Surfactant Nebulization to Prevent Early Intubation in Preterm Infants: A Systematic Review and Meta-Analysis

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Disclosure

- No relevant competing interests

Background

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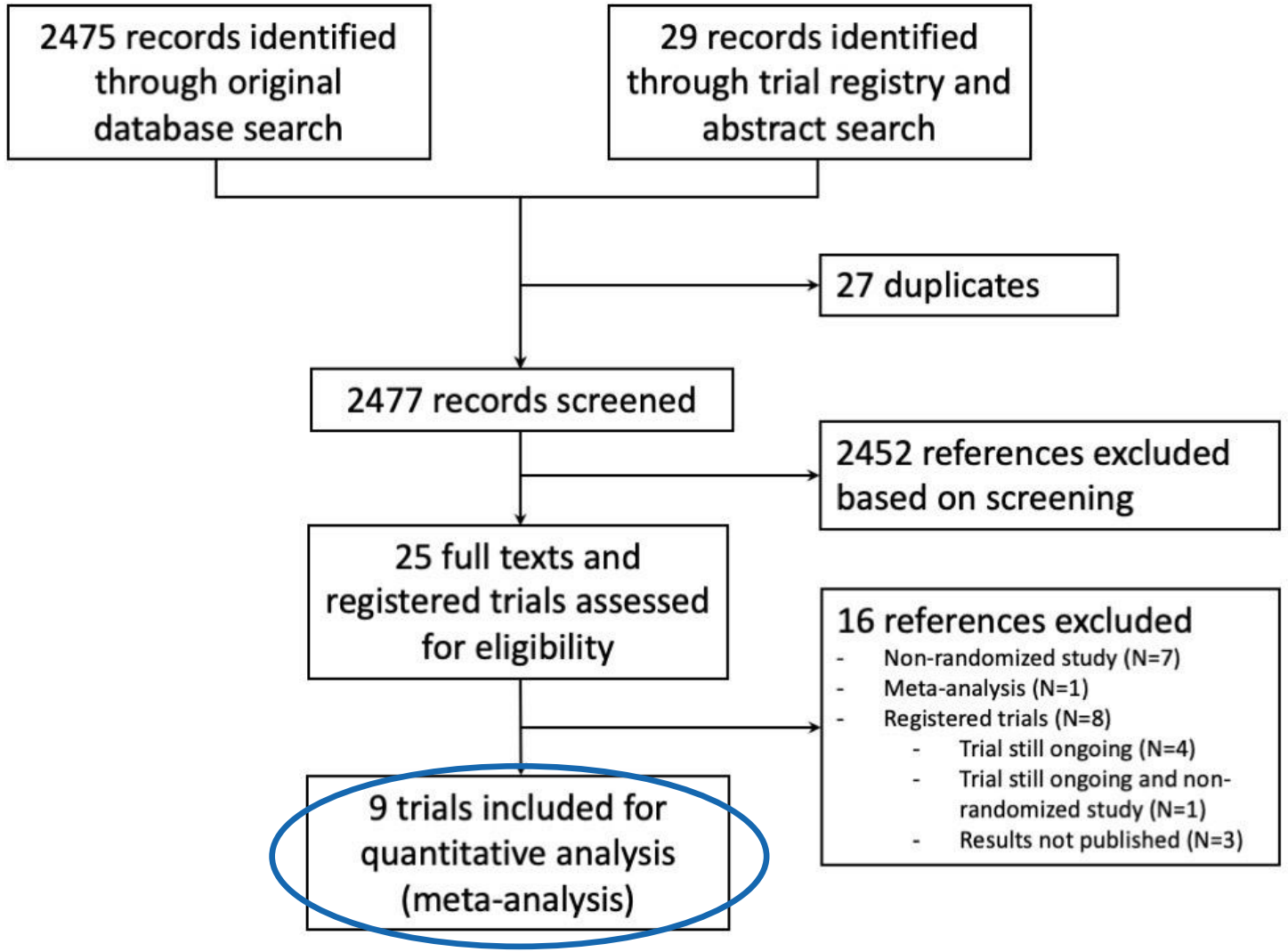
- Objectives:
  - Primary: Determine effectiveness of SN in preventing intubation among preterm infants
  - Secondary: Assess potential effect modifiers and effects on relevant morbidities

Methods

- Data inclusion
  - Data searched through March 23, 2021
- RCTs extracted
  - Population: Preterm infants <37 weeks gestation
  - Intervention: SN
  - Controls: non-invasive respiratory support alone or intratracheal surfactant application
  - Primary Outcome: intubation rate at 72 hours after birth
- Pre-defined subgroup analysis
  - Gestational age, type of nebulizer, surfactant type and surfactant dosage

Flow chart

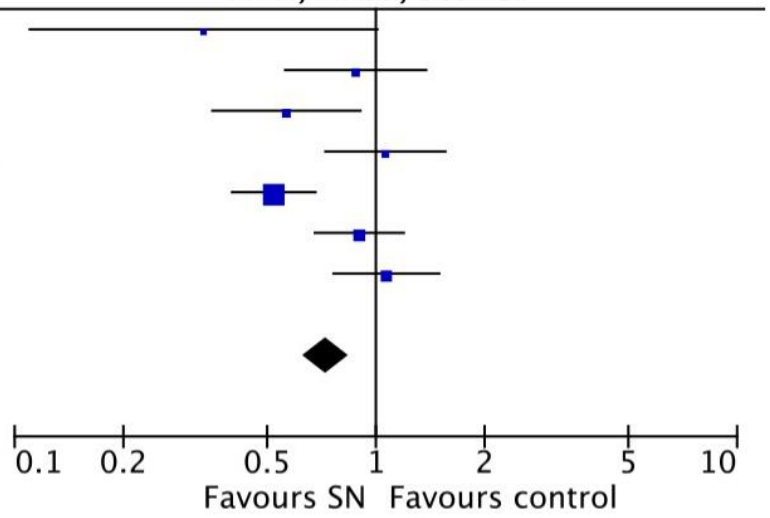

2475 records identified through original database search
29 records identified through trial registry and abstract search
27 duplicates
2477 records screened
2452 references excluded based on screening
25 full texts and registered trials assessed for eligibility
16 references excluded
- Non-randomized study (N=7)
- Meta-analysis (N=1)
- Registered trials (N=8)
  - Trial still ongoing (N=4)
  - Trial still ongoing and non-randomized study (N=1)
  - Results not published (N=3)
9 trials included for quantitative analysis (meta-analysis)

Results – Intubation rate

Study or Subgroup	Nebulized surfactant Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
* Guo 2007	3	16	9	16	3.6%	0.33 [0.11, 1.01]	2007
NCT02074059 2017	18	39	21	40	8.2%	0.88 [0.56, 1.38]	2017
Minocchieri 2019	13	32	23	32	9.1%	0.57 [0.35, 0.91]	2019
NCT02528318 2019	17	24	16	24	6.3%	1.06 [0.73, 1.56]	2019
Cummings 2020	54	202	102	199	40.7%	0.52 [0.40, 0.68]	2020
EUCTR-004547-36 2021	59	110	31	52	16.7%	0.90 [0.68, 1.19]	2021
* NCT02636868 2021	62	142	29	71	15.3%	1.07 [0.76, 1.50]	2021
Total (95% CI)		**565**		**434**	**100.0%**	**0.73 [0.63, 0.84]**	
Total events	226		231				

Heterogeneity: $Chi^2 = 20.62$, df = 6 (P = 0.002); $I^2 = 71\%$

Test for overall effect: Z = 4.41 (P < 0.0001)



Number needed to treat: 8

Results II – Effect modifiers

Effect modifier	RR (95% CI)	p
Gestational age		
- <28 weeks	1.12 (0.74 to 1.70)	0.59
- **≥28 weeks**	**0.70 (0.60 to 0.82)**	**<0.001**
Nebulizer type		
- Capillary	1.02 (0.81 to 1.27)	0.90
- **Jet nebulizer**	**0.52 (0.40 to 0.68)**	**<0.001**
- **Vibrating membrane**	**0.78 (0.61 to 1.00)**	**0.05**
Surfactant dose and type		
- <200 mg/kg synthetic	1.02 (0.81 to 1.27)	0.90
- **≥200 mg/kg animal-derived**	**0.62 (0.52 to 0.75)**	**<0.001**

Results III – Clinical outcomes

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Outcome	N infants	Combined effect RR (95% CI)	p
Death	1,000	0.89 (0.30 to 2.65)	0.83
BPD (oxygen need at 36 wks PMA)	998	0.99 (0.74 to 1.32)	0.96
Severe IVH (≥ grade 3)[34]	994	0.65 (0.29 to 1.44)	0.29
Air leak	1,000	1.03 (0.69 to 1.52)	0.90
Pulmonary hemorrhage	904	0.48 (0.14 to 1.68)	0.25
Sepsis	904	0.90 (0.58 to 1.38)	0.62
Any ROP[35]	423	0.76 (0.37 to 1.54)	0.44
NEC (≥ stage 2)[36]	968	1.13 (0.49 to 2.63)	0.78

Discussion/Outlook

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- SN reduced the intubation rate in preterm infants
- Higher efficacy for higher GA, specific types of nebulizers and higher dose of animal-derived surfactant
- No difference in relevant neonatal morbidities and mortality
- Quality of evidence was low owing to risk of bias and imprecision

- Data from an RCT on *prophylactic* SN is currently being evaluated

Thank you for your attention!

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