Lignocaine/phenylephrine nasal spray does not reduce pain and distress of nasogastric tube insertion in young children: A randomized controlled trial.

Simon Craig, Robert Seith, John Cheek, Kathryn Wilson, Diana Egerton-Warburton, Eldho Paul, Adam West

@DrSimonCraig

Monash Children's Hospital

Funding

- ACEM Emergency Medicine Research Foundation
  - Morson Taylor Research Award, 2012
- Monash Health Senior Medical Staff Association
  - Emerging Investigator Research Award, 2013

Monash Children's Hospital

Background & Importance

Monash Children's Hospital

Leading causes of under 5 mortality

- Preterm birth complications
- Intrapartum-related complications
- Congenital anomalies
- Acute respiratory infections
- Diarrhoea

World Health Organization

Global Health Observatory (GHO) data
Child mortality and causes of death

Monash Children's Hospital

Nasogastric tubes are useful…

- Gastroenteritis / diarrhoea
- Bronchiolitis
  - Maintenance of hydration
  - Prevention of gastric distension when using HFNC
- Surgical conditions (gastric decompression)
- Medication / contrast administration
- Nutritional support

Monash Children's Hospital

Nasogastric tubes hurt!

- Nasogastric tube (NGT) insertion is **the most painful procedure** commonly performed in the emergency department (ED).

Singer AJ, Richman PB, Kowalska A, et al. *Comparison of patient and practitioner assessments of pain from commonly performed emergency department procedures.* Ann Emerg Med. 1999;33:652-658.

Monash Children's Hospital

Nasogastric tubes hurt!

- 98% believed NGT insertion was **uncomfortable** or **painful** for awake and alert patients
- 93% reported use of measures to reduce discomfort
- 28% felt what they do is adequate
- **39% expressed satisfaction** with **current practice**

Juhl GA, Conners GP. *Emergency physicians' practices and attitudes regarding procedural anaesthesia for nasogastric tube insertion.* Emerg Med J. 2005 Apr;22(4):243-5.

Monash Children's Hospital

Pain management – a human right

“According to international human rights law …. failure to take reasonable steps to ensure that people who suffer pain have access to adequate pain treatment may result in the violation of the obligation to protect against cruel, inhuman and degrading treatment.”

Lohman et al. BMC Medicine 2010, 8:8

We can reduce the pain of NGT insertion

…… in adults

Monash Children's Hospital

Local anaesthetic

- Topical nasal spray

Singer AJ, Konia N. *Comparison of topical anesthetics and vasoconstrictors vs lubricants prior to nasogastric intubation: a randomized, controlled trial.* Academic Emergency Medicine 1999;6(3):184-190.

Juhl GA, Conners GP. *Emergency physicians' practices and attitudes regarding procedural anaesthesia for nasogastric tube insertion.* Emergency medicine journal : EMJ. 2005;22(4):243-245.

Nott MR, Hughes JH. *Topical anaesthesia for the insertion of nasogastric tubes.* European Journal of Anaesthesiology. 1995;12(3):287-290.

Wolfe TR, Fosnocht DE, Linscott MS. *Atomized lidocaine as topical anesthesia for nasogastric tube placement: A randomized, double-blind, placebo-controlled trial.* Annals of Emergency Medicine. 2000;35(5):421-425.

Monash Children's Hospital

Local anaesthetic

- Nebulization

Cullen L, Taylor D, Taylor S, Chu K. *Nebulized lidocaine decreases the discomfort of nasogastric tube insertion: a randomized, double-blind trial.* Annals of Emergency Medicine. 2004;44(2):131-137.

Spektor M, Kaplan J, Kelley J, Wheary J, Dalsey W. *Nebulized or sprayed lidocaine as anesthesia for nasogastric intubations.* Academic Emergency Medicine. 2000;7(4):406-408.

- Lignocaine Gel

Ducharme J, Matheson K. *What is the best topical anesthetic for nasogastric insertion? A comparison of lidocaine gel, lidocaine spray, and atomized cocaine.* Journal of Emergency Nursing: JEN 2003;29(5):427-430.

Monash Children's Hospital

Children are....

… different

Monash Children's Hospital

Paediatric research

- RCH Melbourne
- RCT of nebulised lignocaine vs placebo

*"The **study was terminated early** before enrolling the planned 52 patients because of researcher and ED nursing staff concerns about the **level of distress experienced by patients during nebulization**."*

Babl FE, Goldfinch C, Mandrawa C, Crellin D, O'Sullivan R, Donath S. *Does nebulized lidocaine reduce the pain and distress of nasogastric tube insertion in young children? A randomized, double-blind, placebo-controlled trial.* Pediatrics. 2009;123(6):1548-1555

Monash Children's Hospital

The problem…

There are currently ***no studies*** *assessing the effectiveness of a* ***local anesthetic nasal spray*** *for the prevention of pain and distress associated with* ***nasogastric tube insertion in children****.*

Monash Children's Hospital

Study question

Study question

- Does the use of **lignocaine / phenylephrine nasal spray** compared to **0.9% sodium chloride placebo** result in less **pain and distress** for **children aged 6 months to 5 years** receiving a **nasogastric tube**?

Monash Children's Hospital

PICO Format

- P Children aged 6 months – 5 years
  having a NGT inserted as part of their ED treatment
- I Lignocaine / phenylephrine nasal spray
- C 0.9% sodium chloride nasal spray
- O Pain and distress (observer-rated)

Monash Children's Hospital

Population

- Children aged 6 months to 5 years
- Nasogastric tube as part of ED treatment

Monash Children's Hospital

Exclusion criteria

- Allergy to study medication
- Nasal problems
  - Aberrant nasal anatomy
  - Acute or chronic nasal problems
  - Nasal trauma
- Risks of complications from study medication
  - Cardiovascular disease
  - Congenital heart disease
  - Conduction disturbances
  - Neurological conditions
  - Hepatic or renal impairment
  - Asthma

Monash Children's Hospital

Exclusion criteria

- Potential medication interactions
  - Antiarrhythmic drugs
  - Suxamethonium
  - Phenytoin
  - Antidepressants
  - Propranolol
  - Citicoline
- Unable to obtain consent
- Emergent need for NGT insertion
- Non-English speaking and no face-to-face interpreter available.

Monash Children's Hospital

Intervention

- CoPhenylcaine Forte™
- 1 spray = 100 microlitres
  - 5 mg lignocaine
  - 0.5 mg phenylephrine
- 6-12 kg: 1 spray to each nostril
- >12 kg: 2 sprays to each nostril

Monash Children's Hospital

Placebo

- Identical bottle / spray pack
- 0.9% sodium chloride
- 6-12 kg: 1 spray to each nostril
- >12 kg: 2 sprays to each nostril

Monash Children's Hospital

Randomization

- Block randomization (block sizes of 4)
- Randomization allocation sequence and sequentially numbered bottles of study medication were prepared by the Clinical Trials Pharmacy at Monash Health.
- Double-blind (identical spray bottles / kits)

Monash Children's Hospital

Primary outcome: FLACC Score

FLACC score is thought to measure a composite of pain and distress in young children.

"…the FLACC scale is reliable and sensitive to pain for procedural pain assessment."

Crellin DJ, Harrison D, Santamaria N, Huque H, Babl FE.
The Psychometric Properties of the FLACC Scale Used to Assess Procedural Pain.
The journal of pain : official journal of the American Pain Society. 2018;19(8):862-872.

Monash Children's Hospital

Primary outcome: FLACC Score

Criteria	Score - 0	Score - 1	Score - 2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Monash Children's Hospital

Secondary outcomes: VAS

- Visual Analog Scale (100mm)
  - Parent / Carer: Pain
    Distress
  - Observer: Pain
    Distress

Monash Children's Hospital

Secondary outcomes

- Ease of NGT insertion
- Staff member experience
- Procedural complications
- Number of attempts required

Monash Children's Hospital

Baseline

- Observe child in ED cubicle prior to study drug administration.
- Record baseline FLACC score.
- Once score is recorded, administer nasal spray, and move child to procedure room.

Pre-procedure

- Record FLACC score while child is positioned for nasogastric tube insertion

Procedure

- Insert nasogastric tube.
- Record FLACC score during final NGT insertion attempt (whether or not it was successful)
- Once procedure is complete, move child back to ED cubicle

Recovery

- Record FLACC score once child has been returned to ED cubicle

Post Procedure

- Observer completes other data on observer chart (number of attempts, complications, VAS)
- Proceduralist records data on chart (ease of insertion, judgement of active vs placebo)
- Parent / carer asked to complete the parent / carer chart (pain and distress VAS)

Sample size

- Standard deviation of FLACC score assumed to be 2.5 based on earlier pilot data.

Babl FE, Goldfinch C, Mandrawa C, Crellin D, O'Sullivan R, Donath S. Does nebulized lidocaine reduce the pain and distress of nasogastric tube insertion in young children? A randomized, double-blind, placebo-controlled trial. *Pediatrics*. 2009;123(6):1548-1555.

- Minimally clinically significant difference in FLACC approximately 2 (out of maximum score of 10)

Cole J, Shepherd M, Young P. Intranasal fentanyl in 1-3-year-olds: a prospective study of the effectiveness of intranasal fentanyl as acute analgesia. *Emergency medicine Australasia : EMA*. 2009;21(5):395-400.

Monash Children's Hospital

Sample size

- α of 0.05
- Power of 90%

- 35 patients per treatment arm needed to demonstrate a difference of 2/10 in FLACC score

- Allowing for attrition and other factors, we decided on 50 patients per group (100 total)

Monash Children's Hospital

Statistical analysis plan

- Continuous data (FLACC, VAS): non-parametric
  - Results: medians and interquartile ranges (IQRs).
  - Comparison: Wilcoxon rank-sum tests

- Categorical data (e.g. adverse events)
  - Results: numbers (proportions)
  - Comparison: Chi-square or Fisher's exact test as appropriate.

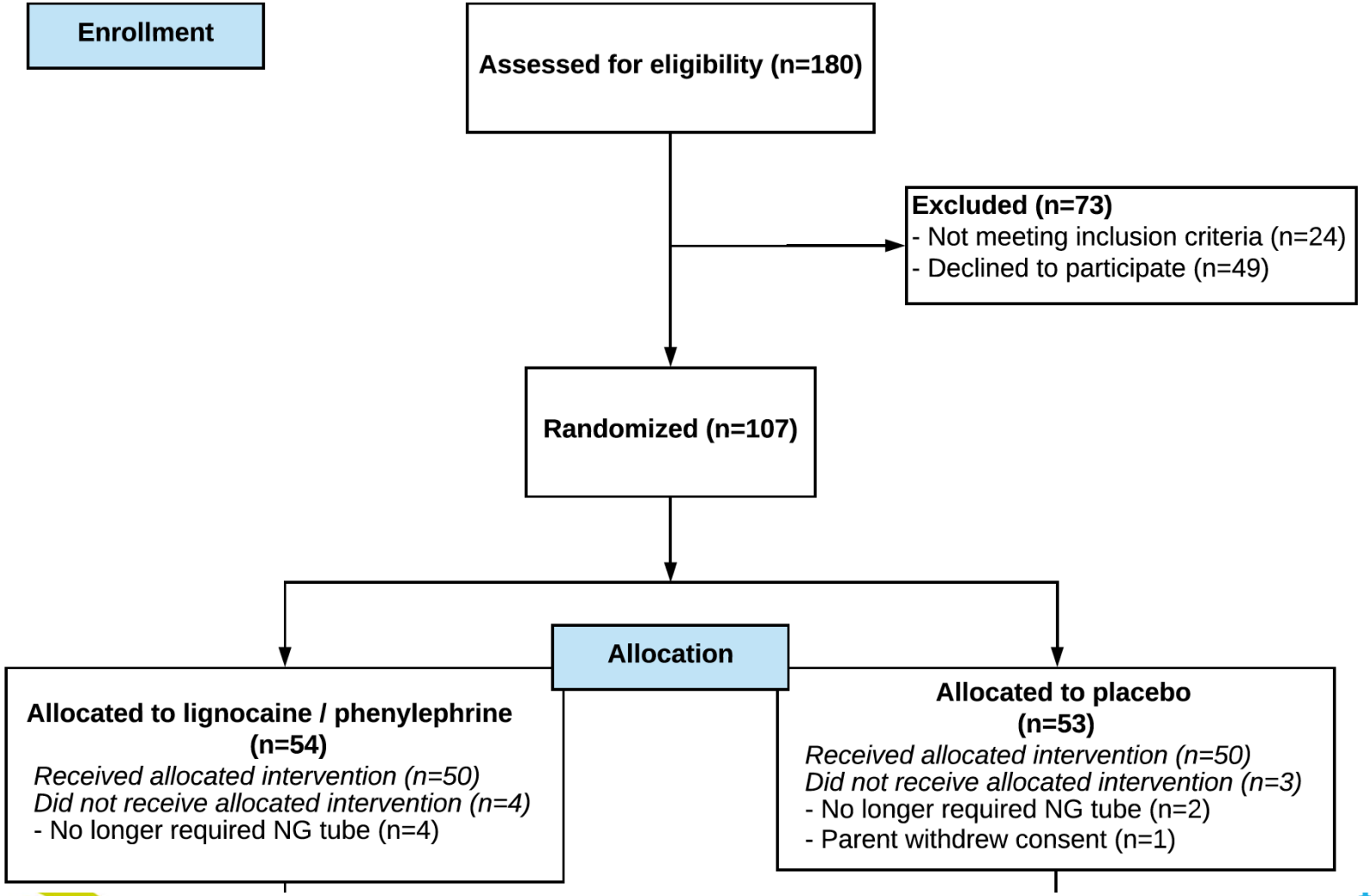
Monash Children's Hospital

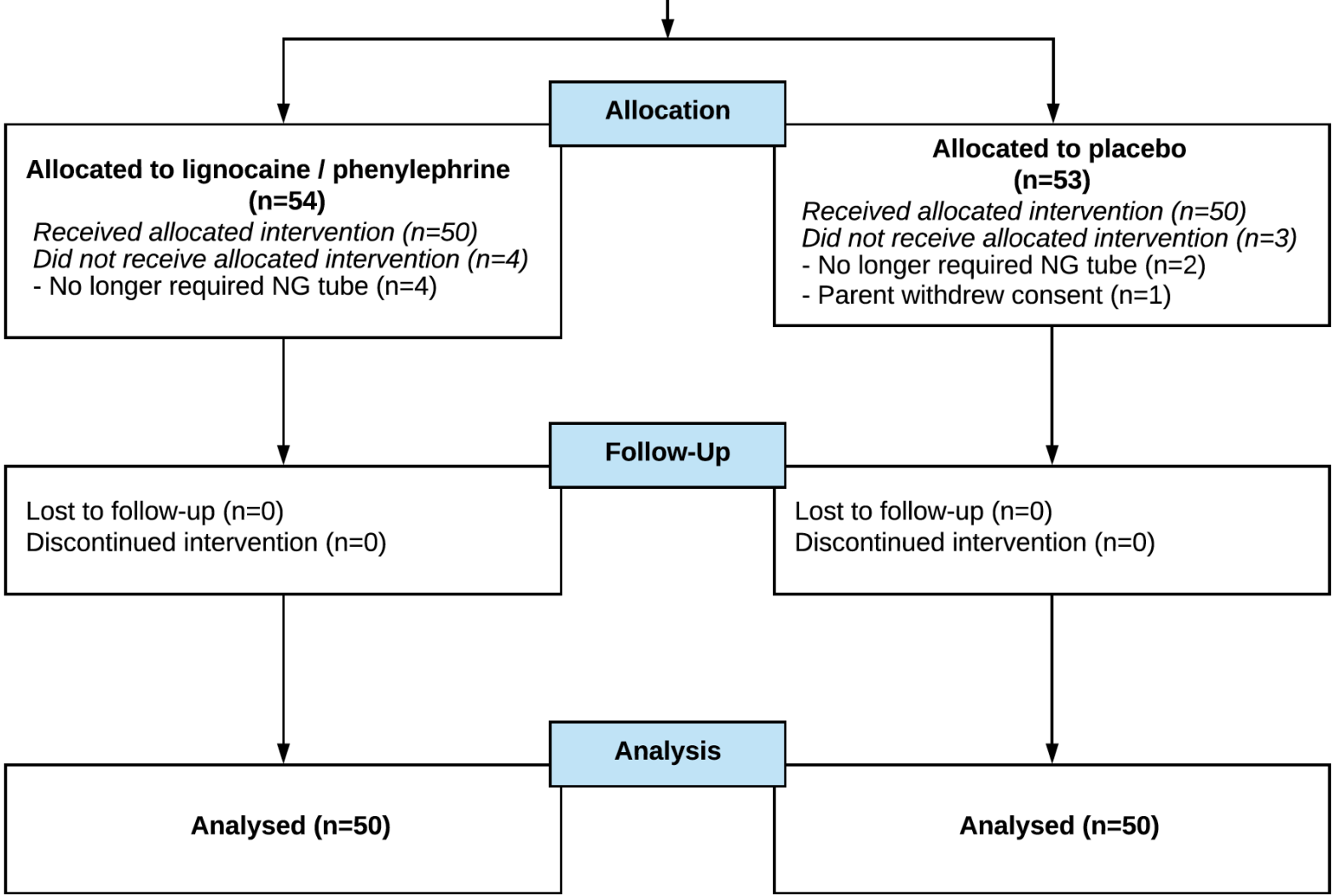
Statistical analysis plan

- Intention to treat
- 2-sided $p<0.05$ indicated statistical significance.
- Stata software version 14
  (StataCorp, College Station, Texas, USA).

Monash Children's Hospital

Results


Enrollment
Assessed for eligibility (n=180)
Excluded (n=73)
- Not meeting inclusion criteria (n=24)
- Declined to participate (n=49)
Randomized (n=107)
Allocation
Allocated to lignocaine / phenylephrine (n=54)
Received allocated intervention (n=50)
Did not receive allocated intervention (n=4)
- No longer required NG tube (n=4)
Allocated to placebo (n=53)
Received allocated intervention (n=50)
Did not receive allocated intervention (n=3)
- No longer required NG tube (n=2)
- Parent withdrew consent (n=1)


Allocation
Allocated to lignocaine / phenylephrine (n=54)
Received allocated intervention (n=50)
Did not receive allocated intervention (n=4)
- No longer required NG tube (n=4)
Allocated to placebo (n=53)
Received allocated intervention (n=50)
Did not receive allocated intervention (n=3)
- No longer required NG tube (n=2)
- Parent withdrew consent (n=1)
Follow-Up
Lost to follow-up (n=0)
Discontinued intervention (n=0)
Lost to follow-up (n=0)
Discontinued intervention (n=0)
Analysis
Analysed (n=50)
Analysed (n=50)

Baseline characteristics

	Lignocaine / Phenylephrine	Placebo
Age, median (IQR), months	13 (9 – 19)	15.5 (12 – 22.5)
Male sex, No. (%),	22 (44)	15 (30)
Weight, median (IQR), kg	9.7 (8.2 – 11)	10.1 (8.7 – 12.7)
Primary **indication for NG insertion**, No. (%)		
Bronchiolitis	4 (8)	7 (14)
Respiratory illness + high-flow nasal cannulae	8 (16)	10 (20)
Dehydration / gastroenteritis	36 (72)	28 (56)

Baseline characteristics

	Lignocaine / Phenylephrine	Placebo
Proceduralist, No. (%)		
Nursing staff	46 (92)	46 (92)
Medical staff	4 (8)	3 (6)
Medical and nursing staff	0 (0)	1 (2)
Proceduralist **experience >5 NGT insertions**	33 (66)	27 (54)
Proceduralist **confidence**, median (IQR), 100mm VAS	8.5 (6.2 – 9.5)	8.3 (6.1 – 9.7)

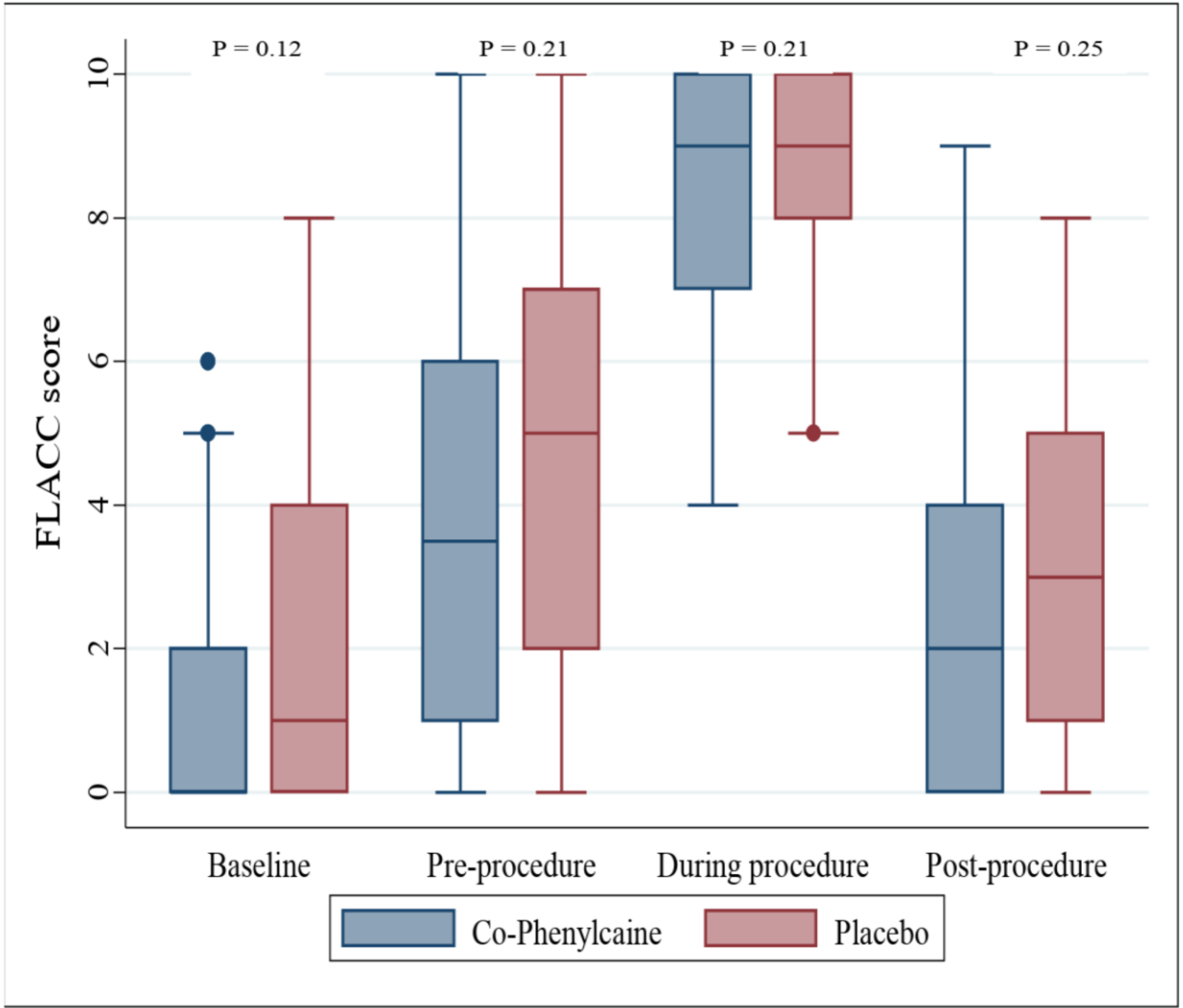
Monash Children's Hospital

Primary Outcome

FLACC Score

Monash Children's Hospital

Primary


P = 0.12
P = 0.21
P = 0.21
P = 0.25
FLACC score
0
2
4
6
8
10
Baseline
Pre-procedure
During procedure
Post-procedure
Co-Phenylcaine
Placebo

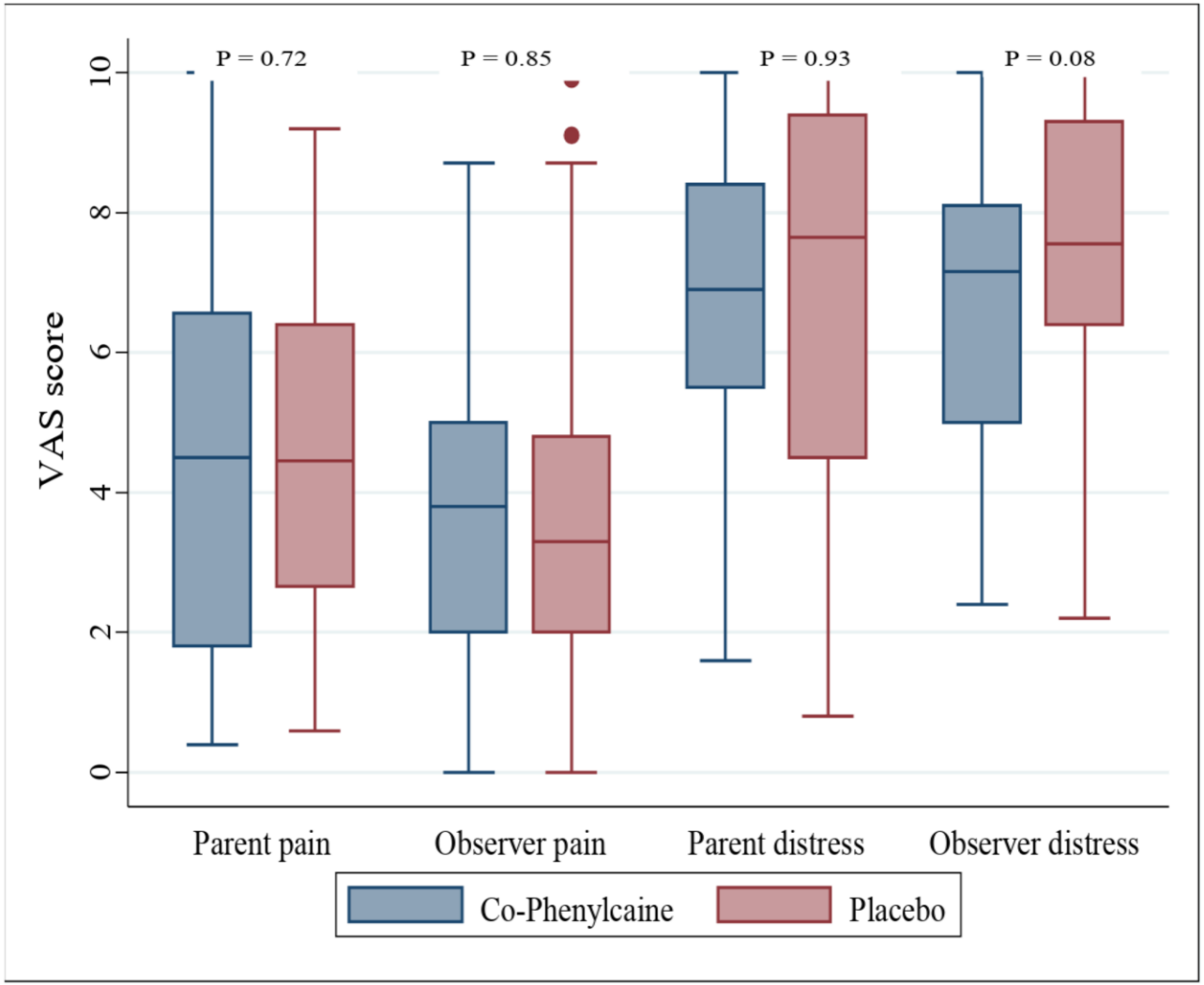
Secondary Outcomes

Observer-rated pain and distress

- Parent / carer
- Staff

Monash Children's Hospital

Secondary


P = 0.72
P = 0.85
P = 0.93
P = 0.08
VAS score
0
2
4
6
8
10
Parent pain
Observer pain
Parent distress
Observer distress
Co-Phenylcaine
Placebo

Complications

	Lignocaine / Phenylephrine	Placebo	P value
Any complication, No. (%)	14 (28)	21 (42)	0.14
Spray complication, No. (%)	2 (4) 1 x dislodged nozzle 1 x irritation / mucus	3 (6) 1 x bleeding 1 x discomfort 1 x unsuccessful on one side	1.00

Monash Children's Hospital

Other Secondary Outcomes

	Lignocaine / Phenylephrine	Placebo	P value
Any NG tube insertion complication, No. (%)	14 (28)	19 (38)	0.29
Bleeding	1 (2)	4 (8)	N/A
Vomiting / gagging / retching	7 (14)	6 (12)	
Bleeding and vomiting	1 (2)	4 (8)	
Misplacement	4 (8)	3 (6)	
Dislodgement	0 (2)	1 (2)	
Other	2 (4) §	1 (2) ¶	

Children's Hospital

Summary

- No difference in primary outcome
- No difference in secondary outcomes
- No difference in complications

- NGT insertion is associated with very high observational scores for pain / distress (FLACC, VAS)

Monash Children's Hospital

Discussion

Monash Children's Hospital

Pain or Distress?

Monash Children's Hospital

Pain and distress in young children

- Difficult to differentiate!

- Similar results (i.e. no benefit for local anaesthetic) for a recent study of lignocaine gel vs placebo for urinary catheterization in young children.

Uspal NG, Strelitz B, Gritton J, Follmer K, Bradford MC, Colton TL, et al. Randomized Clinical Trial of Lidocaine Analgesia for Transurethral Bladder Catheterization Delivered via Blunt Tipped Applicator in Young Children. *Pediatric emergency care*. 2018;34(4):273-279.

Monash Children's Hospital

Other limitations

- Convenience sampling
  - Depended on ED workload / staff availability
- Spectrum bias
  - Easier to recruit those who are “less sick”
- Clinical staff rather than research assistants

Monash Children's Hospital

Timeline

Funding

Ethics

Patient recruitment and data collection

Analysis & write-up

Monash Children's Hospital

Future directions

- Do we need another observational pain scale for young (pre-verbal) children?

- Further RCTs: Midazolam
  Nitrous oxide
  ?Ketamine

Monash Children's Hospital

Conclusion

- Lignocaine / phenylephrine nasal spray is **not superior to saline placebo** in reducing the pain and distress associated with nasogastric tube insertion in young children.

Monash Children's Hospital

Conclusion

- **Further research in young children is needed** to find a way to reduce the pain and distress associated with this common ED procedure.

Monash Children's Hospital

Acknowledgements

- Patients and families
- ED staff at Monash Medical Centre, Clayton
- Emma Ramage, RN, research coordinator, ED
- Renise Teh, Claire Vosk, Sandra Kong and Helen Kopp
  - Trial Pharmacists, Monash Health Pharmacy

Monash Children's Hospital

Questions?

Simon.craig@monash.edu

@DrSimonCraig

Monash Children's Hospital