The Effect of Perioperative Music on Medication Requirement and Hospital Length of Stay
A Meta-analysis

Victor X. Fu, MD,∗† Pim Oomens, MD,∗† Markus Klimek, MD, PhD,‡ Michiel H. J. Verhofstad, MD, PhD,* and Johannes Jeekel, MD, PhD†

Objective: To assess and quantify the effect of perioperative music on medication requirement, length of stay and costs in adult surgical patients.

Methods: A systematic literature search of 8 databases was performed from inception date to January 7, 2019. Randomized controlled trials investigating the effect of perioperative music on medication requirement, length of stay or costs in adult surgical patients were included. Meta-analysis was performed using random effect models, pooled standardized mean differences (SMD) were calculated with 95% confidence intervals (CI). This study was registered with PROSPERO (CRD42018093140) and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines.

Results: The literature search yielded 2414 articles, 55 studies (N = 554) were included. Perioperative music significantly reduced postoperative opioid requirement (pooled SMD −0.31 [95% CI −0.45 to −0.16], \( P < 0.001 \), \( I^2 = 44.3, N = 1398 \)). Perioperative music also significantly reduced intraoperative propofol (pooled SMD −0.72 [95% CI −1.01 to −0.43], \( P < 0.00001 \), \( I^2 = 61.1, N = 554 \)) and midazolam requirement (pooled SMD −1.07 [95% CI −1.70 to −0.44], \( P < 0.001 \), \( I^2 = 73.1, N = 184 \)), while achieving the same sedation level. No significant reduction in length of stay (pooled SMD −0.18 [95% CI −0.43 to 0.067], \( P = 0.15 \), \( I^2 = 56.0, N = 600 \)) was observed.

Conclusions: Perioperative music can reduce opioid and sedative medication requirement, potentially improving patient outcome and reducing medical costs as higher opioid dosage is associated with an increased risk of adverse events and chronic opioid abuse.

Keywords: analgesia, medication requirement, music, opioids, perioperative patient care, propofol, sedation, surgery

(AAnn Surg 2019;xx:xxx–xxx)

A majority of patients continues to experience moderate to severe postoperative pain,1 which is a risk factor for delayed hospital discharge2 and the occurrence of postoperative complications,3,4 persisting chronic pain and the predominant factor for the immediate postsurgical quality of life.5 Opioid analgesics are the primary treatment modality for acute postoperative pain, which is the second most common reason to prescribe opioids.6 However, opioid-related side effects are common,7,8 Opioid use is considered a risk factor for pruritus, nausea, vomiting, drowsiness, urinary retention and the development of delirium.9 Higher opioid doses also increase the incidence of postoperative ileus and respiratory depression.10,11 Moreover, persistent opioid use in surgical patients is quite prevalent.12,13 Earlier studies reported that 5.9% of patients still filled an opioid prescription 3 to 6 months after minor surgical procedures,12 whereas over half of the patients receiving 90 days of continuous opioid medication still use opioid analytics 1 year later.13 Both opioid prescription dosage and duration of use are important predictors for chronic opioid use.6 The concomitant use of benzodiazepines can potentially increase the risk of adverse effects, delirium, and prolonged opioid misuse even more.11,12

Despite these common adverse events and an increase in opioid-related deaths, opioid prescription rates have currently reached epidemic proportions.6 Therefore, there is an increasing interest in nonpharmacological interventions to reduce both postoperative pain and opioid consumption. Recently, several studies have reported beneficial effects of perioperative music.14–16 The purpose of this systematic review and meta-analysis is to assess and quantify the effect of perioperative music as a nonpharmacological intervention on medication requirement before, during and after invasive, surgical procedures. Secondary outcomes are the effect of perioperative music on length of stay and cost reduction.

METHODS

This systematic review and meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines and has been registered with PROSPERO (CRD42018093140).

Literature Search Strategy

A literature search using the exhaustive literature search method was performed with a biomedical information specialist.17 The databases Embase, Medline Ovid, Web-of-science, Scopus, Cochrane central, Cinahl, PsychINFO Ovid, and Google Scholar were searched from date of inception until January 7th, 2019. The full search terms and number of search results of each database are detailed in Appendix A. Also, manual cross-referencing of the included studies was performed.

Study Screening and Selection

Three reviewers (V.F., P.O., and V.E.) independently identified eligible studies using a 2-stage approach. First, title and abstract of all identified papers screened, followed by reading of the full text if eligibility criteria were matched. Inclusion criteria for this systematic review were all available, peer-reviewed, full-text articles of randomized controlled trials in the English language, containing adult patients 18 years old undergoing an inpatient or outpatient invasive,
surgical procedure, investigating the use of recorded music before, during and/or after surgery with either medication requirement, hospital length of stay or direct medical costs as outcome measures. As these predefined outcome measures were often secondary outcomes and therefore not always mentioned in titles or abstracts, the 3 reviewers screened all studies full text for potential review inclusion if during the title and abstract screening process music as a perioperative intervention in adult patients was investigated. The music intervention was predefined as vocal sound, instrumental sound or both, containing the elements melody, harmony, and rhythm. Therefore, studies investigating solely nature sounds were excluded. Studies investigating live music with a music therapist were also excluded, because of the possibility that the effect is caused by the presence of the musical therapist and the irreproducibility of the study. Finally, studies investigating music with an additional, concomitant intervention were excluded, except if this additional intervention was used in both the intervention and control group (for example, the music intervention occurred during bed rest, and the control group received only bed rest). Disagreements between the investigators were resolved by referring to the supervisor (J.J.).

Data Extraction

Study data were independently extracted by the 3 reviewers (V.F., P.O., and V.E.) using a custom, prespecified Microsoft Excel 2010 document. Risk of bias was also independently assessed using the Cochrane Collaboration’s tool for assessing risk of bias in randomized trials.18 Authors of included studies were contacted for additional information if necessary. All data was mutually discussed and disagreements between the investigators were resolved by referring to the supervisor (J.J.).

Statistical Analysis

Data were analyzed with the open-source, meta-analysis software OpenMeta-Analyst, which uses R as the underlying statistical engine.19 Random effect models were used, because heterogeneity between the included studies was assumed to be present. Standardized mean differences (SMD) and absolute mean differences were calculated with 95% confidence interval (CI). Studies were included for meta-analysis if mean values and standard deviations (SDs) of the outcome measures were reported. Opioid doses were converted to milligrams (mg) of morphine equianalgesic (ME), with 1 mg ME being equivalent to 1 mg parenteral morphine. If interquartile ranges or ranges were reported, an approximation of the SD was calculated by dividing the interquartile range by 1.35 and the range by 4. When the standard error of mean was reported, SDs were calculated by multiplying the standard error of mean with the square root of the number of patients.18 Publication bias was visually assessed using funnel plots, if more than ten studies were included for additional information if necessary. All data was mutually discussed and disagreements between the investigators were resolved by referring to the supervisor (J.J.).

RESULTS

The literature search yielded 2414 results. A total of 1524 titles and abstracts were screened after removal of duplicates and 154 articles were assessed full text. Fifty-five studies (4968 patients) were included in the qualitative synthesis and 33 studies (2390 patients)20–53 in the meta-analysis (Fig. 1). There was a high agreement rate of over 85% between the 3 reviewers on study inclusion, risk of bias assessment, and data extraction, and all disagreements could be resolved through mutual discussion.

Study Characteristics

A detailed overview of the study characteristics is presented in Table 1. The music intervention was assessed in a wide range of different surgical procedures. General anesthesia was the most commonly used anesthesia method during surgery in 36 studies (65%), whereas locoregional anesthesia was used in 8 studies (15%). Eight studies (15%) did not report the anesthesia method used and 3 studies (5.5%) contained different surgical procedures with different anesthesia methods. The moment of music intervention varied. Music was played solely preoperatively in 3 (5.5%), intraoperatively in 10 (18%), postoperatively in 25 (45%), and on multiple moments in 15 studies (27%). Two studies by the same author contained both an intraoperative music intervention group and a second music intervention group in which the intervention was solely applied postoperatively.

The music intervention was commonly described as soothing, relaxing, nonlyrical, instrumental music and was preselected by the research team in most studies (45 studies, 82%); patients could select music from a preselected list in 21 studies (38%), whereas no choice was offered in 24 studies (44%). The preferred music of the patient was used in 9 studies (16%), whereas 1 study (1.8%) did not elaborate on the exact music intervention. In a majority of studies, music delivery was achieved using a music player and headphones (41 studies, 75%). Other reported music delivery methods were a music pillow (3 studies, 5.5%), CD-player (3 studies, 5.5%), personal stereo (1 study, 1.8%), an integrated music system in the patient room (1 study, 1.8%), or not specified (6 studies, 11%). The control group consisted of standard care (26 studies, 47%), headphones without music (16 studies, 29%), headphones with white noise or recorded OR noise intraoperatively (5 studies, 9.1%), no music without further specification (3 studies, 5.5%), or an unspecified rest period (3 studies, 5.5%). Two studies (3.6%) had both a standard care and headphones without music group acting as control.

Risk of Bias Assessment

An overview of the risk of bias assessment is presented in Fig. 2 and a more detailed description in Appendix B. A potentially high risk of selection bias was present in several studies (8 studies, 15%),24,29,47,54–58 as sequence generation was done using odd and even numbers, days of the week or hospital record number. Several studies provided insufficient details to assess selection bias (14 studies, 25%).20,22,26–28,30,32,36,38,40,59–62 A moderate to high risk of performance bias was present, as blinding of patients for the music intervention is only possible when the intervention is performed solely intraoperatively during general anesthesia. Blinding of personnel can theoretically be achieved by using headphones for all patients, but is more difficult in practice when patients are free to change music tracks or adjust the volume. Five studies (9.3%) employed a study design in which patients, surgical personnel and outcome assessors were all blinded adequately.18,41,46,63,64 The “other risk of bias” category was reported as unclear in more than half of the studies (36 studies, 65%), because one of the baseline characteristics age, sex, weight, or the duration of surgery, which can influence intraoperative and postoperative medication requirement, was not reported. There was a high risk of other bias because of significant difference in either surgery duration or age between the music and control group in 3 studies.25,36,45 A funnel plot to
investigate publication bias of studies assessing the effect of perioperative music on postoperative opioid requirement showed a near funnel-shaped plot, lacking a small number of studies in the lower-left corner which could be indicative of studies with relatively small samples sizes and small effect sizes being potentially absent (Appendix C).

**Opioid Requirement**

The effect of perioperative music on postoperative opioid requirement was assessed in 42 studies, of which 20 could be included in the meta-analysis. Thirteen studies presented the postoperative opioid dose requirement as morphine equivalents (ME) or parenteral morphine. In 3 studies, postoperative ketobemidone requirement was evaluated, which are equipotent to parenteral morphine (1 mg parenteral ketobemidone = 1 mg ME). Postoperative parenteral tramadol requirement (10 mg parenteral tramadol = 1 mg ME) was assessed in 3 studies and pethidine requirement in 1 study (10 mg pethidine = 1 mg ME). Length of follow-up differed, as 5 studies assessed opioid requirement during the stay in the post-anesthesia care unit, and within the first 2 postoperative hours. Ten studies (50%) assessed opioid requirement for at least 24 hours or more after surgery and involved major surgical procedures. The mean absolute reduction in postoperative opioid requirement of the 8 studies which measured postoperative opioid requirement during the stay in the post-anesthesia care unit or within the first 2 postoperative hours was −1.0 mg ME (95% CI −1.6 to −0.49, P < 0.001, F² = 44.3, N = 1398 patients). The mean absolute reduction in postoperative opioid requirement of the 10 studies which measured postoperative opioid requirement for at least 24 hours or more after surgery was −4.4 mg ME (95% CI −8.2 to −0.65, P = 0.022, F² = 69.6, N = 598 patients). The mean absolute reduction in 5 of these studies which measured opioid requirement for at least 3 postoperative days and involved major surgical procedures was −9.8 mg ME (95% CI −17.9 to −1.70, P = 0.018, F² = 48.8, N = 298 patients).

**FIGURE 1.** PRISMA Flow diagram. N indicates number of studies.
| Study ID | Surgical Procedure | Anesthesia | Intervention | Moment | Duration | N Control | N Outcome Parameters |
|----------|---------------------|------------|--------------|--------|----------|-----------|----------------------|
| Allred, 2010 | Total knee arthroplasty | General or spinal with femoral block | Choice of easy listening, nonlyrical music | Postoperatively | POD 1, 20 min before and after first ambulation | 28 | Quiet rest period | 28 Postoperative opioid requirement |
| Ames, 2017 | Surgical procedures requiring ICU stay | General | MussiCure | Postoperatively | POD 1-2, 50 min, 1-8 times | 20 | 50 min quiet rest | 21 Postoperative opioid requirement |
| Ayoub, 2005 | Urological procedures | Regional | Own favorite music | Intraoperatively | Procedure duration | 31 | Headphones with operation noise recording | 28 Intraoperative propofol requirement |
| Bansal, 2010 | Abdominal, urological, or lower extremity surgery | Spinal | Choice of folk, classical, religious, soothing music | Intraoperatively | Not specified | 50 | Occlusive headphones | 50 PACU length of stay Intraoperative midazolam requirement |
| Binns-Turner, 2011 | Mastectomy | General | Choice of classical, easy-listening, new age, inspirational music | Preoperatively Intraoperatively Postoperatively | Procedure duration and 2 x 30 min daily postoperatively | 32 | Blank iPOD with occlusive headphones | 29 Intraoperative opioid requirement Postoperative opioid requirement |
| Blankfield, 1995 | Coronary artery bypass surgery | General | Dreamflight II by Herb Ernst | Intraoperatively Postoperatively | Procedure duration Total 120 min | 124 | Blank tape intraoperatively and standard care postoperatively | 15 Standard care 34 Standard care | 15 Postoperative opioid requirement Hospital length of stay Intraoperative opioid requirement |
| Chen, 2015 | Total knee replacement | Not specified | Chinese piano and violin music | Preoperatively Postoperatively | Choice of Turkish classical and folk music Preoperatively Postoperatively | 90 min before surgery, after surgery 30 min in ICU and 30 min each day | 34 Standard care | 34 Postoperative opioid requirement |
| Cigerci and Ozbayir, 2016 | Coronary artery bypass surgery | General | Choice of Turkish classical and folk music | Preoperatively Postoperatively | 90 min before surgery, after surgery 30 min in ICU and 30 min each day | 34 Standard care | 34 Postoperative opioid requirement |
| Cutshall, 2011 | Coronary artery bypass graft and/or cardiac valve surgery | General | Choice of 4 CD's | Postoperatively | 2 x 20 min on POD 2-4, 120 min in total | 49 | Standard care with bed rest for 20 min | 51 Postoperative opioid requirement Hospital length of stay Intraoperative propofol requirement Itraoperative propofol requirement Postoperative opioid requirement PACU length of stay | 111 No music | 102 Postoperative opioid requirement PACU length of stay | 38 Headphones without music | 39 PACU length of stay | 39 Postoperative opioid requirement |
| Easter, 2010 | Elective outpatient surgery procedures | Not specified | Choice of easy-listening, country, gospel, rock | Postoperatively | During length of stay in PACU | 111 | No music | 102 Postoperative opioid requirement PACU length of stay | 38 Headphones without music | 39 PACU length of stay | 39 Postoperative opioid requirement |
| Ebneslahidi and Mohseni, 2008 | Elective cesarean section surgery | General | Own favorite music | Postoperatively | 30 min in the recovery room | 38 | Headphones without music | 39 PACU length of stay | 39 Postoperative opioid requirement |
| Finlay, 2016 | Total knee arthroplasty | Spinal with nerve block | Choice of sedative nonlyrical piano, harp, synthesizer orchestral or slow jazz music | Postoperatively | 15 min | 72 | Headphones without music | 17 Postoperative opioid requirement |
| Good, 1995 | Elective, open abdominal surgery | General | 32 tracks with range of genres | Postoperatively | 60 min during the first 2 d after surgery | 21 | Standard care | 21 Postoperative opioid requirement |
| Study ID | Surgical Procedure | Anesthesia | Intervention | Moment | Duration | N Control | N Outcome Parameters |
|---------|--------------------|------------|--------------|--------|----------|-----------|----------------------|
| Good, 1999 | Elective, open, major abdominal surgery | General | Choice of taped soothing music | Preoperatively | First 2 d after surgery | 151 | Standard care 152 | Postoperative opioid requirement |
| Graversen and Sommer, 2013 | Laparoscopic cholecystectomy | General | Musicure using music pillow | Preoperatively | Before surgery start until day care discharge | 40 | Standard care 35 | Intraoperative propofol requirement Postoperative opioid requirement Day care unit length of stay |
| Heitz, 1992* | Para(athyroidectomy or unilateral modified radical mastectomy | General | Choice of 3 instrumental classical tapes | Postoperatively | 15 min after PACU arrival until discharge | 20 | Headphones without music 20 | Postoperative opioid requirement |
| Hook, 2008 | Moderate or major elective surgery | General | Choice of Malay, Western, Chinese, soothing music | Preoperatively | 60 min before and 180 min after surgery | 51 | Headphones without music 51 | Postoperative opioid requirement PACU length of stay |
| Iblher, 2011 | Open heart surgery (coronary bypass, valvular transplant, or both combined) | General | Baroque organ, flute, string orchestra music with 60-80 bpm | Postoperatively | 60 min after ICU admission | 25 | Headphones without music 25 Postoperative opioid requirement |
| Ignacio, 2012 | Elective spine, hip or knee surgery | General | Not specified | Postoperatively | 2 × 30 min | 12 | No music 9 | Postoperative opioid requirement |
| Ikonomodou, 2004 | Laparoscopic sterilization or tubal dyeing | General | Peaceful pan flute music | Preoperatively | 30 min before and after surgery | 29 | Blank compact disk 26 | Postoperative opioid requirement |
| Johnson, 2012 | Gynaecological outpatient surgery | Not specified | Choice of soft country, classical/new age and inspirational music | Preoperatively Intraoperatively | On average 212 min | 43 | Headphones without music 35 Postoperative opioid requirement |
| Kar, 2015* | Elective cardiac surgery under cardiopulmonary bypass | General | Raga therapy (Indian classical music) | Preoperatively Intraoperatively | 30 min before surgery and procedure duration | 17 | Standard care 41 | PACU length of stay Intraoperative sedative requirement Intraoperative propofol requirement |
| Kliempt, 1999 | Diverse range of surgical procedures | General | Classical music Adagio Karajan | Intraoperatively | Procedure duration | 25 | Headphones without music 26 | Intraoperative opioid requirement |
| Koch, 1998* | Outpatient urological procedures | Spinal | Own favorite music | Intraoperatively | Procedure duration | 19 | Standard care 15 | Intraoperative propofol requirement PACU length of stay |
| Koelsch, 2011 | Total hip arthroplasty | Spinal | Joyful instrumental music | Preoperatively Intraoperatively | 120 min before surgery and procedure duration | 20 | Headphones with breaking sea waves noise 20 | Intraoperative propofol requirement |
| Kumar, 2014 | Hernia, breast, appendix and thyroid surgery | Not specified | Raga Ananda Bairavi (Indian classical music) | Preoperatively | At admission and POD 1–3 | 30 | Standard care 30 | Postoperative opioid requirement |
| Study ID                  | Surgical Procedure                        | Anesthesia | Intervention                  | Moment                                  | Duration                              | N  | Control          | N  | Outcome Parameters                       |
|--------------------------|-------------------------------------------|------------|------------------------------|-----------------------------------------|----------------------------------------|----|-----------------|----|-----------------------------------------|
| Laurion and Fetter, 2003 | Gynecological, laparoscopic outpatient day surgery | General    | Piano music                  | Preoperatively                           | 2 times a day before surgery, procedure duration, PACU stay | 28 | Standard care   | 28 | Postoperative opioid requirement, PACU length of stay |
| Lepage, 2001*            | Nononcologic, outpatient or short-stay surgery | Spinal     | Choice of pop, jazz, classical, new age | Preoperatively                           | 30 min daily on POD 1–3               | 56 | Standard care   | 56 | Postoperative patient-controlled analgesia requirement, Postoperative patient-controlled analgesia requirement |
| Liu and Petrini, 2015    | Thoracic surgery                          | General    | Soft, melodious music 60-80 bpm | Postoperatively                          |                                        | 28 | Standard care   | 28 | Postoperative opioid requirement         |
| Macdonald, 2003          | Total abdominal hysterectomy               | Not specified | Own favorite music          | Postoperatively                          | 2–6 h on day of surgery               | 30 | Standard care   | 30 | Postoperative opioid requirement         |
| Masuda, 2005*            | Orthopedic surgery                        | General and spinal | Choice of Noh, Gagaku, classical or Enka music | Postoperatively                          | 20 min                                | 22 | Standard care   | 22 | Hospital length of stay                  |
| Mignault, 2004*          | Gynaecological surgery                    | General    | Choice of jazz, classical, popular new-age or piano music | Intraoperatively                         | Procedure duration                     | 15 | Headphones without music                   | 15 | Intraoperative end-tidal isoflurane requirement, Intraoperative fentanyl requirement, Postoperative opioid requirement |
| Miladinia, 2017*         | Abdominal surgery                         | General    | Relaxing nonlyrical music with a bpm of 60–80 | Postoperatively                          | 3 × 10 min sessions on day of surgery | 30 | Standard care   | 30 | Postoperative opioid requirement         |
| Nielsen, 2018*           | Unspecified orthopedic, urological, gynaecological and general surgery | Epidural, spinal and local | Musicure                      | Intraoperatively                         | Procedure duration                     | 58 | Standard care   | 58 | Intraoperative fentanyl requirement, Intraoperative propofol requirement |
| Nilsson, 2001*           | Elective abdominal hysterectomy           | General    | Relaxing, calming music with sea waves sound | Intraoperatively                         | Procedure duration                     | 30 | Headphones with operation noise recording | 28 | Postoperative opioid requirement, Hospital length of stay, Postoperative opioid requirement |
| Nilsson, 2003a*          | Daycare surgery: varicose veins, open inguinal hernia repair | General    | Soft, relaxing and calming classical music | Postoperatively                         | PACU arrival until patient chose to stop | 62 | Headphones without music                   | 62 | Postoperative opioid requirement         |
| Nilsson, 2003b*          | Daycare surgery: varicose veins, open inguinal hernia repair | General    | Soft instrumental new-age synthesizer music | Intraoperatively                         | Procedure duration                     | 51 | Headphones without music                   | 49 | Postoperative opioid requirement         |
| Nilsson, 2005*           | Open hernia repair (Lichtenstein)         | General    | Soft, new-age synthesizer    | Postoperatively                          | 1 h after PACU arrival, Procedure duration | 51 | Headphones without music                   | 51 | Postoperative opioid requirement         |
| Fu et al Annals of Surgery 2019 The Author(s). Published by Wolters Kluwer Health, Inc.
| Study ID  | Surgical Procedure                  | Anesthesia       | Intervention                                      | Moment        | Duration | N  | Control       | N  | Outcome Parameters                      |
|-----------|-------------------------------------|-------------------|---------------------------------------------------|---------------|----------|----|---------------|----|-----------------------------------------|
| Nilsson, 2009a | Coronary artery bypass graft and/or aortic valve replacement | General | MusiCure using music pillow | Postoperatively | 30 min on POD1 | 20 | Standard care | 20 | Postoperative opioid requirement |
| Nilsson, 2009b* | Coronary artery bypass graft or aortic valve replacement | General | Soft, relaxing, new age style music using music pillow | Postoperatively | 30 min on POD1 | 28 | Standard care | 30 | Postoperative opioid requirement |
| Reza, 2007*  | Elective caesarean section           | General | Soft, instrumental, Spanish style guitar music | Intraoperatively | Procedure duration | 50 | White music | 50 | Postoperative opioid requirement |
| Santhna, 2015 | Total knee replacement surgery       | Not specified    | Choice of soothing and relaxing nonlyrical piano or violin music | Postoperatively | 60 min, 4 times a day | 20 | Standard care | 20 | Postoperative opioid requirement |
| Schwartz, 2009 | Coronary artery bypass graft surgery | General | Light piano music | Postoperatively | Patient’s choice in ICU | 35 | Standard care | 32 | ICU length of stay Hospital costs |
| Sen, 2009a* | Local urological procedures         | Propofol PCS with local infiltration | Own favorite music | Intraoperatively | Procedure duration | 30 | Earphones without music | 30 | Intraoperative propofol requirement |
| Sen, 2009b* | Elective caesarean section          | General | Own favorite music | Preoperatively | 60 min | 50 | Headphones without music | 50 | Postoperative opioid requirement |
| Sen, 2010* | Elective caesarean section          | General | Own favorite music | Postoperatively | 60 min | 35 | No music | 35 | Postoperative opioid requirement |
| Szmuk, 2008 | Laparoscopic hernia or cholecystectomy | General | Choice of pop-rock, classical or Israeli music | Intraoperatively | Procedure duration | 20 | Headphones without music | 20 | Intraoperative end-tidal sevoflurane Postoperative opioid requirement |
| Tse, 2005 | Endoscopic sinus surgery or tubinectomy | Not specified | Choice of Chinese, Western or own favorite music songs | Postoperatively | 2 × 30 min after surgery and on POD1 | 27 | Standard care | 30 | Postoperative analgesic medication requirement |
| Vaajoki, 2012 | Elective major abdominal midline incision surgery | General | Choice of 2000 popular music songs | Postoperatively | Total of 7 × 30 min | 83 | Standard care | 85 | Postoperative opioid requirement Hospital length of stay |
| Zhang, 2005* | Total abdominal hysterectomy         | General with spinal or epidural | Own favorite music | Intraoperatively | Procedure duration | 55 | Headphones without music | 55 | Intraoperative propofol requirement |
| Zhou, 2011* | Radical mastectomy                  | General | Choice of 202 songs | Postoperatively | 2 × 30 min daily | 60 | Standard care Scheduled rest of 30 min | 60 | Hospital length of stay Postoperative opioid requirement |
| Zimmerman, 1996 | Coronary artery bypass graft surgery | General | Choice of 5 soothing music tapes | Postoperatively | 2 × 30 min daily during POD1-3 | 32 | Hospital length of stay | 32 | Postoperative opioid requirement |

*Denotes study included in meta-analysis.

CD indicates compact disk; ICU, intensive care unit; Min, minutes; N, number of patients; PACU, post-anesthesia care unit; PCS, patient-controlled sedation; POD, postoperative day; d, days; h, hours.
blinded did not significantly reduce postoperative opioid requirement (pooled SMD = −0.16 [95% CI −0.63 to 0.31], P = 0.49, F² = 57.1, N = 188 patients).38,41,46 The effect of preoperative and/or intraoperative music on intraoperative opioid requirement was assessed in 7 studies.23,26,29,33,38,40,63 Meta-analysis was not performed because of insufficient data presented, the broad variation in the types of surgery performed and difference in surgery duration.

**Intraoperative Sedative Requirement**

The effect of perioperative music on intraoperative sedative medication requirement was assessed in 13 studies (846 patients). Propofol requirement was assessed in 9,20,26,29,33–35,40,48,51 midazolam requirement in 3,21,33,36 and end-tidal inhalation anesthetics concentration in 2 studies.38,64 In one of these aforementioned studies, both propofol and midazolam were administered intraoperatively for sedation.33 Incremental intraoperative sedative medication doses were administered based on sedation depth, which was either assessed using a bispectral index monitor or a validated sedation scale. The infusion rate was patient-controlled in 4 studies.20,34,36,48 The manner of sedation depth assessment and whether or not infusion rate was patient-controlled is specified in Fig. 4.

Perioperative music significantly reduced intraoperative propofol requirement (pooled SMD = −0.72 [95% CI −1.01 to −0.43], P < 0.00001, F² = 61.1, N = 554 patients, 9 studies) (Fig. 4). All included studies evaluating the effect of music on propofol requirement, except 229,40 that did not specify the manner of sedation depth assessment, reported that the level of sedation did not differ between the music and control group. This reduction in intraoperative propofol requirement remained present when these 2 studies29,40 were excluded from the analysis (pooled SMD = −0.86 [95% CI −1.18 to −0.53], P < 0.00001, F² = 54.9, N = 377 patients, 7 studies), and when the 3 studies with patient-controlled propofol infusion rate were analyzed as a separate subgroup (pooled SMD = −0.82 [95% CI −1.25 to −0.38], P = 0.00025, F² = 40.1, N = 153 patients). Perioperative music also significantly reduced intraoperative midazolam requirement (pooled SMD = −1.07 [95% CI −1.70 to −0.44], N = 421 patients).38,41,46

**FIGURE 3.** Effect of perioperative music on postoperative opioid requirement. Forest plot presenting the effect of perioperative music on postoperative opioid requirement (milligrams of morphine equianalgesics). CI indicates confidence interval; Mean, mean milligrams of morphine equianalgesics; N, total number of patients in study; N_control, number of patients in the control group; N_music, number of patients in the music group; PACU, post-anesthesia care unit; SD, standard deviation in milligrams of morphine equianalgesics; SMD, standardized mean difference.
Perioperative Music Lowers Opioid and Sedative Requirement

**FIGURE 4.** Effect of perioperative music on intraoperative sedative medication requirement. Forest plot presenting the effect of perioperative music on intraoperative propofol (above) and midazolam (below) medication requirement. CI indicates confidence interval; Mean, mean milligrams of propofol or midazolam; N, total number of patients in study; N_C, number of patients in the control group; N_M, number of patients in the music group; OAA/S, observer assessment of alertness/sedation scale; PACU, post-anesthesia care unit; PCS, patient-controlled sedation; SD, standard deviation in milligrams of propofol or midazolam; SMD, standardized mean difference.

**FIGURE 5.** Effect of perioperative music on length of stay. Forest plot presenting the effect of perioperative music on length of stay. CI indicates confidence interval; Mean, mean length of stay; N, total number of patients in study; N_C, number of patients in the control group; N_M, number of patients in the music group; PACU, post-anesthesia care unit; SD, standard deviation; SMD, standardized mean difference.

**P** < 0.001, $I^2$ = 73.1, N = 184 patients) (Fig. 4), while achieving the same sedation depth.

**Length of Stay and Medical Costs**

The effect of perioperative music on length of stay was assessed in 17 studies, of which 9 studies could be included in the meta-analysis. Total length of hospital stay of surgical inpatients was assessed in 4 studies,22,23,37,52 length of stay in the post-anesthesia or day care unit of patients undergoing outpatient surgery in 4 other studies20,26,29,34 and intensive care unit length of stay in 1 study.47 Perioperative music did not significantly reduce length of stay (pooled SMD -0.18 [95% CI -0.43 to 0.07], $P = 0.15$, $I^2$ = 56.0, N = 600 patients) (Fig. 5). When analyzing the studies with outpatient surgical patients (pooled SMD -0.053 [95% CI -0.35 to 0.24], $P = 0.73$, $I^2$ = 13.1, N = 208 patients) and inpatient operations (pooled SMD -0.21 [95% CI -0.66 to 0.25], $P = 0.37$, $I^2$ = 75.2, N = 325 patients) separately, length of stay was also not reduced.

Intensive care unit costs tended to be lower in 1 pilot study [3911 (SD 1566) versus 4365 dollars (SD 2632), $P = 0.09$], as time spent in the intensive care unit was significantly reduced in the music group compared to the control group.47 However, this did not reach statistical significance and overall direct medical costs during hospital length of stay did not differ significantly.

**DISCUSSION**

This systematic review and meta-analysis of 55 randomized controlled trials evaluates the effect of perioperative music on...
intraoperative and postoperative medication requirement and length of stay. Because of the current opioid epidemic, which has increased opioid-related deaths and led to a substantial financial burden, there is an increased interest in nonpharmacological interventions that can reduce both postoperative pain and opioid consumption. Perioperative music reduced opioid consumption by 4.4 mg ME in studies measuring opioid requirement for at least 24 hours or more after surgery. In studies measuring at least 72 hours or more after major surgical procedures, a reduction of 9.8 mg ME was observed. Opioid-related adverse effects have been observed to be dose-dependent and an increased requirement of 3 to 4 mg ME after surgery has been related to the occurrence of 1 additional, clinically meaningful, adverse event. A maximum daily dose exceeding 2 mg of parenteral hydromorphone, equivalent to 10 to 14 mg ME, were significantly associated with the development of postoperative ileus after colorectal surgery, increasing morbidity, length of hospital stay, and direct medical costs. Both a higher daily opioid dose and a prolonged use in opioid-naive patients also increase the risk of chronic opioid use. As more elderly patients are nowadays undergoing surgery, this group would be of particular interest to the use of perioperative music, as they have an increased risk of opioid-related adverse effects and chronic abuse because of polypharmacy and comorbidities.

Perioperative music also significantly reduced both intraoperative propofol and midazolam requirement, whilst achieving the same sedation level. Midazolam is often used during locoregional anesthesia or as a preoperative anxiolytic, but is a risk factor for the occurrence of postoperative delirium. A higher level of preoperative anxiety has been associated with a higher amount of intravenous sedation requirement to induce and maintain adequate sedation level during surgery. Previous studies have reported a beneficial effect of perioperative music on anxiety levels, which could theoretically explain the reduced sedation dosage needed. Although a dose-dependent relation of sedative medication and intraoperative hemodynamic changes has been observed, the predictive outcome capabilities of intraoperative hemodynamics have only been investigated sparingly.

No effect of perioperative music on length of stay was demonstrated. However, only 4 studies assessed total length of stay and organizational rather than patient factors are the most important predictors of delayed discharge. Moreover, almost half of the studies (44%) that assessed length of stay did so in patients undergoing minor surgery in the outpatient setting, making it unlikely to find a clinically relevant difference. Even though opioids are relatively cheap, opioids accounted for 1% of total hospital costs in an observational study of patients undergoing joint replacement surgery. As one of the most commonly performed procedures in the developed world, yearly costs in the United States alone amount to more than $20 billion. It is therefore likely that the beneficial effects of perioperative music on medication requirement will also be observed financially, especially when taking into account the costs that come with opioid-related adverse effects.

This meta-analysis has several strong points. A comprehensive literature search was performed with a dedicated biomedical information specialist. A predefined definition of music was used and studies with live music, a music therapist and concomitant interventions were excluded. In comparison to earlier performed meta-analyses investigating the effects of perioperative music, our focus was solely on medication requirement and length of stay in adult surgical patients. Vetter et al did observe a significant reduction in pain medication requirement by perioperative music in fourteen studies, but this was not significant for the subgroup of patients who received general anesthesia in 9 studies. The meta-analysis by Hole et al combined studies with both surgical and nonsurgical, diagnostic procedures leading to clinical heterogeneity, and did not differentiate between opioid, benzodiazepines, and sedative medication requirement. Nevertheless, this meta-analysis has limitations as well. The included studies contained different surgical patients, surgical procedures, and follow-up duration of the outcome assessment. This was reflected in the moderate to high level of heterogeneity observed. Medication requirement can be influenced by factors such as age, body weight, and the duration of surgery. Some of these baseline characteristics were not reported in the included studies, potentially increasing the risk of bias in interpreting results. Therefore, it is not entirely clear whether perioperative music can have the same beneficial effect size on medication requirement for all surgical procedures. Measurement duration of postoperative opioid requirement in 15 of the 20 studies was 24 hours after surgery or less. Consequently, the mean absolute reduction in mg ME in the music group was relatively low and perhaps does not reflect the full beneficial effect of perioperative music on medication requirement. Although a meta-regression analysis could be performed with covariates such as music intervention duration, music exposure moment relative to the surgical procedure (ie, preoperatively, intraoperatively, postoperatively, or multiple moments), operative severity (ie, minor, moderate, or major surgery), and measurement duration, this was not best appropriate as at least ten studies for each of these factors were recommended. Only postoperative opioids were assessed, as other analgesic medications were often not reported. Some included studies did report that perioperative music also reduced nonopioid analgesic requirement postoperatively.

Our literature search did not include patient-reported outcome measures. However, it should be noted that patients in the included studies were extremely positive towards the use of perioperative music. Almost all patients (88% or higher) found perioperative music to be an enjoyable experience. Likewise, a majority would opt for music again in the future. Patient satisfaction was also markedly increased in the music group, with only the negative comments observed being from those who did not get music or related to the type of available music. Although side-effects of perioperative music could theoretically occur, none of the included studies reported any adverse effects. Specifically, no cardiorespiratory depressions were observed, while McCaffrey et al reported that perioperative music had a significant beneficial effect on delirium and confusion. In some studies, care was taken to restrict music volume and adhere to the noise and hearing loss guidelines to prevent hearing damage, whereas others allowed patients the option to adjust the music volume to their liking. The most well-known implemented nonpharmacological, multimodal interventions in surgical patient care are part of the guidelines collectively known as the Enhanced Recovery After Surgery protocols, which focus on reducing the physiological stress response to surgery by optimizing nutritional state, reducing opioid use and early mobilization. Originally introduced in colorectal surgical patient care, it has subsequently been implemented in a wide range of different surgical specialties with surgery-specific variations. Likewise, the use of perioperative music should be adapted to fit into the operative procedure, individual clinical setting, and wishes and requirements of the medical team. Although it is difficult to draw a firm clinical recommendation based on the data in our meta-analysis, 75% of studies assessing opioid requirement exposed patients to a total of 120 minutes perioperative music on average or less, delivered either before, during and/or on the first 2 days after surgery. Therefore, it seems that a relatively short exposure to music can already be beneficial, with a majority of the studies using a music player and headphones to avoid disrupting communication of the medical staff. Further research could focus on the effect of...
periparative music on postoperative complications, clinical recovery, costs, and implementation.

CONCLUSIONS

Perioperative music can reduce postoperative opioid and intraoperative sedative medication requirement. Therefore, periparative music may potentially improve patient outcome and reduce medical costs, as a higher opioid dosage is associated with an increased risk of adverse events and chronic opioid use. The use of perioperative music seems to be safe and patient-friendly, given the high patients satisfaction reported whilst no adverse effects were observed.

ACKNOWLEDGMENTS

The authors thank W. Bramer, biomedical information specialist of the Medical Library, Erasmus MC University Medical Centre, Rotterdam, for his assistance with the literature search. The authors thank V.P.B. Elbers, BSc, Medical Student, for assistance in the literature screening. The authors thank A. Tomer, MSc, Statistician, for assistance in the statistical analysis.

REFERENCES

1. Gan TJ, Habib AS, Miller TE, et al. Incidence, patient satisfaction, and perceptions of post-surgical pain: results from a US national survey. *Curr Med Res Opin*. 2014;30:149–160.
2. Pavlin DJ, Rapp SE, Polissar NL, et al. Factors affecting discharge time in adult outpatients. *Anesth Analg*. 1998;87:816–826.
3. Ballantyne JC, Carr DB, deFerranti S, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: cumulative meta-analyses of randomized, controlled trials. *Anesth Analg*. 1998;86:598–612.
4. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. *Tale J Biol Med*. 2010;83:11–25.
5. Taylor RS, Ulrich K, Regan S, et al. The impact of early postoperative pain on health-related quality of life. *Pain Pract*. 2013;13:515–523.
6. Shah A, Hayes CJ, Martin BC. Factors influencing long-term opioid use among opioid naive patients: an examination of initial prescription characteristics and pain etiologies. *J Pain*. 2017;18:1374–1383.
7. Dolin SJ, Cashman JN. Tolerability of acute postoperative pain management: nausea, vomiting, sedation, pruritus, and urinary retention. Evidence from published data. *Br J Anaesth*. 2005;95:584–591.
8. Roberts GW, Bekker TB, Carsen HH, et al. Postoperative nausea and vomiting are strongly influenced by postoperative opioid use in a dose-related manner. *Anesth Analg*. 2005;101:1343–1348.
9. Clegg A, Young JB. Which medications to avoid in people at risk of delirium: a systematic review and meta-analysis. *Anesthesiology*. 2011;40:23–29.
10. Gan TJ, Robinson SB, Oderda GM, et al. Closing the gap between methodologists and end-users: R as a computational back-end. *J Stat Softw*. 2012;49:1–15.
11. Yoo GB, Rizk LB, Yaacoub CI, et al. Music and ambient room noise in patients undergoing spinal anesthesia. *Anesth Analg*. 2005;100:1316–1319.
12. Bansal P, Kharouf U, Patel P, et al. The effect of music therapy on sedative requirements and haemodynamic parameters in patients under spinal anaesthesia: a prospective study. *J Clin Diagn Res*. 2010;4:2782–2789.
13. Blankfield RP, Zyzanski SJ, Flocke SA, et al. Taped therapeutic suggestions and taped music as adjuncts in the care of coronary-artery-bypass patients. *Am J Clin Hypn*. 1995;37:32–42.
14. Chen HJ, Chen TY, Huang CY, et al. Effects of music on psychophysiological responses and opioid dosage in patients undergoing total knee replacement surgery. *Jpn J Nurs Sci*. 2015;12:309–319.
15. Ciercy R, Obyahvi T. The effects of music therapy on anxiety, pain and the amount of analgesics following coronary artery surgery. *Turk J Thorac Cardiovasc Surg*. 2016;24:44–50.
16. Cuthall SM, Anderson PG, Prinsen SK. Effect of the combination of music and nature sounds on pain and anxiety in cardiac surgical patients: a randomized study. *Altern Therap Health Med*. 2011;17:16–23.
17. Dubu-Bondoc S, Vadivelu N, Benson J, et al. Hemispheric synchronized sounds and perioperative analgesic requirements. *Anesth Analg*. 2010;110:208–210.
18. Ebnesahid M, Mohseni M. The effect of patient-selected music on early postoperative pain, anxiety, and hemodynamic profile in cesarean section surgery. *J Altern Complement Med*. 2008;14:827–831.
19. Good M. A comparison of the effects of jaw relaxation and music on postoperative pain. *Nurs Res*. 1995;44:52–57.
20. Graversen M, Sommer T. Perioperative music may reduce pain and fatigue in patients undergoing laparoscopic cholecystectomy. *Acta Anaesthesiol Scand*. 2005;47:1010–1016.
21. Heitl Z, Symmeng T, Scamman FL. Effect of music therapy in the postanesthesia care unit: a nursing intervention. *J Post Anesth Nurs*. 1992;7:22–31.
22. Hook L, Sonwathana P, Petichetchnian W. Music therapy with female surgical patients: effect on anxiety and pain. *Thai J Nurs Res*. 2008;12:259–271.
23. Komidou E, Rehnstrom N, Naeho O. Effect of music on vital signs and postoperative pain. *AORN J*. 2004;80:269–274.
24. Kar SK, Ganguly T, Roy SS, et al. Effect of Indian classical music (Raga therapy) on fentanyl, vecuronium, propofol requirements and cortisol levels in cardiopulmonary bypass. *J Anesth Crit Care*. 2015;2:1–5.
25. Koch ME, Kain ZN, Ayoub C, et al. The sedative and analgesic sparing effect of music. *Anesthesiology*. 1998;90:300–306.
26. Koelsch S, Fuermetz J, Sack U, et al. Effects of music listening on cortisol levels and propofol consumption during spinal anesthesia. *Front Psychol*. 2011;2:1–9.
27. Lepage C, Drolet P, Giraud M, et al. Music decreases sedative requirements during spinal anesthesia. *Anesth Analg*. 2001;93:912–916.
28. Masuda T, Miyamoto K, Shimizu K. Effects of music listening on elderly orthopaedic patients during postoperative bed rest. *Nordic J Music Ther*. 2005;14:4–14.
29. Mignaeull B, Giraud F, Albert C, et al. The effect of music on the neurohormonal stress response to surgery under general anesthesia. *Anesth Analg*. 2004;98:527–532.
30. Miladina M, Pishghoie AH, Aliyari S, et al. The comparison of the effect of two complementary medicine methods (music therapy and massage therapy) on postoperative acute pain after abdominal surgery: a randomized clinical trial study. *Iran Red Crescent Med J*. 2017;19:1–7.
31. Nielsen E, Wahlin I, Fristam GH. Evaluating pictures of nature and soft music on anxiety and well-being during elective surgery. *Open Nurs J*. 2018;12:58–66.
32. Nilsson U, Rawal N, Unosson M. Comparison of intra-operative or postoperative music therapy on fentanyl, vecuronium, propofol requirements and cortisol levels in cardiopulmonary bypass. *J Anesth Crit Care*. 2015;2:1–5.
33. Nielsen U, Rawal N, Unosson M. A comparison of intra-operative or postoperative music therapy – a controlled trial of the effects on postoperative pain. *Anesth Analg*. 2005;98:707–711.
34. Nilsson U, Rawal N, Unosson M. Stress reduction and analgesia in patients exposed to calming music postoperatively: a randomized controlled trial. *Eur J Anaesthesiol*. 2005;22:96–102.
Nilsson U. Soothing music can increase oxytocin levels during bed rest after open-heart surgery: a randomised control trial. *J Clin Nurs*. 2009;18:2153–2161.

Reza N, Ali SM, Saeed K, et al. The impact of music on postoperative pain and anxiety following cesarean section. *Middle East J Anesthesiol*. 2007;19:573–586.

Schwartz FJ. A pilot study of patients in postoperative cardiac surgery. *Music Med*. 2009;1:70–74.

Şen H, Atęş F, Sizlan O, et al. Effect of music on sedation during local urological surgeries. *Anatolian J Clin Invest*. 2009;3:131–135.

Şen H, Sizlan O, Yanarates O, et al. The effect of musical therapy on postoperative pain after caesarean section. *TAF Prevent Med Bull*. 2009;8:107–112.

Şen H, Yanarates O, Sizlan A, et al. The efficiency and duration of the analgesic effects of musical therapy on postoperative pain. *Ayer*. 2010;22:145–150.

Zhang XW, Fan Y, Manyande A, et al. Effects of music on target-controlled infusion of propofol requiring durations compared between spinal-epidural analgesia. *Anaesthesia*. 2005;60:980–994.

Zhou KN, Li YM, Yan H, et al. Effects of music therapy on depression and duration of hospital stay of breast cancer patients after radical mastectomy. *Chin Med J (Engl)*. 2011;124:2321–2327.

Zimmerman L, Nieveen J, Barnason S, et al. The effects of music interventions on postoperative pain and sleep in coronary artery bypass graft (CABG) patients... including commentary by Musikowski C. *Scholar Inq Nurs Pract*. 1996;10:153–174.

Easter B, DeBoer L, Settlemyre G, et al. The impact of music on the PACU experience of gynecologic laparoscopic patients. *J Clin Nurs*. 2014;76:357–370.

Liu Y, Petrimi MA. Effects of music therapy on pain, anxiety, and vital signs in patients after thoracic surgery. *Complement Ther Med*. 2015;23:714–718.

McCaferry R, Locsin R. The effect of music on pain and acute confusion in older adults undergoing hip and knee surgery. *Moslit Nurs Pract*. 2006;20:18–22.

Tse MMY, Chan MF, Benzie IFF. The effect of music therapy on postoperative pain and sleep in coronary artery bypass surgery (CABG) patients. *Br J Anaesth*. 2011;108:119–125.

Prasad V, Guerrisi M, Dauri M, et al. Prediction of postoperative pain, heart rate, systolic blood pressure and analgesic use following nasal surgery. *J Pain Palliat Care Pharmacother*. 2005;19:21–29.

Vaajoki A, Pirttia AM, Kankunen P, et al. Effects of listening to music on pain intensity and pain distress after surgery: an intervention. *J Clin Nurs*. 2012;21:708–717.

Johnson SP, Chung KC, Zhong L, et al. Risk of prolonged opioid use among opioid-naïve patients following common hand surgery procedures. *J Hand Surg Am*. 2016;41:947–957.

Kumar TS, Muthuraman M, Krishnakumar R. Effect of the raga anandabhairavi in post operative pain relief management. *Indian J Surg*. 2014;76:31–370.

Laurion S, Fetzer SJ. The effect of two nursing interventions on the postoperative outcomes of gynecologic laparoscopic patients. *J Perinat Nurs*. 2003;18:254–261.

Macdonald RAR, Mitchell LA, Dillon T, et al. An empirical investigation of the anxiolytic and pain reducing effects of music. *Psychol Music*. 2003;31:187–203.

Kilempt P, Ruta D, Ogston S, et al. Hemispheric-synchronisation during anaesthesia: a double blind randomised trial using audiostapes for intraoperative nociception control. *Anaesthesia*. 1999;54:769–773.

Szmuk P, Aroyo N, Ezri T, et al. Listening to music during anesthesia does not reduce the sevoflurane concentration needed to maintain a constant bispectral index. *Anesth Analg*. 2008;107:77–80.

Öhqvist G, Hallin R, Gelinder S, et al. A comparison between morphine, meperidine and ketobemidone in continuous intravenous infusion for postoperative relief. *Acta Anaesthesiol Scand*. 1991;35:44–48.

Grond S, Sablotzki A. Clinical pharmacology of tramadol. *Clin Pharmacokinet*. 2004;43:879–923.

Stanley G, Appadu B, Mead M, et al. Dose requirements, efficacy and side effects of morphine and pethidine delivered by patient-controlled analgesia after gynaecological surgery. *Br J Anaesth*. 1996;76:484–486.

Mohamadi A, Chan JJ, Lian J, et al. Risk factors and pooled rate of prolonged opioid use following trauma or surgery; a systematic review and meta- (regression) analysis. *J Bone Joint Surg Am*. 2018;100:1332–1340.

Zhao SZ, Chung F, Hanna DB, et al. Dose-response relationship between opioid use and adverse effects after ambulatory surgery. *J Pain Sympt Manage*. 2004;28:35–46.

Lowe A, Hamilton M, Greener BM, et al. Fatal overdoses involving hydromorphone and morphine among inpatients: a case series. *CMAJ Open*. 2017;5:E184–E189.

Barletta JF, Asgeirsson T, Senagore AJ. Influence of intravenous opioid dose on postoperative ileus. *Ann Pharmacother*. 2011;45:916–923.

Sun EC, Darnall BD, Baker LC, et al. Incidence of and risk factors for chronic opioid use among opioid-naive patients in the postoperative period. *JAMA Intern Med*. 2016;176:1286–1293.

Chau DL, Walker V, Pai L, et al. Opiates and elderly: use and side effects. *Clin Interv Aging*. 2008;3:273–278.

Inouye SK, Robinson T, Blum C, et al. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. *J Am Coll Surg*. 2015;220:136–148.

Kil HK, Kim WON, Chung WY, et al. Preoperative anxiety and pain sensitivity are independent predictors of propofol and sevoflurane requirements in general anaesthesia. *Br J Anaesth*. 2012;108:119–125.

de Wit F, van Vliet AL, de Wilde RB, et al. The effect of propofol on haemodynamics: cardiac output, venous return, mean systemic filling pressure, and vascular resistances. *Br J Anaesth*. 2016;116:784–789.

Prasad V, Guerrisi M, Dauri M, et al. Prediction of postoperative outcomes using intraoperative hemodynamic monitoring data. *Sci Rep*. 2017;7:1–11.

Challis D, Hughes J, Xie C, et al. An examination of factors influencing delayed discharge of older people from hospital. *Int J Geriatr Psychiatry*. 2014;29:160–168.

Macario A, McCoy M. The pharmacy cost of delivering postoperative analgesia to patients undergoing joint replacement surgery. *J Pain*. 2003;4:22–28.

Lam V, Teutsc S, Fielding J. Hip and knee replacements: a neglected potential savings opportunity. *JAMA*. 2018;319:977–978.5,916–923.

Alfred KD, Byers IF, Sole ML. The effect of music on postoperative pain and anxiety. *Pain Manage Nurs*. 2010;11:15–25.

Ignacio JJ, Fai CM, Hui TEOS, et al. Research in brief — the effect of music on pain, anxiety, and analgesic use on adults undergoing an orthopaedic surgery: a pilot study. *Singapore J Nurs*. 2012;39:49–51.

Nilsson U. The effect of music intervention in stress response to cardiac surgery in a randomized clinical trial. *Heart Lang*. 2009;38:201–207.

Johnson B, Raymond S, Goss J. Perioperative music or headsets to decrease anxiety. *J Peri Anesth Nurs*. 2012;27:146–154.

McCaferry R. The effect of music on acute confusion in older adults after hip or knee surgery. *Appl Nurs Res*. 2009;22:107–112.

Centers for Disease Control and Prevention (CDC). Noise and Hearing Loss Prevention, 2018. Available at: https://www.cdc.gov/niosh/topics/noise/reducenoiseexposure/regguidance.html. Accessed April 7, 2019.

Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. *JAMA Surg*. 2017;152:292–298.
Appendix A. Literature Search Strategy

**Embase**

(music/de OR 'music therapy'/de OR (music OR musical OR musicotherapy):ab,t.i.) AND (surgery/exp OR 'obstetric operation' /exp OR 'postoperative complication'/exp OR 'anesthesiology procedure'/exp OR 'perioperative nursing'/de OR 'postanesthesia nursing'/de OR 'operating room'/de OR 'recovery room'/de OR 'operating room personnel'/de OR (surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operati OR interoperat OR intraoperat OR anesthe OR anaeasthe OR peri-anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe):ab,t.i. OR surgery:link) AND ('economic evaluation' /exp OR 'economic aspect'/exp OR economics/exp OR 'length of stay'/de OR 'drug use'/de OR 'drug therapy'/exp OR 'drug therapy':link OR deprescription/de OR prescription/de OR 'analgesic agent'/exp OR 'anxiety agent'/exp OR 'analgesic' OR 'anxiolytic' OR 'sedative' OR 'narcotic':ab,t.i.)

**Medline Ovid**

(music/ OR "music therapy"/ OR (music OR musical OR musicotherapy):ab,t.i.) AND (exp "Surgical Procedures, Operative"/ OR exp "postoperative complications"/ OR "Anesthesiology"/ OR "perioperative nursing"/ OR "Operating Rooms"/ OR "recovery room"/ OR (surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operati OR interoperat OR intraoperat OR anesthe OR anaeasthe OR peri-anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe):ab,t.i. OR surgery:xs) AND (exp "Economics"/ OR "Length of Stay"/ OR "drug therapy"/ OR "drug therapy",xs OR Drug Prescriptions/ OR Deprescriptions/ OR exp "Analgesics"/ OR exp "Anti-Anxiety Agents"/ OR exp "Hypnotics and Sedatives"/ OR exp "Narcotics"/ OR "economics OR cost OR costs OR ((length OR duration) NEAR/3 (stay OR hospital))") OR ((drug OR drugs OR medication OR paracetamol OR acetaminophen OR opiate OR opioid OR morphine OR morfine OR concentrate OR "pharmacologic" OR agent") NEAR/10 (reduce OR use OR use/used OR user OR users OR "consumption" OR "therapeutic" OR "dose OR dosage OR intake OR demand" OR require)) OR prescri OR deprescri OR analgesic OR anxiolytic OR sedative OR narcotic:ab,t.i.)

**Web-of-science**

TS=((music OR musical OR musicotherapy) NEAR/10 ((surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operation OR operative OR interoperator OR intraoperator OR anesthe OR anaeasthe OR peri anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe)) AND ((econom OR cost OR costs OR ((length OR duration) NEAR/3 (stay OR hospital)) OR ((drug OR drugs OR medication OR paracetamol OR acetaminophen OR opiate OR opioid OR morphine OR morfine OR concentrate OR "pharmacologic" OR agent") NEAR/10 (reduce OR use OR used/used OR user OR users OR "consumption" OR "therapeutic" OR "dose OR dosage OR intake OR demand" OR require)) OR prescri OR deprescri OR analgesic OR anxiolytic OR sedative OR narcotic))

**Scopus**

T I T L E - A B S - KEY (music OR musical OR musicotherapy) W/10 (surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operation OR operative OR interoperator OR intraoperator OR anesthe OR anaeasthe OR peri anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe) AND ((econom OR cost OR costs OR ((length OR duration) W/3 (stay OR hospital)) OR ((drug OR drugs OR medication OR paracetamol OR acetaminophen OR opiate OR opioid OR morphine OR morfine OR concentrate OR "pharmacologic" OR agent") W/10 (reduce OR use OR used/used OR user OR users OR "consumption" OR "therapeutic" OR "dose OR dosage OR intake OR demand" OR require)) OR prescri OR deprescri OR analgesic OR anxiolytic OR sedative OR narcotic))

**PsycINFO Ovid**

(music/ OR "music therapy"/ OR (music OR musical OR musicotherapy):ab,t.i.) AND (exp "Surgery"/ OR "Surgical Patients"/ OR exp "Post-surgical Complications"/ OR exp "Surgical Complications"/ OR "Anesthesiology"/ OR "perioperative nursing"/ OR "postanaesthesia"/ OR "anesthesia"/ OR "anaesthesia"/ OR "anaesthetic"/ OR "anaesthesiologic"/ OR "anesthesiologic"/ OR "anaesthetics"/ OR "anaesthetic"/ OR "anaesthetic":ab,t.i.) AND (exp "Economics"/ OR "Length of Stay"/ OR "drug therapy"/ OR "drug therapy",xs OR Drug Prescriptions/ OR Deprescriptions/ OR exp "Analgesics"/ OR exp "Anti-Anxiety Agents"/ OR exp "Hypnotics and Sedatives"/ OR exp "Narcotics"/ OR "economics OR cost OR costs OR ((length OR duration) ADJ3 (stay OR hospital))") OR ((drug OR drugs OR medication OR paracetamol OR acetaminophen OR opiate OR opioid OR morphine OR morfine OR concentrate OR "pharmacologic" OR agent") ADJ10 (reduce OR "use" OR use/used OR user OR users OR "consumption" OR "therapeutic" OR "dose OR dosage OR intake OR demand" OR require)) OR prescri OR deprescri OR analgesic OR anxiolytic OR sedative OR narcotic:ab,t.i.)

**Cochrane central**

((music OR musical OR musicotherapy):ab,t.i.) AND ((surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operati OR interoperator OR intraoperator OR anesthe OR anaeasthe OR peri-anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe):ab,t.i.) AND ((econom OR cost OR costs OR ((length OR duration) NEAR/3 (stay OR hospital))") OR ((drug OR drugs OR medication OR paracetamol OR acetaminophen OR opiate OR opioid OR morphine OR morfine OR concentrate OR "pharmacologic" OR agent") ADJ10 (reduce OR "use" OR use/used OR user OR users OR "consumption" OR "therapeutic" OR "dose OR dosage OR intake OR demand" OR require)) OR prescri OR deprescri OR analgesic OR anxiolytic OR sedative OR narcotic:ab,t.i.)

**Cinahl**

(MH music+ OR MH "music therapy:" OR T I (music OR musical OR musicotherapy) OR AB (music OR musical OR musicotherapy)) AND (MH "Surgery, Operative:" OR MH "postoperative complications:" OR MH "Anaesthesiology:" OR MH "perioperative nursing:" OR MH "Operating Rooms:" OR MH "Post Anesthesia Care Units:" OR T I (surger OR surgic OR peroperat OR perioperat OR preoperat OR postoperat OR operati OR interoperator OR intraoperator OR anesthe OR anaeasthe OR peri-anesthesiae OR perianesthesiae OR preanesthesiae OR postanesthesiae OR postanesthe)
| Study ID         | Method of Randomization                  | Allocation Concealment | Blinding Participants | Blinding Surgical Staff | Blinding Assessors | Incomplete Adequately Addressed | Reporting | Selective Bias Adequately Addressed |
|------------------|-----------------------------------------|------------------------|-----------------------|-------------------------|--------------------|---------------------------------|-----------|-------------------------------------|
| Allred, 2007     | Sealed envelope system                  | Yes                    | No                    | No                      | Unclear            | Yes. Same number discontinued intervention | Unclear   | Unclear, surgery duration not reported |
| Ames, 2017       | Opaque, sealed envelope                 | Yes                    | No                    | No                      | No                 | Yes, exclusions unrelated to intervention | Low risk  | Unclear, surgery duration and weight not reported |
| Ayoub, 2005      | “Randomized” (unclear)                  | No, randomization and music by nonblinded member | No                    | Yes                     | Yes                | Yes                             | Unclear   | Yes                                 |
| Bansal, 2010     | Lottery method                          | Unclear                | No                    | No                      | No                 | Yes, all enrolled completed the study | Unclear   | Unclear, surgery duration and weight not reported |
| Bimns-Turner,    | Drawing numbers from reclosable plastic bag |           | Yes                    | No                      | No                 | Yes                             | Unclear   | Yes                                 |
| Blankfield, 1995 | “Randomized” (unclear)                  | Unclear                | No                    | No                      | Unclear            | Yes                             | Unclear   | Unclear, surgery duration and weight not reported |
| Chen, 2015       | Sealed envelopes stratified by sex      | Yes                    | No                    | No                      | Unclear            | No, 16/56 excluded and only 30 completed study | Unclear   | Unclear, weight not reported |
| Çügür and Özsayır, 2016 | Randomization by odd and even numbers | No                    | No                    | No                      | Unclear            | Unclear                         | Unclear   | Unclear, surgery duration and weight not reported |
| Cutshall, 2011   | Sealed envelopes                        | Yes                    | No                    | No                      | No                 | Unclear                         | Unclear   | No, patients music group significantly older |
| Dubu-Bondoc, 2010 | “Randomized” (unclear)                  | Unclear                | No                    | Yes                     | Yes                | Unclear                         | Unclear   | Yes                                 |
| Easter, 2010     | Hospital visit number                   | No                     | No                    | No                      | Unclear            | No                              | Unreported | Unclear, surgery duration and weight not reported |
| Ebnesahidi and Mohseni, 2010 | “Randomly assigned” (unclear) | Unclear                | No                    | No                      | No                 | Yes                             | Unclear   | Yes                                 |
| Finlay, 2016     | Computer-generated pseudo-random numerical stratified schedule | Unclear                | No                    | Yes                     | No                 | No                             | Unclear   | Unclear, surgery duration, age, and weight not reported |
| Good, 1995       | Not specified (unclear)                 | Unclear                | No                    | No                      | Unclear            | Unreported                      | Unclear   | 18/102 excluded                      |
| Good, 1999       | Computerized minimization program       | Yes                    | No                    | No                      | No                 | No, 117/617 (19%) excluded, 44% missed at least 1 test | Unclear   | Unclear, surgery duration, age, and weight not reported |
| Graversen and Sommer, 2013 | Randomization by day by picking an envelope | No                    | No                    | No                      | Unclear            | No, 1893 excluded               | Low risk  | Yes                                 |

**Appendix B. Bias Assessment**

Music surgery/operative/operation/perioperative/postoperative/intraoperative/“operating theater”/“recovery Room”/anesthesiological/anesthesia/preanesthetic/postanesthetic/economics/cost/“length stay/hospitalization”/“drug use/usage”
### Appendix B. (Continued)

| Study ID      | Method of Randomization | Allocation Concealment | Blinding Participants | Blinding Surgical Staff | Blinding Assessors | Incomplete Outcome Adequately Addressed | Selective Reporting | Other Bias Adequately Addressed |
|---------------|-------------------------|------------------------|-----------------------|------------------------|-------------------|----------------------------------------|---------------------|-------------------------------|
| Heitz, 1992   | ‘Randomly assigned’ (unclear) | Unclear                | No                    | No                     | Yes               | Unclear                                | Yes                 |                               |
| Hook, 2008    | Envelope method         | Unclear, as safeguards not specified | No                    | No                     | No                | Yes, equal number and reason for exclusion in both groups | Unclear             |                               |
| Ibhzer, 2011  | By lot                  | Unclear                | No                    | No                     | No                | Unclear, 34/160 excluded                | Unclear             |                               |
| Ignacio, 2012 | Computer-generated randomization list | Yes                    | No                    | No                     | No                | Unclear, not specified                  | Unclear             |                               |
| Ikonomodou, 2004 | ‘Randomly assigned’ (unclear) | Unclear                | No                    | Yes                    | Yes               | Yes                                    | Unclear             |                               |
| Johnson, 2012 | ‘Randomized’ (unclear)   | Unclear                | No                    | No                     | No                | Yes                                    | Unclear             |                               |
| Kar, 2015     | Computer-generated randomization | Yes                    | Yes                   | Yes                    | Yes               | Yes, exclusion before intervention and therefore unrelated clear, 2 excluded, group unclear | Unclear             |                               |
| Kliempt, 1999 | Computer-generated random number table | Yes                    | Yes                   | Yes                    | Yes               | Yes                                    | Unclear             |                               |
| Koch, 1998    | Table of random numbers | Unclear whether open allocation | No                    | No                     | No                | Unclear, 34/160 excluded                | Unclear             |                               |
| Koelsch, 2011 | Randomly chosen, identical looking mp3 player | Yes                    | No                    | Yes                    | Yes               | No, 10 / 50 (20%) excluded because of study protocol deviation | Unclear             |                               |
| Kumar, 2014   | Not specified (unclear)  | Unclear                | No                    | No                     | No                | Unclear                                | Unclear             |                               |
| Laurion and Fetzer, 2003 | ‘Randomly assigned’ (unclear) | Unclear                | No                    | No                     | No                | Unclear                                | Unclear             |                               |
| Lepage, 2001  | ‘Randomly assigned’ (unclear) | Unclear                | No                    | No                     | No                | Unclear                                | No, surgery duration longer |                               |
| Liu and Petrini, 2015 | Odd and even day numbers | No                    | No                    | No                     | No                | No, exclusions not evenly divided over groups | Unclear             |                               |
| MacDonald, 2003 | ‘Randomly assigned’ (unclear) | Unclear                | No                    | No                     | No                | Unclear                                | Unclear             |                               |
| Masuda, 2005  | Table of random numbers | Unclear whether open allocation | No                    | No                     | No                | Yes                                    | Unclear             |                               |
| McCaffrey and Loscin, 2006 | Room number | No                    | No                    | No                     | No                | Yes                                    | Unclear             |                               |
| McRee, 2003   | Drawing lots            | Unclear                | No                    | No                     | No                | Unclear                                | Unclear             |                               |
| Migneault, 2004 | ‘Randomly assigned’ (unclear) | Unclear                | Yes                   | Yes                    | Yes               | Unclear                                | Yes                 |                               |
| Miladinia, 2017 | Block randomization     | Yes                    | No                    | No                     | No                | Yes                                    | Low risk            |                               |
| Nielsen, 2018 | ‘Randomized’ (unclear)   | Yes                    | No                    | No                     | No                | Unclear                                | Unclear             |                               |
| Nilsson, 2001 | Computer-generated randomization list | Yes                    | Yes                   | Yes                    | Yes               | Yes                                    | Unclear             |                               |
| Nilsson, 2003a | Computer-generated randomization list | Yes                    | No                    | Yes                    | Yes               | Unclear                                | Unclear             |                               |
| Nilsson, 2003b | Computer-generated randomization list | Yes                    | No                    | Yes                    | Yes               | Unclear                                | Unclear             |                               |
| Nilsson, 2005 | Computer-generated randomization list | Yes                    | No                    | Yes                    | Yes               | Unclear                                | Unclear             |                               |
| Study ID     | Method of Randomization                          | Allocation Concealment | Blinding Participants | Blinding Surgical Staff | Blinding Assessors | Incomplete Outcome Adequately Addressed | Selective Reporting | Other Bias Adequately Addressed |
|-------------|-------------------------------------------------|------------------------|-----------------------|-------------------------|-------------------|----------------------------------------|---------------------|-------------------------------|
| Nilsson, 2009a | Computer-generated randomization list           | Yes                    | No                    | No                      | Yes               | Yes                                    | Unclear             | No, surgery duration in music group significantly longer |
| Nilsson, 2009b | Computer-generated randomization list           | Yes                    | No                    | No                      | Yes               | Yes                                    | Unclear             | Unclear, weight not reported |
| Reza, 2007   | Computer-generated random numbers               | Yes                    | Yes                   | Yes                     | Yes               | Yes                                    | Unclear             | Unclear, weight not reported |
| Santhna, 2015 | Sealed envelopes                               | Yes                    | No                    | No                      | No                | No                                     | Unclear             | Unclear, surgery duration and weight not reported |
| Schwartz, 2009 | Hospital bed                                  | No                     | No                    | No                      | Yes               | Unclear, 5 outliers removed but group not specified | Unclear             | Unclear, surgery duration not reported |
| Sen, 2009a   | Computer-generated                             | Yes                    | No                    | Yes                     | Yes               | Yes                                    | Unclear             | Yes                           |
| Sen, 2009b   | Computer-generated                             | Yes                    | No                    | Yes                     | Yes               | Yes                                    | Unclear             | Yes                           |
| Sen, 2010    | Computer-generated                             | Yes                    | No                    | Unclear                 | Yes               | Yes                                    | Unclear             | Yes                           |
| Szmuk, 2008  | Computer-generated numbers in sequentially numbered opaque envelopes | Yes                    | Yes                   | Yes                     | Yes               | Yes                                    | Unclear             | Yes                           |
| Tse, 2005    | Day of the week                                | No                     | No                    | No                      | No                | Yes                                    | Unclear             | Unclear, surgery duration not reported |
| Vaajoki, 2012 | Odd and even week                             | No                     | No                    | No                      | No                | No, 17% patients excluded during study | Unclear             | Unclear, weight not reported |
| Zhang, 2005  | Computer-generated randomization list          | Yes                    | No                    | Yes                     | Yes               | Yes                                    | Unclear             | Yes                           |
| Zhou, 2011   | Computer-generated random numbers              | Yes                    | No                    | No                      | No                | Yes                                    | Unclear             | Unclear, surgery duration and weight not reported |
| Zimmerman, 1996 | Not specified (unclear)                       | Unclear                | No                    | No                      | No                | Unclear                                | Unclear             | Unclear, surgery duration and weight not reported |

No, high risk of bias; Unclear, unclear risk of bias; Yes, low risk of bias.
Appendix C. Funnel Plot Assessing Publication Bias

Funnel plot assessing publication bias of studies reporting the effect of perioperative music on postoperative opioid requirement.