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Supplemental References

# Supplemental Tables

## eTable 1. List of nodes considered for a network meta-analysis of treatments for acute bronchiolitis in children ≤ 2 years old.

|  |  |  |
| --- | --- | --- |
| Treatment Node | | Treatment definition |
| Placebos/controls | Placebo (neb) | Any nebulised placebo, including isotonic 0.9% saline. |
| Placebo (sys) | Placebos through routes other than inhalation, such as intravenous (IV), intramuscular (IM), or oral delivered placebos, as well as mixed-delivery placebo groups and unspecified placebos. |
| Placebo (air) | Non-nebulised inhaled gas placebos (e.g., oxygen, air-oxygen mixture, low-flow air, etc.) |
| Standard care | Supportive or usual care as defined by trial authors; may include oxygen, fluids, and steroids or bronchodilators at the discretion of the attending physician. |
| Antibiotics | Macrolide | Antibiotics containing a large macrocyclic lactone ring attached to one or more deoxy sugars (e.g., azithromycin). |
| Penicillin-like | Antibiotics containing β-lactam ring fused to a fully-saturated 5-membered ring containing sulfur (e.g., amoxicillin). |
| Broncho-dilators | Epi (neb) | Nebulised epinephrine (adrenaline) and analogues (e.g., norepinephrine). |
| Sal (neb) | Nebulised salbutamol (albuterol). |
| IB (neb) | Nebulised ipratropium bromide. |
| Steroids | Steroid (sys) | Corticosteroids administered systemically (i.e., oral, IM, IV). |
| Steroid (neb) | Nebulised corticosteroids. |
| Non-pharma inhaled treatments | Hypertonic | Hypertonic saline (NaCl) solution of any concentration greater than 0.9% (e.g., 3%, 5%, 7%, etc.) |
| Heliox | Inhaled delivery of a helium and oxygen mixture |
| High flow O2 | High flow oxygen therapy that may or may not be heated and/or humidified. |
| Combined therapies | Epi (neb) + Steroid (sys) | Nebulised epinephrine combined with systemically delivered corticosteroids |
| Epi (neb) + Steroid (neb) | Nebulised epinephrine combined with nebulised corticosteroids |
| Sal (neb) + IB (neb) | Nebulised salbutamol administered with nebulized ipratropium bromide |
| Sal (neb) + Steroid (sys) | Nebulised salbutamol combined with systemically delivered corticosteroids |
| Sal (neb) + Steroid (neb) | Nebulised salbutamol combined with nebulised corticosteroids |
| Hypertonic (neb) + Epi (neb) | Nebulised hypertonic saline administered with nebulised epinephrine |
| Hypertonic (neb) + Sal (neb) | Nebulised hypertonic saline administered with nebulised salbutamol |
| Hypertonic (neb) + Steroid (sys) | Nebulised hypertonic saline administered with a systemic corticosteroid |

## eTable 2. Characteristics of studies meeting the inclusion criteria for a systematic review on treatments of bronchiolitis in children ≤ 2 years old.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study ID (Author, year), Country (Language) | Setting, centers (#), design | Study size (*N*) | Population | | | | | Treatments | | ARD1 | | ARD7 | | LOS | | Overall Risk of Bias |
| Disease severity | | | Age range | Wheeze status | Trial arms | Co-interventions | Rep | NMA | Rep | NMA | Rep | NMA |  |
| Mild | Mod | Sev |
| Abul-Anine 200236, UK (English) | Inpatient, single centre, parallel groups | 38 |  | ● |  | 30 d - 1 y | First episode | Epinephrine (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | N | - | Unclear |
| Abu-Shukair 200137, Jordan (English) | Inpatient, single centre, parallel groups | 140 |  | ● |  | <18 m | First episode | Salbutamol (nebulised);  Epinephrine (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Al-Ansari 201038, Qatar (English) | Inpatient, single centre, parallel groups | 187 |  | ● | ● | 0 - 18 m | First episode | 5% saline (nebulised);  3% saline (nebulised);  0·9% saline (nebulised) | Nebulised epinephrine | N | - | N | - | Y | Y | Low |
| Alansari 201339, Qatar (English) | Inpatient, single centre, parallel groups | 200 |  | ● | ● | 0 - 18 m | First episode | Dexamethasone (oral);  Placebo syrup | Nebulised salbutamol; nebulised 0·9% saline | N | - | N | - | Y | N | Unclear |
| Angoulvant 201740, France (English) | Outpatient, multi-centre (24), parallel groups | 777 |  | ● | ● | 6 w - 12 m | NR | 3% saline (nebulised);  0·9% saline (nebulised) | None | Y | Y | N | - | N | - | Low |
| Anil 201041, Turkey (English) | Outpatient, single centre, parallel groups | 190 | ● | ● |  | 6 w - 24 m | First episode | Epinephrine (nebulised);  Epinephrine + 3% saline (nebulised);  Salbutamol (nebulised);  Salbutamol + 3% saline (nebulised);  0·9% saline (nebulised) | None | Y | Y | N | - | N | - | High |
| Barlas 199842, Turkey (Turkish) | Outpatient, single centre, parallel groups | 90 | ● | ● |  | 0 - 24 m | First episode | Salbutamol (nebulised);  Prednisolone (IV);  Salbutamol (nebulised) + prednisolone (IV);  Epinephrine (nebulised);  Budesonide (nebulised);  Tent mist | NR | Y | Y | N | - | N | - | High |
| Bashir 201843, India (English) | Inpatient, single centre, parallel groups | 189 |  | ● |  | 2 - 18 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Bawazeer 201444, Saudi Arabia (English) | Outpatient, single centre, parallel groups | 162 | ● | ● |  | 1 - 12 m | First episode | Epinephrine (nebulised) + dexamethasone (oral);  Salbutamol (nebulised) + dexamethasone (oral;  Epinephrine (nebulised);  Salbutamol (nebulised) | None | Y | Y | Y | Y | N | - | Low |
| Beck 200745, Israel (English) | Outpatient, single centre, parallel groups | 27 | NR | NR | NR | 2 - 12 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | N | - | Low |
| Beigelman 201546, USA (English) | Inpatient, single centre, parallel groups | 40 | NR | NR | NR | 1 - 18 m | First episode | Azithromycin (oral);  Oral suspension | None | N | - | N | - | Y | Y | High |
| Bentur 200547, Israel (English) | Inpatient, NR, parallel groups | 61 |  | ● | ● | 3 - 12 m | First episode | Dexamethasone (nebulised) + epinephrine (nebulised);  Epinephrine (nebulised) | Oxygen if SpO2 <92% | N | - | N | - | Y | Y | Unclear |
| Berger 199848, Israel (English) | Outpatient, single centre, parallel groups | 42 | NR | NR | NR | 1 - 18 m | First episode | Prednisone (oral);  Placebo syrup | Nebulised salbutamol | Y | Y | N | - | N | - | Unclear |
| Bertrand 200149, Chile (English) | Inpatient, single centre, parallel groups | 30 | ● | ● | ● | <1 y | First episode | Salbutamol + 0·9% saline (nebulised);  Epinephrine + 0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Bilan 200750, Iran (Farsi) | Inpatient, single centre, parallel groups | 100 | NR | NR | NR | 2 - 12 m | First episode | Salbutamol (MDI);  Epinephrine (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Bueno Campana 201451, Spain (English) | Inpatient, multi-centre (2), parallel groups | 75 |  | ● |  | 0 - 6 m | NR | Epinephrine (nebulised) + HHHF oxygen;  Epinephrine (nebulised) + 3% saline (nebulised) | Nebulised epinephrine; nebulised 0·9% saline | N | - | N | - | Y | N | High |
| Bulow 199952, Denmark (English) | Inpatient, multi-centre (3), parallel groups | 147 | NR | NR | NR | < 2 y | NR | Prednisolone (oral or IV);  Quinine hydrochloride (oral) or 0·9% saline (IV) | None | N | - | N | - | Y | Y | Unclear |
| Cade 200053, UK (English) | Inpatient, multi-centre (5), parallel groups | 165 | NR | NR | NR | < 12 m | NR | Budesonide (nebulised);  Nebulisation vehicle | None | N | - | N | - | Y | Y | High |
| Cambonie 200654, France (English) | Inpatient, single centre, parallel groups | 20 |  | ● | ● | <3 m | NR | Heliox;  Air-oxygen | None | N | - | N | - | N | - | Unclear |
| Can 199855, Turkey (English) | Outpatient, single centre, parallel groups | 158 |  | ● |  | 7 w - 24 m | First episode | Salbutamol (nebulised);  0·9% saline (nebulised);  Tent mist | None | N | - | N | - | N | - | High |
| Cengizlier 199756, Turkey (English) | Inpatient, single centre, parallel groups | 31 | ● | ● |  | 6 - 24 m | First episode | Salbutamol (oral);  Salbutamol (MDI);  Standard care | None | N | - | N | - | Y | Y | High |
| Chao 200357, Taiwan (English) | Inpatient, single centre, factorial | 73 | ● | ● |  | < 24 m | Any | Budesonide (nebulised);  Terbutaline (nebulised);  Budesonide (nebulised) + terbutaline (nebulised);  0·9% saline (nebulised) | Oxygen | N | - | N | - | Y | Y | High |
| Chen 201858, USA (English) | Inpatient, nr, parallel groups | 32 |  | ● |  | 0 - 24 m | NR | HHLF oxygen;  Dry oxygen (low flow) | NR | N | - | N | - | Y | N | High |
| Chevallier 199559, France (French) | Inpatient, single centre, parallel groups | 33 |  | ● |  | 34 d - 6 m | NR | Salbutamol (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | Unclear |
| Chowdhury 199560, Saudi Arabia (English) | Inpatient, single centre, factorial | 102 |  | ● | ● | <2 y | First episode | Salbutamol (nebulised);  Ipratropium bromide (nebulised);  Salbutamol (nebulised) + ipratropium bromide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | High |
| Chowdhury 201361, Australia, UK (English) | Inpatient, multi-centre (4), parallel groups | 319 | ● | ● |  | NR | NR | Heliox;  Air-oxygen | None | N | - | N | - | N | - | High |
| Connolly 196962, UK (English) | Inpatient, nr, parallel groups | 100 | ● | ● | ● | 0 - 2 y | NR | Prednisolone (NR);  Placebo (NS) | Ampicillin | N | - | N | - | N | - | High |
| Corneli 200763, USA (English) | Outpatient, multi-centre (20), parallel groups | 600 |  | ● | ● | 2 - 12 m | First episode | Dexamethasone (oral);  Placebo syrup | NR | Y | Y | Y | Y | N | - | Low |
| Daugbjerg 199364, Denmark (English) | Inpatient, multi-centre (5), parallel groups | 123 |  | ● | ● | 1.5 - 18 m | Any | Prednisolone (oral) + terbutaline (nebulised);  Budesonide (nebulised) + terbutaline (nebulised);  Terbutaline (nebulised);  Oral placebo (NR) + nebulised placebo (NR) + 0·9% saline (nebulised) | NR | N | - | N | - | Y | N | Unclear |
| De Boeck 199765, Belgium (English) | Inpatient, single centre, parallel groups | 32 | ● | ● | ● | < 24 m | First episode | Dexamethasone (IV);  Placebo (NS) | Nebulised salbutamol; nebulised ipratropium bromide, oral chloral hydrate | N | - | N | - | Y | N | High |
| Dobson 199866, USA (English) | Inpatient, single centre, parallel groups | 58 |  | ● |  | < 24 m | First episode | Salbutamol (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | High |
| Ejaz 201567, Pakistan (English) | Inpatient, single centre, parallel groups | 80 |  | ● |  | 1 m - 2 y | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | High |
| Ergul 201688, Turkey (English) | Inpatient, single centre, parallel groups | 60 |  | ● | ● | 1 - 24 m | NR | Oxygen (high flow by NC);  Oxygen (high flow by diffuser mask) | NR | N | - | N | - | Y | N | High |
| Everard 201469, UK (English) | Inpatient, multi-centre (10), parallel groups | 317 | NR | NR | NR | <1 y | First episode | 3% saline (nebulised);  Standard care | None | N | - | N | - | Y | Y | Unclear |
| Field 196670, UK (English) | Inpatient, single centre, parallel groups | 52 | ● | ● | ● | NR | NR | Ampicillin (NR);  Placebo (NS) | Ephedrine | N | - | N | - | Y | Y | High |
| Flores 201671, Portugal (English) | Inpatient, single centre, parallel groups | 78 | ● | ● |  | <12 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | Nebulised salbutamol | N | - | N | - | Y | Y | High |
| Flores Gonzales 201572, Spain (English) | Inpatient, single centre, parallel groups | 208 |  | ● |  | <24 m | First episode | 3% saline (nebulised);  3% saline (nebulised) + epinephrine (nebulised) | None | N | - | N | - | Y | Y | High |
| Florin 201473, USA (English) | Outpatient, single centre, parallel groups | 62 |  | ● | ● | 2 - 23 m | First episode | 3% saline (nebulised);  0.9 % saline (nebulised) | None | Y | Y | Y | Y | N | - | Low |
| Franklin 201874, Australia/New Zealand (English) | Inpatient and outpatient, multi-centre (17), parallel groups | 1638 | NR | NR | NR | <12 m | NR | Oxygen (high flow);  Oxygen (low flow) | NR | N | - | N | - | Y | Y | Unclear |
| Gadomski 199475, USA (English) | Outpatient, single centre, factorial | 93 | ● | ● |  | 0 - 15 m | First episode | Salbutamol (nebulised);  Salbutamol (oral);  0·9% saline (nebulised);  Rehydration solution (oral) | NR | Y | Y | N | - | N | - | Unclear |
| Gadomski a 199476, Egypt (English) | Outpatient, single centre, factorial | 128 | ● | ● |  | <18 m | First episode | Salbutamol (nebulised);  Salbutamol (oral);  0·9% saline (nebulised);  Rehydration solution (oral) | NR | N | - | N | - | N | - | Unclear |
| Gheini 201777, Iran (Farsi) | Inpatient, single centre, parallel groups | 80 | ● |  |  | ≤2 y | First episode | Dexamethasone (IM);  Placebo (NS) | NR | N | - | N | - | N | - | Unclear |
| Goebel 200078, USA (English) | Outpatient, multi-centre (2), parallel groups | 51 | ● | ● |  | 0 - 23 m | First episode | Salbutamol (oral or nebulised) + prednisolone (oral);  Salbutamol (oral or nebulised) | NR | Y | N | Y | N | N | - | Unclear |
| Goh 199779, Singapore (English) | Inpatient, single centre, parallel groups | 99 | ● | ● |  | <2 y | First episode | Salbutamol (nebulised);  Ipratropium bromide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | High |
| Gomez-y-Lopez 200780, Mexico (Spanish) | Outpatient, single centre, parallel groups | 49 | ● | ● | ● | 1 - 18 m | NR | Salbutamol (nebulised);  Salbutamol (nebulised) + dexamethasone (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Gonzalez Perez-Yarza 199481, Spain (Spanish) | Inpatient, multi-centre (5), parallel groups | 86 | ● | ● |  | 6 w - 18 m | Any | Terbutaline (nebulised);  Terbutaline (nebulised) + budesonide (nebulised);  Terbutaline (nebulised) + prednisone (oral) | NR | N | - | N | - | Y | N | High |
| Grewal 200982, Canada (English) | Outpatient, single centre, parallel groups | 48 | ● | ● |  | 6 w - 12 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | Nebulised epinephrine | Y | Y | N | - | N | - | Low |
| Gupta 200883, India (English) | Outpatient, single centre, parallel groups | 140 | ● |  |  | <1 y | First episode | Salbutamol (oral);  Placebo syrup | None | Y | N | Y | N | N | - | Low |
| Hariprakash 200384, UK (English) | Outpatient, single centre, parallel groups | 75 | ● | ● | ● | 1 m - 1 y | NR | Epinephrine (nebulised);  0·9% saline (nebulised) | NR | Y | Y | N | - | N | - | Unclear |
| Henry 198385, UK (English) | Inpatient, single centre, parallel groups | 66 | NR | NR | NR | NR | NR | Ipratropium bromide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | High |
| Hilliard 201286, UK (English) | Inpatient, single centre, parallel groups | 19 |  | ● |  | NR | NR | HHHF oxygen;  Headbox-delivered oxygen | NR | N | - | N | - | N | - | High |
| Ho 199187, Australia (English) | Inpatient, single centre, cross-over | 21 | ● | ● |  | 3 w - 6 m | NR | Salbutamol (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Hollman 199888, USA (English) | Inpatient, single centre, hybrid parallel-crossover | 21 | ● | ● | ● | NR | NR | Heliox;  Air-oxygen | None | N | - | N | - | N | - | Low |
| Iglesias Fernandez 200889, Spain (Spanish) | Outpatient, single centre, parallel groups | 96 |  | ● | ● | <15 m | First episode | Heliox-driven nebulisations;  Oxygen-driven nebulisations | Nebulised salbutamol and/or epinephrine | Y | N | Y | N | N | - | Unclear |
| Ipek 201190, Turkey (English) | Outpatient, single centre, factorial | 120 |  | ● |  | <2 y | First episode | Salbutamol (nebulised);  Salbutamol (nebulised) + 3% saline (nebulised);  3% saline (nebulised);  0·9% saline (nebulised) | None | Y | N | N | - | N | - | Unclear |
| Jacobs 201491, USA (English) | Outpatient, single centre, parallel groups | 101 |  | ● | ● | 6 w - 18 m | First episode | 7% saline (nebulised);  0·9% saline (nebulised) | Nebulised epinephrine | Y | Y | N | - | N | - | Unclear |
| Jaquet-Pilloud 201992, Switzerland (English) | Inpatient, multi-centre (2), parallel groups | 122 |  | ● | ● | 6 w - 2 m | First episode | 3% saline (nebulised);  Standard care | None | N | - | N | - | Y | Y | Unclear |
| John 200693, India (English) | Inpatient, single centre, parallel groups | 30 |  | ● | ● | 2 - 24 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Kabir 200994, Bangladesh (English) | Inpatient, multi-centre (5), parallel groups | 327 | NR | NR | NR | <2 y | NR | Ampicillin (IV);  Erythromycin (oral);  Standard care | Nebulised salbutamol; oxygen if SpO2 <90% | N | - | N | - | Y | N | High |
| Kadir 200995, Bangladesh (English) | Inpatient, single centre, parallel groups | 60 |  | ● | ● | <2 y | NR | Salbutamol (nebulised) + ipratropium bromide (nebulised);  Epinephrine (nebulised) | Oxygen; ampicillin and/or gentamicin | N | - | N | - | N | - | High |
| Karadag 200896, Turkey (English) | Inpatient, nr, parallel groups | 70 |  | ● | ● | <1 y | First episode | Salbutamol (nebulised);  Ipratropium bromide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | N | High |
| Kepreotes 201797, Australia (English) | Inpatient, single centre, parallel groups | 202 |  | ● |  | <24 m | NR | HHHF oxygen;  Dry low-flow oxygen | NR | N | - | N | - | Y | Y | High |
| Khanal 2015,98 Nepal (English) | Outpatient, single centre, parallel groups | 100 | ● | ● |  | 6 w - 2 y | First episode | Epinephrine (nebulised) + 3% saline (nebulised);  Epinephrine (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Khashabi 200599, Iran (English) | Outpatient, single centre, parallel groups | 72 | ● | ● | ● | 2 - 24 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised);  0·9% saline (nebulised) | None | Y | Y | N | - | N | - | High |
| Kim 2011100, USA (English) | Outpatient, single centre, parallel groups | 69 |  | ● | ● | 2 - 12 m | NR | Heliox delivery of nebulisations;  Oxygen delivery of nebulisations | Nebulised salbutamol; nebulised epinephrine | Y | N | Y | N | N | - | High |
| Klassen 1991101, Canada (English) | Outpatient, single centre, parallel groups | 83 |  | ● |  | <24 m | NR | Salbutamol (nebulised);  0·9% saline (nebulised) | NR | Y | Y | N | - | N | - | Unclear |
| Klassen 1997102, Canada (English) | Inpatient, single centre, parallel groups | 72 |  | ● | ● | 6 w - 15 m | First episode | Dexamethasone (oral);  Placebo syrup | Nebulised salbutamol; oxygen | N | - | N | - | Y | Y | Low |
| Kneyber 2008103, Netherlands (English) | Inpatient, multi-centre (NR), parallel groups | 71 | ● | ● |  | <24 m | First episode | Azithromycin (oral);  Oral placebo (NR) | None | N | - | N | - | Y | Y | High |
| Kose 2014104, Turkey (English) | Outpatient, single centre, factorial | 56 |  | ● |  | 1 - 24 m | First episode | Salbutamol (nebulised);  Magnesium sulphate (nebulised);  Salbutamol (nebulised) + magnesium sulphate (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Kose 2016105, Turkey (English) | Inpatient, single centre, parallel groups | 106 |  | ● | ● | 1 - 24 m | First episode | Salbutamol (nebulised);  Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) + 7% saline (nebulised) | Steroids if CSS ≥ 10 an hour after treatment | N | - | N | - | Y | Y | High |
| Kristjansson 1993106, Sweden (English) | Inpatient, single centre, parallel groups | 34 |  | ● | ● | <18 m | Any | Epinephrine (nebulised);  Epinephrine vehicle (nebulised) + 0·9% saline (nebulised) | NR | N | - | N | - | N | - | High |
| Kumar 2013107, India (English) | Inpatient, single centre, parallel groups | 40 |  | ● |  | <2 y | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | Nebulised salbutamol; oxygen | N | - | N | - | Y | Y | Unclear |
| Kuyucu 2004108, Turkey (English) | Outpatient, single centre, parallel groups | 90 |  | ● |  | 2 - 21 m | First episode | Epinephrine (nebulised) + dexamethasone (IM);  Salbutamol (nebulised) + dexamethasone (IM);  Epinephrine (nebulised);  Salbutamol (nebulised) | NR | Y | Y | N | - | N | - | High |
| Kuzik 2007109, Canada, UAE (English) | Inpatient, multi-centre (3) , parallel groups | 96 |  | ● |  | <18 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | Unclear |
| Kuzik 2010110, Canada (English) | Outpatient, multi-centre (4), parallel groups | 88 |  | ● |  | 0 - 24 m | Any | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | None | Y | Y | Y | Y | N | - | Low |
| Labbe 1985111, France (French) | Inpatient, single centre, parallel groups | 62 | NR | NR | NR | <24 m | NR | Theopylline (oral or NG);  Placebo (NS) | None | N | - | N | - | Y | N | High |
| Langley 2005112, Canada (English) | Inpatient, single centre, parallel groups | 62 |  | ● |  | 6 w - 2 y | NR | Epinephrine (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Lee 2004113, South Korea (Korean) | Inpatient, single centre, parallel groups | 100 | ● | ● | ● | 0 - 1 y | NR | Epinephrine (nebulised);  Fenoterol (nebulised) | NR | N | - | N | - | Y | N | High |
| Li 2014114, China (Chinese) | Inpatient, single centre, parallel groups | 124 |  | ● |  | 2 - 18 m | First episode | 5% saline (nebulised);  3% saline (nebulised);  0·9% saline (nebulised) | Nebulised ipratropium bromide; nebulised budenoside | N | - | N | - | N | - | Unclear |
| Liet 2005115, Canada (English) | Inpatient, multi-centre (NR), parallel groups | 40 |  |  | ● | <9 m | First episode | Heliox;  Air-oxygen | NR | N | - | N | - | Y | Y | Unclear |
| Lines 1992116, Australia (English) | Inpatient, single centre, parallel groups | 31 | NR | NR | NR | <18 m | NR | Ipratropium bromide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Livni 2010117, Israel (English) | Inpatient, single centre, parallel groups | 65 | ● | ● |  | 1 - 12 m | First episode | Epinephrine (nebulised);  Xylometazoline HCl (nasal drops) | None | N | - | N | - | Y | N | Unclear |
| Luo 2005118, China (Chinese) | Inpatient and outpatient, single centre, parallel groups | 63 | NR | NR | NR | 1 - 10 m | NR | Budesonide (nebulised);  Standard care | None | N | - | N | - | N | - | Unclear |
| Luo 2010119, China (English) | Inpatient, single centre, parallel groups | 93 | ● | ● |  | 0 - 24 m | First episode | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Luo 2011120, China (English) | Inpatient, single centre, parallel groups | 126 |  | ● | ● | <24 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | Low |
| Mazumder 2010121, Bangladesh (English) | Outpatient, single centre, parallel groups | 126 | NR | NR | NR | 1 m - 2 y | NR | Ampicillin (IV);  Erythromycin (oral);  Standard care | Nebulised salbutamol | N | - | N | - | N | - | High |
| McCallum 2013122, Australia (English) | Inpatient, multi-centre (2), parallel groups | 97 | ● | ● |  | 0 - 18 m | NR | Azithromycin (oral);  Placebo syrup | None | N | - | N | - | Y | Y | Unclear |
| McCallum 2015123, Australia (English) | Inpatient, multi-centre (3), parallel groups | 219 | NR | NR | NR | 0 - 24 m | NR | Azithromycin (oral);  Oral placebo (NS) | Oxygen when SpO2 <94% | N | - | N | - | Y | Y | Unclear |
| Menon 1995124, Canada (English) | Outpatient, single centre, parallel groups | 42 |  | ● | ● | 6 w - 12 m | First episode | Salbutamol (nebulised);  Epinephrine (nebulised) | NR | Y | Y | N | - | N | - | Low |
| Mesquita 2009125, Paraguay (English) | Outpatient, single centre, parallel groups | 80 |  | ● |  | 2 - 24 m | First episode | Dexamethasone (oral);  Placebo syrup | Nebulised epinephrine; nebulised 0·9% saline | Y | Y | N | - | N | - | High |
| Milesi 2013126, France (English) | Inpatient, single centre, parallel groups | 19 |  |  | ● | <6 m | NR | Oxygen (CPAP);  Air-oxygen | Oxygen | N | - | N | - | Y | N | Unclear |
| Milesi 2016127, France (English) | Inpatient, multi-centre (5), parallel groups | 142 |  | ● | ● | 1 d - 6 m | NR | Air-oxygen (high flow);  Air-oxygen (CPAP) | None | N | - | N | - | Y | N | Unclear |
| Miraglia 2012128, Italy (English) | Inpatient, single centre, parallel groups | 109 |  | ● | ● | <2 y | First episode | Epinephrine (nebulised);  Epinephrine (nebulised) + 3% saline (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Modaressi 2012129, Iran (English) | Inpatient, multi-centre (2), parallel groups | 40 |  | ● | ● | 1 m - 2 y | First episode | Epinephrine (nebulised);  Salbutamol (nebulised) | None | N | - | N | - | Y | Y | High |
| Modaressi 2015130, Iran (English) | Inpatient, multi-centre (3), parallel groups | 125 |  | ● | ● | <12 m | NR | Magnesium sulfate (nebulised) + epinephrine (nebulised);  Epineprhine (nebulised) | Oxygen if SpO2 <90% | N | - | N | - | Y | N | Unclear |
| Morikawa 2018131, Japan (English) | Inpatient, multi-centre (5), parallel groups | 128 | ● | ● |  | <12 m | First episode | Salbutamol (nebulised);  Salbutamol (nebulised) + 3% saline (nebulised) | Oxygen if SpO2 <95% | N | - | N | - | Y | Y | Unclear |
| Mull 2004132, USA (English) | Outpatient, single centre, parallel groups | 66 |  | ● |  | <12 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised) | NR | Y | Y | N | - | N | - | High |
| Nenna 2014133, Italy (English) | Inpatient, single centre, parallel groups | 42 | ● | ● |  | <12 m | First episode | 7% saline-01% hylronic acid solution (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | N | Unclear |
| NCT01238848134, Argentina (English) | Inpatient, single centre, parallel groups | 100 | NR | NR | NR | 1 m – 2 yr | NR | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | High |
| NCT01238848135, Mexico (English) | Inpatient, single centre, parallel groups | 64 |  | ● | ● | 2 – 24 m | First episode | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | High |
| Ojha 2014136, Nepal (English) | Inpatient, single centre, parallel groups | 72 |  | ● |  | 6 w - 24 m | First episode | 3% saline (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | High |
| Okutan 1998137, Turkey (Turkish) | Outpatient, single centre, parallel groups | 45 | ● | ● |  | 3 - 18 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised);  0·9% saline (nebulised) | Oral chloral hydrate | N | - | N | - | N | - | Unclear |
| Ozyurek 2002138, Turkey (English) | Inpatient, single centre, parallel groups | 42 |  | ● | ● | <24 m | First episode | Salbutamol (nebulised);  Ipratropium bromide (nebulised) | None | N | - | N | - | Y | Y | High |
| Pandit 2013139, India (English) | Inpatient, single centre, parallel groups | 100 |  | ● | ● | 2 - 12 m | First episode | Epinephrine (nebulised) + 3% saline (nebulised);  Epinephrine (nebulised) | NR | N | - | N | - | Y | Y | High |
| Park 1997140, South Korea (Korean) | Inpatient, single centre, parallel groups | 72 | ● | ● |  | 0 - 1 y | Recurrent | Salbutamol (nebulised);  Salbutamol (nebulised) + budesonide (nebulised);  Standard care | Oxygen | N | - | N | - | Y | N | Unclear |
| Park 2005141, South Korea (Korean) | Inpatient, single centre, parallel groups | 80 |  | ● |  | 0 - 1 y | NR | Fenoterol (nebulised);  Fenoterol (nebulised) + 3% saline (nebulised) | NR | N | - | N | - | Y | N | Unclear |
| Patel 2002142, Canada (English) | Inpatient, single centre, parallel groups | 149 | ● | ● | ● | 0 - 12 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised);  0·9% saline (nebulised) | Humidified oxygen if SpO2 ≤95% | N | - | N | - | Y | Y | Low |
| Patel 2003143, Canada (English) | Outpatient, single centre, parallel groups | 129 | ● |  |  | 0 - 12 m | First episode | Salbutamol (oral);  Placebo syrup | NR | Y | N | Y | N | N | - | Low |
| Pinto 2012144, Brazil (English) | Inpatient, multi-centre (2), parallel groups | 185 | NR | NR | NR | <12 m | Any | Azithromycin (oral);  Oral placebo (NS) | None | N | - | N | - | Y | Y | Unclear |
| Plint 2009145, Canada (English) | Outpatient, multi-centre (8), factorial | 800 |  | ● |  | 6 w - 12 m | First episode | Epinephrine (nebulised) + dexamethasone (oral);  Epinephrine (nebulised);  Dexamethasone (oral);  0·9% saline (nebulised) + placebo syrup | Oxygen if SpO2 <92% | Y | Y | Y | Y | N | - | Low |
| Ralston 2005146, USA (English) | Outpatient, single centre, parallel groups | 65 | ● | ● |  | 6 w - 24 m | First episode | Salbutamol (nebulised);  Epinephrine (nebulised);  0·9% saline (nebulised) | None | Y | Y | N | - | N | - | Low |
| Rasul 2008147, Bangladesh (English) | Inpatient, single centre, parallel groups | 60 | NR | NR | NR | 0 - 2 y | First episode | Erythromycin (oral);  Amoxicillin (IV);  Standard care | Oxygen if SpO2 <95% | N | - | N | - | Y | Y | High |
| Ratajczyk 2016148, Poland (English) | Inpatient, single centre, parallel groups | 78 |  | ● |  | 0 - 18 m | NR | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | Low |
| Ray 2002149, India (English) | Outpatient, single centre, parallel groups | 91 | ● | ● | ● | 2 - 24 m | Any | Epinephrine (nebulised);  Salbutamol (nebulised) | None | Y | Y | N | - | N | - | Unclear |
| Reijonen 1995150, Finland (English) | Inpatient, single centre, hybrid parallel-crossover | 100 |  |  | ● | 1 - 24 m | Any | Epinephrine (nebulised), then 0·9% saline (nebulised);  Salbutamol (nebulised), then 0·9% saline (nebulised);  0·9% saline (nebulised), then epinephrine (nebulised);  0·9% saline (nebulised), then salbutamol (nebulised) | Intramuscular epinephrine; oxygen if SpO2 <90% | N | - | N | - | N | - | Unclear |
| Richter 1998151, UK (English) | Inpatient, single centre, parallel groups | 40 | NR | NR | NR | <12 m | First episode | Budesonide (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Roosevelt 1996152, USA (English) | Inpatient, single centre, parallel groups | 122 | NR | NR | NR | <12 m | First episode | Dexamethasone (IM);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Sanchez 1993153, Canada (English) | Inpatient, single centre, cross-over | 32 | ● | ● |  | <1 y | First episode | Salbutamol (nebulised);  Epinephrine (nebulised) | Oral chloral hydrate | N | - | N | - | Y | N | High |
| Sarkar 2018154, India (English) | Inpatient, single centre, parallel groups | 31 |  |  | ● | 28 d - 12 m | NR | Oxygen (CPAP);  Oxygen (high flow) | None | N | - | N | - | Y | N | High |
| Sarrell 2002155, Israel (English) | Outpatient, single centre, parallel groups | 70 | ● | ● |  | 0 - 24 m | First episode | Terbutaline (nebulised);  Terbutaline (nebulised) + 3% saline (nebulised) | NR | N | - | N | - | N | - | High |
| Sarrell 2010156, Israel (English) | Outpatient, multi-centre (2), parallel groups | 330 | NR | NR | NR | 1.5 - 14 m | First episode | Epinephrine (nebulised);  Epinephrine (nebulised) + bromhexine (nebulised);  0·9% saline (nebulised) | None | Y | N | N | - | N | - | Unclear |
| Scarlett 2012157, USA (English) | Inpatient, single centre, parallel groups | 23 | ● | ● |  | 0 - 12 m | First episode | Salbutamol (nebulised);  0·9% saline (nebulised) | NR | N | - | N | - | N | - | High |
| Schreiber 2015158, Italy (English) | Outpatient, multi-centre (2), parallel groups | 133 | NR | NR | NR | 0 - 1 y | NR | 09% saline (nasal irrigation);  3% saline (nasal irrigation);  Standard care | NR | N | - | N | - | N | - | High |
| Schuh 1992159, Canada (English) | Outpatient, single centre, parallel groups | 72 | NR | NR | NR | 6 w - 24 m | First episode | Salbutamol (nebulised) + ipratropium bromide (nebulised);  Salbutamol (nebulised) | None | Y | Y | N | - | N | - | Low |
| Schuh 2002160, Canada (English) | Outpatient, single centre, parallel groups | 71 |  | ● | ● | 8 w - 23 m | First episode | Dexamethasone (oral) + salbutamol (nebulised);  Salbutamol (nebulised) | None | Y | Y | Y | N | N | - | Unclear |
| Schweich 1992161, USA (English) | Outpatient, single centre, parallel groups | 25 |  | ● |  | <2 y | Any | Salbutamol (nebulised);  0·9% saline (nebulised) | None | Y | Y | N | - | N | - | High |
| Seliem 2017162, Egypt (Spanish) | Inpatient, single centre, parallel groups | 125 | ● | ● | ● | 1 m - 2y | NR | Heliox;  Air-oxygen | NR | N | - | N | - | N | - | High |
| Seliem 2018163, Egypt (English) | Inpatient, single centre, parallel groups | 48 |  | ● | ● | 1 m - 2y | NR | Heliox;  Air-oxygen | NR | N | - | N | - | N | - | Unclear |
| Sharma 2013164, India (English) | Inpatient, single centre, parallel groups | 250 |  | ● |  | 1 - 24 m | First episode | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Silver 2015165, USA (English) | Inpatient, single centre, parallel groups | 227 | ● | ● |  | <12 m | Any | 3% saline (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | Unclear |
| Simsek-Kiper 2011166, Turkey (English) | Outpatient, single centre, parallel groups | 80 | ● | ● |  | 2 - 24 m | First episode | Epinephrine (nebulised);  Salbutamol (nebulised) | Oxygen if SpO2 <92% | Y | Y | N | - | Y | N | Unclear |
| Skjerven 2013167, Norway (English) | Inpatient, multi-centre (8), factorial | 404 |  | ● | ● | <12 m | NR | Epinephrine (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | High |
| Stokes 1983168, UK (English) | Inpatient, single centre, parallel groups | 25 | NR | NR | NR | 5 - 48 w | NR | Salbutamol (nebulised);  Ipratropium bromide (nebulised);  Water | None | N | - | N | - | N | - | High |
| Tahan 2007169, Turkey (English) | Inpatient, single centre, parallel groups | 30 | ● | ● | ● | 0 - 7 m | First episode | Clarithromycin (oral);  Placebo syrup | β2-agonist if SpO2<94% or RR>60 breaths/min; Oxygen if SpO2<94% | N | - | N | - | Y | Y | High |
| Tal 2006170, Israel (English) | Inpatient, single centre, parallel groups | 104 |  | ● | ● | 0 - 12 m | First episode | Epinephrine (nebulised);  Epinephrine (nebulised) + 3% saline (nebulised) | NR | N | - | N | - | Y | Y | Unclear |
| Teeratakulpisarn 2007171, Thailand (English) | Inpatient, multi-centre (2), parallel groups | 179 | ● | ● |  | 4 w - 24 m | First episode | Dexamethasone (IM);  Saline (IM) | None | N | - | N | - | Y | Y | High |
| Teunissen 2014172, Netherlands (English) | Inpatient, multi-centre (12), parallel groups | 292 | ● | ● | ● | 0 - 24 m | First episode | 3% saline (nebulised);  6% saline (nebulised);  0·9% saline (nebulised) | Nebulised salbutamol; oxygen if SpO2 ≤93% | N | - | N | - | Y | Y | Unclear |
| Tinsa 2009173, Tunisia (English) | Inpatient, single centre, parallel groups | 36 |  | ● |  | 3 - 12 m | First episode | Terbutaline (nebulised);  0·9% saline (nebulised) | Oxygen if SpO2 <93% | N | - | N | - | Y | N | Unclear |
| Tinsa 2014174, Tunisia (English) | Inpatient, single centre, parallel groups | 97 | ● | ● |  | 1 - 12 m | First episode | 5% saline (nebulised);  5% saline (nebulised) + epinephrine (nebulised);  0·9% saline (nebulised) | Oxygen if SpO2 ≤93% | N | - | N | - | Y | Y | High |
| Totapally 2001175, USA (English) | Inpatient, single centre, cross-over | 20 | NR | NR | NR | <1 y | First episode | Salbutamol (nebulised);  0·9% saline (nebulised) | Oral chloral hydrate | N | - | N | - | Y | N | Unclear |
| Turner 2014176, Australia/New Zealand (English) | Inpatient, multi-centre (3), parallel groups | 55 | NR | NR | NR | <24 m | Any | Aminophylline (IV);  0·9% saline (IV) | Oxygen if SpO2 <95% | N | - | N | - | Y | N | High |
| Uysalol 2017177, Turkey (English) | Outpatient, single centre, factorial | 386 |  | ● |  | 2 - 24 m | First episode | 3% saline (nebulised);  Epinephrine (nebulised);  Epinephrine (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised);  0·9% saline (nebulised) | NR | Y | Y | N | - | N | - | Unclear |
| van Woensel 1997178, Netherlands (English) | Inpatient, single centre, parallel groups | 54 | ● | ● |  | <2 y | NR | Prednisolone (oral);  Oral placebo (NR) | NR | N | - | N | - | Y | Y | Unclear |
| Wainwright 2003179, Australia (English) | Inpatient, multi-centre (4), parallel groups | 194 | ● | ● | ● | <12 m | First episode | Epinephrine (nebulised);  Nebulisation vehicle | NR | N | - | N | - | Y | Y | Unclear |
| Walsh 2008180, USA (English) | Outpatient, multi-centre (2), parallel groups | 721 | NR | NR | NR | 0 - 18 m | Any | Salbutamol (nebulised);  Epinephrine (nebulised) | None | Y | N | N | - | N | - | High |
| Wang 1992181, Canada (English) | Inpatient, single centre, factorial | 62 | ● | ● | ● | 2 m - 2 y | First episode | Salbutamol (nebulised) + ipratropium bromide (nebulised);  Ipratropium bromide (nebulised);  Salbutamol (nebulised);  0·9% saline (nebulised) | None | N | - | N | - | Y | Y | Unclear |
| Wu 2014182, USA (English) | Outpatient, multi-centre (2), parallel groups | 408 |  | ● |  | <24 m | First episode | Salbutamol (nebulised) + 3% saline (nebulised);  Salbutamol (nebulised) | None | Y | Y | N | - | Y | Y | Low |
| Zamani 2015183, Iran (Farsi) | Inpatient, single centre, parallel groups | 70 | ● | ● |  | 2 m - 2 y | NR | Salbutamol (nebulised);  3% saline (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Zhang 2003184, Brazil (English) | Inpatient, single centre, parallel groups | 52 | NR | NR | NR | 4 w - 11 m | First episode | Prednisolone (NR);  Standard care | None | N | - | N | - | Y | Y | High |
| Zhou 2001185, China (Chinese) | Inpatient, multi-centre (2), parallel groups | 72 | NR | NR | NR | 40 d - 10 m | NR | Salbutamol (nebulised);  Salbutamol (nebulised) + budesonide (nebulised) | NR | N | - | N | - | N | - | Unclear |
| Notes: ARD1 = admission rate on Day 1; ARD7 = admission rate up to and including Day 7; LOS = hospital length of stay; NR = Not Reported; Rep =outcome was reported; NMA = contributed data to network meta-analysis; RoB = risk of bias; SpO2 = Oxygen saturation; USA = United States of America; UK = United Kingdom. 150 studies out of 47 countries (65% of studies from high income countries; 35% from middle income; 1% from low income based on World Bank Income Rankings)185 and included 17 studies published in languages other than English (Chinese n=3; Farsi n=3; French n=2; Korean n=3; Spanish n=4; Turkish n=2) | | | | | | | | | | | | | | | | | |

## eTable 3. Risk of Bias assessment for studies included in a network meta-analysis of treatments for acute bronchiolitis in children ≤ 2 years old.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Randomization** | **Allocation** | **Performance bias** | **Detection bias** | **Attrition bias** | **Reporting bias** | **Other bias** | **Overall** |
| Abul-Anine 2002 | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png |
| Abu-Shukair 2001 | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png |
| Alansari 2013 | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\UNCLEAR.png |
| Al-Ansari 2010 | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png |
| Angoulvant 2017 | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png | Z:\common\Bronchiolitis Network Meta-analysis 2016\8.0 Manuscript\Drafts\Tables\Rob_icons\LOW.png |
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## eTable 4. Summary of nodes in a network meta-analysis of the effectiveness of treatments for bronchiolitis on admission rate at day 1 (ARD1).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Node | Definition | Studies in node  (N) | Patients  (N) | Age in months  Mean (SD) | Males  n/N (%) | Severity (%)  Mild/Mild-moderate/ Moderate/Moderate-severe/Severe/NR |
| Placebo (neb)40,41,73, 75,84,99,101,145,146,161,177 | Any nebulised placebo, including 0·9% saline. | 11 | 892 | 4·83 (1·89) | 498/837 (59) | 0/27/55/0/0/18 |
| Placebo (sys)63,75 | Any systemic (i.e., oral, IV, IM) placebo. Includes placebo not specified. | 2 | 317 | 5·11 (0·05) | 178/295 (60) | 0/50/50/0/0/0 |
| Placebo (air) | Inhaled gas placebos (e.g., oxygen, air-oxygen mixture, humidified air, etc.) | 1 | 15 | NR | NR | 0/0/100/0/0/0 |
| Epi (neb)41,42,44,82, 84,91,99,108,124,125,132,145,146,149,166,177 | Nebulised epinephrine | 16 | 695 | 6·00 (1·68) | 335/565 (59) | 0/13/69/6/0/13 |
| Sal (neb)41,42,44,48, 75,99,101,108,109,124,132,146,149,159-161,166,177,182 | Nebulised salbutamol | 19 | 763 | 6·93 (1·50) | 356/597 (60) | 0/26/53/5/0/16 |
| Sal (neb) + IB (neb)159 | Nebulised salbutamol + nebulised ipratropium bromide | 1 | 36 | 9·4 (6·10) | NR | 0/0/0/0/0/100 |
| Steroid (sys)42,63,144 | Systemically delivered steroid | 3 | 519 | 5·06 (0·05) | 317/504 (63) | 0/0/100/0/0/0 |
| Steroid (neb)42 | Nebulised steroid | 1 | 15 | NR | NR | 0/0/100/0/0/0 |
| Hypertonic (neb)40,73,177 | Hypertonic saline (any) | 3 | 493 | 3·89 (1·68) | 287/493 (58) | 0/0/67/0/0/33 |
| Hypertonic (neb) + Epi (neb)41,82,91,177 | Hypertonic saline + epinephrine | 4 | 186 | 7·06 (1·32) | 118/186 (63) | 0/25/50/0/0/0 |
| Hypertonic (neb) + Sal (neb)41,109,182 | Hypertonic saline + nebulised salbutamol | 3 | 291 | 7·27 (1·17) | 191/291 (66) | 0/0/67/0/0/33 |
| Epi (neb) + Steroid (sys)44,108,125,145 | Epinephrine combined with a systemically delivered steroid | 4 | 300 | 5·38 (0·91) | 171/277 (62) | 0/0/100/0/0/0 |
| Sal (neb) + Steroid (sys)42,44,48,108,160 | Salbutamol combined with a systemically delivered steroid | 5 | 134 | 5·78 (1·22) | 41/76 (54) | 0/20/80/0/0/0 |
| All |  |  | 4656 | 5·63 (1·43) | 2492/4121 (60) | 0/21/63/3/0/14 |
| Notes: IV = intravenous; IM = intramuscular injection; NR = not reported; SD = standard deviation | | | | | | |

## eTable 5. Summary of nodes in a network meta-analysis of the effectiveness of treatments for bronchiolitis on admission rate at day 7 (ARD7).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Node | Definition | Studies in node  (N) | Patients (N) | Age in months  Mean (SD) | Males  n/N (%) | Severity (%)  Mild/Mild-moderate/ Moderate/  Moderate-severe/Severe/NR |
| Placebo (neb)41,73,110,143 | Any nebulised placebo, including 0·9% saline. | 4 | 177 | 7·13 (1·90) | 109/177 (62) | 0/50/50/0/0/0 |
| Placebo (sys)63,78,145,160 | Any systemic (i.e., oral, IV, IM) placebo. Includes placebo not specified. | 4 | 554 | 5·15 (0·46) | 337/554 (61) | 0/25/75/0/0/0/0 |
| Epi (neb)41,44,108,132,145,180 | Nebulised epinephrine | 6 | 630 | 5·10 (1·51) | 400/619 (65) | 0/17/83/0/0/0 |
| Hypertonic (neb) + Epi (neb)41 | Hypertonic saline + epinephrine | 1 | 39 | 9·40 (5·00) | 29/39 (74) | 0/100/0/0/0/0 |
| Epi (neb) + Steroid (sys)44,108,145 | Epinephrine combined with a systemically delivered steroid | 3 | 267 | 5·15 (0·64) | 152/244 (62) | 0/0/100/0/0/0 |
| Hypertonic (neb)73,110 | Hypertonic saline (any) | 2 | 75 | 8·02 (0·69) | 47/75 (63) | 0/50/50/0/0/0 |
| Hypertonic (neb) + Sal (neb)41 | Hypertonic saline + nebulised salbutamol | 1 | 36 | 9·70 (6·20) | 23/36 (64) | 0/0/100/0/0/0 |
| Sal (neb)41,44,108, 132,143,180 | Nebulised salbutamol | 6 | 513 | 5·31 (1·29) | 288/501 (57) | 0/33/67/0/0/0 |
| Sal (neb) + Steroid (sys)44,108 | Salbutamol combined with a systemically delivered steroid | 2 | 63 | 5·77 (1·63) | 21/40 (53) | 0/0/100/0/0/0 |
| Steroid (sys)63,78, 145,160 | Systemically delivered steroid | 4 | 564 | 5·08 (0·34) | 355/564 (63) | 0/25/75/0/0/0 |
| All |  |  | 2918 | 5·47 (1·08) | 1761/2849 (62) | 0/27/73/0/0/0 |
| Notes: IV = intravenous; IM = intramuscular injection; NR = not reported; SD = standard deviation | | | | | | | |

## eTable 6. Summary of nodes in a network meta-analysis of the effectiveness of treatments for bronchiolitis on hospital length of stay (LOS).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Node | Definition | Studies in node  (N) | Patients (N) | Age in months  Mean (SD) | Males  n/N (%) | Severity (%)  Mild/Mild-moderate/ Moderate/Moderate-severe/Severe/NR |
| Placebo (neb)43,53,57,59,60,66,79, 109,120,136,142,151,165,167,174,179,181 | Any nebulised placebo, including 0·9% saline. | 17 | 938 | 4·59 (1·13) | 546/907 (60) | 6/18/53/12/0/12 |
| Placebo (sys)46,52,70,103,122,123, 144,169,171,178 | Any systemic (i.e., oral, IV, IM) placebo | 10 | 518 | 6·41 (2·85) | 305/499 (61) | 0/20/0/0/0/80 |
| Placebo (air)72,79,97,115 | Inhaled gas control group (e.g., heated low-flow oxygen, humidified air, tent mist, etc.) | 4 | 886 | 6·60 (1·12) | 576/886 (65) | 0/25/50/0/0/25 |
| Standard care56,69,92,147,184 | Standard or usual care | 5 | 255 | 4·60 (1·96) | 142/240 (60) | 0/0/20/20/0/60 |
| Macrolide46,103,122,123,144,147,169 | Macrolide antibiotics | 7 | 329 | 4·34 (1·29) | 190/307 (62) | 0/0/0/0/0/100 |
| Penicillin-like70,147 | Penicillin-like antibiotics | 2 | 48 | NR | NR | 0/0/0/0/0/100 |
| Epi (neb)38,47,49,50,93,112,128,129, 139,142,167,170, 179 | Nebulised epinephrine | 13 | 720 | 4·42 (5·18) | 381/651 (59) | 0/8/46/38/0/8 |
| Sal (neb)49,50,56,59,60,66,71,79,93, 102,105,107,112,119,129,131,134,135,138,142,148,164, 172,181,182 | Nebulised salbutamol | 25 | 933 | 5·23 (1·93) | 497/803 (62) | 0/16/76/4/0/4 |
| IB (neb) + Sal (neb)60,181 | Nebulised salbutamol + nebulised ipratropium bromide | 2 | 41 | 3·64 (1·8) | 27/41 (66) | 0/0/100/0/0/0 |
| Steroid (sys)52,171,178,184 | Systemically delivered steroid | 4 | 213 | 10·43 (4·39) | 132/213 (62) | 0/50/0/0/0/50 |
| Steroid (neb)53,57,151 | Nebulised steroids | 3 | 121 | 4·70 (1·06) | 70/121 (58) | 0/67/0/0/0/33 |
| Hypertonic (neb)43,69,72,92,109,120,136,165,174 | Hypertonic saline (any) | 9 | 666 | 4·28 (1·73) | 363 (638) | 0/22/44/22/0/11 |
| Heliox115 | Heliox therapy | 1 | 18 | 1·10 (0·85) | 11/18 (61) | 0/0/100/0/0/0 |
| High Flow72,97 | High flow oxygen therapy | 2 | 840 | 6·58 (0·80) | 517/840 (62) | 0/50/0/0/0/50 |
| IB (neb)60,79,138,181 | Ipratropium bromide (nebulised) | 4 | 83 | 4·75 (0·52) | 47/68 (69) | 0/0/0/100/0/0 |
| Epi (neb) + Steroid (neb)47 | Epinephrine combined with a nebulised steroid | 1 | 29 | 3·30 (13·46) | 14/29 (48) | 0/0/0/100/0/0 |
| Sal (neb) + Steroid (sys)102 | Salbutamol combined with a systemically delivered steroid | 1 | 35 | 4·68 (2·96) | 22/35 (63) | 0/0100/0/0/0 |
| Hypertonic (neb) + Epi (neb)38,72,128,139,170,174 | Hypertonic saline + epinephrine | 6 | 394 | 3·36 (0·94) | 197/343 (57) | 0/0/50/50/0/0 |
| Hypertonic (neb) + Sal (neb)71,105,107,119,131,134,135,148,164,172,182 | Hypertonic saline + nebulised salbutamol | 11 | 684 | 5·17 (1·41) | 358/614 (58) | 0/9/73/9/0/9 |
| All |  |  | 7751 | 5·35 (1·68) | 4398/7253 (61) | 1/17/45/13/0/24 |
| Notes: IV = intravenous; IM = intramuscular injection; NR = not reported; SD = standard deviation | | | | | | | |

## eTable 7. Confidence in a Network Meta-Analysis (CINeMA) assessment for admission rate at day 1 (ARD1)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comparison | Number of studies | Within-study bias | Reporting bias | Indirectness | Imprecision | Heterogeneity | Incoherence | Confidence rating |
| Epi (neb) vs Epi (neb) + Hypertonic (neb) | 4 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs Epi (neb) + Steroid (sys) | 4 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) vs Hypertonic (neb) | 1 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs Hypertonic (neb) + Sal (neb) | 1 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs Placebo (air) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs Placebo (neb) | 6 | Some concerns | Undetected | No concerns | Some concerns | No concerns | No concerns | Low |
| Epi (neb) vs Sal (neb) | 11 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs Sal (neb) + Steroid (sys) | 3 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs Steroid (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs Steroid (sys) | 2 | No concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Moderate |
| Epi (neb) + Hypertonic (neb) vs Hypertonic (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Hypertonic (neb) + Sal (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Placebo (neb) | 2 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Epi (neb) + Hypertonic (neb) vs Sal (neb) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Major concerns | Very low |
| Epi (neb) + Steroid (sys) vs Placebo (neb) | 1 | No concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Moderate |
| Epi (neb) + Steroid (sys) vs Sal (neb) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs Sal (neb) + Steroid (sys) | 2 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Epi (neb) + Steroid (sys) vs Steroid (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Hypertonic (neb) vs Placebo (neb) | 3 | No concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Moderate |
| Hypertonic (neb) vs Sal (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs Placebo (neb) | 1 | Some concerns | Undetected | No concerns | No concerns | Some concerns | No concerns | Low |
| Hypertonic (neb) + Sal (neb) vs Sal (neb) | 3 | No concerns | Undetected | No concerns | Some concerns | No concerns | No concerns | Moderate |
| Placebo (air) vs Sal (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs Sal (neb) + Steroid (sys) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs Steroid (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Placebo (air) vs Steroid (sys) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs Placebo (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs Sal (neb) | 7 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Placebo (neb) vs Steroid (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Placebo (sys) vs Sal (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Placebo (sys) vs Steroid (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Sal (neb) vs Sal (neb) + IB (neb) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Sal (neb) vs Sal (neb) + Steroid (sys) | 5 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Sal (neb) vs Steroid (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) vs Steroid (sys) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + Steroid (sys) vs Steroid (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + Steroid (sys) vs Steroid (sys) | 1 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Low |
| Steroid (neb) vs Steroid (sys) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs Placebo (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) vs Sal (neb) + IB (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Epi (neb) + Hypertonic (neb) vs Epi (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Placebo (air) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Placebo (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) + Hypertonic (neb) vs Sal (neb) + IB (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Epi (neb) + Hypertonic (neb) vs Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Hypertonic (neb) vs Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs Hypertonic (neb) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) + Steroid (sys) vs Hypertonic (neb) + Sal (neb) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) + Steroid (sys) vs Placebo (air) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs Placebo (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) + Steroid (sys) vs Sal (neb) + IB (neb) | 0 | No concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Moderate |
| Epi (neb) + Steroid (sys) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) vs Placebo (air) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs Placebo (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) vs Sal (neb) + IB (neb) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) vs Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs Steroid (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Sal (neb) vs Placebo (air) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs Placebo (sys) | 0 | No concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Moderate |
| Hypertonic (neb) + Sal (neb) vs Sal (neb) + IB (neb) | 0 | No concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Moderate |
| Hypertonic (neb) + Sal (neb) vs Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs Steroid (sys) | 0 | No concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Moderate |
| Placebo (air) vs Placebo (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs Sal (neb) + IB (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs Sal (neb) + IB (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Placebo (neb) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (sys) vs Sal (neb) + IB (neb) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Placebo (sys) vs Sal (neb) + Steroid (sys) | 0 | No concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Moderate |
| Placebo (sys) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + IB (neb) vs Sal (neb) + Steroid (sys) | 0 | No concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Moderate |
| Sal (neb) + IB (neb) vs Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + IB (neb) vs Steroid (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |

## eTable 8. Confidence in a Network Meta-Analysis (CINeMA) assessment for admission rate up to day 7 (ARD7)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comparison | Number of studies | Within-study bias | Reporting bias | Indirectness | Imprecision | Heterogeneity | Incoherence | Confidence rating |
| Epi (neb) vs. Epi (neb) + Steroid (sys) | 3 | No concerns | Undetected | No concerns | Some concerns | No concerns | No concerns | Moderate |
| Epi (neb) vs. Hypertonic (neb) + Epi (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs. Hypertonic (neb) + Sal (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs. Placebo (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs. Placebo (sys) | 1 | No concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Moderate |
| Epi (neb) vs. Sal (neb) | 5 | Major concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Sal (neb) + Steroid (sys) | 2 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) vs. Steroid (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Epi (neb) + Steroid (sys) vs. Placebo (sys) | 1 | No concerns | Undetected | No concerns | No concerns | No concerns | No concerns | High |
| Epi (neb) + Steroid (sys) vs. Sal (neb) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) + Steroid (sys) vs. Sal (neb) + Steroid (sys) | 2 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Epi (neb) + Steroid (sys) vs. Steroid (sys) | 1 | No concerns | Undetected | No concerns | No concerns | No concerns | Some concerns | Moderate |
| Hypertonic (neb) vs. Placebo (neb) | 2 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. Hypertonic (neb) + Sal (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Placebo (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Sal (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Placebo (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Sal (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Placebo (neb) vs. Sal (neb) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Placebo (sys) vs. Steroid (sys) | 4 | No concerns | Undetected | No concerns | Some concerns | No concerns | No concerns | Moderate |
| Sal (neb) vs. Sal (neb) + Steroid (sys) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs. Hypertonic (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs. Hypertonic (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs. Hypertonic (neb) + Epi (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (sys) vs. Placebo (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Hypertonic (neb) + Epi (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (sys) vs. Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Placebo (sys) vs. Sal (neb) + Steroid (sys) | 0 | No concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Moderate |
| Sal (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Sal (neb) + Steroid (sys) vs. Steroid (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |

## eTable 9. Confidence in a Network Meta-Analysis (CINeMA) assessment for hospital length of stay (LOS)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Comparison | Number of studies | Within-study Bias | Reporting Bias | Indirectness | Imprecision | Heterogeneity | Incoherence | Overall Confidence |
| Hypertonic (neb) + Sal (neb) vs. Sal (neb) | 9 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Low |
| Epi (neb) vs. Sal (neb) | 6 | Some concerns | Undetected | No concerns | No concerns | Major concerns | No concerns | Very low |
| Hypertonic (neb) vs. Placebo (neb) | 6 | Some concerns | Undetected | No concerns | No concerns | Some concerns | No concerns | Low |
| Macrolide vs. Placebo (sys) | 6 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Placebo (neb) vs. Sal (neb) | 6 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Low |
| Epi (neb) vs. Hypertonic (neb) + Epi (neb) | 4 | Some concerns | Undetected | No concerns | No concerns | Some concerns | No concerns | Low |
| IB (neb) vs. Sal (neb) | 4 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Very low |
| Epi (neb) vs. Placebo (neb) | 3 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Low |
| IB (neb) vs. Placebo (neb) | 3 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Very low |
| Placebo (neb) vs. Steroid (neb) | 3 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Very low |
| Placebo (sys) vs. Steroid (sys) | 3 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| High Flow vs. Placebo (air) | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) vs. Hypertonic (neb) + Epi (neb) | 2 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Standard care | 2 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Placebo (neb) | 2 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Sal (neb) | 2 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. IB (neb) + Sal (neb) | 2 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Epi (neb) vs. Epi (neb) + Steroid (neb) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Heliox vs. Placebo (air) | 1 | Some concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Placebo (neb) | 1 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | No concerns | Low |
| IB (neb) vs. Placebo (air) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Penicillin-like | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Standard care | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Penicillin-like vs. Placebo (sys) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Standard care | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Placebo (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Sal (neb) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Very low |
| Sal (neb) vs. Sal (neb) + Steroid (sys) | 1 | No concerns | Undetected | No concerns | Major concerns | No concerns | No concerns | Low |
| Sal (neb) vs. Standard care | 1 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Standard care vs. Steroid (sys) | 1 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Heliox | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. High Flow | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Hypertonic (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Hypertonic (neb) + Epi (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. IB (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. IB (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Macrolide | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Penicillin-like | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Placebo (air) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Placebo (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) + Steroid (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Heliox | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. High Flow | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Hypertonic (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs. IB (neb) | 0 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| Epi (neb) vs. IB (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Macrolide | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Epi (neb) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Epi (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. High Flow | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Hypertonic (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Hypertonic (neb) + Epi (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. IB (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. IB (neb) + Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Placebo (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Heliox vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Hypertonic (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Hypertonic (neb) + Epi (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. IB (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. IB (neb) + Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Placebo (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Standard care | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| High Flow vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. IB (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. IB (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Epi (neb) vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Epi (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. IB (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. IB (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Macrolide | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Penicillin-like | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Placebo (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) + Sal (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Sal (neb) + Steroid (sys) | 0 | No concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) + Sal (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) + Sal (neb) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Hypertonic (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) vs. IB (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) vs. IB (neb) + Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| Hypertonic (neb) vs. Sal (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Hypertonic (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Hypertonic (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) + Sal (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Macrolide | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Penicillin-like | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| IB (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Placebo (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Macrolide vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Placebo (air) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Placebo (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Penicillin-like vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Placebo (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Standard care | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (air) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Placebo (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (neb) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Some concerns | No concerns | Some concerns | Low |
| Placebo (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (sys) vs. Sal (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (sys) vs. Sal (neb) + Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Placebo (sys) vs. Standard care | 0 | Major concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Very low |
| Placebo (sys) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + Steroid (sys) vs. Standard care | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Sal (neb) + Steroid (sys) vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) + Steroid (sys) vs. Steroid (sys) | 0 | Some concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) vs. Steroid (neb) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Sal (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |
| Standard care vs. Steroid (neb) | 0 | Some concerns | Undetected | No concerns | Some concerns | Some concerns | Some concerns | Low |
| Steroid (neb) vs. Steroid (sys) | 0 | Major concerns | Undetected | No concerns | Major concerns | No concerns | Some concerns | Very low |

# Appendices

## Appendix 1: PRISMA Checklist of Items to Include When Reporting A Systematic Review Involving a Network Meta-analysis

|  |  |  |  |
| --- | --- | --- | --- |
| Section/Topic | Item # | Checklist Item | Reported on Page # |
| TITLE |  |  |  |
| Title | 1 | Identify the report as a systematic review incorporating a network meta-analysis (or related form of meta-analysis). | Page 1 |
|  |  |  |  |
| ABSTRACT |  |  |  |
| Structured summary | 2 | Provide a structured summary including, as applicable:  Background: main objectives  Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and *synthesis methods, such as network meta-analysis.*  Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.  Discussion/Conclusions: limitations; conclusions and implications of findings.  Other: primary source of funding; systematic review registration number with registry name. | Page 4 |
|  |  |  |  |
| INTRODUCTION |  |  |  |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known*, including mention of why a network meta-analysis has been conducted.* | Page 5 |
| Objectives | 4 | Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | Page 5 |
|  |  |  |  |
| METHODS |  |  |  |
| Protocol and registration | 5 | Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web address); and, if available, provide registration information, including registration number. | Page 6 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. *Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).* | Page 6-7 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | Page 6 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | Page 6 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | Page 6 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | Page 7 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | Page 7 |
| Geometry of the network | S1 | Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers. | Page 8 |
| Risk of bias within individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | Page 8 |
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses. | Page 8 |
| Planned methods of analysis | 14 | Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to:  Handling of multi-arm trials;  Selection of variance structure;  Selection of prior distributions in Bayesian analyses; and  Assessment of model fit. | Page 8 |
| Assessment of Inconsistency | S2 | Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found. | Page 8 and Appendix 4 |
| Risk of bias across studies | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | Page 8 |
| Additional analyses | 16 | Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following:  Sensitivity or subgroup analyses;  Meta-regression analyses;  Alternative formulations of the treatment network; and  Use of alternative prior distributions for Bayesian analyses (if applicable). | Page 8 |
|  |  |  |  |
| RESULTS† |  |  |  |
| Study selection | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | Figure 1 |
| Presentation of network structure | S3 | Provide a network graph of the included studies to enable visualization of the geometry of the treatment network. | Figure 3 |
| Summary of network geometry | S4 | Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure. | Page 9, Appendix 5 |
| Study characteristics | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | eTable2 |
| Risk of bias within studies | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment. | Figure 2, eTable 3 |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. *Modified approaches may be needed to deal with information from larger networks.* | eTables 4-6 |
| Synthesis of results | 21 | Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented. | Figure 4 |
| Exploration for inconsistency | S5 | Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, *P* values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network. | Appendix 5 |
| Risk of bias across studies | 22 | Present results of any assessment of risk of bias across studies for the evidence base being studied. | eTables 7-9 |
| Results of additional analyses | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses*, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses,* and so forth). | Page 10, Appendices 7-9 |
|  |  |  |  |
| DISCUSSION |  |  |  |
| Summary of evidence | 24 | Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers). | Page 11 |
| Limitations | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). *Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).* | Page 12-13 |
| Conclusions | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | Page 13 |
|  |  |  |  |
| FUNDING |  |  |  |
| Funding | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network. | Title page  Role of Funders: Page 8 |

PICOS = population, intervention, comparators, outcomes, study design.

\* Text in italics indicates wording specific to reporting of network meta-analyses that has been added to guidance from the PRISMA statement.

† Authors may wish to plan for use of appendices to present all relevant information in full detail for items in this section.

## Appendix 2. Reported Protocol Deviations

In the current report only the two primary outcomes are presented: proportion of outpatient visits resulting in admission (i.e., admission rate; AR) and length of stay in days (LOS). Subsequent manuscripts will report on secondary outcomes of interest as outlined in the protocol (e.g. clinical score, respiratory rate, etc.). The Protocol was updated in Prospero on the 26th March 2019, to reflect these amendments.

This review deviated from the original protocol in the following ways:

Contacting study authors for missing data

Because the majority of studies reporting the primary outcomes were able to be included in the analysis, an *ad hoc* decision was made not to sink resources into contacting study authors for missing data.

Pairwise analysis

As a result of how we approached defining “Placebo”, a number of placebo nodes were included in the analysis (Placebo [Neb]), Placebo [systemic], Placebo [air], standard care). It was unfeasible to split the pairwise comparisons by their placebos for comparative purposes.

Reporting of GRADE

We utilised a new approach and web application that simplifies the evaluation of confidence in the findings from network meta-analysis (CINeMA).1,2

**References:**

1. Salanti, G., et al. (2014). "Evaluating the quality of evidence from a network meta-analysis." PLOS ONE 9(7): e99682

2. Nikolakopoulou, A., et al. (2019). "Assessing confidence in the results of network meta-analysis (CINeMA)." 597047

## Appendix 3. Search strategy

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Search Title: Bronchiolitis-NMA

Strategy:

|  |
| --- |
| 1. Bronchiolitis/  2. Bronchiolitis, Viral/  3. Metapneumovirus/  4. Parainfluenza Virus 3, Human/  5. Respiratory Syncytial Viruses/  6. Respiratory Syncytial Virus, Human/  7. Respiratory Syncytial Virus Infections/  8. bronchioliti\*.tw,kf.  9. ((first\* or recurr\*) adj3 wheez\*).tw,kf.  10. metapneumovirus\*.tw,kf.  11. ((para-influenza or parainfluenza) adj virus adj2 ("3" or three)).tw,kf.  12. respiratory s#nc#t#al vir\*.tw,kf.  13. RSV.tw,kf.  14. or/1-13 [Combined MeSH and text words for bronchiolitis]  15. Child, Preschool/  16. exp Infant/  17. exp Pediatrics/  18. (baby\* or babies or infan\* or neo-nat\* or neonat\* or newborn\* or post-matur\* or postmatur\* or pre-matur\* or prematur\* or pre-term\* or preterm\*).tw,jw,kf.  19. (child\* or pre-school\* or preschool\* or toddler\*).tw,jw,kf.  20. p?ediatric\*.tw,jw,kf.  21. or/15-20 [Combined MeSH and text words for infants]  22. and/14,21 [Combined concept for bronchiolitis and infants]  23. controlled clinical trial.pt.  24. randomized controlled trial.pt.  25. drug therapy.fs.  26. group?.ab.  27. placebo.ab.  28. random\*.ab.  29. trial.ab.  30. or/23-29  31. exp animals/ not humans/  32. (animal or animal-model\* or animals or bovine or calves or camel\* or canine\* or cat or cats or dog or dogs or equine or feline or felines or goat\* or hamster or hamsters or llama\* or mice or monkey or monkeys or mouse or pig or piglet or piglets or pigs or porcine or primate\* or rabbit or rabbits or rat or rats or rodent or rodents or sheep or simian\* or swine or swines).ti.  33. 30 not (31 or 32) [Modified Cochrane Highly Sensitive search strategy for identifying randomized trials - http://handbook.cochrane.org/]  34. and/22,33 [RCT filter applied]  35. remove duplicates from 34 |

Known item test:

36. (11919104 or 17543129 or 9773910 or 11288210 or 10648365 or 16537867 or 9695300 or 9124056 or 7735418 or 7598441 or 23509160 or 17652648 or 9427901 or 5323069 or 26572729 or 8283363 or 8190575 or 10791133 or 9364884 or 17722445 or 18695272 or 22100741 or 1929514 or 9781732 or 27688541 or 18042975 or 22147778 or 2019938 or 9042119 or 18085694 or 19450268 or 15491380 or 16356437 or 18411235 or 24086334 or 7776075 or 19445861 or 23056893 or 14757602 or 12461499 or 12756382 or 22748516 or 19439742 or 16082697 or 9602198 or 8709687 or 8419602 or 2213394 or 11815760 or 1437435 or 17050564 or 17394255 or 19537014 or 11983043 or 12840089 or 12969212).ui. (57)

37. remove duplicates from 36 (56)

38. 37 not 35 (1)

Note: strategy did not find this cross-over study (excluded because of RCT filter)

Kneyber MC, van Heerde M, Twisk JW, Plötz FB, Markhors DG. Heliox reduces respiratory system resistance in respiratory syncytial virus induced respiratory failure. Critical care. 2009 May 15;13(3):1. PMID: 19450268

Database: Ovid Embase 1974 to 2016 Week 42

Search Title: Bronchiolitis-NMA\_1

Strategy:

|  |
| --- |
| 1. bronchiolitis/  2. human metapneumovirus/  3. human parainfluenza virus 3/  4. exp human respiratory syncytial virus/  5. viral bronchiolitis/  6. bronchioliti\*.tw,kw.  7. ((first\* or recurr\*) adj3 wheez\*).tw,kw.  8. metapneumovirus\*.tw,kw.  9. ((para-influenza or parainfluenza) adj virus adj2 ("3" or three)).tw,kw.  10. respiratory s#nc#t#al vir\*.tw,kw.  11. RSV.tw,kw.  12. or/1-11 [Combined Emtree and text words for bronchiolitis]  13. exp infant/  14. exp pediatrics/  15. preschool child/  16. toddler/  17. (baby\* or babies or infan\* or neo-nat\* or neonat\* or newborn\* or post-matur\* or postmatur\* or pre-matur\* or prematur\* or pre-term\* or preterm\*).tw,jx,kw.  18. (child\* or pre-school\* or preschool\* or toddler\*).tw,jx,kw.  19. p?ediatric\*.tw,jx,kw.  20. or/13-19 [Combined Emtree and text words for infants]  21. and/12,20 [Combined concept for bronchiolitis and infants]  22. crossover procedure/  23. clinical trial/  24. double blind procedure/  25. placebo/  26. prospective study/  27. randomization/  28. randomized controlled trial/  29. single blind procedure/  30. (allocat\* adj2 random\*).tw.  31. double blind\*.tw.  32. placebo\*.tw.  33. randomi?ed controlled trial\*.tw.  34. RCT.tw.  35. single blind\*.tw.  36. ((treble or triple) adj blind\*).tw.  37. or/22-36  38. abstract report/  39. case study/  40. letter/  41. (case adj (report\* or stud\*)).ti.  42. or/38-41  43. 37 not 42  44. exp animals/ not exp humans/  45. (animal or animal-model\* or animals or bovine or calves or camel\* or canine\* or cat or cats or dog or dogs or equine or feline or felines or goat\* or hamster or hamsters or llama\* or mice or monkey or monkeys or mouse or pig or piglet or piglets or pigs or porcine or primate\* or rabbit or rabbits or rat or rats or rodent or rodents or sheep or simian\* or swine or swines).ti.  46. 43 not (44 or 45) [Modified SIGN Embase RCT filter - http://www.sign.ac.uk/methodology/filters.html#random]  47. and/21,46 [RCT filter applied]  48. remove duplicates from 47 |

Database: Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley Cochrane Library (inception to present)

Search Title: Bronchiolitis-NMA

Strategy:

|  |
| --- |
| 1. [mh ^Bronchiolitis]  2. [mh ^"Bronchiolitis, Viral"]  3. [mh ^Metapneumovirus]  4. [mh ^"Parainfluenza Virus 3, Human"]  5. [mh ^"Respiratory Syncytial Viruses"]  6. [mh ^"Respiratory Syncytial Virus, Human"]  7. [mh ^"Respiratory Syncytial Virus Infections"]  8. bronchioliti\*:ti,ab,kw  9. ((first\* or recurr\*) near/3 wheez\*):ti,ab,kw  10. metapneumovirus\*:ti,ab,kw  11. ((para-influenza or parainfluenza) near/1 virus near/2 ("3" or three)):ti,ab,kw  12. "respiratory s?nc?t?al vir\*":ti,ab,kw  13. RSV:ti,ab,kw  15. [mh ^"Child, Preschool"]  16. [mh Infant]  17. [mh Pediatrics]  18. (baby\* or babies or infan\* or neo-nat\* or neonat\* or newborn\* or post-matur\* or postmatur\* or pre-matur\* or prematur\* or pre-term\* or preterm\*):ti,ab,kw,so  19. (child\* or pre-school\* or preschool\* or toddler\*):ti,ab,kw,so  20. p\*diatric\*:ti,ab,kw,so  21. [OR #15-#20]  22. #14 AND #21  23. #14 AND #21 in Trials |

Database: CINAHL Plus with Full Text via EBSCOhost (1937 to the present)

Search Title: Bronchiolitis-NMA

Strategy:

|  |
| --- |
| S1. (MH "Bronchiolitis")  S2. (MH "Respiratory Syncytial Virus Infections")  S3. (MH "Respiratory Syncytial Viruses")  S4. bronchioliti\*  S5. ((first\* or recurr\*) N3 wheez\*)  S6. metapneumovirus\*  S7. ((para-influenza or parainfluenza) N1 virus N2 ("3" or three))  S8. "respiratory s?nc?t?al vir\*"  S9. RSV  S10. S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9  S11. (MH "Child, Preschool")  S12. (MH "Infant+")  S13. (MH "Pediatrics+")  S14. (baby\* or babies or infan\* or neo-nat\* or neonat\* or newborn\* or post-matur\* or postmatur\* or pre-matur\* or prematur\* or pre-term\* or preterm\*)  S15. (child\* or pre-school\* or preschool\* or toddler\*)  S16. (p#ediatric or p#ediatrics)  S17. S11 OR S12 OR S13 OR S14 OR S15 OR S16  S18. S10 AND S17  S19. PT clinical trial  S20. (MH "Clinical Trials+")  S21. (MH "Placebos")  S22. (MH "Quantitative Studies")  S23. (MH "Random Assignment")  S24. (allocat\* N1 random\*)  S25. (blind\* N1 (doubl\* OR singl\* OR trebl\* OR tripl\*)  S26. (clinic\* N1 trial\*)  S27. (mask\* N1 (doubl\* OR singl\* OR trebl\* OR tripl\*)  S28. placebo\*  S29. "randomi?ed controlled trial"  S30. S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29  S31. ((MH "Vertebrates+") NOT MH Human)  S32. TI(animal or animal-model\* or animals or bovine or calves or camel\* or canine\* or cat or cats or dog or dogs or equine or feline or felines or goat\* or hamster or hamsters or llama\* or mice or monkey or monkeys or mouse or pig or piglet or piglets or pigs or porcine or primate\* or rabbit or rabbits or rat or rats or rodent or rodents or sheep or simian\* or swine or swines)  S33. S30 NOT (S31 OR S32) [Modified SIGN CINAHL RCT filter - http://www.sign.ac.uk/methodology/filters.html#random  S34. S18 AND S33 [RCT filter applied] |

Trial Registry: ClinicalTrials.gov

URL: <https://clinicaltrials.gov/>

Strategy:

|  |
| --- |
| Advanced Search >  Study Type: Interventional Studies  Age: Child  Conditions: "Bronchiolitis" OR "Bronchiolitis, Viral" OR "respiratory syncytial virus" OR "respiratory syncytial viruses" OR RSV  First Received: From 01/01/2014 to 10/20/2016 |

Trial Registry: World Health Organization International Clinical Trials Registry Platform (WHO ICTRP)

URL: <http://apps.who.int/trialsearch/>

Strategy:

|  |
| --- |
| Advanced Search >  Search for clinical trials in children  Recruitment status is: ALL  Conditions: bronchiolitis OR respiratory syncytial virus OR respiratory syncytial viruses OR RSV  Date of registration: From 01/01/2014 to 10/11/2016 |

## Appendix 4. CINeMA methods and Grading decisions

We assessed the confidence in estimates of the main outcomes (AR and LOS) with Confidence in Network Meta‐Analysis (CINeMA), an adaptation of the Grading of Recommendations Assessment, Development and Evaluation framework (GRADE) specifically developed for network meta‐analysis.1,2

The level of confidence in the evidence for each pair of nodes in the network is rated on five domains: study limitations (i.e., the risk of bias in each study); indirectness of the evidence; inconsistency (including heterogeneity and incoherence); imprecision (i.e., whether the 95% confidence interval includes values potentially leading to different clinical decisions); and publication bias. The confidence ratings for each pair of nodes was then used to assess the overall confidence in the evidence across the entire network.

**Decision Rules**

1. Within Study Bias

We classified an overall risk of bias for every study based on the individual risk of bias items3, and summarized the within study bias for each comparison using the weighted average score for each relative effect estimate according to the percentage contribution of studies at each bias level. For the weighted average, we used the percentage contribution matrix to approximate the contribution of each study, and assigned scores of −1, 0 and 1 to low, moderate and high risk of bias.

2. Reporting Bias

We set all as undetected based on the completeness of our search, prior empirical evidence (clinical expert judgments considerations) related to this field, and the high proportion of trials that reported AR and LOS in their respective settings (60% of outpatient studies reported on admission rate, and 76% of inpatient studies reported on LOS). We could not use quantitative approaches such as funnel plots to assess publication bias because all but one comparison in each network were assessed by a small number of studies (<8).

3. Indirectness

We controlled for transitivity by using tight inclusion criteria; only studies investigating a specified treatment intervention in children aged ≤ 24months, with a clinical diagnosis of bronchiolitis were included. We qualitatively assessed the distribution of effect modifiers (sex, age, disease severity, and wheeze status) across the comparisons and concluded that there was no indirectness in any of the studies included.

4. Imprecision

For our dichotomous outcomes (ARD1 and ARD7) odds ratios lower than 0.800 or higher than 1.25 were considered clinically meaningful. The clinically meaningful thresholds were set at mean differences of ±0.5 days for the continuous outcome of LOS. If the confidence interval crossed the clinically meaningful threshold the comparison was downgraded one level. Crossing both thresholds resulted in a downgrading of two levels.

5. Heterogeneity

We evaluated the degree of concern due to heterogeneity by comparing the clinical inference determined by the 95% confidence intervals (CI) and the 95% prediction interval (PrI),4,5 the latter reflecting the degree of heterogeneity. Applying the same clinically meaningful thresholds as above, we considered there to be no concerns in heterogeneity when the two judgements matched (e.g., neither 95% CI nor 95% PrI crossed a threshold for clinically important effects), some concerns when they differed by one degree (e.g., if the a boundary of the 95% PrI crossed a threshold for clinically important effects where the 95% CI did not), and major concerns when they differed by two degrees (e.g., no concern based on 95% CI but 95% PrI crossed into clinically important effects in both directions).

6. Incoherence

We assessed incoherence both globally using the design-by-treatment interaction model and locally using the Separate Indirect from Direct Evidence (SIDE, or node-splitting approach).6,7

With respect to incoherence, we did not downgrade comparisons that had only direct evidence. The same judgement was made for comparisons with mixed evidence for which the contribution of direct evidence was more than 90%. We used the rules described by Salanti, 20142 to infer confidence regarding incoherence in network treatment effects informed by less than 90% direct evidence, which were downgraded for large inconsistency measures (i.e., difference of mean differences >0.5 or < -0.5 or ratio of ratios <0.8 or >1.25).

As there will always be concerns around inconsistency for indirect evidence, comparisons with only indirect evidence we downgraded for incoherence by one or two levels depending on whether the p < 0.01 for the design by treatment interaction model.2

7. Overall assessment:

To assess overall confidence in the evidence for each comparison, we followed the guidance outlined by the developers of the CINeMA framework.2 Each comparison started at ‘high’ confidence and was downgraded 1 level for each domain with a rating of with some concerns and downgraded 2 levels for each domain with major concerns. However, the six domains assessed by CINeMA should be considered jointly rather than in isolation, avoiding downgrading the overall level of confidence more than once for related concerns. Because imprecision, heterogeneity and incoherence are interconnected, comparisons were downgraded only once based on a combined assessment of these domains. Comparisons were downgraded 2 steps for a rating of “major concerns” in any one of these 3 domains, while a rating of “some concerns” in imprecision, heterogeneity or incoherence resulted in downgrading 1 step.

Table: Evaluation schema for overall confidence in the evidence provided by each comparison.

|  |  |
| --- | --- |
| Domain(s) | Downgrading criteria |
| Within-study bias | No Concerns = No downgrading  Some Concerns = ↓  Major Concerns = ↓↓ |
| Reporting bias | Undetected = No downgrading  Detected = ↓↓ |
| Indirectness | No Concerns = No downgrading  Some Concerns = ↓  Major Concerns = ↓↓ |
| Imprecision and Inconsistency (Heterogeneity, Incoherence) | No Concerns = No downgrading  Some Concerns = ↓  Major Concerns = ↓↓ |

**References:**

1. Nikolakopoulou, A., et al. (2019). "Assessing confidence in the results of network meta-analysis (CINeMA)." 597047.

2. Salanti, G., et al. (2014). "Evaluating the quality of evidence from a network meta-analysis." PLOS ONE 9(7): e99682.

3. Higgins, J. P., et al. (2011). "The Cochrane Collaboration's tool for assessing risk of bias in randomised trials." BMJ 343: d5928

4. Higgins, J. P., et al. (2012). "Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies." Res Synth Methods 3(2): 98-110.

5. Riley, R. D., et al. (2011). "Interpretation of random effects meta-analyses." 342: d549.

6. White, I. R., et al. (2012). "Consistency and inconsistency in network meta-analysis: model estimation using multivariate meta-regression." Research synthesis methods 3(2): 111-125.

7. Dias, S., et al. (2010). "Checking consistency in mixed treatment comparison meta-analysis." Statistics in medicine 29(7-8): 932-944.

## Appendix 5. Summary of Each Network

The contribution matrices for each network showing the percentage of contributions from the direct comparisons for the mixed and indirect estimates can be made available upon request.

**ARD1 Network**

Usable data on 4656 patients were available from 27 of 35 studies reporting on ARD1 (eTable 2). Studies analysed for the ARD1 network enrolled a median of 83 patients (range: 25 to 800). A majority of studies included in the network were carried out in North America (Canada: n=7; USA: n=8). Eight studies restricted eligibility to patients ≤12 months. 21 of the 27 studies limited enrolment to first-time wheezers only. For studies contributing to the ADR1 network, the overall risk of bias was low for 11 studies (41%), high for 7 studies (26%), and unclear for 9 studies (33%).

The ARD1 network was well connected. The most evaluated nodes in the ARD1 network were: nebulised salbutamol (19 studies) and nebulised epinephrine (16 studies) (Table 2). The only node not contained within a closed loop was nebulised salbutamol combined with ipratropium bromide, which was evaluated in only one comparison (against nebulised salbutamol alone). Direct evidence was available for 38 of 78 (49%) possible comparisons and indirect evidence was available for all comparisons without direct evidence.

**ARD7 Network**

Usable data on ARD7 were available for 3107 patients in 13 of 35 studies, most of which were carried out in Canada (n=4) or the USA (n=6) (eTable 2). Studies analysed for the ARD7 network enrolled a median of 90 patients (range: 51 to 800). Of the 13 studies, 6 restricted eligibility criteria to patients ≤12 months. Ten studies restricted inclusion criteria to only first-time wheezers. The overall risk of bias for studies contributing to the ADR7 network was low for 6 studies, high for 5 studies, and unclear for 2 studies.

Among the ARD7 studies two isolated networks were initially identified, of which one included only one a single study comparing heliox to air-type placebo. This study was therefore excluded from further analysis and the network was built using the remaining 12 studies. In the refined network, the most frequent nodes were also nebulised epinephrine (6 studies) and nebulised salbutamol (6 studies). Nebulised hypertonic saline was the only node not included in a closed loop.

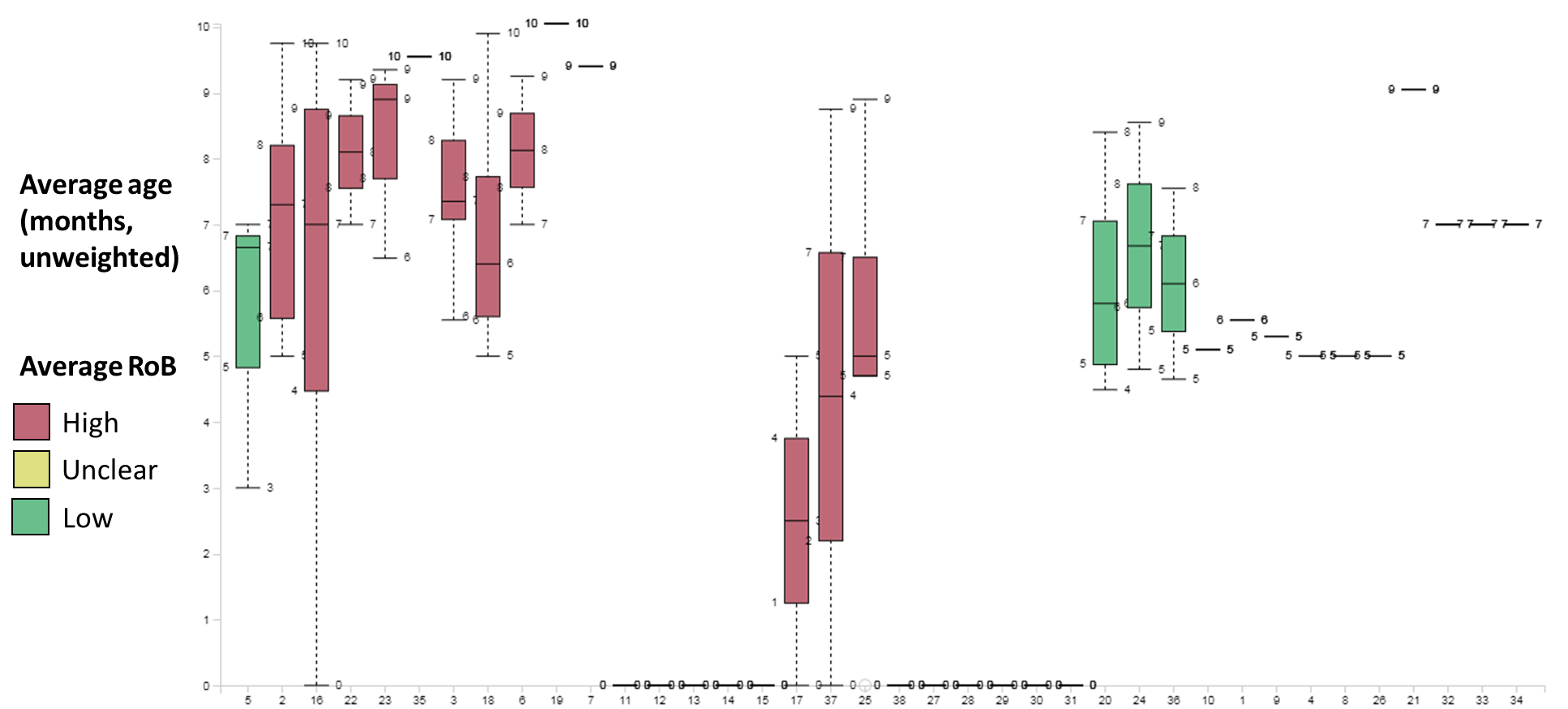
**LOS connectivity**

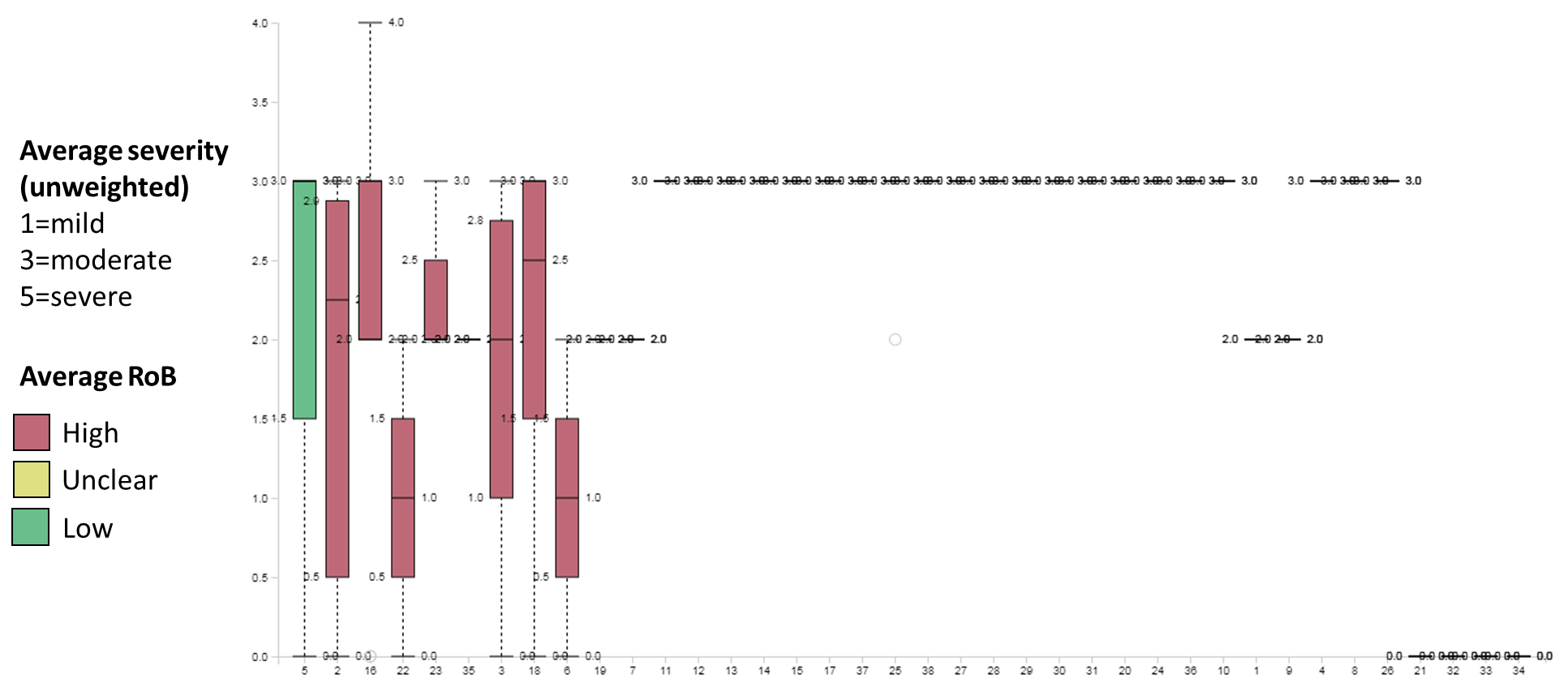
Usable data for LOS in nodes of interest were available on 7751 patients from 59 of the 83 studies reporting on this outcome (eTable 2). Studies were carried out in 31 countries, most frequently Canada (n=6), Australia (n=5), India (n=5), Turkey (n=4), the United Kingdom (n=4) and the United States (n=4). Studies analysed for the LOS network enrolled a median of 97 patients (range: 30 to 1638). Twenty-two studies restricted eligibility to patients ≤12 months. Overall, 43 enrolled only first-time wheezers while 13 studies did not report on wheeze status. Of studies contributing to the LOS network had an unclear risk of bias (n=28, 51%); risk of bias was low in 6 studies, and high in 25 studies (eTable 2).

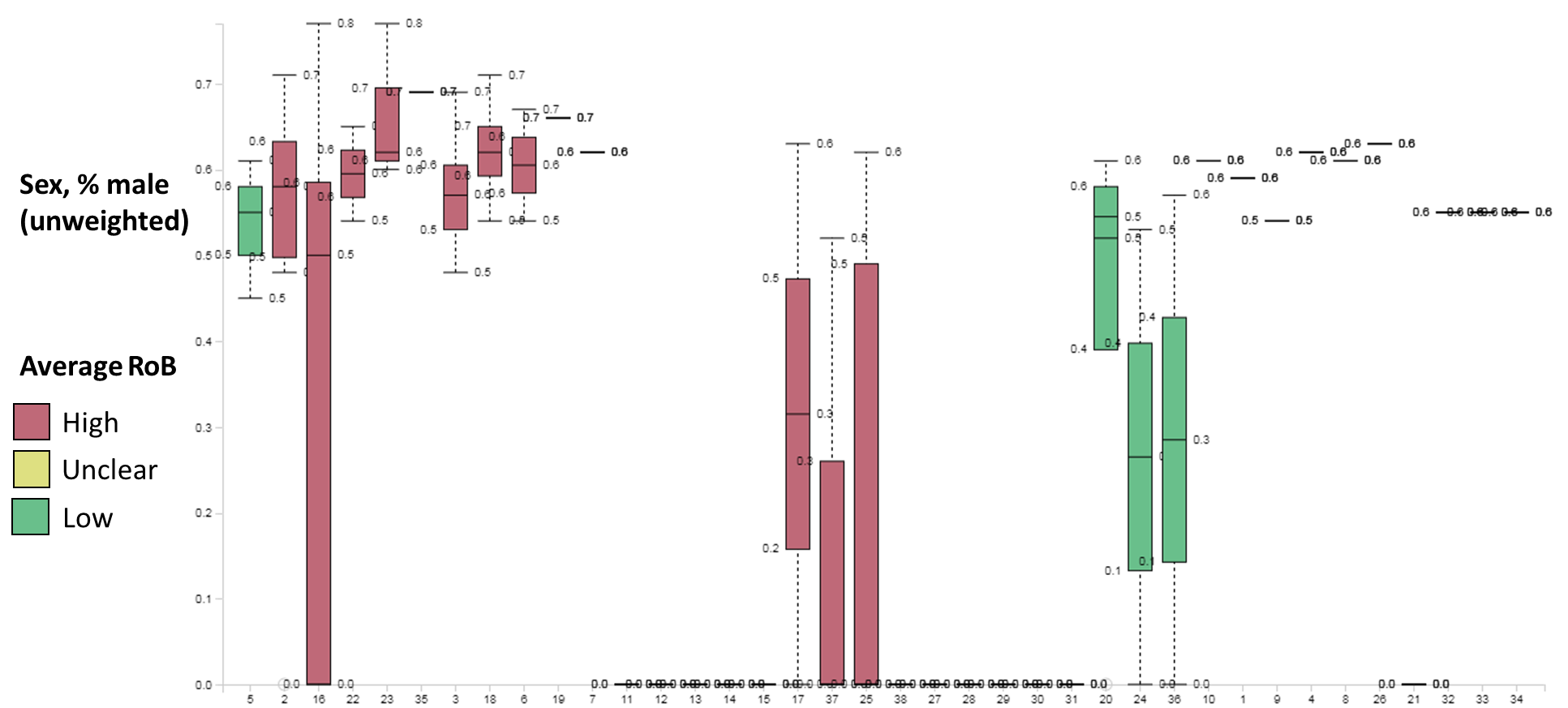
The most frequently evaluated nodes in the LOS network included were nebulised salbutamol (25 studies), nebulised placebo (17 studies), and nebulised epinephrine (13 studies). The LOS network was less well-connected than the ARD1 network, and several nodes were not included in any closed loops. Six nodes were included in only one direct comparison each: high flow oxygen therapy (2 studies); heliox therapy (1 study); nebulised epinephrine plus steroid (1 study); nebulised steroid (3 studies); nebulised salbutamol plus systemic steroid (1 study); and hypertonic saline nebulised with salbutamol (11 studies). Overall, direct evidence was available for 30/171 (18%) of possible comparisons; indirect evidence was available for all comparisons without direct evidence.

## Appendix 6. Qualitative evaluations of clinical transitivity assumptions.

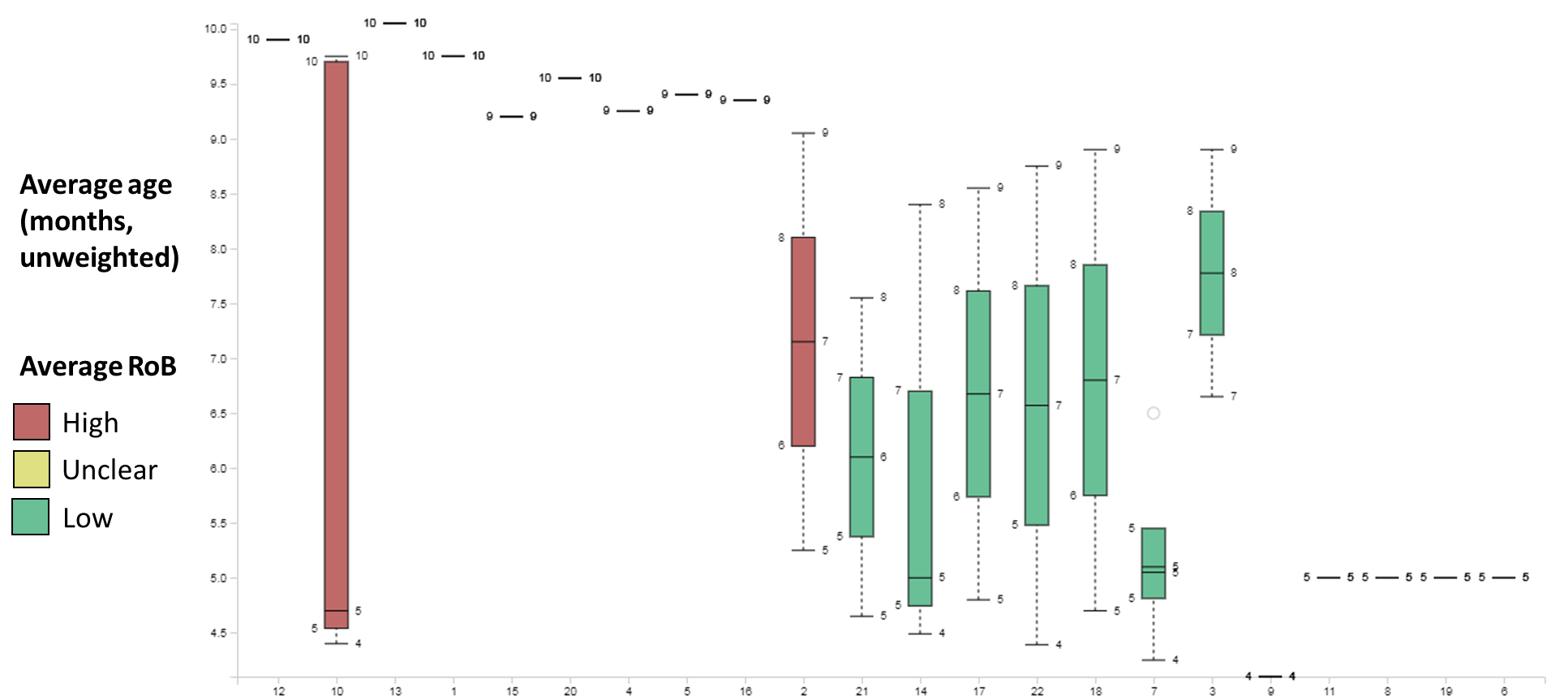
ARD1 – By comparison

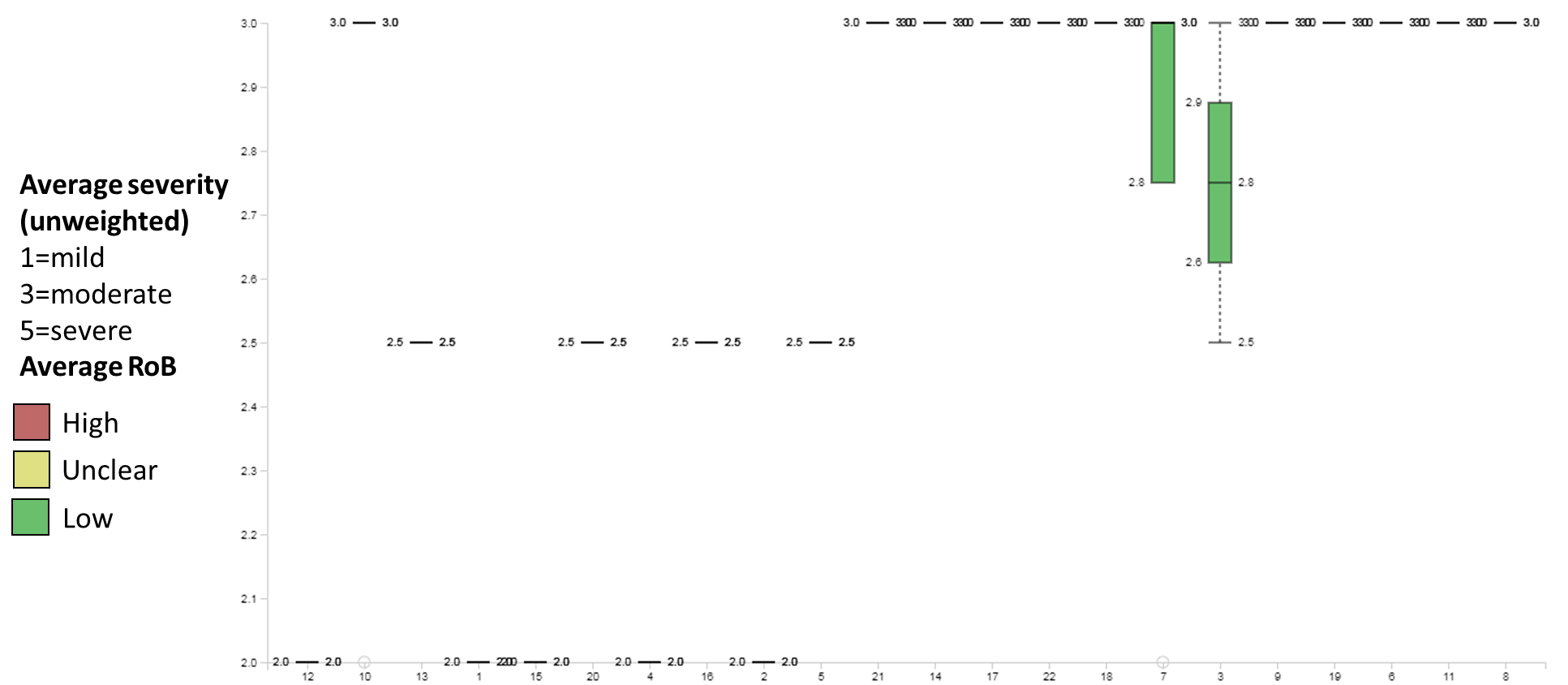


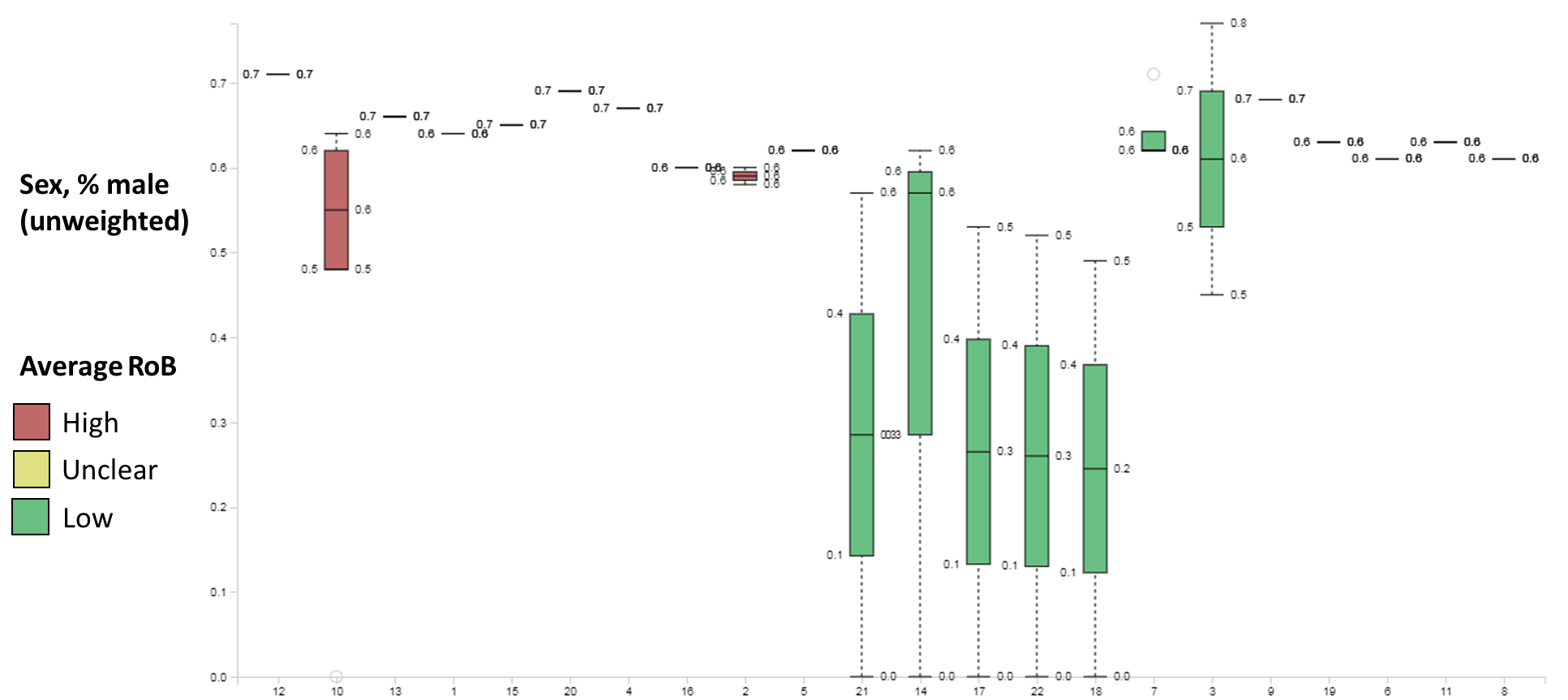




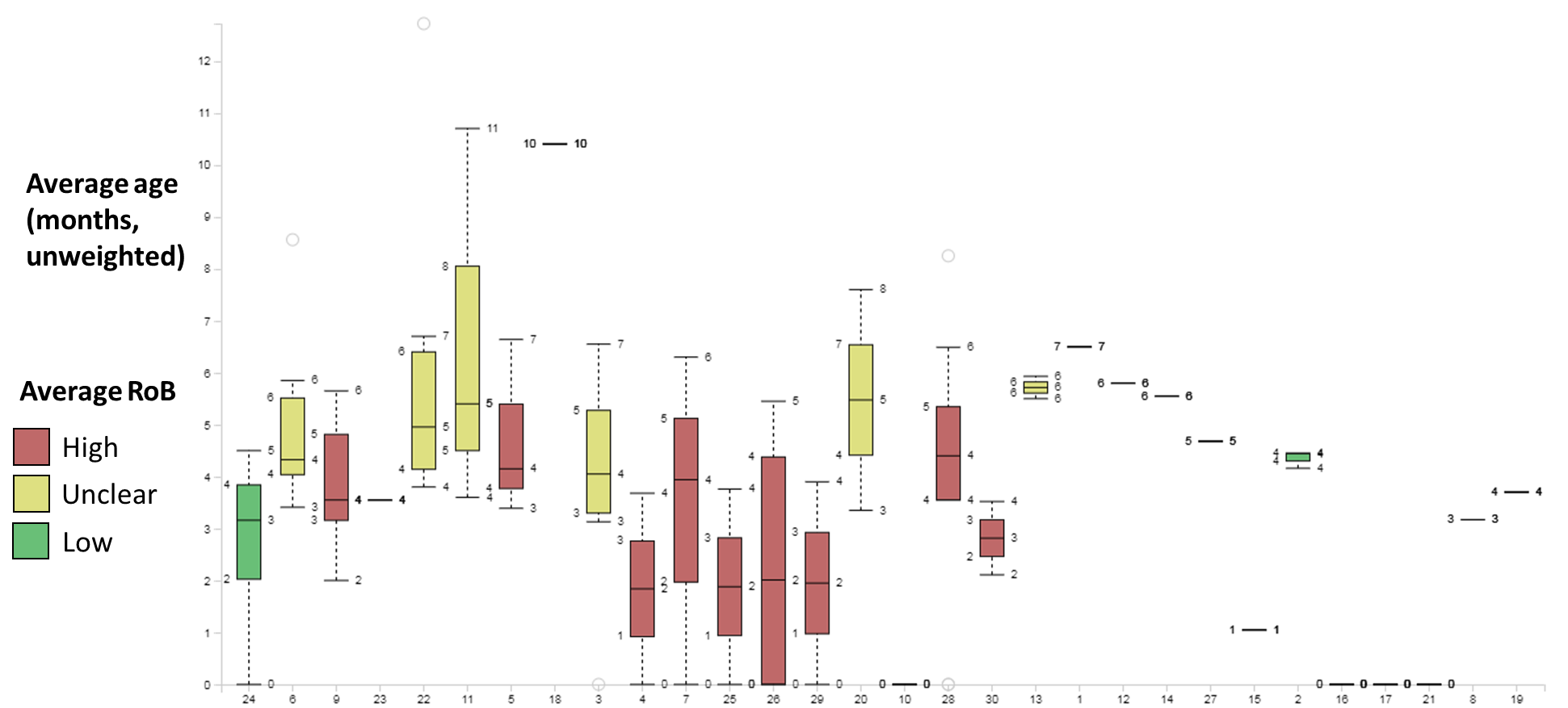
ARD7 – By comparison

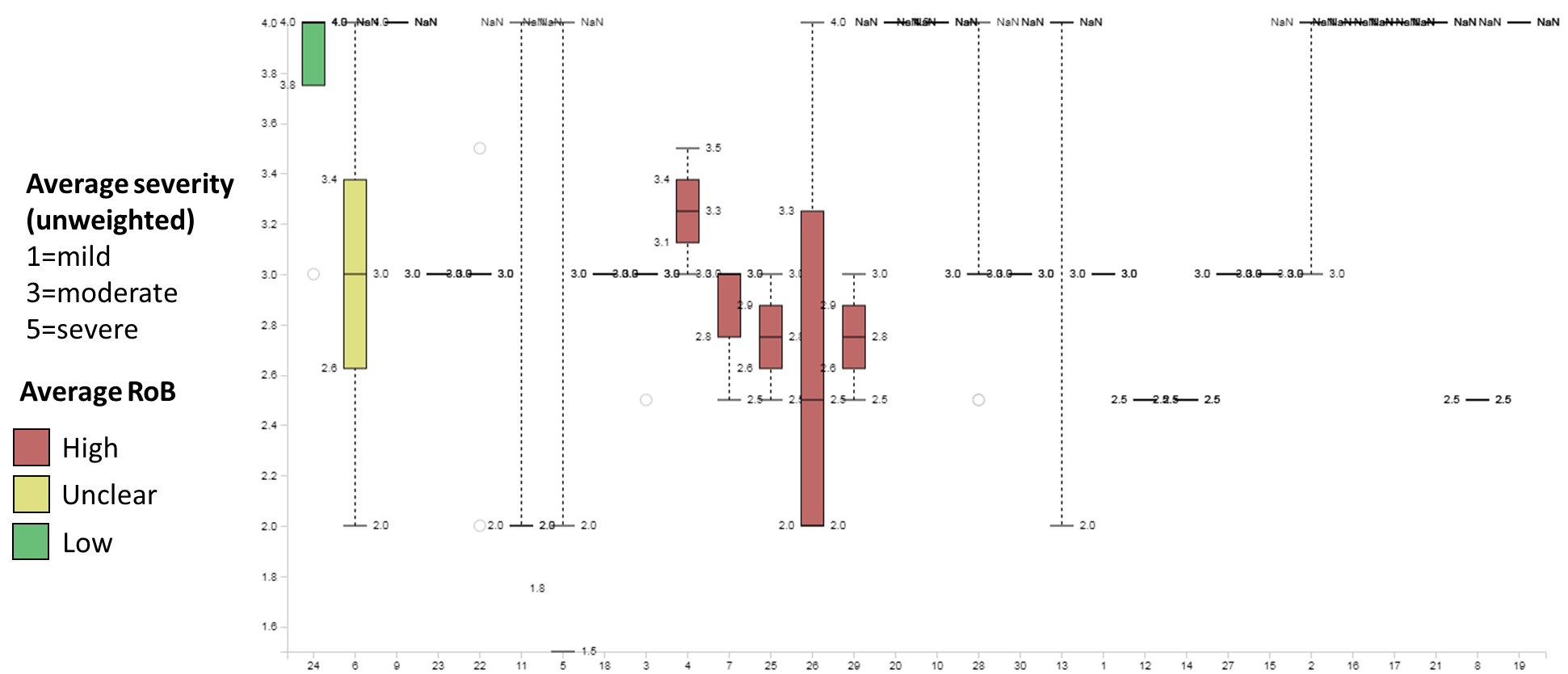


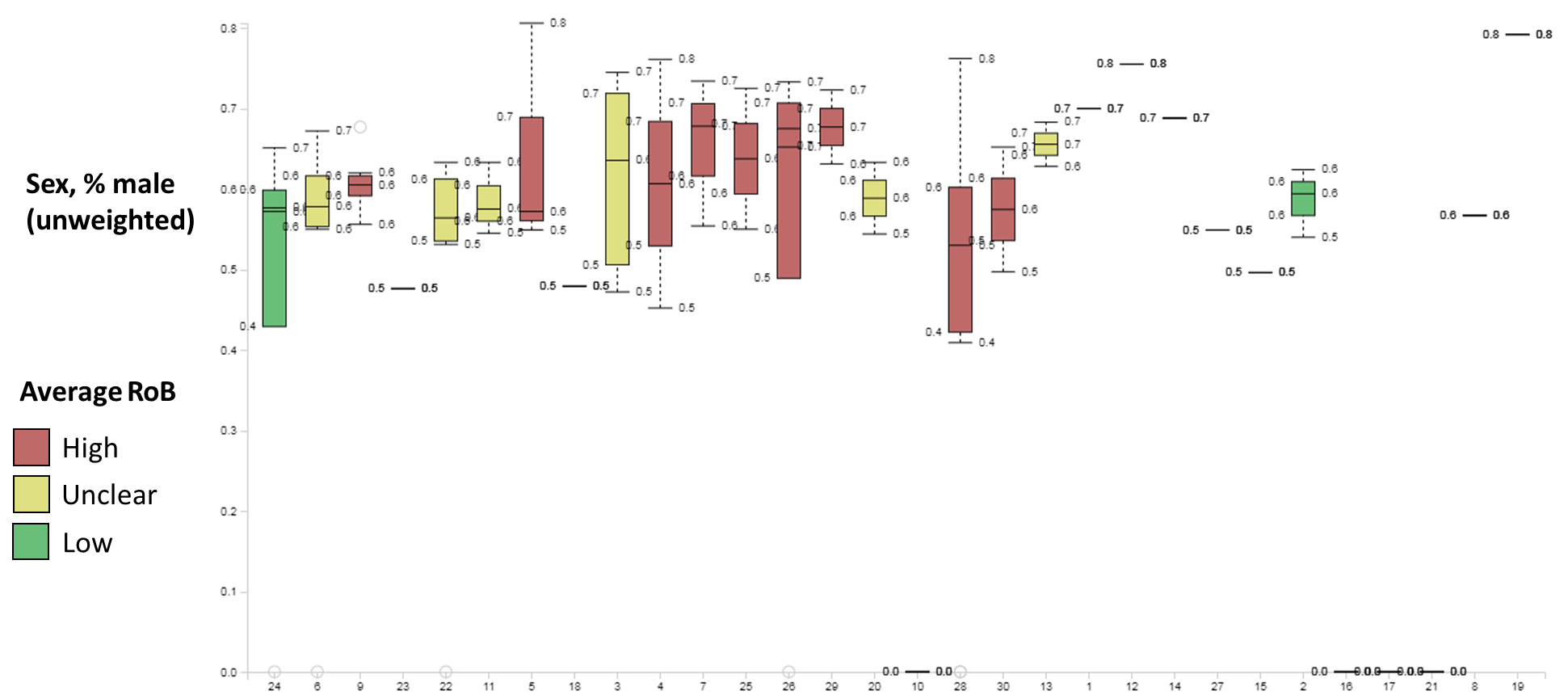




LOS – By comparison



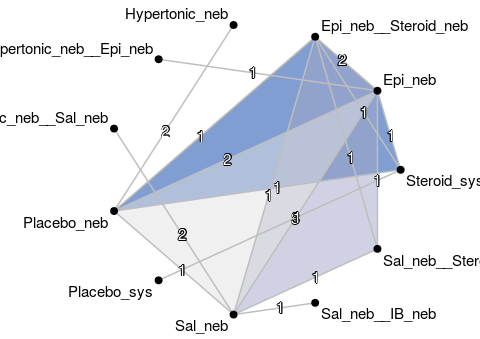


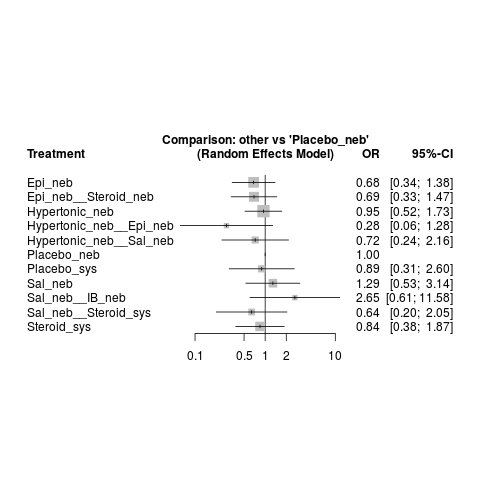


## Appendix 7. Results of sensitivity analyses – ARD1

ARD1 Low vs. High/Unclear ROB

*Low ROB studies:*

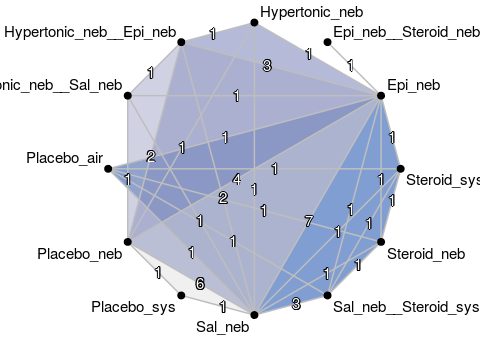
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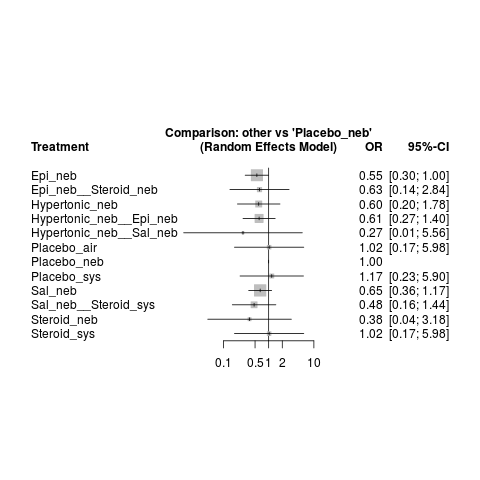
**

*ARD1 Treatment rankings in Low ROB studies*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) + Epi (neb) | . | 0.41 (0.11; 1.58) | . | . | . | . | . | . | . | . |
| 0.44 (0.08; 2.40) | Sal (neb) + Steroid (sys) | 0.75 (0.23; 2.42) | 0.74 (0.23; 2.32) | . | . | . | . | . | 0.82 (0.25; 2.68) | . |
| 0.41 (0.11; 1.58) | 0.94 (0.33; 2.65) | Epi (neb) | 1.18 (0.60; 2.34) | . | 0.93 (0.40; 2.15) | . | . | 0.74 (0.35; 1.58) | 0.46 (0.20; 1.07) | . |
| 0.40 (0.09; 1.82) | 0.93 (0.32; 2.65) | 0.99 (0.51; 1.92) | Epi (neb) + Steroid (sys) | . | 0.71 (0.30; 1.67) | . | . | 0.60 (0.26; 1.40) | 1.11 (0.36; 3.45) | . |
| 0.39 (0.07; 2.07) | 0.89 (0.25; 3.14) | 0.95 (0.35; 2.56) | 0.96 (0.33; 2.77) | Hypertonic (neb) + Sal (neb) | . | . | . | . | 0.56 (0.30; 1.06) | . |
| 0.33 (0.07; 1.58) | 0.76 (0.23; 2.57) | 0.81 (0.37; 1.77) | 0.82 (0.37; 1.84) | 0.86 (0.26; 2.80) | Steroid (sys) | 0.95 (0.46; 1.93) | . | 0.85 (0.37; 1.93) | . | . |
| 0.31 (0.06; 1.74) | 0.72 (0.18; 2.95) | 0.77 (0.27; 2.21) | 0.78 (0.26; 2.27) | 0.81 (0.20; 3.22) | 0.95 (0.46; 1.93) | Placebo (sys) | . | . | . | . |
| 0.30 (0.06; 1.53) | 0.68 (0.18; 2.52) | 0.72 (0.29; 1.83) | 0.73 (0.28; 1.92) | 0.76 (0.22; 2.67) | 0.89 (0.33; 2.43) | 0.94 (0.28; 3.23) | Hypertonic (neb) | 0.95 (0.52; 1.73) | . | . |
| 0.28 (0.06; 1.28) | 0.64 (0.20; 2.05) | 0.68 (0.34; 1.38) | 0.69 (0.33; 1.47) | 0.72 (0.24; 2.16) | 0.84 (0.38; 1.87) | 0.89 (0.31; 2.60) | 0.95 (0.52; 1.73) | Placebo (neb) | 0.71 (0.16; 3.15) | . |
| 0.22 (0.05; 1.02) | 0.50 (0.17; 1.48) | 0.53 (0.25; 1.14) | 0.54 (0.23; 1.25) | 0.56 (0.30; 1.06) | 0.65 (0.24; 1.78) | 0.69 (0.20; 2.36) | 0.73 (0.25; 2.15) | 0.78 (0.32; 1.89) | Sal (neb) | 0.49 (0.15; 1.57) |
| **0.11 (0.02; 0.74)** | 0.24 (0.05; 1.20) | 0.26 (0.06; 1.05) | 0.26 (0.06; 1.11) | 0.27 (0.07; 1.04) | 0.32 (0.07; 1.49) | 0.34 (0.06; 1.84) | 0.36 (0.07; 1.75) | 0.38 (0.09; 1.65) | 0.49 (0.15; 1.57) | Sal (neb) + IB (neb) |

*ARD1 High/Unclear ROB Studies*

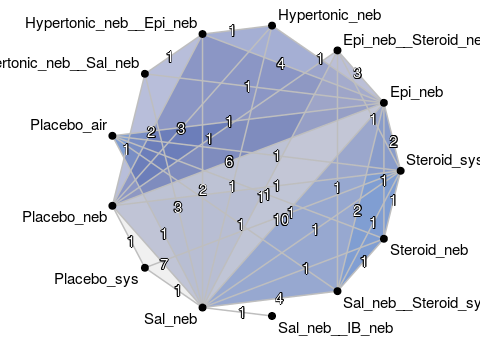
**

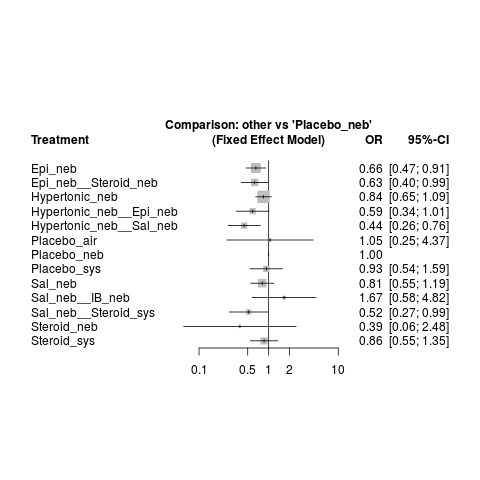
**

*ARD1 Treatment rankings in High/unclear ROB studies*

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) + Sal (neb) | . | . | 0.52 (0.02; 17.39) | . | 0.35 (0.01; 9.74) | . | 0.32 (0.01; 8.99) | . | . | . | 0.51 (0.02; 16.94) |
| 0.72 (0.02; 27.39) | Steroid (neb) | 0.56 (0.06; 5.50) | 3.21 (0.11; 93.01) | . | . | . | 0.56 (0.06; 5.50) | 0.37 (0.04; 3.31) | 0.37 (0.04; 3.31) | . | . |
| 0.57 (0.02; 13.38) | 0.79 (0.10; 6.37) | Sal (neb) + Steroid (sys) | 5.74 (0.23; 142.93) | . | . | . | 0.67 (0.26; 1.76) | 0.66 (0.09; 4.66) | 0.66 (0.09; 4.66) | . | . |
| 0.49 (0.02; 10.04) | 0.69 (0.08; 5.69) | 0.87 (0.29; 2.56) | Epi (neb) | 1.18 (0.33; 4.17) | 1.09 (0.50; 2.39) | 0.88 (0.22; 3.50) | 0.87 (0.47; 1.59) | 0.12 (0.00; 2.69) | 0.12 (0.00; 2.69) | . | **0.48 (0.24; 0.98)** |
| 0.45 (0.02; 10.58) | 0.63 (0.06; 6.41) | 0.79 (0.19; 3.37) | 0.91 (0.31; 2.66) | Hypertonic (neb) | 0.81 (0.23; 2.88) | . | 2.06 (0.48; 8.87) | . | . | . | 0.59 (0.17; 1.98) |
| 0.44 (0.02; 9.15) | 0.62 (0.07; 5.56) | 0.77 (0.22; 2.69) | 0.89 (0.43; 1.85) | 0.98 (0.31; 3.08) | Hypertonic (neb) + Epi (neb) | . | 1.95 (0.56; 6.74) | . | . | . | 0.81 (0.27; 2.42) |
| 0.43 (0.02; 11.89) | 0.60 (0.05; 7.53) | 0.76 (0.13; 4.41) | 0.88 (0.22; 3.50) | 0.96 (0.17; 5.54) | 0.98 (0.20; 4.69) | Epi (neb) + Steroid (sys) | . | . | . | . | . |
| 0.42 (0.02; 8.51) | 0.58 (0.07; 4.57) | 0.73 (0.28; 1.90) | 0.85 (0.49; 1.47) | 0.93 (0.31; 2.80) | 0.95 (0.42; 2.15) | 0.97 (0.22; 4.30) | Sal (neb) | 0.66 (0.09; 4.66) | 0.66 (0.09; 4.66) | 0.75 (0.12; 4.55) | 0.58 (0.30; 1.13) |
| 0.26 (0.01; 8.28) | 0.37 (0.04; 3.31) | 0.47 (0.08; 2.56) | 0.54 (0.09; 3.06) | 0.59 (0.08; 4.33) | 0.60 (0.09; 3.82) | 0.61 (0.07; 5.68) | 0.63 (0.12; 3.39) | Steroid (sys) | 1.00 (0.16; 6.31) | . | . |
| 0.26 (0.01; 8.28) | 0.37 (0.04; 3.31) | 0.47 (0.08; 2.56) | 0.54 (0.09; 3.06) | 0.59 (0.08; 4.33) | 0.60 (0.09; 3.82) | 0.61 (0.07; 5.68) | 0.63 (0.12; 3.39) | 1.00 (0.16; 6.31) | Placebo (air) | . | . |
| 0.23 (0.01; 6.89) | 0.32 (0.02; 4.36) | 0.41 (0.06; 2.61) | 0.47 (0.09; 2.45) | 0.51 (0.08; 3.44) | 0.52 (0.09; 3.04) | 0.54 (0.06; 4.64) | 0.55 (0.11; 2.74) | 0.87 (0.09; 8.84) | 0.87 (0.09; 8.84) | Placebo (sys) | 1.78 (0.25; 12.87) |
| 0.27 (0.01; 5.56) | 0.38 (0.04; 3.18) | 0.48 (0.16; 1.44) | 0.55 (0.30; 1.00) | 0.60 (0.20; 1.78) | 0.61 (0.27; 1.40) | 0.63 (0.14; 2.84) | 0.65 (0.36; 1.17) | 1.02 (0.17; 5.98) | 1.02 (0.17; 5.98) | 1.17 (0.23; 5.90) | Placebo (neb) |

*ARD1 Complete Network Meta-analysis - Fixed effects*



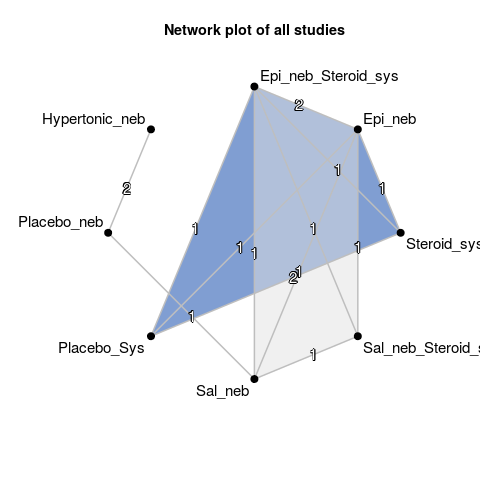


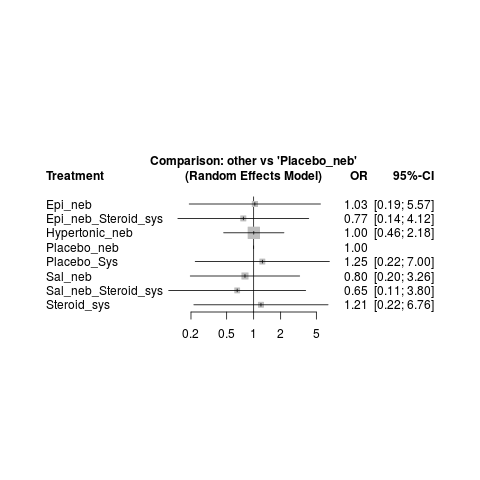
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) + Sal (neb) | . | . | 0.35 (0.01; 8.91) | . | 0.52 (0.02; 15.99) | 0.55 (0.38; 0.80) | . | . | . | . | 0.51 (0.02; 15.58) | . |
| 0.86 (0.43; 1.73) | Sal (neb) + Steroid (sys) | 1.79 (0.21; 15.46) | . | 0.74 (0.28; 1.92) | 0.90 (0.35; 2.31) | 0.68 (0.36; 1.30) | . | 0.66 (0.11; 3.99) | 0.66 (0.11; 3.99) | . | . | . |
| 1.15 (0.17; 7.61) | 1.34 (0.20; 8.74) | Steroid (neb) | . | . | 3.21 (0.12; 85.20) | 0.56 (0.06; 4.82) | . | 0.37 (0.05; 2.89) | 0.37 (0.05; 2.89) | . | . | . |
| 0.76 (0.38; 1.50) | 0.88 (0.40; 1.90) | 0.66 (0.10; 4.44) | Hypertonic (neb) + Epi (neb) | . | 0.76 (0.45; 1.30) | 2.03 (0.69; 5.99) | 1.23 (0.45; 3.39) | . | . | . | 0.78 (0.33; 1.86) | . |
| 0.71 (0.38; 1.30) | 0.82 (0.42; 1.60) | 0.61 (0.09; 4.00) | 0.93 (0.50; 1.76) | Epi (neb) + Steroid (sys) | 0.87 (0.55; 1.37) | 1.11 (0.43; 2.85) | . | 0.71 (0.40; 1.26) | . | . | 0.60 (0.34; 1.05) | . |
| 0.68 (0.41; 1.14) | 0.79 (0.42; 1.46) | 0.59 (0.09; 3.77) | 0.90 (0.55; 1.48) | 0.96 (0.63; 1.47) | Epi (neb) | 0.73 (0.48; 1.10) | 1.18 (0.43; 3.23) | 0.87 (0.51; 1.50) | 0.12 (0.01; 2.45) | . | 0.63 (0.43; 0.92) | . |
| 0.55 (0.38; 0.80) | 0.64 (0.35; 1.15) | 0.48 (0.07; 3.03) | 0.73 (0.41; 1.29) | 0.78 (0.48; 1.26) | 0.81 (0.57; 1.15) | Sal (neb) | 0.49 (0.14; 1.69) | 0.66 (0.11; 3.99) | 0.66 (0.11; 3.99) | 0.75 (0.15; 3.84) | 0.67 (0.40; 1.13) | 0.49 (0.18; 1.31) |
| 0.53 (0.29; 0.95) | 0.61 (0.31; 1.22) | 0.46 (0.07; 2.99) | 0.70 (0.39; 1.25) | 0.75 (0.45; 1.24) | 0.78 (0.52; 1.16) | 0.96 (0.61; 1.51) | Hypertonic (neb) | . | . | . | 0.85 (0.65; 1.10) | . |
| 0.52 (0.28; 0.97) | 0.60 (0.30; 1.22) | 0.45 (0.07; 2.88) | 0.69 (0.36; 1.31) | 0.73 (0.44; 1.22) | 0.76 (0.48; 1.20) | 0.94 (0.57; 1.57) | 0.98 (0.59; 1.65) | Steroid (sys) | 1.00 (0.19; 5.35) | 0.95 (0.68; 1.31) | 0.85 (0.50; 1.43) | . |
| 0.43 (0.10; 1.84) | 0.49 (0.12; 2.11) | 0.37 (0.05; 2.89) | 0.56 (0.13; 2.51) | 0.60 (0.14; 2.57) | 0.63 (0.15; 2.60) | 0.77 (0.19; 3.19) | 0.81 (0.19; 3.44) | 0.82 (0.20; 3.41) | Placebo (air) | . | . | . |
| 0.48 (0.24; 0.96) | 0.56 (0.26; 1.20) | 0.42 (0.06; 2.74) | 0.64 (0.31; 1.30) | 0.68 (0.38; 1.23) | 0.71 (0.41; 1.22) | 0.88 (0.49; 1.57) | 0.91 (0.50; 1.65) | 0.93 (0.67; 1.28) | 1.13 (0.26; 4.84) | Placebo (sys) | 1.78 (0.29; 11.04) | . |
| 0.44 (0.26; 0.76) | 0.52 (0.27; 0.99) | 0.39 (0.06; 2.48) | 0.59 (0.34; 1.01) | 0.63 (0.40; 0.99) | 0.66 (0.47; 0.91) | 0.81 (0.55; 1.19) | 0.84 (0.65; 1.09) | 0.86 (0.55; 1.35) | 1.05 (0.25; 4.37) | 0.93 (0.54; 1.59) | Placebo (neb) | . |
| 0.27 (0.09; 0.77) | 0.31 (0.10; 0.98) | 0.23 (0.03; 1.89) | 0.35 (0.11; 1.11) | 0.38 (0.13; 1.14) | 0.39 (0.14; 1.12) | 0.49 (0.18; 1.31) | 0.51 (0.17; 1.50) | 0.52 (0.17; 1.57) | 0.63 (0.11; 3.53) | 0.56 (0.18; 1.75) | 0.60 (0.21; 1.73) | Sal (neb) + IB (neb) |

## Appendix 8. Results of sensitivity analyses – ARD7

ARD7 Low vs. High/Unclear ROB

*Low ROB studies:*

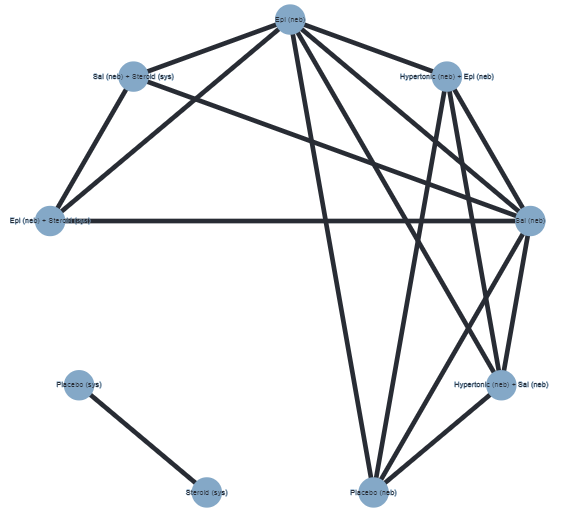
**

**

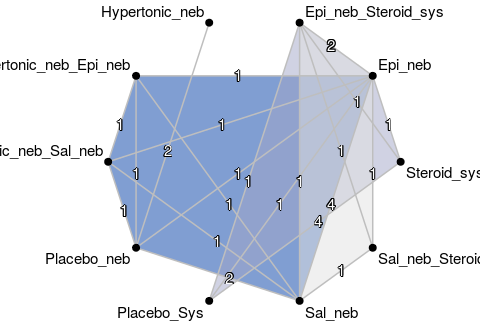
*ARD7 Treatment rankings in Low ROB studies*

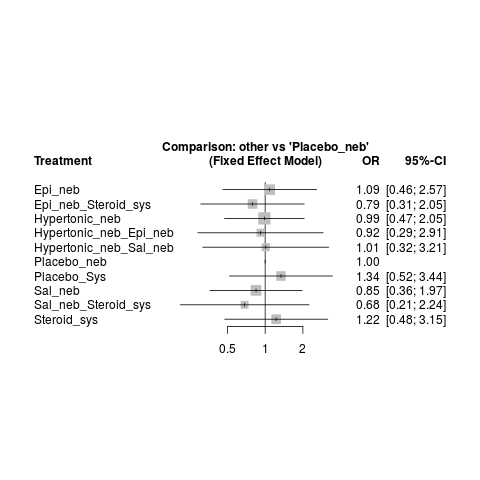
|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Sal (neb) + Steroid (sys) | 0.74 [0.27; 2.03] | 0.82 [0.28; 2.36] | . | . | 0.75 [0.26; 2.13] | . | . |
| 0.85 [0.34; 2.17] | Epi (neb) + Steroid (sys) | 1.11 [0.41; 3.02] | . | . | 0.74 [0.44; 1.24] | 0.60 [0.33; 1.09] | 0.58 [0.32; 1.04] |
| 0.82 [0.28; 2.36] | 0.96 [0.38; 2.41] | Sal (neb) | . | 0.80 [0.20; 3.26] | 0.92 [0.33; 2.58] | . | . |
| 0.65 [0.10; 4.46] | 0.76 [0.12; 4.86] | 0.80 [0.16; 3.97] | Hypertonic (neb) | 1.00 [0.46; 2.18] | . | . | . |
| 0.65 [0.11; 3.80] | 0.77 [0.14; 4.12] | 0.80 [0.20; 3.26] | 1.00 [0.46; 2.18] | Placebo (neb) | . | . | . |
| 0.63 [0.25; 1.63] | 0.74 [0.44; 1.24] | 0.78 [0.31; 1.97] | 0.97 [0.15; 6.22] | 0.97 [0.18; 5.24] | Epi (neb) | 0.90 [0.51; 1.60] | 0.87 [0.49; 1.53] |
| 0.54 [0.20; 1.49] | 0.64 [0.37; 1.08] | 0.66 [0.24; 1.80] | 0.83 [0.13; 5.51] | 0.83 [0.15; 4.65] | 0.86 [0.51; 1.42] | Steroid (sys) | 0.97 [0.67; 1.39] |
| 0.52 [0.19; 1.44] | 0.61 [0.36; 1.04] | 0.64 [0.24; 1.74] | 0.80 [0.12; 5.32] | 0.80 [0.14; 4.49] | 0.83 [0.50; 1.37] | 0.97 [0.67; 1.39] | Placebo (sys) |

*ARD7 High ROB Studies*

**

*ARD7 Complete Network Meta-analysis - Fixed effects*





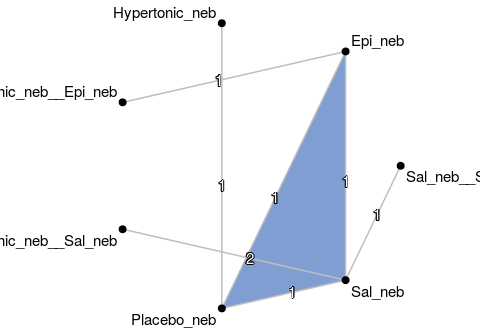
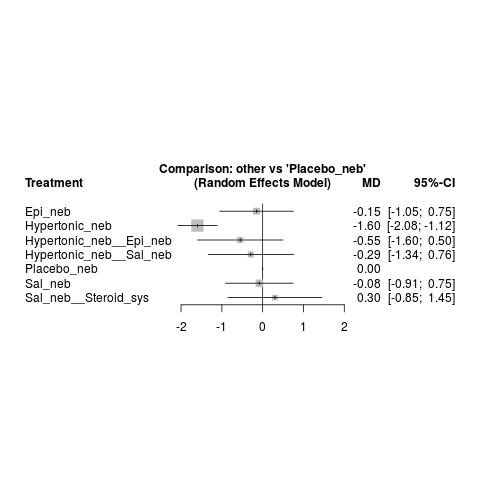
*Treatment rankings for ARD7 under a fixed effects model.*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Sal (neb) + Steroid (sys) | 0.74 (0.28; 1.92) | 0.82 (0.30; 2.23) | . | . | . | . | 0.75 (0.28; 2.01) | . | . |
| 0.86 (0.37; 2.04) | Epi (neb) + Steroid (sys) | 1.11 (0.43; 2.85) | . | . | . | . | 0.73 (0.47; 1.12) | **0.60 (0.37; 0.97)** | **0.58 (0.35; 0.93)** |
| 0.81 (0.35; 1.89) | 0.94 (0.58; 1.52) | Sal (neb) | 0.89 (0.25; 3.20) | . | 0.82 (0.32; 2.08) | 0.81 (0.22; 2.93) | 0.79 (0.60; 1.05) | . | . |
| 0.75 (0.20; 2.83) | 0.86 (0.28; 2.67) | 0.92 (0.32; 2.64) | Hypertonic (neb) + Epi (neb) | . | 0.94 (0.27; 3.22) | 0.91 (0.26; 3.13) | 0.81 (0.24; 2.66) | . | . |
| 0.70 (0.17; 2.80) | 0.80 (0.24; 2.67) | 0.86 (0.28; 2.63) | 0.93 (0.24; 3.65) | Hypertonic (neb) | 0.99 (0.47; 2.05) | . | . | . | . |
| 0.68 (0.21; 2.24) | 0.79 (0.31; 2.05) | 0.85 (0.36; 1.97) | 0.92 (0.29; 2.91) | 0.99 (0.47; 2.05) | Placebo (neb) | 0.97 (0.28; 3.34) | 0.86 (0.26; 2.84) | . | . |
| 0.68 (0.18; 2.58) | 0.78 (0.25; 2.44) | 0.84 (0.29; 2.41) | 0.91 (0.26; 3.13) | 0.98 (0.25; 3.84) | 0.99 (0.31; 3.15) | Hypertonic (neb) + Sal (neb) | 0.89 (0.27; 2.94) | . | . |
| 0.63 (0.27; 1.45) | 0.73 (0.48; 1.11) | 0.78 (0.59; 1.03) | 0.84 (0.29; 2.42) | 0.91 (0.29; 2.81) | 0.92 (0.39; 2.18) | 0.93 (0.32; 2.68) | Epi (neb) | 0.90 (0.57; 1.43) | 0.87 (0.55; 1.37) |
| 0.56 (0.23; 1.36) | **0.65 (0.42; 0.99)** | 0.69 (0.43; 1.11) | 0.75 (0.24; 2.31) | 0.80 (0.24; 2.66) | 0.82 (0.32; 2.10) | 0.83 (0.27; 2.56) | 0.89 (0.59; 1.32) | Steroid (sys) | 0.92 (0.71; 1.18) |
| 0.51 (0.21; 1.25) | **0.59 (0.39; 0.91)** | 0.63 (0.39; 1.02) | 0.69 (0.22; 2.12) | 0.74 (0.22; 2.44) | 0.75 (0.29; 1.93) | 0.76 (0.24; 2.34) | 0.81 (0.55; 1.21) | 0.92 (0.71; 1.18) | Placebo (sys) |

## Appendix 9. Results of sensitivity analyses - LOS

*Low vs. High/Unclear ROB*

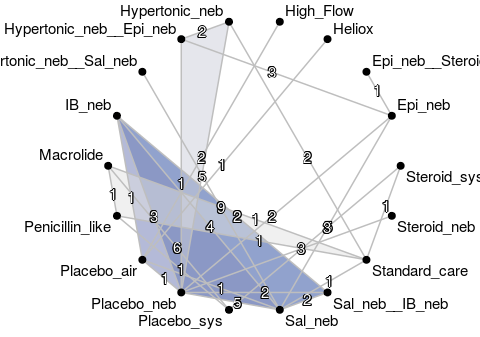
*Low ROB studies*

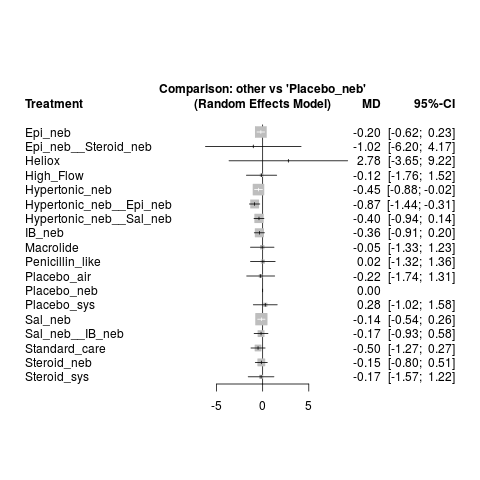
* *

LOS Treatment rankings in Low ROB studies

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) | . | . | . | . | **-1.60 (-2.08; -1.12)** | . |
| -1.05 (-2.20; 0.10) | Hypertonic (neb) + Epi (neb) | . | -0.40 (-0.93; 0.13) | . | . | . |
| **-1.31 (-2.46; -0.16)** | -0.26 (-1.52; 1.00) | Hypertonic (neb) + Sal (neb) | . | -0.21 (-0.85; 0.43) | . | . |
| **-1.45 (-2.48; -0.42)** | -0.40 (-0.93; 0.13) | -0.14 (-1.28; 1.00) | Epi (neb) | -0.07 (-1.01; 0.87) | -0.15 (-1.05; 0.75) | . |
| **-1.52 (-2.48; -0.56)** | -0.47 (-1.55; 0.61) | -0.21 (-0.85; 0.43) | -0.07 (-1.01; 0.87) | Sal (neb) | -0.08 (-0.91; 0.75) | -0.38 (-1.18; 0.42) |
| **-1.60 (-2.08; -1.12)** | -0.55 (-1.60; 0.50) | -0.29 (-1.34; 0.76) | -0.15 (-1.05; 0.75) | -0.08 (-0.91; 0.75) | Placebo (neb) | . |
| **-1.90 (-3.15; -0.65)** | -0.85 (-2.20; 0.50) | -0.59 (-1.62; 0.43) | -0.45 (-1.69; 0.79) | -0.38 (-1.18; 0.42) | -0.30 (-1.45; 0.85) | Sal (neb) + Steroid (sys) |

*LOS High ROB Studies*

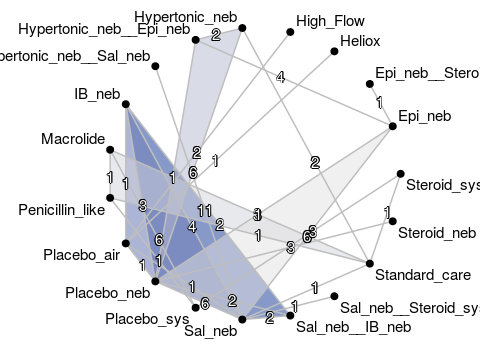
**

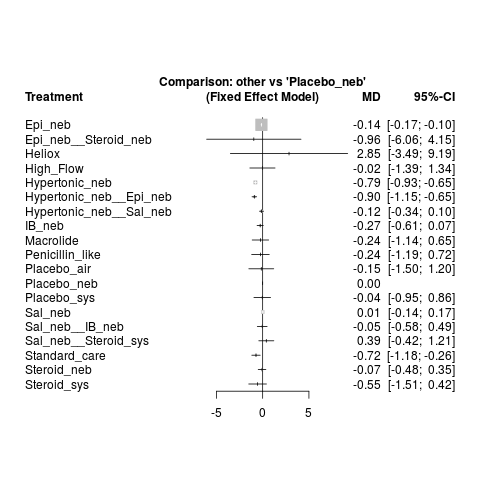
**

*LOS Treatment rankings in High/unclear ROB studies*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) + Epi (neb) | . | -0.57 (-1.32; 0.19) | . | . | . | . | . | -0.57 (-1.16; 0.02) | . | . | . | . | . | . | -0.98 (-2.77; 0.81) | . | . |
| -0.37 (-1.24; 0.49) | Standard care | 0.09 (-0.65; 0.84) | . | . | . | . | -1.00 (-3.21; 1.21) | . | . | . | . | -0.50 (-1.67; 0.67) | -1.00 (-2.60; 0.60) | -0.10 (-1.34; 1.14) | . | . | . |
| -0.42 (-0.99; 0.15) | -0.05 (-0.73; 0.63) | Hypertonic (neb) | . | . | . | . | . | . | . | . | . | . | . | . | -0.47 (-0.95; 0.00) | . | . |
| -0.48 (-1.17; 0.21) | -0.10 (-0.99; 0.78) | -0.05 (-0.71; 0.60) | Hypertonic (neb) + Sal (neb) | . | . | . | . | . | . | . | . | . | -0.26 (-0.62; 0.11) | . | . | . | . |
| 0.14 (-5.05; 5.34) | 0.52 (-4.72; 5.75) | 0.56 (-4.63; 5.76) | 0.62 (-4.58; 5.81) | Epi (neb) + Steroid (neb) | . | . | . | -0.82 (-5.99; 4.35) | . | . | . | . | . | . | . | . | . |
| -0.52 (-1.26; 0.22) | -0.14 (-1.06; 0.77) | -0.10 (-0.77; 0.58) | -0.04 (-0.68; 0.60) | -0.66 (-5.86; 4.54) | IB (neb) | -0.30 (-1.91; 1.31) | . | . | -0.12 (-1.00; 0.76) | . | . | . | -0.27 (-0.84; 0.30) | . | -0.33 (-0.98; 0.32) | . | . |
| -0.66 (-2.26; 0.94) | -0.28 (-1.98; 1.41) | -0.24 (-1.81; 1.34) | -0.18 (-1.75; 1.38) | -0.80 (-6.20; 4.59) | -0.14 (-1.67; 1.39) | Placebo (air) | . | . | . | -0.10 (-0.72; 0.53) | . | . | -0.10 (-1.74; 1.54) | . | -0.35 (-1.95; 1.25) | . | -3.00 (-9.25; 3.25) |
| -0.70 (-2.15; 0.75) | -0.33 (-1.49; 0.84) | -0.28 (-1.63; 1.07) | -0.23 (-1.69; 1.24) | -0.84 (-6.21; 4.52) | -0.18 (-1.67; 1.30) | -0.04 (-2.10; 2.01) | Steroid (sys) | . | . | . | . | . | . | . | . | -0.53 (-1.23; 0.18) | . |
| **-0.68 (-1.18; -0.17)** | -0.30 (-1.13; 0.52) | -0.26 (-0.79; 0.28) | -0.20 (-0.73; 0.33) | -0.82 (-5.99; 4.35) | -0.16 (-0.77; 0.45) | -0.02 (-1.57; 1.53) | 0.02 (-1.40; 1.45) | Epi (neb) | . | . | . | . | 0.03 (-0.42; 0.48) | . | -0.25 (-0.89; 0.39) | . | . |
| -0.70 (-1.61; 0.21) | -0.33 (-1.38; 0.73) | -0.28 (-1.13; 0.58) | -0.22 (-1.06; 0.62) | -0.84 (-6.07; 4.39) | -0.18 (-0.97; 0.61) | -0.04 (-1.70; 1.62) | 0.00 (-1.57; 1.57) | -0.02 (-0.83; 0.79) | Sal (neb) + IB (neb) | . | . | . | -0.21 (-1.10; 0.68) | . | 0.02 (-0.82; 0.86) | . | . |
| -0.75 (-2.47; 0.97) | -0.38 (-2.18; 1.42) | -0.33 (-2.02; 1.36) | -0.28 (-1.96; 1.41) | -0.90 (-6.33; 4.53) | -0.24 (-1.89; 1.42) | -0.10 (-0.72; 0.53) | -0.05 (-2.20; 2.09) | -0.08 (-1.75; 1.59) | -0.05 (-1.83; 1.72) | High flow | . | . | . | . | . | . | . |
| -0.73 (-1.59; 0.14) | -0.35 (-1.36; 0.66) | -0.31 (-1.09; 0.48) | -0.25 (-1.10; 0.60) | -0.87 (-6.10; 4.36) | -0.21 (-1.07; 0.65) | -0.07 (-1.73; 1.59) | -0.03 (-1.57; 1.52) | -0.05 (-0.83; 0.73) | -0.03 (-1.03; 0.97) | 0.03 (-1.74; 1.80) | Steroid (neb) | . | . | . | -0.15 (-0.80; 0.51) | . | . |
| -0.83 (-2.16; 0.51) | -0.45 (-1.48; 0.57) | -0.41 (-1.64; 0.82) | -0.35 (-1.71; 1.00) | -0.97 (-6.30; 4.36) | -0.31 (-1.68; 1.06) | -0.17 (-2.15; 1.81) | -0.13 (-0.92; 0.66) | -0.15 (-1.46; 1.16) | -0.13 (-1.60; 1.34) | -0.07 (-2.15; 2.00) | -0.10 (-1.54; 1.34) | Macrolide | . | 0.40 (-0.72; 1.52) | . | -0.39 (-0.83; 0.05) | . |
| **-0.73 (-1.32; -0.15)** | -0.36 (-1.17; 0.45) | -0.31 (-0.85; 0.23) | -0.26 (-0.62; 0.11) | -0.88 (-6.06; 4.31) | -0.22 (-0.75; 0.32) | -0.07 (-1.60; 1.45) | -0.03 (-1.45; 1.39) | -0.06 (-0.44; 0.33) | -0.03 (-0.79; 0.73) | 0.02 (-1.62; 1.67) | -0.01 (-0.77; 0.76) | 0.10 (-1.21; 1.40) | Sal (neb) | . | -0.07 (-0.58; 0.45) | . | . |
| -0.89 (-2.29; 0.50) | -0.52 (-1.62; 0.58) | -0.47 (-1.76; 0.82) | -0.42 (-1.83; 0.99) | -1.04 (-6.38; 4.31) | -0.38 (-1.81; 1.05) | -0.23 (-2.25; 1.78) | -0.19 (-1.23; 0.85) | -0.22 (-1.59; 1.16) | -0.19 (-1.72; 1.33) | -0.14 (-2.25; 1.97) | -0.17 (-1.66; 1.33) | -0.07 (-0.89; 0.76) | -0.16 (-1.52; 1.20) | Penicillin-like | . | 0.31 (-0.84; 1.46) | . |
| **-0.87 (-1.44; -0.31)** | -0.50 (-1.27; 0.27) | **-0.45 (-0.88; -0.02)** | -0.40 (-0.94; 0.14) | -1.02 (-6.20; 4.17) | -0.36 (-0.91; 0.20) | -0.22 (-1.74; 1.31) | -0.17 (-1.57; 1.22) | -0.20 (-0.62; 0.23) | -0.17 (-0.93; 0.58) | -0.12 (-1.76; 1.52) | -0.15 (-0.80; 0.51) | -0.05 (-1.33; 1.23) | -0.14 (-0.54; 0.26) | 0.02 (-1.32; 1.36) | Placebo (neb) | . | . |
| -1.16 (-2.51; 0.20) | -0.78 (-1.83; 0.26) | -0.74 (-1.99; 0.51) | -0.68 (-2.05; 0.69) | -1.30 (-6.64; 4.04) | -0.64 (-2.03; 0.75) | -0.50 (-2.49; 1.49) | -0.46 (-1.14; 0.23) | -0.48 (-1.81; 0.85) | -0.46 (-1.94; 1.03) | -0.40 (-2.49; 1.68) | -0.43 (-1.89; 1.02) | -0.33 (-0.75; 0.09) | -0.42 (-1.75; 0.90) | -0.26 (-1.08; 0.56) | -0.28 (-1.58; 1.02) | Placebo (sys) | . |
| -3.66 (-10.11; 2.80) | -3.28 (-9.76; 3.19) | -3.24 (-9.68; 3.21) | -3.18 (-9.63; 3.26) | -3.80 (-12.06; 4.46) | -3.14 (-9.58; 3.30) | -3.00 (-9.25; 3.25) | -2.96 (-9.54; 3.62) | -2.98 (-9.42; 3.46) | -2.96 (-9.43; 3.51) | -2.90 (-9.19; 3.38) | -2.93 (-9.40; 3.54) | -2.83 (-9.39; 3.73) | -2.93 (-9.36; 3.51) | -2.77 (-9.33; 3.80) | -2.78 (-9.22; 3.65) | -2.50 (-9.06; 4.06) | Heliox |

*Complete Network Meta-Analysis LOS - Fixed effects*





*Treatment rankings for LOS based on a fixed effects model.*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Hypertonic (neb) + Epi (neb) | **-0.66 (-1.12; -0.20)** | . | . | . | . | . | . | **.** | **-0.54 (-0.83; -0.24)** | . | . | . | . | . | -0.98 (-2.58; 0.62) | . | . | . |
| -0.11 (-0.38; 0.16) | Hypertonic (neb) | -0.10 (-0.56; 0.36) | . | . | . | . | . | . | . | . | . | . | . | . | **-0.84 (-0.99; -0.70)** | . | . | . |
| -0.18 (-0.69; 0.33) | -0.07 (-0.51; 0.37) | Standard+ care | -1.00 (-3.06; 1.06) | . | . | -0.50 (-1.34; 0.34) | -0.10 (-1.04; 0.84) | . | . | . | . | . | . | . | . | -1.00 (-2.38; 0.38) | . | . |
| -0.35 (-1.34; 0.64) | -0.24 (-1.20; 0.71) | -0.17 (-1.02; 0.67) | Steroid (sys) | . | . | . | . | . | . | . | . | . | . | **-0.53 (-0.93; -0.14)** | . | . | . | . |
| 0.06 (-5.05; 5.17) | 0.17 (-4.94; 5.27) | 0.24 (-4.89; 5.36) | 0.41 (-4.79; 5.60) | Epi (neb) + Steroid (neb) | . | . | . | . | -0.82 (-5.92; 4.28) | . | . | . | . | . | . | . | . | . |
| **-0.63 (-1.05; -0.21)** | **-0.52 (-0.89; -0.16)** | -0.45 (-1.02; 0.11) | -0.28 (-1.30; 0.74) | -0.69 (-5.80; 4.43) | IB (neb) | . | . | -0.30 (-1.69; 1.09) | . | . | . | . | -0.13 (-0.78; 0.52) | . | -0.36 (-0.78; 0.06) | -0.24 (-0.62; 0.15) | . | . |
| -0.66 (-1.58; 0.27) | -0.55 (-1.44; 0.34) | -0.48 (-1.25; 0.29) | -0.31 (-0.74; 0.13) | -0.71 (-5.90; 4.47) | -0.03 (-0.98; 0.93) | Macrolide | 0.40 (-0.37; 1.17) | . | . | . | . | . | . | **-0.22 (-0.43; -0.01)** | . | . | . | . |
| -0.66 (-1.64; 0.32) | -0.55 (-1.50; 0.40) | -0.48 (-1.32; 0.36) | -0.31 (-0.99; 0.37) | -0.72 (-5.91; 4.48) | -0.03 (-1.04; 0.98) | -0.00 (-0.57; 0.56) | Penicillin-like | . | . | . | . | . | . | 0.31 (-0.51; 1.13) | . | . | . | . |
| -0.75 (-2.12; 0.62) | -0.64 (-2.00; 0.72) | -0.57 (-1.99; 0.85) | -0.40 (-2.05; 1.26) | -0.81 (-6.09; 4.47) | -0.12 (-1.48; 1.24) | -0.09 (-1.71; 1.53) | -0.09 (-1.74; 1.56) | Placebo (air) | . | . | . | -0.13 (-0.35; 0.09) | . | . | -0.35 (-1.73; 1.03) | -0.10 (-1.53; 1.33) | . | -3.00 (-9.20; 3.20) |
| **-0.76 (-1.01; -0.51)** | **-0.65 (-0.80; -0.51)** | -0.58 (-1.04; -0.13) | -0.41 (-1.37; 0.55) | -0.82 (-5.92; 4.28) | -0.13 (-0.47; 0.21) | -0.11 (-1.00; 0.79) | -0.10 (-1.06; 0.85) | -0.01 (-1.36; 1.34) | Epi (neb) | . | . | . | . | . | **-0.13 (-0.17; -0.09)** | -0.17 (-0.34; 0.00) | . | . |
| **-0.78 (-1.11; -0.44)** | **-0.67 (-0.93; -0.41)** | **-0.60 (-1.11; -0.10)** | -0.43 (-1.41; 0.56) | -0.84 (-5.95; 4.27) | -0.15 (-0.52; 0.23) | -0.12 (-1.04; 0.80) | -0.12 (-1.10; 0.86) | -0.03 (-1.39; 1.33) | -0.02 (-0.24; 0.21) | Hypertonic (neb) + Sal (neb) | . | . | . | . | . | -0.13 (-0.30; 0.03) | . | . |
| **-0.83 (-1.32; -0.35)** | **-0.72 (-1.16; -0.29)** | **-0.65 (-1.27; -0.04)** | -0.48 (-1.53; 0.57) | -0.89 (-6.01; 4.23) | -0.20 (-0.74; 0.34) | -0.18 (-1.16; 0.81) | -0.17 (-1.22; 0.87) | -0.08 (-1.50; 1.33) | -0.07 (-0.49; 0.35) | -0.05 (-0.53; 0.42) | Steroid (neb) | . | . | . | -0.07 (-0.48; 0.35) | . | . | . |
| -0.88 (-2.27; 0.51) | -0.77 (-2.14; 0.61) | -0.70 (-2.14; 0.74) | -0.52 (-2.20; 1.15) | -0.93 (-6.22; 4.35) | -0.24 (-1.62; 1.13) | -0.22 (-1.85; 1.42) | -0.22 (-1.88; 1.45) | -0.13 (-0.35; 0.09) | -0.11 (-1.48; 1.26) | -0.10 (-1.48; 1.28) | -0.04 (-1.47; 1.39) | High+ Flow | . | . | . | . | . | . |
| **-0.85 (-1.44; -0.26)** | **-0.74 (-1.29; -0.19)** | -0.67 (-1.37; 0.03) | -0.50 (-1.60; 0.60) | -0.91 (-6.04; 4.22) | -0.22 (-0.79; 0.35) | -0.19 (-1.23; 0.85) | -0.19 (-1.29; 0.90) | -0.10 (-1.54; 1.34) | -0.09 (-0.62; 0.45) | -0.07 (-0.63; 0.49) | -0.02 (-0.70; 0.66) | 0.02 (-1.43; 1.48) | Sal (neb) + IB (neb) | . | 0.07 (-0.52; 0.67) | -0.15 (-0.81; 0.51) | . | . |
| -0.86 (-1.79; 0.08) | -0.75 (-1.64; 0.15) | -0.68 (-1.46; 0.10) | **-0.50 (-0.89; -0.11)** | -0.91 (-6.10; 4.27) | -0.22 (-1.19; 0.74) | -0.20 (-0.40; 0.01) | -0.19 (-0.76; 0.37) | -0.11 (-1.73; 1.52) | -0.09 (-1.00; 0.81) | -0.08 (-1.00; 0.85) | -0.02 (-1.02; 0.97) | 0.02 (-1.62; 1.66) | -0.00 (-1.05; 1.05) | Placebo (sys) | . | . | . | . |
| -0.90 (-1.15; -0.65) | **-0.79 (-0.93; -0.65)** | **-0.72 (-1.18; -0.26)** | -0.55 (-1.51; 0.42) | -0.96 (-6.06; 4.15) | -0.27 (-0.61; 0.07) | -0.24 (-1.14; 0.65) | -0.24 (-1.19; 0.72) | -0.15 (-1.50; 1.20) | **-0.14 (-0.17; -0.10)** | -0.12 (-0.34; 0.10) | -0.07 (-0.48; 0.35) | -0.02 (-1.39; 1.34) | -0.05 (-0.58; 0.49) | -0.04 (-0.95; 0.86) | Placebo (neb) | 0.06 (-0.27; 0.39) | . | . |
| **-0.91 (-1.21; -0.62)** | **-0.80 (-1.01; -0.60)** | **-0.73 (-1.21; -0.26)** | -0.56 (-1.53; 0.41) | -0.97 (-6.08; 4.14) | -0.28 (-0.62; 0.05) | -0.25 (-1.16; 0.65) | -0.25 (-1.22; 0.71) | -0.16 (-1.51; 1.19) | -0.15 (-0.30; 0.00) | -0.13 (-0.30; 0.03) | -0.08 (-0.52; 0.36) | -0.04 (-1.41; 1.33) | -0.06 (-0.60; 0.48) | -0.06 (-0.97; 0.86) | -0.01 (-0.17; 0.14) | Sal (neb) | -0.38 (-1.18; 0.42) | . |
| **-1.29 (-2.15; -0.44)** | **-1.18 (-2.01; -0.36)** | **-1.11 (-2.05; -0.18)** | -0.94 (-2.20; 0.32) | -1.35 (-6.52; 3.82) | -0.66 (-1.53; 0.21) | -0.63 (-1.84; 0.57) | -0.63 (-1.89; 0.62) | -0.54 (-2.11; 1.03) | -0.53 (-1.35; 0.29) | -0.51 (-1.33; 0.31) | -0.46 (-1.38; 0.46) | -0.42 (-2.00; 1.17) | -0.44 (-1.41; 0.52) | -0.44 (-1.65; 0.78) | -0.39 (-1.21; 0.42) | -0.38 (-1.18; 0.42) | Sal (neb) + Steroid (sys) | . |
| -3.75 (-10.10; 2.60) | -3.64 (-9.99; 2.70) | -3.57 (-9.93; 2.79) | -3.40 (-9.81; 3.02) | -3.81 (-11.95; 4.34) | -3.12 (-9.46; 3.23) | -3.09 (-9.50; 3.32) | -3.09 (-9.50; 3.33) | -3.00 (-9.20; 3.20) | -2.99 (-9.33; 3.36) | -2.97 (-9.32; 3.38) | -2.92 (-9.27; 3.44) | -2.87 (-9.08; 3.33) | -2.90 (-9.26; 3.47) | -2.89 (-9.30; 3.51) | -2.85 (-9.19; 3.49) | -2.84 (-9.18; 3.51) | -2.46 (-8.85; 3.94) | Heliox |

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