

Amethocaine (Ametop™) versus EMLA™ for successful intravenous cannulation in a children's emergency department



A randomised, double-blind controlled study
Clinton Newbury and Dr. David Herd



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Acknowledgements

- Clinton Newbury, 4th year medical student.

Statement of Author Contributions

CN designed the study, undertook the data collection and drafted the manuscript. DH conceived the study idea, helped with study design, analysed the data. CN and DH edited the manuscript. DH takes responsibility for the paper as a whole.



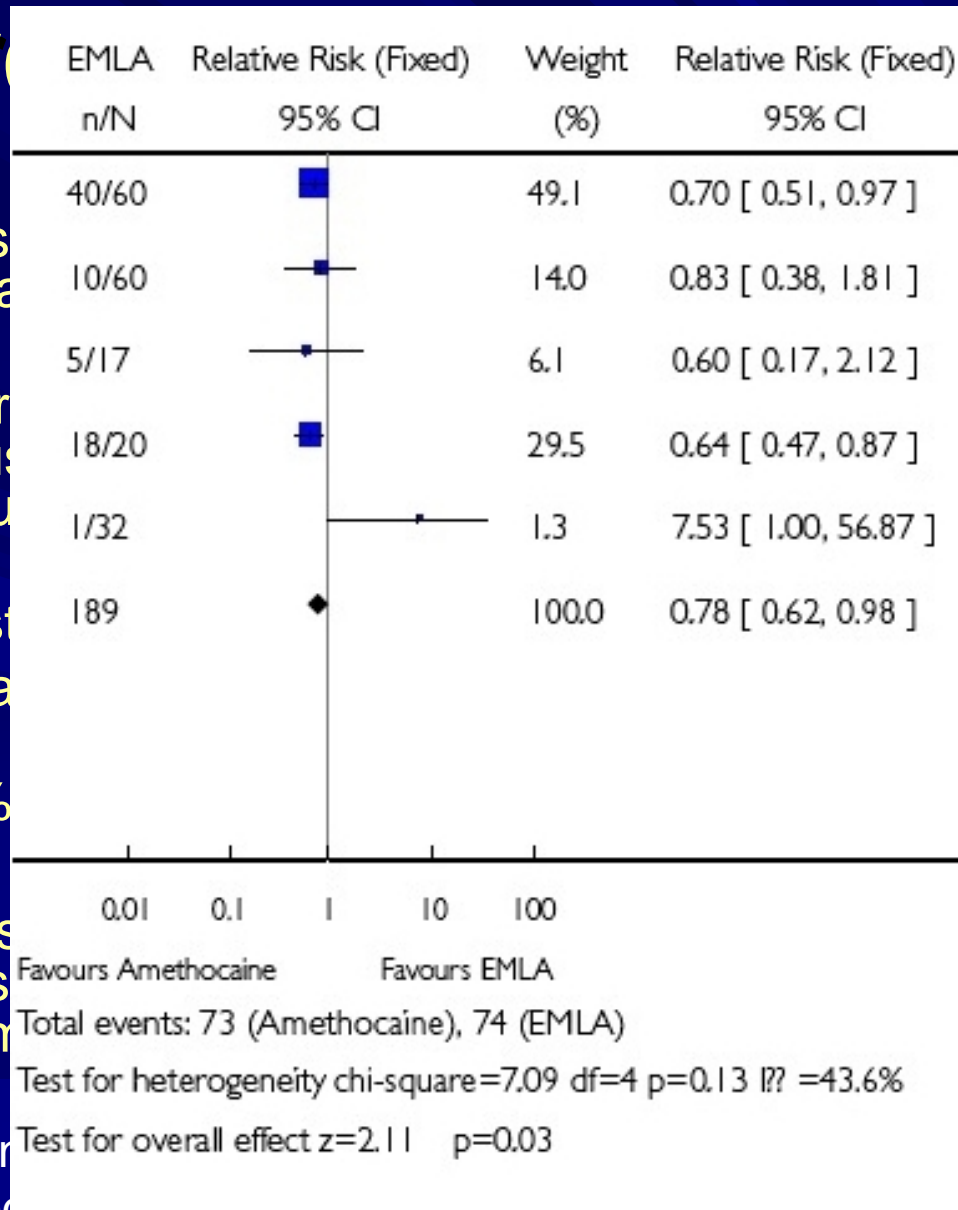
Acknowledgements

- Clinton Newbury, 4th year medical student.
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- Staff of the Starship Children's Emergency Department and the children and their families.



Background

- Topical anaesthetic cream is the standard treatment for acute pain in children.
- Starship emergency department is the standard for intravenous analgesia for children with acute pain.
- Cochrane systematic review found that amethocaine reduces pain in children with acute pain. RR 0.78 (95% CI 0.62, 0.98).
- Two questions remain:
 - 1. Do topical anaesthetics increase the risk of adverse events?
 - 2. Are the cost implications of amethocaine worth the reduction in pain?



Lander JA. EMLA and children's pain associated with needle insertion. CD004236. Issue 3, 2006

and Amethocaine for reduction of children's pain associated with needle insertion (Review)


Lander JA, Weltman BJ, So SS



THE COCHRANE COLLABORATION®

Cochrane review prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library*

<http://www.thecochranelibrary.com>



WILEY
Publishers Since 1807

Review for reduction of children's pain associated with needle insertion (Review)
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Background

- Amides and esters
- Amides metabolised in liver, risk of systemic toxicity higher
- Esters metabolised by esterases in skin, blood. By product PABA is a potent allergen.
- The ideal topical anaesthetic cream and reality?

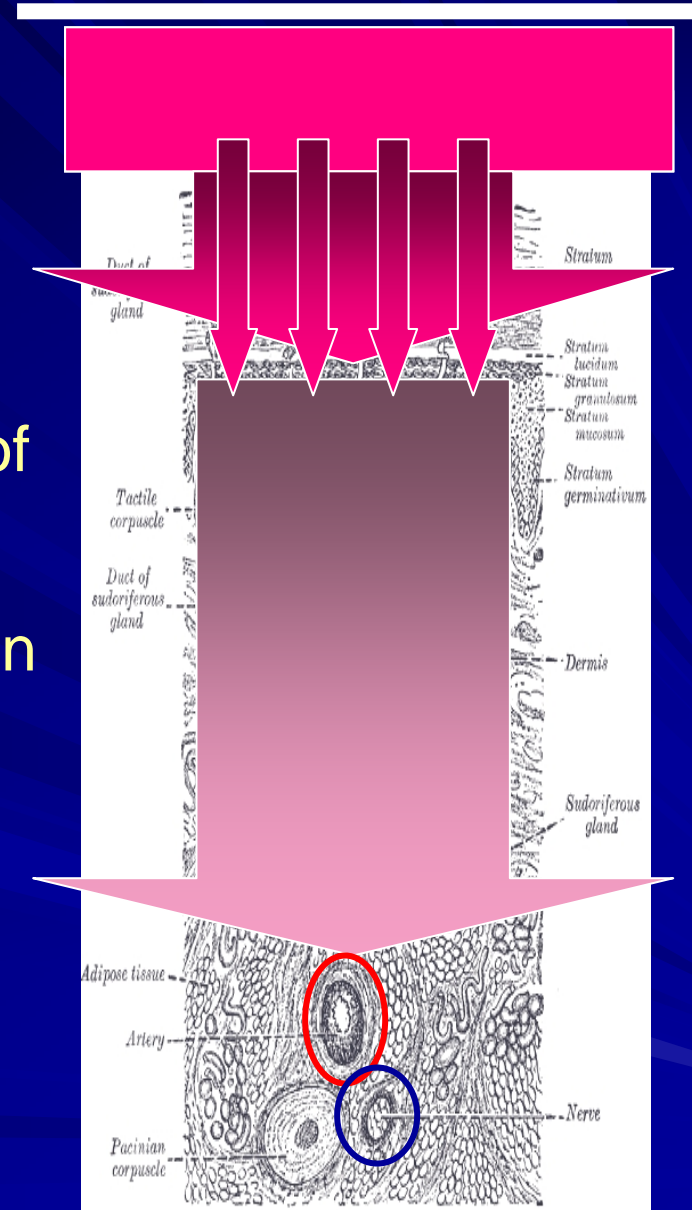


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Topical anaesthetic agents

- EMLA Since before 1983 worldwide
- Amethocaine
 - Ametop (UK, NZ, not US)
 - AnGel (Australia)
 - S-caine peel (US)
- Lignocaine
- Liposomal lignocaine
 - ELA-max (US, Canada)
- [Synera (US)]
- [Iontophoresis]
- [Lasers]
- [Zingo!]

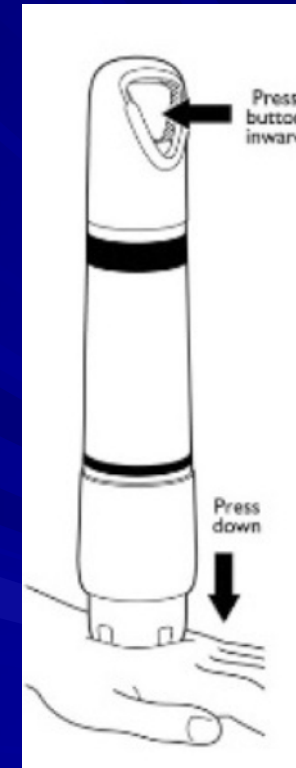




Image from FDA.com



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EMLA versus Ametop

	EMLA 	Ametop 
Age	Use above three months	Use above three months
Minimum application time	60-90 minutes (1.5 hours)	30-45 minutes
Removal time	1-4 hours	45 min post application
Duration of pain relief	Minimum of 2 hours post removal	4-6 hours post removal
Prescribing advice	< 12 months 2g total dose > 12 months 2g per site	1.5g sufficient for 2 sites, up to 30cm ²
Skin changes	Blanching	Erythema

Note: Recommendations as per Acute Pain Service: October 2006.

EMLA comes in 5g tubes. Ametop comes in 1.5g tubes.



Hypotheses

1. Ametop may increase the success of intravenous cannulation compared to EMLA due to less vasoconstriction.
2. Ametop has previously proved more effective in ward and clinic settings. Would this be the case in a children's emergency department?
3. Could ametop save money and time due to its faster onset of action.



Aims

1. To determine if Ametop increases the success of intravenous cannulation compared to EMLA?
2. To determine if Ametop provides superior pain relief to EMLA in the Children's Emergency Department.
3. To develop an economic evaluation model.



Method

Randomised, double-blind controlled study

- Children aged 3 months to 15 years offered topical anaesthesia for intravenous cannulation were eligible

- **First step**

Conducted at triage by nurses
Consent and Randomisation



- **Second step**

Intravenous cannula inserted by doctor
Doctor completes data collection form
Pain of procedures observed in a convenience sample



Method

- Power calculation based on 70% success rate with a 10% clinically significant increase, $p = 0.05$ and power 0.8 requires 330 children in each group
- Power was not calculated for the secondary observed cohort as we had a limited time span and resources
- Northern X Ethics Committee approval NTX06/10/128 with special dispensation for verbal consent at triage.
- ADHB research number A+3584
Australian Clinical Trials Register:
ACTRN012606000409572



First step

Standardised explanation of trial

Verbal consent?

YES

NO

Normal practice

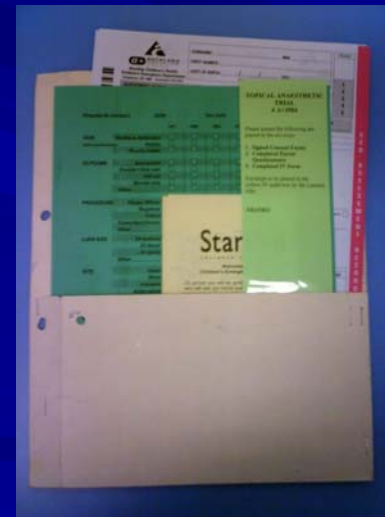
Randomised

Cream applied

Used tube collected

Note removal time

Written consent form given



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Second step

Doctors inserts cannula and completes the data form



Written consent form signed by the caregiver and the questionnaire done



Data form placed in collection box



	Hospital ID: (sticker)	DOB:	Sex (m/f):				Date:
			1ST	2ND	3RD	4TH	
VEIN <small>(before transillumination)</small>	Visible & distended	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Visible	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Poorly visible	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
OUTCOME	Successful	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Couldn't find vein	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Fell out	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Bloods only	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
PROCEDURE	House Officer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Registrar	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Fellow	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Consultant/Senior	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
LUER SIZE	24 (yellow)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	22 (blue)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	20 (pink)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
SITE	Hand	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Wrist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Forearm	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Antecubital	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Foot	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
PRESENT <small>(multiple allowed)</small>	Nurse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Caregiver	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Play specialist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
POSITION	Wrapped	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Lying flat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Being cuddled	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Sitting or inclined	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
ANALGESIA	None (why?)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	EMLA	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Ethyl Chloride	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Sucrose	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Entonox	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other _____	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
WEESIGHT (transillumination)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Topical Amethocaine versus EMLA

Data Collection Form v 1.0 (4 September 2006)



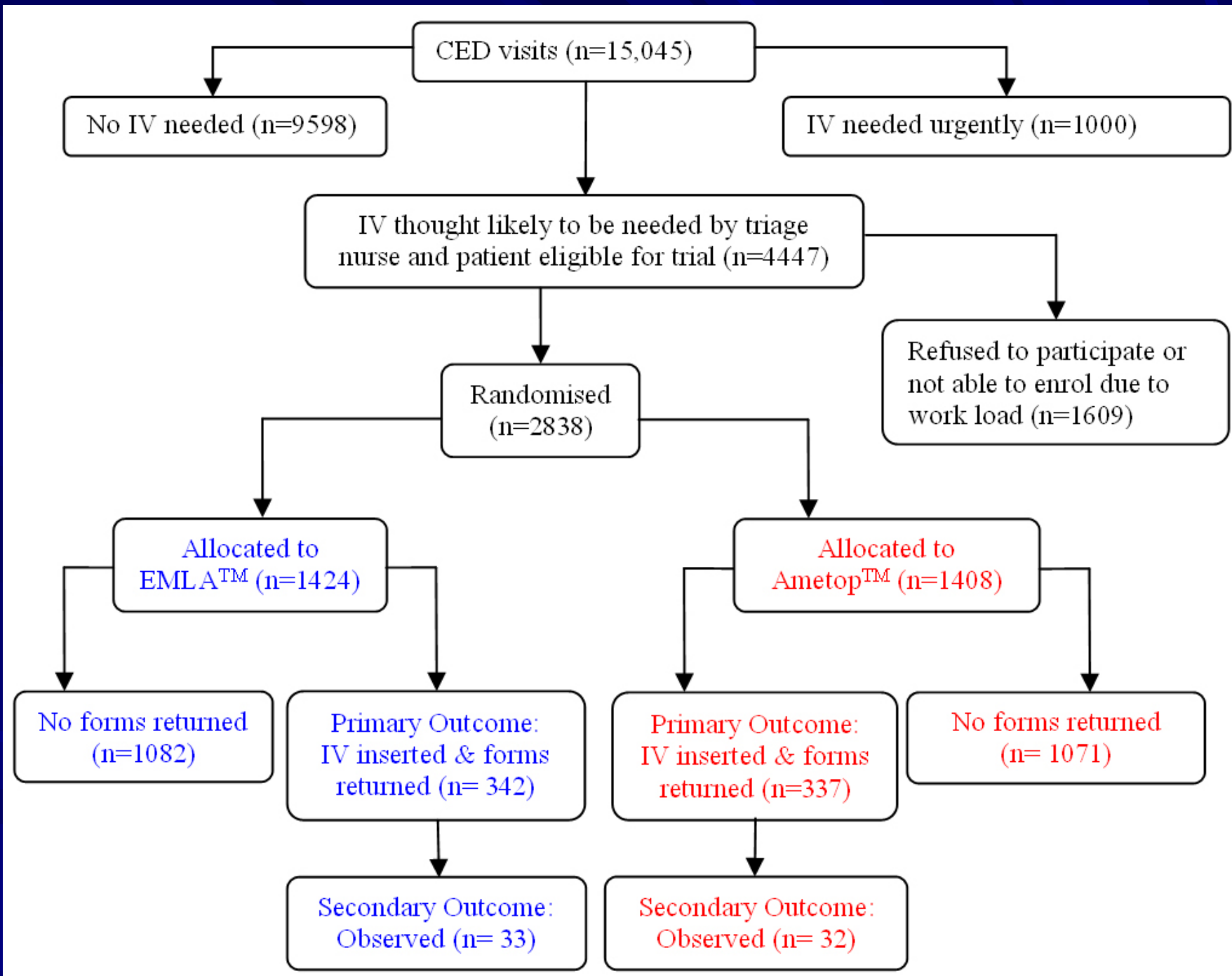
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Results

- Participants analysed on an intention to treat basis
- Primary outcome was successful first attempt at cannulation
- Secondary outcome was distress using the VAS and the FLACC score to assess pain.





Primary Outcome

Successful first attempt at cannulation



EMLA



Ametop™

Successful

253 (73.9%)

255 (75.5%)

Not successful

89

81

342

336

Chi-square ($p=0.56$)

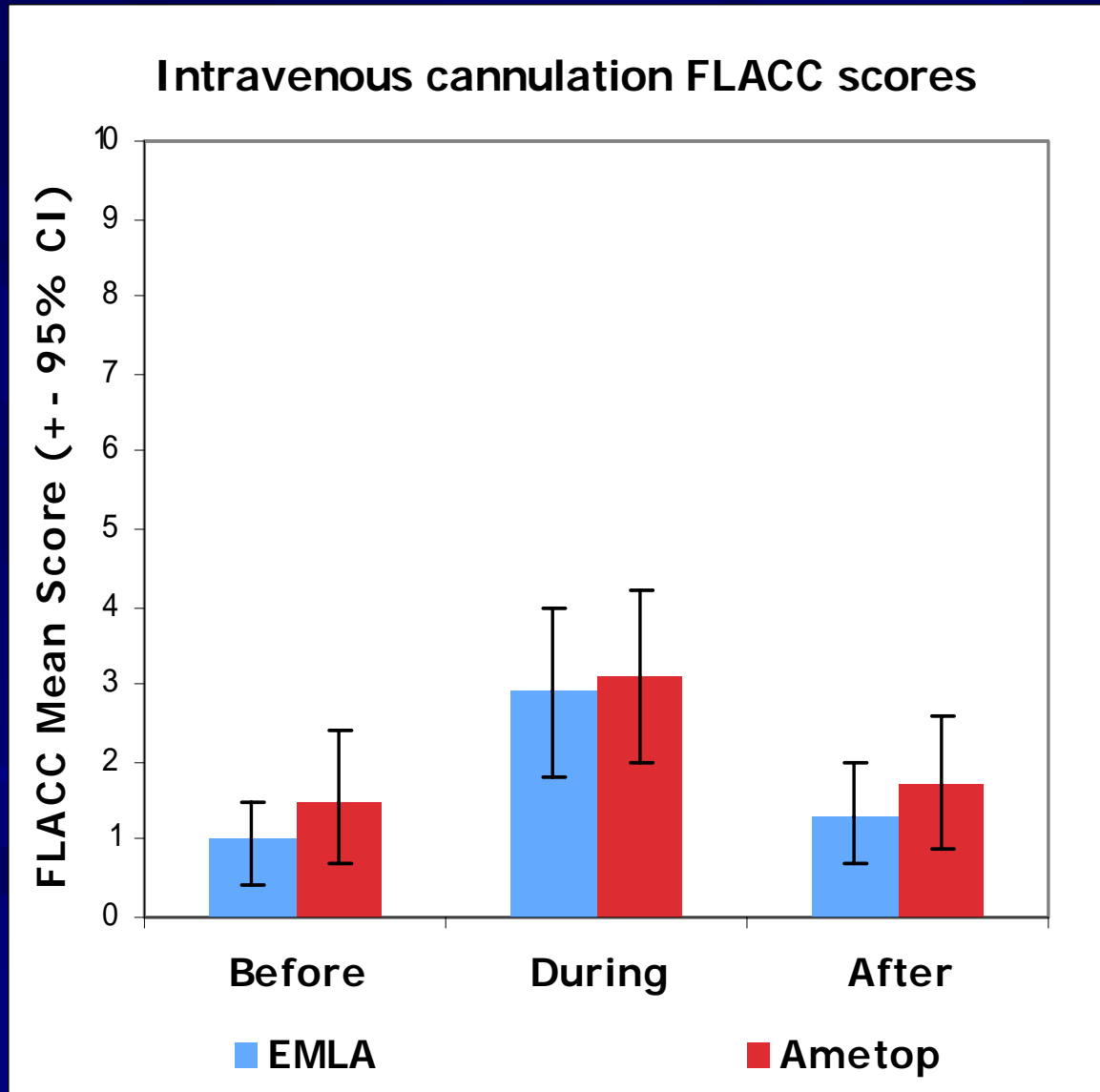
Power 80%



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Secondary Outcome



No statistically significant difference on the VAS scores or the FLACC scale using both a parametric t-test and a non-parametric Wilcoxon test.



Other outcomes

- No significant adverse effects were seen or reported during either cohort
- 61% of caregivers said they would use the cream again

	EMLA™	Ametop™
Reported skin changes	12.6%	22.5%
Thought it was a problem	11.6%	12.0%
Cream removed early	4.4%	2.7%
Average weight of cream used	2.65 g (SD 0.82)	1.09 g (SD 0.31)



Discussion

Summary



- There was no statistically significant difference in first attempt intravenous cannulation success
- Observed pain scores were similar between Ametop™ (amethocaine) and EMLA™



Discussion

Limitations

- Large group of patients not enrolled
- Difficulty in blinding could result in bias
- Allocation concealment could be circumvented



Discussion

Arendts, Stevens and Fry, BJA 2008



British Journal of Anaesthesia 100 (4): 521–4 (2008)
doi:10.1093/bja/aen003 Advance Access publication February 20, 2008

BJA

Topical anaesthesia and intravenous cannulation success in paediatric patients: a randomized double-blind trial

G. Arendts*, M. Stevens and M. Fry

Department of Emergency Medicine, St George Hospital, Kogarah NSW 2217, Australia

**Corresponding author. E-mail: glenn.arendts@sesiahs.health.nsw.gov.au*

Background. It is not known whether the choice of topical anaesthetic influences the likelihood of successful i.v. cannulation in the paediatric population. The null hypothesis of this study was that no difference exists in the initial success rate of cannulation between two commonly used topical anaesthetics.



Methods. A randomized double-blind trial conducted on patients between the age of 12 months and 12 yr presenting to a tertiary hospital emergency department. Patients requiring cannulation were randomized to either 4% amethocaine gel (AnGEL) or 5% lidocaine and prilocaine in a 1:1 emulsion (EMLA). The primary endpoint was success of initial attempt at i.v. cannulation.

Results. One hundred and seventy-seven patients were analysed of 203 enrolled. The success rate of AnGEL (73/97, 75%) and EMLA (59/80, 74%) did not significantly differ (χ^2 0.05, $P=0.82$).

Conclusions. No difference exists in the cannulation success rates between the two anaesthetics. The choice of topical anaesthetic in paediatric cannulation should be based on other

Discussion

Advantages of amethocaine

	EMLA 	Ametop 
Age	Use above three months	Use down to one month
Minimum application time	60-90 minutes	30-45 minutes
Duration of pain relief	Minimum of 2 hours post removal	4-6 hours post removal
Prescribing advice	< 12 months 2g total dose > 12 months 2g per site	1.5g sufficient for 2 sites, up to 30cm ²
methaemaglobinaemia	Rare	None
Cost	\$ 9.00 per 5g tube	\$ 6.17 per 1.5g tube (AnGel \$2.50)



Discussion Cost

Cost effectiveness of amethocaine (Ametop™) compared to EMLA™ for intravenous cannulation in a children's emergency department.



Herd DW¹, Newbury C², Brown PM³

¹ Starship Children's Hospital,

² Auckland Medical School,

³ Auckland University School of Population Health



Background

Intravenous cannulation is a common distressing procedure performed in the children's emergency department (CED). Topical anaesthetics (e.g. EMLA™) are proven to reduce discomfort. A recent Cochrane review significantly favoured amethocaine over EMLA for pain relief.¹

Aims

We set out to determine if amethocaine is more cost-effective than EMLA™ in our children's emergency department.

Method

Step One

Design a decision tree that follows each child through the department.

Step Two

Probability data sourced from a concurrent randomised controlled trial² and an intravenous quality assurance audit.³ Calculate terminal probabilities for each outcome (i-vii).

Step Three

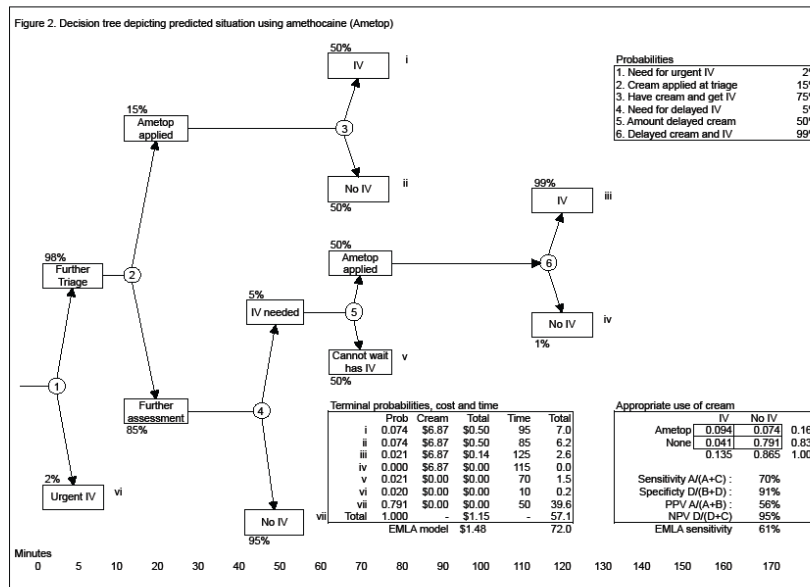
Calculate cost for each outcome using data from ADHB purchasing.

Step Four

Sensitivity analyses. Vary probability and cost points to determine most sensitive variables.

Step Five

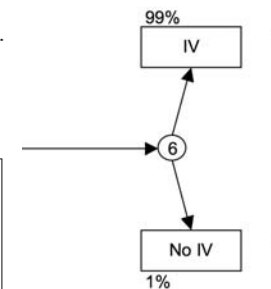
Modelling. Use predicted values to determine cost and success of new services (e.g. amethocaine).



Results

Over six months 15,045 children presented to CED and 2,858 had topical anaesthetic, 795 had cannula recorded. Of the children who had a cannula 61% received topical anaesthetic. A decision tree model for current situation has been developed (figure 1). Using this model the EMLA™ service costs NZ\$1.48 per child presenting to the department. The model is very sensitive to proportion of cream applied at triage. A

1. Need for urgent IV	2%
2. Cream applied at triage	15%
3. Have cream and get IV	75%
4. Need for delayed IV	5%
5. Amount delayed cream	2%
6. Delayed cream and IV	99%



Appropriate use of cream

	IV	No IV	
EMLA	0.083	0.222	0.304
None	0.053	0.642	0.696
	0.136	0.864	1.000

Sensitivity A/(A+C) :	61%
Specificity D/(B+D) :	74%
PPV A/(A+B) :	27%
NPV D/(D+C) :	92%

140 150 160 170



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Conclusion



- Amethocaine (Ametop™) is not more successful than EMLA™ for first attempt intravenous cannulation in children
- Amethocaine (Ametop™) has a number of other advantages over EMLA™



