

Management of routine postoperative pain for children undergoing cardiac surgery: a Paediatric Acute Care Cardiology Collaborative Clinical Practice Guideline

Guidelines

Cite this article: Gal DB, Clyde CO, Colvin EL, Colyer J, Ferris AM, Figueroa MI, Hills BK, Lagergren SM, Mangum J, Mann JL, McKeta AS, Patel SS, Reeves JF, Richter M, Ring LM, Rosenblum JM, Tindel K, Weiner JG, Williams KG, Zabala LM, and Madsen NL (2022). Management of routine postoperative pain for children undergoing cardiac surgery: a Paediatric Acute Care Cardiology Collaborative Clinical Practice Guideline. *Cardiology in the Young*, page 1 of 13. doi: [10.1017/S1047951122003559](https://doi.org/10.1017/S1047951122003559)

Received: 9 June 2022

Revised: 18 October 2022

Accepted: 19 October 2022

Keywords:

Clinical practice guideline; postoperative pain; CHD

Author for correspondence:

Dana B. Gal, 3333 Burnett Ave., Cincinnati, OH 45229, USA. Tel: +1 513 803 4574; Fax: +1 513 803 4493.

E-mail: dana.gal@cchmc.org

Dana B. Gal¹ , Caitlin O. Clyde², Erin L. Colvin³, Jessica Colyer⁴, Anne M. Ferris⁵, Mayte I. Figueroa⁶, Brittney K. Hills¹, Sarah M. Lagergren⁷ , Jordan Mangum⁸, Jessica L. Mann⁶, Angela S. McKeta⁹ , Sonali S. Patel¹⁰, Jennifer F. Reeves¹¹, Molly Richter¹² , Lisa M. Ring⁸, Joshua M. Rosenblum¹³, Kaitlin Tindel², Jeffrey G. Weiner¹⁴, Kimberly G. Williams¹⁵, Luis M. Zabala² and Nicolas L. Madsen²

¹The Heart Institute, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA; ²UT Southwestern Medical Center, Heart Center at Children's Health, Dallas, TX, USA; ³Heart Institute, Division of Pediatric Cardiothoracic Surgery, UPMC Children's Hospital of Pittsburgh, Pittsburgh, PA, USA; ⁴Heart Center, Seattle Children's Hospital, Seattle, WA, Division of Pediatrics, University of Washington, Seattle, WA, USA; ⁵Department of Pediatrics, Columbia University Vagelos College of Physicians and Surgeons and New York-Presbyterian Morgan Stanley Children's Hospital, New York, NY, USA; ⁶Division of Pediatric Cardiology, Washington University School of Medicine, St. Louis, MO, USA; ⁷Heart Center, Children's Mercy Hospital, Kansas City, MO, USA; ⁸Children's National Heart Institute, Children's National Hospital, Washington, DC, USA; ⁹Pediatric Cardiology, Medical University of South Carolina, Charleston, SC, USA; ¹⁰Pediatric Cardiology, University of Colorado School of Medicine, Aurora, CO, USA; ¹¹Division of Pediatric Cardiac Surgery, Shawn Jenkins Children's Hospital at Medical University of South Carolina, Charleston, SC, USA; ¹²Heart Center, Seattle Children's Hospital, Seattle, WA, USA; ¹³Division of Cardiac Surgery, Children's Healthcare of Atlanta and Emory University School of Medicine, Atlanta, GA, USA; ¹⁴Thomas P. Graham Jr. Division of Pediatric Cardiology, Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN, USA and ¹⁵Division of Cardiology, Lucile Packard Children's Hospital Stanford, Palo Alto, CA, USA

Abstract

Background: Pain following surgery for cardiac disease is ubiquitous, and optimal management is important. Despite this, there is large practice variation. To address this, the Paediatric Acute Care Cardiology Collaborative undertook the effort to create this clinical practice guideline. **Methods:** A panel of experts consisting of paediatric cardiologists, advanced practice practitioners, pharmacists, a paediatric cardiothoracic surgeon, and a paediatric cardiac anaesthesiologist was convened. The literature was searched for relevant articles and Collaborative sites submitted centre-specific protocols for postoperative pain management. Using the modified Delphi technique, recommendations were generated and put through iterative Delphi rounds to achieve consensus. **Results:** 60 recommendations achieved consensus and are included in this guideline. They address guideline use, pain assessment, general considerations, preoperative considerations, intraoperative considerations, regional anaesthesia, opioids, opioid-sparing, non-opioid medications, non-pharmaceutical pain management, and discharge considerations. **Conclusions:** Postoperative pain among children following cardiac surgery is currently an area of significant practice variability despite a large body of literature and the presence of centre-specific protocols. Central to the recommendations included in this guideline is the concept that ideal pain management begins with preoperative counselling and continues through to patient discharge. Overall, the quality of evidence supporting recommendations is low. There is ongoing need for research in this area, particularly in paediatric populations.

Surgery is integral to the management of CHD, and pain is an expected component of the postoperative period. Pain exposure early in life can make children more susceptible to prolonged pain following subsequent injuries.^{1,2} Pain also impacts haemodynamics through heart rate and blood pressure changes, and adequate postoperative pain control reduces the risk of bleeding and cardiac events.³ For these reasons, dedicated pain management strategies for children and neonates are warranted. Despite the importance of pain management and the ubiquity of postoperative pain, no national or society guidelines currently exist specific to pain in the CHD population. Efforts directed towards enhanced recovery after surgery have addressed pain management, but are not comprehensive in their scope. While numerous review articles have been published on pharmacotherapy strategies, they do not provide actionable guidance for practitioners.²⁻⁹ An international survey of 15 centres found significant practice variation in

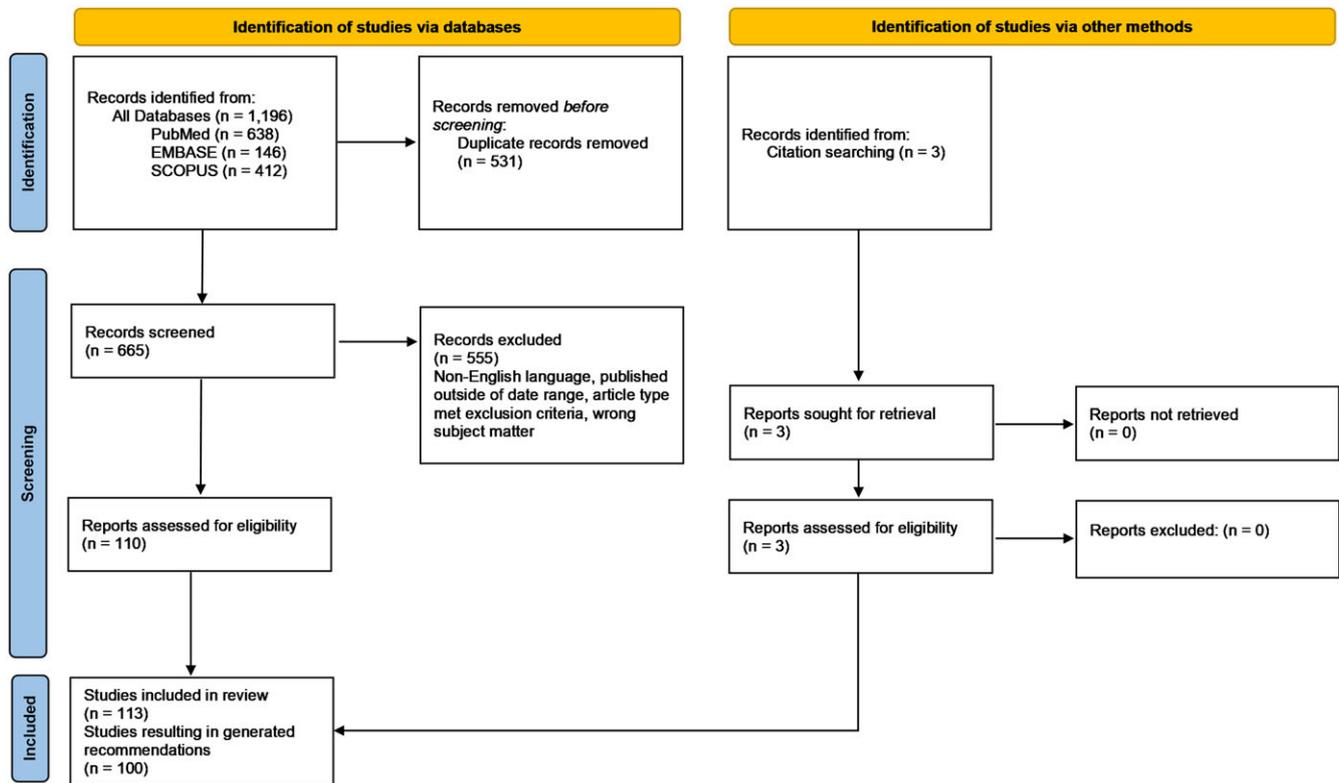


Figure 1 Results of literature search. Dates of searches: PubMed 9/18/21, EMBASE and SCOPUS 9/28/21.

choice of analgesics and dosing.¹⁰ Furthermore, a national survey of heart centres conducted by the Paediatric Acute Care Cardiology Collaborative in 2021 revealed only 6 of 34 respondents reported having an institutional written policy regarding pain management, three reported standardised practice among providers but no written policy, and the remaining 25 said there was no standardisation among providers within their institution.

Challenges to creating management guidelines for children with CHD include the current variability in practice, the relative infrequency combined with wide heterogeneity of lesions, changes in baseline physiology with different ages of childhood, and the lack of consensus regarding meaningful endpoints in study design. For pain, specifically, another challenge is presented by the inherent impact of analgesic agents on haemodynamics. In the face of these challenges, it has been suggested that collaborative learning networks such as Paediatric Acute Care Cardiology Collaborative are well suited to undertake the task of creating and disseminating management guidelines.⁸ Clinical pathways and clinical practice guidelines have been shown to reduce practice variation, facilitate incorporation of up-to-date research into clinical practice, and improve healthcare quality and outcomes.^{11–14} To confer these benefits to children undergoing cardiac surgery, we aimed to create an evidence-based clinical practice guidelines that could be utilised broadly to improve quality of pain management among children undergoing cardiac surgery and reduce practice variability.

Methods and results

Panel composition

Paediatric Acute Care Cardiology Collaborative convened a 19-member panel with expertise in paediatric cardiology and

postoperative care including paediatric cardiologists, advanced practice practitioners, pharmacists, a paediatric cardiothoracic surgeon, and a paediatric cardiac anaesthesiologist. This panel was tasked with reviewing the literature and evidence as well as existing site-specific pain management protocols and formulating recommendations.

Target audience and scope

The intent of this clinical practice guidelines is to provide guidance on management of routine postoperative pain among children undergoing cardiac surgery. It is intended to address term gestational infants, children, and adolescents undergoing cardiac surgery who are extubated within 24 hours of surgery. The intended audience is any healthcare provider who manages pain in such patients. Sedation, delirium, chronic pain, pain related to cardiac procedures but not surgery such as catheterisation or electrophysiology studies, habituation, and withdrawal are outside of the scope of this clinical practice guidelines.

Evidence review

The panel collectively determined the scope and key questions as well as inclusion criteria to guide the evidence review. The literature was searched using PubMed, SCOPUS, EMBASE, and the Agency for Healthcare Research and Quality (formerly National Guideline Clearinghouse) (Supplemental Table). Articles were excluded if they were published prior to the year 2000 or not available in English. Case reports, editorials, letters, and commentaries were also excluded. Search results and article retrieval are detailed in Figure 1. Searches were conducted on 9/18/21 and 9/28/21. References from searched articles were also considered and included if they met above criteria. Search criteria included terms

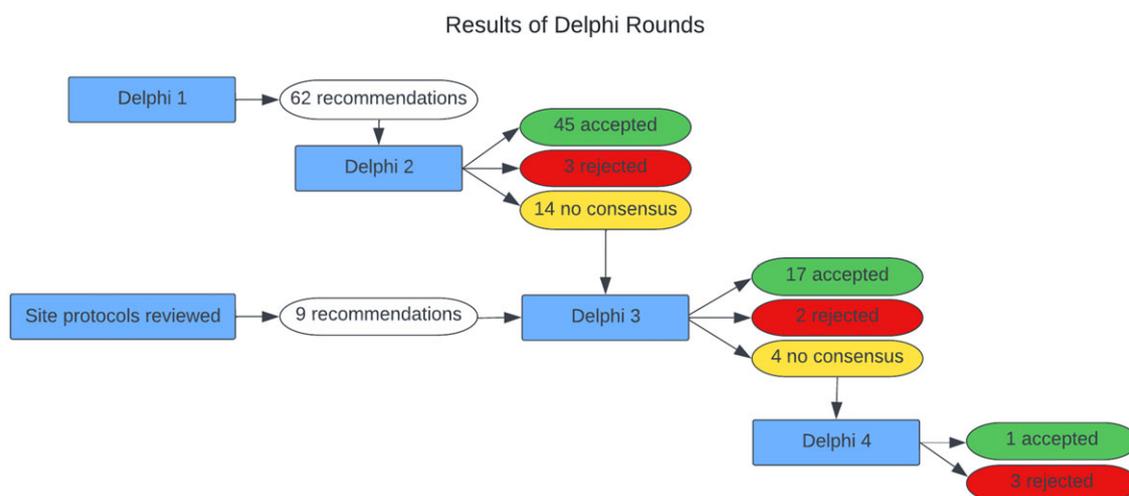


Figure 2 Results of Delphi Rounds. Three recommendations were removed after completion of the Delphi rounds as they were felt to be repetitive or non-contributory.

related to the paediatric population but adult data were included if the studies offered reliable, robust data, and strength of recommendation was downgraded if based on adult data exclusively. Articles were categorised by broad topics and each article was reviewed by two-panel members from different centres. If the two-panel members disagreed about the quality of the evidence or strength of recommendation to be generated from the article, a third-panel member from a third centre also read the article and adjudicated the decision.

Searching of the databases resulted in 1196 articles, 531 of which were duplicates. Further screening resulted in 113 eligible articles which were reviewed in full for inclusion. Articles addressing preoperative and intraoperative topics were included if they also studied impact of interventions on postoperative pain.

In addition to review of the published literature, Paediatric Acute Care Cardiology Collaborative sites were contacted and asked to share any existing site-specific protocols. These were reviewed after completion of the literature review and panel members had the opportunity to generate recommendations based on expert opinion of these protocols if not otherwise addressed in the literature.

Grading of the evidence and recommendations

The panel rated the quality of the evidence and strength of recommendation using methods described by the Grading of Recommendations Assessment, Development, and Evaluation) Working Group.^{15–17} The quality of the evidence was rated as high, moderate, low, or very low, and the strength of recommendation was rated as strong or weak. Generally, quality of the evidence assessment is based on the study design, study limitations, and criticality of outcomes. Recommendations based on high-quality evidence are unlikely to change in the future, even if new research is published. In contrast, recommendations based on low- or very low-quality evidence have a high likelihood of changing in the future based on new evidence. The strength of recommendation is largely based on how clearly the potential benefits of following the recommendation outweigh the potential risks or harms of not following the recommendation. For weak recommendations, choosing whether to follow it must be based on consideration of individual circumstances including personal preferences and values of patients and clinicians. A strong strength of

recommendation does not necessarily correlate with high quality of the evidence and vice versa. If a recommendation is supported by multiple articles with differing levels of quality of the evidence or strength of recommendation, the highest quality of the evidence and strength of recommendation are reported. For recommendations based on expert opinion, on which there is no available peer-reviewed literature, quality of the evidence is denoted as not applicable (N/A) and strength of recommendation is based on the panel consensus. Specific age ranges in recommendations reflect the populations in the supporting studies.

Guideline development process

The panel met virtually in September 2021. The scope and key definitions were agreed upon during that meeting. A modified Delphi technique was then employed.¹⁸ For Round 1 of the Delphi, panel members reviewed a subset of the identified literature (as described above) and created an initial set of potential recommendations. Of the 113 included articles (8 included adult data), 110 served as the basis for potential recommendations which were voted on in Delphi Round 2. After analysis of the results of Delphi Round 2, site-specific protocols were distributed to panel members who then had the opportunity to submit recommendations based on expert opinion addressing any topics for which peer-reviewed literature was unavailable. This was intentionally completed after evidence review to limit bias when assessing the literature. Round 3 of the Delphi was focused on these expert recommendations, as well as literature-based recommendations which had not previously achieved consensus. In total, 4 Delphi rounds were completed and 63 recommendations were accepted (Fig 2). Two recommendations were based solely on adult data. In subsequent review, 3 recommendations were felt to be repetitive or non-contributory and were removed. For all Delphi rounds subsequent to Round 1, consensus was defined as greater than two-thirds majority and was required for approval or rejection of recommendations, but the panel aimed for unanimity or near unanimity. Except in one specific case, there were no reported conflicts of interest, and all panellists voted on all recommendations. One panellist reported a conflict of interest related to review of an article they had authored and therefore recused themselves from voting on that specific recommendation.

The panel finalised the recommendations in April 2022. Once recommendations were finalised, a guideline was drafted and reviewed by all panellists for editing. Once panellists agreed upon the written guideline, it was shared with the Paediatric Acute Care Cardiology Collaborative Executive Committee, comprised of 30 members from 16 centres in North America plus two patient family representatives, for peer review. After another round of revisions among the clinical practice guidelines panel, the guideline was finalised and submitted for external peer review.

Recommendations

Clinical practice guidelines use and general information

Recommendation	Quality of the evidence	Strength of recommendation
Because of significant practice variation, difficulty in studying rare diseases, lack of consensus surrounding meaningful endpoints, and lack of consensus surrounding inclusion/exclusion criteria for trials in CHD, collaboratives such as the Paediatric Cardiac Critical Care Consortium and Paediatric Acute Care Cardiology Collaborative are well positioned to create common protocols that could then be used as the basis for trials. ¹⁹	High	Strong
Clinical judgement should be used when applying clinical practice guidelines, particularly with high-risk populations such as patients with pulmonary hypertension, systemic hypertension, residual lesions, haemodynamic compromise (arrhythmias, bleeding), and others. ³	Moderate	Strong
Multimodal analgesia should be considered as medications may act synergistically and allow for lower doses of individual drugs thereby potentially avoiding certain side effects such as constipation from opioids. ²⁰	Low	Weak
Implementation of new protocols or practices for postoperative patients should involve a multidisciplinary approach with representation of all staff involved in patient care. ²¹	Low	Strong
It is reasonable to invest in education for nurses regarding standardised approaches to pain and sedation management as adherence to such programmes may decrease overall exposure to opioid and benzodiazepine agents. ²²⁻²⁴	Moderate	Strong

One challenge to developing protocols and clinical practice guidelines in paediatric cardiology is the significant heterogeneity of disease. When addressing postoperative pain management, the wide variety of underlying disease and various surgical options challenges the ability to decrease practice variability. Collaboratives offer the opportunity to amass multi-centre data and experiences, thereby increasing understanding of a given topic, such as postoperative pain management.¹⁹ While clinical practice guidelines are helpful in providing guidance to clinicians, it is

important to recognise that they cannot address all patient populations and judgement must be used when applying them. Individual patients and high-risk populations may not benefit from application of clinical practice guidelines.³ Involvement of all stakeholders and participants in clinical care is important when developing protocols. Bedside nurses, in particular, are well positioned to improve associated processes as they frequently assess and treat pain.²¹⁻²⁴

Pain assessment

Recommendation	Quality of the evidence	Strength of recommendation
Pain should be assessed using validated, age-appropriate tools, response to intervention should be regularly assessed, and management of pain requires acknowledgement of underlying cardiac disease and selection of appropriate agents. ^{6,7}	Moderate	Strong
There is insufficient evidence to suggest superiority of any of the multiple validated scoring tools to assess pain in infants and children. However, medical units should select a specific tool and use it consistently, so providers are best able to interpret pain scores. Providers within a unit should be trained to use the same tool among themselves to promote consistency. ^{6,7,25-27}	Moderate	Strong
As novel approaches to objective pain assessment are developed, including machine learning, Analgesia Nociception Index, and Nociception Level Index, plans to study these tools in infants and children should be developed so this population may also benefit from the objective assessment of pain. Strategies should also be considered for development of less costly objective pain assessment tools. ⁵	Very low	Strong
Children's individual coping mechanisms and cultural backgrounds may influence pain perception and reporting therefore providers may consider these factors while managing pain. ^{6,28}	Very low	Strong
It is possible underlying genetic variants such as <i>COMT</i> are responsible for differential propensity for pain among individuals. Pain management should be adjusted for individual experience of pain and reaction to interventions including undertreatment and overtreatment. ⁵	Moderate	Strong
Parents/caregivers' assessments of their child's pain should be taken into consideration, most importantly for children who are developmentally unable to express their own pain level. ²⁹	Low	Strong

Undertreatment or reluctance to treat pain among children with cardiac disease is likely common and often related to concerns that analgesics may have unfavourable haemodynamic effects. However, undertreatment may negatively result in increased stress response which may have negative long- and short-term consequences.^{6,7} A variety of tools have been developed to assess pain in infants and children, utilising both subjective and objective information. There is insufficient evidence to suggest that any of these tools is superior, however consistent use and unit-wide acceptance of a given tool improves consistency of pain assessment and subsequent treatment.^{6,7,25–27} Pain assessment among infants and children, particularly those who are non-verbal, relies on a combination of factors including objective data such as vital sign changes and subjective information such as patient-reported symptoms or family assessment.²⁹ There are currently efforts to develop additional tools to objectively measure pain; however, these efforts have been primarily limited to adult populations.⁵ Children would benefit from such tools, especially non-verbal children or children who are developmentally unable to express their pain. It is important to recognise that social and cultural factors may influence the experience of pain and treatment should be adjusted based on individual response.^{5,6,28} Though we did not identify literature examining the impact of implicit bias or racism on the treatment of pain among children undergoing congenital heart surgery, this is a known problem in medicine^{30–32} and pain should never be managed differentially based solely on a patient's race or ethnicity.

General principles

Recommendation	Quality of the evidence	Strength of recommendation
Thoracotomies may be more painful than sternotomies and may require additional consideration for analgesia. ³³	Very low	Weak
While chest tubes remain in place, patients may require higher levels of analgesia so it is reasonable to continue use of scheduled analgesics.	N/A	Strong
As patients progress postoperatively, is it appropriate to reduce the frequency or amount of scheduled analgesics and transition analgesia to be used as needed. It is reasonable to continue medications with the lowest side effect profiles as scheduled for the longest period of time and to first transition those with higher side effect profiles, such as opioids, to as needed.	N/A	Strong
Additional medications should be used to mitigate known, common side effects of analgesics such as bowel regimen medications for patients taking opiates. It is reasonable to consider H2 blockers or proton-pump inhibitors for patients taking NSAIDs, particularly if enteral intake is limited or poor.	N/A	Strong
To reduce reliance on individual bedside providers' perception of pain, concrete parameters, such as	N/A	Strong

ranges of validated pain scores, should be used to determine when to administer medications which are prescribed to be given as needed.		
Pain inconsistent in location or intensity with surgery or postoperative time course, or associated with vital sign changes, respiratory distress, or fever should prompt evaluation and consideration of new diagnoses such as wound dehiscence, sepsis, tight dressings, ileus, and more.	N/A	Strong
Discrepancy between self or family-reported pain and provider observations of pain should be addressed with further evaluation.	N/A	Strong
Painful procedures in the postoperative period should be addressed with additional analgesia and non-pharmaceutical interventions. It is reasonable to consider use of anxiolytics for painful procedures.	N/A	Strong

Pain in the postoperative period should be considered in the context of the individual patient and their risk factors for ongoing pain. Specifically, the incision type and presence of chest tubes may predispose patients to ongoing pain, requiring additional analgesia.³³ Additionally, timing within a hospitalisation should be taken into account given the temporally associated reduction of pain as patients' progress from their surgery. As patients' pain improves and their need for analgesia diminishes, it is most appropriate to first discontinue or reduce frequency of administration of medications with the highest risk for side effects and continue those medications which have fewer side effects. It is appropriate to utilise additional medications to treat known and common side effects of commonly used analgesics. In particular, a bowel regimen should be implemented for patients taking opioid medications as opioids are associated with constipation.

Pain that does not follow the anticipated course over time, or that is inconsistent in type or location, or is associated with other signs and symptoms such as vital sign changes or respiratory distress is cause for rapid and thorough evaluation for other causes. Similarly, additional evaluation is needed when patient or family reports of pain are discrepant from provider's assessment of pain.

Preoperative considerations

Recommendation	Quality of the evidence	Strength of recommendation
Standardised education with preoperative counselling for parents/patients on postoperative pain management, including realistic expectations and measurable goals for pain management, may improve alignment of the care team and the family and may improve nurse/parent collaboration. ^{29,34}	Very low	Strong
Provide developmentally appropriate toys and video games to patients in the preoperative setting to help reduce stress and anxiety. ³⁵	Low	Strong

Families and providers often have discrepant expectations for postoperative pain level and management which can challenge the therapeutic relationship needed to assist children in their recovery. Preoperative counselling should therefore address realistic expectations for postoperative pain and aim to establish understanding with families regarding what their child may experience and how it will be addressed.^{29,34} Discussions related to goals of pain management should emphasise functionality rather than complete elimination of pain. Additionally, management of stress and anxiety in the preoperative setting has been associated with reduced postoperative pain.³⁵

Intraoperative considerations

Recommendation	Quality of the evidence	Strength of recommendation
Intraoperative multimodal pain management may be used to reduce intraoperative opioids need. ⁴	Very low	Weak

It has been suggested that multimodal pain management during surgery, including use of acetaminophen, local anaesthesia and postoperative nausea and vomiting treatments, may reduce the need for intraoperative opioids and improve postoperative pain outcomes.⁴ There have been a number of studies examining the use of intraoperative methadone and its impact on postoperative pain but based on the current evidence, this panel does not currently have a recommendation related to its use.^{36–38}

Regional anaesthesia

Recommendation	Quality of the evidence	Strength of recommendation
Transversus thoracis muscle plane block should be used in children 2–12 years old undergoing sternotomy. ^{39–41}	High	Strong
Paravertebral block may be considered for patients undergoing cardiac surgery but there is insufficient evidence to recommend it uniformly. ^{42,43}	Moderate	Weak
It is reasonable to consider continuous infusion catheters such as erector spinae plane blocks or use of parasternal intercostal blocks but there is insufficient evidence to recommend it uniformly. Lidocaine may be used safely in such infusions, even among patients who require cardiopulmonary bypass. Lidocaine, bupivacaine, and ropivacaine have been studied but there is insufficient evidence to support any specific agent. ^{44–51}	High	Weak
Caudal analgesia is a safe intervention for children undergoing cardiac surgery in that adverse events or effects are rare, however there is conflicting evidence regarding whether it improves postoperative pain outcomes. Caudal	Moderate	Weak

analgesia may be considered as the evidence suggests minimal harm but further research is needed to demonstrate benefits. ^{52–56}		
It is reasonable to use spinal anaesthesia as it may decrease postoperative opiate requirement in uncomplicated cardiac surgery. ⁵⁷	Moderate	Weak
Continuous incision infusions of local anaesthetic should be considered to enhance analgesia after congenital heart surgery. ^{54,58,59}	Moderate	Weak

The use of regional anaesthesia has gained interest and acceptance as a means of reducing intraoperative and postoperative opioid requirements. Currently, centre-specific considerations are required for use of regional anaesthesia-based experience of anaesthesiologists and availability of providers to manage such modalities outside of the operating room such as consultative pain services. Multiple studies have examined specific types of regional anaesthesia in the context of paediatric congenital heart surgery and it has widely been found to be safe. Specifically for transversus thoracis plane blocks, studies have shown improved pain scores, decreased intraoperative and postoperative opioid requirements, shorter time to extubation and shorter ICU length of stay compared to patients not receiving nerve blocks.^{39–41} Similar endpoints have been used in studies of paravertebral block and have shown promise though the body of evidence is insufficient currently to uniformly recommend paravertebral block.^{42,43} Additionally, erector spinae plane blocks and parasternal intercostal blocks using continuous infusions shown to be safe but there is inconclusive evidence to suggest uniform adoption of such approaches.^{45–51} No specific anaesthetic agent has shown superiority in these studies. Caudal analgesia has been shown to be safe with minimal harm. However, there is controversy regarding its impact on postoperative pain as studies comparing use of caudal analgesia to children not receiving regional anaesthesia have not consistently demonstrated improved outcomes; therefore it is reasonable to consider caudal analgesia but as it does not have clear benefits, it is not uniformly recommended.^{52–56} Spinal anaesthesia may improve pain scores and reduce postoperative opioid requirement however only one study with a small sample size of 20 patients has demonstrated this.⁵⁷ While many forms of regional anaesthesia have conflicting evidence, continuous infusion of local anaesthetic at incision sites has been shown to reduce postoperative pain scores and opioid requirements and should be considered, though some evidence to support this comes from adult studies.^{54,58,59} Further research is needed to explore the efficacy of these various regional anaesthetic techniques in order to identify which patients might benefit from regional anaesthesia.

Opioids

Recommendation	Quality of the evidence	Strength of recommendation
For children receiving weight-based dosing, morphine doses should not exceed 0.2 mg/kg as doses >0.2 mg/kg are not incrementally effective in increasing effective analgesia. ⁶⁰	Moderate	Strong
Patients with preoperative cyanosis due to CHD do not have differing	Moderate	Strong

opioid sensitivity or pain scores compared to acyanotic patients and should be prescribed normal doses of opioids for analgesia. ⁶¹		
Patient-controlled analgesia should be considered for developmentally appropriate patients who require IV opioid administration as they may improve patient satisfaction with pain management while reducing overall opioid exposure. There is insufficient evidence to recommend for or against continuous infusion with patient-controlled analgesia. ^{62,63}	Moderate	Weak
Children with Trisomy 21 and CHD show no difference in morphine metabolism compared to those without Down syndrome and therefore should receive the same approach to opioid-based analgesia. ⁶⁴⁻⁶⁷	Moderate	Strong
Patients with CHD do not metabolise morphine differently than the general population and should therefore receive the same doses as individuals without CHD. ⁶⁸	Low	Weak
It is reasonable to consider limiting morphine use in patients with renal dysfunction due to risk of accumulation of toxic metabolites. ⁶⁸	Low	Weak

Despite side effects and risk for habituation, opioids remain a mainstay of postoperative pain management and offer effective analgesia.⁶⁹ There are some specific considerations regarding opioid use among children undergoing cardiothoracic surgery. In animal studies, chronic hypoxaemia has been associated with increased sensitivity to opioid medications. Studies among humans with obstructive sleep apnoea and chronic hypoxaemia have shown similar results prompting consideration of whether children with cyanotic CHD may also have variable sensitivity to opioids. When studied, however, children with cyanotic lesions were not found to have differing sensitivity to opioids and therefore should be prescribed typical doses.⁶¹

Another specific consideration relates to children with Trisomy 21 and CHD. Previous reports have suggested possible altered pharmacokinetics or pharmacodynamics among children with Trisomy 21; however, multiple studies have found no difference among children with and without Trisomy 21, and these children should therefore receive opioids at typical doses.⁶⁴⁻⁶⁷

There have been limited published reports related to decreased opioid clearance among individuals with decreased systemic blood flow prompting consideration for need to dose opioids differentially among individuals with CHD.^{68,70} Despite these reports, modelling of pharmacokinetics has shown that children with CHD do not metabolise morphine significantly differently from children without CHD and should therefore be treated with conventional doses.⁶⁸ Patients with renal dysfunction, a common issue following cardiac surgery, are at risk for toxic accumulation of metabolites of morphine.⁶⁸

Among certain populations, patient-controlled analgesias have been shown to have increased effectiveness of analgesia compared to provider-initiated intermittent boluses.⁶⁹ Limited studies among children undergoing cardiac surgery have shown similar findings.^{62,63} Because of the potential for better analgesia, higher satisfaction, and overall reduction in opioid exposure, patient-

controlled analgesias should be considered for children who require intravenous opioids and are developmentally appropriate.

Opioid-sparing

Recommendation	Quality of the evidence	Strength of recommendation
Opioid exposure should be minimised as reduced opioid exposure may enhance postoperative recovery and facilitate "fast-track" recovery. ⁷¹	High	Strong
Standard pain management protocols should be used as they are safe and effective and can facilitate an opioid-sparing approach to postop pain management. ⁷¹	High	Strong
Multimodal pain management including consideration of regional anaesthesia, acetaminophen, and NSAIDs should be used to reduce need for opioid medications. ⁷¹	High	Strong
For patients with anticipated extubation within 3 hours of ICU admission, continuous infusions of opioids and/or benzodiazepines should be avoided and instead scheduled acetaminophen and IV ketorolac may be used. ⁷²	Moderate	Strong

Due to increased awareness of risks associated with opioid medications including habituation, withdrawal, and side effects including constipation and respiratory depression, as well as evidence that opioid-sparing approaches may facilitate postoperative recovery, there is significant interest in developing protocols and approaches to postoperative pain management which minimise opioid exposure.^{69,71} Multimodal pain management has been utilised successfully to reduce opioid exposure postoperatively.⁴ Additionally, increased awareness of the likely trajectory of patients in the immediate postoperative period, particularly those who are likely to tolerate extubation soon after arrival in the ICU, has facilitated opioid-sparing approaches.⁷¹ In a randomised controlled trial of children recovering from cardiothoracic surgery, there was no difference in pain control among those who received continuous versus intermittent opioids but use of continuous infusions resulted higher total doses of opioids and longer length of stay.⁷² Increased examination of whether continuous infusions are needed for individual patients may result in decreased reflexive use of them and improved patient outcomes.

Non-opioid medications

Recommendation	Quality of the evidence	Strength of recommendation
Non-steroidal anti-inflammatory drugs (NSAIDs) should be considered in patients >28 days old, including those with complex CHD, as NSAIDs may reduce overall opioid exposure and may not be associated with significant adverse effects such as bleeding or acute kidney injury in	Moderate	Strong

patients without additional risk factors. ⁷²⁻⁷⁸		
NSAIDs should routinely be utilised for pain management in patients >6 months as this may reduce opioid exposure and may not be associated with significant adverse effects such as bleeding or acute kidney injury in patients without additional risk factors. ^{73,74,77-81}	Moderate	Strong
Acetaminophen should be used early in the postoperative period to facilitate pain management and reduce overall opioid exposure. There is no clear clinical advantage to use of IV acetaminophen over enteral administration though there is increased cost to IV administration. ⁸²⁻⁸⁵	Moderate	Strong
Acetaminophen may be used but with caution in patients undergoing surgery for CHD with impaired hepatic metabolism given reduced clearance. ⁸⁶	Moderate	Weak
Prospective studies and randomised controlled trials are needed to improve understanding of the efficacy and adverse effects related to acetaminophen and NSAIDs in neonatal and paediatric cardiac populations. Studies should include consideration of renal and/or hepatic function and focus on paediatric populations, ideally with the full age spectrum and with all types of CHD represented. ^{74,81} Multi-centre studies should also address any associated reduction in opiate use. ⁸⁷	High	Strong
While NSAIDs may not be associated with clinical bleeding in patients without other risk factors, they may impact platelet function and research is needed to better understand the impact of NSAID-mediated platelet inhibition in children. ^{73,75,88}	Moderate	Weak
The effect of magnesium on postoperative pain in infants, children and neonates should be studied as it has been shown to have positive effect among adults with minimal adverse effects. It is reasonable to ensure serum magnesium levels are within normal range in the postoperative period. ⁵	Very low	Weak
Research is needed regarding safety and efficacy of gabapentinoids in infants and children. Caution will be needed when studying these medications among patients with heart failure. ⁵	Very low	Strong
It is reasonable to consider use of muscle relaxants such as cyclobenzaprine, diazepam, and methocarbamol as adjunctive options for pain management, particularly in children older than 12 years of age. Research is needed regarding the utility of muscle relaxants in postoperative patients.	N/A	Weak

Multimodal pain management relies largely, though not exclusively, upon NSAIDs and acetaminophen. While NSAIDs are used in neonates and infants for indications such as closure of the patent ductus arteriosus, retinopathy of prematurity, and prevention of intraventricular haemorrhage, there has been reluctance to use NSAIDs as a primary means of analgesia among infants less than 6 months of age.^{89,90} Additionally, there is significant variation in practice related to NSAID and acetaminophen or paracetamol use in children. A systematic review of guidelines for anti-pyresis among children identified 55 guidelines addressing use of ibuprofen and 69 addressing use of paracetamol. There was minimal agreement between guidelines regarding appropriate population, dosing, frequency, duration of treatment, or conditions in which to avoid or use caution prior to initiating the drug.⁹¹ Additionally, for many of the age-based recommendations against use of NSAIDs or acetaminophen in young children, there was either no published evidence or low quality of evidence to support those recommendations.⁹¹ More recent publications have examined use of NSAIDs in younger children and found them to be safe.⁹⁰

Multiple studies have examined use of ibuprofen or ketorolac in postoperative infants and children, some as young as 28 days. In addition to focusing on achieving analgesia, these studies have largely used creatinine or blood urea nitrogen as endpoints.⁷⁴⁻⁷⁶ These are known to be imperfect markers of true renal function and, while they were found to be increased among patients receiving NSAIDs, the clinical implication of that rise is unclear, particularly as the values did not always fall outside of the range of normal. Acute kidney injury following cardiac surgery is common but is multifactorial in aetiology and not directly related to nephrotoxin exposure, including ibuprofen and ketorolac.⁹² Additionally, studies examining the risk of bleeding and changes to platelet function while receiving NSAIDs have found platelet function is altered but there is no increase in clinically significant bleeding.^{73-76,79,88} It is unclear what the implication of changed platelet function is, and this warrants further research, particularly considering the additional risk factors in this population including cardiopulmonary bypass, presence of chest tubes, and surgical wounds.

In addition to NSAIDs and acetaminophen, there have been a few studies examining use of other non-opioid analgesics among adults and there have been suggestions to study these among children. Perioperative administration of magnesium has been shown to decrease postoperative pain and opioid consumption among adults.⁵ While there are no data, to our knowledge, among children, it is a worthwhile consideration given the relative ease of monitoring magnesium levels (something that is often already occurring in postoperative patients) and the low risk of side effects when administered enterally or slowly if parenterally. Additionally, gabapentinoids have been identified as potentially useful in children recovering from cardiac surgery. Pregabalin, in particular, appears to be effective for acute pain and has been studied among adults recovering from cardiac surgery.⁵ We could not identify any data related to spasmolytic medications but in practice, these are commonly utilised after CHD surgery, particularly in adolescents and young adults. Further research is warranted to explore these, and other, non-opioid medications for treatment of pain in children.

Non-pharmaceutical pain management

Recommendation	Quality of the evidence	Strength of recommendation
Non-pharmacologic methods of pain management may be areas of weakness for clinicians and pain management protocols should incorporate such methods as a component of developmental care of infants and children undergoing cardiac surgery as this developmental care may have long-term impact on neurodevelopmental outcomes. ⁹³	Very low	Strong
Music, music videos, and music therapy, when available, should be used in the postoperative period to reduce pain, anxiety and distress. ⁹³⁻⁹⁷	Low	Strong
Massage therapy should be used in the postoperative period to reduce anxiety and distress and improve patient and family satisfaction. There is insufficient evidence regarding impact of massage therapy on opioid use but it has been shown to reduce benzodiazepine requirements. ⁹⁸⁻¹⁰⁰	Moderate	Strong
Physical therapy should be utilised for patients after cardiac surgery as it is associated with decreased overall pain. ¹⁰¹	Very low	Strong
Children should be offered age and developmentally appropriate toys and educational materials in the postoperative period once they are awake and alert. ¹⁰²	Very low	Strong
When available, Paediatric Integrative Medicine services, including complementary therapies such as Reiki, massage therapy, and acupuncture, should be offered to children in the postoperative period. ¹⁰³	Very low	Strong
Skin-to-skin care for infants should be considered when feasible in the postoperative period. ¹⁰⁴	Low	Strong
The physical environment of postoperative patients should be optimised with consideration of sound and music as well as lighting and having caregivers at bedside. ⁶	Very low	Strong

Non-pharmacologic approaches to analgesia are widely accepted as an important component of postoperative care, but may be underutilised among children undergoing and recovering from cardiac surgery.^{69,93} Reasons for underutilisation include lack of resources and inadequate awareness of benefits but services such as music therapy, massage therapy, acupuncture, and others have been shown to improve postoperative pain scores in this population.^{93-95,97-100,103} Additionally, not all non-pharmacologic approaches are resource intensive – indeed, skin-to-skin contact has been shown to improve comfort among infants undergoing cardiac surgery and increase physiologic stability.¹⁰⁴ Other interventions as simple as providing developmentally appropriate toys and optimising environmental factors such as lighting and noise

can also improve postoperative outcomes related to pain.^{6,102} Other non-pharmacologic analgesia modalities have been shown to be effective among adults undergoing thoracic surgery, chiefly transcutaneous electrical nerve stimulation.⁶⁹ Transcutaneous electrical nerve stimulation has also been shown to be effective in reducing procedural pain for children.¹⁰⁵ Efforts should be made to determine if transcutaneous electrical nerve stimulation is effective among children undergoing cardiac surgery, particularly considering the lack of side effects and ease of use. Importantly, there is minimal risk associated with these non-pharmacologic modalities.

Discharge considerations

Recommendation	Quality of the evidence	Strength of recommendation
Acetaminophen and NSAIDs should be strongly considered as first-line pain management agents at time of discharge. ⁷¹	Low	Strong
It is reasonable to limit the number of opiate doses prescribed at discharge to 5–10. ^{106,107}	Moderate	Weak
Some diagnoses, such as atrial septal defects, may not require prescription of opiates at time of discharge. ¹⁰⁷	Moderate	Weak
Due to significant variation related to hospital/practice and not patient-specific factors demonstrated among adult patients, research is needed to better understand best practices surrounding opioid prescription at time of discharge for children after cardiac surgery. ¹⁰⁸	Low	Weak
Exposure to and awareness of guidelines can decrease number of opioid doses prescribed at time of discharge and help standardise prescribing practices. ¹⁰⁶	Low	Weak

Children are likely to need ongoing analgesia after discharge home following cardiac surgery. Discharge teaching may even include consideration that pain can transiently worsen as children become more mobile in their home environments. Acetaminophen and NSAIDs should be used as the first-line medications for treatment of pain in the home environment – children still requiring frequent administration of opioids may not yet be ready for discharge.⁷¹ To that end, Monitto et al studied the effectiveness of analgesia following discharge for a variety of paediatric surgeries including cardiac surgery and found that despite low levels of use of opioids at home, analgesia was largely good or excellent at 1–2 days following discharge and 10–14 days following discharge.¹⁰⁷ Because so few patients require frequent opioid administration at home and the majority of prescribed doses are unused, it is reasonable to limit the number of prescribed doses and some patients may not require opioids at all.^{106,107} In this study, atrial septal defects made up the majority of included patients making it easiest to apply their findings clinically to that population. However, it should be noted that much of the postoperative pain experienced by patients is related to incision sites (sternotomy, thoracotomy, chest tubes when in place) rather than the heart itself and therefore the specific form of CHD likely has little impact on

postoperative pain and rather the extent of the incision, first time versus redo incision, incision healing, and features such as delayed sternal closure play heavily into the experience of pain.

Studies of opioid prescription at discharge among adults undergoing cardiac surgery have shown that the greatest predictor of amount of opioid prescribed is hospital, not patient or surgery-specific factors.¹⁰⁸ There remains a need for research to better understand best practices surrounding opioid prescription at time of discharge for children undergoing cardiac surgery, particularly given the risks of undertreating pain in the home environment relative to the risks of overuse or misuse of opioid medications. Studies targeting opioid prescription variability for postoperative children have shown that institutional guidelines available to prescribing physicians can reduce variability and decrease overall opioid prescription at time of discharge, though these results have not been reproduced among children undergoing cardiac surgery.¹⁰⁶

Limitations

In aiming to address postoperative pain management, this guideline does not address sedation or delirium. It also does not address habituation or withdrawal for patients who may require prolonged infusions of narcotics. Agents such as dexmedetomidine, propofol, ketamine, and others often play an important role in postoperative pain management in the ICU setting but were not addressed in this guideline due to the lack of literature providing data on their use in extubated children. Additionally, because the scope of this work was limited to patients who extubate early, there are no intensive care providers on our panel. The panel was intentionally comprised of individuals from a large variety of centres geographically and with a variety of programme styles; however, recruitment did occur via Paediatric Acute Care Cardiology Collaborative which may introduce some bias. Panellists were not required to have recently published articles related to pain management and therefore may not be considered the most expert; however, this also may have limited bias in that no panellists were reviewing their own research.

Conclusions

Postoperative pain among children following cardiac surgery is currently an area of significant practice variability despite a large body of literature and the presence of centre-specific protocols. After a review of the evidence and these protocols, a panel of experts convened by Paediatric Acute Care Cardiology Collaborative created these recommendations, which were subsequently approved by the Paediatric Acute Care Cardiology Collaborative executive committee. Central to the recommendations is the concept that ideal pain management begins with pre-operative counselling and continues through to patient discharge. While general principles may be applied, pain management must be tailored to individual patient experience and response to intervention. Standardised approaches to assessing and addressing pain are needed. Opioid medications remain a mainstay of pain management but multimodal approaches, non-opioid medications, and non-pharmacologic interventions are effective in minimising opioid exposure and improving postoperative pain measures.

The panel identified numerous gaps in the available evidence and found that the quality of existing evidence was overall low – only 9 of the 63 recommendations have a high quality of the evidence and many have a low or very low quality of the evidence.

There is ongoing need for research, particularly in children, related to objective methods of pain assessment, the utility of regional anaesthesia, intraoperative pain management strategies, and non-opioid analgesics. The aim of this clinical practice guidelines is to address this variability and support providers in their development of more standard approaches to postoperative pain management.

Supplementary material. To view supplementary material for this article, please visit <https://doi.org/10.1017/S1047951122003559>

Acknowledgements. We thank and appreciate the support of Paediatric Acute Care Cardiology Collaborative staff in assisting with logistical aspects of creating this work.

Financial support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of interest. None.

References

- Schwaller F, Fitzgerald M. The consequences of pain in early life: injury-induced plasticity in developing pain pathways. *Eur J Neurosci* 2014; 39: 344–352.
- Pollak U, Serraf A. Pediatric cardiac surgery and pain management: after 40 years in the desert, have we reached the promised land? *World J Pediatr Congenit Heart Surg* 2018; 9: 315–325.
- Fuller S, Kumar SR, Roy N, et al. The American Association for Thoracic Surgery Congenital Cardiac Surgery Working Group 2021 consensus document on a comprehensive perioperative approach to enhanced recovery after pediatric cardiac surgery. *J Thorac Cardiovasc Surg* 2021; 162: 931–954.
- Roy N, Parra MF, Brown ML, et al. Initial experience introducing an enhanced recovery program in congenital cardiac surgery. *J Thorac Cardiovasc Surg* 2020; 160: 1313–1321.
- Pollak U, Bronicki RA, Achuff BJ, Checchia PA. Postoperative pain management in pediatric patients undergoing cardiac surgery: where are we heading? *J Intensive Care Med* 2019; 885066619871432.
- Diaz LK. Anesthesia and postoperative analgesia in pediatric patients undergoing cardiac surgery. *Pediatr Drugs* 2006; 8: 223–233.
- Hehir DA, Easley RB, Byrnes J. Noncardiac challenges in the cardiac ICU: feeding, growth and gastrointestinal complications, anticoagulation, and analgesia. *World J Pediatr Congenit Heart Surg* 2016; 7: 199–209.
- Thompson EJ, Foote HP, King CE, et al. A systematic review of the evidence supporting post-operative medication use in congenital heart disease. *Cardiol Young* 2021; 31: 707–733.
- Wolf AR, Jackman L. Analgesia and sedation after pediatric cardiac surgery. *Paediatr Anaesth* 2011; 21: 567–576.
- Zeilmaker-Roest GA, Wildschut ED, Van Dijk M, et al. An international survey of management of pain and sedation after paediatric cardiac surgery. *BMJ Paediatr Open* 2017; 1: 1.
- Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E (eds). *Clinical Practice Guidelines We Can Trust*. Washington (DC), 2011.
- Rotter T, Kinsman L, James E, et al. Clinical pathways: effects on professional practice, patient outcomes, length of stay and hospital costs. *Cochrane Database Syst Rev* 2010CD006632.
- Plishka CT, Rotter T, Penz ED, et al. Effects of clinical pathways for COPD on patient, professional, and systems outcomes: a systematic review. *Chest* 2019; 156: 864–877.
- Neame MT, Chacko J, Surace AE, Sinha IP, Hawcutt DB. A systematic review of the effects of implementing clinical pathways supported by health information technologies. *J Am Med Inform Assoc* 2019; 26: 356–363.
- Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ* 2008; 336: 1049–1051.
- Guyatt GH, Oxman AD, Kunz R, et al. What is "quality of evidence" and why is it important to clinicians? *BMJ* 2008; 336: 995–998.

17. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008; 336: 924–926.
18. Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs* 2000; 32: 1008–1015.
19. Thompson EJ, Foote HP, King CE, et al. A systematic review of the evidence supporting post-operative medication use in congenital heart disease. *Cardiol Young* 2021; 31: 707–733.
20. Bignami E, Castella A, Pota V, et al. Perioperative pain management in cardiac surgery: a systematic review. *Minerva Anesthesiol* 2018; 84: 488–503.
21. Bastero P, DiNardo JA, Pratap JN, Schwartz JM, Sivarajan VB. Early perioperative management after pediatric cardiac surgery: review at PCICS 2014. *World J Pediatr Congenit Heart Surg* 2015; 6: 565–574.
22. Van Valen R, Van Vuuren H, Van Domburg RT, Van Der Woerd D, Hofland J, Bogers AJJC. Pain management after cardiac surgery: experience with a nurse-driven pain protocol. *Eur J Cardiovasc Nur* 2012; 11: 62–69.
23. Lincoln PA, Whelan K, Hartwell LP, et al. Nurse-implemented goal-directed strategy to improve pain and sedation management in a pediatric cardiac ICU. *Pediatr Crit Care Med* 2020; 21: 1064–1070.
24. Magner C, Valkenburg AJ, Doherty D, et al. The impact of introducing nurse-led analgesia and sedation guidelines in ventilated infants following cardiac surgery. *Intens Crit Care Nur* 2020; 60: 102879.
25. Franck LS, Ridout D, Howard R, Peters J, Honour JW. A comparison of pain measures in newborn infants after cardiac surgery. *Pain* 2011; 152: 1758–1765.
26. Cury MR, Martinez FE, Carlotti AP. Pain assessment in neonates and infants in the post-operative period following cardiac surgery. *Postgrad Med J* 2013; 89: 63–67.
27. Bai J, Hsu L, Tang Y, Van Dijk M. Validation of the COMFORT Behavior Scale and the FLACC Scale for pain assessment in Chinese children after cardiac surgery. *Pain Manag Nurs* 2012; 13: 18–26.
28. Bai J, Hsu L. Pain status and sedation level in Chinese children after cardiac surgery: an observational study. *J Clin Nurs* 2013; 22: 137–147.
29. Huth MM, Broome ME, Mussatto KA, Morgan SW. A study of the effectiveness of a pain management education booklet for parents of children having cardiac surgery. *Pain Manag Nurs* 2003; 4: 31–39.
30. Sabin JA, Greenwald AG. The influence of implicit bias on treatment recommendations for 4 common pediatric conditions: pain, urinary tract infection, attention deficit hyperactivity disorder, and asthma. *Am J Public Health* 2012; 102: 988–995.
31. Strand NH, Mariano ER, Goree JH, et al. Racism in pain medicine: we can and should do more. *Mayo Clin Proc* 2021; 96: 1394–1400.
32. Fanta M, Ladzekpo D, Unaka N. Racism and pediatric health outcomes. *Curr Probl Pediatr Adolesc Health Care* 2021; 51: 101087.
33. Karuppiah N, Pehora C, Haller C, Taylor K. Surgical closure of atrial septal defects in young children - a review of anesthesia care in sternotomy and thoracotomy approaches. *J Cardiothorac Vasc Anesth* 2021; 35: 123–127.
34. Harvey KA, Kovalesky A. Post-operative pain and comfort in children after heart surgery: a comparison of nurses and families pre-operative expectations. *J Pediatr Nurs* 2018; 43: 9–15.
35. Kumar A, Das S, Chauhan S, Kiran U, Satapathy S. Perioperative anxiety and stress in children undergoing congenital cardiac surgery and their parents: effect of brief intervention—a randomized control trial. *J Cardiothorac Vasc Anesth* 2019; 33: 1244–1250.
36. Iguidbashian JP, Chang PH, Iguidbashian J, Lines J, Maxwell BG. Enhanced recovery and early extubation after pediatric cardiac surgery using single-dose intravenous methadone. *Ann Card Anaesth* 2020; 23: 70–74.
37. Barnett AM, Machovec KA, Ames WA, et al. The effect of intraoperative methadone during pediatric cardiac surgery on postoperative opioid requirements. *Paediatr Anaesth* 2020; 30: 773–779.
38. Robinson JD, Caruso TJ, Wu M, Kleiman ZI, Kwiatkowski DM. Intraoperative methadone is associated with decreased perioperative opioid use without adverse events: a case-matched cohort study. *J Cardiothorac Vasc Anesth* 2020; 34: 335–341.
39. Abdelbaser II, Mageed NA. Analgesic efficacy of ultrasound guided bilateral transversus thoracis muscle plane block in pediatric cardiac surgery: a randomized, double-blind, controlled study. *J Clin Anesth* 2020; 67: 110002.
40. Zhang Y, Chen S, Gong H, Zhan B. Efficacy of bilateral transversus thoracis muscle plane block in pediatric patients undergoing open cardiac surgery. *J Cardiothorac Vasc Anesth* 2020; 34: 2430–2434.
41. Cakmak M, Isik O. Transversus thoracic muscle plane block for analgesia after pediatric cardiac surgery. *J Cardiothorac Vasc Anesth* 2021; 35: 130–136.
42. Türköz A, Balcı ST, Can Güner M, et al. Anesthesia management with single injection paravertebral block for aorta coarctation in infant. *Paediatr Anaesth* 2013; 23: 1078–1083.
43. Sahajanandan R, Varsha AV, Kumar DS, et al. Efficacy of paravertebral block in "Fast-tracking" pediatric cardiac surgery - experiences from a tertiary care center. *Ann Card Anaesth* 2021; 24: 24–29.
44. Otu C, Vo V, Staffa SJ, et al. The use of regional catheters in children undergoing repair of aortic coarctation. *J Cardiothorac Vasc Anesth* 2021; 35: 3694–3699.
45. Macaire P, Ho N, Nguyen T, et al. Ultrasound-guided continuous thoracic erector spinae plane block within an enhanced recovery program is associated with decreased opioid consumption and improved patient postoperative rehabilitation after open cardiac surgery - a patient-matched, controlled before-and-after study. *J Cardiothorac Vasc Anesth* 2019; 33: 1659–1667.
46. Roy N, Brown ML, Parra MF, et al. Bilateral erector spinae blocks decrease perioperative opioid use after pediatric cardiac surgery. *J Cardiothorac Vasc Anesth* 2021; 35: 2082–2087.
47. Caruso TJ, Lin C, O'Connell C, et al. Systemic absorption of lidocaine from continuous erector spinae plane catheters after congenital cardiac surgery: a retrospective study. *J Cardiothorac Vasc Anesth* 2020; 34: 2986–2993.
48. Kaushal B, Chauhan S, Magoon R, et al. Efficacy of bilateral erector spinae plane block in management of acute postoperative surgical pain after pediatric cardiac surgeries through a midline sternotomy. *J Cardiothorac Vasc Anesth* 2020; 34: 981–986.
49. Chaudhary V, Chauhan S, Choudhury M, Kiran U, Vasdev S, Talwar S. Parasternal intercostal block with ropivacaine for postoperative analgesia in pediatric patients undergoing cardiac surgery: a double-blind, randomized, controlled study. *J Cardiothorac Vasc Anesth* 2012; 26: 439–442.
50. Moga FX, Lo Galbo MD, Overman DM, Friedrichsdorf SJ. Post-cardiotomy parasternal nerve block with bupivacaine may be associated with reduced post-operative opioid use in children: a retrospective cohort study. *Children (Basel)* 2020; 7: 7.
51. Kaushal B, Chauhan S, Saini K, et al. Comparison of the efficacy of ultrasound-guided serratus anterior plane block, pectoral nerves II block, and intercostal nerve block for the management of postoperative thoracotomy pain after pediatric cardiac surgery. *J Cardiothorac Vasc Anesth* 2019; 33: 418–425.
52. Samantaray DJ, Trehan M, Chowdhry V, Reedy S. Comparison of hemodynamic response and postoperative pain score between general anaesthesia with intravenous analgesia versus general anaesthesia with caudal analgesia in pediatric patients undergoing open-heart surgery. *Ann Cardiac Anaesth* 2018; 22: 35–40.
53. Nguyen KN, Byrd HS, Tan JM. Caudal analgesia and cardiothoracic surgery: a look at postoperative pain scores in a pediatric population. *Paediatr Anaesth* 2016; 26: 1060–1063.
54. Nasr JA, Abdelhamid HM. The efficacy of caudal dexmedetomidine on stress response and postoperative pain in pediatric cardiac surgery. *Ann Cardiac Anaesth* 2013; 16: 109–114.
55. Evans MA, Monahan A, Abhold E, Hajduk J, Vu E, Suresh S. The utilization of caudal hydromorphone for fast-tracking in congenital cardiac surgery in a tertiary-care children's hospital: an audit. *J Clin Anesth* 2021; 72: 72.
56. Maharramova M, Taylor K. A systematic review of caudal anesthesia and postoperative outcomes in pediatric cardiac surgery patients. *Semin Cardiothorac Vasc Anesth* 2019; 23: 237–247.

57. Hammer GB, Ramamoorthy C, Cao H, et al. Postoperative analgesia after spinal blockade in infants and children undergoing cardiac surgery. *Anesth Analg* 2005; 100: 1283–1288.
58. Tirotta CF, Munro HM, Salvaggio J, et al. Continuous incisional infusion of local anesthetic in pediatric patients following open heart surgery. *Paediatr Anaesth* 2009; 19: 571–576.
59. Paladini G, Di Carlo S, Musella G, et al. Continuous wound infiltration of local anesthetics in postoperative pain management: safety, efficacy and current perspectives. *J Pain Res* 2020; 13: 285–294.
60. Elkomy MH, Drover DR, Galinkin JL, Hammer GB, Glotzbach KL. Pharmacodynamic analysis of morphine time-to-remedication events in infants and young children after congenital heart surgery. *Clin Pharmacokinet* 2016; 55: 1217–1226.
61. Murray-Torres TM, Tobias JD, Winch PD. Perioperative opioid consumption is not reduced in cyanotic patients presenting for the Fontan procedure. *Pediatr Cardiol* 2021; 42: 1170–1179.
62. Mota FA, Marcolan JF, Pereira MH, Milanez AM, Dallan LA, Diccini S. Comparison study of two different patient-controlled anesthesia regimens after cardiac surgery. *Rev Bras Cir Cardiovasc* 2010; 25: 38–44.
63. Epstein HM. Postoperative patient-controlled analgesia in the pediatric cardiac intensive care unit. *Crit Care Nurse* 2017; 37: 55–61.
64. Goot BH, Kaufman J, Pan Z, et al. Morphine pharmacokinetics in children with down syndrome following cardiac surgery. *Pediatr Crit Care Med* 2018; 19: 459–467.
65. Valkenburg AJ, Calvier EA, van Dijk M, et al. Pharmacodynamics and pharmacokinetics of morphine after cardiac surgery in children with and without Down syndrome. *Pediatr Crit Care Med* 2016; 17: 930–938.
66. Vogel ER, Staffa SJ, DiNardo JA, Brown ML. Dosing of opioid medications during and after pediatric cardiac surgery for children with Down syndrome. *J Cardiothorac Vasc Anesth* 2022; 36: 195–199.
67. Van Driest SL, Shah A, Marshall MD, et al. Opioid use after cardiac surgery in children with Down syndrome. *Pediatr Crit Care Med* 2013; 14: 862–868.
68. Elkomy MH, Drover DR, Glotzbach KL, et al. Pharmacokinetics of morphine and its metabolites in infants and young children after congenital heart surgery. *AAPS J* 2016; 18: 124–133.
69. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain* 2016; 17: 131–157.
70. Dagan O, Klein J, Bohn D, Barker G, Koren G. Morphine pharmacokinetics in children following cardiac surgery: effects of disease and inotropic support. *J Cardiothorac Vasc Anesth* 1993; 7: 396–398.
71. Frankel WC, Maul TM, Chrysostomou C, et al. A minimal opioid postoperative management protocol in congenital cardiac surgery: safe and effective. *Semin Thorac Cardiovasc Surg* 2020.
72. Penk JS, Lefaiver CA, Brady CM, Steffensen CM, Wittmayer K. Intermittent versus continuous and intermittent medications for pain and sedation after pediatric cardiothoracic surgery; a randomized controlled trial. *Crit Care Med* 2018; 46: 123–129.
73. Savva DA, Kishk OA, Morgan JA, Biggs JM, Seung H, Bauer C. Post-operative non-steroidal anti-inflammatory drug use for pain in infant and paediatric cardiac surgery patients. *Cardiol Young* 2019; 29: 1440–1444.
74. Saini A, Maher KO, Deshpande SR. Nonopioid analgesics for perioperative and cardiac surgery pain in children: current evidence and knowledge gaps. *Ann Pediatr Cardiol* 2020; 13: 46–55.
75. Moffett BS, Wann TI, Carberry KE, Mott AR. Safety of ketorolac in neonates and infants after cardiac surgery. *Paediatr Anaesth* 2006; 16: 424–428.
76. Dawkins TN, Barclay CA, Gardiner RL, Krawczeski CD. Safety of intravenous use of ketorolac in infants following cardiothoracic surgery. *Cardiol Young* 2009; 19: 105–108.
77. Gupta A, Daggett C, Drant S, Rivero N, Lewis A. Prospective randomized trial of ketorolac after congenital heart surgery. *J Cardiothorac Vasc Anesth* 2004; 18: 454–457.
78. Jalkut MK. Ketorolac as an analgesic agent for infants and children after cardiac surgery: safety profile and appropriate patient selection. *AACN Adv Crit Care* 2014; 25: 23–30.
79. Gupta A, Daggett C, Ludwick J, Wells W, Lewis A. Ketorolac after congenital heart surgery: does it increase the risk of significant bleeding complications? *Paediatr Anaesth* 2005; 15: 139–142.
80. Inoue M, Caldaroni CA, Frndova H, et al. Safety and efficacy of ketorolac in children after cardiac surgery. *Intens Care Med* 2009; 35: 1584–1592.
81. Acharya M, Dunning J. Does the use of non-steroidal anti-inflammatory drugs after cardiac surgery increase the risk of renal failure? *Interact Cardio Thorac Surg* 2010; 11: 461–467.
82. Jelacic S, Bollag L, Bowdle A, Rivat C, Cain KC, Richebe P. Intravenous acetaminophen as an adjunct analgesic in cardiac surgery reduces opioid consumption but not opioid-related adverse effects: a randomized controlled trial. *J Cardiothorac Vasc Anesth* 2016; 30: 997–1004.
83. Mallama M, Valencia A, Rijs K, Rietdijk WJR, Klimek M, Calvache JA. A systematic review and trial sequential analysis of intravenous vs. oral perioperative paracetamol. *Anaesthesia* 2021; 76: 270–276.
84. Ahlers SJ, Van Gulik L, Van Dongen EP, Bruins P, Tibboel D, Knibbe CA. Aminotransferase levels in relation to short-term use of acetaminophen four grams daily in postoperative cardiothoracic patients in the intensive care unit. *Anaesth Intensive Care* 2011; 39: 1056–1063.
85. Cattabriga I, Pacini D, Lamazza G, et al. Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial. *Eur J Cardiothorac Surg* 2007; 32: 527–531.
86. Mian P, Valkenburg AJ, Allegaert K, et al. Population pharmacokinetic modeling of acetaminophen and metabolites in children after cardiac surgery with cardiopulmonary bypass. *J Clin Pharmacol* 2019; 59: 847–855.
87. Donnellan A, Sawyer J, Peach A, Staveski S, Nelson DP, Pratap JN. Reducing exposure to opioid and benzodiazepine medications for pediatric cardiac intensive care patients: a quality improvement project. *Pediatr Crit Care Med* 2019; 20: 340–349.
88. Kim JS, Kaufman J, Patel SS, Manco-Johnson M, Di Paola J, da Cruz EM. Antiplatelet effect of ketorolac in children after congenital cardiac surgery. *World J Pediatr Congenit Heart Surg* 2018; 9: 651–658.
89. Aranda JV, Salomone F, Valencia GB, Beharry KD. Non-steroidal anti-inflammatory drugs in newborns and infants. *Pediatr Clin North Am* 2017; 64: 1327–1340.
90. Ziesenitz VC, Zutter A, Erb TO, van den Anker JN. Efficacy and safety of ibuprofen in infants aged between 3 and 6 months. *Paediatr Drugs* 2017; 19: 277–290.
91. Green C, Krafft H, Guyatt G, Martin D. Symptomatic fever management in children: a systematic review of national and international guidelines. *PLoS One* 2021; 16: e0245815.
92. Uber AM, Montez-Rath ME, Kwiatkowski DM, Krawczeski CD, Sutherland SM. Nephrotoxin exposure and acute kidney injury in critically ill children undergoing congenital cardiac surgery. *Pediatr Nephrol* 2018; 33: 2193–2199.
93. Miller TA, Lisanti AJ, Witte MK, et al. A collaborative learning assessment of developmental care practices for infants in the cardiac intensive care unit. *J Pediatr* 2020; 220: 93–100.
94. Van Der Heijden MJE, Araghi SO, Van Dijk M, Jeekel J, Hunink MGM. The effects of perioperative music interventions in pediatric surgery: a systematic review and meta-analysis of randomized controlled trials. *PLoS ONE* 2015; 10: e0133608.
95. Huang YL, Lei YQ, Liu JF, Cao H, Yu XR, Chen Q. The music video therapy in postoperative analgesia in preschool children after cardiothoracic surgery. *J Cardiac Surg* 2021; 36: 2308–2313.
96. Huang YL, Lei YQ, Liu JF, Cao H, Yu XR, Chen Q. Comparison of the effectiveness of music video therapy and music therapy on pain after cardiothoracic surgery in preschool children. *Heart Surg Forum* 2021; 24: E299–E304.
97. Kakar E, Billar RJ, van Rosmalen J, Klimek M, Takkenberg JJM, Jeekel J. Music intervention to relieve anxiety and pain in adults undergoing cardiac surgery: a systematic review and meta-analysis. *Open Heart* 2021; 8: e001474.

98. Staveski SL, Boulanger K, Erman L, et al. The impact of massage and reading on children's pain and anxiety after cardiovascular surgery: a pilot study. *Pediatr Crit Care Med* 2018; 19: 725–732.
99. Harrison TM, Brown R, Duffey T, et al. Effects of massage on postoperative pain in infants with complex congenital heart disease. *Nurs Res* 2020; 69: S36–S46.
100. Albert NM, Gillinov AM, Lytle BW, Feng J, Cwynar R, Blackstone EH. A randomized trial of massage therapy after heart surgery. *Heart Lung: J Acute Crit Care* 2009; 38: 480–490.
101. Araujo AS, Klamt JG, Vicente WV, Garcia LV. Pain and cardiorespiratory responses of children during physiotherapy after heart surgery. *Rev Bras Cir Cardiovasc* 2014; 29: 163–166.
102. Chen LL, Lei YQ, Liu JF, Cao H, Yu XR, Chen Q. Application and effects of an early childhood education machine on analgesia and sedation in children after cardiothoracic surgery. *J Cardiothorac Surg* 2021; 16.
103. Mayan M, Alvadaj T, Punja S, Jou H, Wildgen S, Vohra S. Parents' experiences of an inpatient pediatric integrative medicine service for symptom management. *Explore (NY)* 2019; 15: 415–418.
104. Lisanti AJ, Demianczyk AC, Costarino A, et al. Skin-to-skin care is a safe and effective comfort measure for infants before and after neonatal cardiac surgery. *Pediatr Crit Care Med* 2020; 21: E834–E841.
105. Lander J, Fowler-Kerry S. TENS for children's procedural pain. *Pain* 1993; 52: 209–216.
106. Irfan A, Martin LY, Canner J, et al. The impact of post-operative opioid guidelines on prescribing behaviors in the pediatric population. *Pediatr Surg Int* 2020; 36: 1339–1343.
107. Monitto CL, Hsu A, Gao S, et al. Opioid prescribing for the treatment of acute pain in children on hospital discharge. *Anesth Analg* 2017; 125: 2113–2122.
108. Holst KA, Dearani JA, Schaff HV, et al. What drives opioid prescriptions after cardiac surgery: practice or patient? *Ann Thorac Surg* 2020; 110: 1201–1208.