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Risk Factors for Pediatric Asthma Readmissions: A Systematic Review

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Objective: To systematically review the literature on pediatric asthma readmission risk factors.

Study design: We searched PubMed/MEDLINE, CINAHL, Scopus, PsycINFO, and Cochrane Central Register of Controlled Trials for published articles (through November 2019) on pediatric asthma readmission risk factors. Two authors independently screened titles and abstracts and consensus was reached on disagreements. Full-text articles were reviewed and inclusion criteria applied. For articles meeting inclusion criteria, authors abstracted data on study design, patient characteristics, and outcomes, and four authors assessed bias risk.

Results: Of 5,749 abstracts, 74 met inclusion criteria. Study designs, patient populations, and outcome measures were highly heterogeneous. Risk factors consistently associated with early readmissions (≤ 30 days) included prolonged length of stay (odds ratio range, 1.1-1.6) and chronic comorbidities (1.7-3.2). Risk factors associated with late readmissions (> 30 days) included female sex (1.1-1.6), chronic comorbidities (1.5-2), summer discharge (1.5-1.8), and prolonged length of stay (1.04-1.7). Across both readmission intervals, prior asthma admission was the most consistent readmission predictor (1.3-5.4).

Conclusions: Pediatric asthma readmission risk factors depend on the readmission interval chosen. Prior hospitalization, length of stay, sex, and chronic comorbidities were consistently associated with both early and late readmissions.

Trial registration CRD42018107601

Pediatric asthma readmissions are costly and common. Hospitalizations account for over one-third of asthma spending, and create substantial financial burdens for patients, families, and the healthcare system.[1–3] Hospital readmissions double the cost of pediatric inpatient care.[4] Early readmissions (≤ 30 days post discharge) have come under scrutiny as markers of hospital quality and potential metrics for reimbursement penalties. But late readmissions (> 30 days) in pediatric asthma are far more common, with 17% to 54% of children readmitted for another episode of asthma within a year.[5,6] These high asthma readmission rates are concerning, given that asthma is an ambulatory-care-sensitive condition for which timely, appropriate outpatient care could prevent hospitalization.[7,8] There is an urgent need to identify risk factors associated with asthma readmissions so that children at highest risk can be targeted for tailored, evidence-based interventions.

As greater pressure is put on hospital systems to decrease readmissions, identifying risk factors for those readmissions is crucial. Consideration of all potential risk factors by researchers and clinicians may help target discharge care for children at highest risk for readmission. Prior systematic reviews of pediatric asthma readmission risk factors were incomplete, contained errors (i.e., included studies had the incorrect outcome measure [9,10] or inappropriate inclusion criteria [11]), or conflated emergency-department revisits and inpatient readmissions [12,13]). A more thorough and rigorous investigation is needed to inform the next generation of readmission risk-reduction interventions. The study objective was to systematically review all risk factors for pediatric asthma readmissions and to identify factors associated with early and with late readmission.

METHODS

This systematic review was conducted and reported using a registered protocol (PROSPERO registration number CRD42018107601) based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines.[14]

Literature Search and Study Selection

A clinical health-sciences librarian performed our comprehensive electronic search of publications using the following databases: PubMed Medline, Cumulative Index to Nursing and Allied Health Literature via EBSCO, Scopus via Elsevier, Cochrane Central Register of Controlled Trials via Wiley, and PsycInfo via EBSCO (Table I; available at www.jpeds.com) All results were collected from database inception through November 14, 2019. Additionally, the ISRCTN Registry and ClinicalTrials.gov were searched through December 13, 2019. Search terms included a previously validated search string to identify pediatric studies,[15] and a combination of MeSH terms, title, abstract, keywords for asthma, and readmissions. Only articles published in English were included in the final review. Original-research articles from journals were included; commentaries, case reports, editorials, dissertations, letters to the editor, and conference proceedings were excluded. Clinical trials, and cross-sectional, case-control, prospective cohort, and quality-improvement studies were included. The full search strategy is available both in the supplemental information (Table 1) and in the protocol registration. Additional records were found by compiling forward citations—articles citing the included studies—and bibliographies in all full-text records that were selected for inclusion. Forward citations were identified using Scopus or Google Scholar citation tracking. Bibliographies were compiled from Scopus or from the full text. Duplicates were identified and removed via ProQuest RefWorks (Legacy version). Only studies of asthma-specific readmissions, as opposed to all-cause readmissions, were included. Asthma readmission risk factors were determined to be

related to early readmissions (≤ 30 days after index hospitalization discharge) or late readmissions (> 30 days). No upper limit for the readmission interval was pre-specified to fully capture all possible articles related to pediatric asthma readmission risk factors.

Data Abstraction

Prior to screening all titles and abstracts, two authors independently screened a random sample of 166 titles and abstracts for which they were blinded to authors and journals. The first test of agreement was weak (Cohen K = 0.48). Consequently, the reviewers discussed rating differences and reviewed another random sample of 166 titles and abstracts, for which moderate agreement (Cohen K = 0.71) was achieved. The two reviewers then independently screened all titles and abstracts, still blinded to author and journal titles, using an Excel workbook designed specifically for screening.[16] Data were compiled into a single Excel workbook, and disagreements were settled by consensus. Two authors independently reviewed articles for consideration, and article inclusion was either reached by consensus or by adjudication of a third reviewer.

Risk-of-Bias Assessment

Study quality was evaluated by paired evaluators using the Newcastle-Ottawa scale for non-randomized trials[17] and Cochrane risk-of-bias assessment tool for randomized controlled trials.[18] Discrepancies in quality assessment were first discussed and ultimately resolved by a third reviewer when necessary.

RESULTS

A total of 5,749 titles and abstracts were screened, 374 full text articles were evaluated, and 74 studies were included for final analysis (Figure 1; available at www.jpeds.com). Included

studies had marked variability in design and analysis strategies (Table 2). Due to this heterogeneity, meta-analysis could not be performed; instead, a qualitative synthesis of study results, applicability, and limitations is presented (Table 3; available at www.jpeds.com). Overall, 36% of studies tested associations with early readmissions and 80% examined associations with late readmissions. There were 21 distinct risk factors identified for early readmissions and 46 for late readmissions (Table 4). Risk factors assessed with multivariable adjustment, or as case-control studies, are displayed in Figure 2 as forest plots without quantitative synthesis. Risk of bias for included studies was moderate (Figure 3; available at www.jpeds.com).

Sociodemographic Risk Factors

Female sex was consistently associated with late readmissions.[5,6,19–24] with aORs ranging from 1.00 to 1.6. Age >12 years old was associated with increased early readmission risk (aOR and aHR range 0.78-2.5; four of five studies with significant associations),[5,25–27] but associations with late readmissions were mixed. Two studies reported an association of each increasing year of age with late readmission.[28,29] Eight studies found that young children had increased late readmission risk vs. teenagers (aOR and aHR range 1.1-4.36)[6,19–21,30–34]; however, one high-quality national study found the opposite across multiple readmission intervals.[5]

Fifteen studies investigated the association of Black/African-American (hereafter referred to as Black) race/ethnicity with early asthma readmission. A large matched cohort analysis (>11,000 pairs) using Medicaid claims data found that Black race was not associated with early readmissions (OR, 0.96; 95% CI, 0.88-1.05).[35] Studies reporting multiple readmission time frames found decreased[36] or no association of Black race/ethnicity with early readmissions,

but significantly increased associations with late readmissions.[5,36,37] Of 29 studies investigating the association between African American race/ethnicity and late readmissions, two found a decreased odds of readmission (aOR, 0.72-0.83), eight found an increased association (aOR/aHR range, 1.18-1.94),[5,21,36–43] and the remainder found no association. One study used directed acyclic graphs and inverse probability weighting to account for an extensive list of measured variables. In the unadjusted analysis, Black children were over twice as likely as white children to be readmitted; however, this disparity no longer persisted after adjustment for relevant covariates.[44]

Latino race/ethnicity was not significantly associated with early readmission in any of the seven studies that investigated this potential association. In 20 studies assessing Latino race/ethnicity and late readmissions, five studies found an increased association.[5,21,37,40,41] One single-center study found Latino ethnicity was associated with lower odds of late readmission vs. white children; the study population, however, was >50% Latino and therefore may not be generalizable.[45] No studies reported on racial/ethnic associations of Asian American, Pacific Islander, American Indian/Alaska Native, or multiracial children with asthma readmissions.

Eleven US studies investigated the association of public insurance with early readmission. No studies conducted outside the US reported associations with insurance status. After multivariable adjustment, two out of three studies found an increased risk of readmission (20-59%) with public vs. private insurance. [26,27] Of 14 studies on late readmissions, public insurance was associated with an increased risk of readmission in only three (aOR, 1.09-1.33).[5,21,33,46] One study found that the interaction of Black race/ethnicity and public insurance was associated with a higher odds of readmission (aOR, 1.28), but no significant

association was found when either factor was considered individually.[46] Another study revealed that the type of public insurance was associated with increased readmissions—patients in fee-for-service plans had 1.5 greater adjusted odds of readmission than those in managed-care plans.[47]

A variety of measures were used to explore associations between socioeconomic status and late readmissions. Three studies compared low vs high income (either by lowest quartile or < \$60,000/year in combined family income), and found significant associations between poverty and late readmission (aOR range: 1.27 to 3.1).[21,48,49] Studies investigating neighborhood and geographic risk factors were contradictory. One study found that, after adjusting for other geographic and socioeconomic risk factors, neighborhood poverty and crowded housing conditions were not associated with readmissions.[33] This study did find, however, that children living in predominantly minority neighborhoods had a 43% higher hazard of readmission. Another study from 2012 assessed a geographic risk score's association with late readmissions.[50] It found high-risk areas had a significantly higher readmission hazard (aHR, 1.75). In contrast, a more recent study tested whether the Overall Child Opportunity Index—a comprehensive metric comprising geographic access to education, health, and economic opportunities—was associated with readmission.[51] Although the index was associated with initial pediatric asthma hospitalization rates, the score was not significantly associated with readmissions.

Comorbidities

Obesity was the most frequently assessed individual comorbidity risk factor. Four studies assessed the association between obesity and pediatric asthma readmission.[52–55] Early readmissions were evaluated in three studies yielding mixed results. Studies using adjusted

analyses provided conflicting assessments: one study found that obesity was associated with 26% greater odds of early asthma readmission, compared with children of normal weight,[53] whereas another revealed no association of BMI with early or late readmissions.[54] Similarly, a more recent study showed no association of obesity with late readmission.[55] Other individual risk factors assessed included history of prematurity and associated sequelae, such as bronchopulmonary dysplasia. History of prematurity was associated with early[52,56] and late readmissions.[57] Studies of administrative datasets regularly utilized complex chronic conditions (CCCs) as an aggregate measure of multiple comorbidities. CCC is a validated measure of a chronic illness expected to last greater than one year and involving multiple organ systems, or involving one organ system but requiring specialty pediatric care and hospitalization.[58] CCCs were associated with early (aOR and aHR range, 1.7-3.2)[5,25,27,56] and late readmissions (aOR, 1.5-2).[5,25,57]

Environmental Factors

Environmental exposures, including environmental tobacco smoke (ETS), traffic-related air pollution, and fungus/yeast in the home, were assessed using a variety of methods, including direct measures, serum biomarkers, geographic air sampling, and parental report. ETS was assessed in three studies of early readmissions and six studies of late readmissions.[44,49,55,56,59–63] ETS assessed by self-report was not associated with readmissions in any study. One study assessed both self-report of ETS exposure and serum and salivary cotinine.[62] Reported ETS exposure was not associated with readmission (OR, 1.18; 95% CI, 0.79-1.89), whereas serum and salivary cotinine were significantly associated with late readmission (OR, 1.59; 95% CI, 1.02-2.48; and OR, 2.35; 95% CI, 1.22-4.55, respectively). Of note, among patients with no reported ETS exposure, 70% had detectable salivary cotinine

levels. Ten studies tested the association of season with asthma readmissions. Summer admission was consistently associated with both early [56] and late readmissions.[33,47,64] Dust-mite allergens were associated with late readmissions in two studies.[64,65] Other environmental exposures associated with late readmissions in only single studies included food allergies,[64] inhalant allergens,[66] airborne fungus,[67] and traffic-related air pollution.[49]

Markers of Episode Severity

Twelve studies evaluated the association of length of stay (LOS) of the index admission with early readmissions. Most found no association, but two showed that prolonged LOS (variably defined in each study) was associated with early readmissions (aOR/aHR, 1.3-1.6).[27,56] LOS was associated with late readmissions in only five of 14 studies. All five studies found prolonged LOS in the initial hospitalization was associated with higher late readmission odds or hazards (aOR/aHR, 1.04-1.55).[5,21,31,33,40]

Six studies examined pediatric intensive care unit (PICU) use and early readmission.[5,35,52,59,60,68] Only one study indicated an association: PICU admission was associated with lower odds of early and late readmissions (OR range 0.4 to 0.9 over multiple readmission timeframes).[5] PICU utilization and late readmissions were investigated in four studies. Two found PICU stays were associated with late readmission in bivariate analysis,[68,69] one reported this association in multivariable analysis,[21] and one indicated PICU admissions were associated with reduced odds of late readmission.[5]

Use of Health Services

Three studies found that previous asthma admissions (variably defined, but generally defined as an asthma admission in the six to twelve months prior to index hospitalization) were associated with significantly higher odds of early readmissions.[5,56,60] Prior admissions were

associated with late readmissions in all studies which assessed the risk factor. Whether reported as probability of readmission,[70] HRs,[38,46,71], ORs in a case-control study, [57] or ORs from logistic regression[5,6,30,38,47,71–73], all studies reported a significantly higher risk of late readmission (Figure 2).

Three studies tested the association of primary-care or medical-home access with readmissions. One study found no association of medical-home access with readmissions.[59] In contrast, the other two studies indicated that poor medical-home access was associated with almost double the odds of late readmission.[38,39] Studies on follow-up with pulmonology after initial hospital discharge were contradictory. One showed pulmonary consultation in the year post-discharge was associated with higher late readmission odds,[23] whereas another found lower odds.[63]

Studies on the association of medication use with readmissions have yielded a diverse range of outcomes, many of which are difficult to interpret. Some studies investigated medications that have fallen out of favor, such as theophylline[6] and cromolyn sodium.[23,63,64] Multiple studies reported that use of medications known to reduce asthma hospitalizations and readmissions are actually associated with increased rates of readmission, including inhaled corticosteroids (ICS) and oral corticosteroids (OCS)[47]; failing to account for confounding by indication likely contributes to these associations. One study examined the relationship between medication fills prior to discharge and readmissions. A study of Medicaid claims found that filling either a beta-agonist, ICS, or OCS prescription prior to discharge was associated with a decreased odds of early readmission.[74] Filling all three medications prior to discharge was associated with a significant reduction in early readmissions (OR, 0.32; 95% CI, 0.16-0.60). For late readmissions, filling ICS alone prior to discharge was associated with 13%

reduced odds of readmission; when ICS, OCS, and short-acting beta agonist (i.e., albuterol) prescriptions all were filled prior to discharge, there was a significantly lower odds of readmission (OR, 0.83; 95% CI, 0.72-0.97).[74]

Regional and Institutional Factors

The Joint Commission previously mandated that pediatric asthma patients have a written asthma treatment plan on hospital discharge.[75] A large, multi-site, cross-sectional study found that provision of asthma treatment plans to patients at hospital discharge had no association with readmissions at seven, 30, or 90 days.[76] In contrast, two multi-modal quality-improvement projects revealed that sustained high rates of asthma treatment plan completion are associated with decreased late readmissions.[77,78]

There were significant regional and seasonal differences associated with readmissions. Some findings are of limited utility outside particular regions: Sweden and Denmark have higher readmission rates vs. Norway,[79] and New York City hospitals have higher readmission rates vs. Philadelphia and Pittsburgh.[80] More broadly applicable, however, are findings that rural hospitals have lower readmission rates than urban hospitals.[27,81]

Family Factors

Tests of parental asthma knowledge, in the absence of formal education programs, have shown either no association[28] or marginal associations[38] with readmissions.

Unstudied Risk Factors

No study examined associations of eosinophilia, fractional excretion of nitrous oxide, or limited English proficiency (LEP) with readmissions.

DISCUSSION

This systematic review reveals certain urgent priorities and unanswered questions, and provides a research agenda for reducing pediatric asthma readmissions.

Prior admissions were the most consistent risk factor for both early and late readmissions. Severity indicators of acute asthma attacks (e.g. LOS) and medical complexity (e.g. CCC) were both associated with early and late readmissions. How to leverage these findings to reduce readmissions is less clear. Although previous interventions to reduce asthma readmissions have found infrequent or limited success, this systematic review can be used to help refine target populations for intervention to optimize chances of future success. Studies in adult populations indicate that a team-based approach including a case manager can be moderately successful in reducing frequent asthma ED visits[82] and hospitalizations.[83] Whether these approaches are effective in children is unknown. Interventions that have been shown to decrease readmission for the medically complex child, such as dedicated medical homes, could be a model for these children identified to be at highest readmission risk.

The association of young age and late readmission informs a key research priority: the proper definition of the asthma cohort is lacking. Included studies used discrepant age inclusion criteria—these criteria therefore urgently need standardization. Many studies, especially large nationwide studies, included all children under < 19 years. This is likely inappropriate, as the most common cause of wheezing in a child < 2 years old is bronchiolitis, not asthma.[84] As bronchiolitis is the most common cause of hospitalization of children < 2 years old, the misclassification bias of readmissions, especially in retrospective database analyses, is too great. As such, children < 2 years old should be excluded from these types of analyses. In light of this,

we have not displayed the association of age <5 years in Figure 2 as five of seven studies included children < 2 years old in their analysis.

The final association with readmissions needing urgent investigation is seasonality—specifically summer admissions/discharges. Asthma is a seasonal disease, with admissions that peak in fall and winter, and nadir in summer. Those with worse disease severity and those with greater susceptibility to allergic environmental triggers may be more prone to hospitalization during the summer and subsequent readmission when viral illnesses are circulating in the fall and winter. These findings suggest that targeted interventions that focus on intensive allergen-reduction efforts and chronic asthma management for these children are urgent priorities.

Although this review identified numerous risk factors associated with asthma readmissions, there are unstudied risk factors and methodologies worthy of further investigation. There are certain noteworthy absences from the extensive list of readmission risk factors. Many studies investigated associations with race/ethnicity; however, none reported directly on LEP. LEP is associated with increased adverse events,[85] and directly impacts critical transitions of care that must occur during and after hospital discharges.[86,87] Social determinants of health, including racism, poverty, inadequate housing, housing instability,[88] and inability to access healthcare, are all interrelated. Attempts to create composite measures, such as the Child Opportunity Index, or geographic risk scores, have had mixed results. In the current administrative systems—optimized for billing and not prognostic accuracy—these data, however, are not captured reliably. How to measure social determinants of health while balancing accuracy and feasibility needs elucidation.

The utility of biomarkers also remains an unanswered question. Despite guidelines[89] identifying eosinophilia and fractional extraction of nitric oxide as risk factors for exacerbations, neither marker was examined in any readmission study. ETS is a known trigger for asthma exacerbations; however, self-reported ETS was not associated with readmissions in any study. Serum and salivary cotinine, ETS biomarkers, were associated with readmissions in one study.[62] It is unknown if this finding can be replicated or translated into action to aid in parental tobacco-cessation counseling. In addition, whereas e-cigarettes are associated with increased asthma exacerbations,[90] it is unknown if their use is also a risk factor for pediatric asthma readmissions.

Most studies employed traditional regression techniques—either Cox proportional hazards or logistic regressions—and some went beyond and used propensity matching to reduce confounding. Only one study, however, used newer machine-learning methods to model readmission risk.[91] These newer methodologies may reinforce previously discovered patterns of risk factors, or may reveal previously unknown risk-factor associations.[92] The utility of these novel methods is a key unanswered question.

Although readmission risk factors continue to deserve quantification and elucidation, interventions to reduce readmission risk ought to be the highest research priority. Only two RCTs were identified in this review, and they showed a small but real improvement in readmission reduction through nurse-led programs.[71,73] Potential opportunities for readmission reduction interventions are listed in Table 6.

Readmission reduction interventions, if effective, should preferentially target those at highest readmission risk; however, poor-quality datasets and modeling hinder this goal. Better

readmission prediction will require improvements in the quality of administrative databases. Retrospective studies of administrative databases lacking critical variables, such as social determinants of health, asthma severity on admission, and validated metrics of acute asthma severity, impair researchers' and quality-improvement scientists' ability to predict readmissions. Our systematic review suggests that, at a minimum, the risk factors identified herein (age, sex, race/ethnicity, admission season, and prior asthma hospitalization) should be incorporated into any dataset designed to measure or predict readmissions, but are likely insufficient to provide an adequate assessment of readmission risk.

Deeper exploration of some unexplained associations is needed. The association of female sex and late readmissions was surprisingly consistent. A recent systematic review examining risk factors associated with pediatric asthma exacerbations found no meaningful association between sex and exacerbation risk.[93] This discrepancy with sex as a clear risk factor for readmissions has a number of potential explanations, such as potential bias in acute asthma management based on sex, biological differences, etc., which deserve further investigation. Discovering the drivers of this association, which affects half the pediatric population, should urgently be investigated and addressed. The association of older age (>12 years old) and early readmissions was similarly consistent. This finding has been reported before, but the causes have not been fully described.[12] Qualitative interviews of key stakeholders (i.e., parents, primary care providers, and/or inpatient clinicians) may shed light on this and other risk factors for readmission.

Our findings have policy implications. Asthma is an ambulatory-care-sensitive condition and readmissions have been proposed as a marker of quality. Incentivizing early readmission-reduction programs is unlikely to be a good use of resources, given that the outcome is

uncommon and generally not preventable. Late readmissions are far more common; however, the degree of preventability is largely unknown. Incentivizing prevention of these late readmissions has the potential reduce waste, as some proportion of these readmissions should be amenable to appropriate outpatient care. There is some evidence that they are modifiable, and dedicated quality-improvement teams have decreased late readmissions through multi-modal efforts which have included not just a focus on asthma treatment plans, but ensuring outpatient follow-up, medications in-hand on discharge, and even discharge with an extra course of systemic corticosteroids.[91,92] These types of intensive programs have borne good results. The broad policy of mandating adherence to a home-management care plan on discharge from hospitalization, however, was not found to be associated with reduced readmission risk.[76] Without knowledge of the drivers, preventability, and downstream effects of readmissions, implementation of readmission reduction interventions that have an insufficient evidence base are unlikely to be effective.

Certain study limitations should be noted. Despite the participation of an experienced medical librarian, and previously validated pediatric search strings,[15] it is possible that not all pediatric asthma readmission risk factors were identified. Another limitation is the heterogeneity of methods used in published studies to identify readmission risk factors. We deliberately cast a wide net, including all pediatric age ranges and study designs; the resulting heterogeneous study findings therefore could not be combined in a meta-analysis. One systematic review that chose to conduct a meta-analysis also found most risk factors too heterogeneous to quantitatively synthesize. For some more commonly reported factors—sex, race/ethnicity, SES, and prior ED or hospital admission—those particular authors chose to calculate pooled estimates of effect

sizes.[13] We chose instead to report qualitative summaries and forest plots without quantitative synthesis in the attached tables (Figure 2 and Table 3). We believe that these choices resulted in the most inclusive systematic review to date of pediatric asthma readmission risk factors.

This systematic review identified prior admissions, index hospitalization LOS, and CCCs to be associated with both early and late pediatric asthma readmissions. Age, female sex, poverty, and seasonality were also found to be important predictors of readmissions. Addressing these risk factors in innovative, evidence-based, effective interventions will be critical in reducing pediatric asthma readmissions.

ABBREVIATIONS

aOR: adjusted odds ratio; aHR: adjusted hazard ratio; ETS: environmental tobacco smoke; CCC: complex chronic conditions; LOS: length of stay; PICU: pediatric intensive care unit; CI: confidence interval; ICS: inhaled corticosteroid; OCS: oral corticosteroid; LEP: limited English proficiency

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FIGURE LEGENDS

FIGURE 1; online: Selection of studies investigating pediatric asthma readmission risk factors

FIGURE 2: Forest plots of risk factors for early and late pediatric asthma readmission

Journal Pre-proof

TABLE 1, online: Database search strategy

Database	Search strategy	Hits
PubMed/Medline (National Library of Medicine, including Pre-MEDLINE and non-MEDLINE; 1945 to November 2019)	("Asthma"[Mesh] OR asthma*[tw]) AND ("Patient Readmission"[Mesh] OR readmit*[tw] OR readmis*[tw] OR re-admit*[tw] OR re-admis*[tw] OR rehospita*[tw] OR re-hospita*[tw] OR revisit*[tw] OR re-visit*[tw] OR reutiliz*[tw] OR (future[tw] AND admit*[tw]) OR (future[tw] AND admis*[tw]) OR (future[tw] AND hospita*[tw]) OR (future[tw] AND visit*[tw]) OR (future[tw] AND utiliz*[tw]) OR (repeat[tw] AND admit*[tw]) OR (repeat[tw] AND admis*[tw]) OR (repeat[tw] AND hospita*[tw]) OR (repeat[tw] AND visit*[tw]) OR (repeat[tw] AND utiliz*[tw]) OR (subsequent[tw] AND admit*[tw]) OR (subsequent[tw] AND admis*[tw]) OR (subsequent[tw] AND hospita*[tw]) OR (subsequent[tw] AND visit*[tw]) OR (subsequent[tw] AND utiliz*[tw])) AND (infan*[tw] OR newborn*[tw] OR new-born*[tw] OR perinat*[tw] OR neonat*[tw] OR baby[tw] OR baby*[tw] OR babies[tw] OR toddler*[tw] OR minors[tw] OR minors*[tw] OR boy[tw] OR boys[tw] OR boyfriend[tw] OR boyhood[tw] OR girl*[tw] OR kid[tw] OR kids[tw] OR child[tw] OR child*[tw] OR children*[tw] OR schoolchild*[tw] OR schoolchild[tw] OR school child[tw] OR school child*[tw] OR adolescen*[tw] OR juvenil*[tw] OR youth*[tw] OR teen*[tw] OR under*age*[tw] OR pubescen*[tw] OR pediatrics[mh] OR pediatri*[tw] OR peadiatric*[tw] OR school[tw] OR school*[tw] OR prematur*[tw] OR preterm*[tw])	1590
Scopus (Elsevier; 1966 to November 2019)	Title-Abstract-Keyword: (asthma* AND (readmit* OR readmis* OR re-admit* OR re-admis* OR rehospita* OR re-hospita* OR revisit* OR re-visit* OR reutiliz* OR (future AND admit*) OR (future AND admis*) OR (future AND hospita*) OR (future AND visit*) OR (future AND utiliz*) OR (repeat AND admit*) OR (repeat AND admis*) OR (repeat AND hospita*) OR (repeat AND visit*) OR (repeat AND utiliz*) OR (subsequent AND admit*) OR (subsequent AND admis*) OR (subsequent AND hospita*) OR (subsequent AND visit*) OR (subsequent AND utiliz*))) AND (infan* OR newborn* OR new-born* OR perinat* OR neonat* OR baby OR baby* OR babies OR toddler* OR minors OR minors* OR boy OR boys OR boyfriend OR boyhood OR girl* OR kid OR kids OR child OR child* OR children* OR schoolchild* OR schoolchild OR school child OR school child* OR adolescen* OR juvenil* OR youth* OR teen* OR under*age* OR pubescen* OR pediatri* OR peadiatric* OR school OR school* OR prematur* OR preterm*)	1731
Cochrane Central Register of Controlled Trials	All Text: asthma* AND (readmit* OR readmis* OR re-admit* OR re-admis* OR rehospita* OR re-hospita* OR revisit* OR re-visit* OR reutiliz* OR (future AND admit*) OR (future AND admis*))	709

(CENTRAL) (Wiley; through November 2019)	OR (future AND hospital*) OR (future AND visit*) OR (future AND utiliz*) OR (repeat AND admit*) OR (repeat AND admis*) OR (repeat AND hospital*) OR (repeat AND visit*) OR (repeat AND utiliz*) OR (subsequent AND admit*) OR (subsequent AND admis*) OR (subsequent AND hospital*) OR (subsequent AND visit*) OR (subsequent AND utiliz*)) AND (infan* OR newborn* OR new-born* OR perinat* OR neonat* OR baby OR baby* OR babies OR toddler* OR minors OR minors* OR boy OR boys OR boyfriend OR boyhood OR girl* OR kid OR kids OR child OR child* OR children* OR schoolchild* OR schoolchild OR school child OR school child* OR adolescen* OR juvenil* OR youth* OR teen* OR under*age* OR pubescen* OR pediater* OR peadiatric* OR school OR school* OR prematur* OR preterm*)	
CINAHL (Ebsco; 1937 to November 2019)	MH "Asthma+" AND (MH "Readmission" OR TX readmit* OR TX re-admit* OR TX re-admis* OR TX readmis* OR TX rehospital* OR TX re-hospital* OR TX revisit* OR TX re-visit* OR TX reutiliz* OR (TX future AND TX admit*) OR (TX future AND TX admis*) OR (TX future AND TX hospital*) OR (TX future AND TX visit*) OR (TX future AND TX utiliz*) OR (TX repeat AND TX admit*) OR (TX repeat AND TX admis*) OR (TX repeat AND TX hospital*) OR (TX repeat AND TX visit*) OR (TX repeat AND TX utiliz*) OR (TX subsequent AND TX admit*) OR (TX subsequent AND TX admis*) OR (TX subsequent AND TX hospital*) OR (TX subsequent AND TX visit*) OR (TX subsequent AND TX utiliz*)) AND (MH "Child+" OR MH "Adolescence+" OR MH "Minors(Legal)")	999
PsycInfo (Ebsco; 1887 to November 2019)	TX asthma* AND (TX readmit* OR TX readmis* OR TX re-admit* OR TX re-admis* OR TX rehospital* OR TX re-hospital* OR TX revisit* OR TX re-visit* OR TX reutiliz* OR (TX future AND TX admit*) OR (TX future AND TX admis*) OR (TX future AND TX hospital*) OR (TX future AND TX visit*) OR (TX future AND TX utiliz*) OR (TX repeat AND TX admit*) OR (TX repeat AND TX admis*) OR (TX repeat AND TX hospital*) OR (TX repeat AND TX visit*) OR (TX repeat AND TX utiliz*) OR (TX subsequent AND TX admit*) OR (TX subsequent AND TX admis*) OR (TX subsequent AND TX hospital*) OR (TX subsequent AND TX visit*) OR (TX subsequent AND TX utiliz*)) AND (TX infan* OR TX newborn* OR TX new-born* OR TX perinat* OR TX neonat* OR TX baby OR TX baby* OR TX babies OR TX toddler* OR TX minors OR TX minors* OR TX boy OR TX boys OR TX boyfriend OR TX boyhood OR TX girl* OR TX kid OR TX kids OR TX child OR TX child* OR TX children* OR TX schoolchild* OR TX schoolchild OR TX school child OR TX school child* OR TX adolescen* OR TX juvenil* OR TX youth* OR TX teen* OR TX under*age* OR TX pubescen* OR TX pediater* OR TX peadiatric* OR TX school OR TX school* OR TX	268

	prematur* OR TX preterm*)	
ClinicalTrials.gov (through December 2019)	Condition or disease: Asthma in Children Other terms: readmission	7
ISRCTN Registry (through December 2019)	asthma AND readmission	9

TABLE 3; online: Study Description of Included Articles

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Design: Randomized Control trial					
Fisher 2009[70]	RCT with Logistic regression	US	306	24 months	Asthma coach intervention 0.43 (0.23-0.81) Prior year admission 3.09 (1.59-6.02)
Madge 1997[68]	RCT with Cox regression	UK	201	2-14 months	Asthma home management training program: 0.39 (0.17-0.90) One prior admission 3.98 (1.12-14.21) Two+ prior admissions 8.34 (2.74-25.41)
Design: Comparative effectiveness					
Pinto 2019[93]	Multivariable logistic	US	214	1, 12 months	Bivariate: No difference in time to readmission for those in a multimodal, nurse-driven inpatient intentioned program 145.4 days (116.6-174.3) vs. 159.3 days (115.4-203.3) p=0.61
Design: Prospective Cohorts					
Auger 2013[37]	Multivariable Cox	US	601	12 months	Low medical home access 1.56 (1.06-2.32) Black/African American race 1.48 (1.02-2.17) Past inhaled steroid use 1.49 (1.03-2.15) Total "Parent's Perception of Primary Care" score not associated
Auger 2015[36]	Multivariable Cox	US	601	12 months	Asthma knowledge 1.04 (1.001-1.07) Black/African American race 1.58 (1.08-2.23) Prior hospitalization 1.91 (1.28-2.84) Poor medication adherence 1.61 (1.10-2.36) Poor medical home access 1.52 (1.01-2.30)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Beck 2012[47]	Multivariable Cox	US	601	12 months	Children living in high geographic risk areas: 1.75 (1.2-2.58) *Extreme poverty rate above national median, median home value below national median, or rate of adults with less than high school degree was above national median (total score range = 0-3)
Beck 2014[40]	Multivariable Cox with propensity weighting	US	774	12 months	Unadjusted African American race vs. white 1.98 (1.42-2.77) reduced to 1.44 (1.07-1.96) after adjusting for all available variables (SES variables, asthma severity, and financial hardship variables)
Beck 2016[41]	Multivariable Cox with propensity weighting	US	450	12 months	Unadjusted African American race vs. white 2.26 (1.56-3.26) reduced to 1.18 (0.87-1.6) after adjusting for all available variables using IPW.
Chen 2003a[69]	Multivariable logistic	US	115	12 months	Prior asthma admission 5.36 (1.9-15.14) Parents less bothered emotionally by their child's asthma (*emotion subscale of the PACQLQ) 1.64 (1.00-2.70) Parental report of less mastery with respect to their child's illness (on Impact of Family Scale) 0.68 (0.46-1.0)
Henry 1995[28]	Multivariable logistic	Australia	456	12 months	Age per year 1.1 (1.03-1.21) Parental asthma knowledge score not associated (primary outcome)
Howrylak 2014[59]	Multivariable logistic	US	774	12 months	Report of exposure: 1.18 (0.79-1.89) Serum cotinine 1.59 (1.02-2.48) Salivary cotinine 2.35 (1.22-4.55)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Kenyon 2018[56]	Multivariable logistic	US	2438	1 month	No significant difference for each 1-10 point increasing access composite score. 0.93 (0.79-1.10)
Mitchell 1987[61]	Bivariate	New Zealand	200	12 months	Single vs. multiple readmissions: Age of first asthma attack: 24.6 (16.3) vs. 32(24.4) months p=0.022 Unknown trigger for asthma attacks: 39.7 vs. 15.6 p<0.001 Changes in weather 36.2 vs. 60.7 p=0.044 Number of bad months per year: 1.8 (SD 2.4) vs. 2.6 (SD 2.3) p=0.021 Summer months were less problematic for single admits vs. multiple admits group (no p value reported) Allergies to food single 20.8 vs. 35.8 p=0.032, Dust mites: 25.0 vs. 49.1 p=0.001 Missed days of school in prior year 9.3 vs. 16.5 p=0.019 Differences in drugs prescribed: Theophylline 17% vs. 49% p=0.041 Sodium cromoglycate 14.1% vs. 29% p=0.005 Antibiotics 9% vs. 4% p=0.021
Moncrief 2014[45]	Multivariable logistic	US	526	12 months	≥ 1 night away from home per week 1.5 (1.2-2.0) Income <\$60,000 2.6 (1.1-6.4)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Newman 2014[46]	Multivariable Cox	US	758	12 months	Multivariable: Traffic related air pollution: 3.0 (1.1-8.1) for white children, 1.1 (0.6-1.8) for Black/African Americans Household income <\$60,000/year 3.1 (1.1-8.2) Controller medication use 0.5 (0.3-0.83)
Sporik 1993[94]	Bivariate	UK	83	5 to 6 months	Sensitized and still exposed to mite allergens (83% vs. 32% P<0.001)
Wever-Hess 2001[63]	Bivariate	Netherlands	100	12 months	Age 0-1 years, eczema protective (20% vs. 59% P=0.006) Age 2-4 years, antibodies against inhalant allergens 1.54 (1.22-1.95)
Design: retrospective cohorts					
Abe 2019[95]	Bivariate	Japan	216	36 months	Rhinovirus infection on index admission associated with readmission with Rhinovirus on future asthma hospitalization P<0.01)
Abu-Kishk 2016[66]	Bivariate	Israel	94	>120 months	PICU in index admission 42.5% vs. 25.5%, p=0.022
Aragona 2016[52]	Multivariable logistic	US	333	12 months	No association between obesity and readmission 1.1 (0.6 - 2.0)
Ash 2006[96]	Multivariable logistic	US	1068	24 months	White race vs. Black/African American race 15.8% vs. 22.5% Multivariable: Age 5-14 years vs. 15-39 years 0.85 (0.71-1.02)
Beck 2017[48]	Multivariable logistic	US	2539	12 months	No association between Overall Child Opportunity Index Categories or by sub categories (Education, Health and Environment, Social and Economic)
				Readmission	Results, Odds Ratio or Hazard Ratio

Citation	Analysis	Location	N	Timeframe	(95% CI)
Bettenhausen 2015[51]	Multivariable logistic	US	518	1, 3 months	BMI for age not associated with readmission.
Bloomberg 2003[43]	Multivariable Cox	US	8761	120 months	Black vs. White/other race 0.83 (0.73-0.94) Medicaid or self-pay not significant alone 1.02 (0.84-1.26) Interaction of Medicaid/self-pay and Black race 1.28 (1.03-1.58) with commercial, insurance/ or white other race as reference Probability of readmission increases with each subsequent admission
Brittan 2017[44]	Multivariable logistic	US	9288	15 - 90 days	Post discharge outpatient OCS prescription fill had highest association with readmission 3.2 (2.4 - 4.6) Preceding hospitalization 2.9 (2.0 - 4.0) OCS prescription fill 2 (1.5-2.7) preceding ED visit 1.5 (1.1-1.9) Medicaid fee for service plan vs. managed care plan 1.5 (1.1-2.1) Summer vs. fall discharge 1.5 (1.1-2.0) Summer dc vs. fall dc height chance of readmit 1.5 OR Spring was protective 0.65 (0.45-0.85)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Bucholz 2018[25]	Multivariable Cox	US	170177	7, 15, 30 days	1-7 days: 14-17 years vs. <4 years 1.74 (1.23-2.48) Number of chronic conditions: 2-3 1.57 (1.21-2.04), 4+ 5.1 (3.48-7.52) 8-15d: Number of chronic conditions: 2-3 1.49 (1.15-1.92), 4+ 4.90 (3.58-6.69); 16-30d: Age (referent: < 5 years old): 5-9 years old 0.74 (0.55-0.98) 10-13 years old 0.70 (0.54-0.91) Number of chronic conditions: 2-3 1.70 (1.29-2.24), 4+ 5.68 (4.23-7.62)
Chabra 1998[38]	Multivariable logistic	US	6844	12 months	African American 1.94 (1.49-2.49) Latino 1.34 (1.04-1.72) LOS >4 days 1.35 (1.05-1.74)
Chen 2003b[19]	Multivariable Cox	Canada	86863	36 months	Age (15-19 years as reference) <1 year 2.36 (2.15-2.59), 1-4 years 1.54 (1.41-1.69). 5-9 and 10-14 not significantly different Female increased readmission risk for 10-14 years (1.47(1.34-1.60)) and age 15-19 (1.35 (1.22-1.49)) No gender difference at ages <1, 1-4, or 5-9
Delmas 2011[20]	Multivariable logistic (with sub-analysis stratified bivariate)	France	87598	7 days, 12 months	Bivariate stratified by age: 10-14 years, Female vs. Male: 1.31 (1.07-1.60) 10-20 Female vs. Male 1.54 (1.13-2.10) Bivariate: Age with 2-4 years as reference: 5-9 0.81 (0.73-0.89), 10-14 years 0.87 (0.78-0.98); 15-19 years 0.69 (0.59-0.81)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
DeWolfe 2018[97]	Multivariable Cox	US	2427	3 days, 1 month	No significant difference between hospitalist with residents vs. hospitalist with advanced practice providers: 3 days: 1.1 (0.9-6.7) 1 month 1.3 (0.6-2.6) No significant difference at 3 or 30 days between HRS and HAPPS.
Douglas 2019[98]	Multivariable linear propensity score	US	5334	7 days, 1, 3 months	Azithromycin not associated with readmission risk: 0.89 (0.46-1.72)
Farber 1998[30]	Multivariable logistic	US	277	12 months	Age <5 years vs. 5-13 years 4.36 (1.02-9.41) Prior admission 2.34 (1.19-4.60) Asthma class within six months of discharge not significant (primary outcome)
Fisher-Owens 2006[99]	Multivariable logistic	US	17406	3 days, 12 months	Black/African American race vs. White race 3-day readmission 0.28 vs. 0.42 p=0.002 12-month 11.4 vs. 7.7 P<0.0001 Multivariable results not presented numerically or with tests of association: "black patients almost twice as likely as whites to return to the hospital within the year"

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Gay 2019[100]	Multivariable logistic	US	53503	15 days	Shorter LOS associated with 15-day readmission rate. Beta coefficient -1.22, $p=0.03$ 81.8 additional days were required with a cost of \$2,502/day (or \$204,638 for 81.8 additional bed-days)
Giarola 2014[58]	Bivariate	Australia	200	12 months	No significant difference between Indigenous vs. Non-indigenous children (27.5% vs. 27.5% $P=0.99$)
Jroundi 2019[21]	Multivariable Cox	US	66835	6, 12, 60 months	ICU admission 1.23 (1.17-1.30) (Primary); Age (12-17 reference) 2-5 years 1.21 (1.14-1.28), 6-11 years 1.07 (1.01-1.14) Female 1.07 (1.03-1.11) Race/ethnicity (white race reference) Black 1.44 (1.37-1.53), Hispanic 1.27 (1.20-1.35); Other race 1.17 (1.09-1.26) Median household income (top quartile reference) 51st-75th income percentile 1.07 (0.99-1.14), 26th-50th income percentile 1.08 (1.01-1.16), 0 to 25th income percentile 1.27 (1.19-1.35) Payer (Private insurance reference) Medicaid 1.10 (1.05-1.15), Other 1.03 (0.96-1.11) LOS per day 1.05 (1.04-1.06)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Kenyon 2014[5]	Multivariable logistic	US	44204	7, 15 days; 1, 2, 6, 12 months	Significant at all time points (7 days, 15 days, 1, 2, 6, 12 months) Prior year asthma admission (OR range 1.3-1.4) Age 12-18 years (OR range 1.1-4.7) CCC (OR range 1.5-2.4) Discharging hospital has high readmission rate (OR range 1.3-1.4) Discharged to home [protective] (OR range 0.3-0.8) ICU stay [protective] (OR range 0.4-0.9) Associated at 12 months and beyond: Female sex Non-Hispanic Black: 1.8 (1.6-1.9) Hispanic 1.3 (1.2-1.4) Public insurance 1.3 Magnesium given 1.3 LOS >1 day (OR range 1.3-1.6)
Kenyon 2015[71]	Multivariable Cox	US	31658	15 days, 3 months	0-15 days: Beta agonist fill 0.67 (0.51-0.87) ICS fill 0.59 (0.42-0.85) If filled all 3: 0.32 (0.16-0.60) 15-90d: ICS fill 0.87 (0.77-0.98) Absolute risk reduction of 5.27 to 4.62% (-13%). If filled all 3: 0.83 (0.72-0.97)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Knighton 2013[26]	Multivariable logistic	US	4965	1 month	Asthma severity Major vs. Mild 1.71 (1.05-2.76); Age with 1-4 years reference: <1 year 2.58 (1.69-3.93), 15-17 years 2.52 (1.37-4.64) Payer Medicare/Medicaid vs. private insurance 1.59 (1.17-2.18) Index LOS 1.04 (0.98-1.10) (primary outcome).
Kocevar 2004[76]	Multivariable Cox	Denmark, Sweden, Norway, and Finland	9635	24 months	With Norway as reference group, Sweden 1.24 (1.11-1.38) and Denmark 1.18 (1.06- 1.32)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Liu 2009[33]	Multivariable Cox	US	2919	48 months	Public insurance: 1.40 (1.1-1.78) Age 0-4 reference 5-10 0.58 (0.44-0.78) 11-18 0.57 (0.40-0.81) Season Winter reference: Summer 1.83 (1.31-2.54) Fall 1.39 (1.07-1.81) Spring Not associated 1.23 (0.94-1.61) LOS 3+ days 1.65 (1.28-2.10) vs. 1 day. High proportion of minority residents 1.33 (1.02-1.74) High proportion of neighborhood poverty and high crowded housing conditions NOT associated with higher readmission rates. Readmission rate for children living in predominantly minority neighborhoods was 43% higher than children living in predominantly white communities 1.43 (1.10-1.85)
Macarthur 1996[60]	Bivariate	Canada	68	12 months	Follow-up on discharge with pediatrician or pulmonologist 0.48 (0.29-0.79) ICS or sodium cromoglycate use 0.52 (0.28-0.97)
Mitchell 1984[101]	Multivariable logistic	New Zealand	3625	12 months	Polynesians readmitted more than Europeans 34.9% vs. 23.8% $P < 0.001$

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Mitchell 1994[6]	Multivariable Cox	New Zealand	1034	33 months	Female: 1.23 (1.04-1.45); Age <5 1.71 (1.41-2.08); Prior admissions: 1: 1.32 (1.03-1.70) 2: 1.68 (1.24-2.26) 3: 2.00 (1.47-2.71) 4+: 2.80 (2.23-3.51) Medications during index admit: IV treatment 1.29 (1.08-1.55); Theophylline 0.51(0.28-0.92)
Okubo 2017[50]	Multivariable logistic	Japan	38679	1 month	Obese vs. normal weight 1.26 (1.03-1.54) Underweight and overweight not associated with readmission.
Parikh 2017[35]	Multivariable generalized linear mixed effects	US	3906	1, 3, 6, 12 months	1 month: No significant difference by race/ethnicity at 1 month 3 months: Non-Hispanic White (reference) Non-Hispanic black 1.3 (1.2-1.5) Hispanic 0.9 (0.8-1.1), Other 0.9 (0.8-1.1) 6 months: Non-Hispanic White (reference) Non-Hispanic black 1.6 (1.4-1.7) Hispanic 1.1 (1-1.2), Other 1 (0.9-1.1) 12 months: Non-Hispanic White (reference) Non-Hispanic black 1.7 (1.6-1.8) Hispanic 1.1 (1-1.2), Other 1 (0.9-1.1)
Raymond 1998[102]	Bivariate	Australia	121	12 months	Decrease in "negative perceived consequences" of asthma: 0.31 (0.12-0.83). Example statements: "Treating my child for his asthma is very frustrating"

				Readmission	Results, Odds Ratio or Hazard Ratio
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Citation	Analysis	Location	N	Timeframe	(95% CI)
Rottem 2005[31]	Bivariate	Israel	1,208	12 months	Longer LOS for index admission (3.3 vs. 2.7 days $P=0.002$); Seasonal difference for readmissions: Fall 30.2, Winter 26.3, 25.0 % spring, 16.0 Summer ($p<0.0001$). fewer readmissions for 0-3 year olds.
Ryan 2019[49]	Bivariate	US	328	1 month	Older age 11.8 +- 3.1 vs. 8.9 +-3.4 years $p=0.01$ Weight 57 +/-21.9 vs. 39.2 +- 22.6 kg $p=0.02$ Severity classification moderate or severe 89% vs. 47% $p=0.01$ Prior intubation 33 vs. 4% $p<0.01$ History of prematurity 55% vs. 7% $p<0.01$ Pediatric Asthma Severity Score poorly predicted unplanned readmission Area- Under-the-Curve 0.28 (0.11-0.44).
Sazonov Kocevar 2005[103]	Multivariable Cox	Norway	2,961	24 months	Allergic rhinitis 1.72 (1.34 - 2.21)
Schaubel 1996[67]	Bivariate	Canada	16,429	>30 months	Probability of asthma readmission: 1 prior hospitalization 42%, 3 prior hospitalizations 59%, 3 prior hospitalizations 76%
Senthilselvan 1995 [24]	Multivariable linear regression	Canada	19,934	12 months	10-14 year-old girls: 1.6 (1.3-1.9)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Silber 2003[77]	Multivariable Cox	US	38,310	21 days	Readmission from NYC children's hospital vs. Philadelphia/Pittsburg 3.38 (P<0.0001) Odds of readmission in general hospital in NYC vs. general hospital in Philadelphia/Pittsburgh: 2.33 (P<0.001) General hospitals outside of NYC vs. outside of Pittsburg/Philadelphia 2.38 (P<0.0001). No difference comparing intra state readmission rates (NYC Children's Hospital vs. NYC general hospital 1.04 P=0.63), Pittsburgh/Philadelphia children's vs. Pittsburgh/Philadelphia general (0.72 P = 0.33)
Silber 2017[34]	Matched cohort	US	22,158	10 days, 1 month	No difference at 10 days: Black patients 0.9% vs. 1.0% p=0.68, No difference at 30 days: Black patients 2.6% vs. White patients 2.5% p=0.49.
Shin 2018 [88]	Machine learning	US	3,678	12 months	Random forest based algorithm had 66% accuracy predicting readmissions using census tract sociodemographic data. Most important variables were age and LOS.
To 1996 [32]	Bivariate	Canada	28,646	12 months	0-4 years vs. 5-17 years 1.39 (1.30-1.46)
Tolomeo 2009 [29]	Multivariable logistic	US	298	12 months	Age 1.102 (1.003-1.21) Prior asthma related ED visit 3.12 (1.16-8.33)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Tse 2017 [65]	Multivariable Cox	Canada	26,168	1, 3, 6, 12, 36, 60 months	6-month readmission: ICU 8.8% vs. Non-ICU 6.5% (P=0.005) 12-month readmission: ICU 13.8% vs. Non-ICU 10.4% (P=0.002) 36-month readmission: ICU 24.1% vs. Non-ICU 18.1% (P<0.001) 60-month readmission: ICU 28.3% vs. Non-ICU 22.8% (P<0.001)
Valovirta 2002[104]	Bivariate	Finland	1,488	12 months	2-5 years vs. 6-14 years: 25.7% vs. 5.8% (P not reported).
Veeranki 2018[27]	Multivariable Cox	US	12,842	1 month	Age 12-18 vs. 6-11 1.59 (1.22-2.07) Private insurance vs. Medicaid 0.69 (0.51-0.95) Central county >1million population 1.50 (1.00-2.24), Micropolitan 2.46 (1.36-4.45) LOS: >4 days vs.<2 days 1.56 (1.02-2.38) Teaching status rural hospital as reference: Urban, no teaching 2.11 (1.02-4.32), Urban teaching 2.25 (1.16-4.39) Discharge disposition: skilled facility vs. home/home healthcare 2.53 (1.33-4.79); CCC 3.21 (2.31-4.47).
Vicendese 2014[22]	Multivariable logistic	Australia	33,559	1, 12 months	1 month: Girls vs. Boys 1.15 (1.004-1.32) 12 months: Girls vs. Boys 1.11 (1.05-1.19)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Wallace 2004[39]	Case cohort	USA	21016	6 months	(White as reference, no P value or 95% CI reported) Female: 1-4 years Black 1.6, Hispanic 1.7; 5-9 years Black 2.4, Hispanic 2.5 10-14 years Black race 3.0, Hispanic ethnicity 2.2; Male: 1-4 years Black 1.7, Hispanic 1.7; 5-9 years Black 2.1, Hispanic 2.4 10-14 years Black race 2.2, Hispanic ethnicity 1.6;
Design: Case Control					
Alshehri 2005[54]	Multivariable logistic	Saudi Arabia	28	2 months	Prior admission 2.21 (1.08-9.10) NICU at birth 4.44 (1.7-9.34) Bronchopulmonary dysplasia 3.06 (2.01- 8.7.95) Recurrent aspiration 1.96 (1.08-4.63) >5 days asthma symptoms on presentation 0.15 (0.03-0.42) Infiltrate on CXR 0.04 (0.011-0.13) IV steroids 0.104 (0.016-0.32)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Cohen 2000[53]	Case Control	US	107	1 month	Prior admit for asthma 4.88 (99% CI 3.24-7.26) Prematurity 5.2 (99% CI 1.72-15.4) History of other co-morbid disease 4.3 (99% CI 1.89-9.82) White race 2.81 (99% CI 1.69-4.66) Admission from clinic 2.38 (99% CI 1.02-5.56) Fall/Winter admission vs. Spring/Summer 1.94 (99% CI 1.23-3.06) LOS >3 days 2.67 (99% CI 1.0-7.12) Anticholinergic medication on discharge 3.7 (99% CI 1.24-10.77) Oral steroid on discharge 3.26 (99% CI 2.68-3.96)
Minkovitz 1999[23]	Bivariate	US	119	12 months	Female 63% vs. 29% P<0.001 Other chronic conditions 69 vs. 49% p=0.049 Medications: Albuterol sulfate 89% vs. 69% p=0.02 Cromolyn sodium 49% vs. 21% p=0.003 Inhaled corticosteroids 17% vs. 5% p=0.03 Pulmonary consult 23% vs. 4% p=0.001 Pulmonary consult in year post discharge 37% vs. 12% p=0.002
Reznik 2006[57]	Case Control	US	445	1 month	Prior admission 1.89 (1.10-3.25)
Rushworth 1995[78]	Case Control	Australia	*	2 weeks to 6 months	Rural 8.9% vs. Metropolitan 19.1% p<0.001

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Vicendese 2015[64]	Multivariable logistic	Australia	44	24 months	Airborne fungus: Cladosporium 1.68 (1.04-2.72) Total fungi and yeast not significant. Odds readmission with Cladosporium doubling. 1.52 for yeast Frequency of vacuuming frequently vs. infrequently 15.69 (2.82-87.18) Carpet in children's bedroom 4.07 (1.03-16.06) Bedding synthetic vs. feather doona 14.62 (1.26-169.4)
Design: Cross-sectional					
Morse 2011[105]	Multivariable logistic	US	37267	7 days, 1, 3 months	No association with 5% improvement in CAC-3 compliance with readmissions at 7 days, 30 days, 90 days
Quality Improvement					
Bergert 2014[75]	Interrupted Time Series	US	1,295	1, 3, 6 months	CAC-3 compliance intervention at 91-180 days: 0.29 (0.11-0.78) Not significant at 0-30 or 31-90 days
Fassl 2012[74]	Multivariable logistic	US	1865	6 months	Pre-post implementation of asthma pathway 0.67 (0.50-0.91) adjusted odds of readmission. Key intervention was prolonged CAC-3 compliance.
Krupp 2017[106]	Quality Improvement	US	526	1 month	Multifaceted QI intervention decreased readmission rate to 1.65-2.40 from 3.5-7.98%
Lo 2018[107]	Quality Improvement	US	3261	3, 7, 14 days	No significant difference when changing discharge criteria from albuterol every 4 hours to every 3 hours at 3 days 0.94 (0.42-2.10), 7 days 1.24 (0.64-2.40), 14 days 1.21 (0.68-2.18)

Citation	Analysis	Location	N	Readmission Timeframe	Results, Odds Ratio or Hazard Ratio (95% CI)
Zipkin 2017[42]	Multivariable logistic	US	1,176	6 months	CAC-3 full compliance vs. none/partial 0.81 (0.53-1.22) (primary analysis), If CAC-3 full and partial vs. none: 0.63 (0.41-0.95) Age (reference 13-17) 2-5 years 0.44 (0.44-0.79), 6-12 years 0.58 (0.390-0.88) Hispanic ethnicity 0.58 (0.39-0.88)
Abbreviations: 95% CI: 95% Confidence interval; RCT: Randomized controlled trial; US: United States; UK: United Kingdom; SES: Socioeconomic status; IPW: Inverse propensity weighting; PACQLQ: Pediatric Asthma Caregiver's Quality of Life Questionnaire; PICU: Pediatric intensive care unit; BMI: Body mass index; OCS: Oral corticosteroids; ED: Emergency department; LOS: Length of stay; NYC: New York City; CAC-3: Children's Asthma Care Measure 3 * = data not reported.					

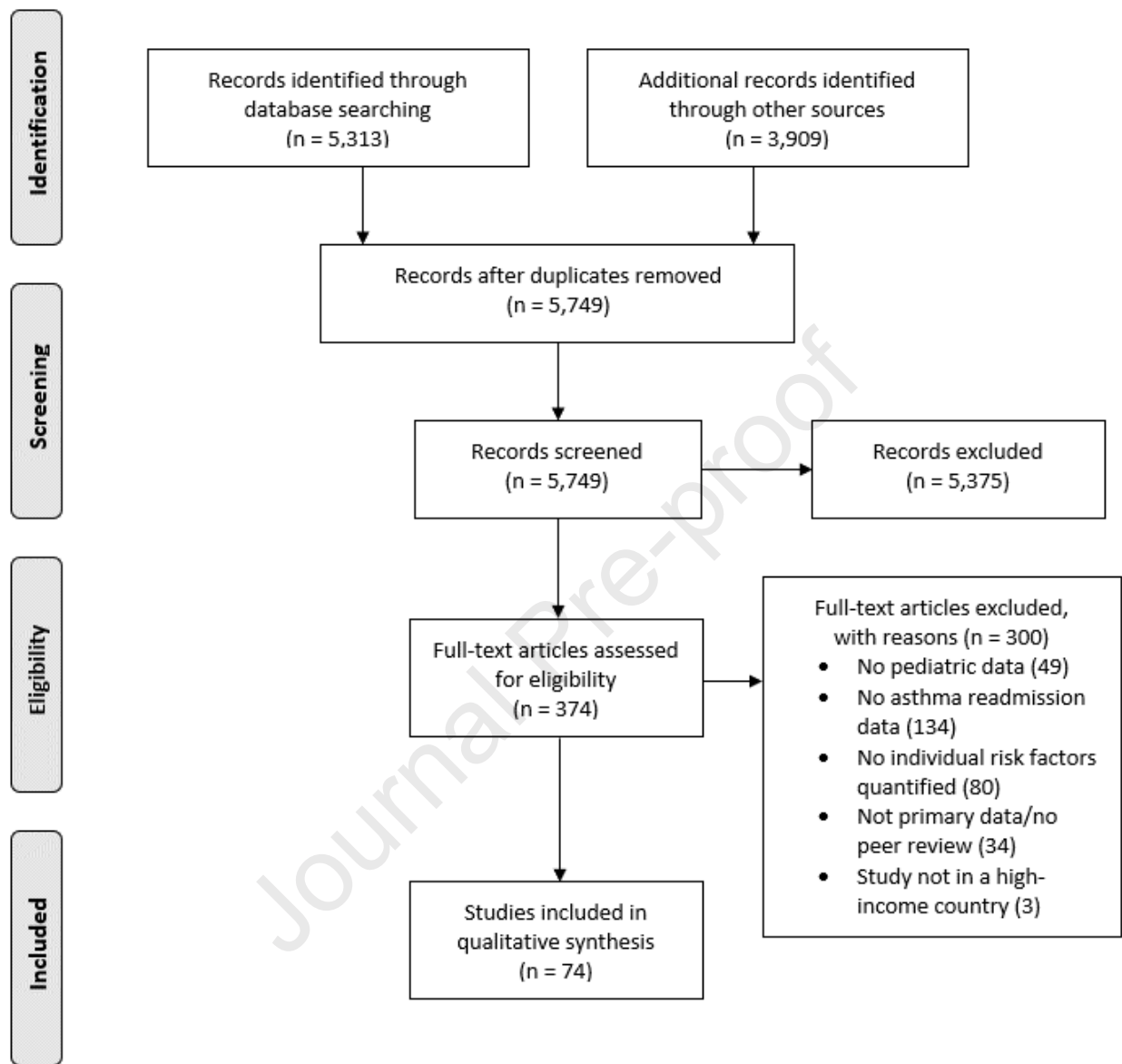
FIGURE 1; online. Selection of studies investigating pediatric asthma readmission risk factors

TABLE 5; online. Risk-of-bias assessment for included studies

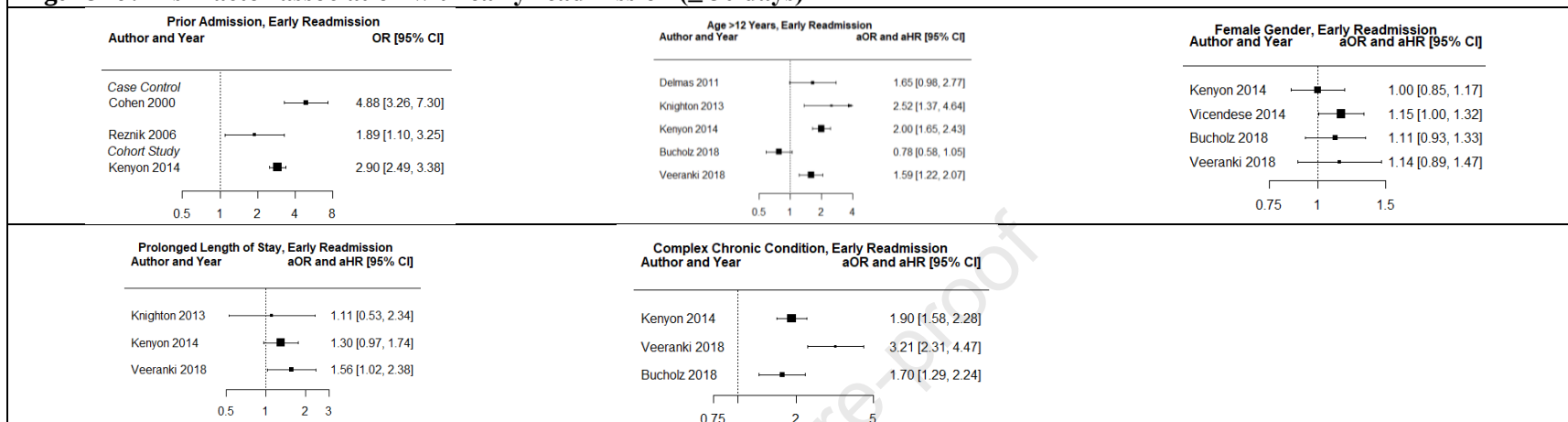
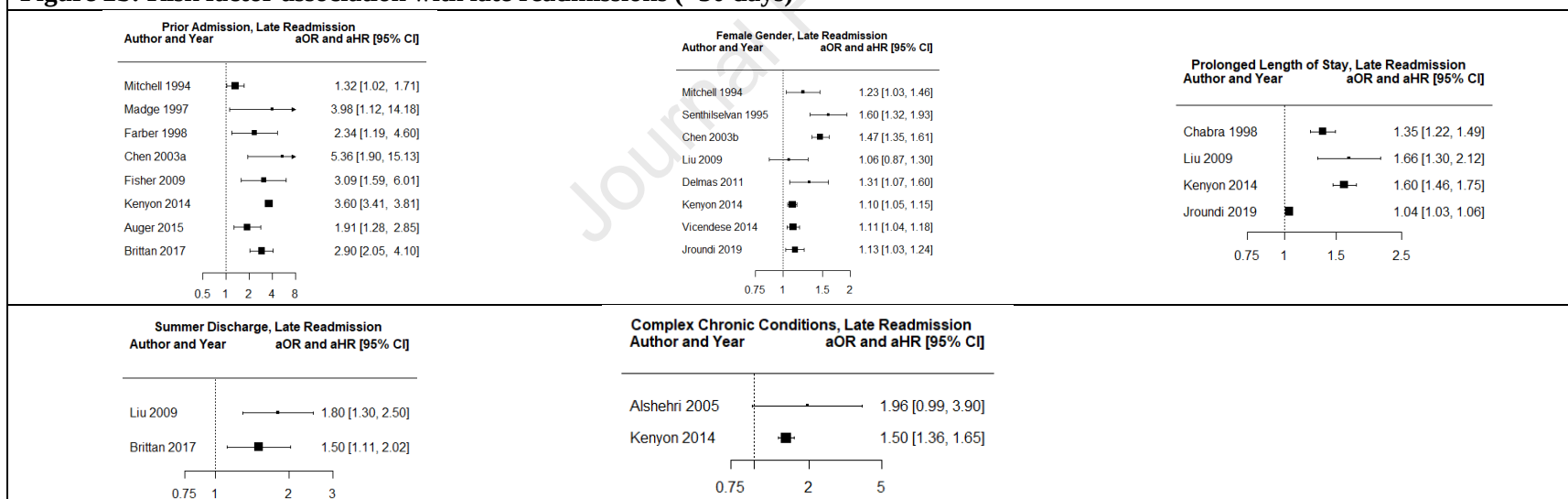
Design: randomized controlled trials						
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Fisher 2009						
Madge 1997						
Design: comparative effectiveness						
	Selection		Comparability		Outcome	
Pinto 2019	★★★★		★★		★★★	
Design: prospective cohorts						
	Selection		Comparability		Outcome	
Auger 2013	★★★★		★★		★★	
Auger 2015	★★★★		★★		★★	
Beck 2012	★★★★		★		★★★★	
Beck 2014	★★★★		★★		★★★★	
Beck 2016	★★★★		★★		★★★★	
Chen 2003a	★★★★		★★		★★★★	
Henry 1995	★★★		★★		★★	
Howrylak 2014	★★★★		★★		★★★★	
Kenyon 2018	★★★★		★★		★★	
Mitchell 1987	★★★★		★★		★★★★	
Moncrief 2014	★★★★		★★		★★	
Newman 2014	★★★★		★★		★★★★	
Wever-Hess 2001	★★★				★★★★	
Design: retrospective cohort						
	Selection		Comparability		Outcome	
Abe 2019	★★				★★★★	
Abu-Kishk 2016	★★★★		★		★★	

	Selection	Comparability	Outcome
Aragona 2016	★★★★	★★	★★★
Ash 2006	★★★★	★★	★★★
Beck 2017	★★★★	★★	★★★
Bettenhausen 2015	★★★★	★	★★★
Bloomberg 2003	★★★★	★★	★★★
Brittan 2017	★★	★★	★★★
Bucholz 2018	★★★★	★	★★★
Chabra 1998	★★★★	★★	★★★
Chen 2003b	★★★★	★	★★★
Delmas 2011	★★★★		★★★
DeWolfe 2018	★★★★	★★	★★★
Douglas 2019	★★★★	★★	★★★
Farber 1998	★★★★	★	★★★
Fisher-Owens 2006	★★★★	★★	★★★
Gay 2019	★★★★		★★★
Giarola 2014	★★★★	★★	★★★
Jroundi 2019	★★★★	★★	★★★
Kenyon 2014	★★★★	★★	★★★
Kenyon 2015	★★★★	★★	★★★
Knighton 2013	★★★★	★★	★★★
Kocevar 2004	★★★★	★	★★★
Liu 2009	★★★★	★★	★★★
Macarthur 1996	★★★★	★	★★★
Mitchell 1984	★★★★	★	★★★
Mitchell 1994	★★★★	★★	★★★
Okubo 2017	★★★★	★	★★★
Parikh 2017	★★★★	★★	★★★
Raymond 1998	★★★★	★★	★★★
Rottem 2005	★★★★	★★	★★★
Ryan 2019	★★★★	★★	★★★
Sazonov Kocevar 2005	★★★★	★	★★★
Schaubel 1996	★★★★		★★★
Senthilselvan 1995	★★★★	★	★★★
Silber 2003	★★★★	★★	★★★
Silber 2017	★★★	★★	★★★
Shin 2018	★★★★	★★	★★★
To 1996	★★★★		★★★
Tolomeo 2009	★★★★	★★	★★★

	Selection	Comparability	Outcome
Tse 2017	★★★★	★★	★★★
Valovirta 2002	★★★★	★	★★★
Veeranki 2018	★★★★	★★	★★★
Vicendese 2014	★★★★	★	★★★
Wallace 2004	★★★★	★	★★★
Design: case-control			
	Selection	Comparability	Exposure
Alshehri 2005	★★★★	★	★★★
Cohen 2000	★★	★★	★★★
Minkovitz 1999	★★★★	★	★★★
Reznik 2006	★★★★	★	★★★
Rushworth 1995	★★★★	★	★★★
Vicendese 2015	★★★	★★	★★★
Design: cross-sectional			
	Selection	Comparability	Outcome
Morse 2011	★★★★	★★	★★★
Design: quality improvement			
	Selection	Comparability	Outcome
Bergert 2014	★★★★	★	★★★
Fassl 2012	★★★★	★★	★★★
Krupp 2017	★★★★	★	★★★
Lo 2018	★★★★	★★	★★★
Zipkin 2017	★★★★	★★	★★★

TABLE 2. Study design and statistical analysis by asthma readmission outcome

Characteristic	Early Readmission (≤ 30 days)	Late Readmission (>30 days)
N	26	60
Study design, n (%)		
Randomized controlled trial	0 (0)	2 (3.3)
Prospective cohort	1 (3.8)	13 (21.7)
Retrospective cohort	19 (73.1)	37 (61.6)
Case-control	2 (7.7)	4 (6.6)
Cross-sectional	1 (3.9)	1 (1.6)
Quality improvement	3 (11.5)	3 (5.0)
Analysis, n (%)		
Bivariate	3 (11.5)	13 (21.6)
Logistic regression	15 (57.7)	28 (46.7)
Cox proportional-hazards	6 (23.1)	14 (23.3)
Regression with propensity adjustment	1 (3.9)	3 (5.0)
Interrupted time series	1 (3.9)	1 (1.7)
Machine learning	0 (0)	1 (1.7)
Publication year by NHLBI Guideline		
Pre EPR-1 (pre-1991)	0 (0)	2 (3.3)
EPR-1 (1991-1996)	0 (0)	8 (13.3)
EPR-2 (1997-2001)	1 (3.8)	6 (10.0)
EPR-2 update (2002-2006)	3 (11.5)	11 (18.3)
EPR-3 2007 (2007-2019)	22 (84.6)	33 (55.0)
NB: 12 studies investigated both early and late readmission outcomes		
Abbreviations: NHLBI: National Heart Lung and Blood Institute; EPR: Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma		

FIGURE 2. Forest plots of risk factors for early and late pediatric asthma readmission**Figure 2a: Risk factor association with early readmission (≤ 30 days)****Figure 2b: Risk factor association with late readmissions (>30 days)**

Adjusted odds ratios and hazard ratios displayed together to demonstrate consistency of effect. Meta-analysis not performed due to heterogeneity of study methods. Therefore, summary statistics are not presented.

TABLE 6. Potential interventions for reducing asthma readmissions identified in a systematic review of the literature.

Potential Interventions
“Medications-in-hand” for patients at discharge [108]
Bluetooth-enabled inhalers [109]
Single maintenance and reliever therapy (SMART) [110]
Parent mentors or community health workers [111]

TABLE 4. Categorization of risk factors associated with early and late pediatric asthma readmissions

Risk Factors for Early Readmission (≤ 30 days)	Risk Factors for Late Readmission (> 30 days)
<i>Sociodemographic:</i>	<i>Sociodemographic:</i>
Age	Age:
< 5 years old [20,25,26]	Age <5 years old [6,19–21,30,32–34]
>12 years old[25–27,52,59]	Age >12 years old -Increased association[5] -No association[43]
	Age increasing per year [28,29]
Female sex [20,22,27]	Female sex [5,6,19–24]
Black race/ethnicity -Decreased association[36] -No association[5,35,37]	Black race/ethnicity -Increased association [5,21,36–43] -No association [44]
Latino race/ethnicity -No association [37]	Latino race/ethnicity -Increased association [5,21,37,40,41] -Decreased association [45]
Public insurance[5,26,27]	Public insurance [5,21,33,46]
	SES or low income[21,48,49]
<i>Comorbidities</i>	<i>Comorbidities</i>
CCC [5,25,27,56]	CCC [5,25,57]
Prematurity [52,56]	Prematurity [57]
Obesity -Increased association [53] -No association[54]	Obesity -Increased association [54] -No association [55]
<i>Environmental factors</i>	<i>Environmental factors</i>
	Summer season [33,47,64]
<i>Episode severity</i>	<i>Episode severity</i>
Long LOS -Increased association [27,56] -No association [26]	Long LOS [5,21,31,33,40]
ICU stay -Decreased association[5] -No association [68]	PICU stay -Increased association [21,69] -Decreased association [5]
Asthma severity [26,52]	
<i>Use of health services</i>	<i>Use of health services</i>
Prior asthma admission [5,56,60]	Prior admission [5,6,30,31,38,47,59,64,70–74]
Non-home disposition [5,27]	ED Visits [29,47]
	Low medical-home access [38,39]
	Pulmonologist follow-up [23,63]

Risk Factors for Early Readmission (≤ 30 days)	Risk Factors for Late Readmission (> 30 days)
<i>Institutional factors</i>	<i>Institutional factors</i>
Asthma treatment plan -No association[76]	Asthma treatment plan -No association[76]
	Asthma treatment plan and multimodal QI -Decreased association [77,78]
	<i>Family factors</i>
	Asthma knowledge -Increased association [38,72] -No association [28]
	Less emotionally bothered by asthma/negative perceived consequences of asthma [72,94]
Risk factors identified in only one study: New York City vs Philadelphia [80]; Central country > 1 million population [27]; Micropolitan [27] ; Medication fill prior to discharge [74]; High readmission hospitals [5]; Ethnicity (international)[95] NS[61]; Medicaid fee for service vs managed care[47]; Geographic risk score[50]; Sleeping away from home one night per week [48]; Eczema [66]; Allergic rhinitis [96]; Inhaled allergens [66]; Fungus [67]; Frequent vacuuming, carpet in kids room; Objective environmental tobacco smoke marker (serum/salivary cotinine) [62]; Traffic pollution [49]; Changes in weather[64]; Food allergies [64]; Sweden vs Denmark[79]; Metropolitan vs rural [81]; missed days of school [64]; Prescription fill on discharge (Protective) [74] Oral corticosteroid[47];	
Interventions: Quality improvement intervention [protective][97]; Asthma coach intervention protective [73] Quality improvement asthma pathway protective [77] High completion rate of Asthma Action Plan [78] NS[98]; nurse home management program [71]	
Abbreviations: CCC: Complex chronic conditions; LOS: Length of stay; ICU: Intensive care unit; ED: Emergency department; QI: Quality improvement	



PRISMA 2009 Checklist: Risk Factors for Pediatric Asthma Readmissions

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	49 Sup Table 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	N/A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A



PRISMA 2009 Checklist: Risk Factors for Pediatric Asthma Readmissions

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, 27 Fig. 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	30
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	45
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	28
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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