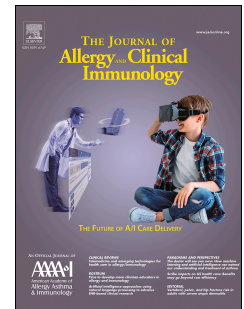


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Socioeconomic disparities in asthma healthcare utilization, exacerbations and mortality: A systematic review and meta-analysis

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Socioeconomic disparities in asthma healthcare utilization, exacerbations and mortality: A systematic review and meta-analysis

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Roche/Genentech Inc, Glaxo Smith Kline, Amgen, Genentech / Hoffman la Roche, Astra Zeneca, Aerocrine and Vitalograph. LH has given lectures supported by Novartis, Hoffman la Roche/Genentech Inc, Sanofi, Glaxo Smith Kline, Astra Zeneca, Teva and Circassia. LH reports support for attending meetings from Astra Zeneca, Boehringer Ingelheim, Chiesi, Glaxo Smith Kline and Napp Pharmaceuticals. LH has taken part in advisory boards supported by Novartis, Hoffman la Roche/Genentech Inc, Sanofi, Evelo Biosciences, Glaxo Smith Kline, Astra Zeneca, Teva, Theravance and Circassia. The rest of the authors declare that they have no relevant conflicts of interest.

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Abstract

Introduction Prior studies investigating the effect of socio-economic status (SES) on asthma healthcare outcomes have been heterogeneous in their populations studied and methodologies employed.

Objectives: To systematically synthesize evidence investigating the impact of SES on asthma healthcare utilization, exacerbations and mortality.

Methods We searched Embase, Medline and Web of Science for studies reporting differences in primary care attendance, exacerbations, emergency department (ED) attendance, hospitalization, ventilation / intubation, readmission and asthma mortality by SES. Study quality was assessed using the Newcastle Ottawa Scale and meta-analyses conducted using random-effects models. We conducted several pre-specified subgroup analyses, including by healthcare system (insurance-based vs. universal government funded) and time-period (pre-2010 vs. post-2010).

Results 61 studies, comprising 1,145,704 patients, were included. Lower SES was consistently associated with increased secondary healthcare utilization including ED attendance (OR: 1.61; 95%CI: 1.40-1.84), hospitalization (OR: 1.63; 95%CI 1.34-1.99) and readmission (OR: 1.31; 95%CI 1.19-1.44). Substantial associations were also found between SES and ventilation / intubation (OR: 1.76; 95%CI: 1.13-2.73) although there was no association with primary care attendances (OR: 0.79; 95%CI: 0.51-1.24). We found evidence of borderline significance for increased exacerbations (OR: 1.18; 95%CI: 0.98-1.42) and mortality (OR: 1.12; 95%CI: 0.92-1.37) among more deprived groups. There was no convincing evidence that disparities were

associated with country-level healthcare funding models, or that disparities have narrowed over time.

Conclusions Patients with a lower SES have substantially increased secondary care healthcare utilization. We found evidence suggestive of increased exacerbations and mortality risk although confidence intervals were wide. These disparities have been consistently reported worldwide, including within countries offering universally funded healthcare systems.

Systematic review registration number CRD42020173544.

Capsule summary: Patients from lower socioeconomic backgrounds have substantially increased secondary healthcare utilization. It is unclear to what extent this is driven by an increased risk of exacerbations or the funding model of their local healthcare system.

Key Messages:

- Patients with a lower SES have substantially increased secondary healthcare utilization.
- We found evidence suggestive of increased exacerbations and mortality risk although confidence intervals were wide.
- These disparities have been consistently reported worldwide, including within countries offering universally funded healthcare systems.

Keywords: asthma, socioeconomic status, disparities, inequalities

82 Abbreviations:

- 83 ACT: American College Testing
- 84 BMI: Body Mass Index
- 85 DAG: Directed acyclic graph
- 86 ED: Emergency department
- 87 CI: Confidence interval
- 88 COVID-19: Coronavirus disease
- 89 EA: Enumeration area
- 90 HMO: Health maintenance organization
- 91 ICS: Inhaled corticosteroids
- 92 IQR: Inter quartile range
- 93 OCS: Oral corticosteroids
- 94 OR: Odds ratio
- 95 SES: Socio-economic status
- 96 ZSDS: Zung Self-Rating Depression Scale

Introduction

Asthma is a highly prevalent chronic condition affecting 3.6% of the global population ^[1]. It is neither curable nor preventable, with the economic burden of the disease primarily attributed to lifelong management of the condition, disease severity, emergency treatment following exacerbations, and indirect societal costs. It is estimated that the cost of asthma exceeds \$80 billion annually in the U.S.A ^[2] and \$1.5 billion annually in the U.K. ^[3], with severe asthma patients contributing disproportionately to these costs. Exacerbations are common in all severities of asthma ^[4] and are associated with short-term suffering and long-term functional decline ^[5].

Deprived communities are known to suffer increased morbidity across several chronic disease areas including respiratory and cardiovascular diseases ^[6-8]. In asthma, a broad literature has previously demonstrated poorer healthcare outcomes among deprived communities within Europe and the U.S.A. ^[9, 10], and investigation into the interaction between socioeconomic factors and asthma has recently been highlighted as a key research priority ^[11]. Several mechanisms have been proposed as potential contributors to socioeconomic disparities in asthma including higher smoking rates, poor housing conditions and less effective self-management. Studies have previously linked lower socio-economic status (SES) to inadequate health literacy ^[12, 13], which could mediate the relationship with poor asthma outcomes through lower levels of asthma control ^[14], increased emergency department (ED) utilization ^[15], improper inhaler technique ^[16], and poor adherence to medications ^[17].

Whilst several studies have previously investigated the effect of SES on asthma healthcare outcomes, these have been heterogeneous in their study populations, countries, healthcare systems and methodologies. This review systematically brings together the relevant evidence-

122 base, providing an overview of the impact of SES on asthma healthcare utilization,
123 exacerbations and mortality across a variety of exposures and populations. It also explores
124 heterogeneity between studies in an effort to identify specific populations where disparities are
125 largest, and interventions might be prioritized.

Methods

2.1 Protocol and registration

A detailed protocol for this review was developed in conjunction with the search strategy and subsequently registered with the International Prospective Register of Systematic Reviews (PROSPERO; www.crd.york.ac.uk/prospero/, reference CRD42020173544), prior to data extraction.

2.2 Search strategy and study selection

Searches were conducted in Web of Science, Embase and Medline from inception to November 2019 (Figure E1). Our search included terms for asthma, those related to SES including income, poverty, education, employment status and healthcare insurance coverage. Our specific outcomes of interest were primary care attendance, exacerbations, ED attendance, hospitalization, ventilation / intubation, hospital readmission, and asthma mortality. Studies were eligible if they were reported in English language peer-reviewed journals and all participants had either self- or clinician-diagnosed asthma. We excluded ecological studies as these are open to the ecological fallacy^[18]. Title and abstract screening were conducted in duplicate by two independent reviewers (CR and AA). Decisions from both reviewers were compared, with any disagreements resolved through consensus, or referred to the third independent reviewer (JB).

2.3 Data extraction and quality assessment

Data extraction was performed independently and in duplicate by two reviewers (CR and AA) using a bespoke data extraction form (Table E1). Data extracted included study location, data collection period and setting, sample size, and study population demographic characteristics.

Study quality was assessed using an adapted version of the Newcastle Ottawa Scale for case-control, cohort and cross-sectional studies^[19, 20]. Studies were scored across three domains: selection of participants, comparability, and ascertainment or assessment of the exposure and outcome. Domain scores were totaled, and each exposure-outcome pairing was awarded an overall quality rating (poor, fair, good).

2.4 Data synthesis and statistical methods

Crude and adjusted odds ratios (with 95% confidence intervals) were extracted from each study. Only one estimate from each study was presented in a meta-analysis to preserve statistical independence. To achieve this we applied a hierarchy of exposures: SES, insurance coverage and education/employment status. Therefore, in a study reporting differences by both SES and insurance coverage, only the SES estimate was displayed. For all studies, estimates reflect the comparison between the highest and lowest SES group (Table E2). Our approach of combining data on multiple facets of SES, and of comparing the lowest vs. highest SES groups has been widely implemented in other reviews including of childhood inflammation, chronic kidney disease, adiposity and dental caries^[21-24].

Meta-analyses were conducted using DerSimonian-Laird random-effects models with the statistical heterogeneity evaluated using the I^2 statistic^[25] and interpreted using the thresholds defined by the Cochrane Handbook^[26]. Hazard ratios and relative risks were treated as odds ratios to facilitate the pooling of estimates. We conducted sensitivity analysis restricting our analysis to studies deemed good quality and investigated if any single study was having substantial influence on our pooled estimates using a 'leave-one-out' analysis. Additionally, we performed several pre-specified subgroup analyses to investigate heterogeneity including by specific exposure (SES, education/employment status, insurance coverage), healthcare

172 financing (public vs. private), patient age (pediatric vs. adult), study timeframe (pre- vs. post-
173 2010), and data collection setting. The association between pooled effect estimates (by country)
174 and their corresponding Gini coefficients were tested using Spearman's rank correlation for
175 studies with evidence from at least five countries. The Gini coefficient is a commonly used
176 measure of relative inequality with a higher number representing a greater degree of income
177 inequality ^[27]. Publication bias was considered for each meta-analysis with at least 10 studies
178 ^[28], through visual inspection of funnel plots and the application of Egger's tests. Data analysis
179 was performed in STATA (version 14) ^[29].

Results

Our electronic search returned 8,559 records after removal of duplicates (Figure 1). Full texts were retrieved for 288 records, with 227 excluded due to not reporting a relevant outcome/exposure (n=160, 44%), including non-asthmatics (n=59, 26%), or not being published in English (n=8, 4%). This left 61 studies, comprising 1,145,704 patients, meeting the inclusion criteria. Two studies presented only narrative results [30, 31], meaning that 59 studies were included in the meta-analysis.

3.1 Quality assessment and small study effects

Overall, 41 (35%) of the estimates extracted during the study were rated as good quality, one (1%) as fair and 75 (64%) as poor (Table E3). The primary reason for a 'poor' rating was lack of adjustment for at least age and sex, which occurred in all 75 of the poor-quality estimates. Within the cohort studies, we also observed potential issues with outcome ascertainment due to patient self-report (n=28, 37%), while in cross-sectional studies there was frequently a lack of detail on non-responders (n=26, 81%). In general, studies varied substantially in the level of case-mix adjustment. Of those that performed some case-mix adjustment, most (68%) adjusted for age and sex while several others accounted for additional factors including ethnicity/race (34%) or lifestyle factors (23%) (Table E4). There was no evidence of small study effects for ED visits ($p=0.698$) or readmission ($p=0.621$), although some asymmetry was noted for hospitalizations ($p=0.012$) (Figures E2 to E4).

3.2 Study characteristics

The majority of studies were from the U.S.A. (n=40, 66%), with Canada (n=5), U.K. (n=4) and Australia (n=3) the only other countries contributing more than one study (Table 1). Single studies were included from each of Brazil, China, Colombia, France, Poland, Saudi Arabia,

South Africa, Sweden, and Thailand. The median number of participants was 804 (IQR: 251, 2919) although this ranged from 60 in a Canadian study^[32], to 760,418 in a study exploring in-hospital mortality within the USA^[33]. The median age of study populations was 27.9 years (IQR: 7.9, 40.8), with 22 reporting on pediatric patients only. Studies were conducted in a variety of settings, with general population surveys (n=15; 25%), hospitalization records (n=14; 23%) and ED records (n=9; 15%) most common. Thirty (49%) studies reported differences by SES, 26 (43%) by employment or education, and 29 (48%) by insurance status. The most frequently reported outcomes were ED visits (n=25; 41%), hospitalization (n=22; 36%), and hospital readmission (n=10; 16%). Fewer studies investigated differences in exacerbations (n=7; 11%), ventilation / intubation (n=7; 11%), mortality (n=5; 8%) and primary care attendance (n=5; 8%).

3.3 The effect of SES on healthcare utilization

There was no clear evidence of differences in primary care attendances among SES groups (OR: 0.79; 95% CI: 0.51, 1.24; $I^2=95.1\%$) (Table 2, Figure E5). However, lower levels of SES were consistently associated with increased asthma secondary healthcare utilization (Table 2). The odds of ED attendance were increased by 1.61 (95% CI 1.40, 1.84) among the lowest SES group when compared to the highest (Figure 2). Findings of higher ED attendances were consistent across 88% of individual studies, however substantial heterogeneity existed ($I^2=83.1$), with the largest estimate from a Saudi-Arabian study which reported 50% of patients in the lowest SES group attended ED compared to only 7.6% in the highest SES group (OR: 9.0; 95% CI: 3.0, 26)^[34]. The odds of hospitalization (OR: 1.63; 95% CI: 1.34, 1.99; $I^2=78.4\%$) (Figure 3) were also elevated among the lowest SES groups, as were the odds of ventilation / intubation (OR: 1.76; 95% CI: 1.13, 2.73; $I^2=82.5\%$) (Figure E6), although there was

substantial heterogeneity between studies in both cases. Again, there was consistent evidence of higher utilization in the lowest SES groups for readmission (OR: 1.31; 95% CI: 1.19, 1.44; $I^2=45.3\%$) (Figure 4), although the magnitude of this differed between studies.

3.4 The effect of SES on asthma exacerbations and mortality

Fewer studies investigated the association between SES and asthma exacerbations or mortality (Table 2). There was evidence suggestive of increased exacerbation rates (OR: 1.18; 95% CI: 0.98, 1.42; $I^2=70.8\%$) (Figure E7) and mortality (OR: 1.12; 95% CI: 0.92, 1.37; $I^2=64.2\%$) (Figure E8) among the lowest SES group when compared to the highest, although confidence intervals were wide. Of the studies investigating mortality, 4 (80%) reported an increased risk of death associated with lower SES, with the largest effect estimate reported by an Australian study (OR: 1.94; 95% CI: 0.70, 5.38)^[35]. Conversely, one large study from the U.S.A. reported slightly reduced in-hospital mortality among patients residing in the poorest quartile of areas (OR: 0.94; 95% CI: 0.84, 1.05)^[33].

3.5 Sensitivity and Subgroup Analysis

Our overall conclusions were unchanged in sensitivity analysis when restricted to studies deemed good quality (Table 2). The pooled estimate for hospitalizations was substantially attenuated for good quality studies (OR: 1.19; 95% CI: 1.06, 1.34; $I^2=0\%$), although a moderate attenuation was also observed for other outcomes including ED attendances and readmissions. Importantly, we found little evidence of heterogeneity among studies investigating differences in ED attendances, hospital admissions and readmissions when restricting to good quality studies despite substantial heterogeneity in the unrestricted analyses (Table 2). The finding of marginally higher exacerbations and mortality among the lowest SES group remained when

restricting to good quality studies (Table 2). Of note, none of the seven studies investigating differences in ventilation / intubation were deemed good quality. The leave-one-out analysis demonstrated that no single study had undue influence on our pooled estimate, although significantly increased exacerbations (OR: 1.24; 95% CI: 1.05, 1.46) and mortality (OR: 1.24; 95% CI: 1.07, 1.44) were observed among the lowest SES group when leaving out the study with the lowest estimated effect (Table E5).

There was little evidence of differential effects by exposure type, with relatively consistent pooled estimates observed when separately combining studies investigating differences in SES, employment/education and insurance status, although heterogeneity was reduced in some cases (Figures 2 to 4 & E5 to E8). There was some inconsistent evidence of a temporal reduction in SES disparities in our review, with a notable reduction observed among studies conducted post-2010 compared to pre-2010 for hospitalizations (1.33 vs 1.85, $p<0.001$) (Table 3, Table E6). Although the estimated SES effect was slightly reduced among pediatric studies for ED visits (1.54 vs 1.69, $p<0.001$), it was elevated for readmissions (1.37 vs 0.99, $p=0.027$).

Of note, there was no compelling evidence that SES disparities were elevated in countries with an insurance-based healthcare system when compared to those with a universal government funded system, although a moderate increase in disparities was observed for hospital readmissions (1.35 vs. 1.00, $p=0.023$) (Table 3). We were unable to assess the correlation between SES disparities and the Gini coefficient for most outcomes due to studies being set within a limited pool of countries; however, we did not find any evidence of an association for hospitalizations ($\rho=0.00$, $p=1.000$) (Figure E9).

Discussion

This systematic review and meta-analysis investigating the effect of SES on asthma healthcare utilization, exacerbations and mortality found that patients with a lower SES had substantially increased secondary healthcare utilization, with evidence suggestive of increased risk of exacerbations and mortality. There was substantial heterogeneity in our estimates, however this was largely negated when restricting to high-quality studies. There was inconsistent evidence of a reduction in SES disparities over time, but notably there was no convincing evidence of a difference between countries with a universally funded healthcare system compared to those based on private insurance coverage.

We did not investigate the drivers of SES disparities, however several mechanisms are possible that could lead to poorer asthma control and health outcomes among more deprived groups. Previous studies have shown poor adherence to maintenance medications among lower SES groups^[36-38], which has been prospectively linked with increased asthma morbidity and health care utilization^[17]. Worse living conditions among more deprived communities may also play an important role possibly due to increased aeroallergen exposure^[39, 40]. Lifestyle factors also contribute to the development and severity of asthma symptoms experienced, with smoking^[41] and obesity^[42] more prevalent among deprived populations^[43]. Our findings that wide socioeconomic disparities in secondary healthcare utilization persist despite only moderate differences in exacerbations, and no evidence of increased primary care attendances, suggests that differences in healthcare seeking behavior may be an important factor. Others have noted an increased propensity for patients from more deprived areas to favor emergency care^[44-46], which could be related to lower levels of health literacy within this patient group^[47-49], or a perception of higher-quality and more accessible care within hospitals⁽⁵⁰⁾. However, the root of socioeconomic inequalities remains uncertain, and solutions are unlikely to be straightforward.

299

300 Few interventions aiming to improve medication adherence have been shown to be cost-
301 effective despite this being frequently suggested as a potential lever to tackle inequalities ^[51].
302 A nascent literature exploring interventions to improve health literacy has demonstrated their
303 promise as a means to reduce disparities, however, further consideration of the costs of
304 providing these interventions, and an exploration on their impact on healthcare outcomes is
305 required ^[52]. Other issues such as poorer housing conditions are likely to require far-reaching
306 and costly public health interventions to resolve. Recent evidence from the U.S.A. suggests
307 that the childhood SES status of a parent had an effect on their children's asthma outcomes
308 independent of their current economic circumstances ^[53], suggesting that the time-scales
309 required to fully address inequalities are likely to be generational. There is clearly scope and
310 opportunity for novel interventions, with an established literature supporting the possible
311 components of an integrated intervention, such as Episodic Future Thinking ^[54] and framing
312 and commitment devices ^[55]. However, public health practitioners trying to improve the
313 outcomes for people with a chronic disease like asthma must also recognize that upstream
314 determinants such poverty and disadvantage also affect behavioral economic traits and
315 decision-making agency. Thus "personalized prevention" must be balanced with whole
316 population approaches to mitigate increasing inequalities ^[56].

317

318 There was some inconsistent evidence that SES disparities may have decreased over time
319 although understanding the causes of this is difficult due to the complex landscape of multiple
320 intertwining public health interventions acting in each country at any time. This finding should
321 be interpreted with caution as it is open to temporal confounding due to changes in
322 methodology and study populations, particularly as other studies have reported widening SES
323 disparities in mortality over time ^[57, 58]. It was perhaps surprising that SES disparities were

similar within the U.S.A. healthcare system, which is often criticized for entrenching inequality^[59], and other countries such as the U.K. and Canada which offer universal healthcare systems to all residents regardless of ability to pay. Typically, financial barriers to accessing healthcare for chronic conditions are perceived as an obvious mechanism for worse outcomes^[60, 61]. However, our findings may suggest that the provision of chronic disease management, mediated through acute healthcare contacts and the organizational integration of the healthcare system itself^[62, 63], may be a more important driver of disparities^[64]. It is also recognized that even in universal healthcare systems, poor engagement with healthcare systems and lack of adherence with treatment is common across lower SES groups^[65], suggesting that the mechanisms for worse outcomes are not simply economic, but also incorporate the influence of social and cultural factors^[64].

We found that the studies included within our review took a varying approach to statistical adjustment, which made it difficult to compare their results. Some studies eschewed any adjustment which could lead to spurious SES differences driven by unmodifiable factors such as variation in age or sex. Conversely, other studies adjusted for a broad range of covariates such as asthma severity, smoking status and medication adherence which could plausibly lie on the causal pathway between SES and asthma outcomes. Adjusting for these factors could lead to over-adjustment bias and serve to conceal important inequalities^[66]. Future studies should carefully consider their analytical strategy and ensure their statistical models are based upon a robust conceptual framework^[67] separating potential confounders and mediators of the direct SES effect. Recently Jackson has provided an elegant framework for this and highlighted the need to distinguish between ‘allowable’ (essentially those related to need) and ‘non-allowable’ factors (those perceived to be unjust determinants of outcomes) within a plausible directed acyclic graph (DAG)^[68].

349

350 The main strength of this review was in summarizing a diverse literature of primary research
351 investigating the effect of SES on asthma healthcare utilization and healthcare outcomes, which
352 provides an at-a-glance overview for policymakers, clinicians and researchers. We
353 implemented a broad search strategy and included studies, which investigated proxies of SES
354 such as employment/education and insurance status. Pooled estimates for all three domains of
355 SES were similar, suggesting that combining these exposures was a valid approach, although
356 the suitability of such proxies has been questioned elsewhere ^[69]. Our review also facilitated a
357 novel investigation of SES disparities over time and between patient subgroups, which was not
358 undertaken in any single study previously.

359

360 We also acknowledge several potential weaknesses in our study. We did not aim to capture
361 data on potential pathways to healthcare utilization, in particular medication prescribing and
362 adherence data, or the effect of health literacy in mediating the relationship between SES and
363 health disparities, as other reviews have previously investigated the effect of SES in these areas
364 ^[49, 51]. In concordance with similar reviews investigating SES disparities ^[65, 70], there was
365 substantial heterogeneity in our primary analysis which could be related to differences in
366 outcome classification, exposure definition, methodology (e.g. type of effect estimate) or study
367 definition and may hinder the interpretability of our results. However, this was largely
368 mitigated when restricting to high-quality studies and our overall conclusions of increased
369 secondary healthcare utilization among low SES groups was unchanged. The majority of the
370 studies included in this review were based in the U.S.A. which may limit the external validity
371 of our findings. We believe that this is an important finding in itself and may suggest a lack of
372 research into the magnitude and drivers of asthma SES disparities within many countries. This
373 is particularly important as our results indicate that SES disparities in asthma healthcare

outcomes are far from a solely U.S.A.-based phenomenon. For pragmatic reasons we limited our search to English language studies, it is possible that eligible studies published in other languages were excluded. Similarly, our finding of potential small-study effects among the studies investigating disparities in hospitalizations could possibly suggest publication bias.

In conclusion, patients with a lower SES have substantially increased asthma healthcare utilization, with evidence suggestive of increased exacerbations and mortality. These socioeconomic disparities have been consistently reported worldwide, including within countries offering universally funded healthcare systems, and are entrenched over several decades. Further research is required to understand the mechanisms underlying these disparities.

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720 **Tables**721 **Table 1 - Summary characteristics of studies included in review.**

Study Name (Year)	Country	Participants	Mean Age, years (SD)	% Male	Clinical Setting	Exposure	Outcome
Davidson (1994) ^[71]	USA	170	7.4 (NR)	62	ED Rec	Ins	ED, Hosp
Stoddard (1994) ^[72]	USA	667	NR	NR	Gen Pop	SES, Ins	PC
Leson (1995a) ^[73]	USA	300	7.7 (2.4)	55	Hosp Rec	SES, Emp/Edu	Int
Leson (1995b) ^[74]	USA	143	16.4 (2.3)	52	Hosp Rec	SES, Emp/Edu	Int
LeSon (1995c) ^[75]	USA	375	40.8 (13.5)	35	Hosp Rec	SES, Emp/Edu	Int
Boulet (1996) ^[32]	Canada	60	40.5 (20)	53	ED Rec	SES, Emp/Edu	ED
LeSon (1996) ^[76]	USA	550	27.9 (4.2)	36	Hosp Rec	SES, Emp/Edu	Int
Mowat (1998) ^[77]	UK	1,504	NR	NR	Gen Prac	SES	ED, Hosp, PC
Adams (2000) ^[78]	Australia	293	42.0 (18.0)	33	Sec Care	Emp/Edu	ED, Hosp
Finkelstein (2000) ^[79]	USA	12,935	7.5 (4.9)	57	Sec Care	Ins	ED, Hosp
Stanford (2000) ^[80]	USA	2,738	41.0 (11.0)	30	ED Rec	Ins	Hosp
Bair (2001) ^[81]	USA	478	46.2 (NR)	26	Gen Prac	Emp/Edu, Ins	ED
Eisner (2001) ^[82]	USA	242	40.5 (7.3)	27	Gen Prac	SES, Emp/Edu	Hosp
Ferris (2001) ^[83]	USA	965	7.9 (4.1)	60	ED Rec	Ins	Hosp, Int
Ortega (2001) ^[84]	USA	804	5.3 (2.5)	63	Gen Pop	Ins	ED, Hosp
Al-Dawood (2002) ^[34]	Saudi Arabia	141	10.7 (3.1)	100	Gen Pop	SES	ED
Amre (2002) ^[85]	Canada	404	NR	56	ED Rec	Emp/Edu	ED, Hosp, PC
Bloomberg (2003) ^[86]	USA	8,761	NR	63	Hosp Rec	Ins	ReAd
Spurrier (2003) ^[87]	Australia	135	4.9 (3.0)	NR	ED Rec	Emp/Edu	ED
Ather (2004) ^[88]	USA	15,864	NR	29	Hosp Rec	Ins	ReAd
Chen (2004) ^[89]	Canada	8,333	NR	30	Hosp Rec	SES	ReAd

Pesola (2004) ^[90]	USA	237	40.4 (13.2)	38	ED Rec	Emp/Edu, Ins	ED, Hosp
Barton (2005) ^[35]	Australia	251	NR	NR	Other	Emp/Edu	Mort
Grant (2005) ^[91]	USA	152	NR	38	Gen Pop	SES, Emp/Edu	ED, Hosp
Lasmar (2006) ^[92]	Brazil	202	NR	67	Sec Care	SES, Emp/Edu	ReAd
Meng (2006) ^[93]	USA	4,359	NR	39	Gen Pop	SES, Emp/Edu, Ins	ED
Van der Merwe (2006) ^[94]	South Africa	90	30.9 (12.3)	32	Sec Care	SES	Hosp
DeWalt (2007) ^[95]	USA	150	7.7 (2.8)	NR	Sec Care	SES, Emp/Edu	ED, Hosp
Forbes (2007) ^[96]	UK	921	NR	63	Gen Prac	SES	ED
Wainwright (2007) ^[31]	UK	1,674	NR	40	Gen Prac	SES	Hosp
Horner (2008) ^[97]	USA	183	8.8 (1.2)	59	Gen Pop	SES, Ins	ED, Hosp
Peters (2008) ^[98]	USA	1,315	46.2 (12.7)	30	Ter Care	Ins	ED, Hosp
To (2008) ^[99]	Canada	269	NR	60	ED Rec	SES	ED, Ex
Kim (2009) ^[100]	USA	982	NR	64	Gen Pop	SES, Emp/Edu, Ins	ED
Liu (2009) ^[101]	USA	2,919	NR	60	Hosp Rec	Ins	ReAd
Wright (2009) ^[102]	USA	1,313	NR	62	Gen Pop	Ins	ED
Carroll (2010) ^[103]	USA	306	8.1 (4.3)	58	Hosp Rec	Ins	ReAd
Piper (2010) ^[104]	USA	1,630	NR	61	Gen Pop	SES, Ins	PC
Lutfiyya (2011) ^[105]	USA	30,323	NR	35	Gen Pop	SES	ED, Ex, PC
Zejda (2012) ^[106]	Poland	186	11.1 (2.2)	62	Gen Pop	Emp/Edu	Hosp
Auger (2013) ^[107]	USA	601	NR	64	Hosp Rec	SES, Emp/Edu, Ins	ReAd
Roberts (2013) ^[108]	UK	116,457	46.0 (18.0)	35	Hosp Rec	SES	Mort
Rodriguez-Martinez (2013) ^[109]	Colombia	101	NR	60	Sec Care	Emp/Edu	ReAd
Chang (2014) ^[110]	USA	11,027	8.2 (6.9)	43	Ins	Ins	ED, Hosp
Kenyon (2014) ^[111]	USA	36,601	NR	61	Hosp Rec	Ins	ReAd
To (2014) ^[112]	Canada	NS	NR	NR	Ins	SES	Mort
Kaur (2015) ^[33]	USA	760,418	NR	33	Hosp Rec	SES, Ins	Int, Mort
Dilokthornsakul (2016) ^[113]	Thailand	1,982	40.3 (24.0)	61	Sec Care	Ins	Hosp
Hasegawa (2016) ^[114]	USA	1,928	NR	41	ED Rec	Ins	ED, Hosp, Int
Yan (2016) ^[115]	China	1,546	55.8 (16.8)	41	Hosp Rec	SES, Emp/Edu	Ex
Backman (2017) ^[10]	Sweden	2,055	45.4 (NR)	45	Other	Emp/Edu	Mort

Denlinger (2017) ^[30]	USA	709	NR	41	Other	SES, Emp/Edu	Ex
Xie (2017) ^[116]	USA	27,604	NR	27	Sec Care	Ins	Ex
Zhang (2017) ^[117]	USA	5,535	NR	57	Gen Pop	SES, Emp/Edu	ED
Grunwell (2018) ^[118]	USA	579	NR	58	Sec Care	SES, Emp/Edu	Hosp, Int
Mazalovic (2018) ^[119]	France	255	29.6 (6.9)	43	Gen Prac	SES, Emp/Edu	Ex, Hosp
Gushue (2019) ^[120]	USA	854	NR	NR	Gen Pop	Emp/Edu, Ins	Ex
Jroundi (2019) ^[9]	USA	66,835	6.5 (4.1)	61	Hosp Rec	SES, Ins	ReAd
Seibert (2019) ^[121]	USA	342	30.9 (6.1)	22	Gen Pop	SES	ED, Hosp
Shechter (2019) ^[122]	USA	200	NR	61	Other	Ins	ED
Sullivan (2019) ^[123]	USA	6,751	11.5 (NR)	59	Gen Pop	SES, Emp/Edu, Ins	Ex

722

723 Abbreviations: ED (ED Visit), Ex (Exacerbation), Hosp (Hospitalization), Mort (Mortality), PC (Primary Care Attendance), ReAd

724 (Readmission), Int (Ventilation / Intubation), SES (Socioeconomic status), Emp (Employment), Edu (Education), Ins (Insurance), ED Rec (ED

725 Records), Gen Pop (General Population), Gen Prac (General Practice), Hosp Rec (Hospitalization Records), Ins (Insurance Database), Sec Care

726 (Secondary Care), Ter Care (Tertiary Care), NR (not reported), NS (not specified)

727 **Table 2 – Pooled effect of SES on asthma healthcare utilization**

Outcome	All Studies			Good Quality		
	N	OR (95% CI's)	I ²	N	OR (95% CI's)	I ²
Health Care Utilization						
Primary Care Attendance	5	0.79 (0.51, 1.24)	95.1	2	0.96 (0.61, 1.51)	25.7
ED Visit	25	1.61 (1.40, 1.84)	83.1	10	1.41 (1.29, 1.54)	0.0
Hospitalization	22	1.63 (1.34, 1.99)	78.4	6	1.19 (1.06, 1.34)	0.0
Ventilation / Intubation	7	1.76 (1.13, 2.73)	82.5			
Readmission	10	1.31 (1.19, 1.44)	45.3	4	1.29 (1.22, 1.36)	0.0
Exacerbations and Mortality						
Exacerbations	7	1.18 (0.98, 1.42)	70.8	3	1.05 (0.72, 1.53)	58.7
Mortality	5	1.12 (0.92, 1.37)	64.2	3	1.10 (0.88, 1.39)	79.3

728

729 **Table 3 - Additional Subgroup Analysis**

Subgroup	ED Visit				Hospitalization				Readmission			
	N	OR (95% CI's)	I ²	p	N	OR (95% CI's)	I ²	p	N	OR (95% CI's)	I ²	p
Age				<0.001				0.133				0.027
Adult	7	1.69 (1.32, 2.15)	93.5		7	1.59 (1.11, 2.28)	90.4		2	0.99 (0.79, 1.24)	0.0	
Pediatric	13	1.54 (1.25, 1.90)	53.4		9	1.66 (1.24, 2.23)	62.0		6	1.37 (1.16, 1.63)	27.8	
Time period				0.008				<0.001				0.515
Pre-2010	19	1.63 (1.33, 2.00)	69.8		15	1.85 (1.40, 2.43)	74.6		5	1.27 (1.04, 1.55)	57.9	
Post-2010	6	1.55 (1.20, 2.01)	93.4		7	1.33 (1.03, 1.73)	77.1		5	1.31 (1.18, 1.45)	38.8	
Healthcare System				0.185				0.301				0.023
Insurance based	17	1.63 (1.40, 1.90)	87.0		17	1.57 (1.27, 1.95)	79.9		7	1.35 (1.24, 1.47)	42.7	
Universal Government Funded	8	1.56 (1.03, 2.39)	60.7		5	2.10 (1.15, 3.83)	75.7		3	1.00 (0.78, 1.26)	0.0	
Data Collection Setting				0.973				<0.001				NA
General Population	15	1.56 (1.32, 1.84)	88.1		10	1.50 (1.16, 1.96)	74.7					
Secondary / Tertiary Care	10	1.69 (1.24, 2.31)	63.0		12	1.70 (1.29, 2.25)	74.6		10	1.31 (1.19, 1.44)	45.3	

730

Figure Legends

Figure 1: PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

*Studies were excluded at this stage for several reasons (not all participants had asthma, a relevant outcome/exposure was not reported, the data was not grouped into relevant comparison categories in the analysis and the full article was not published in English.

Figure 2: Forest Plot of odds ratios for asthma related ED Visits, sub grouped by exposure type

Figure 3: Forest Plot of odds ratios for asthma related hospitalization, sub grouped by exposure type

Figure 4: Forest Plot of odds ratios for asthma related readmission, sub grouped by exposure type

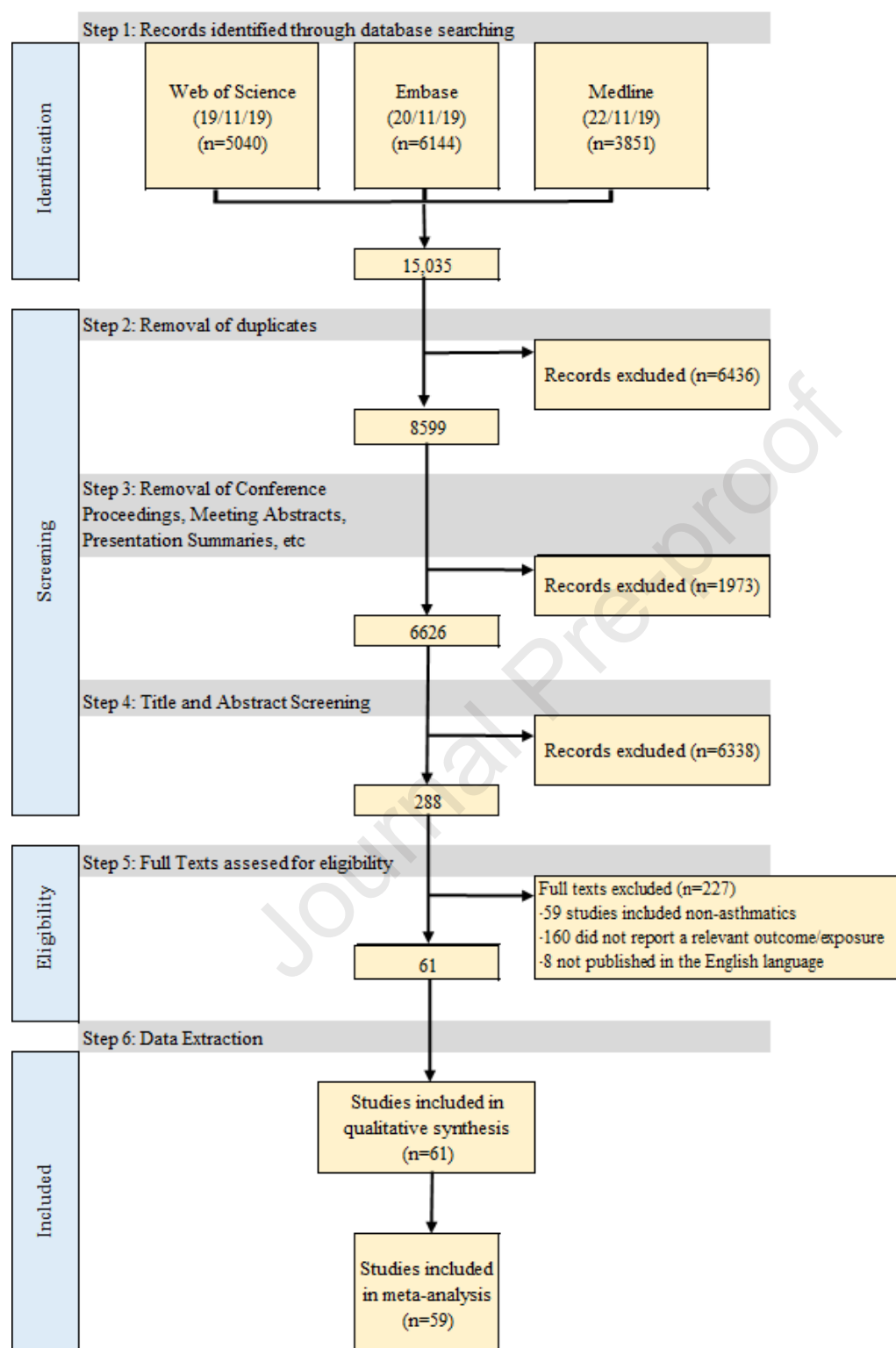


Figure 1

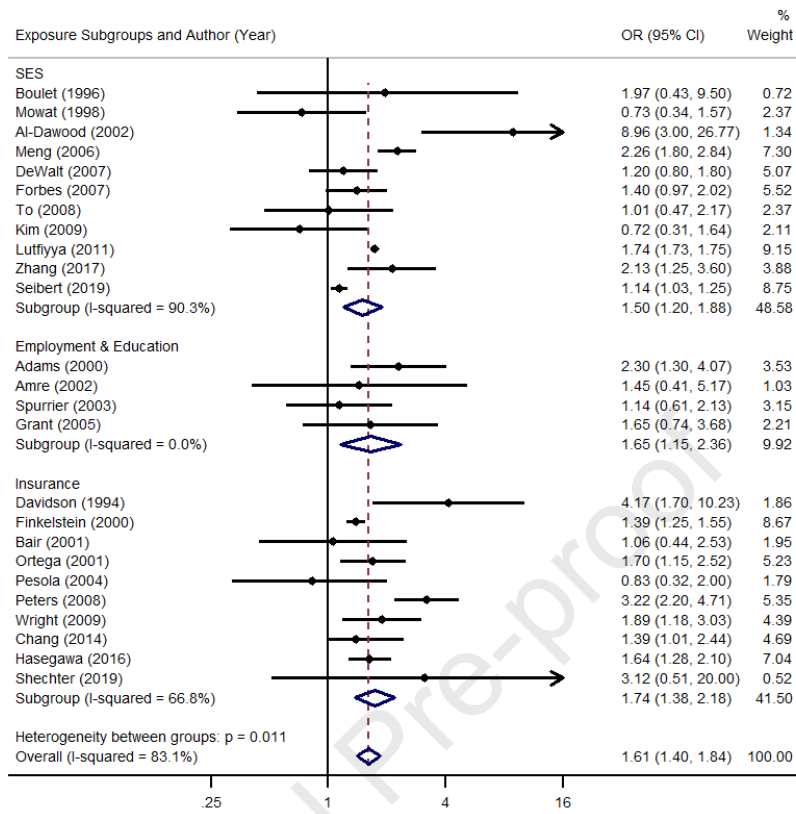


Figure 2

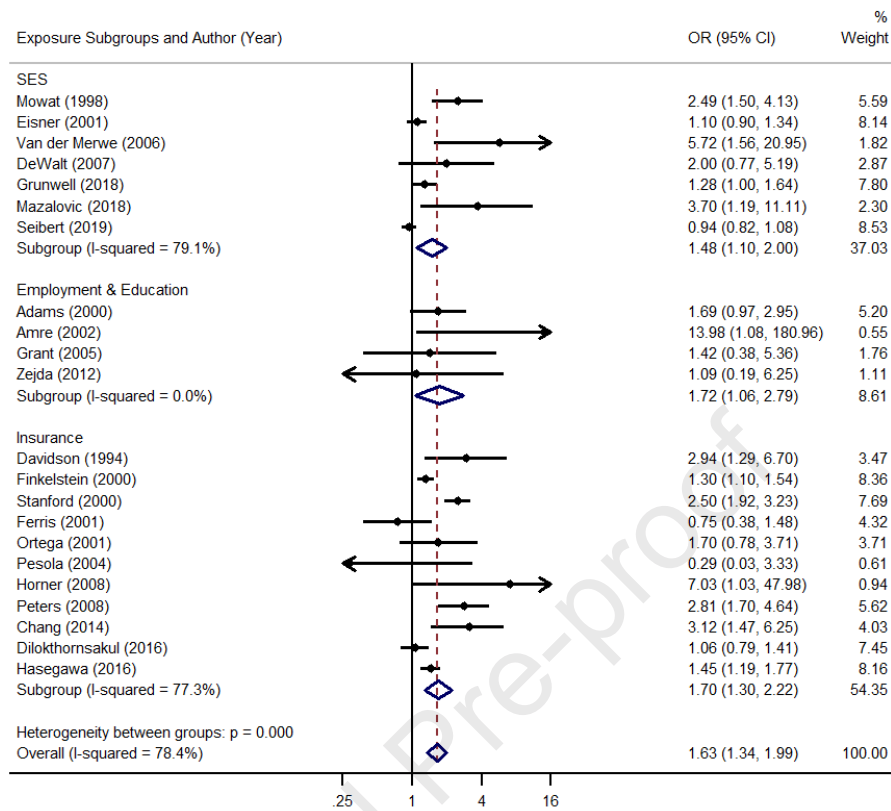


Figure 3

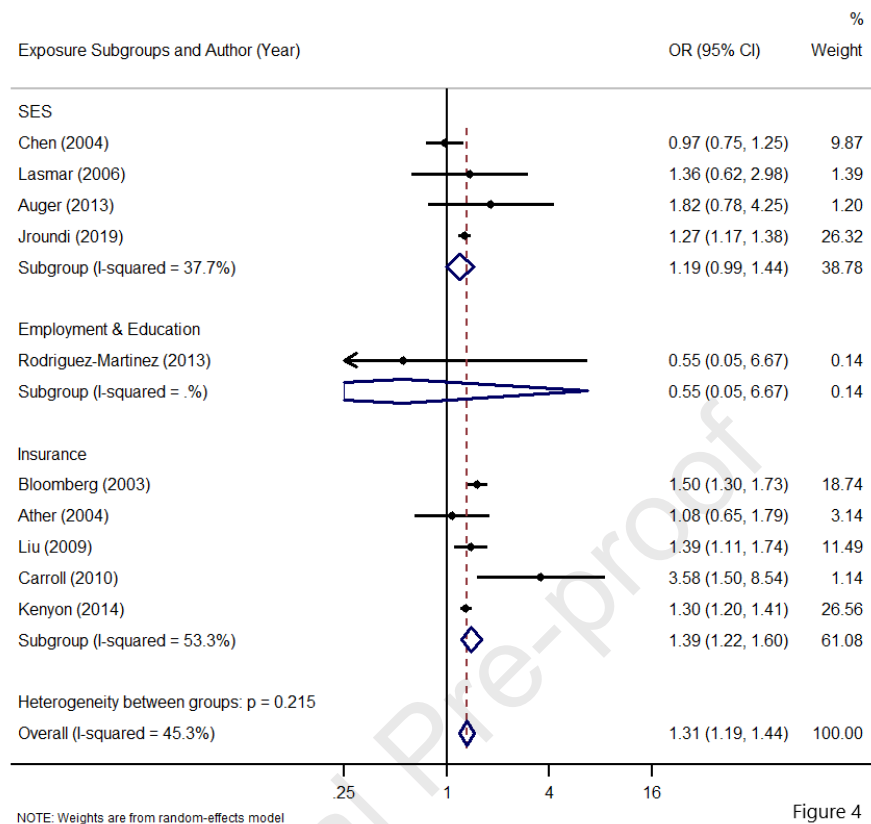


Figure 4

Online Repository

Title: Socioeconomic disparities in asthma healthcare utilization, exacerbations and mortality: A systematic review and meta-analysis

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20 **Figure E1: Search terms used in the Web of Science database**

21 *Identical terms were used to search the Embase and Medline databases.*

TS= (asthma)

AND

TS= (socioeconomic* OR sociodemographic OR SES OR psychosocial OR income OR salary OR poverty OR *employ* OR "social class" OR disadvantage* OR depriv* OR insur* OR "managed care")

AND

TS= (mortality OR death* OR morbidity OR exacerbat* OR vent* OR "emergency department" OR ED OR (accident near/2 emergency) OR A&E OR readmission* OR hospitali?ation OR admission* OR "primary care" OR GP OR "general pract*" OR *attend* or consult* or utili*)

22

23 **Table E1: List of data fields collected during data extraction.**

Study details	Categorical variable options
Country	
Sample size	
Cohort description	
Data collection setting	General practice, hospitalization records, ED records, secondary care, tertiary care, insurance database, general population, other
Data collection period	
Study design	Case control, cohort, cross-sectional
Mean Age (SD/SE)	
Age range	
Percentage males	
ICS (%)	
OCS (%)	
Severe asthma (%)	
Asthma severity of group	Not disclosed, mild, moderate, severe, other
FEV1 average	

Study comparison data	Categorical variable options
Exposure	SES, income, poverty, employment, occupation, education, social class, deprivation, insurance
How groups were compared (e.g. low income vs high income)	
Reference group summary	
Estimate group summary	
For continuous exposures what an increase in 1 unit represents	
Outcome	Mortality, exacerbations, ventilation / intubation, ED visit, hospitalization, readmission, primary care attendance
Statistical method used	Odds ratio, risk ratio, hazard ratio, chi squared
How the outcomes were compared (e.g. odds of hospital admission vs not)	
Estimate	
Lower CI	
Upper CI	
Confidence level (%)	
P value	
Standard error	
Are estimates adjusted?	Yes, no
Variables adjusted for	
Were estimates calculated manually?	Yes, no
Outline how estimate was calculated	

25 **Table E2: Exposure comparison groups for each study included in the meta-analysis.**

First author (Publication Year)	Exposure	Comparison	Outcome
Davidson (1994)	Insurance	Medicaid vs private insurance	ED Visit
	Insurance	Medicaid vs private insurance	Hospitalization
Stoddard (1994)	Income	<100% poverty level vs $\geq$ 400% of the poverty level	Primary Care Attendance
	Insurance	Uninsured vs insured	Primary Care Attendance
LeSon (1995a)	Education	Little formal parental education vs assumed significant formal parental education	Ventilation / Intubation
	SES	Low SES vs assumed moderate/high SES	Ventilation / Intubation
LeSon (1995b)	Education	Little formal education vs assumed significant formal education	Ventilation / Intubation
	SES	Low SES vs assumed moderate/high SES	Ventilation / Intubation
LeSon (1995c)	Education	Little formal education vs assumed significant formal education	Ventilation / Intubation
	SES	Low SES vs assumed moderate/high SES	Ventilation / Intubation
Boulet (1996)	Income	Low vs high income	ED Visit
	Education	Primary vs University Education	ED Visit
	Employment	Unemployed vs employed	ED Visit
LeSon (1996)	Employment	Unemployed vs employed	Ventilation / Intubation
	SES	Low SES vs assumed high SES	Ventilation / Intubation
	Education	Little formal education vs assumed significant formal education	Ventilation / Intubation
Mowat (1998)	Deprivation	High vs low deprivation	ED Visit
	Deprivation	High vs low deprivation	Primary Care Attendance
	Deprivation	High vs low deprivation	Hospitalization
Adams (2000)	Employment	Unemployed vs employed	Hospitalization
	Employment	Unemployed vs employed	ED Visit
	Education	$\leq$ 10 years vs $>$ 10 years of education	Hospitalization
	Education	$\leq$ 10 years vs $>$ 10 years of education	ED Visit
Finkelstein (2000)	Insurance	Medicaid vs non-Medicaid (commercial payers)	Hospitalization
	Insurance	Medicaid vs non-Medicaid (commercial payers)	ED Visit
Stanford (2000)	Insurance	Indemnity vs managed care	Hospitalization
Bair (2001)	Education	Less than high school education vs graduate/professional education	ED Visit
	Insurance	Medicaid vs non-Medicaid	ED Visit
Eisner (2001)	Education	Educational attainment in years	Hospitalization
	Income	Household income per \$10,000 decrement	Hospitalization

Ferris (2001)	Insurance	Medicaid vs Indemnity	Hospitalization
	Insurance	Medicaid vs Indemnity	Ventilation / Intubation
Ortega (2001)	Insurance	Medicaid vs Private insurance	Hospitalization
	Insurance	Medicaid vs Private insurance	ED Visit
Al-Dawood (2002)	SES	Lower vs upper socioeconomic class	ED Visit
Amre (2002)	Occupation	Fathers Occupational Group 4 (Students and unemployed) vs 1 (Highest economic category)	ED Visit
	Occupation	Fathers Occupational Group 4 (Students and unemployed) vs 1 (Highest economic category)	Hospitalization
	Occupation	Fathers Occupational Group 4 (Students and unemployed) vs 1 (Highest economic category)	Primary Care Attendance
Bloomberg (2003)	Insurance	Medicaid or self-pay vs Commercial	Readmission
Spurrier (2003)	Education	Tertiary qualifications vs some years of high school	ED Visit
	Occupation	Parental occupational prestige score	ED Visit
Ather (2004)	Insurance	Medicaid vs indemnity	Readmission
Chen (2004)	Income	<\$15,000 vs \$30,000+ average personal income	Readmission
Pesola (2004)	Education	At least high school education vs less than high school education	ED Visit
	Education	At least high school education vs less than high school education	Hospitalization
	Insurance	Insured vs uninsured	ED Visit
	Insurance	Health insurance present vs absent	Hospitalization
	Employment	Employed vs unemployed	ED Visit
	Employment	Employed vs unemployed	Hospitalization
Barton (2005)	Employment	Unemployed vs employed	Mortality
Grant (2005)	Education	High school or less vs some college or more	Hospitalization
	Education	High school or less vs some college or more	ED Visit
Lasmar (2006)	Education	0-3 years educational level of mother vs >3 years	Readmission
	Income	Income ≤ 3 times the minimum wage vs > 3 times the minimum wage	Readmission
Meng (2006)	Income	Low vs high income	ED Visit
	Insurance	Medicaid/other public insurance vs employment based or private insurance	ED Visit
	Education	Less than high school vs College or greater	ED Visit
Van der Merwe (2006)	Income	No formal income vs formal income	Hospitalization
DeWalt (2007)	Income	Household annual income <\$15,000 vs ≥\$15,000	ED Visit
	Education	≤ 12th grade vs >12th grade	ED Visit
	Income	Household annual income <\$15,000 vs ≥\$15,000	Hospitalization
	Education	≤ 12th grade vs >12th grade	Hospitalization
Forbes (2007)	Deprivation	4th Quartile of Townsend deprivation score vs 1st	ED Visit
Horner (2008)	Insurance	Health insurance vs no insurance	Hospitalization

Peters (2008)	Insurance	Medicaid vs non-Medicaid	Hospitalization
	Insurance	Medicaid vs non-Medicaid	ED Visit
To (2008)	Income	Low SES vs (assumed) high SES	ED Visit
	Income	Low SES vs (assumed) high SES	Exacerbation
Kim (2009)	Insurance	Public vs private insurance	ED Visit
	Education	Low vs high education	ED Visit
	Income	family income <100% of the poverty line vs >= 400% of the poverty line	ED Visit
Liu (2009)	Insurance	Public vs private insurance	Readmission
Wright (2009)	Insurance	Employer based insurance vs not	ED Visit
Carroll (2010)	Insurance	Public vs private insurance	Readmission
Piper (2010)	Income	Income >\$20,000 vs <\$20,000	Primary Care Attendance
	Insurance	Public vs private insurance	Primary Care Attendance
Lutfiyya (2011)	SES	Low vs high SES	Primary Care Attendance
	SES	Low vs high SES	Exacerbation
	SES	Low vs high SES	ED Visit
Zejda (2012)	Education	Parental education high school or more vs less	Hospitalization
Auger (2013)	Insurance	Medicaid vs private	Readmission
	Education	Maternal education < high school vs >=4 years college degree	Readmission
	Income	Total annual household income <\$14,999 vs >\$90,000	Readmission
Roberts (2013)	Deprivation	Most vs least deprived	Mortality
Rodriguez-Martinez (2013)	Education	College, university or higher vs primary	Readmission
Chang (2014)	Insurance	Private insurance vs Medicaid	Hospitalization
	Insurance	Private insurance vs Medicaid	ED Visit
Kenyon (2014)	Insurance	Public vs private insurance	Readmission
To (2014)	Deprivation	Most vs least deprived	Mortality
Kaur (2015)	Income	Lowest vs highest median household income quartile	Ventilation / Intubation
	Income	Highest vs lowest income quartile	Mortality
	Insurance	Medicare/Medicaid vs Private	Ventilation / Intubation
	Insurance	Private including HMO vs Medicare/Medicaid	Mortality
Dilokthornsakul (2016)	Insurance	Civil Servant Medical Benefit Scheme(CSMBS) vs Universal Coverage Scheme(UC scheme)	Hospitalization
Hasegawa (2016)	Insurance	Public vs private insurance	ED Visit
	Insurance	Public vs private insurance	Hospitalization
	Insurance	Public vs private insurance	Ventilation / Intubation

Yan (2016)	Education	Middle and lower school education level vs high school or university and higher	Exacerbation
	Income	Income lower vs higher than Per Capita Disposable income	Exacerbation
Backman (2017)	Occupation	Professionals and executives vs manual workers in service	Mortality
Xie (2017)	Insurance	Medicaid vs Private Insurance	Exacerbation
Zhang (2017)	Income	High vs low income	ED Visit
	Education	College graduate vs <= high school education	ED Visit
Grunwell (2018)	Poverty	Residing in a region with a higher vs lower percentage of residents having income below the poverty line	Hospitalization
Mazalovic (2018)	Education	Education higher than a bachelor's degree vs lower	Exacerbation
	Occupation	Skilled vs unskilled occupation	Exacerbation
	SES	Medium/High vs Low SES	Hospitalization
Gushue (2019)	Education	Higher education vs high school or less	Exacerbation
	Insurance	Continuous public vs continuous private insurance	Exacerbation
Jroundi (2019)	Income	First vs Forth quartile	Readmission
	Insurance	Medicaid vs private insurance	Readmission
Seibert (2019)	Income	Regression on income categories: <15k, 15-29,999, 30k-50k, >50k	Hospitalization
	Income	Regression on income categories: <15k, 15-29,999, 30k-50k, >50k	ED Visit
Shechter (2019)	Insurance	Private insurance vs Medicaid	ED Visit
Sullivan (2019)	Insurance	Medicaid vs private insurance	Exacerbation
	Education	Parents education < vs >= high school	Exacerbation
	Income	Poor vs high income	Exacerbation

27 **Table E3: Quality Ratings of all studies included in the meta-analysis, broken down by individual exposure-outcome pairings. (Y=Yes,**
 28 **N=No)**

Cohort Studies

Study	Exposure	Outcome	Selection				Comparability	Outcomes			Quality Rating
			Representative-ness	Selection	Exposure Ascertainment	Outcome not present at start of study	Comparability	Outcome Assessment	Sufficient follow-up period	Adequacy of follow-up	
Leson (1995a)	Edu	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
	SES	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
Leson (1995b)	Edu	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
	SES	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
LeSon (1995c)	Edu	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor
	SES	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor
LeSon (1996)	Edu	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
	Emp	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
	SES	Int	Y	Y	N	Y	N	Y	Y	Y	Poor
Mowat (1998)	Dep	ED	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Dep	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Dep	PC	Y	Y	Y	Y	N	Y	Y	Y	Poor
Adams (2000)	Edu	ED	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Edu	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Emp	ED	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Emp	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
Finkelstein (2000)	Ins	ED	Y	Y	Y	N	Y	Y	Y	Y	Good
	Ins	Hosp	Y	Y	Y	N	Y	Y	Y	Y	Good
Stanford (2000)	Ins	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
Eisner (2001)	Edu	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
	Inc	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
Ferris (2001)	Ins	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Ins	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor

Ortega (2001)	Ins	ED	Y	Y	Y	Y	Y	N	Y	Y	Good
	Ins	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
Amre (2002)	Occ	ED	Y	Y	Y	Y	N	N	Y	Y	Poor
	Occ	Hosp	Y	Y	Y	Y	N	N	Y	Y	Poor
	Occ	PC	Y	Y	Y	Y	N	N	Y	Y	Poor
Bloomberg (2003)	Ins	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
Spurrier (2003)	Edu	ED	Y	Y	N	Y	N	N	Y	Y	Poor
	Occ	ED	Y	Y	N	Y	N	N	Y	Y	Poor
Ather (2004)	Ins	ReAd	Y	Y	Y	Y	Y	Y	Y	Y	Good
Chen (2004)	Inc	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
Pesola (2004)	Edu	ED	Y	Y	Y	Y	Y	N	Y	Y	Good
	Edu	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
	Emp	ED	Y	Y	Y	Y	Y	N	Y	Y	Good
	Emp	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
	Ins	ED	Y	Y	Y	Y	Y	N	Y	Y	Good
	Ins	Hosp	Y	Y	Y	Y	Y	N	Y	Y	Good
Lasmar (2006)	Edu	ReAd	Y	Y	N	Y	N	Y	Y	Y	Poor
	Inc	ReAd	Y	Y	N	Y	N	Y	Y	Y	Poor
DeWalt (2007)	Edu	ED	Y	Y	Y	Y	N	N	Y	Y	Poor
	Edu	Hosp	Y	Y	Y	Y	N	N	Y	Y	Poor
	Inc	ED	Y	Y	Y	Y	N	N	Y	Y	Poor
	Inc	Hosp	Y	Y	Y	Y	N	N	Y	Y	Poor
Peters (2008)	Ins	ED	N	Y	Y	Y	N	N	Y	Y	Poor
	Ins	Hosp	N	Y	Y	Y	N	N	Y	Y	Poor
To (2008)	Inc	ED	Y	Y	Y	Y	Y	N	Y	Y	Good
	Inc	Ex	Y	Y	Y	Y	Y	N	Y	Y	Good
Liu (2009)	Ins	ReAd	Y	Y	Y	Y	Y	Y	Y	Y	Good
Carroll (2010)	Ins	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
Auger (2013)	Edu	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Inc	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Ins	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor
Roberts (2013)	Dep	Mort	Y	Y	Y	Y	Y	Y	Y	Y	Good
Rodriguez-Martinez (2013)	Edu	ReAd	Y	Y	Y	Y	N	Y	Y	Y	Poor

Chang (2014)	Ins	ED	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Ins	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
Kenyon (2014)	Ins	ReAd	Y	Y	Y	Y	Y	Y	Y	Y	Good
To (2014)	Dep	Mort	Y	Y	Y	Y	Y	Y	Y	Y	Good
Kaur (2015)	Inc	Mort	Y	Y	Y	Y	Y	Y	Y	Y	Good
	Inc	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Ins	Mort	Y	Y	Y	Y	Y	Y	Y	Y	Good
	Ins	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor
Dilokthornsakul (2016)	Ins	Hosp	Y	Y	Y	Y	Y	Y	Y	Y	Good
Hasegawa (2016)	Ins	ED	Y	Y	Y	Y	Y	Y	Y	Y	Good
	Ins	Hosp	Y	Y	Y	Y	N	Y	Y	Y	Poor
	Ins	Int	Y	Y	Y	Y	N	Y	Y	Y	Poor
Backman (2017)	Occ	Mort	Y	Y	Y	Y	N	Y	Y	Y	Poor
Mazalovic (2018)	Edu	Ex	N	Y	N	Y	N	N	Y	Y	Poor
	Occ	Ex	N	Y	N	Y	N	N	Y	Y	Poor
	SES	Hosp	N	Y	N	Y	N	N	Y	Y	Poor
Jroundi (2019)	Inc	ReAd	Y	Y	Y	Y	Y	Y	Y	Y	Good
	Ins	ReAd	Y	Y	Y	Y	Y	Y	Y	Y	Good
Seibert (2019)	Inc	ED	Y	Y	N	Y	N	N	Y	N	Poor
	Inc	Hosp	Y	Y	N	Y	N	N	Y	N	Poor

Cross Sectional Studies

Study	Exposure	Outcome	Selection				Comparability	Exposures		Quality Rating
			Representative-ness	Sample size	Response rate	Exposure Ascertainment	Comparability	Outcome Assessment	Statistical test	
Davidson (1994)	Ins	ED	Y	Y	N	N	N	Y	Y	Poor
	Ins	Hosp	Y	Y	N	N	N	Y	Y	Poor
Stoddard (1994)	Inc	PC	Y	Y	N	Y	Y	Y	Y	Good
	Ins	PC	Y	Y	N	Y	Y	Y	Y	Good
Bair (2001)	Edu	ED	Y	Y	Y	Y	Y	Y	Y	Good
	Ins	ED	Y	Y	Y	Y	Y	Y	Y	Good
Al-Dawood (2002)	SES	ED	Y	Y	Y	Y	N	Y	Y	Poor
Grant (2005)	Edu	ED	Y	Y	N	Y	N	Y	N	Poor
	Edu	Hosp	Y	Y	N	Y	N	Y	N	Poor
Meng (2006)	Edu	ED	Y	Y	Y	Y	N	Y	Y	Poor
	Inc	ED	Y	Y	Y	Y	N	Y	Y	Poor
	Ins	ED	Y	Y	Y	Y	Y	Y	Y	Good
Horner (2008)	Ins	Hosp	Y	Y	N	Y	N	Y	Y	Poor
Kim (2009)	Edu	ED	Y	Y	N	Y	N	Y	Y	Poor
	Inc	ED	Y	Y	N	Y	Y	Y	Y	Good
	Ins	ED	Y	Y	N	Y	N	Y	Y	Poor
Wright (2009)	Ins	ED	Y	Y	N	Y	N	Y	Y	Poor
Piper (2010)	Inc	PC	Y	Y	N	Y	Y	Y	Y	Good
	Ins	PC	Y	Y	N	Y	Y	Y	Y	Good
Lutfiyya (2011)	SES	ED	Y	Y	N	Y	N	Y	Y	Poor
	SES	Ex	Y	Y	N	Y	N	Y	Y	Poor
	SES	PC	Y	Y	N	Y	N	Y	Y	Poor
Zejda (2012)	Edu	Hosp	Y	Y	N	Y	Y	Y	Y	Good
Yan (2016)	Edu	Ex	Y	Y	N	Y	N	Y	Y	Poor
	Inc	Ex	Y	Y	N	Y	N	Y	Y	Poor
Zhang (2017)	Edu	ED	Y	Y	N	Y	N	Y	Y	Poor
	Inc	ED	Y	Y	N	Y	N	Y	Y	Poor

Gushue (2019)	Edu	Ex	Y	Y	N	Y	Y	Y	Y	Good
	Ins	Ex	Y	Y	N	Y	Y	Y	Y	Good
Sullivan (2019)	Edu	Ex	Y	Y	N	Y	N	Y	N	Poor
	Inc	Ex	Y	Y	N	Y	N	Y	N	Poor
	Ins	Ex	Y	Y	N	Y	N	Y	N	Poor

Case Control Studies

Study	Exposure	Outcome	Selection				Comparability	Outcomes			Quality Rating
			Case Definition	Representative-ness	Control Selection	Control Definition	Comparability	Exposure Ascertainment	Consistent between cases and controls	Non-Response rate	
Boulet (1996)	Edu	ED	Y	Y	N	Y	Y	N	Y	Y	Good
	Emp	ED	Y	Y	N	Y	Y	N	Y	Y	Good
	Inc	ED	Y	Y	N	Y	Y	N	Y	Y	Good
Barton (2005)	Emp	Mort	Y	Y	N	Y	N	N	N	N	Poor
Van der Merwe (2006)	Inc	Hosp	Y	Y	N	Y	N	Y	Y	N	Poor
Forbes (2007)	Dep	ED	Y	Y	Y	Y	Y	Y	Y	N	Good
Xie (2017)	Ins	Ex	Y	Y	N	Y	Y	Y	Y	Y	Good
Grunwell (2018)	Pov	Hosp	Y	Y	N	Y	N	Y	Y	Y	Poor
Shechter (2019)	Ins	ED	Y	N	N	Y	Y	Y	Y	Y	Fair

30 **Table E4: Variables adjusted for in each study (Y=Yes, N=No)**

Study Name	Exposure	Outcome	Age	Sex	Race/ Ethnicity	Smoker (Self or Parents)	Asthma Severity	Medications	Hospital Admissions	Co- morbidities	Pet Ownership / Exposure	Length of Stay	Urban/ Rural Residence	Literacy (Parents or self)	Poverty	ED Visits	Family History of Asthma	Additional Variables Adjusted For
Shechter (2019)	Ins	ED	Y	Y	Y	Y	N	Y	N	N	N	N	N	N	N	N	N	Distance from hospital, Presence of asthma action plan, Spanish speaking
Gushue (2019)	Ins	Ex	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Born in the USA, Health Status, Household Structure, USA census region
	Edu	Ex	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	
Jroundi (2019)	SES	ReAd	Y	Y	Y	N	N	N	N	N	N	Y	N	N	N	N	N	
	Ins	ReAd	Y	Y	Y	N	N	N	N	N	N	Y	N	N	N	N	N	
Seibert (2019)	SES	ED	N	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	Year/Season of interview
	SES	Hosp	N	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	
Grunwell (2018)	SES	Hosp	Y	N	Y	N	Y	N	Y	Y	N	N	N	N	N	N	Y	
Xie (2017)	Ins	Ex	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	BMI
Yan (2016)	SES	Ex	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	FEV1 less than 50% before discharge, Mean ACT score of 15 or less in 1 year follow-up
	Edu	Ex	N	N	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	
Dilokthornsakul (2016)	Ins	Hosp	Y	Y		N	Y	Y	N	Y	N	N	N	N	N	N	N	
Hasegawa (2016)	Ins	ED	Y	Y	Y	N	N	N	Y	N	N	N	N	N	N	N	N	
Kaur (2015)	SES	Mort	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Admission day (weekday/weekend), Hospital region, Quartile month, Teaching vs non-teaching hospital
	Ins	Mort	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Complex chronic condition, Home disposition, Hospital admission rate performance
Kenyon (2014)			Y	Y	Y	N	N	Y	Y	N	N	Y	N	N	N	N	N	
	Ins	ReAd																
To (2014)	SES	Mort	Y	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N	
Auger (2013)	Ins	ReAd	Y	N	Y	N	N	Y	N	N	N	N	N	N	N	N	N	
	Edu	ReAd	Y	N	Y	N	N	Y	N	N	N	N	N	N	N	N	N	
	SES	ReAd	Y	N	Y	N	N	Y	N	N	N	N	N	N	N	N	N	
Roberts (2013)	SES	Mort	Y	Y	N	N	N	N	N	Y	N	N	N	N	N	N	N	Year

Rodriguez-Martinez (2013)			Y	N	N	Y	N	Y	Y	N	Y	N	N	N	N	N	N	Maternal allergic rhinitis, Score of asthma knowledge questionnaire, Score of ZSDS
Zeida (2012)	Edu	ReAd																Lung disease or allergy in parents, Number of asthma attacks in the past year, Number of siblings
Piper (2010)	Edu	Hosp	Y	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N	Health status, Region
	SES	PC	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	
	Ins	PC	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	
Kim (2009)																		Family size, Region of residence, Residence in metropolitan statistical area
	SES	ED	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	
Liu (2009)																		Same zip code as hospital, Season of index hospitalization, Year of index hospitalization
	Ins	ReAd	Y	Y	Y	N	N	N	N	N	N	Y	N	N	Y	N	N	
Wright (2009)																		Family type, If current condition limits activities, Level of symptoms in the last 12 months
	Ins	ED	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	
To (2008)	SES	Ex	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	Cold/sinus infection as trigger, had acute asthma episodes in the last 6 months, Had walk-in clinic visit in the past year, Wash bed linen in hot water weekly
			Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	
	SES	ED																
Horner (2008)	Ins	Hosp	N	Y	N	N	N	N	N	N	N	N	N	N	N	N	Y	N
DeWalt (2007)	Edu	Hosp	Y	N	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N	Parental asthma knowledge, Site of care
	SES	Hosp	Y	N	Y	Y	Y	Y	N	N	N	N	N	Y	N	N	N	
	Edu	ED	Y	N	Y	Y	Y	Y	N	N	N	N	N	N	N	N	N	
	SES	ED	Y	N	Y	Y	Y	Y	N	N	N	N	N	Y	N	N	N	
Forbes (2007)	SES	ED	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	
Meng (2006)																		English proficiency, Frequency of asthma symptoms, Reason for delay in asthma care, Self-reported health status, Usual source of care
			Y	Y	Y	Y	N	N	N	N	N	N	Y	N	N	N	N	
	Ins	ED																
Chen (2004)																		Percentage of EA population with University degree, Province
	SES	ReAd	Y	N	N	N	N	N	N	N	N	Y	N	N	N	N	N	
Ather (2004)	Ins	ReAd	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	
Pesola (2004)	Edu	Hosp	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	Daily use of peak flow meter, Duration of asthma, Living with spouse/significant other
	Emp	Hosp	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	
	Ins	Hosp	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	
	Ins	ED	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	
	Edu	ED	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	
	Emp	ED	Y	Y	N	Y	Y	N	Y	N	Y	N	N	N	N	N	N	

Amre (2002)	Emp	Hosp	N	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Age of mother at childbirth, Hospitalization at first diagnosis, Routine follow-up physician visits for control of asthma
	Emp	ED	N	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Routine follow-up physician visits for control of asthma
Eisner (2001)	Edu	Hosp	Y	Y	Y	Y	Y	N	Y	N	N	N	N	N	N	N	N	Gastric acid suppression medication, Aspirin allergy history, Atopic history
	SES	Hosp	Y	Y	Y	Y	Y	N	Y	N	N	N	N	N	N	N	N	Aspirin allergy history, Atopic history
Ferris (2001)	Ins	Hosp	N	N	Y	N	Y	Y	N	Y	N	N	N	N	N	N	N	Duration of symptoms, O2 saturation, Pulmonary index score
Bair (2001)	Ins	ED	Y	Y	Y	N	Y	N	N	Y	N	N	N	N	N	N	N	Mental and physical health score, Reported access problems
	Edu	ED	Y	Y	Y	N	Y	N	N	Y	N	N	N	N	N	N	N	Reported access problems
Ortega (2001)	Ins	ED	Y	Y	N	N	Y	Y	N	N	N	N	N	N	N	N	N	Frequency of asthma-related primary care visits in the last year, Practice type of primary provider
	Ins	Hosp	Y	Y	N	N	Y	Y	N	N	N	N	N	N	N	N	N	Frequency of asthma-related primary care visits in the last year, Practice type of primary provider
Stanford (2000)	Ins	Hosp	Y	N	N	N	N	N	N	Y	N	N	N	N	N	N	N	
Finkelstein (2000)	Ins	ED	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	
	Ins	Hosp	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	
Boulet (1996)	Edu	ED	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	Atopy, Duration of asthma
	Emp	ED	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	
	SES	ED	Y	Y	N	Y	N	Y	N	N	N	N	N	N	N	N	N	
Stoddard (1994)	Ins	PC	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Family size, Population density, Region
	SES	PC	Y	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	Region

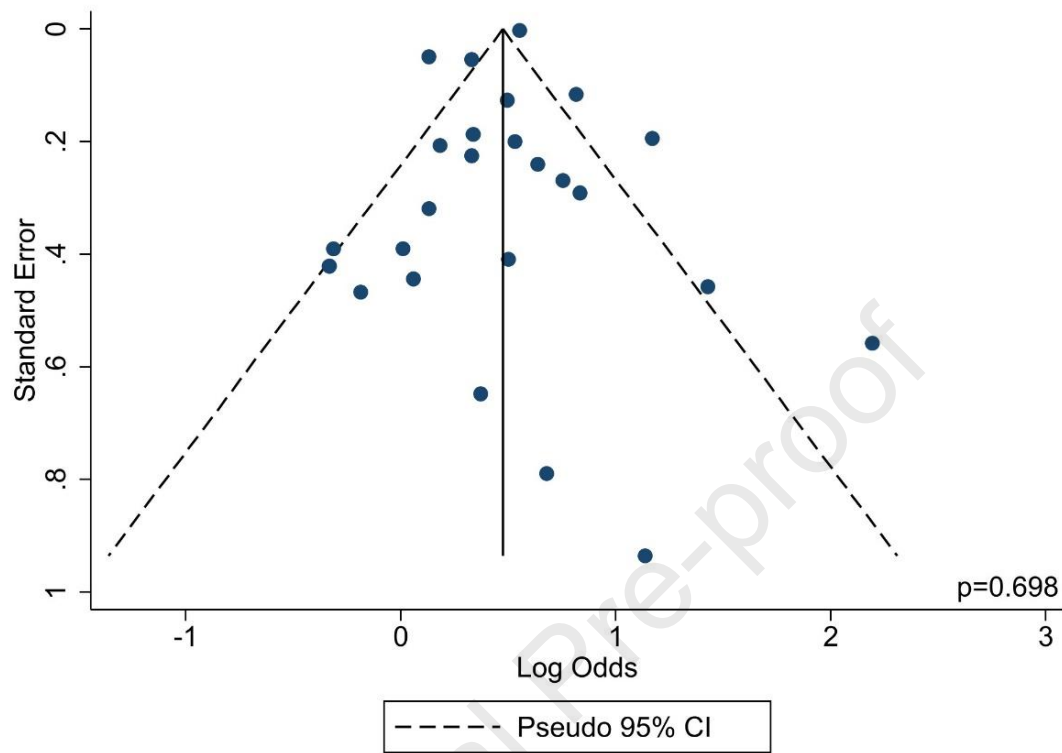
31 Abbreviations: ED (ED Visit), Ex (Exacerbation), Hosp (Hospitalization), Mort (Mortality), PC (Primary Care Attendance), ReAd

32 (Readmission), Int (Ventilation / Intubation), SES (Socioeconomic status), Emp (Employment), Edu (Education), Ins (Insurance), ED Rec (ED

33 Records), Gen Pop (General Population), Gen Prac (General Practice), Hosp Rec (Hospitalization Records), Ins (Insurance Database), Sec Care

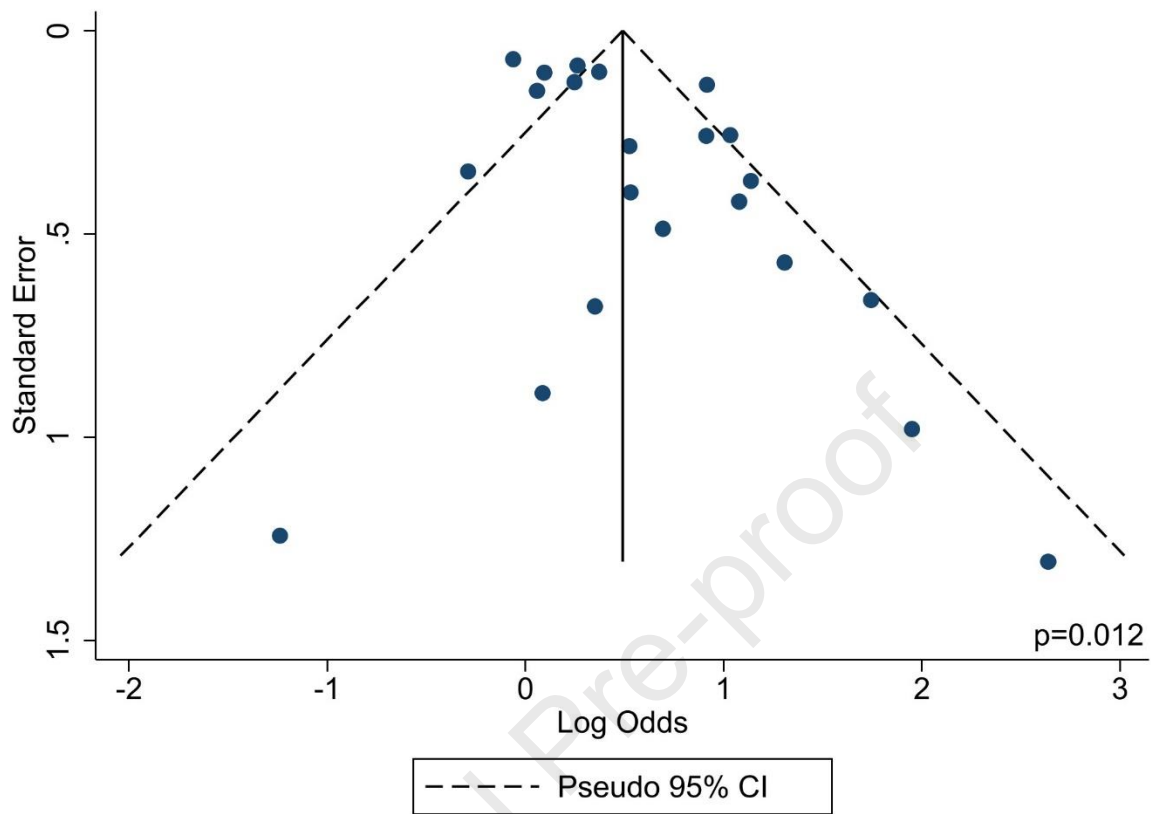
34 (Secondary Care), Ter Care (Tertiary Care), NR (not reported), NS (not specified)

35 **Figure E2: Funnel plot for data included in the emergency department visit meta-**
36 **analysis.**



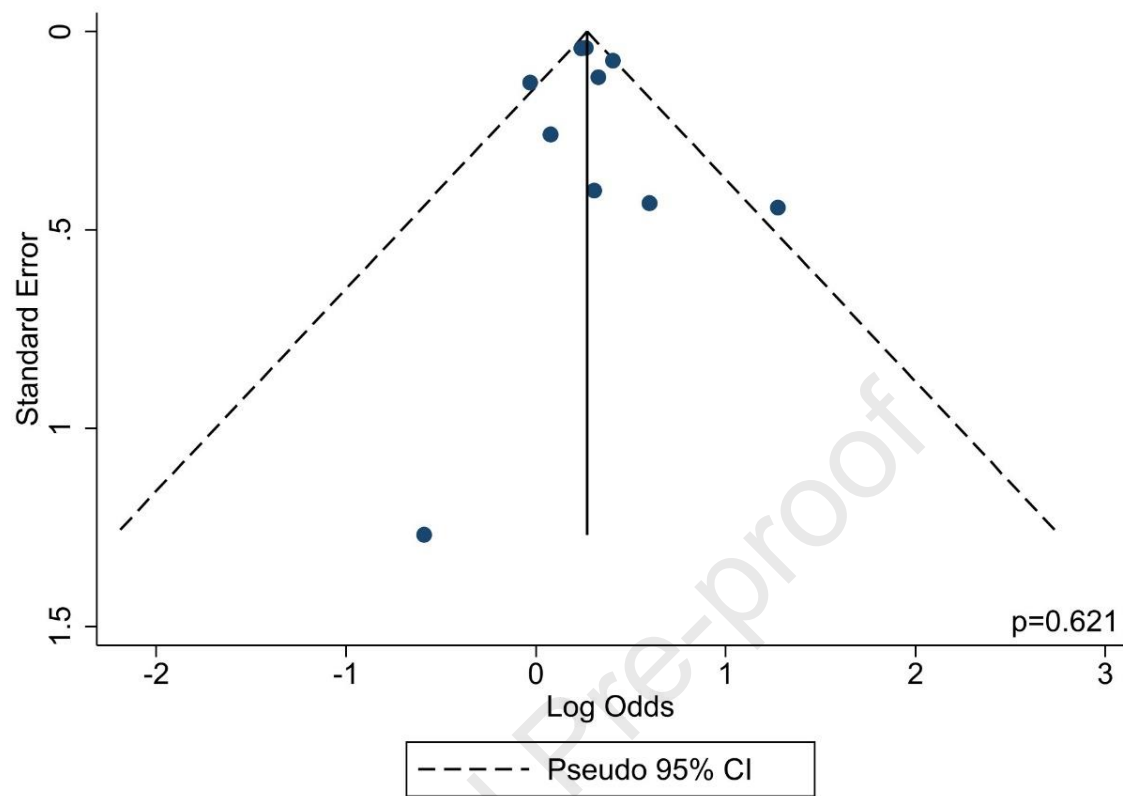
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38 **Figure E3: Funnel plot for data included in the hospitalization meta-analysis.**



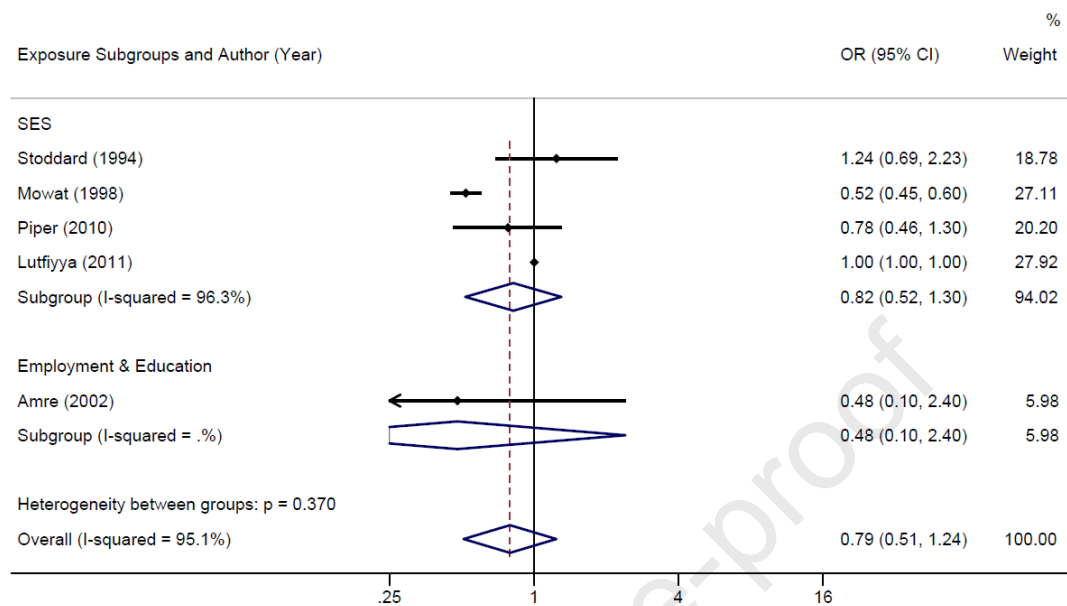
39

40 **Figure E4: Funnel plot for data included in the readmission meta-analysis.**

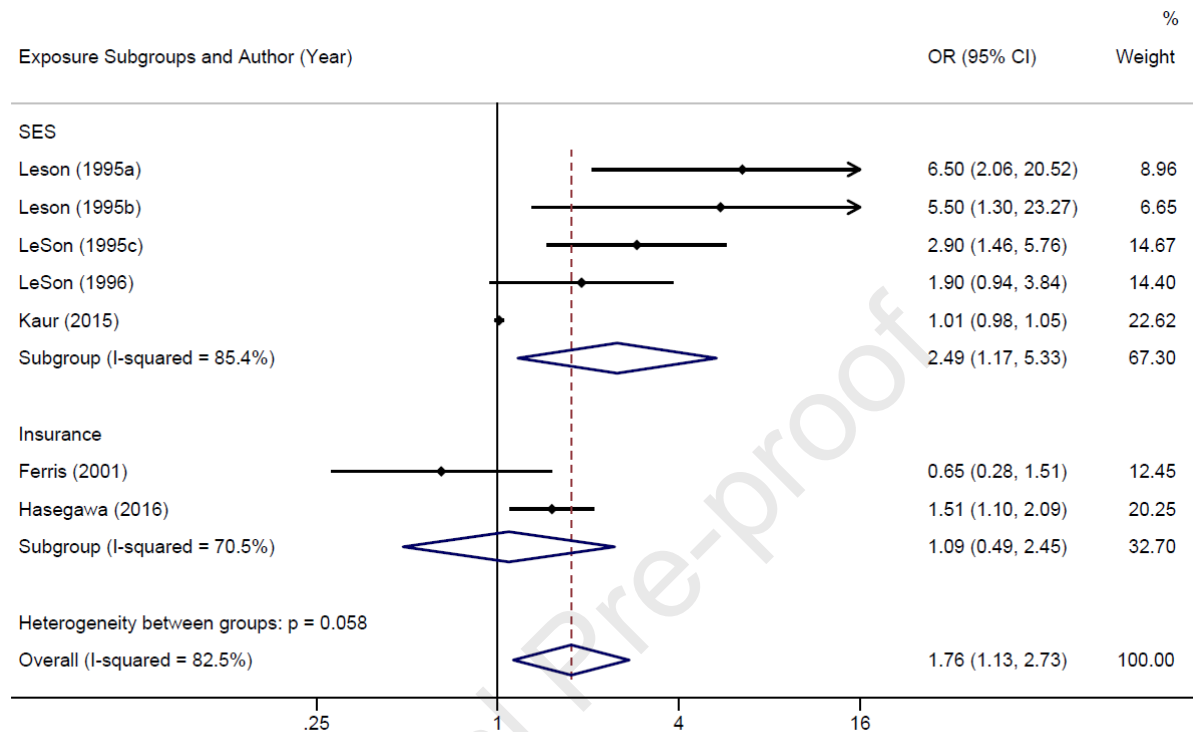


41

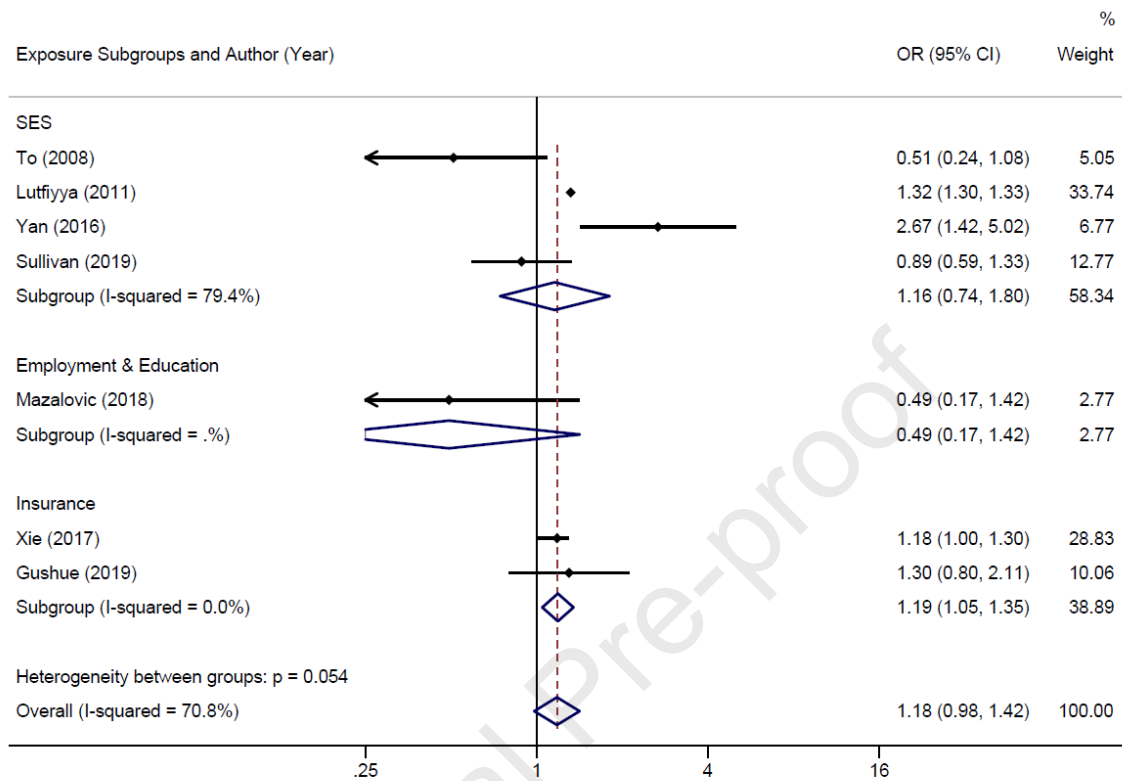
42 **Figure E5: Forest Plot of odds ratios for asthma related Primary Care Attendance, sub**
 43 **grouped by exposure type**



45 **Figure E6: Forest Plot of odds ratios for asthma related Ventilation / Intubation, sub**
 46 **grouped by exposure type**

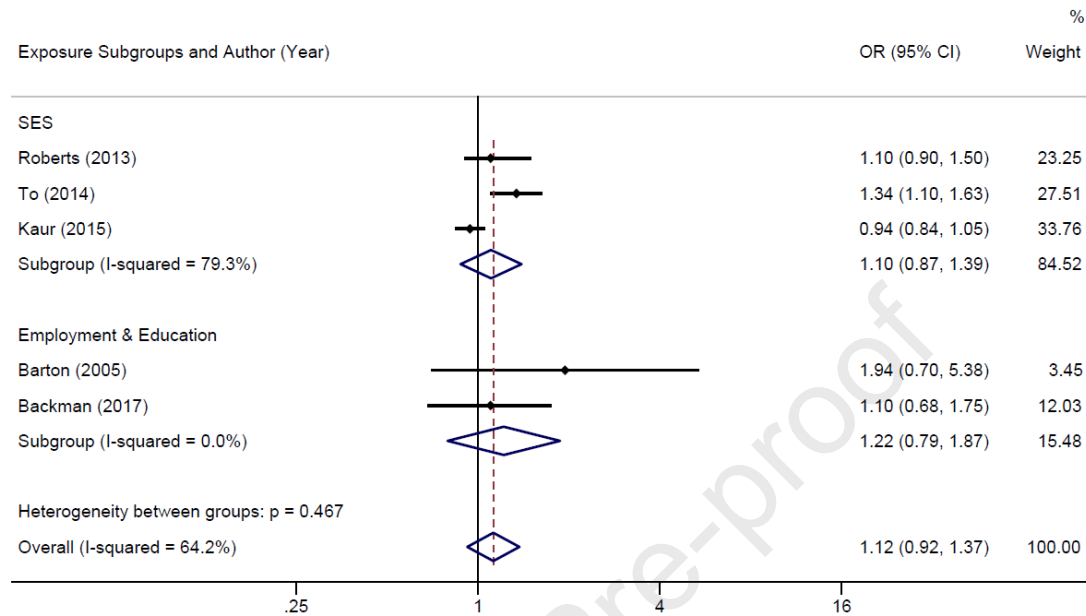


48 **Figure E7: Forest Plot of odds ratios for asthma related Exacerbations, sub grouped by**
 49 **exposure type**



NOTE: Weights are from random-effects model

51 **Figure E8: Forest Plot of odds ratios for asthma related Mortality, sub grouped by**
 52 **exposure type**



54 **Table E5: Leave-one-out meta-analysis summary**

Outcome	Primary analysis estimate (95% CI)	Minimum estimate (95% CI)	Maximum estimate (95% CI)
Health Care Utilization			
Primary Care Attendance	0.79 (0.51, 1.24)	0.72 (0.43, 1.19)	1.00 (1.00, 1.00)
ED Visit	1.61 (1.40, 1.84)	1.54 (1.35, 1.77)	1.67 (1.47, 1.89)
Hospitalization	1.63 (1.34, 1.99)	1.54 (1.28, 1.85)	1.70 (1.37, 2.11)
Readmission	1.31 (1.19, 1.44)	1.27 (1.16, 1.40)	1.34 (1.24, 1.45)
Ventilation / Intubation	1.76 (1.13, 2.73)	1.51 (1.00, 2.28)	2.09 (1.22, 3.57)
Exacerbations and Mortality			
Exacerbations	1.18 (0.98, 1.42)	1.08 (0.77, 1.52)	1.24 (1.05, 1.46)
Mortality	1.12 (0.92, 1.37)	0.99 (0.88, 1.12)	1.24 (1.07, 1.44)

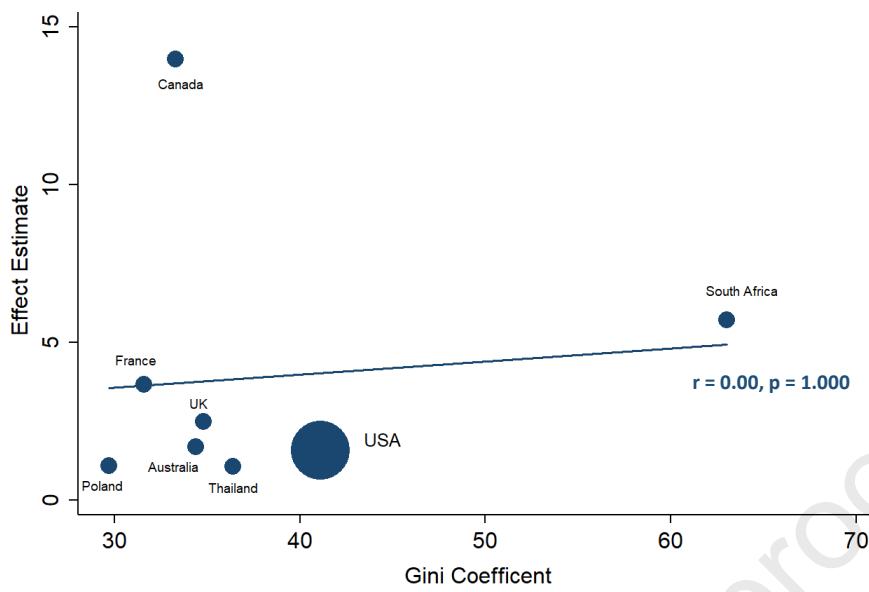
55

56 **Table E6: Subgroup Analyses for exacerbations, mortality, primary care attendance and ventilation / intubation**

Subgroup	Primary Care Attendance				Exacerbations				Ventilation / Intubation				Mortality			
	N	OR (95% CI's)	I ²	p	N	OR (95% CI's)	I ²	p	N	OR (95% CI's)	I ²	p	N	OR (95% CI's)	I ²	p
Exposure Group				0.370				0.054				0.058				0.467
SES	4	0.82 (0.52, 1.30)	96.3		4	1.16 (0.74, 1.80)	79.4		5	2.49 (1.17, 5.33)	85.4		3	1.10 (0.87, 1.39)	79.3	
Employment & Education	1	0.48 (0.10, 2.40)	N/A		1	0.49 (0.17, 1.42)	N/A						2	1.22 (0.79, 1.87)	0.0	
Insurance					2	1.19 (1.05, 1.35)	0.0		2	1.09 (0.49, 2.45)	70.5					
Age				<0.001				0.014				0.066				N/A
Adult	1	1.00 (1.00, 1.00)	N/A		3	1.35 (0.70, 2.58)	75.4		1	1.51 (1.10, 2.09)	N/A		1	1.10 (0.85, 1.42)	N/A	
Pediatric	2	0.52 (0.45, 0.60)	0.0		1	0.51 (0.24, 1.08)	N/A		1	0.65 (0.28, 1.51)	100.0					0.229
Time period				<0.001				0.014				<0.001				
Pre-2010	3	0.71 (0.35, 1.42)	74.9		1	0.51 (0.24, 1.08)	N/A		5	2.40 (1.13, 5.08)	71.0		1	1.94 (0.70, 5.38)	N/A	
Post-2010	2	1.00 (1.00, 1.00)	0.0		6	1.24 (1.05, 1.46)	65.5		2	1.20 (0.81, 1.77)	83.5		4	1.10 (0.90, 1.34)	69.1	
Healthcare System				<0.001				0.014				N/A				0.003
Insurance based	3	1.00 (1.00, 1.00)	0.0		6	1.24 (1.05, 1.46)	65.5		7	1.76 (1.13, 2.73)	82.5		1	0.94 (0.84, 1.05)	N/A	
Universal Government Funded	2	0.52 (0.45, 0.60)	0.0		1	0.51 (0.24, 1.08)	N/A						4	1.24 (1.07, 1.44)	0.0	
Data Collection Setting				0.370				0.123				N/A				0.003
General Population	4	0.82 (0.52, 1.30)	96.3		4	1.11 (0.83, 1.49)	57.2						3	1.32 (1.10, 1.58)	0.0	
Secondary / Tertiary Care	1	0.48 (0.10, 2.40)	N/A		3	1.20 (0.60, 2.39)	82.1		7	1.76 (1.13, 2.73)	82.5		2	0.97 (0.86, 1.11)	18.2	

57

58 **Figure E9: Gini coefficient vs effect estimate for hospitalization by country**



59