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A Double-Blind, Randomised, Placebo-Controlled Trial of **Ondansetron** to reduce vomiting in children receiving **Intranasal Fentanyl** and **N_2O** for procedural sedation

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Disclosure

I have had no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial service(s) discussed in this presentation.

Background

- Intranasal fentanyl + N_2O = non parenteral combination for painful procedures
- N_2O alone = 2-8% vomiting rate
- Intranasal fentanyl + N_2O = 20-30% vomiting rate

Can we do better?

Study Question

How much can ondansetron reduce the vomiting rate in children receiving intranasal fentanyl and N_2O for procedural sedation?

Study Design

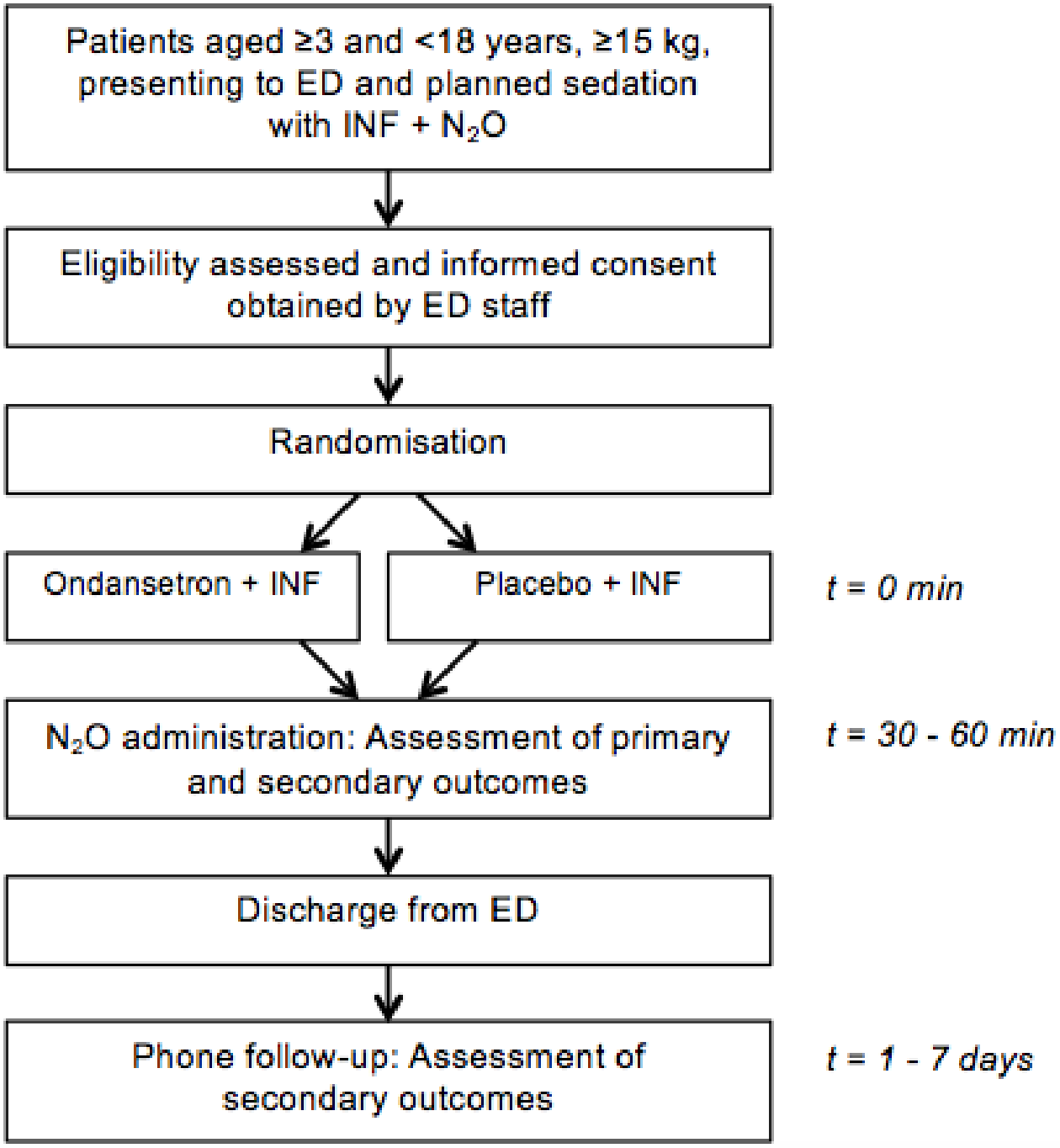
- Randomised, double-blind, placebo controlled trial
- Intervention: **oral** ondansetron or placebo 30-60 min before sedation with intranasal fentanyl and N_2O
- Sample size to show 10% reduction in vomiting at 80% power = **442 participants**

Participants

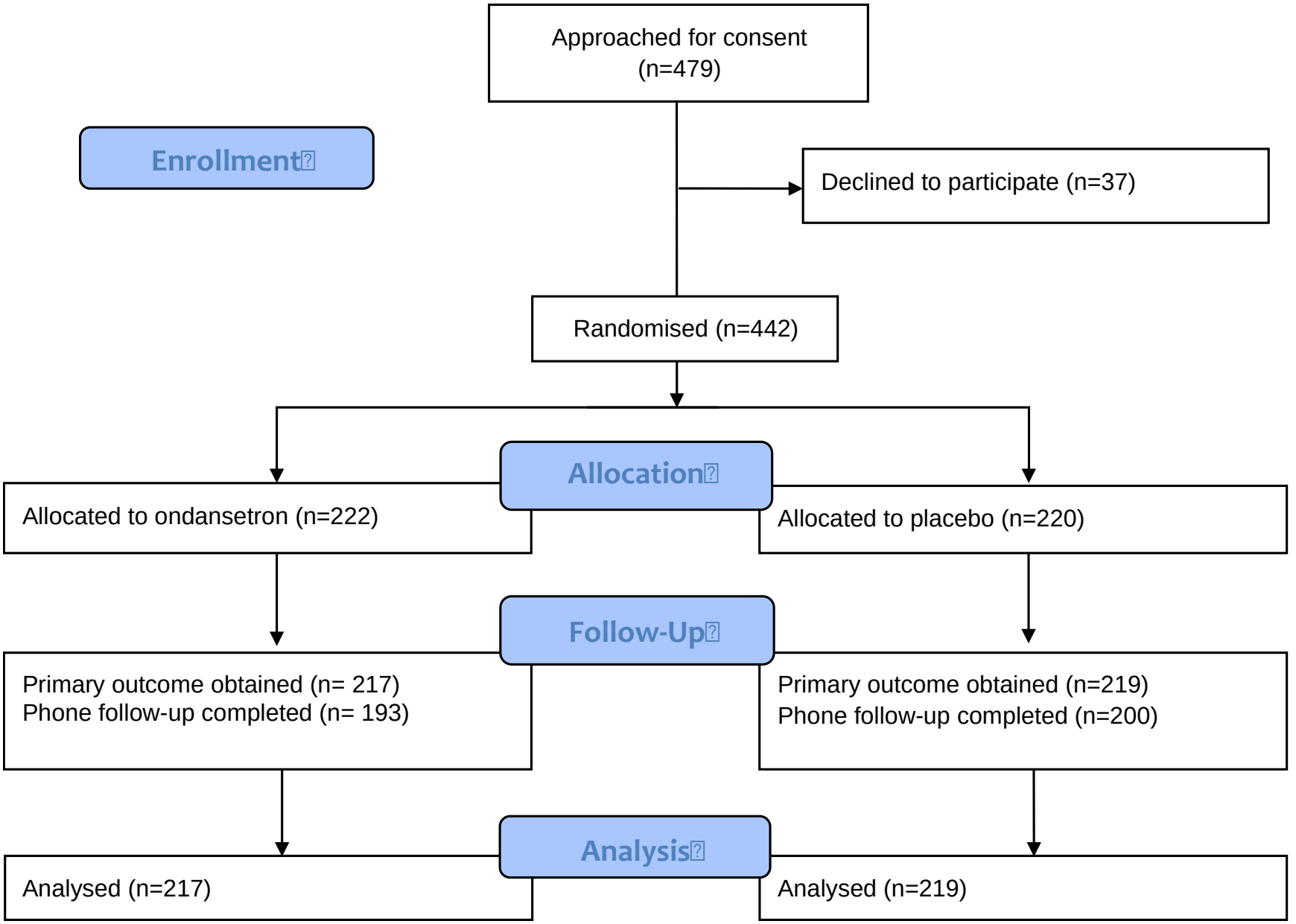
- Children 3-18 years, ≥15 kg, planned sedation with intranasal fentanyl (1.5mcg/kg) and N_2O (70%)
- Stratified by weight 15-30 kg and ≥30 kg
- Exclusion: contraindication to sedation, allergy to agents, concussed or actively vomiting

Outcomes

- Primary: early vomiting = during and up to 1 hour after sedation
- Secondary:
  - number of vomits during sedation
  - retching during procedural sedation
  - vomiting 1 to 24 hours post sedation
  - sedation duration and quality
  - adverse events


Patients aged ≥3 and <18 years, ≥15 kg, presenting to ED and planned sedation with INF + N_2O
Eligibility assessed and informed consent obtained by ED staff
Randomisation
Ondansetron + INF
Placebo + INF
t = 0 min
N_2O administration: Assessment of primary and secondary outcomes
t = 30 - 60 min
Discharge from ED
Phone follow-up: Assessment of secondary outcomes
t = 1 - 7 days

CONSORT flow diagram



Results

Baseline characteristics		
	Ondansetron	Placebo
	n=217	n=219
Age (years) mean (SD)	8.8 (3.4)	8.8 (3.3)
Male gender n (%)	136 (63)	135 (62)
Weight group n (%)		
15-30 kg	109 (50)	111 (51)
≥30kg	108 (50)	108 (49)
Procedure type n (%)		
Fracture reduction	160 (74)	169 (77)
Dislocation reduction	7 (3)	10 (5)
Splint/cast application	16 (7)	13 (6)
Laceration repair	15 (7)	12 (5)
Abscess drainage	3 (1)	8 (4)
Other	18 (8)	10 (5)

Results

Baseline characteristics		
	Ondansetron	Placebo
	n=201	n=205
Fasting status		
Hours, median (IQR)	3.9 (2.9,5.6)	5.0 (3.9,6.3)
Proportion ≥1 hour liquid	197 (99)	203 (99)
Proportion ≥2 hours liquid	178 (89)	191 (93)
Proportion ≥4 hours liquid	103 (52)	116 (57)
Proportion ≥6 hours liquid	43 (22)	42 (20)
Proportion ≥2 hours solid	190 (95)	201 (99)
Proportion ≥4 hours solid	131 (65)	151 (74)
Proportion ≥6 hours solid	68 (34)	66 (32)

Results

Primary Outcome							
	Ondansetron n=217		Placebo n=219		Difference in proportions	(95% CI)	p-value
Early vomiting*, n/N (%)	26/217	(12)	36/ 219	(16)	-4.6	(-11.1,2.0)	0.18

*Defined as vomiting during the sedation until discharge or within one hour from the start of the sedation (whichever comes first)

Results

Secondary Outcomes							
	Ondansetron n=217		Placebo n=219		Difference in proportions	(95% CI)	p-value
If vomited, number of vomits, n/N (%)							
1	24/26	(92)	29/34	(85)			
2	2/26	(8)	4/34	(12)			
Unknown	0/26	(0)	1/34	(3)			
Retching during procedure, n/N (%)	27/217	(12)	33/217	(15)	-2.8	(-9.3,3.7)	0.41
Any vomiting*, n/N (%)	41/196	(21)	63/204	(31)	-9.9	(-18.5,-1.4)	0.02

*Up to 24 hours after the start of the procedure

Results

Secondary Outcomes							
	Ondansetron n=217		Placebo n=219		Difference in proportions	(95% CI)	p-value
Procedure affected by vomiting, n/N (%)	14/217	(6)	11/219	(5)	1.5	(-2.8,5.8)	0.53
abandoned, n/N (%)	4/217	(2)	4/219	(2)	0.0	(-2.8,2.9)	0.99
prolonged, n/N (%)	6/217	(3)	6/219	(3)	-0.1	(-3.2,2.9)	0.99
other, n/N (%)	4/217	(2)	1/219	(0)	1.9	(-1.7,5.5)	0.21
Optimal sedation, n/N (%)	203/217	(94)	192/217	(88)	5.0	(-0.3,10.4)	0.07

There were only 2 minor adverse events, both in the placebo group.

Limitations

- Use of ondansetron syrup vs wafer
- Generalisability in settings using lower concentrations of N_2O or performing less painful procedures
- Did not address higher risk sub-groups (preprocedural nausea or individuals known to vomit easily)

Discussion

- Largest trial describing this sedation technique, first to study premedication
- Early vomiting lower than previously reported, may explain null findings
- Very few adverse events other than vomiting

Conclusion

Ondansetron does not significantly reduce vomiting during or shortly after procedural sedation with combined intranasal fentanyl and N_2O.

Merci! Thank you!

Thank you to all **families** who have participated

Study team:

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Extra slides

Table 1: Baseline characteristics		
	Ondansetron	Placebo
	n=217	n=219
Study related procedures		
Prior non-procedural fentanyl, n (%)	65 (30)	71 (32)
Prior non-procedural fentanyl dose (mcg/kg), mean (SD)	1.7 (0.7)	1.9 (1.1)
Spat out (within 10 minutes) study drug, n (%)	1 (0)	1 (0)
Procedural fentanyl dose (mcg/kg), mean (SD)	1.4 (0.4)	1.4 (0.2)
Total fentanyl dose (mcg/kg), mean (SD)	2.0 (0.9)	2.0 (1.1)
Time between last non-procedural INF and procedure start (min), mean (SD)	152.7 (56.8)	159.2 (70.5)
Time between procedural INF and procedure start (min), mean (SD)	42.8 (16.8)	42.1 (15.6)
Time between study drug and procedure start (min), mean (SD)	43.2 (16.8)	44.3 (17.4)
Duration of sedation procedure (min), mean (SD)	13.5 (6.7)	14.0 (7.3)