | - | - | - | - | - | - | | *p*>0.05‡ † in all groups |
| Verbal empathy/ touch: | - | - | - | - | - | - | - | - | - | - | |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Diette GB,  et al 200350 | Audio-visual | STAI | Audio-visual: | 43.2 | - | - | - | *p*>0.05 | 44.8 | - | - | - | - | | *p*=0.084 |
| Comparator: | 43.8 | - | - | - | 45.6 | - | - | - | - | |
| Drahota A, et al 200851 | Audio-visual | STAI | Audio-visual: | 41.4 | - | 12.5 | - | - | 27.91 | - | 9.86 | - | - | | - |
| Comparator: | 39.2 | - | 13 | - | - | 27.2 | - | 7.44 | - | - | | - |
| Eslami J, et al 201852 | Aromatherapy | STAI | Lavandula angustifolia: | 43.9 | - | 9.71 | - | - | 31.1 | - | 6.44 | - | - | | *P*<0.001‡ |
| Citrus aurantium L.: | 43.9 | - | 7.88 | - | - | 30.17 | - | 5.59 | - | - | | *P*<0.001‡ |
| Comparator: | 39.7 | - | 10.02 | - | - | 40.7 | - | 9.69 | - | - | | *P*=0.975 † Compared to comparator |
| Fang AS, et al 201653 | Audio-visual | STAI | Video glasses: | 36 | - | 11.3 | - | *p*=0.40 | -7.7\* | - | 9.9 | - | - | | *p*=0.0335 |
| Comparator: | 33.8 | - | 12.3 | - | -4.4\* | - | 9.4 | - | - | |
| Frank LS, et al 200754 | Massage therapeutic touch & reflexology | Nervousness | Therapeutic touch: | 69.9 | - | 42.6 | - | *p*=0.76 | −41\* | - | 46 | - | - | | *p*=0.77 |
|  | Comparator: | 67.1 | - | 34.8 | - | −44\* | - | 41 | - | - | |
| Tense | Therapeutic touch: | 66.1 | - | 33.4 | - | *p*=0.71 | −40\* | - | 46 | - | - | | *p*=0.80 |
|  | Comparator: | 69.2 | - | 36.7 | - | −37\* | - | 41 | - | - | |
| Fearful | Therapeutic touch: | 60.6 | - | 43.8 | - | *p*=0.86 | −35\* | - | 55 | - | - | | *p*=0.43 |
|  | Comparator: | 67.7 | - | 34.8 | - | −43\* | - | 48 | - | - | |
| Hayes A, et al 200355 | Audio | STAI | Music: | 36.7 | - | 9.1 | - | - | 32.3 | - | 10.4 | - | - | | *p*=0.007 |
| Comparator: | 36.1 | - | 8.3 | - | - | 34.6 | - | 11.5 | - | - | |
| Heidaria F, et al 201756 | Therapeutic touch | STAI | Hand reflexology: | 49.82 | - | 1.74 | - | *p*=0.78 | 42.67 | - | 1.47 | - | - | | *p*=0.001 |
| Comparator: | 49.71 | - | 1.65 | - | 48.66 | - | 1.78 | - | - | |
| Hızlı F, et al 201557 | Hypnosis | BAI | Hypnotherapy: | 6 | - | - | 0–28 | - | 2 | - | - | 0–23 | - | | *p*=0.001 |
| Comparator: | 9 | - | - | 0–28 | - | 8 | - | - | 0–34 | - | |
| HAS | Hypnotherapy: | 11 | - | - | 2 –29 | - | 6 | - | - | 0–22 | - | | *p*=0.005 |
| Comparator: | 11.5 | - | - | 0–31 | - | 11.5 | - | - | 1–38 | - | |
| Hozumi H, et al 201758 | Aromatherapy | Anxiety VAS (1-10mm) | Vehicle (sham): | - | - | - | - | - | 3 | - | 7‡ | - | - | | *P*>0.05 |
| Lavender: | - | - | - | - | - | 3 | - | 6‡ | - | - | | *P*>0.05 |
| Grapefruit: | - | - | - | - | - | 2 | - | 8‡ | - | - | | *P*>0.05 |
| Osmanthus: | - | - | - | - | - | 2 | - | 7‡ | - | - | | *P*<0.05 |
| Comparator: | - | - | - | - | - | 3 | - | 8‡ | - | - | | *P>*0.05 |
| Hu PH, et al 201059 | Aromatherapy | STAI | Neroli: | 41.79 | - | 10.28 | - | *p*=0.734 | 30.79 | - | 3.89 | - | - | | *p*=0.079 |
| Comparator: | 43.46 | - | 10.41 | - | 36.46 | - | 9.31 | - | - | |
| Hudson BF, et al 201560 | Audio,  Audio-visual, interaction & stress ball | STAI | Music: | 38.6 | - | 8.78 | - | - | 38.6 | - | 10.31 | - | - | | *p*=0.03 |
| DVD: | 39.86 | - | 10.3 | - | - | 37.56 | - | 10.28 | - | - | |
| Interaction: | 37.74 | - | 9.19 | - | - | 35.29 | - | 8.94 | - | - | |
| Stress ball: | 41.54 | - | 11.0 | - | - | 38.54 | - | 8.58 | - | - | |
| Comparator: | 39 | - | 7.72 | - | - | 41.29 | - | 9.72 | - | - | |
| S-NRS | Music: | 4.49 | - | 2.71 | - | - | 3.79 | - | 2.42 | - | - | | *p*=0.06 |
| DVD: | 4.65 | - | 2.32 | - | - | 3.31 | - | 2.24 | - | - | |
| Interaction: | 4.33 | - | 2.31 | - | - | 3 | - | 1.96 | - | - | |
| Stress ball: | 4.8 | - | 2.43 | - | - | 3.6 | - | 2 | - | - | |
| Comparator: | 4.33 | - | 2.13 | - | - | 4.38 | - | 2 | - | - | |
| A-NRS | Music: | - | - | - | - | - | 4.76 | - | 0.06 | - | - | | - |
| DVD: | - | - | - | - | - | 4.7 | - | 0.06 | - | - | | - |
| Interaction: | - | - | - | - | - | 4.64 | - | 0.06 | - | - | | - |
| Stress ball: | - | - | - | - | - | 4.7 | - | 0.06 | - | - | | - |
| Comparator: | - | - | - | - | - | 4.58 | - | 0.06 | - | - | | - |
| Jiménez-Jiménez M, et al 201361 | Audio | STAI Control of intraoperative stress feeling | Music: | 33.7 | - | 9.3 | - | *p*=0.78 | - | - | - | - | - | | - |
| Comparator: | 34.1 | - | 10 | - | - | - | - | - | - | | - |
| Music: | - | - | - | - | - | 1.31 | - | 0.3 | - | - | | *p*=0.02 |
| Comparator: | - | - | - | - | - | 2.36 | - | 0.3 | - | - | |
| Kekecs Z,  et al 201462 | Education/ information | STAI | Education / therapeutic suggestion: | 41.59 | - | 10.1 | - | *p*=0.254 | - | - | - | - | - | | - |
| Comparator: | 44.22 | - | 11.5 | - | - | - | - | - | - | | - |
| Wellbeing (scale 1-9) | Education / therapeutic suggestion: | 6 | - | - | 3–9 | *p*=0.98 | 6 | - | - | 3–9 | - | | *p*=0.084 |
| Comparator: | 6 | - | - | 2–9 | 6 | - | - | 2–9 | - | |
| Calmness (scale 1-7) | Education / therapeutic suggestion: | 4.5 | - | - | 2–7 | *p*=0.37 | 4.5 | - | - | 2 –7 | - | | *p*=0.039 |
| Comparator: | 4 | - | - | 2–7 | 4 | - | - | 3 –7 | - | |
|  |  |  | High-info. |  |  |  |  |  |  |  |  |  |  | |  |
| Kola S, et al 201363 | Education/ information | STAI | Low monitor: | 17.75 | - | 6.79 | - | - | 13.75 | - | 5.27 | - | - | | - |
| High monitor: | 18.94 | - | 7.12 | - | - | 12.75 | - | 3.26 | - | - | | - |
| Low-info. Low monitor |  | - |  | - | - |  | - |  | - | - | | - |
| Low monitor: | 17.39 | - | 6.59 | - | - | 13.33 | - | 4.41 | - | - | | - |
| High monitor: | 16.75 | - | 5.48 | - | - | 12.81 | - | 4.11 | - | - | | - |
| Comparator |  | - |  | - | - |  | - |  | - | - | | - |
| Low monitor: | 18.79 | - | 5.83 | - | - | 14.3 | - | 5.24 | - | - | | - |
| High monitor: | 16.89 | - | 5.09 | - | - | 13.42 | - | 3.43 | - | - | | - |
| Kwekkeboom KL, et al 200364 | Audio & distraction | STAI | Music: | 36.2 | - | 13.0 | - | - | 32.1 | - | 12.46 | - | - | | - |
| Distraction: | 42.8 | - | 13.0 | - | - | 36.5 | - | 12.46 | - | - | | - |
| Comparator: | 36.2 | - | 13.0 | - | - | 29.2 | - | 12.46 | - | - | | - |
| Lang EV, et al 200065 | Empathic attention & hypnosis | Anxiety VAS (1-10) | Attention: | 3.8 | - | - | - | - | 2.5 | - | - | - | - | | - |
| Hypnosis: | 3.8 | - | - | - | - | 1 | - | - | - | - | | - |
| Comparator: | 3.5 | - | - | - | - | 3.8 | - | - | - | - | | - |
| LEE WL, et al 201766 | Audio | STAI | Meditative: | 40.26 | - | 5.68 | - | *p*=0.50 | 34.97 | - | 6.73 | - | - | | *p*=0.02 |
| Comparator: | 37.73 | - | 6.73 | - | 38.38 | - | 5.66 | - | - | |
| McSherry, T, et al 201867 | Virtual reality | Anxiety VNS (1-10) | Immersive virtual reality (IVR) - 1st dressing: change | 4.8 | - | 2.9 | - | - | 3.5 | - | 3 | - | - | | *P*>0.05 |
| IVR - 2nd dressing change: | 4.1 | - | 2.4 | - | - | 3.5 | - | 2.6 | - | - | |
| Ng MY, et al 201668 | Audio | STAI | Music: | - | 10 | - | 7, 13 | *P*=0.328 | - | 8 | - | 6, 10 | - | | *p*=0.721 |
| Comparator: | - | 10 | - | 8, 13 | - | 9 | - | 6, 12.5 | - | |
| Navidian A, et al 201869 | Audio-visual | Willingness to repeat the clinical procedure (% survey) | Music: | - | - | - | - | - | - | - | - | - | - | | *p*=0.04‡ †favours music |
| Comparator: | - | - | - | - | - | - | - | - | - | - | |
| Nilsson U, et al 200970 | Audio | Anxiety NRS (1-10) | Music: | - | 2 | - | 0, 4 | *p*=0.479 | - | - | - | - | - | | - |
| Comparator: | - | 2 | - | 0, 4 | - | - | - | - | - | | - |
| Relaxation NRS (1-10) | Music: | - | - | - | - | - | - | 8 | - | 5, 9 | - | | *p*=0.218 |
| Comparator: | - | - | - | - | - | - | 8 | - | 4, 9 | - | |
| Short STAI | Music: | - | - | - | - | - | - | 15 | - | 14, 15 | - | | *p*=0.932 |
| Comparator: | - | - | - | - | - | - | 15 | - | 13, 15 | - | |
| Discomfort NRS (1-10) | Music: | - | - | - | - | - | - | 0.5 | - | 0, 2 | - | | *p*=0.193 |
| Comparator: | - | - | - | - | - | - | 1 | - | 0, 3 | - | |
| Nilsson U, et al 201271 | Audio | Anxiety NRS (1-10) | Music: | 5.3 | - | 2 | - | - | - | - | - | - | - | | - |
| Comparator: | 5.4 | - | 2.4 | - | - | - | - | - | - | - | | - |
| Enviroment NRS (1-10) | Music: | - | - | - | - | - | 9 | - | 1.7 | - | - | | *p*<0.0001‡ †favours music |
| Comparator: | - | - | - | - | - | 7.7 | - | 3 | - | - | |
| Relaxation NRS (1-10) | Music: | - | - | - | - | - | 5.6 | - | 3 | - | - | |
| Comparator: | - | - | - | - | - | 6 | - | 3.1 | - | - | |
| Discomfort NRS (1-10) | Music: | - | - | - | - | - | - | 0.8 | - | 0–10 | - | |
| Comparator: | - | - | - | - | - | - | 2 | - | 0–8 | - | |
| Packiam VT,  et al 201872 | Audio | STAI | Music: | 33.7 | - | 8.9 | - | *p*=0.61 | - | - | - | - | - | | - |
| Comparator: | 34.4 | - | 9.9 | - | - | - | - | - | - | | - |
| Satisfaction VAS (0-10) | Music: | - | - | - | - | - | 8.8 | - | 1.6 | - | - | | *p*= 0.29 |
| Comparator: | - | - | - | - | - | 8.5 | - | 1.9 | - | - | |
| Willingness to repeat VAS  (0-10) | Music: | - | - | - | - | - | 8.2 | - | 2.7 | - | - | | *p*= 0.92 |
| Comparator: | - | - | - | - | - | 8.1 | - | 2.2 | - | - | |
| Padam A,  et al 201773 | Audio | STAI | Vedic chants: | 40.4 | - | 8.8 | - | - | 38.5 | - | 10.7 | - | - | | - |
| Music: | 41.8 | - | 9.9 | - | - | 38 | - | 8.6 | - | - | | - |
| Comparator: | 40.5 | - | 8.7 | - | - | 39.1 | - | 8.8 | - | - | | - |
| Ripley L, et al 201474 | Audio | Short STAI | Music: | - | - | - | - | - | 8 | - | - | 7-11 | - | | *p*=0.36 |
| Comparator: | - | - | - | - | - | 9 | - | - | 8-12 | - | |
| Rosen J, et al 201375 | Massage, therapeutic touch  & reflexology | STAI | Massage: | 37.67 | - | 12.5 | - | *p*=0.427 | 31.15 | - | 1.54 | - | - | | *p*=0.9720 |
| Attention: | 40.45 | - | 12.9 | - | 31.83 | - | 2.23 | - | - | |
| Schupp CJ, et al 200576 | Empathic attention & hypnosis |  | Low STAI (<43) |  |  |  |  |  |  |  |  |  |  | |  |
| STAI | Attention: | 31.1 | - | 6.9 | - | *p*>0.05 | - | - | - | - | - | | - |
| Hypnosis: | 33.5 | - | 5.7 | - | - | - | - | - | - | | - |
| Comparator: | 34 | - | 5.5 | - | - | - | - | - | - | | - |
| Time course of patients’ anxiety self-rating (0-10) | Attention: | - | - | - | - | - | 4.85 | - | - | - | - | | *p*>0.05 |
| Hypnosis: | - | - | - | - | - | 1.98 | - | - | - | - | |
| Comparator: | - | - | - | - | - | 2.03 | - | - | - | - | |
|  | High STAI (≥43) |  |  |  |  |  |  |  |  |  |  | |  |
| STAI | Attention: | 53.8 | - | 7.5 | - | *p*<0.05 | - | - | - | - | - | | - |
| Hypnosis: | 51.1 | - | 6.6 | - | - | - | - | - | - | | - |
| Comparator: | 53.3 | - | 7.7 | - | - | - | - | - | - | | - |
| Time course of patients’ anxiety self-rating (0-10) | Attention: | - | - | - | - | - | 3.84 | - | - | - | - | | *P*=0.06 |
| Hypnosis: | - | - | - | - | - | 3.35 | - | - | - | - | |
| Comparator: | - | - | - | - | - | 2.03 | - | - | - | - | |
| Shabanloei R, et al 201077 | Audio | STAI | Music: | 52.9 | - | 6.94 | - | *P*=0.852 | 43.24 | - | 5.41 | - | - | | *P*=0.27 |
| Comparator: | 52.18 | - | 7.29 | - | 46.42 | - | 7.2 | - | - | |
| Shahsavari H, et al 201778 | Reflexology | Anxiety VAS  (1-10mm) | Reflexology: | 4.35 | - | 0.33 | - | *p*=0.2 | 2.83 | - | 0.23 | - | - | | *p*>0.001 |
| Comparator: | 3.78 | - | 0.29 | - | 4.88 | - | 0.34 | - | - | |
| Shenefelt PD, et al 201379 | Cognitive behavioural therapy | Anxiety SUD (0-10) | Guided imagery live: | 3.31 | - | - | 0 -7 | *P*>0.05 | 0.77 | - | - | 0-3 | - | | *P*>0.05 |
| Guided imagery recorded: | 3.38 | - | - | 0-8 | 0.77 | - | - | 0-5 | - | |
| Comparator: | 3.15 | - | - | 0-10 | 1.15 | - | - | 0-4 | - | |
| Simmons D,  et al 200480 | Massage, verbal coaching & breathing techniques | Anxiety Likert (0-10) | Massage: | - | - | - | - | - | 3.65 | - | - | 1.7 | - | | - |
| Verbal coaching/ slow breathing: | - | - | - | - | - | 3.1 | - | - | 2.2 | - | | - |
| Massage/ verbal coaching: | - | - | - | - | - | 2.75 | - | - | 1.5 | - | | - |
| Comparator: | - | - | - | - | - | 5.85 | - | - | 1.9 | - | | - |
| Discomfort Likert (0-10) | Massage: | - | - | - | - | - | 4.3 | - | - | 2 | - | | - |
| Verbal coaching/ slow breathing: | - | - | - | - | - | 3.5 | - | - | 2.2 | - | | - |
| Massage/ verbal coaching: | - | - | - | - | - | 4.15 | - | - | 2.3 | - | | - |
| Comparator: | - | - | - | - | - | 5.95 | - | - | 1.9 | - | | - |
| Snow A,  et al 201281 | Hypnosis | VAS-A  (1-100mm) | Hypnosis: | - | - | - | - | - | -22\* | - | 18‡ | - | - | | *p*=0.026 |
| Comparator: | - | - | - | - | - | -13\* | - | 6‡ | - | - | |
| Sobana R, et al 201582 | Audio | Short STAI | Music: | - | - | - | - | - | -6.1\* | - | 4.19 | - | - | | - |
| Comparator: | - | - | - | - | - | 0.06\* | - | 1.2 | - | - | | - |
| Trambert T, et al 201483 | Aromatherapy | STAI | Lavender-sandalwood: | - | - | - | - | - | -11\* | - | - | 35,4 | - | | - |
| Orange-peppermint: | - | - | - | - | - | -6\* | - | - | -33,10 | - | | - |
| Comparator: | - | - | - | - | - | -4\* | - | - | -28,23 | - | | - |
| Ugras GA, et al 201884 | Audio | STAI | Natural sounds: | 39.11 | - | 4.71 | - | *p*<0.001 | 34.38 | - | 4.71 | - | - | | *p*<0.001 |
| Turkish music: | 41.71 | - | 9.89 | - | 35.44 | - | 7.66 | - | - | |
| Classical music: | 41.93 | - | 9.51 | - | 35.71 | - | 10.28 | - | - | |
| Comparator: | 43.51 | - | 6.64 | - | 44.09 | - | 6.47 | - | - | |
| Walker MR, et al 201485 | Virtual reality | VAS-A  (1-100mm) | Virtual reality: | 4.9 | - | - | - | - | 5.6 | - | - | - | - | | - |
| Unpleasant VAS  (1-100mm) | 5.2 | - | - | - | - | 5.1 | - | - | - | - | | - |
| VAS-A  (1-100mm) | Comparator: | - | - | - | - | - | 6.2 | - | - | - | - | | - |
| Unpleasant VAS  (1-100mm) | - | - | - | - | - | 5.3 | - | - | - | - | | - |
| Weeks BP,  et al 201186 | Audio | Anxiety NRS | Loudspeaker music: | - | - | - | - | - | 2 | - | - | 1–9 | - | | *p*<0.05 |
| Focused music: | - | - | - | - | - | 2 | - | - | 1–8 | - | | *p*<0.05 |
| Comparator: | - | - | - | - | - | 5 | - | - | 1–10 | - | | *p*>0.05 |
| Wu KL, et al 201487 | Education/ information | STAI | Accessibility-enhanced multimedia informational education: | - | - | - | - | - | 16.33 | - | - | - | - | | *p*<0.05 |
| Instructional DVD education: | - | - | - | - | - | 13.25 | - | - | - | - | | *p*>0.05 |
| Comparator: | - | - | - | - | - | 10.16 | - | - | - | - | | *p*>0.05 |
| Xiaolian J,  et al 201588 | Visual & Audio-visual | STAI | Visual: | 33.35 | - | 10.3 | - | p=0.637 | 28.2 | - | 6.93 | - | - | | *p*=0.169 |
| Audio-visual: | 34.13 | - | 8.85 | - | 29.18 | - | 7.08 | - | - | |
| Comparator: | 35 | - | 9.3 | - | 30.88 | - | 9.32 | - | - | |