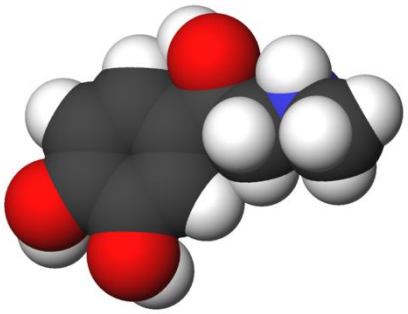
EVIDENCE BASED MEDICINE OF

ADRENALINE

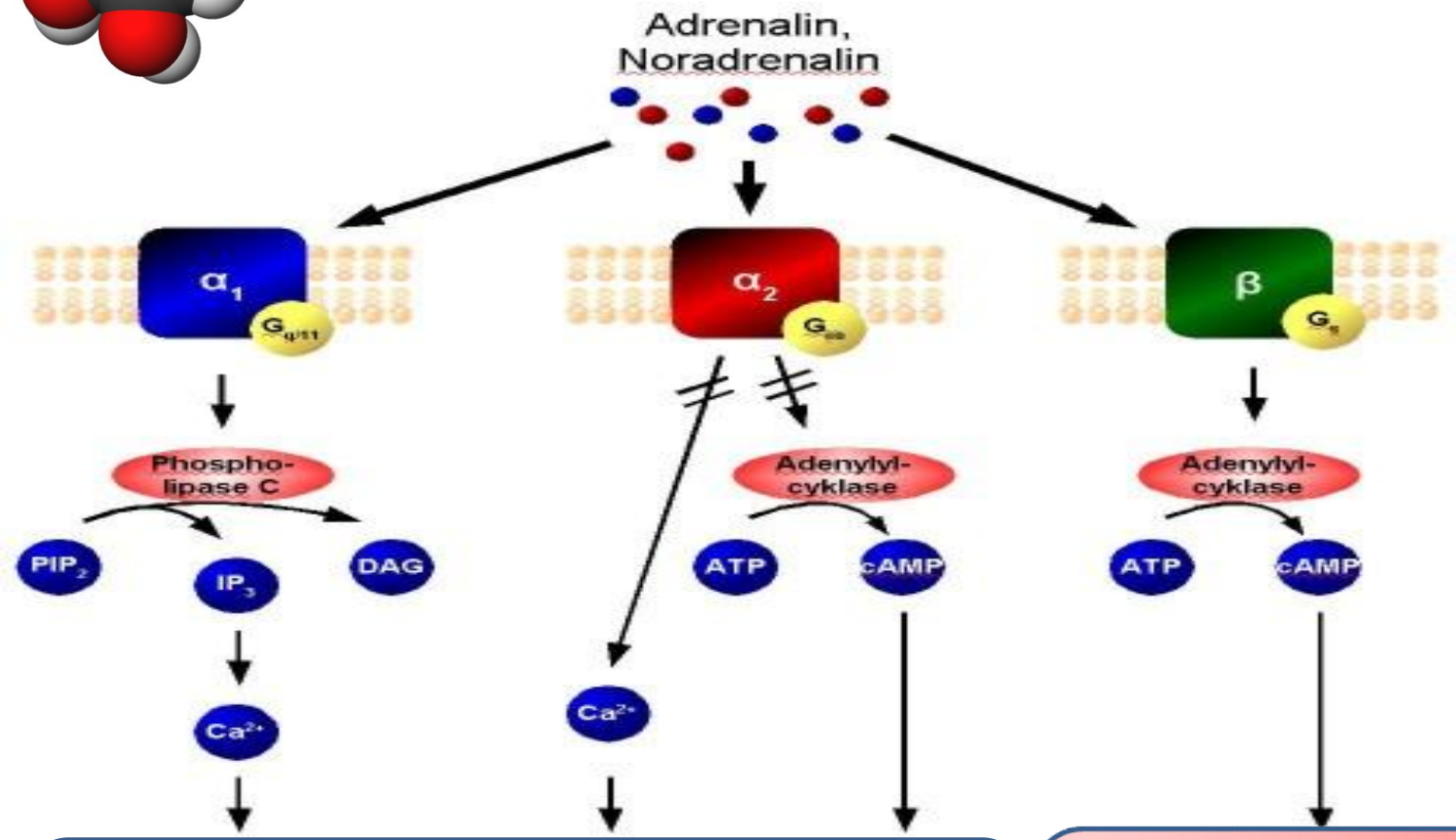
FOR TREAMENT IN ACUTE BRONCHIOLITIS.

DR HUYEN TON NU THUY MY

RESPIRATORY DEPARTMENT



ADRENALINE



Reduction in respiratory secretions and mucosa edema

Relaxation of airway smooth muscle And inhibition of inflammatory process

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Diagnosis and Management of Bronchiolitis

Subcommittee on Diagnosis and Management of Bronchiolitis

Pediatrics 2006;118;1774-1793
DOI: 10.1542/peds.2006-2223

2006: BRONCHIOLATORS IN BRONCHIOLIS

- **RECOMMENDATION 2B**
- Inhaled bronchodilators should be continued only if there is a documented positive clinical response.
- The AHRQ evidence report notes that nebulized Adrenaline has “some potential for being efficacious.
- The Cochrane: Use Adrenaline for inpatients and Outpatients

American Academy of Pediatrics : Diagnosis and management of bronchiolitis 2006

Management of Bronchiolitis in 2010

TABLE 3 Summary of Recent Evidence for Therapies Used for Bronchiolitis

Therapy	Summary	Recommendation
Bronchodilators	No improvement in duration of illness or hospitalization[58,59]	No routine use
	May improve short-term clinical scores in a subset of children[58]	Use only after proven benefit in a trial of therapy, if chosen as an option
Corticosteroids	No improvement in duration of illness or hospitalization[7,83]	No routine use
Leukotriene receptor antagonists	No improvement in duration of illness[67,75]	Not recommended
Nebulized hypertonic saline	May reduce length of inpatient hospitalization[70]	None

Evidence Based Guideline for The Management of bronchiolitis in Pediatrics 2010; 125; 342-349

ADRENALINE IN BRONCHIOLITIS

2011 WHAT'S NEW ?

Steroids and Bronchodilators for Acute Bronchiolitis in the first two years of life: Systematic Review And Meta-Analysis

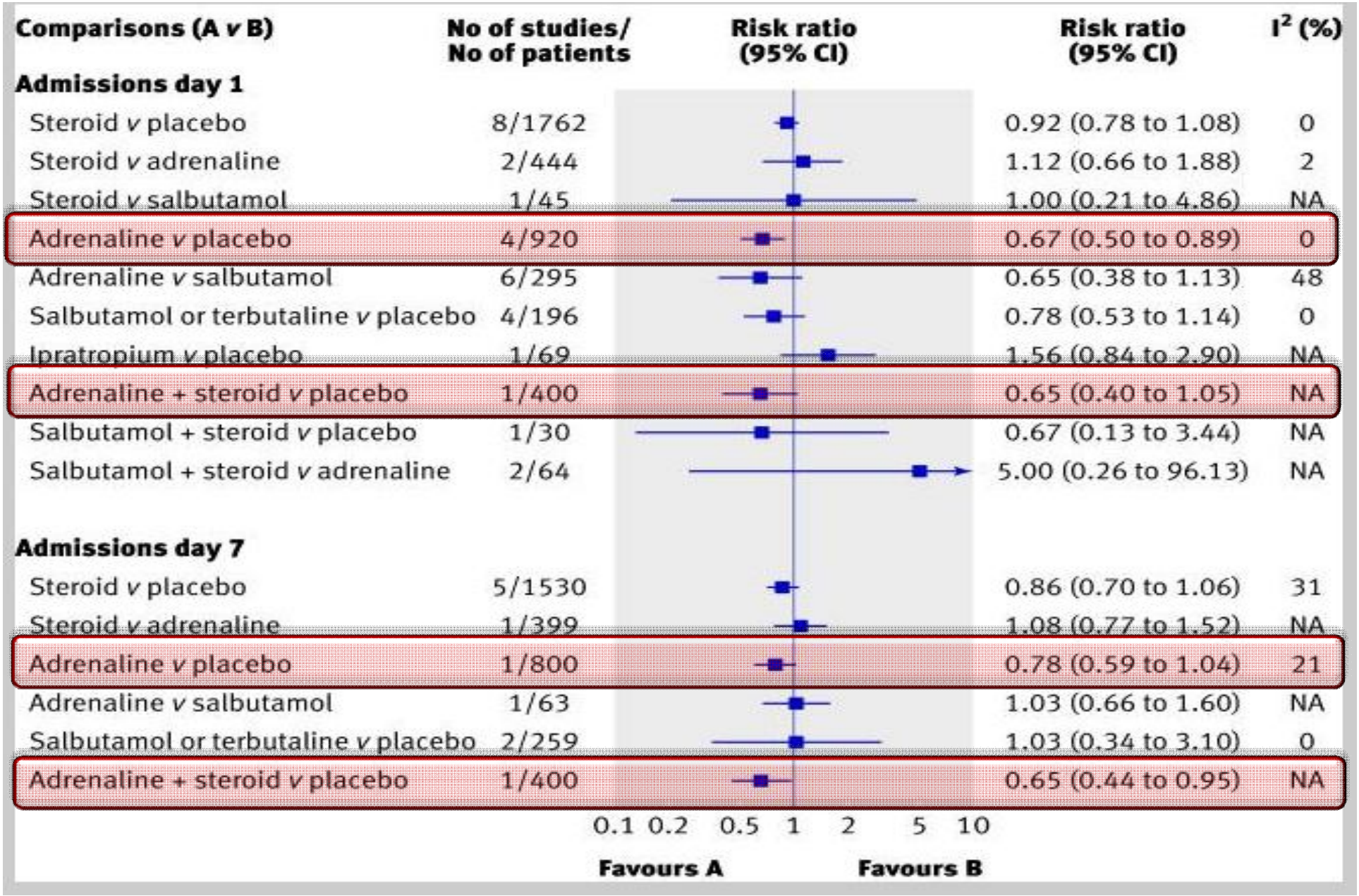
The Cochrane library and The treatment of Bronchiolitis in 2011
British Medical journal: January – 27 – 2011
Published online: April – 6 - 2011

SYSTEMATIC REVIEW AND META - ANALYSIS

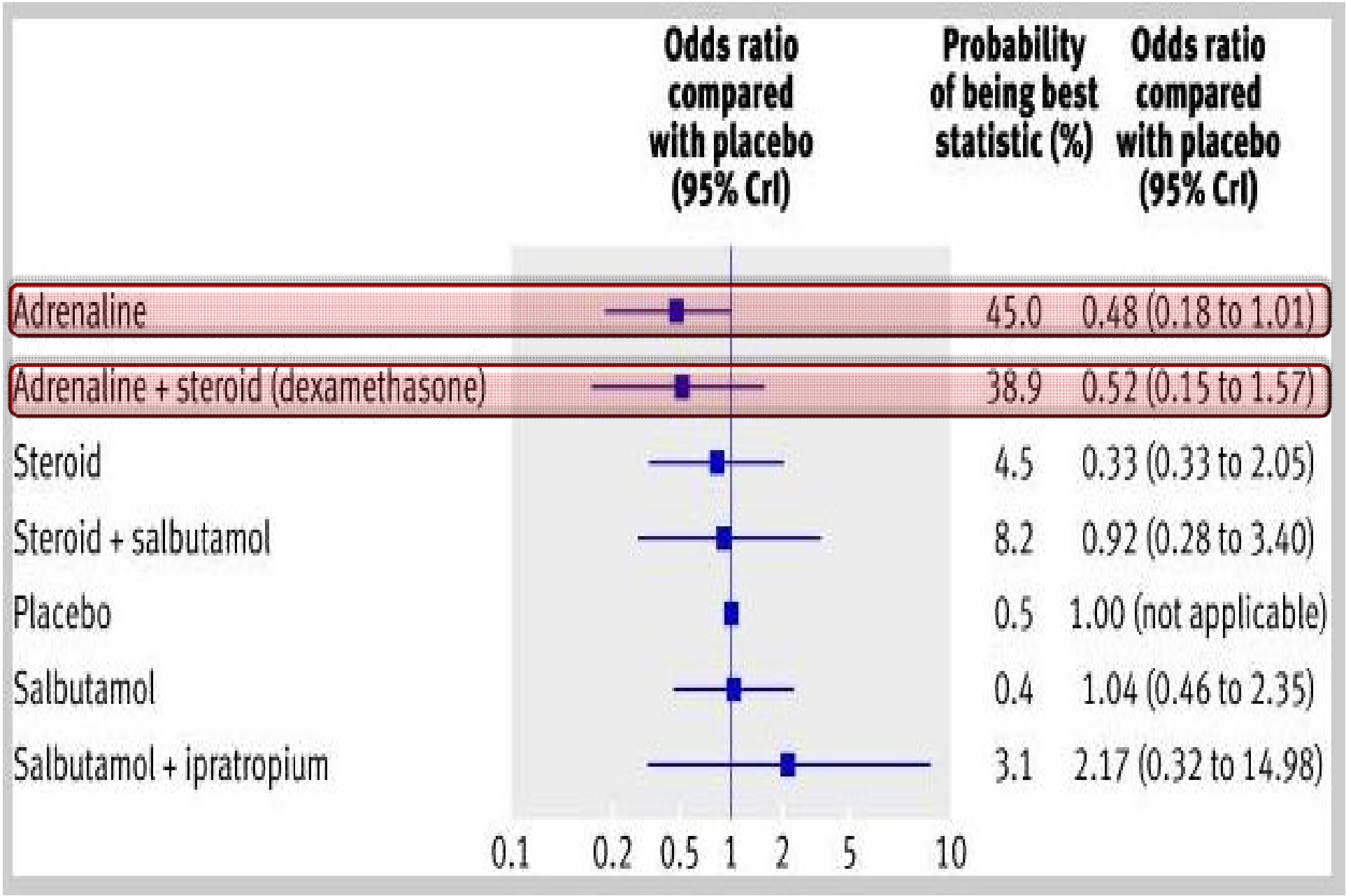
- 48 studies (4897 patients).
- RCTs of Children aged < 24 month.
- First Episode of Bronchiolitis with wheezing.
- Bronchodilator or steroid, alone or combined, with placebo or another intervention.
- Rate of admission for outpatients (day 1 and up to day 7) and length of stay for inpatients.

BRONCHODILATORS AND GLUCOCORTICOIDS FOR TREATMENT OUTPATIENTS IN ACUTE BRONCHIOLITIS.

The Cochrane library and The treatment of Bronchiolitis in 2011
British Medical journal: January – 27 – 2011
Published online: April – 6 - 2011



Results from meta-analysis of direct comparisons for admission rates from emergency department (day 1 and day 7) in outpatients.



Results of mixed treatment analysis for admissions at day 1.

OUTPATIENT OUTCOMES

Outcome	Comparison	Number of subjects (studies)	Measure of effect (95% CI)	I^2	Quality of evidence (GRADE)
Hospitalization rate on day 1	Glucocorticoid *vs* placebo	1730 (8)	RR: 0.92 (0.78, 1.08)	0%	High
	Epinephrine*vs*placebo	**920 (4)**	**RR: 0.67 (0.50, 0.89)[a]**	**0%**	**Moderate**
	Epinephrine and glucocorticoid *vs* placebo	401 (1)	RR: 0.64 (0.40, 1.04)	—	Low
	Epinephrine *vs* bronchodilator	295 (6)	RR: 0.65 (0.38, 1.13)	48%	Moderate
	Glucocorticoid *vs* epinephrine	444 (2)	RR: 1.12 (0.66, 1.88)	2%	Moderate
Hospitalization rate within 7 days	Glucocorticoid *vs* placebo	1498 (5)	RR: 0.86 (0.70, 1.06)	31%	Moderate
	Epinephrine *vs* placebo	800 (1)	RR: 0.78 (0.59, 1.05)	21%	Low
	Epinephrine and glucocorticoid*vs*placebo	**400 (1)**	**RR: 0.65 (0.44, 0.95)[b]**	—	**Low**
	Epinephrine *vs* bronchodilator	63 (1)	RR: 1.03 (0.66, 1.60)	—	Low
	Glucocorticoid *vs* epinephrine	399 (1)	RR: 1.08 (0.77, 1.52)	—	Moderate

OUTPATIENT OUTCOMES

Clinical score at 60 minutes	Glucocorticoid *vs* placebo	1006 (4)	SMD: − 0.04 (−0.16, 0.09)	0%	High
	Epinephrine*vs*placebo	**900 (4)**	**SMD:−0.45 (−0.66, −0.23)[a]**	**40%**	**High**
	Epinephrine and glucocorticoid*vs*placebo	**399 (1)**	**SMD:−0.34 (−0.54, −0.14)[b]**	**—**	**Moderate**
	Epinephrine *vs* bronchodilator	248 (6)	SMD: − 0.11 (−0.36, 0.14)	0%	Moderate
	Glucocorticoid and bronchodilator *vs* placebo	30 (1)	SMD: − 0.30 (−1.02, 0.42)	—	Low
	Glucocorticoid*vs*epinephrine	**442 (2)**	**SMD: 0.31 (0.12, 0.50)[a]**	**0%**	**High**
Clinical score at 120 minutes	Glucocorticoid *vs* placebo	214 (3)	SMD: − 0.17 (−0.55, 0.21)	43%	Moderate
	Glucocorticoid and bronchodilator *vs* placebo	30 (1)	SMD: − 0.22 (−0.94, 0.50)	—	Low
	Epinephrine*vs*placebo	**30 (1)**	**SMD:−0.83 (−1.58, −0.08)[a]**	**—**	**Low**
	Epinephrine *vs* bronchodilator	207 (4)	SMD: − 0.09 (−0.37, 0.18)	0%	Moderate

RESULTS

- For outpatients with bronchiolitis, nebulized Adreanline decreased hospitalization rate on day one by 33%. (Grade: Moderate)
- Netbulized Adrenaline + glucocorticoids, there was a reduction of similar magnitude for hospitalization rate within seven days. (Grade: Low)
- Outpatients treated with epinephrine (High) or epinephrine and glucocorticoid combined both had significantly lower clinical scores at 60 minutes. (Grade: Moderate)

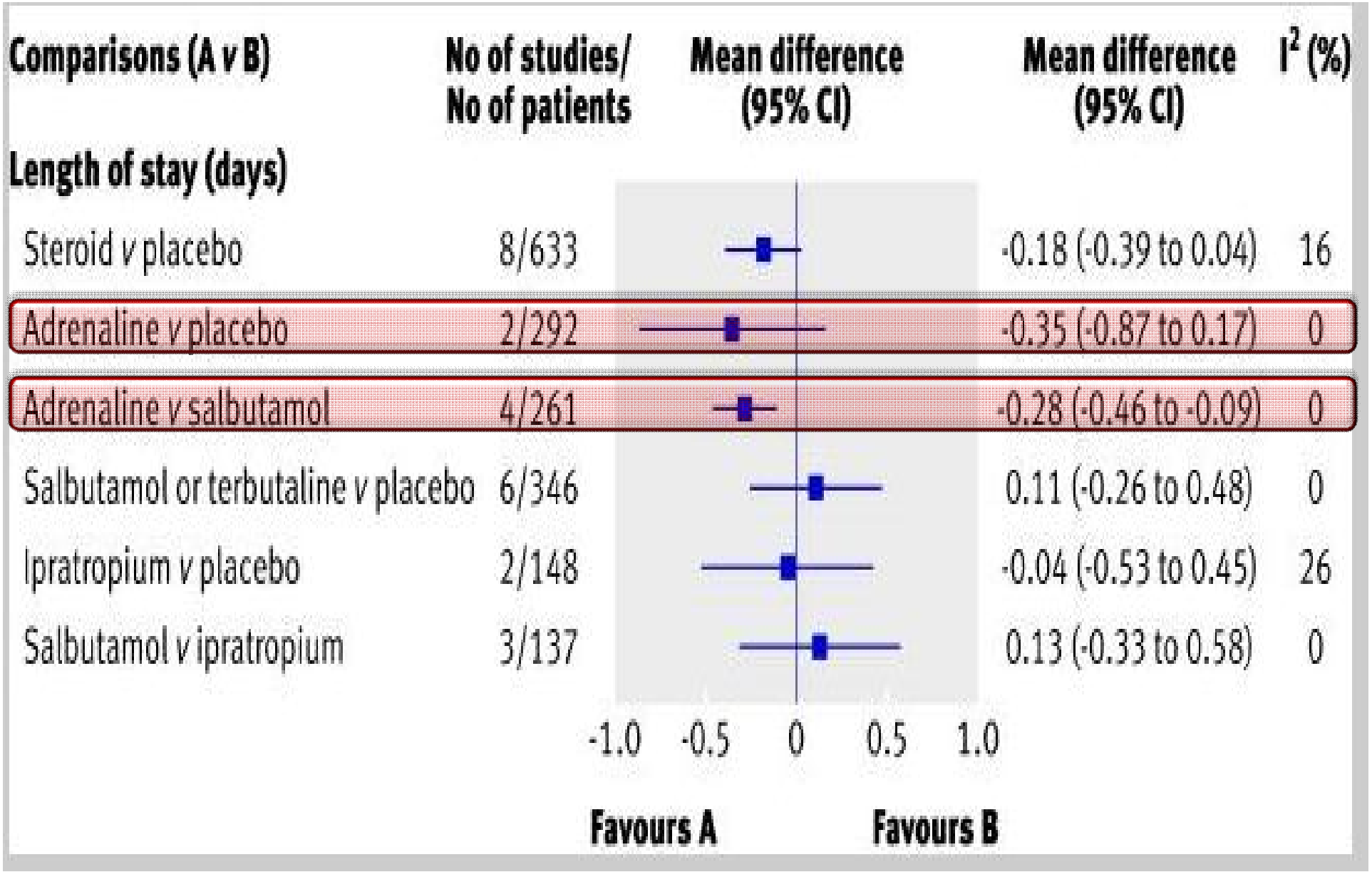
Authors' Conclusions

- For outpatients with bronchiolitis, nebulized Adrenaline can be effective in avoiding hospitalization.
- Systemic glucocorticoids such as dexamethasone cannot be recommended as a routine therapy given the current level of evidence and potential for adverse events.

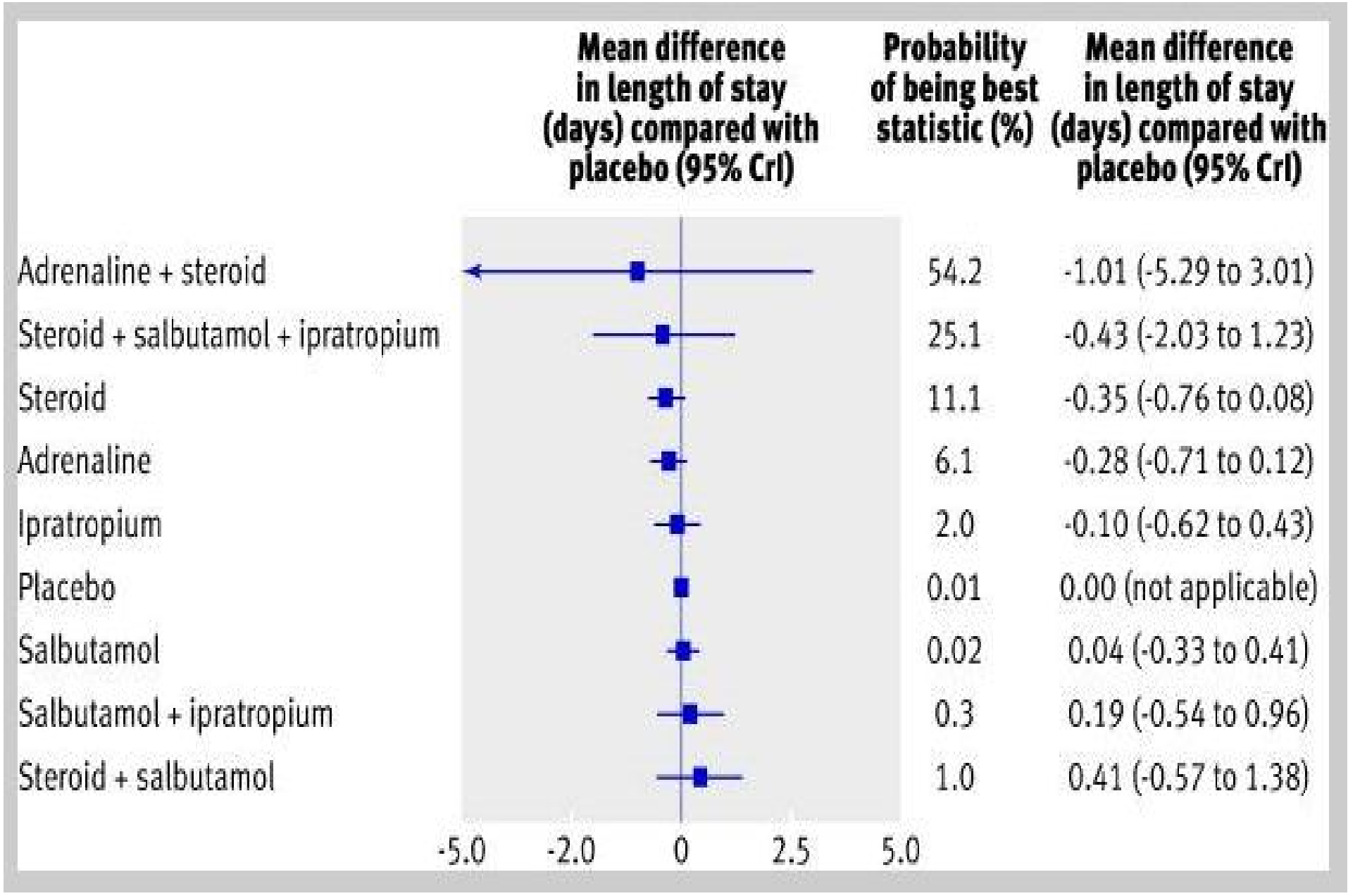
The Cochrane library and The treatment of Bronchiolitis in 2011

BRONCHODILATORS AND GLUCOCORTICOIDS FOR TREATMENT IN-PATIENTS IN ACUTE BRONCHIOLITIS

The Cochrane library and The treatment of Bronchiolitis in 2011
British Medical journal: January – 27 – 2011
Published online: April – 6 - 2011



Results from meta-analysis of direct comparisons for length of stay in inpatients.



Results of mixed treatment analysis for length of stay.

INPATIENT OUTCOMES

Outcome	Comparison	Number of subjects (studies)	Measure of effect (95% CI)	I^2	Quality of evidence (GRADE)
Length of stay	Glucocorticoid *vs* placebo	633 (8)	MD: − 0.18 (−0.39, 0.04)	16%	High
	Bronchodilator *vs* placebo	349 (6)	MD: 0.06 (−0.27, 0.39)	0%	Moderate
	Epinephrine *vs* placebo	292 (2)	MD: − 0.35 (−0.87, 0.17)	0%	Moderate
	Epinephrine*vs*bronchodilator	**261 (4)**	**MD:−0.28 (−0.46, −0.09)[a]**	**0%**	**Moderate**
	3% hypertonic saline*vs*0.9% saline	**282 (4)**	**MD:−1.16 (−1.55, −0.77)[b]**	**0%**	**Moderate**
	Chest physiotherapy *vs* standard care or other drainage/breathing technique	172 (3)	MD: 0.07 (−0.58, 0.73)	0%	Low
Re-admissions between 2 days and 4 months	Glucocorticoid *vs* placebo	359 (3)	RR: 1.04 (0.12, 8.72)	66%	Low
	Inhaled corticosteroid *vs* placebo	309 (4)	RR: 1.15 (0.60, 2.22)	45%	Moderate
	Epinephrine *vs* placebo	192 (2)	RR: 0.29 (0.05, 1.86)	0%	Low
Re-admissions between 3 months and 1 year	Inhaled corticosteroid *vs* placebo	358 (5)	RR: 1.05 (0.63, 1.75)	29%	Moderate
Clinical score at 60 minutes	**Epinephrine*vs*bronchodilator**	**248 (4)**	**SMD:−0.79 (−1.45, −0.13)[a]**	**79%**	**Low**
	Epinephrine *vs* placebo	232 (2)	SMD: − 0.04 (−0.49, 0.40)	46%	Moderate
Clinical score at 120 minutes	**Epinephrine*vs*bronchodilator**	**140 (1)**	**SMD:−0.52 (−0.86, −0.18)[a]**	—	**Low**
Clinical score at 1–3 days	Glucocorticoid *vs* placebo	113 (4)	SMD: − 0.74 (−1.48, 0.01)	70%	Low

RESULTS

- For inpatients, nebulized Adrenaline versus bronchodilator decreased length of stay. Adrenaline decreased length of stay by seven hours.(Grade: Moderate)
- For inpatients, epinephrine versus bronchodilator led to a significantly lower clinical score at both 60 mins and 120 mins. (Grade: Low)

Authors' Conclusions

- For inpatients, nebulized Adrenaline and systemic and inhaled glucocorticoids cannot be recommended for inpatients given the weak level of evidence.

The Cochrane library and The treatment of Bronchiolitis in 2011

Side-effects of Netbulized Adrenaline

- Adrenaline inhalation is generally safe.
- Life-threatening Cardiac Arrhythmia after a Single Dose of Nebulized Adrenaline could be unpredictable in Pediatric Emergency Department. (Oxford Journals).

Oxford Journals: Journal of Tropical Pediatrics 2011

The safety of nebulization with 3 to 5 ml of adrenaline (1:1000)

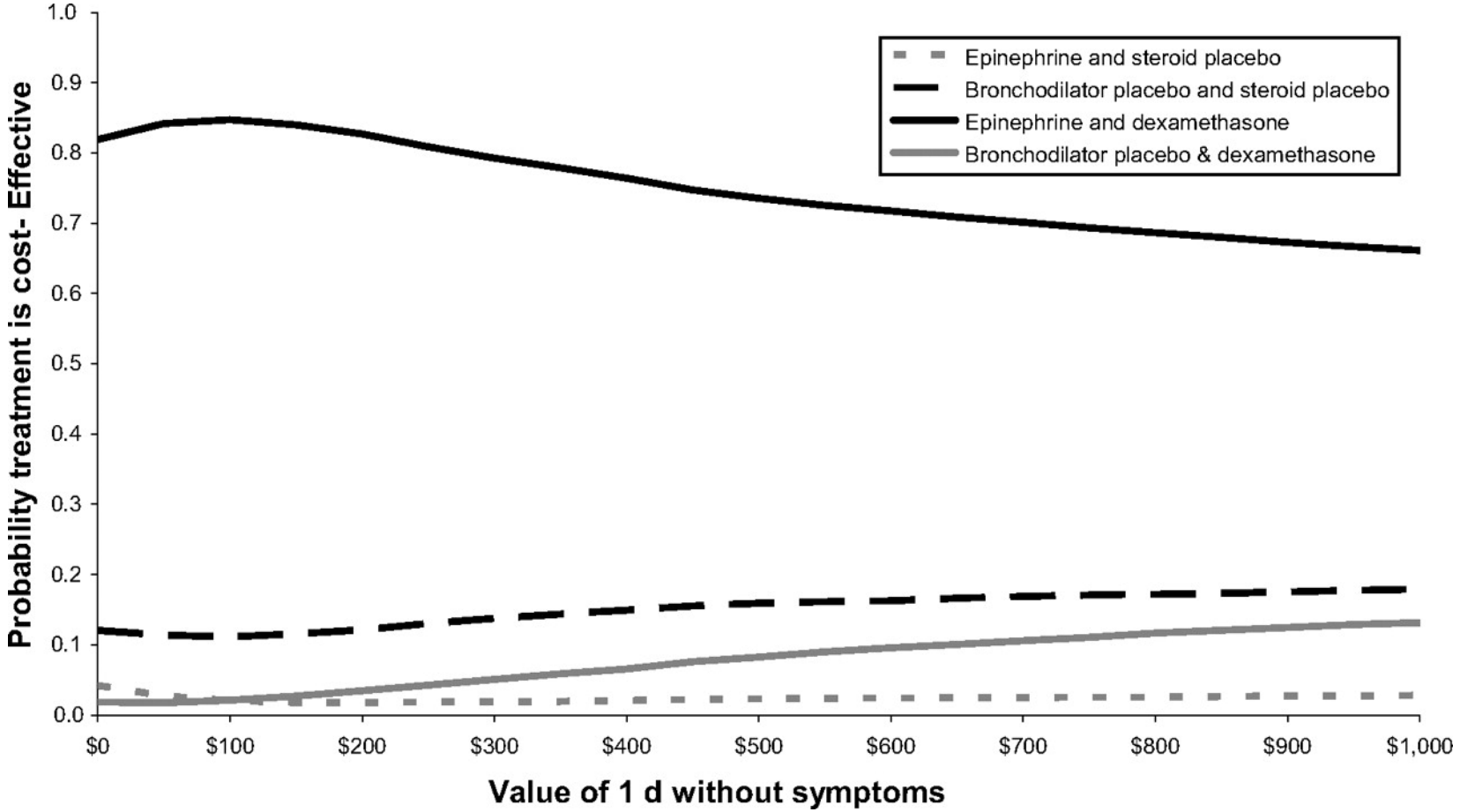
- An evidence based review. (review article of “Jornal the pediatria”).
- Evidence shows that nebulization with 3 to 5 ml of adrenaline (1:1000) is a safe therapy, with minor side-effects, for children with acute inflammatory airway obstruction.

Cost-effectiveness of Adrenaline and Dexamethasone in Bronchiolitis

- The Research group Pediatric Emergency Research Canada.
- This analysis is based on a double-blind RCT of 800 infants (Age: 6 w-12 m-M: 5 m). During 3 bronchiolitis seasons from 2004 through 2007.
- The most cost-effective treatment option
- The most effective in controlling symptoms and is associated with the least costs.

American Academy of Pediatrics in 2010

Cost-effectiveness acceptability curve.



Sumner A et al. Pediatrics 2010;126:623-631

PEDIATRICS®

CONCLUSION & DISCUSSION

- This review provides some important directions for clinical practice and future research.
- Adrenaline seems to be beneficial for short term outcomes among outpatients, including admission rates from the emergency department.
- Furthermore, adrenaline combined with dexamethasone showed longer term effects, reducing admission rates up to seven days after the emergency department visit.
- For inpatients, none of the interventions examined showed clear benefits for length of stay.

THANK YOU FOR ATTENTION!