**Supplementary appendix 1**: Methodology

Eligibility criteria

We included all RCT's and quasi-RCT's in which either individual newborn infants or clusters of newborn infants were randomized to CPAP and/or HFNC withdrawal strategies. Infants had to be born before 37 weeks' gestation, receiving noninvasive respiratory support with CPAP or HFNC and be ready for a weaning attempt. Noninvasive respiratory support could be applied by different interfaces: via face mask, nasal mask, nasal prongs, or a single nasopharyngeal tube.

Search methods

We searched MEDLINE, EMBASE, the Cochrane Central Register of controlled trials and CINAHL from inception to December 2019. Ongoing or unpublished trials were searched through trial registers (clinicaltrials.gov, EU clinical trial register, Australia and New Zealand's clinical register) and if needed by contacting the author of the study. References lists were also searched.

We used the following strategy: MeSH search terms "infant, premature", "infant", "very low birth weight" OR the text word "VLBW", "infant*", "preterm*", "premature*", "low birth weight", "neonat*", "newborn*" AND MeSH search terms "continuous positive airway pressure", "oxygen inhalation therapy", "noninvasive ventilation" OR the text words "CPAP", "high-flow", "nasal cannula", "NC", "high-flow nasal cannula", "HFNC", "heated humidified high-flow nasal cannula", "HHHFNC", "positive pressure", "distending pressure", "positive expiratory pressure", "positive end expiratory pressure", "PEEP" AND MeSH search term "ventilator weaning" OR the text words "wean*", "decreas*", "ceasing", "cessation", "stop*", "stopping", "discontinue", "withdraw*"

Study selection, Risk of bias and quality of the evidence

On search completion and following duplicate removal, two investigators (BVD/FVGD) independently performed the first screening of the retrieved studies based on title and abstract, and subsequently also the following screening based on full-text. Data were extracted by one author (BVD) and checked for accuracy by a second author (CVD). Extracted data included characteristics regarding the study (setting, publication year, etc.), the population, the intervention and the outcomes. A third author (FC) acted as adjudicator when an agreement could not be reached.

Two investigators (BVD/JL) assessed independently the risk of bias in individual studies using the Cochrane tool for bias assessment in RCT's [1]. We assessed studies using the following criteria: random sequence generation, allocation concealment, blinding of intervention, completeness of follow-up and blinding of outcome measurement assigning a rating of "Yes" (no risk), "No" (high risk) or "Unknow" for each category.

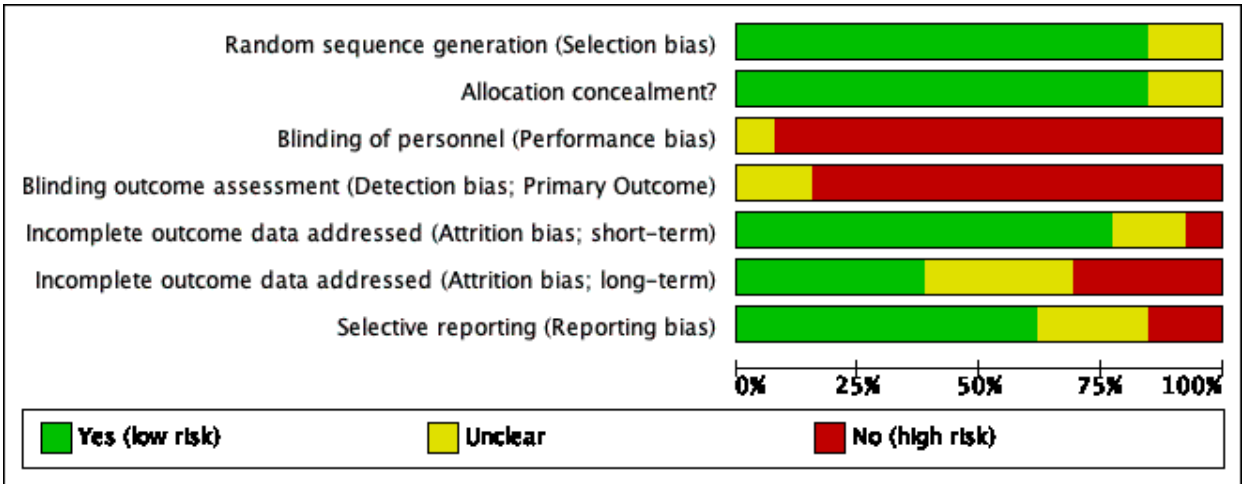
Under the assumption that true heterogeneity between studies would be present, the random-effects model was used for all meta-analyses.

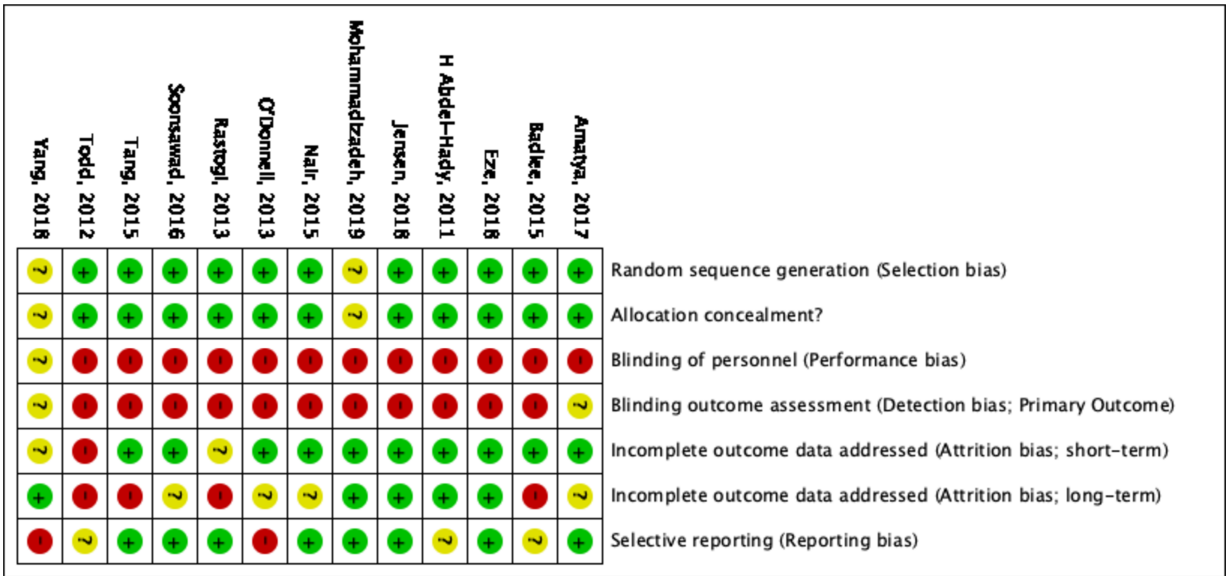
Statistical analysis

The statistical analyses were performed using RevMan 5.3 (Cochrane Collaboration). Under the assumption that true heterogeneity between studies would be present, the random-effects model was used for all meta-analyses. Treatment effects for categorical data were expressed as a risk ratio (RR) and for continuous outcomes as a mean differences (MD) using the Mantel-Haenzel and inverse variance method. For studies[9–11,16,17] only reporting medians and interquartile (IQR), we estimated the mean and standard deviation (SD) using the methods proposed by Hozo et al[2]. Studies with multiple interventions arms for the same weaning strategy were handled as follows: either only one intervention arm of that study was included in the meta-analysis (i.e. when the other intervention arm was considered to be less consistent with the review question), or both arms were included in the same meta-analysis, thereby splitting the control group in equal parts (i.e. in case both intervention arms were considered to be of equal importance to the review question). The 95% confidence interval (CI) was reported on all estimates. We assessed heterogeneity using the chi-squared test for homogeneity and the $I^2$ statistic. If statistical heterogeneity was found (chi-square values of $p<0.10$ or $I^2$ values >50%) we explored the possible reason for this heterogeneity.

Risk of bias and Quality of evidence assessments

Eleven trials[7–10, 15 – 17] have a low risk of bias for group allocation. Random-sequence was generated using a computer-based system, and allocation was concealed using sealed envelopes in the majority of the studies. Yang et al[18] and Mohammadizadeh et al[19] did not clearly described the methodology of their study. The type of intervention did not allow for blinding, hence, all included trials are at risk of performance bias. The number of participants with missing data was not or insufficiently described in eight trials.






References:

1. Higgins JG: Cochrane handbook for systematic reviews of interventions, 2011
2. Hozo SP, Djulbegovic B and Hozo I: Estimating the mean and variance from the median, range and the size sample. *BMC Medical Research Methodology* 2005; 5 (13): p. 1 – 10