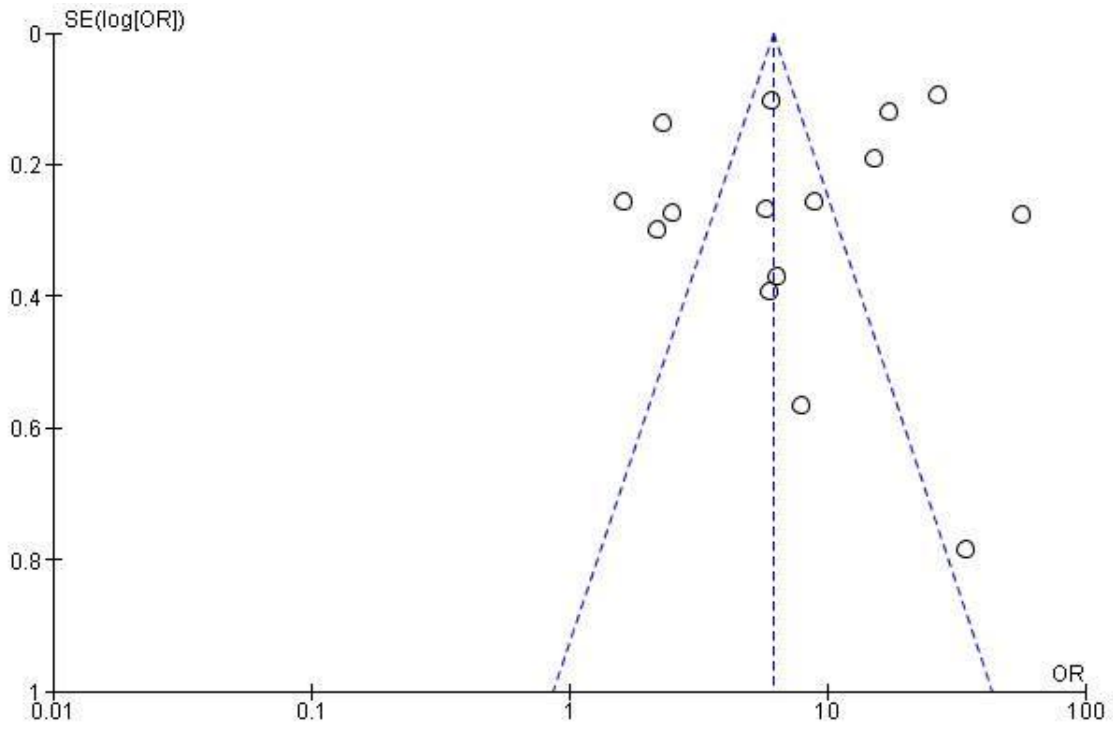
SUPPLEMENT



Supplemental Figure 1 – Funnel Plot Incorporating 16 Populations from the 11 Studies Included in the Meta-Analysis

Studies included - Alsheri *et al.,* 2020; Costa *et al.,* 2018; Covar *et al.,* 2008; Emerman *et al.,* 2001; Engelkes *et al.,* 2016; Engelkes *et al.,* 2020; Quezada *et al.,* 2016; Triasih *et al.,* 2011; Turner *et al.,* 2018; van den Bosch *et al.,* 2012; Wu *et al.,* 2011.

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Supplemental Table I – Positive Predictive Values for Studies Stratified by Methodology

Study Design	Author	Outcome	Positive Predictive Value
Randomised Controlled Trial	Covar *et al*., 2008	≥1 prednisone course in prior year + exacerbation during follow-up	0.43
	Wu *et al*., 2011	ED visit or hospitalisation in year prior to randomisation + exacerbation during follow-up	0.58
	Quezada *et al*., 2016	Unscheduled visit in prior year + future exacerbation	0.77
Prospective Cohort Study	Emerman *et al*., 2001	Hospitalisation in prior year + future exacerbation	0.31
	Chen *et al*., 2003	Hospitalisation + readmission in following year	0.30
	Miller *et al*., 2008	ED visit + urgent care visit in following 6 months	0.14
	To *et al*., 2008	ED visit + exacerbation in following 6 months	0.54
Routinely Acquired Data	Tolomeo *et al*., 2009	Hospitalisation + ED visit in following year	0.28
	Kenyon *et al*., 2014	Hospitalisation + readmission in following year	0.17
	Engelkes *et al*., 2016	Exacerbation in year prior to cohort entry + exacerbation during follow-up	0.28
	To *et al*., 2018	ED visit + ED visit in following year	0.12
	Turner *et al*., 2018	Exacerbation in baseline year + exacerbation in outcome year	0.43
	Engelkes *et al*., 2020	Exacerbation + future ED visit/hospitalisation CPRD SIDIAP IPCI AUH PEDIANET	 0.15 0.13 0.19 0.08 0.06
Retrospective Case-Control	van den Bosch *et al*., 2012	Hospitalisation + future PICU admission	0.73
	Visitsunthorn *et al*., 2013	Hospitalisation + readmission	0.26
	Costa *et al*., 2018	≥3 ED visits in prior year + exacerbation at baseline	0.78
	Alsheri *et al*., 2020	PICU admission + future PICU admission	0.25

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Abbreviations used: AUH – Aarhus University Prescription Database, CPRD – Clinical Practice Research Datalink, ED – Emergency Department, IPCI – Integrated Primary Care Information, PICU – Paediatric Intensive Care Unit, SIDIAP - Sistema d'Informació per al Desenvolupament de la Investigació en Atenció Primària.

Search Strategy

Ovid MEDLINE(R) – 1946 to December Week 5 2020

1. exp Asthma/
2. asthma$.tw.
3. (asthma$ adj3 attack$).tw.
4. (asthma$ adj3 exacerbation$).tw.
5. (p?ediatric adj3 asthma$).tw.
6. (acute adj3 asthma$).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp Child/
9. p?ediatric$.tw.
10. 8 or 9
11. (risk adj3 factor$).tw.
12. 7 and 10 and 11

Limits → English language, Human studies, no Review articles, publication year 2000-current

Ovid EMBASE classic + EMBASE – 1947 to 2021 January 08

1. exp Asthma/
2. asthma$.tw.
3. (asthma$ adj3 attack$).tw.
4. (asthma$ adj3 exacerbation$).tw.
5. (p?ediatric adj3 asthma$).tw.
6. (acute adj3 asthma$).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp Child/
9. p?ediatric$.tw.
10. 8 or 9
11. (risk adj3 factor$).tw.
12. 7 and 10 and 11

Limits → English language, Human studies, no Review articles, publication year 2000-current

APA PsycInfo 1806 to January Week 1 2021

1. exp Asthma/
2. asthma$.tw.
3. (asthma$ adj3 attack$).tw.
4. (asthma$ adj3 exacerbation$).tw.
5. (p?ediatric adj3 asthma$).tw.
6. (acute adj3 asthma$).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. child$.tw.
9. p?ediatric$.tw.
10. 8 or 9
11. (risk adj3 factor$).tw.
12. 7 and 10 and 11

Limits → English language, Human studies, no Review articles, publication year 2000-current

EBSCO CINAHL

S1. (MH “Asthma+”)
S2. TX asthma*
S3. TX asthma* attack*
S4. TX asthma* exacerbation*
S5. TX p?ediatric asthma*
S6. TX acute asthma*
S7. (MH “Child+”)
S8. TX p?ediatric*
S9. TX risk factor*
S10. S1 or S2 or S3 or S4 or S5 or S6
S11. (S1 or S2 or S3 or S4 or S5 or S6) AND (S7 or S8)
S12. ((S1 or S2 or S3 or S4 or S5 or S6) AND (S7 or S8)) AND (S9)
S13. (((S1 or S2 or S3 or S4 or S5 or S6) AND (S7 or S8)) AND (S9)) NOT PT review article

Limits → English language, publication year 2000-2021

Rules applied during scoring

Under the selection bias domain, studies were awarded a rating based on how likely the selected population is to be representative of the target population, and, where applicable, the percentage of selected individuals that agreed to participate.

Under the study design domain, studies were awarded a strong rating if they used data from a randomised controlled trial and a moderate rating if they were a case-control or cohort study.

Under the confounders domain, studies were awarded a strong rating if either there were no important differences between groups, or if they controlled for confounders in their analysis, such as through the use of multivariate models.

Under the data collection methods domain, studies were awarded a strong rating if a database of routinely acquired data was used, or if extra measures were taken to ensure the reliability of the data collected. Studies were awarded a moderate rating if methods such as medical record review or parental interviews were used.

Under the withdrawals and drop-outs domain, studies were awarded a rating based on whether drop-outs were reported in terms of numbers and reasons and also the percentage of individuals completing the study. Retrospective case-control studies were awarded a not applicable status for this domain in accordance with the EPHPP tool guidance.

The global rating was determined based on the number of weak ratings each study had received, with a strong global rating being awarded to studies with no weak domains, a moderate global rating for studies with one weak domain and a weak rating for studies with two or more weak domains.

Results of Quality Assessment

Overall, there was a moderate risk of selection bias across the included studies with 14 awarded a strong rating, 11 awarded a moderate rating and one awarded a weak rating. Chen *et al*., 2003 received a weak rating because, even though the identified individuals were deemed very likely to be representative of the target population, only 44% of selected individuals agreed to participate, increasing the likelihood that these individuals were not representative of the overall target population. Although the majority of studies were awarded a strong rating for selection bias because the individuals selected were likely to be representative of the target population identified in the study, their results may not necessarily be generalisable to the wider asthma population as they often used children admitted to hospital, or seen in the ED, and these children may represent a more severe subset of the childhood asthma population.

The majority of studies received a moderate rating for study design as they were either cohort or case-control studies, with only four receiving a strong rating as they used data from randomised controlled trials.

All but one of the studies received a strong rating in the confounders domain due to there either being no differences between the groups in the study or use of appropriate statistical analysis, with multivariate models used to control for potential confounders. Quezada *et al*., 2016 received a weak rating as there was no effort to control for confounding variables either in the methodology or analysis, reducing the validity of the results.

In the data collection methods domain, 16 received a strong rating and 10 received a moderate rating. The latter rating was due to there being a risk of recall bias in these 10 studies due to use of parental and child interviews, or medical record reviews as their means of data collection. There are differences in the way, and the level of detail, that medical professionals document clinical information based on deemed relevance and importance, and therefore medical records are also not a completely reliable source of data. However, due to the retrospective nature of the majority of these studies, these data collection methods were the only ones available.

Within the withdrawals and drop-out domains, six studies had a retrospective case-control design and therefore received a not applicable rating. Of the remaining 20 studies, 12 received a strong rating and seven received a moderate rating. There was a risk of attrition bias in these seven studies due to not reporting withdrawals and drop-outs in terms of both numbers and reasons. However, for all of these studies, greater than 80% of participants completed the study. Haselkorn *et al*., 2009

received a weak rating due to its use of data from the TENOR study which did not report information regarding drop-outs or the percentage of participants completing the study.