RUTGERS HEALTH
School of Nursing
Nurse Anesthesiology Program

The Effectiveness of Intravenous Dexmedetomidine Compared to Other Intravenous Anesthetics in Reducing the Incidence of Delirium in Pediatric Patients Undergoing General Anesthesia for Cardiac Surgery: A Systematic Review

Russell Lynn Memorial Student Lecture Series

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Objectives

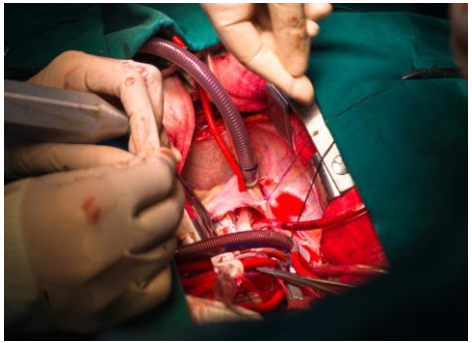
- Evaluate the effectiveness of intravenous dexmedetomidine compared to other IV anesthetics used in general anesthesia in reducing postoperative emergence delirium (ED) in pediatric cardiac surgery patients
- Provide evidence-based insights for anesthesia providers to improve pediatric perioperative care
- Address the lack of recent (within the last ten years) comprehensive reviews on this topic
- Highlight the need for further large-scale studies to validate current findings

Systematic Review Question

What is the effectiveness of intravenous dexmedetomidine compared to other intravenous anesthetics in reducing the incidence of delirium in pediatric patients undergoing general anesthesia for cardiac surgery?

Purpose of Review

- ✓ Evaluate the effectiveness of intravenous dexmedetomidine compared to other intravenous anesthetics in reducing the incidence of delirium in pediatric patients undergoing general anesthesia for cardiac surgery
- ✓ Provide a current and comprehensive review on the potential benefits of dexmedetomidine use during cardiac surgery
- ✓ Dissemination of evidence-based research with the potential to drive practice changes that improve patient outcomes and enhance satisfaction for patients, caregivers, and providers



Background

Prevalence

- Cardiac birth defects occur in approximately 4 to 8 per 1,000 live births
- Congenital heart disease is the leading cause of mortality among pediatric patients undergoing cardiac surgery
- Around 10,000 children require general anesthesia for cardiac defect repairs annually

Emergence Delirium

- Defined as sudden perceptual disturbances and psychomotor agitation within 45 minutes of recovery from anesthesia
- Presentation may include confusion, thrashing, psychomotor disorders, hallucinations, excitability, restlessness, purposeless hyperactive physical behavior
- Incidence in children after general anesthesia ranges from 10-80%

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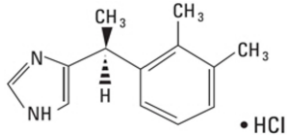
Background (continued)

Contributing Factors

- Preschool-aged children⟶ highest risk
- Short-acting general anesthetic agents, most notably sevoflurane, have been linked emergence delirium in children

Dexmedetomidine

- Highly selective alpha-2 adrenergic agonist
- Sedative, analgesic, and anxiolytic properties
- Maintains cardiovascular stability⟶ ideal for patients with cardiac disease
- Anesthetic sparing and neuroprotective effects



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Significance

The development of emergence delirium negatively affects patients, family members, healthcare providers and the organization as a whole

- Risk of falls
- Premature extubations
- Dislodgement of IV lines
- Increased length of stay
- Wound dehiscence and surgical site bleeding
- Prolonged PACU times
- Injury to providers
- Increased staff requirements
- Higher overall medical costs
- Patient, family, and provider dissatisfaction

Methods

Systematic Review and Meta-Analysis

- Comprehensive search of 4 databases was conducted to identify relevant published and unpublished studies
- Screening, quality appraisal, and data extraction were independently performed by 3 independent reviewers
- PRISMA 2020 reporting guidelines for systematic reviews and meta-analyses were followed
- A random-effect model meta-analysis using SPSS software was conducted to assess relevant outcomes and determine the proportion of patients who developed delirium in the dexmedetomidine and control groups

Participants

Children

0-18 years old

Heart disease

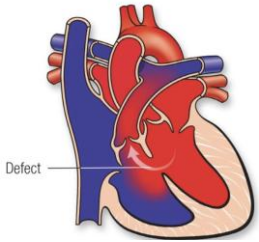
Included any congenital or acquired cardiac structural abnormalities of the valves, major blood vessels and chambers

Cardiac surgery

Procedures included but were not limited to replacement of heart valves, repair of major blood vessels, repair of septal defects, and other cardiac surgeries

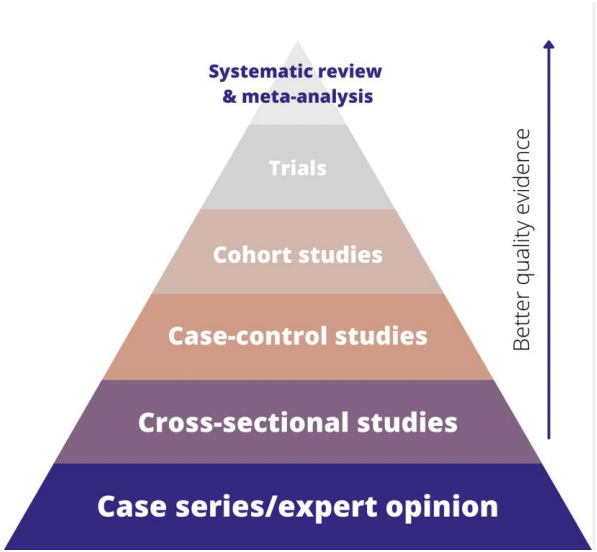
Exclusion criteria

- Greater than 18 years of age
- Lack of heart disease
- Pre-existing cognitive dysfunction



Types of Studies

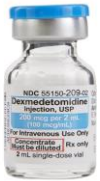
- Experimental and non-experimental study designs considered
  - Randomized controlled trials
  - Non-randomized trials
  - Case-control studies
  - Analytical cohort studies
- Studies included were both randomized controlled trials (RCTs) ⟶ “Gold Standard”
  - Directly compare patients who received dexmedetomidine with those who did not



Intervention and Control

Intervention

- Perioperative administration medium-dose Dexmedetomidine at 0.2 mcg/kg/hr, high-dose Dexmedetomidine at 0.4 mcg/kg/hr of dexmedetomidine during cardiac surgery (Ming et al., 2021)
- Dexmedetomidine 0.5 mcg/kg bolus over 10 minutes, followed by infusion at 0.5 mcg/kg/hour until end of surgery (Sun et al., 2017)



Control

- Volume-matched 0.9% normal saline infusion
- Other agents commonly used preoperatively during cardiac surgery for children
  - Including but not limited to propofol, midazolam, ketamine, and fentanyl

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Search Strategy

3-step search strategy to find all published and unpublished studies:

1

- Initial search of MEDLINE (PubMed)
- Text words contained in the titles and abstracts of relevant articles, and the index terms used to describe these articles, were used

2

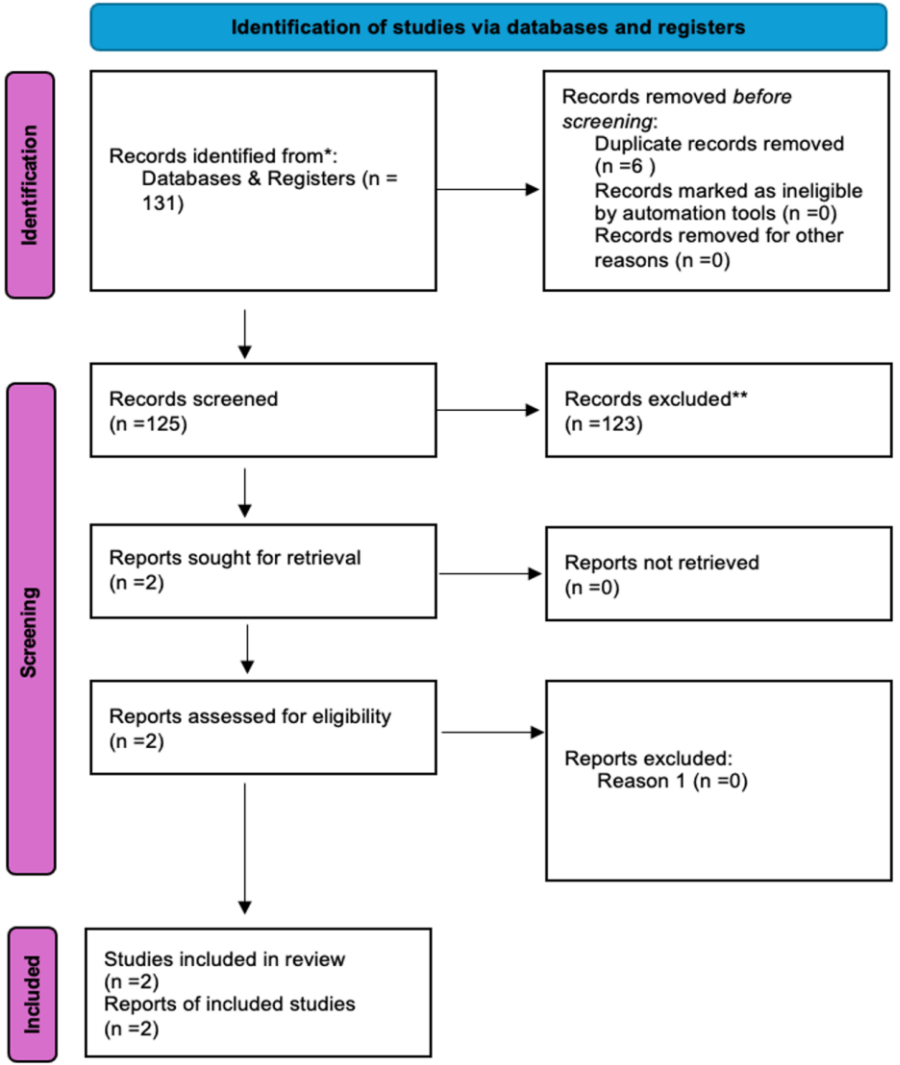
- A second search using all identified keywords and index terms was undertaken across all included databases
  - Embase, Scopus, ProQuest Dissertation and Theses

3

- The reference lists of all identified studies were screened as part of the third search for additional studies

- Only studies published in the English language considered for inclusion
- A search range based on the year of publication was not set to allow greater sensitivity

PRISMA Diagram



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Concept Map

Keywords:

- Dexmedetomidine
- Delirium
- Children
- Cardiac surgery

Component	Search Strategy	# Citations
Dexmedetomidine	"dexmedetomidine"[Mesh] OR "dexmedetomidine" OR "precedex"	9,364
Pediatric	(("Child"[Mesh]) OR "Adolescent"[Mesh]) OR "Infant"[Mesh] OR "pediatr*" OR "paediatr*"	4,616,906
Cardiac Surgery	("Thoracic surgery"[Mesh]) OR "cardiac surgical procedures"[Mesh] OR "cardiac surger*" OR "congenital heart surger*" OR "heart surger*" OR "heart procedure*"	315,142
Total	(("dexmedetomidine"[Mesh] OR "dexmedetomidine" OR "precedex") AND ((("Child"[Mesh]) OR "Adolescent"[Mesh]) OR "Infant"[Mesh] OR "pediatr*" OR "paediatr*")) AND (("Thoracic surgery"[Mesh]) OR "cardiac surgical procedures"[Mesh] OR "cardiac surger*" OR "congenital heart surger*" OR "heart surger*" OR "heart procedure*")	160

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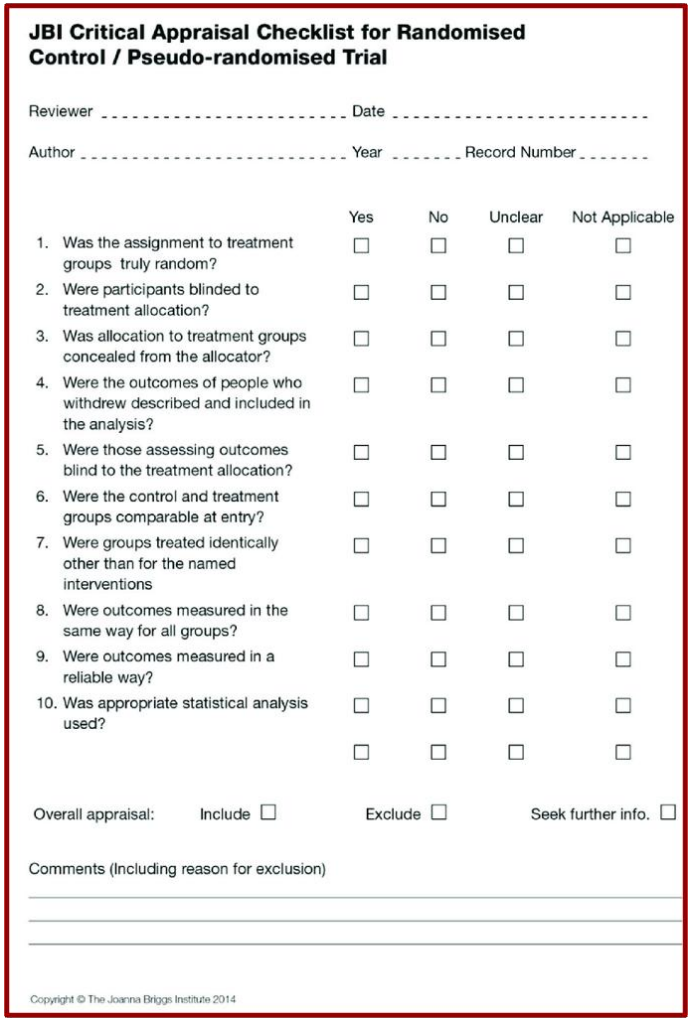
Quality Appraisal

- Studies were reviewed against inclusion and exclusion criteria
- Two full text studies were included in this review
- **Included studies:**
  - Selected studies were critically appraised by 3 independent reviewers for methodological quality
  - The standardized critical appraisal instruments from the Joanna Briggs Institute were utilized
  - Included studies had an 80% response as “met” on appraisal checklist
  - Disagreements were resolved through discussion or with an additional reviewer
- No studies were excluded based on methodological quality alone

Quality Appraisal (continued)

- Two RCTs were compiled into a table of evidence and reviewed by three independent reviewers
- Quality assessed using standard JBI critical Appraisal Checklist and deemed good quality
- Common methodological flaws:
  - Lack of clarity on whether allocation to treatment groups was concealed
  - Uncertainty about whether follow-up was completed in both groups



JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Data Extraction

- The data extracted from papers included specific details about study participants, design, and outcome measures
- Disagreements between reviewers were resolved by discussion or an additional reviewer

Data extraction

- Study design
- Study participants (age & gender)
- Settings (procedures)
- Duration of anesthesia, cross-clamp time, time to extubation
- Intervention
- Comparators
- Study results
- Statistical analysis
- All other relevant data
  - Funding, conflicts of interest

Outcome measures

- Presence of emergence delirium

Pediatric Anesthesia Emergence Delirium (PAED) Scale

Point	Description of items	Not at all	Just a little	Quite a bit	Very much	Extremely
1	The child makes eye contact with the caregiver	4	3	2	1	0
2	The child's actions are purposeful	4	3	2	1	0
3	The child is aware of his/her surroundings	4	3	2	1	0
4	The child is restless	0	1	2	3	4
5	The child is inconsolable	0	1	2	3	4

Findings

Two RCTs representing a total of 110 patients were included

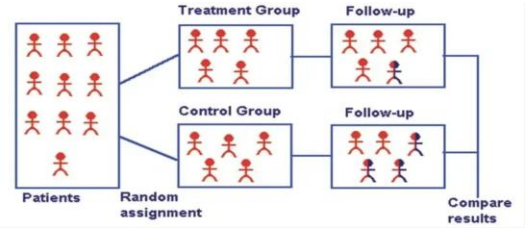
- Published between 2017-2024
- Conducted in China
- Elective repair of ASD or VSD under GA on CPB
- Reported the incidence of emergence delirium as a primary or secondary outcome

Study #1 (Ming et al., 2021)

- 50 patients total (mean age: 2.5 years)
- ED defined as 2-5 on the 5-point scale
- Lower overall incidence of ED in the dexmedetomidine groups
    - Most prominent difference seen in moderate agitation

Study #2 (Sun et al., 2017)

- 90 patients total (mean age: 28-30 months)
- ED defined as $\geq$ 10 on the PAED scale
- Significantly lower incidence of ED in the dexmedetomidine group
    - Mean PAED Dexmedetomidine group: 3
    - Mean PAED saline group: 9



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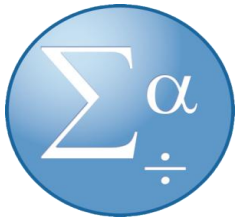
Data Synthesis and Analysis

- Quantitative data was pooled in a statistical meta-analysis
- SPSS version 28.0 software (IBM Statistics for Windows. Armonk, NY: IBM Crop) was used for statistical analysis
- Random effect model utilized for meta-analysis
- Effect sizes expressed as odds ratio (for categorical data) calculated for analysis
- Heterogeneity tested statistically using the chi-squared and I-squared tests



$$\chi^2 = \sum \frac{(O-E)^2}{E}$$

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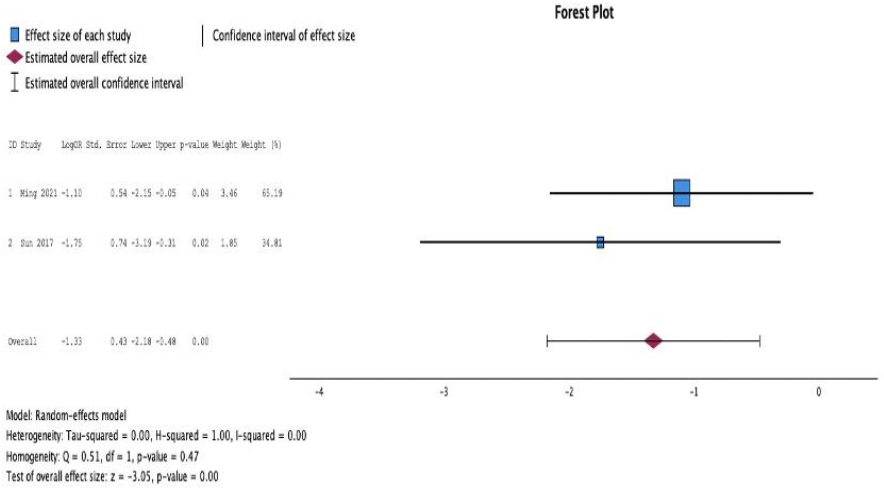
Meta-Analysis

- A pooled odds ratio was calculated using a random-effect model to determine the effect of Dex
- **The overall odds ratio:**
  - -1.326 (95% CI -2.176 to -0.475)
  - Statistically significant (p = 0.002), indicating a lower incidence of delirium in the Dex group
- q-value of 0.513 (p = 0.474) indicated homogeneity between the studies (p > 0.1)
- I^2 value of 0 confirmed no variability between the studies



Heterogeneity Measures

Overall	Tau-squared	.000
	H-squared	1.000
	I-squared (%)	.0

Test of Homogeneity

	Chi-square (Q statistic)	df	Sig.
Overall	.513	1	.474

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Discussion

Findings summary

- The results of this systematic review are similar to previous reviews on the use of dexmedetomidine for ED in pediatric patients
- Previously published reports focused on different populations of pediatric patients, but showed that dexmedetomidine effectively reduced delirium in those undergoing general anesthesia for various surgeries
- The use of dexmedetomidine leads to a decreased incidence of pediatric ED across various surgical settings

Clinical significance

- Evidence from this review expands knowledge on the use of dexmedetomidine in children undergoing cardiac surgery
- Providers should use dexmedetomidine in similar clinical scenarios to reduce complications related to the development of ED

Recommendations

- Further studies on the use of dexmedetomidine in pediatric cardiac surgery should be conducted, as the sample size in this systematic review is small

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Limitations

- Search strategy was restricted to English
- Some studies had methodological flaws, limiting validity of results
- Small number of participants in most studies
- Studies were conducted in one country (China), which potentially limits generalizability of the results to a larger patient population

Large-scale studies with rigorous methodology are needed to validate these findings across broader patient populations

Conclusions

Summary of findings

- Dexmedetomidine can be effective in the prevention of ED among pediatric patients undergoing cardiac surgery

Implications for clinical practice

- Development of clinical practice guidelines related to the prevention of emergence delirium in pediatric cardiac surgery
- Educational development for anesthesia providers regarding the implications of emergence delirium

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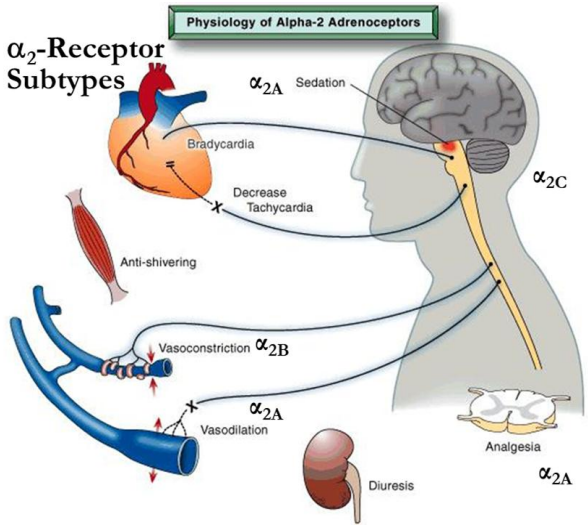
Conclusions (continued)

Call to action

- Clinicians should consider the use of dexmedetomidine to improve the post-operative experience of children and their families
- Advocate for further research into the prevention of emergence delirium in children undergoing general anesthesia
- Investigating the effects of different dosages may yield insights into achieving the best balance between efficacy and safety
- Studies examining the patho-pharmacological mechanisms by which dexmedetomidine reduces emergence delirium in pediatric cardiac patients may lead to further advancements in management and prevention



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Knowledge Translation

- Present the information to statewide organizations, such as the New Jersey Association of Nurse Anesthesiologists
    - Poster presentations
    - The Russell Lynn Memorial Lecture Series
- Enable nurse anesthesiologists statewide to:
    - Learn from the research
    - Apply the evidence and recommendations to their clinical practices
- Share findings at individual hospital grand rounds to ensure broader dissemination
- Develop clinical practice guidelines in the future to support and inform clinical decision-making

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