

Supplemental Digital Content

Figure 1: Funnel plot for the Therapeutic failure

Funnel plot of standard error (log RR) by the risk ratio(RR) for therapeutic failure for the studies included in the meta-analysis. Each dot corresponds to one study and the dotted line in the center shows the pooled RR estimate of the meta-analysis. Given the low number of studies, these results are not conclusive.

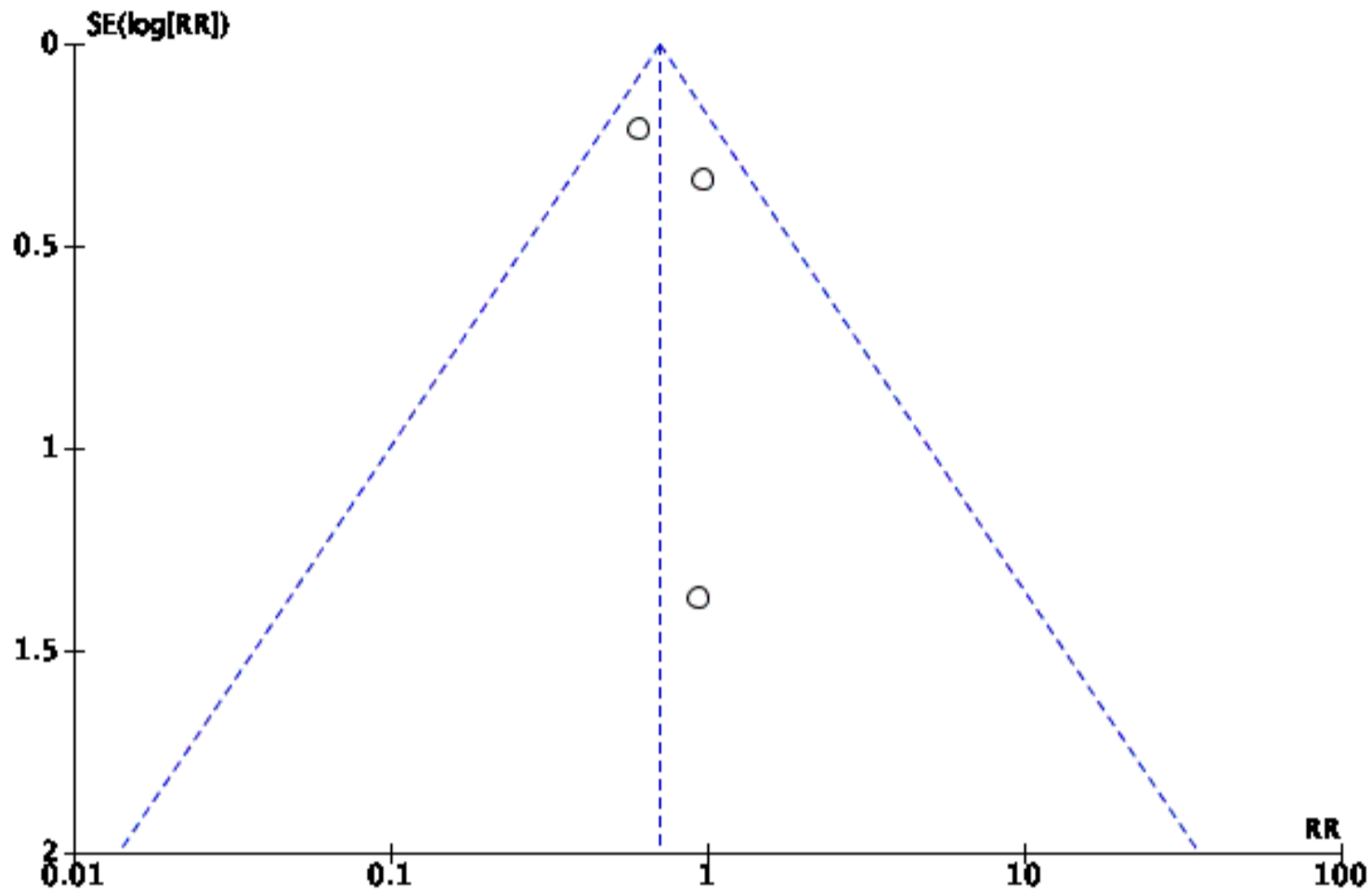


Figure 2: Funnel plot for the invasive mechanical ventilation:

Funnel plot of standard error (log RR) by the risk ratio (RR) for invasive mechanical ventilation for the studies included in the meta-analysis. Each dot corresponds to one study and the dotted line in the center shows the pooled RR estimate of the meta-analysis. Given the low number of studies, these results are not conclusive.

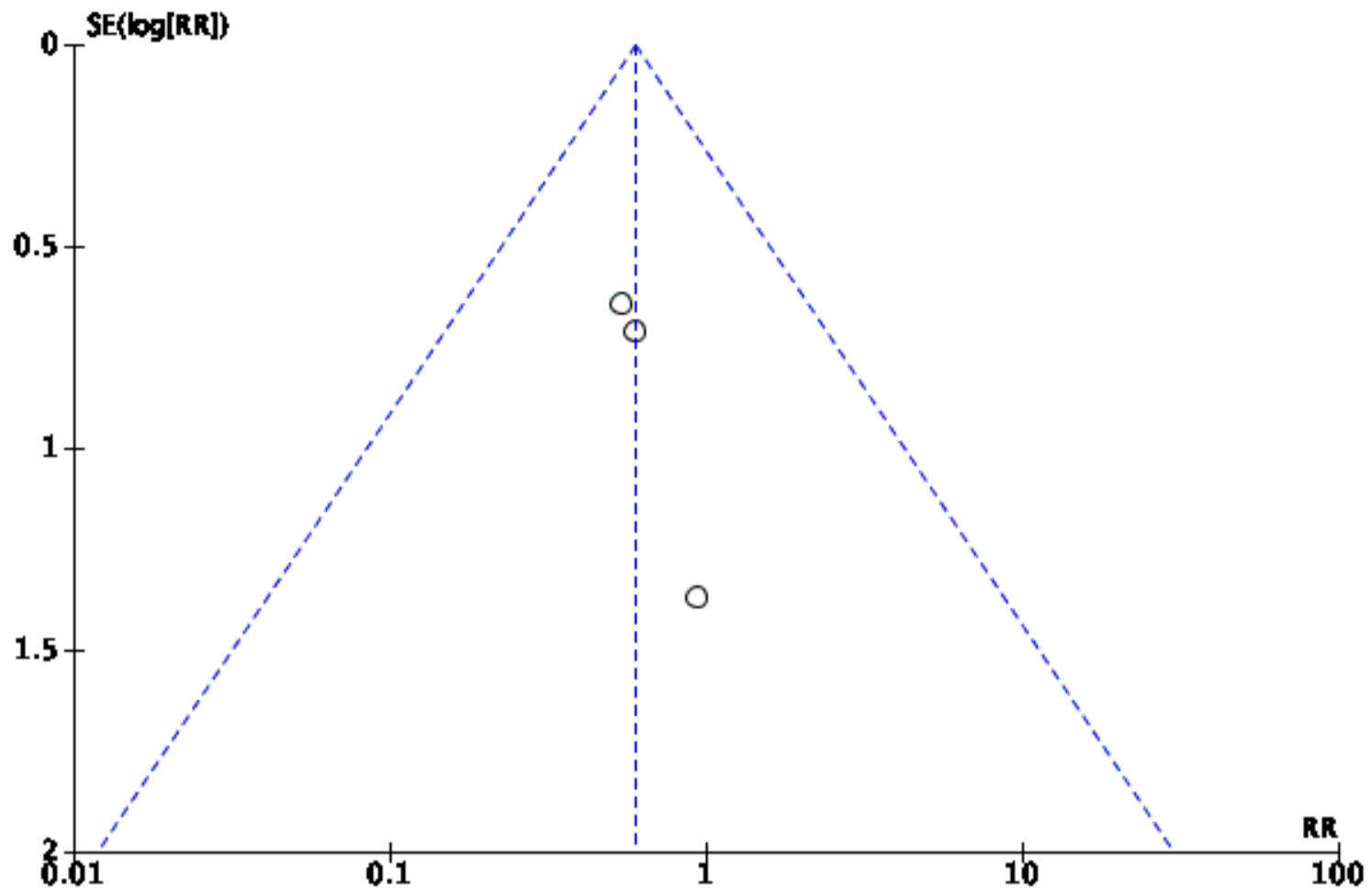


Figure 3: Length of therapy.

Forest plot shows the mean difference (MD) for the length of therapy, in days. Horizontal bars denote 95% confidence intervals (95% CIs). Studies are represented as blue squares centered on the point estimate of the result of each study. The area of the square represents the weight given to the study in the meta-analysis. The black diamond represents the overall combined estimated effect and its 95% CI.

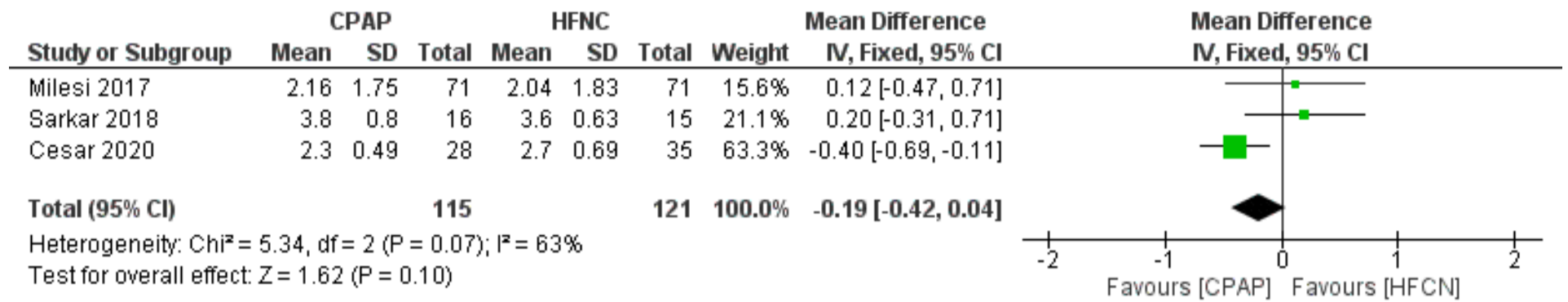


Figure 4: Length of no invasive ventilatory therapy.

Forest plot shows mean difference (MD) for the length of no invasive ventilatory therapy, in days. Horizontal bars denote 95% confidence intervals (95% CIs). Studies are represented as blue squares centered on the point estimate of the result of each study. The area of the square represents the weight given to the study in the meta-analysis. The black diamond represents the overall combined estimated effect and its 95% CI.

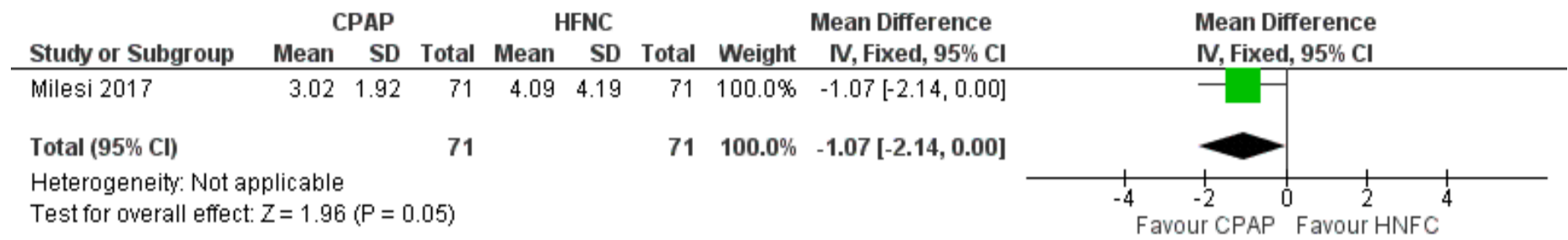


Figure 5. GRADE summary of findings table with all the outcomes. This figure displays the Summary of Findings (SOF) table, which described the quality of the evidence per outcome according to the GRADE working group approach. Explanations in the footnotes provide justification for the rating of the evidence

Nasal Continuous positive airway pressure (CPAP) compared to high-flow nasal cannula (HFNC) for infants and children with moderate to severe bronchiolitis					
Patient or population: infants and children with moderate to severe bronchiolitis					
Intervention: Nasal Continuous positive airway pressure (CPAP)					
Comparison: High-flow nasal cannula (HFNC)					
Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with HFNC	Risk difference with CPAP
Therapeutic failure	236 (3 RCTs)	⊕⊕○○ LOW ^{a,b}	RR 0.70 (0.50 to 0.99)	413 per 1,000	124 fewer per 1,000 (207 fewer to 4 fewer)
Invasive Mechanical Ventilation	236 (3 RCTs)	⊕⊕○○ LOW ^{a,c}	RR 0.60 (0.25 to 1.43)	107 per 1,000	43 fewer per 1,000 (81 fewer to 46 more)
Apnea	205 (2 RCTs)	⊕⊕⊕○ MODERATE ^{c,d}	RR 0.40 (0.08 to 1.99)	47 per 1,000	28 fewer per 1,000 (43 fewer to 47 more)
Time until therapeutic failure	205 (2 RCTs)	⊕⊕⊕○ MODERATE ^a	-	The mean time until therapeutic failure was 6.7 hours	MD 3.16 hours higher (1.55 higher to 4.77 higher)
Length of Therapy	236 (3 RCTs)	⊕○○○ VERY LOW ^{a,c,e}	-	The mean length of Therapy was 2.79 days	MD 0.19 days lower (0.42 lower to 0.04 higher)
Length of non-invasive ventilation	142 (1 RCT)	⊕⊕⊕○ MODERATE ^f	-	The mean length of non-invasive ventilation was 3.02 days	MD 1.07 days lower (2.14 lower to 0)
Length of PCCU stay	236 (3 RCTs)	⊕⊕○○ LOW ^{a,c}	-	The mean length of PCCU stay was 5.02 days	MD 0.02 days higher (0.38 lower to 0.42 higher)
Length of stay	63 (1 RCT)	⊕⊕○○ LOW ^{c,g}	-	The mean length of stay was 8 days	MD 0 days (0.57 lower to 0.57 higher)
Adverse events	235 (3 RCTs)	⊕⊕⊕○ MODERATE ^h	RR 2.47 (1.17 to 5.22)	58 per 1,000	86 more per 1,000 (10 more to 246 more)

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio; MD: Mean difference

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Explanations

a. The three studies had high or unclear risk of selection and performance biases

b. Imprecise, because the 95%CI was very wide. This means the effect may range from a relative reduction of the risk of 1% to a reduction of 50%

c. Imprecise, because on one side of the 95%CI CPAP increases the risk (increases the risk of events, or increases the mean of the continuous outcome), and on the other, it reduces the risk (reduces the risk of events, or reduces the mean of the continuous outcome)

d. Although both trials (Milesi et al. 2017 and Cesar et al. 2020) were unblinded, it is very unlikely this may have affected the outcome (apnea) which we considered to be a hard outcome. Thus, we did not rate down due to the risk of bias.

e. Moderate heterogeneity ($I^2=63\%$)

f. The only study that provided data for this outcome (Milesi et al 2017) was unblinded

g. The only study that provided data for this outcome (Cesar et al. 2020) had high risk of bias because interventions were not blinded

h. Of the three studies, 2 had high and unclear risk of biases (performance and detection biases) (Milesi et al. 2017 and Cesar et al. 2020), Sarkar et al. study had high risk of bias, and this study provided more than half of the weight in the meta-analysis

Search Strategies

MEDLINE

OID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE

1. "Viral Bronchiolit*".ab,kw,sh,ti.
2. "Bronchiolit*".ab,kw,sh,ti.
3. "Bronchopneumon*".ab,kw,sh,ti.
4. "Respiratory Syncytial Virus*".ab,kw,sh,ti.
5. "Respiratory Syncytial Virus* Infection*".ab,kw,sh,ti.
6. 1 or 2 or 3 or 4 or 5
7. "positive-pressure respiration*".ab,kw,sh,ti.
8. "continuous positive airway pressur*".ab,kw,sh,ti.
9. "CPAP Ventilation*".ab,kw,ti.
10. "Bilevel Continuous Positive Airway Pressur*".ab,kw,ti.
11. "Biphasic Continuous Positive Airway Pressur*".ab,kw,ti.
12. "Noninvasive Ventilation*".ab,kw,sh,ti.
13. "positive end expiratory pressur*".ab,kw,ti.
14. nppv.ab,kw,ti.
15. nippv.ab,kw,ti.
16. "Oxygen Inhalation Therap*".ab,kw,sh,ti.
17. "Respiratory therap*".ab,kw,sh,ti.
18. "Cannula* nasal".ab,kw,ti.
19. "High-flow nasal cannula*".ab,kw,ti.
20. "high flow nasal*".ab,kw,ti.
21. hfnc.ab,kw,ti.
22. hfnp.ab,kw,ti.
23. hhfnox.ab,kw,ti.
24. CPAP.ab,kw,ti.
25. nCPAP.ab,kw,ti.
26. PEEP.ab,kw,ti.
27. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28. 6 and 27

EMBASE

1. Viral Bronchiolit\$.ab,kw,sh,ti.
2. Bronchiolit\$.ab,kw,sh,ti.
3. Bronchopneumon\$.ab,kw,sh,ti.
4. Respiratory Syncytial Virus\$.ab,kw,sh,ti.
5. or/1-4
6. positive-pressure respiration\$.ab,kw,sh,ti.
7. continuous positive airway pressur\$.ab,kw,sh,ti.
8. CPAP.ab,kw,ti.
9. Bilevel Continuous Positive Airway Pressur\$.ab,kw,ti.
10. Bi?level.ab,kw,ti.
11. Biphasic Continuous Positive Airway Pressur?.ab,kw,ti.
12. Non?invasive Ventilation\$.ab,kw,sh,ti.
13. n?ppv.ab,kw,ti.
14. Oxygen Inhalation Therap\$.ab,kw,sh,ti.
15. Respiratory therap\$.ab,kw,sh,ti.

16. nasal cannula\$.ab,kw,ti.
17. High-flow nasal cannula\$.ab,kw,ti.
18. High flow nasal cannula\$.ab,kw,ti.
19. high flow nasal\$.ab,kw,ti.
20. hfn\$.ab,kw,ti.
21. hfnox.ab,kw,ti.
22. peep.mp. or exp positive end expiratory pressure/
23. or/6-22
24. 5 and 23

LILACS

(tw:((tw:(ventilación no invasiva)) OR (tw:(Noninvasive Ventilation)) OR (tw:(Respiración con Presión Positiva)) OR (tw:(Respiração com Pressão Positiva)) OR (tw:(Positive Pressure Respiration)) OR (tw:(Respirator* Therap*)) OR (tw:(Terapi* Respiratori*)) OR (tw:(Respiration, Artificial)) OR (tw:(Respiración Artificial)) OR (tw:(Oxygen Inhalation Therap*)) OR (tw:(Oxigeno terapi)) OR (tw:(High-flow nasal cannula)) OR (tw:(cánula de alto flujo)) OR (tw:(PEEP)) OR (tw:(CPAP)))) AND (tw:((tw:(Bronquiolitis)) OR (tw:(bronchiolitis)) OR (tw:(bronquiolite)) OR (tw:(virus sincitial* respiratorio*)) OR (tw:(Respiratory Syncytial Virus*)) OR (tw:(Vírus Sincicia* Respiratório))))