Office of Evidence Based Practice (EBP) – Critically Appraised Topic: Ipratropium Bromide for Asthma Exacerbation in the Emergency Department or Urgent Care Center

Specific Care Question

In the patient greater than 2 years old and less than 5 years old who presents to the ED/UCC with an asthma exacerbation, should ipratropium bromide (IB) be considered as an adjunct to standard treatment with albuterol for severe asthma at presentation, or asthma that does not respond to initial treatment to reduce hospital admissions and adverse effects and improve tests of pulmonary function?

Question Originator

The Asthma in the Emergency Department/ Urgent Care Center Clinical Practice Guideline Team

Literature Summary

Background. Standard treatment for acute asthma exacerbations includes albuterol and corticosteroids (GINA, 2018, p 74). For exacerbations that are moderate to severe at initial presentation or do not respond to initial treatment, anticholinergic agents such as IB are recommended (GINA, 2018, p. 119;Griffiths & Ducharme, 2013)

Study characteristics*.* The search for suitable studies was completed on February 21, 2018. One Cochrane Database Systematic Review (Griffiths & Ducharme, 2013) that included 20 relevant studies and two RCTs published since the CDSR are included (see Figure 1). The included studies were randomized trials that compared treatment with anticholinergics (IB) with short-term beta-agonists (SABA) to treatment with SABA alone. Subjects were between the age of 18 months and 18 years. Overall, there was low risk of bias across the included studies (see Figure 2). Subjects were being treated for an acute asthma exacerbation.

Key results. We concur with the (GINA, 2018) guideline and recommend IB be used in conjunction with albuterol and corticosteroids in patients with severe asthma exacerbations, or exacerbations that do not respond to initial therapy. This recommendation is based on high quality evidence that the addition of IB decreases hospital admissions in the population (*OR* = 0.6, 95% CI [0.45, 0.60]), and moderate quality evidence that the change from baseline forced expiratory volume in 1 second, percent predicted (FEV1, % predicted) at 60 minutes past the IB treatment is greater (*Mean difference* = 10.08, 95% CI [6.25, 13.92].

Summary by Outcome

Hospital Admission. Sixteen trials (2842 subjects) were included for this outcome. The trials were placed in the following sub-groups a) severe, b) moderate-severe, c) moderate, d) mild-moderate, and e) mild. Subjects in the moderate, mild-moderate and mild sub-groups did not have decrease in hospital admission. Importantly, for subjects in the severe and moderate-severe sub-groups those that were treated with IB with SABA had significantly less hospital admissions than those treated with SABA alone (*OR* = 0.6, 95% CI [0.45, 0.60]. See Table 1 and Figure 3.

Change from baseline FEV_1, % predicted at 60 minutes. Five trials (402 subjects) were included for this outcome. Subjects treated with IB plus SABA had greater increase in % predicted FEV_1 at 60 minutes past last treatment than did subjects treated with SABA alone *Mean difference* = 10.08, 95% CI [4.11, 14.89]. (See Table 2 and Figure 4)

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Change in clinical score at 120 minutes (± 30 minutes). Four trials (1134 subjects) were included for this outcome. Various scoring tools were used in each trial. Subjects treated with IB plus SABA had greater reduction in the clinical score than subjects treated with SABA alone *Mean difference* = 0.39, 95% CI [-0.66, 0.11] (see Table 2 and Figure 5).

Relapse. Nine trials (1389 subjects) were included for this outcome. Relapse was defined as less than 72 hours in five trials, within 48 hours in one trial, and no definition was given in three trials. Relapse rate was not different between the group treated with IB plus SABA and the group treated with SABA alone *OR* = 1.08, 95% CI, [0.66, 1.77] (See Table 2 and Figure 6).

Adverse Events. Three adverse events (AE) were reported upon. For the outcome Tremor seven trial were included (542 subjects). Subjects in the IB plus SABA group had significantly less tremor than those in the SABA alone group *OR* = 0.53, 95% CI, [.31, .90]. For the outcome Nausea, seven trials (757 subjects) were included. Subjects in the IB plus SABA group had significantly less nausea than those in the SABA alone group *OR* = 0.54, 95% CI [.31, .93]. Finally, for the outcome Vomiting, eight trials (1230 subjects) were included. There was no difference in the occurrence of vomiting when groups treated with IB plus SABA and groups treated with SABA alone *OR* = 0.87, 95% CI [0.47, 1.61].

Search Strategy and Results (see PRISMA diagram)

PubMed - (asthma OR wheez* OR respiratory sounds) AND (random* OR trial* OR placebo* OR comparative study OR controlled study OR double blind OR single-blind) AND (child OR children OR infan* OR adolescen* OR pediatr* OR paediatr*) AND (emergenc* OR acute*) AND (ipratropium* OR anticholinerg* OR atropin*) Filters: From 2012/01/01 to 2018/12/31

Thirty-five articles were identified in the PubMed search. Amanda Nedved, MD, Erin Scott, DO and Irene Walsh MD reviewed the 35 titles and abstracts found in the search and identified 14 articles believed to answer the question. After an in-depth review 3 articles answered the question. One of the three was the CDSR by (Griffiths & Ducharme, 2013)), which included 20 trials. Therefore, the total number of trials is 22 trials (Griffiths (2013), the 20 trials analyzed by (Griffiths & Ducharme, 2013) and two new trials (Memon, Parkash, Ahmed Khan, Gowa, & Bai, 2016; Wyatt, Borland, Doyle, & Geelhoed, 2015).

Studies Included in this Review (in Alphabetical Order)

Studies with * are from in Griffiths & Ducharme, 2013

*Beck, Robertson, Galdes-Sebaldt, & Levison (1985)
*Benito Fernandez, Mintegui Raso, Sanchez Echaniz, Vazquez Ronco, & Pijoan Zubizarreta (2000)
*BI (2009)
*Calvo, Calvo, Marin, & Moya (1998)
*Chakraborti, Lodha, Pandey, & Kabra (2006)
*Cook, Fergusson, & Dawson (1985)
*Ducharme & Davis (1998)
*Guill, Maloney, & DuRant (1987)
*Iramain et al. (2011)
Memon, Parkash, Ahmed Khan, Gowa & Bai (2016)
*Peterson et al. (1996)
*Phanichyakam, Kraisarin, & Sasisakulporn (1990)

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*Qureshi, Zaritsky, & Lakkis 1997)
*Qureshi, Pestian, Davis, & Zaritsky (1998)
*Reisman, Galdes-Sebalt, Kazim, Canny, & Levison (1988)
*Schuh, Johnson, Callahan, Canny, & Levison (1995)
*Sharma & Madaan (2004)
*Sienra Monge, Bermijo Guevara, del Rio Navarro, Rosas Vargas, & Rayes Ruiz (2000)
*Watanasomsiri & Phipatanakul (2006)
*Watson, Becker, & Simons (1988)
Wyatt, Borland, Doyle & Geelhoed (2015)
*Zorc, Pusic, Ogborn, Lebet, & Duggan (1999)

Studies Not Included in this Review with Exclusion Rationale (in Alphabetical Order)

Authors	Reason for exclusion
(Castro-Rodriguez, G, & C, 2015)	Overview of reviews
(Everard et al., 2005)	Includes patients < 2 years of age
(Nomura et al., 2017)	Article in Japanese
(Hon & Leung, 2017)	Narrative review
(Lebedenko & Semernik, 2015)	Article in Russian
(Pardue Jones, Fleming, Otillio, Asokan, & Arnold, 2016)	Narrative review
(Rodrigo & Neffen, 2017)	Medication is a controller medication, not for an exacerbation
(Salo et al., 2006)	Included adults only
(Teoh et al., 2012)	The pre-Griffiths CDSR
(Vezina, Chauhan, & Ducharme, 2014)	Hospitalized patients

Method Used for Appraisal and Synthesis

The Cochrane Collaborative computer program, Review Manager (Higgins & Green, 2011)[a] was used to synthesize the 2 included studies. GRADEpro GDT (Guideline Development Tool) is the tool used to create the Summary of Findings Tables for this analysis.

[a]Higgins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cohcrane Collaboration, 2011.

EBP Scholar's responsible for analyzing the literature

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EBP team member responsible for reviewing, synthesizing, and developing this document

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Acronyms used in this document:

Acronym	Explanation
CDSR	Cochrane Database of Systematic Reviews
FEV_1	Forced expiratory volume in one second
IB	Ipratropium bromide
SABA	Short acting beta-agonist

Date Developed/Updated: May 1 2018

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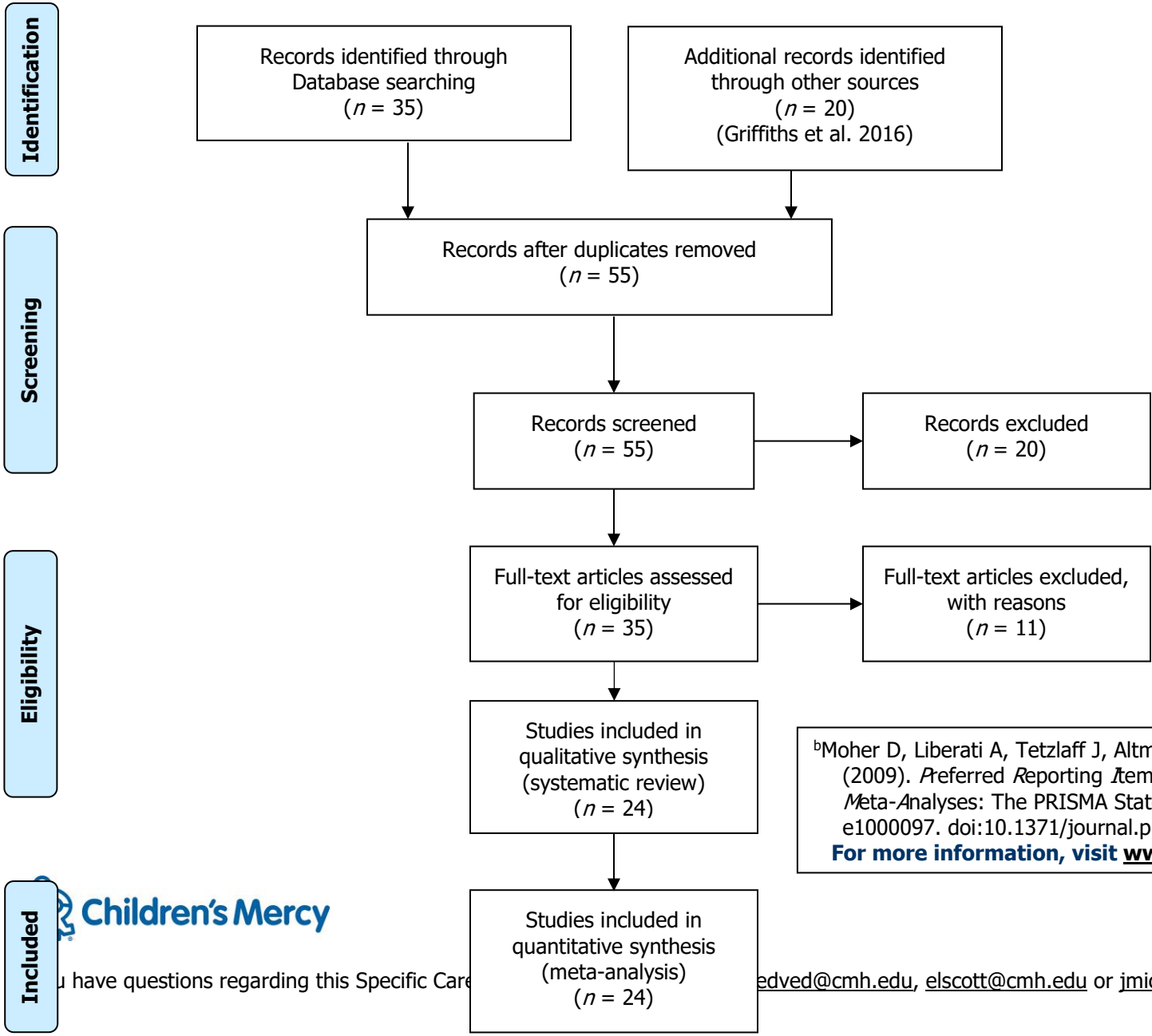
Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA)[b]



[b]Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Figure 2
Risk of Bias Summary

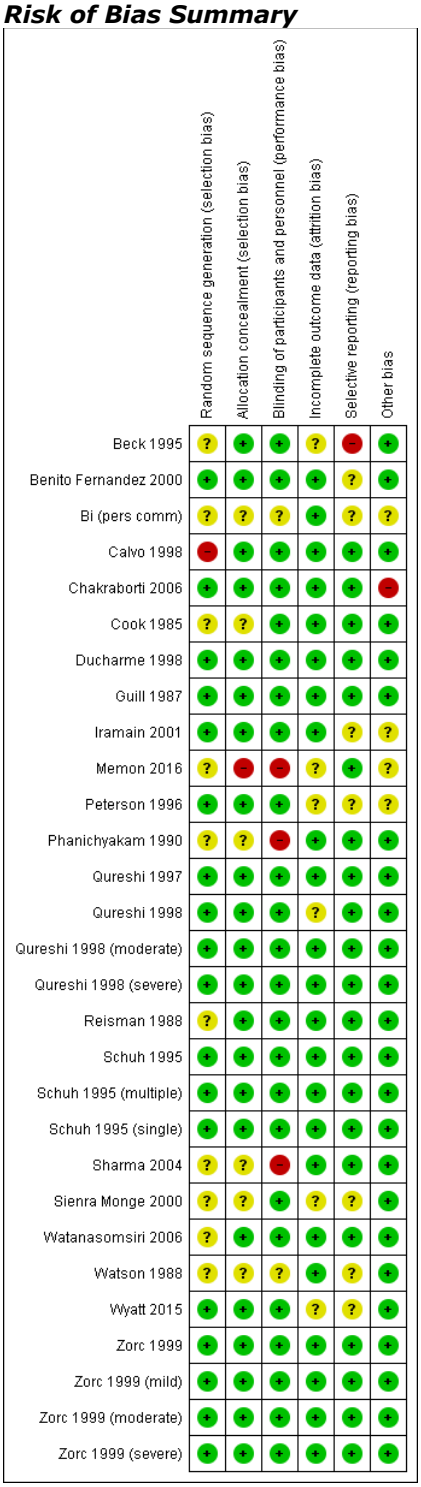


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Table 1
Summary of Findings Table

Anticholinergic (IB) and SABA Compared to SABA Alone for Asthma Exacerbation in the ED or UCC: Hospital Admission											
Certainty assessment							**Summary of findings**				
№ of participants (studies) Follow-up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty of evidence**	**Study event rates (%)**		**Relative effect (95% CI)**	**Anticipated absolute effects**	
							With SABA Alone	**With Anticholinergic (IB) and SABA**		**Risk with SABA Alone**	**Risk difference with Anticholinergic (IB) and SABA**
Hospital Admission											
2842 (19 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ HIGH	395/1397 (28.3%)	346/1445 (23.9%)	**OR 0.73** (0.60 to 0.88)	283 per 1,000	**59 fewer per 1,000** (91 fewer to 25 fewer)
Hospital Admission - Severe											
1188 (8 RCTs)	not serious	not serious	not serious	serious [a]	none	⨁⨁⨁◯ MODERATE	173/580 (29.8%)	139/608 (22.9%)	**OR 0.60** (0.45 to 0.80)	298 per 1,000	**95 fewer per 1,000** (138 fewer to 45 fewer)
Hospital Admission - Moderate-severe											
371 (4 RCTs)	not serious	not serious	not serious	serious [a,b]	none	⨁⨁⨁◯ MODERATE	49/182 (26.9%)	30/189 (15.9%)	**OR 0.51** (0.30 to 0.86)	269 per 1,000	**111 fewer per 1,000** (170 fewer to 29 fewer)
Hospital Admission - Moderate											

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Anticholinergic (IB) and SABA Compared to SABA Alone for Asthma Exacerbation in the ED or UCC: Hospital Admission											
Certainty assessment							**Summary of findings**				
808 (4 RCTs)	not serious	not serious	not serious	serious [b,c]	none	⨁⨁⨁◯ MODERATE	145/406 (35.7%)	148/402 (36.8%)	**OR 1.04** (0.73 to 1.48)	357 per 1,000	**9 more per 1,000** (69 fewer to 94 more)

Hospital Admission - Mild-moderate											
358 (2 RCTs)	not serious	not serious	not serious	very serious [a]	none	⨁⨁◯◯ LOW	24/172 (14.0%)	23/186 (12.4%)	**OR 0.85** (0.46 to 1.59)	140 per 1,000	**18 fewer per 1,000** (70 fewer to 65 more)
Hospital Admission - Mild											
117 (1 RCT)	not serious	not serious	not serious	very serious [d]		-	4/57 (7.0%)	6/60 (10.0%)	**OR 1.47** (0.39 to 5.51)	70 per 1,000	**30 more per 1,000** (42 fewer to 224 more)

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Low number of subjects categorized as severe asthma exacerbation.
b. One study reported no hospitalizations in either group,
c. Low number of subjects categorized as moderate asthma exacerbation.
d. Only one trial is included for this sub-group *n* = 117

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Table 2
Summary of Findings Table

Anticholinergic (IB) and SABA compared to SABA Alone for health problem or population *Asthma Exacerbation in the ED or UCC: Change in baseline FEV1, Change in clinical score, and Relapse*											
Certainty assessment							**Summary of findings**				
№ of participants (studies) Follow-up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty of evidence**	**Study event rates (%)**		**Relative effect (95% CI)**	**Anticipated absolute effects**	
							With SABA Alone	**With Anticholinergic (IB) and SABA**		**Risk with SABA Alone**	**Risk difference with Anticholinergic (IB) and SABA**
Change from baseline in % predicted FEV1, 60 minutes post last ipratropium											
402 (5 RCTs)	not serious	not serious	not serious	serious [a]	none	⨁⨁⨁◯ MODERATE	180	222	-	The mean change from baseline in % predicted FEV1, 60 minutes post last ipratropium was **0**	MD **10.08 higher** (6.24 higher to 13.92 higher)
Change in clinical score at 120 minutes (+/- 30 minutes)											
1134 (4 RCTs)	serious [b]	not serious	not serious	serious [c]	none	⨁⨁◯◯ LOW	573	561	-	The mean change in clinical score at 120 minutes (+/- 30 minutes) was **0**	MD **0.39 lower** (0.66 lower to 0.11 lower)

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Anticholinergic (IB) and SABA compared to SABA Alone for health problem or population *Asthma Exacerbation in the ED or UCC: Change in baseline FEV1, Change in clinical score, and Relapse*											
Certainty assessment							**Summary of findings**				
Relapse											
1389 (10 RCTs)	not serious	not serious	not serious	serious [d]		-	30/666 (4.5%)	37/723 (5.1%)	**OR 1.08** (0.66 to 1.77)	45 per 1,000	**3 more per 1,000** (15 fewer to 32 more)

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Low number of subjects in the included trials (*N* = 402, IB +SABA group *n* = 222; IB alone group *n* = 180)
b. One of the four studies did not conceal allocation nor blind subjects, personnel, nor outcome assessors.
c. Low number of subjects in the included trials (*N* = 561, IB +SABA group *n* = 573; IB alone group *n* = 180)
d. Wide confidence intervals across all studies

Table 3
Characteristics of Studies
(Characteristics of Studies tables, and Risk of Bias tables from the CDSR can be found in (Griffiths & Ducharme, 2013).

Memon 2016

Methods	RCT
Participants	**Setting:** Emergency department, Pakistan from October 1, 2009, to March 31, 2010, **Randomized into study:** *N* = 200 • **Group 1 (salbutamol):** *n* = 100 • **Group 2 (salbutamol plus ipratropium bromide):** *n* = 100 **Completed Study:** *N* = 177 • **Group 1 (salbutamol):** *n* = 84 • **Group 2 (salbutamol plus ipratropium bromide):** *n* = 93 **Gender, males:** • **Group 1(salbutamol):** *n* = 58 (58%) • **Group 2 (salbutamol plus ipratropium bromide):** *n* = 54 (54%) **Age, years**: • **Group 1 (salbutamol):** 9.1±3

	○ 2-6 years: *n* = 18 ○ 7-11 years: *n* = 57 ○ >11 years: *n* = 25 • **Group 2 (salbutamol plus ipratropium bromide):** 9.3±2.8 ○ 2-6 years: *n* = 15 ○ 7-11 years: *n* = 63 ○ >11 years: *n* = 22 **Inclusion Criteria:** • Ages 2-14 years • Visiting emergency department for acute severe asthma ○ For asthma evaluation, clinical score by Bentur Modification (BM) 5-10 (moderate) and >10 (serve exacerbation) was used. Bentur Modification is based on 4 parameters: heart rate (HR), respiratory rate (RR), wheezing, accessory muscle usage. Each parameter has minimum 0 and maximum 3 score. **Exclusion Criteria:** • None disclosed . **Power Analysis: "**The sample size was calculated on the basis of frequency of asthma disease being 8.5%. It was calculated at 95% confidence interval (CI) with 4% precision, using EPI software 6."
Interventions	• **Group 1 (salbutamol):** received 3 doses of salbutamol (0.03 ml/kg/dose) only 15 minutes apart • **Group 2 (salbutamol plus ipratropium bromide):** received 3 doses of ipratropium (250 microgram/dose) in combination with salbutamol (0.03 ml/kg/dose) with same time interval Response to treatment was assessed after 15 minutes of the last dose and a change in severity category (improvement) from baseline to lower category was taken as improvement.
Outcomes	**Primary outcome(s):** · Clinical score, specifically Bentur Modification score
Notes	They only report the clinical score of those subjects whose score after treatment was less than 10.

Risk of bias table

Bias	Scholars' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	The authors did not describe the method of randomization. "The patients were randomly allocated to two equal groups."
Allocation concealment (selection bias)	High risk	Not described

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Blinding of participants and personnel (performance bias)	High risk	Not described
Incomplete outcome data (attrition bias)	Unclear risk	No missing outcome data
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Unclear risk	

Wyatt 2015

Methods	Randomized, single-blinded controlled trial
Participants	**Setting:** Princess Margaret Hospital for Children (PMH) Emergency Department, Australia **Randomized into study:** *N* = 416 • **Group 1:** *n = 209* • **Group 2:** *n = 207* **Completed Study:** *N= 410* • **Group 1:** *n = 205* • **Group 2:** *n = 205* **Gender, males** • **Group 1:** *n = 105 (60%, reported from per protocol 174)* • **Group 2:** *n = 110 (64%, reported from per protocol 173)* **Age, years** (median) (Q1, Q3) • **Group 1:** 4.3 (2.8, 6.4) • **Group 2:** 4.1 (3.0, 6.3) **Inclusion Criteria** • Age 2 to 15 years old • Presenting with acute wheezing illness of moderate severity based on criteria suggested by the National Asthma Council Australia. Includes one or more of the following; oxygen saturations of 90-94%, speaking in phrases, and moderate to loud wheeze. **Exclusion Criteria**

	• Age less than 2 years to avoid overlap with bronchiolitis • Adolescents 16 and older due to upper age limit of institution's ED acceptance • Severe asthma defined with oxygen saturations less than 90%, cyanosis, inability to speak secondary to breathlessness, silent chest or abnormal conscious state • Current chronic respiratory illness • Had received Ipratropium Bromide in the preceding 6 hours **Power Analysis** • The study is an equivalence trial with a 15% margin of equivalence, using the outcome: Hospital admission. • With a sample size of 173 subjects per group, there would be 80% power to detect a significant difference ($p < 0.05$).
Interventions	• **Group 1:** Salbutamol + Prednisolone + Ipratropium ○ Salbutamol, Metered Dose Inhaler (MDI) (100 mcg/actuation) with spacer 3 times at 20 minute intervals (age 2 to 5 years 6 actuations per dose, age 6 to 15 years 12 actuations per dose) ○ PLUS Oral Prednisolone 1 mg/kg to maximum 50 mg dose. ○ PLUS Ipratropium Bromide MDI (21 mcg/actuation) with spacer 3 times at 20 minute intervals (age 2 to 5 years 4 actuations per dose, age 6-15 years 8 actuations per dose) • **Group 2:** Salbutamol + Prednisolone ○ Salbutamol MDI 100 mcg/actuation with spacer 3 times at 20 minute intervals (age 2 to 5 years 6 actuations per dose, age 6 to 15 years 12 actuations per dose) PLUS Oral Prednisolone 1 mg/kg to maximum 50mg dose.
Outcomes	• **Primary outcome(s)** ○ Rate of hospital admission • **Secondary outcome(s**) • **Safety outcomes**
Notes	Unable to double blind this intervention. However, the treating providers were blinded to the intervention.

Risk of bias table

Bias	Scholar's judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	Blocked computerized random number generation
Allocation concealment (selection bias)	Low risk	Concealed in opaque envelopes

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Blinding of participants and personnel (performance bias)	Low risk	Doctor managing patient was not present during administration by nursing staff and exact treatment was not documented in patient record
Incomplete outcome data (attrition bias)	Unclear risk	17% of the group randomized to receive ipratropium and 16% of the group who did not receive ipratropium were not included in the analysis. The reason of excluding appears to be balanced between among the same reasons between groups.
Selective reporting (reporting bias)	Unclear risk	
Other bias	Low risk	

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Figure 3

***Comparison Anticholinergic + SABA vs. SABA*, Outcome: Hospital Admission (Lower is better)**

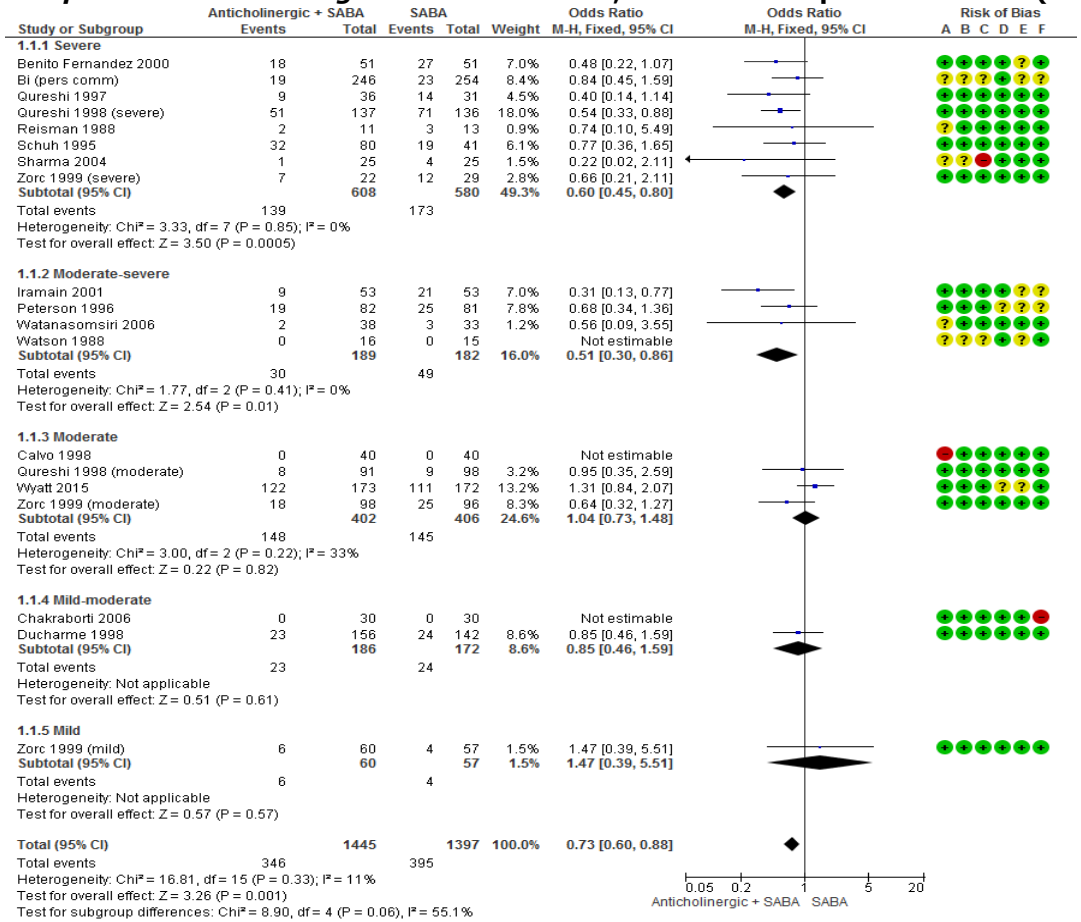

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Figure 4
Comparison Anticholinergic + SABA vs. SABA, Outcome: Change from baseline in % predicted FEV_1 (Higher is better)

	Anticholinergic + SABA			SABA				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year
Watson 1988	89.3	13.2	16	80	14	15	16.0%	9.30 [-0.29, 18.89]	1988
Schuh 1995 (single)	23.4	20.6	39	13.1	12.5	19	20.1%	10.30 [1.73, 18.87]	1995
Schuh 1995 (multiple)	26	29	40	13.1	12.5	20	13.3%	12.90 [2.37, 23.43]	1995
Peterson 1996	14.7	0	82	13.1	0	81		Not estimable	1996
Qureshi 1997	33.6	11.3	45	24.1	14.6	45	50.6%	9.50 [4.11, 14.89]	1997
Total (95% CI)			**222**			**180**	**100.0%**	**10.08 [6.24, 13.92]**	

Heterogeneity: $Chi^2 = 0.35$, $df = 3$ ($P = 0.95$); $I^2 = 0\%$
Test for overall effect: $Z = 5.15$ ($P < 0.00001$)

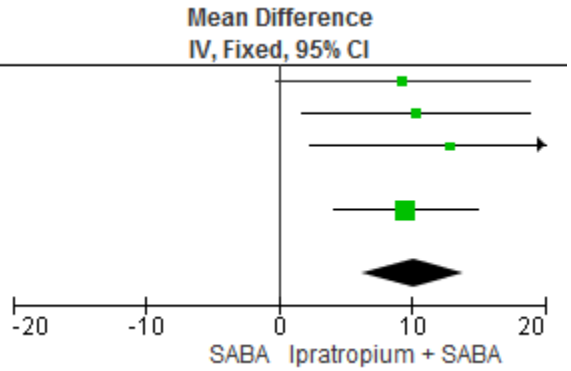

Figure 5 ***Comparison Anticholinergic + SABA vs. SABA, Outcome: Change in clinical score at 120 minutes (Lower is better)***

	Anticholinergic + SABA			SABA				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year
Bi (pers comm)	-6.7	0	246	-6.4	0	254		Not estimable	
Qureshi 1998 (moderate)	-3.95	1.18	79	-3.65	1.3	84	51.7%	-0.30 [-0.68, 0.08]	1998
Qureshi 1998 (severe)	-4.54	2.05	136	-4.07	2.21	135	29.1%	-0.47 [-0.98, 0.04]	1998
Memon 2016	4.4	2.4	100	4.9	2.1	100	19.2%	-0.50 [-1.13, 0.13]	2016
Total (95% CI)			**561**			**573**	**100.0%**	**-0.39 [-0.66, -0.11]**	

Heterogeneity: $Chi^2 = 0.43$, $df = 2$ ($P = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 2.78$ ($P = 0.006$)

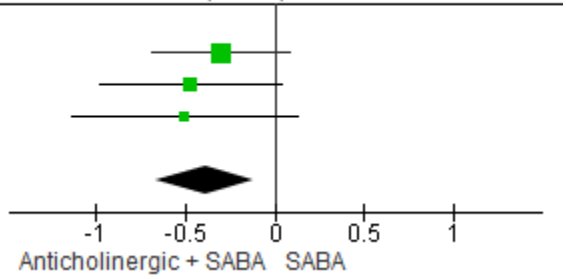

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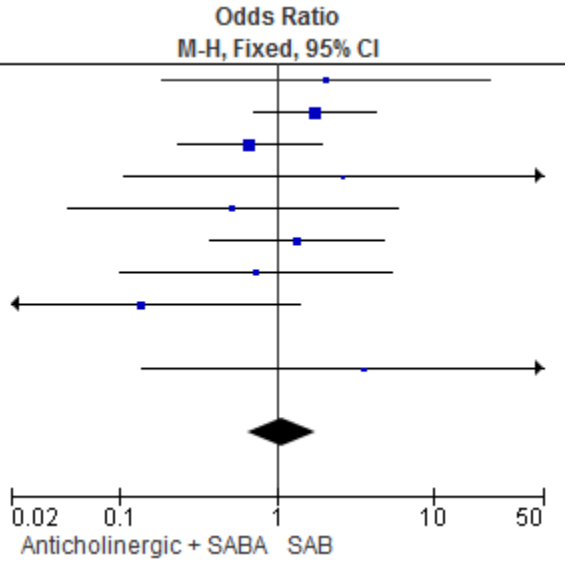
Figure 6 ***Comparison Anticholinergic + SABA vs. SABA, Outcome: Relapse (within 72 hours, Lower is better)***

Study or Subgroup	Anticholinergic + SABA Events	Total	SABA Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bi (pers comm)	2	246	1	254	3.2%	2.07 [0.19, 23.02]
Ducharme 1998	15	133	8	118	24.9%	1.75 [0.71, 4.28]
Peterson 1996	7	63	9	57	27.8%	0.67 [0.23, 1.92]
Qureshi 1997	1	36	0	31	1.7%	2.66 [0.10, 67.72]
Qureshi 1998 (moderate)	1	71	2	75	6.4%	0.52 [0.05, 5.88]
Qureshi 1998 (severe)	7	85	4	64	13.9%	1.35 [0.38, 4.81]
Reisman 1988	2	11	3	13	7.5%	0.74 [0.10, 5.49]
Schuh 1995	1	47	3	22	13.2%	0.14 [0.01, 1.41]
Watson 1988	0	16	0	15		Not estimable
Zorc 1999 (severe)	1	15	0	17	1.4%	3.62 [0.14, 95.78]
Total (95% CI)		**723**		**666**	**100.0%**	**1.08 [0.66, 1.77]**
Total events	37		30			

Heterogeneity: $Chi^2 = 6.62$, $df = 8$ ($P = 0.58$); $I^2 = 0\%$

Test for overall effect: $Z = 0.30$ ($P = 0.77$)



Children's Mercy

If you have questions regarding this Specific Care Question – please contact anedved@cmh.edu, elscott@cmh.edu or jmichael@cmh.edu