

# WORKING P A P E R

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## Estimating the Impact of Improving Asthma Treatment

### A Review and Synthesis of the Literature

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## PREFACE

Over 30 million Americans are suffering from asthma and it is the most common chronic disease among children. While asthma has become an inherently treatable disease, actual treatment continues to fall short of recommended care. And, in spite of their higher prevalence of disease, minority children are less likely to receive adequate treatment. Thus, many asthma attacks could be avoided - and much suffering prevented, if nationally accepted treatment guidelines were consistently followed. Better treatment could also reduce healthcare spending, since a substantial proportion of cost is due to potentially avoidable hospital admissions and emergency room visits.

Improving asthma care is also not simple. As it is a multifactorial disease, treatment has to go beyond pharmacologic therapy and has to address environmental factors, allergens and lifestyle. Disadvantaged populations who face real and perceived barriers to access of care are disproportionately affected. Innovative ways of delivering and financing care are therefore needed.

This report, funded by the Merck Childhood Asthma Network, Inc., tries to inform the debate about better ways to care for asthma by synthesizing the research on the cost and benefits of better asthma care:

- 1) What are the gaps in the quality of asthma care for children and all patients;
- 2) What are the clinical and policy implications of those gaps (e.g., excess morbidity and mortality, avoidable hospitalizations, loss school/work days);
- 3) What would it cost to close the quality gaps; and
- 4) What would be the return on investment/cost-benefit ratio of better asthma care?

For this work, RAND scanned over 2700 publications from the peer-reviewed and other literature and extracted information into a database.

The data were analyzed to find patterns and commonalities in the published evidence.

The results show that although the quality of asthma care is an area of active research, it is impossible to derive reasonably bounded consensus estimates for the cost and benefits of better asthma care, because there is not enough research that assesses the economic impact of better care and because researchers used a staggering variety of criteria to recruit their study patients and a staggering number of study outcomes, making it all but impossible to compare results across studies. While it was not possible to obtain reasonable estimates of the costs or benefits of care, some important findings did emerge. Consistent with previously published reports, quality of asthma care has substantial gaps and disadvantaged populations appear to receive worse care.

Our findings suggest the need for more economic evaluations of the impact of gaps in asthma care and of interventions to improve asthma control and that such research should use standard definitions to allow comparison across studies and aggregation of data.

The report is based on research conducted by RAND Health. Rand Health furthers RAND's mission of helping improve policy and decisionmaking through research and analysis, by working to improve health care systems and advance understanding of how the organization and financing of care affects cost, quality and access.

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## EXECUTIVE SUMMARY

### Introduction and Background

In 2002, over 30 million Americans reported ever having been diagnosed with asthma; 106 per 1000 adults and 122 per 1000 children, making it the most common chronic disease among children (NCHS, 2006). In 2002, the estimated annual cost of treating asthma was around \$ 14 billion, of which hospital care accounted for almost a third of direct costs, and the indirect cost of asthma care was \$ 4.6 billion (NHLBI, 2002).

Recent advances in pharmacotherapy have made asthma a highly treatable disease. Current treatment guidelines define the appropriate uses for three categories of agents: 1) anti-inflammatory medications (inhaled corticosteroids [ICS] and leukotriene inhibitors), 2) bronchodilators (methylxanthines and long-acting beta-agonists [LABA]), and 3) rescue treatments (systemic steroids and short-acting beta-agonists (SABA). However, research suggests that treatment often falls short of recommended care. According to a 2001 study, 74 percent of children with moderate to severe asthma in a national sample did not receive adequate treatment. (Haltermann et al., 2001) And, in spite of their higher prevalence of the disease, minority children are less likely than white children to receive adequate treatment (AAFA, 2005). Adults with asthma fare no better: A recent RAND study showed that only 43 percent of patients who used a rescue inhaler at least three times a day were put on maintenance treatment (McGlynn, 2003). Recognition of the discrepancy between recommended care and care that is actually received has led to initiatives to improve the quality of asthma care, such as the Healthy People 2010 Initiative.

Although the quality of asthma care, treatment options, and the effect of the disease have been addressed extensively by the research community, no attempt has been made to date to provide consensus estimates for the costs (that is, for medications and other medical care) and benefits (such as avoided hospitalizations and ER visits, reduction in lost school or work days, and improved workplace productivity) of quality asthma care.

We conducted a project aimed at bridging this gap by synthesizing the existing evidence from literature and non-literature sources to address the following questions:

1. What are the gaps in the quality of asthma care for children and adults?

2. What are the clinical and policy implications of those gaps (e.g., excess morbidity and mortality, avoidable hospitalizations, lost school/work days)?
3. What would it cost to close the quality gaps?
4. What would be the return on investment/cost-benefit ratio of better asthma care?

This report provides the results of our literature synthesis and attempts to answer the questions, with the hope of guiding policy directed at improving the quality of asthma care.

### **Approach and Methods**

To answer the questions, we conducted a comprehensive review of the literature dating from 1995 to 2006 to identify relevant publications as well as unpublished material. To obtain articles published in peer-reviewed journals, we searched the traditional health literature databases, such as Medline, EMBASE, and Cinahl, as well as Psycinfo, Social Sciences Abstracts, and Econlit. Relevant articles were referenced for additional articles to retrieve. We also searched the websites of relevant governmental professional and advocacy organizations as well as a number of databases for "grey" literature sources.

Two researchers independently reviewed the titles of identified items to assess whether the content of the article was likely to provide relevant information. If available, the abstracts were obtained for all items flagged by one of the two reviewers as potentially relevant. Two reviewers then independently reviewed the abstracts or, in some cases, the full publications to determine whether they contained relevant information. Differences in opinion were resolved by consensus. Reports were omitted from further consideration if they did not contain any relevant information, were not conducted in the United States, were review or opinion articles, or were duplicative publications of the same data.

A comprehensive coding tool (form) was developed to abstract the relevant data from each report, including study design, findings (such as quality gaps), outcomes resulting from quality gaps, and cost estimates. These data were entered into a database for further analysis. As a first step, we conducted a qualitative analysis, seeking common themes and findings across the sources.

In the second part of the analysis, we attempted to take differences in population characteristics into account and to recalculate the outcomes measured in the first part of the analysis using common metrics

in order to facilitate cross-study comparisons. Three outcome measures were chosen: use of inhaled corticosteroids, hospitalizations, and emergency room (ER) visits. For each outcome measure, all findings were re-estimated to express them in the same terms, and where possible study durations were extrapolated to one year. We tested four categories of explanatory variables to account for differences: disease severity, age, race/ethnicity, and data source.

## **Results**

Of the 2,786 reports identified by the initial searches, all but 164 were omitted from further review because they were determined not to meet the inclusion criteria.

### ***Initial Analysis***

***Findings on the Quality of Asthma Care.*** The majority of reports that addressed care quality focused on pharmacologic treatment. Reported utilization rates for all three categories of asthma medications exhibited considerable variability. Utilization rates for anti-inflammatory drugs ranged from 0 percent to 94 percent and for bronchodilators from 0 to 98 percent, but median rates for anti-inflammatory drugs (32 percent) were considerably higher than for bronchodilators (17 percent). Use of rescue treatment also ranged from 0 percent to almost 100 percent. The types of utilization measures varied widely among studies.

Nevertheless, three patterns of utilization emerged. First, use of anti-inflammatory medications was well below 100 percent. Second, bronchodilators were used less frequently than anti-inflammatory drugs, reflecting their decreasing role in asthma treatment. Third, utilization rates for rescue drugs varied substantially, but few studies expressly looked into the adequacy of treatment with rescue drugs.

***Findings on the Outcomes of Care.*** Among the studies that examined care outcomes, most examined hospitalization rates and/or emergency room visit rates; a much smaller number measured lost school days, symptom days, symptom-free days, or complications associated with asthma, and only a few studies attempted to directly relate the outcomes to gaps in quality of care. Further complicating attempts to synthesize findings across multiple studies, the units used to measure and express a particular outcome (e.g., hospitalization rate) tended to vary considerably among studies. Nonetheless, comparing studies that used a similar metric revealed a wide range of estimates. For example, the incidence of at least one hospitalization in the preceding 3 to 12 months was generally below 10 percent, although 35 percent of patients

in a study conducted at an urban hospital were hospitalized during the month of the study. Too few studies assessed outcomes in terms of complications or symptom-free/symptom days to permit any comparisons.

**Findings on the Cost of Closing Gaps in Care.** We found insufficient evidence to estimate the cost of reducing the gaps in quality and the return on investment for interventions - such as disease management programs - that attempt to close the gap.

### **Secondary Analyses**

**Findings on ICS Utilization.** ICS utilization ranged from 10 to 94 percent of a study sample. Greater use was associated with disease severity (that is, the stringency of the study's inclusion/exclusion criteria for participant enrollment, compared with, say, the HEDIS criteria), being white, and being an adult; also, self-reported use was greater than use rates obtained from other data sources. Thus, use rates are lower than they should be, and blacks and Hispanics are disproportionately affected.

**Findings on ER Visits.** The number of ER visits varied from zero to 80 per 100 patient years. ER visit rates mirrored the findings on ICS utilization. Thus, ER visits were associated with disease severity, the proportion of whites and adults in the population, and with self-report.

**Findings on Hospitalization Rates.** The rate of hospitalization also varied widely: from zero to 53 admissions per 100 patient years. Hospitalization also mirrored ICS utilization and ER visits.

**Results of Two-way Tabulations and Multivariate Regression.** When the results were tabulated by both disease severity and racial/ethnic composition of the sample, few combinations of disease severity and racial/ethnic composition contained more than one or two studies; nevertheless, the findings generally reflected those for the individual explanatory variables. However, multivariate regression found no statistically significant effect of any of the explanatory variables.

### **Discussion**

This study showed that although the quality of asthma care is an area of active research, it is impossible to derive reasonably bounded consensus estimates for the cost and benefits of better asthma care. Two limitations accounted for this problem. First, most publications focused on only one aspect of the question, e.g., estimating ICS treatment rates or hospital admission rates; however, no study tried to relate variation in endpoints explicitly to gaps in care. For example, no study examined the potential association between higher hospital admission rates and lower use of ICS treatment (except in the context of a multifaceted

intervention, making it impossible to isolate the effect of ICS treatment). Second, and more importantly (*and more surprisingly,*) researchers used a staggering variety of criteria to recruit their study patients and a staggering number of study outcomes. Similarly, as the key determinant of both treatment intensity and patient outcomes, *disease severity* was often insufficiently defined, that is, not defined according to well-established criteria. This finding is somewhat surprising, considering the availability of well-established patient identification and risk stratification criteria that can be applied to utilization data (HEDIS criteria) or clinical data (NHBLI and ATS criteria).

While it was not possible to obtain reasonable estimates of the costs or benefits of care, some important findings did emerge. Consistent with previously published reports, disadvantaged populations appear to receive worse care. ICS treatment rates were lower in studies with a high proportion of minority patients (and/or Medicaid) beneficiaries, a finding previously reported by others.

Another important finding was that both ICS treatment rates and ER and hospital utilization rates were typically higher in studies that relied on self-reported data than in studies that used health insurance claims or medical records as their sources. This finding implies that study outcome findings that have been derived from different types of data sources cannot simply be pooled but that, instead, it is necessary to take the data source into account when interpreting results.

Our findings suggest the need for more economic evaluations of the impact of gaps in asthma care and of interventions to improve asthma control and that such research should use standard definitions to allow comparison across studies and aggregation of data. Public and private funding agencies should use their influence to move the asthma research community toward more standardization of definitions. Arriving at such definitions is no easy feat, as it requires forming consensus and achieving buy-in of multiple stakeholders. But MCAN, with its ties to both the federal and non-federal funding agencies, the advocacy community, and academic researchers, is in an excellent position to broker such a consensus.

Finally, the second important conclusion of our study is that, given the enormous variability of results, overly confident statements about the gaps in asthma care or their impact should be avoided, as any estimates will strongly depend on their context. Thus, for the present, policymakers and other stakeholders should carefully review the sources of - and methods used to generate - existing data, when relying on them as the basis for critical decisions.

#### **ACKNOWLEDGMENTS**

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## 1. BACKGROUND

Childhood asthma is the most common chronic disease among U.S. children, affecting 4.8 million of America's 70 million children under age 18. In 1995, children were hospitalized for treatment of asthma nearly 170,000 times at a total cost of about \$387 million. The debilitating effects of this condition cause 10 million missed school days each year. (AHRQ, 2000) Overall asthma prevalence has increased by about 75 percent since the early 1980s, from 30.7 per 1000 population in 1980 to 53.8 per 1000 population in 1993/1994 (NHLBI, 1999). In 2002, the estimated annual cost of treating asthma was around \$ 14 billion, of which hospital care accounted for almost a third of direct costs, and the indirect cost of asthma care was \$ 4.6 billion (NHLBI, 2002).

Asthma is an inherently treatable disease, particularly with recent advances in drug therapy that targets its inflammatory component (Knorr et al., 1998; Lazarus et al. 2001). Pharmacological treatment of asthma is a two-pronged approach: So-called controller drugs aim at stabilizing the disease and so-called rescue drugs (e.g., short-acting beta-agonists (SABA or systemic steroids) at fast symptom relief. The two main groups of controller drugs are the anti-inflammatory drugs (inhaled corticosteroids [ICS] and leukotriene inhibitors) and the bronchodilators (long-acting beta-agonists [LABA] and methylxanthines<sup>1</sup>). Rescue treatment can also aim at reducing the inflammatory component of the disease through systemic steroids or at reducing airway constriction through fast-onset bronchodilator (short-acting beta-agonists (SABA) and methylxanthines). The appropriate use of these agents and other management techniques is documented in nationally accepted guidelines, such as those published by the National Asthma Education and Prevention Program (NAEPP). However, actual treatment falls short of recommended care, suggesting substantial problems with quality of care for asthma. For example, 74 percent of children with moderate to severe asthma in a national sample did not receive adequate treatment (Halterman et al., 2001). In another study evaluating care, only between 11 and 33 percent of all children hospitalized for asthma had received prior anti-inflammatory maintenance treatment (Homer, 1996). And, in spite of their higher prevalence of the disease, minority children are less likely than white children to receive adequate treatment (AAFA, 2005). Adults with

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<sup>1</sup> Because of their narrow therapeutic margin, the role of the methylxanthines, such as theophylline, is diminishing.

asthma fare no better: A recent RAND study showed that only 43 percent of patients who used a rescue inhaler at least three times a day were put on maintenance treatment (McGlynn, 2003).

This gap between recommended and actual treatment, and the enormous clinical effects and policy implications have alerted clinicians, researchers, and policymakers to the need for some action. This recognition is manifested, for example, in the targets for asthma treatment in the HealthyPeople 2010 initiative, which strives to achieve better overall health care quality and the elimination of disparities (DHHS, 2000).

While there is a wealth of publications on problems affecting asthma care quality, treatment options, and the impact of the disease, a comprehensive review that integrates the existing evidence and provides consensus estimates for the cost (e.g., medication cost and medical charges) and benefits (e.g., avoided hospitalizations and ER visits, reduction in lost school or work days, improved workplace productivity) for better care is lacking. Thus, the purpose of this project was to try to bridge this gap by consolidating the existing evidence from literature and non-literature sources to address the following questions:

1. What are the gaps in the quality of asthma care for children and adults?
2. What are the clinical and policy implications of those gaps (e.g., excess morbidity and mortality, avoidable hospitalizations, loss school/work days)?
3. What would it cost to close the quality gaps?
4. What would be the return on investment/cost-benefit ratio of better asthma care?



## 2. ASSESSMENT OF THE EVIDENCE BASE

### METHODS

We consolidated existing evidence from literature and non-literature sources to address the following questions:

1. What are the gaps in the quality of asthma care?
2. What are the clinical and policy implications of those gaps?
3. What would it cost to close the quality gaps?

### LITERATURE SEARCH

We conducted a comprehensive search of the peer-reviewed literature as well as other sources to identify relevant publications. The search covered the traditional health literature databases such as Medline, EMBASE, and Cinahl. We also searched Psycinfo and Social Sciences Abstracts. Another important database that was reviewed was Econlit, which includes economic journals, books, dissertations, and working papers. Any relevant articles obtained through our searches were also "reference mined," i.e. the reference lists were reviewed for additional articles to retrieve. We also searched the websites of relevant governmental professional and advocacy organizations (see Appendix B for a full list).

Because some studies may not have been published in academic journals, we also searched the following "grey" literature sources from outside the world of peer-reviewed journals for relevant studies or data:

- *New York Academy of Medicine (NYAM) Grey Literature collection* - NYAM publishes a bimonthly Grey Literature Report featuring documents related to public health and medicine. The focus is on research material, rather than consumer health material. The Report encompasses materials that are not otherwise indexed, not produced by commercial publishers, and not available through normal, commercial distribution channels. Materials in the collection are published by government agencies, non-profit non-governmental organizations, universities, and independent research centers. The documents come from organizations as diverse as the American Association of Retired Persons (AARP), American Association of Health Plans (AAHP), and United Hospital Fund. Document types include but are not limited to case studies,

conference proceedings, discussion papers, fact sheets, government documents, issue briefs, research reports, statistical reports, and white papers.

- *Conference Papers Index* - Preliminary results from studies are often presented at scientific or business conferences before or instead of being published in journals.
- *Worldcat* - This catalogue is maintained collectively by over 9,000 member institutions around the world. It is the leading bibliographic database in the world, and references books, web sites, recordings, films, and magazines.

The searches covered all English publications after 1995. Search terms are listed in Appendix A.

#### **Assessment of Identified Articles**

Following the literature search, two researchers independently reviewed the titles of identified items to assess whether the content of the article was likely to provide relevant information. If available, the abstracts were obtained for all items flagged by one of the two reviewers as potentially relevant. Two reviewers then independently reviewed the abstracts or, in some cases, the full publication and made a determination whether the article contained relevant information. Differences in opinion were resolved by consensus. Studies were discarded if they did not contain any relevant information, were not conducted in the United States, were review or opinion articles, or were duplicative publications of the same data.

#### **Abstraction of Literature**

We developed a comprehensive coding tool that allowed organization of the data and information found in the identified studies. The tool covered the following categories for each item:

- Identifying information (author, publication year, etc.)
- Study design (comparison strategy, sample size and composition, etc.)
- Findings that identify gaps in - or other evidence of poor quality - asthma care (inhaled steroid treatment rates, etc.)

- Effect of treatment gaps (hospital admission rates, lost school days, etc.)
- Information on or estimates of cost to close the quality gaps (program cost for disease management, etc.)

The full abstraction tool can be found in Appendix D. The coding tool was used to create a Microsoft Access database into which all relevant information was abstracted.

#### **Assessment of Content**

The information coded into the database was analyzed to determine the number of studies that provided data on the quality of asthma treatment (i.e. whether treatment was according to professional standards and guidelines), effect of asthma on clinical and other endpoints (hospitalizations, ER visits, school/work days lost, mortality, and symptom days or symptom free days) and the efficacy of asthma disease management interventions.

Taking into account the data sources for the studies (public claims data, private claims data, self reported, medical records/charts) and the populations (general asthma population, high-risk asthma population), we attempted to identify patterns and commonalities across studies.

#### **RESULTS**

Our literature search identified 2,786 reports that met our initial search criteria. Based on the initial screening, many of the reports (2,459) were deemed to be irrelevant and were excluded from the subsequent analysis. An additional 164 reports were also discarded because they did not describe a study of a US-based population (39), contained no relevant information (94 reports), were an opinion piece or literature review (22 reports), or were duplicative study reports (9). (see Figure 2.1)

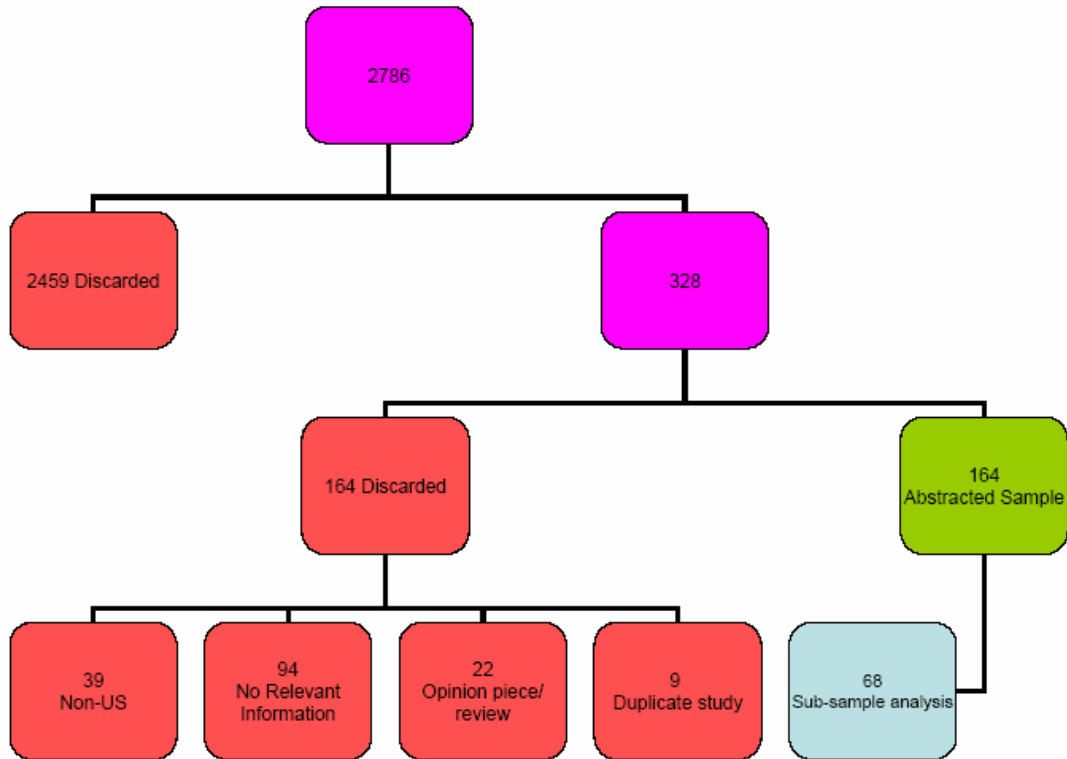


Figure 2.1 Lit Search Flowchart

### Findings on Quality of Asthma Care

The focus of most studies that assessed asthma care quality was pharmacological treatment. We identified 72 studies that examined use of anti-inflammatory medication (11 Leukotriene Modifiers, 59 Inhaled Corticosteroids, and 18 unspecified anti-inflammatory drugs), 34 studies that examined bronchodilator (26 theophylline, 10 LABA, and 3 unspecified bronchodilators) utilization rates, and 62 studies that examined utilization of rescue treatments (8 looked at systemic steroid use and 57 studies examined utilization rates of SABA).

Reported utilization rates for all three categories of asthma medications exhibited considerable variability, as can be seen in Table 2.1. Only 10 percent of subjects in one study (Study 145) used an anti-inflammatory drug while the use rate in another study (Study 297) was 94 percent. Similar variability existed in estimates of use of bronchodilators and rescue treatments. Half of studies reported theophylline utilization rates between 10 and 30 percent, although one study reported a rate of 63 percent (Study 144). Use of bronchodilators

was somewhat lower - half of studies found use rates of 10 to 24 percent - although one study (Study 106) reported a utilization rate of 98 percent. Use of rescue treatment ranged from under 6 percent (Study 119) to almost 100 percent (study 17), with half of studies reporting rates between 36 percent and 85 percent.

Despite the variability in these reported rates, three important patterns did emerge. First, utilization of anti-inflammatory medication was low with the median treatment rate across studies being 38 percent. While we did not have sufficient clinical information to determine for each study what the appropriate treatment rate should have been<sup>2</sup>, the fact that studies commonly recruited patients with frequent or costly encounters with the health care system suggests that much higher treatment rates are warranted. (Please see Section 3 for a detailed analysis)

Consistently, use of ICS by whites was higher than in minority populations. Second, anti-inflammatory medications appear to be more widely used than LABA and Theophylline, reflecting the fact that guidelines now emphasize anti-inflammatory treatment over bronchodilators: While the median rate of anti-inflammatory drug use was 32.5 percent, the median rates of bronchodilator use was only 16.9 percent. Third, utilization rates for rescue treatment varied substantially, but few studies expressly looked into the adequacy of treatment with rescue inhalers. Some but not all studies suggested higher use of rescue inhalers in black populations than in non-black populations.

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<sup>2</sup> For example, individuals classified with mild-intermittent cases of asthma do not have an indication for long-term anti-inflammatory treatment.

**Table 2.1: Range of Estimated Asthma Medication Utilization Rates<sup>3</sup>**

	Mean	Minimum	25th Percentile	Median	75th Percentile	Maximum	Number of Studies
<b>Anti-Inflammatory Drugs</b>	34.5%	0.0%	15.7%	32.5%	49.6%	94.0%	68
<b>Bronchodilators</b>	27.5%	0.26%	9.1%	16.9%	44.8%	98.0%	34
<b>Rescue Treatment</b>	50.0%	0.56%	14.1%	52.8%	84.1%	96.0%	48

**Findings on Outcomes of Care**

We identified 83 studies that examined hospitalization rates and 78 that assessed ER visit rates for asthma patients; however, other outcome measures were much less common. A total of 22 studies measured lost school days. Two studies measured symptom free days and five symptom days as an outcome, and seven studies looked at comorbidities associated with asthma. Most notably, only very few studies attempted to attribute the outcomes to gaps in quality of care, such as by correlating anti-inflammatory treatment with the risk of hospital admission. Those studies on ICS treatment that did report such analyses were usually intervention studies, in which changes in treatment and subsequent effects on outcomes were attributed to the intervention. As those interventions were typically multi-faceted, such studies do not allow disentangling the effect of higher treatment rates and the effect of other changes, such as improvements of air quality or reduction in allergen exposure.

One of the difficulties in detecting patterns across these studies was that many different metrics were used to express the rates at which the outcomes of interest occurred. For instance, some studies report the

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<sup>3</sup> Studies were included in Table 2.1 if they reported some measure of the fraction of subjects who took a particular drug. Therefore, the number of studies reported in the table may be smaller than the number of studies that have any information on utilization of a class of asthma medication. Note that the utilization measures vary from study to study. For instance, some report the percentage of individuals for whom an insurance claim for the purchase of a particular drug was filed, while other studies report the percent of study subjects who indicated they used a given drug in some interval of time. In the text, we report findings on the range of estimates of inhaled corticosteroid (ICS) utilization reported in studies that used a common utilization measure.

number of hospitalizations in terms of events per 1000 person years, whereas others simply report the fraction of patients with any hospitalization in a certain interval of time, and those intervals also varied across studies. Nonetheless, comparing studies that used a similar metric revealed a wide range of estimates. The incidence of at least one hospitalization in the preceding 3 to 12 months was generally below 10 percent, although 35 percent of patients in a study conducted at an urban hospital were hospitalized in the month of the study (Study 362). Similarly, most studies reported that fewer than 15 percent of study subjects had an ER visit, although some estimates were above 40 percent.

Studies that measured lost school days consistently reported relationships between asthma and absenteeism, although the lack of uniformity in the metric used to measure absenteeism makes it difficult to compare the results across studies. Some studies reported absenteeism in terms of ever missing a day of school in some interval of time. For instance, one study of children who suffered from nighttime asthma attacks found that 35 percent had missed at least one day of school in the preceding four weeks (Study 226). Other studies examined the average number of days missed. In one such study, children in the sample missed an average of 7 days per year (Study 230).

The fact that very few studies measure symptom-free days made it very difficult to detect any generalizable patterns for this outcome. To illustrate, asthma limited at least one activity of 18 percent of the subjects in one study (202), but another study reported a disability rate associated with asthma of 43 percent (229). Assessments of symptom-free days or symptom days were relatively uncommon in the studies that examined this outcome. In one such study, participants enjoyed fewer than three symptom-free days in the prior two weeks (Study 324)

### **Findings on the Cost of Closing Gaps in Care**

In an effort to obtain estimates of the cost of reducing the gaps in care, we searched for studies that examined the efficacy of asthma disease management programs (ADMP) or similar interventions, such as school-based or community-based outreach programs. While numerous studies described such interventions, we found only 45 studies that formally evaluated their effect and only six that contained any information on the cost of the intervention or the savings it achieved

relative to the no-intervention baseline. All six of these studies, all on disease management for asthma, found the interventions to be cost-effective.<sup>4</sup> One intervention that provided 60- to 90-minute, one-on-one educational sessions was even found to have produced annual net savings of almost \$2,000 per patient (Study 96). However, a recent RAND review of the effectiveness of disease management interventions found no conclusive evidence that disease management for asthma can reduce direct medical costs. (Mattke, Seid, Ma, 2006)

To summarize, we found insufficient evidence to try to answer our questions on the cost of reducing the gap in quality and the return on investment for programs that attempt to close the gap.

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<sup>4</sup> Note that the meaning - and measures - of "cost-effectiveness" varies across the studies. One reported the reduction in costs borne by the insurer that occurred after the implementation of the program (Study 138), whereas another found that the cost of achieving an additional symptom-free day fell by \$9.20 (Study 97). In the latter example, the program may have increased total care expenditures.



### 3. ANALYSIS OF SELECTED ENDPOINTS

One of the key findings that emerged from the preceding discussion was the enormous variability in the reported rates of particular outcomes, such as pharmacological treatment rates or hospital admission rates, which made it very difficult to detect any patterns and to consolidate the evidence into consensus estimates. Part of the variability can be explained by differences in the patient populations studied and the data sources used. Another problem, as mentioned above, was that studies used a variety of different operational definitions for similar concepts, which makes it difficult to compare outcomes. In this second part of the analysis, we attempted to account for differences in population characteristics and to recalculate outcomes using common metrics in order to facilitate cross-study comparisons. It should be emphasized that the unit of analysis was the individual study, i.e. we tried to capture the overall composition of the study sample, which may have ignored substantial heterogeneity within the sample.

#### **METHODS**

##### **Selection of Endpoints**

In this part of the analysis we chose to focus on three patient outcomes:

1. ICS treatment
2. Hospital admissions
3. ER visits

These outcomes were selected because we identified a relatively large number of studies that measured them, which would make it possible to investigate quantitatively if variation in sample characteristics and other study features explained the overall variability in the estimates across studies.

For this analysis, we included only studies with baseline data for any of these three outcomes. Studies that began collecting outcome data only after the initiation of an intervention were discarded, as it would not be possible to distinguish the effect of the intervention from typical patterns of care.

We rebased ICS treatment as the percent of study subjects treated, hospital admissions and ER visits as events per 100 patient years. Some assumptions and conventions had to be adopted to permit us to convert

the various forms used to express the three outcomes into common metrics:

- For intervention studies that collected both baseline and post-intervention data, we used only baseline data as we were less interested in the effects of a particular intervention than in typical treatment patterns.
- For intervention studies with a control group, we attempted to pool the baseline data for the intervention and control groups. If this was not possible because of heterogeneity or insufficient information, we used only the data for the control group.
- If study duration was less than a full year, we extrapolated data to a year.
- If hospital admissions or ER visits were expressed as a percent of study patients admitted, we assumed one event per study participant.

Obviously, such assumptions have the potential for introducing error and even bias. For example, extrapolation of partial year data to a full year does not account for seasonality effects. In addition, some studies had to be excluded because their data could not be converted based on the published information, e.g., we could not convert hospital admissions data from one study because the study measured admissions over the patient's lifetime (Study 2750). Other studies had to be excluded to avoid confounding, e.g., if a study recruited its population from patients who visited an ER, it could obviously not be included in analyses that used ER visits as an outcome. Our final sample consisted of 34 studies with information on ICS use, 42 that measured ER visits, and 42 that measured hospitalizations (see Appendix B).<sup>5</sup>

#### **Selection of Explanatory Variables**

We attempted to account for the variance across study samples with four types of explanatory variables:

- *Disease severity.* The vast majority of studies identified patients based on healthcare utilization. Thus, we decided to use the

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<sup>5</sup> Studies that did not have information on one the stratifying variables were not included in the respective analyses. Therefore the sample size in the tables does not always agree with the total number of studies cited here.

NCQA's proposed criteria for identifying asthma patients from insurance claims data. In short, those criteria identify patients as having moderate to severe asthma, if they have (1) at least one hospital admission, (2) at least one ER visit, (3) at least four prescription drug claims for asthma drugs, or (4) at least four office visits and two prescription drug claims in a year. We categorized all studies that explicitly selected patients based on those criteria or selected patients that would have met those criteria as reporting on "average severity" study populations. Studies covering populations that would not have met the criteria, e.g., that identified patients based on only one office visit, were categorized as "Low severity." And studies of populations that were of considerably higher risk, such as those identified based on multiple ER visits, were labeled as "high" severity. It is important to keep in mind that the severity classification refers to the typical severity of patients that were included in a given study. Thus, for example, some individuals in the "low severity" studies may also have had severe cases of asthma. Several studies used other criteria for diagnosis, such as National Heart, Lung, and Blood Institute (NHLBI)<sup>6</sup> (seven studies) and American Thoracic Society (ATS) (two studies) criteria, both of which assess disease severity on the basis of symptoms and pulmonary function tests. As only two studies used the ATS criteria, we dropped those from the analysis. We included the studies based on the NHLBI criteria, but could not stratify those studies by the NHLBI categories of patient severity because of the small number and because most did not provide enough information to stratify patients.

- *Age.* The populations of the included studies were divided into five age categories: children (0-12), adolescents (12-18), non-adults (0-18), adults (18+), and all ages.
- *Race/ethnicity.* For racial/ethnic composition, we collected data on the percentage of study subjects who were white, black, Hispanic<sup>7</sup>, or other/unknown. Studies were then grouped into four mutually-exclusive categories: >40 percent black, >25 percent

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<sup>6</sup> Those criteria are sometimes also referred to as NIH or NAEPP criteria.

<sup>7</sup> We were unable to differentiate Hispanic subgroups based on the reported information, which constitutes a limitation, because disease prevalence and probably severity varies among those subgroups.

Hispanic and <40% black, >50 percent white and no information on the racial/ethnic makeup of the sample.

- *Data source.* We classified studies into one of four groups: claims (private insurer), claims (public insurer), medical records/charts, and self-reported information.

It should be emphasized that forming those categories represents an attempt to find a workable solution to the problem of imperfect information. As with the outcomes described above, studies frequently failed to provide detailed information on sample composition and patient identification or information that would allow stratifying outcomes by disease severity within a study. Thus, the resulting categories still allow for substantial heterogeneity, as illustrated in Table 3.1. For example, studies that we labeled as using less stringent criteria than the NCQA criteria to select subjects may still include large numbers of patients who would have been selected using a more rigorous standard. Finally, the fact that our stratification approach is based on utilization of care may have introduced bias into the analysis, as our outcomes also reflect utilization.

**Table 3.1: Examples of Identification Criteria Used in Reviewed Studies**

Study ID	Criteria for study population	Disease Severity Classification
4	Recent clinic visit with a diagnosis of asthma, or a recent prescription for a bronchodilator or inhaled anti-inflammatory agent	Low
45	At least one medical claim with a primary diagnosis of asthma	Low
53	Patients were frequent users of the emergency department	High
55	Patients diagnosed as having asthma by a physician or a nurse practitioner during 1 ambulatory encounter, 1 hospitalization with a primary diagnosis of asthma, or 1 emergency department visit for asthma between October 1, 1991 and September 28, 1994	Low
61	At least one ED visit or observation during the last year.	Average
99	Pharmacy claims in the following categories: inhaled beta-agonists, inhaled corticosteroids, leukotriene modifiers, cromolyn, nedocromolin, ipratropium	Low
113	HEDIS criteria: 1) at least 4 asthma medication dispensing events, 2) at least 1 emergency department visit with asthma as the primary diagnosis (ICD-9 code 493.xx), 3) at least one hospitalization with asthma as the primary diagnosis (ICD-9 code 493.xx), 4) at least 4 outpatient asthma visits with asthma as one of the listed diagnoses and at least 2 asthma medication dispensing events	Average
146	Patient had 2 or more emergency department visits for asthma exacerbation in the 6 months prior to the survey	NHLBI criteria
154	2 or more asthma related emergency department visits or a hospitalization due to asthma exacerbation	High
226	Patients selected based on administrative and/or pharmacy claims. Children with two or more visits for asthma in last 12 months (ICD-9 code 493.xx) and/or 1 or more dispensations of a drug commonly prescribed for asthma	Low

### **Analytic Approach**

For each of the outcomes, we began the analysis by tabulating the reported estimates by groups defined by the explanatory variables. These one-way tabulations provide information on the association between a given outcome and the explanatory variables we considered. We further refined these comparisons by conducting two-way tabulations as well as multivariate regressions.

### **Results for One-way Tabulations**

#### ICS Utilization

The first set of columns in Table 3.2 shows the distribution of reported rates of ICS treatment stratified by each of the explanatory variables. Utilization rates range from 10 percent to 94 percent with a mean of 43 percent. Some of this variability appears to be influenced by the selected explanatory variables. For instance, utilization rates were higher in studies that examined a population with more severe asthma: The median estimate in studies that selected subjects using more stringent requirements than the HEDIS criteria was 69% compared with only 32% in studies that used HEDIS-like criteria. Another pattern is that ICS utilization was lower in studies in which the sample comprised a large percentage of racial and ethnic minorities. The median estimate in studies where at least 40 percent of the subjects were black was 32 percent compared to 51 percent in studies where the sample was at least 50 percent white (although the study with the lowest ICS utilization rate had a majority-white sample). ICS utilization rates are also somewhat higher in studies of adults than in studies of children or non-adults. Finally, ICS treatment rates are also correlated with the data source: Studies based on self-reported data tend to find higher utilization rates, whereas those that use claims data - data from public insurers, in particular - report the lowest.

Despite the fact that estimates of ICS utilization appear to be related to the explanatory variables, there is considerable variability even within the categories we constructed. In the five studies that use a more restrictive definition than the HEDIS criteria to select subjects, the estimates range from 39 percent to 80 percent, and in the studies that use criteria less stringent than those of HEDIS, the estimates range from 10 to 72 percent.

Similar patterns exist for the other stratifying variables, as well. In studies where the sample was at least 50 percent white, the estimates range from 10 percent to 94 percent, and the range is 17 to 80 percent in the studies where at least 40 percent of the sample was black. And although studies based on claims data generally have lower ICS utilization rates than studies that use other sources of data, there is a relatively wide range of estimates (10 to 56 percent) among the nine studies that use public insurer claims data.

Even with this high degree of variability, at least three important qualitative conclusions can be drawn from these results. First, ICS use rates in almost all studies are well below 100 percent, even when the subjects are selected on the basis of having moderate to severe asthma and thus have a clear treatment indication. This finding suggests the presence of sizable gaps in adequate asthma care, although variation in the actual estimates is too high for us to be able to quantify these gaps in any reliable fashion. Second, insufficient quality of care appears to disproportionately affect disadvantaged populations, as ICS utilization was lower in studies with large numbers of blacks or Hispanics and also in studies of Medicaid populations. Third, ICS utilization rates vary by the source of data. Studies that use claims data tend to report lower ICS utilization rates than do studies based on self-reported data or information from medical records.

**Table 3.2: Tabulations of Estimates of ICS Utilization by Sample Characteristics and Source of Data**

	ICS utilization rate			
<b>Severity</b>	<b>Min</b>	<b>Median</b>	<b>Max</b>	<b># Studies</b>
Less than HEDIS	10%	36%	72%	14
HEDIS	15%	32%	94%	9
More than HEDIS	39%	69%	80%	5
NHLBI	19%	39%	78%	4
Total	10%	40%	94%	32
<b>Race/Ethnicity</b>				
No Race Info	17%	40%	55%	9
> 40% black	17%	32%	80%	7
>25% Hispanic and <40% Black	15%	26%	78%	5
Majority White	10%	51%	94%	12
Total	10%	40%	94%	33
<b>Age</b>				
Children	26%	26%	26%	1
Non adults	10%	35%	80%	15
Adults	31%	52%	78%	9
All	15%	42%	94%	8
Total	10%	40%	94%	33
<b>Data Source</b>				
Claims (private)	17%	40%	55%	7
Claims (public)	10%	27%	56%	9
Medical Records	26%	33%	80%	5
Self Reported	26%	67%	78%	11
Self Reported/claims				
Self Reported/med. Records	94%	94%	94%	1
Total	10%	40%	94%	33



ER Visits

The patterns for reported rates of ER visits are similar to those for ICS utilization. Studies of patients with more severe asthma generally reported higher estimates of ER visit rates. The median number of ER visits was 3.6 per 100 patient years in studies where asthma was diagnosed with criteria less strict than the HEDIS criteria, compared to 5.0 in the four studies that used stricter criteria than HEDIS. Estimates of ER utilization were also higher in studies where the sample had a higher fraction of whites, in studies of adults, and in studies that used self-reported data.

The most striking pattern was again the wide range of estimates. The median ER visit rate was 3.9 visits per 100 patient years, but a number of studies had much higher rates (the 75<sup>th</sup> percentile - not reported in the table - is 13.8).

**Table 3.3: Tabulations of Estimates of ER Visits by Sample Characteristics and Source of Data**

Severity	ER Visits per 100 patient years			
	Min	Median	Max	# Studies
Less than HEDIS	0.0	3.6	58.3	21
HEDIS	0.0	3.7	66.7	12
More than HEDIS	2.2	5.0	80.0	4
NHLBI	0.0	9.9	32.0	5
Total	0.0	3.9	80.0	42
<b>Race/Ethnicity</b>				
No Race Info	0.1	4.5	58.3	16
> 40% black	0.0	3.6	80.0	5
>25% Hispanic and <40% Black	0.0	0.5	23.4	9
Majority White	0.1	13.7	66.7	12
Total	0.0	3.9	80.0	42
<b>Age</b>				
Children	.	.	.	0
Non adults	0.0	3.3	47.0	16
Adults	0.1	5.3	80.0	12
All	0.0	2.5	61.6	14
Total	0.0	3.9	80.0	42
<b>Data Source</b>				
Claims (private)	0.1	5.3	66.7	16
Claims (public)	0.0	0.2	58.3	13
Medical Records	3.6	6.7	9.9	2
Self Reported	0.6	6.4	80.0	7
Self Reported/claims	9.8	9.8	9.8	1
Self Reported/med. Records	23.4	42.5	61.6	2
Total	0.0	3.6	80.0	41

Hospital Admissions

The results for hospitalizations largely mirror those for ER visits. Hospitalization rates vary widely, even within the categories based on the explanatory variables. In spite of this variability, some patterns can be seen. Hospitalization rates increase with asthma severity, although it should be noted that there are only three studies that examine hospital visits and use criteria more stringent than those of NCQA. The highest estimates of hospitalizations come from studies based on self-reported data. Of the eight studies that use only self-reported data, the median estimate is 9.2 hospital admissions per 100 patient years, and the largest estimate is 53.3 per 100 patient years. Unlike ICS utilization and ER visits, hospital admission rates are highest in studies with a large fraction of black patients. The median and maximum estimates in the six studies with at least 40 percent black patients are higher than in the studies that cover our other race/ethnicity categories.

**Table 3.4: Tabulations of Estimates of Hospital Visits by Sample Characteristics and Source of Data**

Severity	Hospital admissions per 100 patient years			
	Min	Median	Max	# Studies
Less than HEDIS	0.0	1.7	13.0	20
HEDIS	0.0	3.9	33.3	14
More than HEDIS	0.7	2.9	53.3	3
NHLBI	0.0	2.0	9.9	4
Total	0.0	2.3	53.3	41
<b>Race/Ethnicity</b>				
No Race Info	0.0	2.0	11.0	16
> 40% black	0.0	9.0	53.3	6
>25% Hispanic and <40% Black	0.0	0.1	10.0	9
Majority White	0.0	5.3	33.3	11
Total	0.0	2.4	53.3	42
<b>Age</b>				
Children	17.3	22.2	27.0	2
Non adults	0.0	2.6	13.0	16
Adults	0.0	3.3	53.3	12
All	0.0	0.6	19.6	12
Total	0.0	2.4	53.3	42
<b>Data Source</b>				
Claims (private)	0.0	2.5	33.3	15
Claims (public)	0.0	0.1	13.0	13
Medical Records	0.7	2.4	4.0	2
Self Reported	0.0	9.2	53.3	8
Self Reported/claims	3.8	3.8	3.8	1
Self Reported/med. Records	9.9	14.7	19.6	2
Total	0.0	2.3	53.3	41

### **Results for two-way tabulations and regression analyses**

In an attempt to further control for heterogeneity across studies, we tabulated the results by asthma severity and the racial/ethnic makeup of the sample. Table 3.5 shows the minimum and maximum estimates for the three patient outcomes in each of the 16 cells generated by crossing the categories defined by these two explanatory variables.<sup>8</sup> The range of estimates is generally smaller than in the one-way tabulations, but this observation is largely an artifact of the numerous cells that have just one or two studies. In most of the cells with more than two studies, the range of estimates remains large. For instance, consider first the results for ICS utilization. In the four studies that have a sample that is majority white and that use less than the HEDIS criteria to select patients into the sample, ICS utilization rates range from 10 percent to 72 percent. The studies with a relatively large proportion of Hispanic typically reported ICS utilization rates that ranged between 16 and 33 percent, although one study that used stricter criteria than those of HEDIS reported a utilization rate of 80 percent. For each asthma severity category, only one study included a sample that was at least 40 percent black, so for these studies it is not possible to gauge the variability of estimates within a cell, although it is worth noting that the study that used a selection procedure similar to the HEDIS algorithm had the lowest ICS utilization rate (16 percent).

Similar variability is also seen for ER and hospital visits. In the studies that use less than the HEDIS algorithm and have a majority white sample, average ER visits range from 0.8 to 42 per 100 patient years, and average hospital visits range from 0.5 to 13 per 100 patient years. In studies that use more than the HEDOS algorithm to select subjects and where the sample was at least 25 percent Hispanic, ER visits range from 3.6 to 80 per 100 patient years, and hospital visits range from 0.7 to 53 per 100 patient years. In contrast, the estimates in the studies that use a HEDIS-like algorithm and have a sample comprising at least 40 percent blacks fell in a reasonably tight range: between zero and 1.5 per 100 patient years for ER visits, and between zero and 0.75 per 100 patient years for hospital visits.

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<sup>8</sup> We chose to focus on the two-way tabulation based on the racial/ethnic makeup of the sample and the severity of the patient's asthma because these two variables had a relatively strong, monotonic relationship with the three patient outcomes.

<b>Table 3.5: Tabulations of Estimates of Utilization by Racial and Ethnic Makeup of Sample and Asthma Severity for ICS Utilization</b>				
	<b>Less than HEDIS</b>	<b>HEDIS</b>	<b>More than HEDIS</b>	<b>NHLBI</b>
	0.172	0.55		0.351
<b>No Race Info</b>	0.523	0.55		0.351
	7	1		1
	0.167	0.255	0.39	
<b>&gt;25% Hispanic and &lt;40% Black</b>	0.333	0.32	0.8	
	2	3	2	
	0.26	0.151	0.77	0.19
<b>&gt; 40% black</b>	0.26	0.151	0.77	0.78
	1	1	1	2
	0.1	0.268	0.41	0.43
<b>Majority White</b>	0.721	0.94	0.69	0.43
	4	4	2	1
Note: Each cell contains the minimum estimate (top number), maximum estimate (bottom number), and number of studies.				

<b>Table 3.6: Tabulations of Estimates of Utilization by Racial and Ethnic Makeup of Sample and Asthma Severity for ER Visits</b>				
	<b>Less than HEDIS</b>	<b>HEDIS</b>	<b>More than HEDIS</b>	<b>NHLBI</b>
	0.081	5.9		
<b>No Race Info</b>	58.29	47		
	14	2		0
	0.017		3.55	
<b>&gt;25% Hispanic and &lt;40% Black</b>	0.02		80	
	2	0	3	
	3	0.003		0.034
<b>&gt; 40% black</b>	3	1.49		23.44
	1	6	0	2
	0.763	13.8	2.22	0.13
<b>Majority White</b>	41.7	66.7	2.22	32
	4	4	1	3
Note: Each cell contains the minimum estimate (top number), maximum estimate (bottom number), and number of studies.				

<b>Table 3.7: Tabulations of Estimates of Utilization by Racial and Ethnic Makeup of Sample and Asthma Severity for Hospital Visits</b>				
	<b>Less than HEDIS</b>	<b>HEDIS</b>	<b>More than HEDIS</b>	<b>NHLBI</b>
	0.002	2.5		
<b>No Race Info</b>	9.3	11		
	14	2		0
	0.014	17.3	0.72	
<b>&gt;25% Hispanic and &lt;40% Black</b>	0.16	27	53.3	
	2	2	2	
	10	0.0010		0.011
<b>&gt; 40% black</b>	10	0.76		9.89
	1	6	0	2
	0.526	5.3	2.93	0.015
<b>Majority White</b>	13	33.3	2.93	4
	3	4	1	2
Note: Each cell contains the minimum estimate (top number), maximum estimate (bottom number), and number of studies.				

**Results of Multivariate Regression**

Another approach to controlling for multiple dimensions of heterogeneity is to use multivariate regression. Table 3.8 shows the estimates of a regression of one of the three patient outcomes on the percentage of the sample that was white and two variables denoting asthma severity: less than HEDIS and HEDIS/more than HEDIS (the excluded group was studies that used the NHLBI standard). For none of the patient outcomes were any of these explanatory variables statistically



significant. Although the one-way tabulations suggested that asthma severity and the racial makeup of the sample were related to these outcomes, these results show that they explain little of the variance across studies (the R-Squared in all cases was below 0.13).<sup>9</sup>

<b>Table 3.8: Regression Results</b>			
	<b>ICS Utilization</b>	<b>ER Visits</b>	<b>Hospital Visits</b>
% White	0.218	10.978	-6.623
	(0.178)	(18.807)	(9.839)
Less than HEDIS	-0.161	-2.656	0.648
	(0.169)	(14.155)	(8.703)
HEDIS or More than HEDIS	-0.019	8.218	7.008
	(0.155)	(13.110)	(7.878)
Intercept	0.385*	6.641	7.241
	(0.153)	(15.450)	(8.741)
R-squared	0.130	0.050	0.106
N	22	25	24
Note: Standard errors in parentheses			

<sup>9</sup> In addition to the regression results in Table 3, we also ran univariate regressions to examine the relationship between the outcomes and each of the explanatory variables. These results also did not yield any statistically significant findings.

## DISCUSSION

The goal of this project was to identify the body of evidence on gaps in the quality of care for asthma, their impact on patient outcomes, and the potential cost of closing the quality gap, with the intent to provide consensus estimates for the policy debate. Our review demonstrated that the quality of asthma care is a very actively researched area, as the initial screening of the last ten years yielded 2786 publications, most of them in the peer-reviewed literature, and a large number of institutions that provided information on their websites. However, in spite of the large number of publications, it proved impossible to derive reasonably bounded consensus estimates for the cost and benefits of better asthma care. Two limitations accounted for this problem.

First, most publications focused on only one aspect of the question, e.g., they provided estimates only for ICS treatment rates or hospital admission rates. But no study tried to explicitly attribute variation in endpoints to gaps in care, i.e., tried to relate higher hospital admission rates to lower use of anti-inflammatory treatment, except in the context of an intervention. And those intervention studies were typically multifaceted, e.g. tried to address asthma triggers together with improved pharmacologic treatment. Thus, the variation in endpoints was attributed to the effect of the overall intervention and not necessarily related to pharmacologic treatment specifically, i.e. the results cannot be used to derive estimates for the effect of anti-inflammatory treatment.

Second, and more importantly, authors used a staggering variety of criteria for the identification of their study patients and a staggering number of definitions of their study endpoints. Similarly, as the key determinant both of treatment intensity and patient outcomes, disease severity was often insufficiently defined, that is, not defined according to well-established criteria. This observation was somewhat surprising, as, for example, well-established patient identification and risk stratification criteria exist that can be applied to assess utilization data (NCQA's HEDIS criteria) or clinical data (NHBLI and ATS criteria). But many authors still used their own criteria for disease severity or did not provide their criteria at all. For example, Study 11 selected their study population according to the NHBLI criteria but did not stratify their findings according to severity.

This failure of the research field to converge on common definitions is even more surprising if one considers that in 1996, the

National Asthma Education and Prevention Program's Task Force on the Cost Effectiveness, Quality of Care, and Financing of Asthma Care issued a call for more economic evaluations of asthma care and for the development of a standardized approach for such studies (Sullivan et al., 1996).

We attempted to overcome the limitations of the published information by standardizing endpoints to common definitions and by accounting for commonly used explanatory variables, such as racial/ethnic composition of the sample, age structure, disease severity, and data source. But even that attempt did not produce reasonably bounded estimates for three common endpoints (ICS treatment rates, hospital admission rates and ER visit rates). The challenge was that only a subset of the studies could be converted to those standardized endpoints, reducing the sample size to 34 studies with information on ICS usage, 42 for ER visits, and 42 for hospital admissions. Those samples did not allow us to conduct true multivariate analyses, which would simultaneously adjust for the effect of different explanatory variables. In addition, re-basing the reported information as standard outcomes and explanatory variables required the use of restrictive assumptions. Our results showed that ICS treatment rates, as well as ER and hospital utilization rates were higher in the studies of samples that we categorized as covering higher-risk patients (i.e., identification of criteria that were more stringent than the HEDIS criteria), suggesting that we were able to explain some of the variance. But the relatively crude adjustment that the reported data allowed implies that substantial heterogeneity remained unaccounted for in particular in the disease severity categories.

While no consensus estimates could be constructed, some important findings did emerge. Consistent with previously published reports, disadvantaged populations appear to receive worse care. ICS treatment rates were lower in studies with a high proportion of minority patients and/or Medicaid beneficiaries. This finding had previously been reported by others, for example, by Cooper and colleagues, who examined claims data for Medicaid patients in Tennessee and found that black children were less likely to have a prescription filled for an ICS, than white children (Cooper et al, 2001). Similarly, an article by Finkelstein and colleagues compared ambulatory visit patterns, rates of medication use, and emergency room and hospital use for asthmatic children enrolled in Medicaid and asthmatic children enrolled in the same HMO, but with a commercial payer (2000). These researchers found that significantly fewer children enrolled in Medicaid were dispensed a controller medication than the children enrolled in the commercial HMO (2000).

However, overall, a consistent result was that ICS treatment rates were far below 100 percent in a sample of studies in which most patients were likely to have had an indication for treatment.. This finding was consistent across study settings and study populations, highlighting that care for asthma patients is still far from optimal.

Some of our findings were counterintuitive: Our results suggested that rates of ER visits were higher in non-minority populations than in minorities and higher in adults than in children. The results by age are largely explained by the fact that the studies on adults tend to include more severe cases than the studies on non-adults. For instance, 7 out of 16 studies (43 percent) of non-adults used less stringent criteria than the HEDIS criteria to select subjects, compared to only 4 in 12 (33 percent) of the studies of adults. When looking only at studies that used less stringent criteria than HEDIS to select subjects, the median estimate of ER utilization rates was much lower for adults than for non-adults (9.8 versus 2.0).

No obvious explanation for the counterintuitive finding of higher ER utilization rates in studies covering non-minorities than in studies of minority groups could be found. There are no clear differences in severity definition, age composition, or source of data between the studies made up of a majority of whites relative to studies where the sample is at least 40 percent black. Moreover, the differences in ER utilization are large and not driven by outliers but quite consistent. Two qualifications have to be kept in mind, however, that may have contributed to those results. First, we use rather crude criteria<sup>10</sup> to label study sample as "minority" or "non-minority" and may have insufficiently captured important differences. Second, we compare studies with different samples rather than assess differences in utilization by race or ethnicity *within* a study sample.

Another important finding was that both ICS treatment rates and ER and hospital utilization rates were typically higher in studies based on self-reported data than in studies that used health insurance claims or medical records as their sources. This finding implies that findings that have been derived from different types of data sources cannot simply be pooled but that instead, it is necessary to take the data source into account when interpreting results.

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<sup>10</sup> We labeled studies as covering a "non-minority" population, if the majority of the sample was white, and a "minority" population, if at least 40 percent of the sample was black.

## IMPLICATIONS

Our findings suggest that more economic evaluations of the impact of asthma and of interventions to improve asthma control are clearly needed and that such research should use standard definitions to allow comparison across studies and aggregation of data. For example, one might use large databases of health insurance claims to identify groups of patients ranging in asthma severity, determine their ICS treatment rates, and compare treatment to subsequent ER visits and hospital admissions and the cost of care. This process would allow estimates to be derived for the cost-effectiveness of improved drug treatment of asthma.

Public and private funding agencies should use their influence to move the asthma research community toward more standardization. Ideally, researchers would have to commit themselves to using a set of standard definitions for disease severity, treatment intensity, and outcomes, such as hospital admissions, in order to qualify for funding. In some cases, the standard definitions might reflect mere conventions, such as expressing hospital utilization as admissions per 100 patient years. In other cases, the definitions might rely on past empirical research, such as the NHLBI categorization scheme for asthma severity. Obviously, if the particular context of a study requires the use of different operational definitions, researchers should be free to make the case for those. But unless a clear reason exists to deviate from the standard definitions, they should be used by default.

Arriving at such definitions is no easy feat, as it requires forming consensus and achieving buy-in of multiple stakeholders. MCAN, with its ties both to the federal and non-federal funding agencies, the advocacy community, and academic researchers, is in an excellent position to broker such a consensus. This effort seems worthwhile and could be more influential in achieving the goal of providing better data to decisionmakers than any individual research project.

Finally, the second important conclusion of our study is that, given the enormous variability of results, overly confident statements

about the gaps in asthma care or their impact should be avoided, as any estimates will strongly depend on their context. Thus, before better evidence is generated, policymakers and other stakeholders should carefully review the sources of - and methods used to generate - existing data, when basing critical decisions on them.

**Appendix**

**A. ASTHMA QUALITY OF CARE - SEARCH METHODOLOGIES**

**TOPIC #1: GAPS IN ASTHMA QUALITY OF CARE**

**STRATEGY 1A-**

**DATABASE SEARCHED:** PUBMED

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma[majr] OR asthma[ti] OR (asthma AND (ethnology OR epidemiology))  
AND  
quality of care OR treatment OR care OR therapy  
AND  
disparit\* OR inadequa\* OR variability OR differential OR inequit\* OR gap  
OR variation OR variance OR  
(medication AND (use OR adherence OR utilization)) OR (guideline\* AND  
adherence) OR disease management OR socioeconomic factors OR race OR  
racial OR poverty OR income OR minorities OR minority  
AND  
united states

**NUMBER OF ITEMS RETRIEVED:** 1681

**STRATEGY 1B-**

**DATABASES SEARCHED:** DISSERTATION ABSTRACTS

ECONLIT  
PAIS INTERNATIONAL  
PAPERS FIRST  
PROCEEDINGS  
PSYCINFO  
SOCIAL SCIENCE ABSTRACTS  
SOCIAL SERVICES ABSTRACTS  
SOCIOLOGICAL ABSTRACTS  
WORLDCAT  
WORLDCAT DISSERTATION

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma  
AND  
quality of care OR treatment OR care OR therapy  
AND  
disparit\* OR inadequa\* OR variability OR differential OR inequit\* OR gap  
OR variation OR variance OR (guideline adherence) OR (disease  
management) OR (medication AND (use OR adherence OR utilization))

OR

Asthma

AND  
quality  
AND  
socioeconomic\* or race or racial or poverty or income

**TOTAL NUMBER OF ITEMS RETRIEVED: 154**

**STRATEGY 1C-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**  
asthma in Subject Heading  
AND  
quality  
AND  
treat\* OR therap\*

**NUMBER OF ITEMS RETRIEVED: 288**

**STRATEGY 1D-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**  
asthma in Subject Heading  
AND  
quality  
AND  
medication OR prescription\* OR guideline\* OR "disease management"  
NOT  
"quality of life"

**NUMBER OF ITEMS RETRIEVED: 204**

**STRATEGY 1E-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**  
asthma in Subject Heading  
AND  
quality  
AND  
socioeconomic\* OR race OR racial OR poverty OR income

**NUMBER OF ITEMS RETRIEVED: 108**



**STRATEGY 1F-**

**DATABASES SEARCHED:**

New York Academy of Medicine Grey Literature Database

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:** asthma

**NUMBER OF ITEMS RETRIEVED:** 59

**TOPIC #2 - CLINICAL & POLICY IMPLICATIONS OF THE QUALITY GAP**

**STRATEGY 2A-**

**DATABASE SEARCHED:** PUBMED

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma[majr] OR asthma[ti] OR (asthma AND (ethnology OR epidemiology))  
AND  
morbidity OR mortality OR hospitaliz\* OR (hospital AND (admission OR  
admissions OR utilization OR use OR stay OR stays OR visit OR visits))  
OR (((emergency AND (room OR department OR departments)) OR ((ER OR ED)  
AND (admission OR admissions OR readmission\* OR utilization OR use OR  
stay OR stays OR visit OR visits)) OR ((loss OR lost OR absences OR  
absence OR missed OR attendance) AND (work OR employment OR workdays or  
workday OR school)) OR attendance OR absenteeism OR presenteeism  
AND  
United States  
NOT  
results of Search Topic #1

**NUMBER OF ITEMS RETRIEVED:** 1414

**STRATEGY 2B-**

**DATABASES SEARCHED:**

DISSERTATION ABSTRACTS  
ERIC  
ECONLIT  
PAIS INTERNATIONAL  
PAPERS FIRST  
PROCEEDINGS  
PSYCINFO  
SOCIAL SCIENCE ABSTRACTS  
SOCIAL SERVICES ABSTRACTS  
SOCIOLOGICAL ABSTRACTS  
WORLDCAT  
WORLDCAT DISSERTATION

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

Asthma

AND

impact OR effect OR morbidity OR mortality OR hospitalization OR hospital OR admission OR utilization OR use OR stay OR visit OR (emergency room) OR (emergency department) OR ER OR ED OR loss OR lost OR absences OR missed OR attendance OR work OR employment OR job OR workdays OR school OR absenteeism OR presenteeism

**Total NUMBER OF ITEMS RETRIEVED: 240**

**STRATEGY 2C-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

Asthma in Subject Heading

AND

(impact OR effect OR effects OR morbidity OR mortality) IN TITLE

NOT

drug therapy IN Subject Heading

**NUMBER OF ITEMS RETRIEVED: 255**

**STRATEGY 2D-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

Asthma in Subject Heading

AND

hospitalization OR (hospital\* AND (readmi\* OR re-admi\* OR admission OR admit\* OR utiliz\* OR stay)

NOT

drug therapy IN Subject Heading

**NUMBER OF ITEMS RETRIEVED: 330**

**STRATEGY 2E-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

Asthma in Subject Heading  
AND  
emergency in Subject Heading  
AND  
admission OR admit\* OR utiliz\* OR use OR stay  
NOT  
drug therapy IN Subject Heading

**NUMBER OF ITEMS RETRIEVED: 118**

**STRATEGY 2F-**

**DATABASES SEARCHED: CINAHL**

**TIME PERIOD COVERED: 1995-2006**

**OTHER LIMITERS: English**

**SEARCH STRATEGY:**

Asthma in Subject Heading  
AND  
loss OR lost OR absen\* OR presentee\*  
NOT  
drug therapy IN Subject Heading

**NUMBER OF ITEMS RETRIEVED: 139**

**SEARCH TOPIC #3 - COSTS OF CLOSING THE QUALITY GAP**

**STRATEGY 3A-**

**DATABASE SEARCHED: PubMed**

**TIME PERIOD COVERED: 1995-2006**

**OTHER LIMITERS: English**  
Human

**SEARCH STRATEGY:**

Asthma [majr] OR Asthma [ti]  
AND  
((Quality of Health Care) OR (quality of care) OR ((treatment OR care OR therapy) AND (disparity OR disparities OR inadequate OR inadequacy OR inadequacies OR variability OR differential OR inequity OR inequities OR gap OR variation OR variance)) OR (medication and (use OR adherence OR utilization)) OR (guideline\* AND adherence) OR (disease management))  
AND  
((Survivor Analysis) OR (morbidity) OR (mortality) OR (hospitalization) OR (hospital AND (admission OR utilization OR use OR stay OR visit) OR ((emergency AND (room OR department)) OR (ER) OR (ED)) AND (admission OR utilization OR use OR stay OR visit)) OR (((loss) OR (lost) OR (absences) or (missed) OR (attendance)) AND ((work) OR (employment) OR (workdays) OR (school))) OR (attendance) OR (absenteeism) OR (presenteeism))  
AND  
improvement\* OR progress OR enhancement\* OR improved OR better OR enhanced OR increased OR intervention OR program  
AND  
Cost OR (return on investment) OR budget OR expenditure\* OR spending OR expense OR savings OR ROI OR Health Care Costs

OR

Asthma [majr] OR Asthma [ti]

AND

(Quality of Health Care) OR (quality of care) OR (treatment OR care OR therapy)

AND

disparity OR disparities OR inadequate OR inadequacy OR inadequacies OR variability OR differential OR inequity OR inequities OR gap OR variation OR variance OR (medication and (use OR adherence OR utilization)) OR (guideline\* AND adherence) OR (disease management))

AND

(Survivor Analysis) OR morbidity OR mortality OR hospitalization OR (hospital AND (admission OR utilization OR use OR stay OR visit) OR ((emergency AND (room OR department)) OR (ER) OR (ED)) AND (admission OR utilization OR use OR stay OR visit)) OR (loss OR lost OR absences OR missed OR attendance) AND (work OR employment OR workdays OR school) OR attendance OR absenteeism OR presenteeism

AND

Health Care Costs

OR

Asthma [majr]

AND

improvement\* OR progress OR enhancement\* OR improved OR better OR enhanced OR increased OR intervention OR program

AND

Health Care Costs

OR

Asthma [majr]

AND

Quality of Health Care [MeSH]

AND

Health Care Costs

**NUMBER OF ITEMS RETRIEVED: 412**

**STRATEGY 3B-**

**DATABASES SEARCHED:**

DISSERTATION ABSTRACTS

ERIC

ECONLIT

PAIS INTERNATIONAL

PAPERS FIRST

PROCEEDINGS

PSYCINFO

SOCIAL SCIENCE ABSTRACTS

SOCIAL SERVICES ABSTRACTS

SOCIOLOGICAL ABSTRACTS

WORLDCAT

WORLDCAT DISSERTATION

**TIME PERIOD COVERED: 1995-2006**

**OTHER LIMITERS: English**

**SEARCH STRATEGY:**

asthma

AND

improv\* OR progres OR enhance\* OR better OR increased OR intervention OR program\*

AND

cost\* OR (retrurn on investment) OR budget\* OR expenditure\* OR spending OR expense\* OR saving\*

**TOTAL NUMBER OF ITEMS RETRIEVED: 90**

**STRATEGY 3C-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma in Subject Heading

AND

quality

AND

improv\* OR progress\* OR enhanc\* OR better OR increas\* OR interven\* OR program\*

AND

cost\* OR "return on investment" OR budget\* OR expen\* OR spend\* OR savings

**NUMBER OF ITEMS RETRIEVED: 117**

**STRATEGY 3D-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma in Subject Heading

AND

improv\* OR progress\* OR enhanc\* OR better OR increas\* OR interven\* OR program\*

AND

(cost\* OR "return on investment" OR budget\* OR expen\* OR spend\* OR savings) IN TITLE

**NUMBER OF ITEMS RETRIEVED: 47**

**STRATEGY 3E-**

**DATABASES SEARCHED:** CINAHL

**TIME PERIOD COVERED:** 1995-2006

**OTHER LIMITERS:** English

**SEARCH STRATEGY:**

asthma in Subject Heading

AND

improv\* OR progress\* OR enhanc\* OR better OR increas\* OR interven\* OR  
program\*

AND

cost\* OR "return on investment" OR budget\* OR expen\* OR spend\* OR  
savings

**NUMBER OF ITEMS RETRIEVED: 329**

**STRATEGY 3F-**

**DATABASES SEARCHED: CINAHL**

**TIME PERIOD COVERED: 1995-2006**

**OTHER LIMITERS: English**

**SEARCH STRATEGY:**

asthma in Subject Heading

AND

improv\* OR progress\* OR enhanc\* OR better OR increas\* OR interven\* OR  
program\*

AND

econom\*

NOT

cost\* OR "return on investment" OR budget\* OR expen\* OR spend\* OR  
savings

**NUMBER OF ITEMS RETRIEVED: 133**

**B. LITERATURE SEARCH WEBSITES**

**Government, professional and advocacy organization websites visited  
for literature search**

<b>Website/Organization</b>	<b>URL</b>
Agency for Healthcare Research and Quality	<a href="http://www.ahrq.gov">www.ahrq.gov</a>
Asthma and Allergy Foundation of America (AAFA)	<a href="http://www.aafa.org/">www.aafa.org/</a>
Allies Against Asthma (Michigan)	<a href="http://www.asthma.umich.edu/">www.asthma.umich.edu/</a>
American Lung Association	<a href="http://www.lungusa.org">www.lungusa.org</a>
California's Regional Asthma Management and Prevention (RAMP) Initiative	<a href="http://www.rampasthma.org">www.rampasthma.org</a>
California Health Department Asthma Program	<a href="http://www.dhs.ca.gov/asthma">www.dhs.ca.gov/asthma</a>
Center for Health Care Strategies	<a href="http://www.chcs.org">www.chcs.org</a>
Chicago Asthma Consortium	<a href="http://www.chicagoasthma.org/">http://www.chicagoasthma.org/</a>
New York City Asthma Partnership	<a href="http://www.asthma-nyc.org">www.asthma-nyc.org</a>
National Initiative for Children's Health Care Quality (NICHQ)	<a href="http://www.nichq.org">www.nichq.org</a>

Institute for Healthcare Improvement (IHI)	<a href="http://www.ihl.org">www.ihl.org</a>
National Institutes of Health (NIH)	<a href="http://www.nih.gov">www.nih.gov</a>
National Heart, Lung, and Blood Institute (NHLBI)	<a href="http://www.nhlbi.nih.gov/">www.nhlbi.nih.gov/</a>
National Institute of Allergy and Infectious Diseases (NIAID)	<a href="http://www.niaid.nih.gov">www.niaid.nih.gov</a>
National Institute of Environmental Health Sciences (NIEHS)	<a href="http://www.niehs.nih.gov">www.niehs.nih.gov</a>
Robert Wood Johnson Foundation	<a href="http://www.rwjf.org">www.rwjf.org</a>
CDC Asthma Program	<a href="http://www.cdc.gov/asthma/">http://www.cdc.gov/asthma/</a>
American Academy of Allergy Asthma and Immunology (AAAAI)	<a href="http://www.aaaai.org/">www.aaaai.org/</a>
WHO Global Alliance Against Chronic Respiratory Diseases (GARD)	<a href="http://www.who.int/respiratory/gard/en/">www.who.int/respiratory/gard/en/</a>
International Study of Asthma and Allergies in Childhood (ISAAC)	<a href="http://isaac.auckland.ac.nz/">http://isaac.auckland.ac.nz/</a>

Literature Search Wesites, continued

EPA Asthma and Indoor Environments	<a href="http://www.epa.gov/asthma/">www.epa.gov/asthma/</a>
American College of Allergy, Asthma and Immunology (ACAAI)	<a href="http://www.acaai.org/">www.acaai.org/</a>
Global Institute for Asthma	<a href="http://www.ginasthma.com">www.ginasthma.com</a>
DHHS	<a href="http://www.hhs.gov/">www.hhs.gov/</a>
Social Science Research Network (SSRN)	<a href="http://www.ssrn.com">www.ssrn.com</a>
National Bureau of Economic Research	<a href="http://www.nber.org/">www.nber.org/</a>
Kaiser Family Foundation	<a href="http://www.kff.org">www.kff.org</a>
Canadian Lung Association	<a href="http://www.lung.ca/asthma/">www.lung.ca/asthma/</a>
Asthma UK	<a href="http://www.asthma.org.uk/">www.asthma.org.uk/</a>
Asthma Foundation of Victoria (Australia)	<a href="http://www.asthma.org.au/">www.asthma.org.au/</a>
Merck Childhood Asthma Network (MCAN)	<a href="http://www.mcanonline.org">www.mcanonline.org</a>



**C. ARTICLES INCLUDED IN THE REVIEW**

<u>ID</u>	<u>Citation</u>
248	Allen, F. C. (2000) "Temporal trends in prescribing of anti-inflammatory medications for asthma management." DAI 61(03B): 116.
30	Allen-Ramey, F. C. Duong P. T. Goodman D. C. Sajjan S. G. Nelsen L. M. Santanello N. C. and Markson L. E. (2003). "Treatment effectiveness of inhaled corticosteroids and leukotriene modifiers for patients with asthma: an analysis from managed care data." Allergy Asthma Proc 24(1): 43-51
329	American Lung Association "Trends in Morbidity and Mortality Report." May 2005 <a href="http://www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/ASTHMA1.PDF">http://www.lungusa.org/atf/cf/%7B7A8D42C2-FCCA-4604-8ADE-7F5D5E762256%7D/ASTHMA1.PDF</a>
114	Anderson, M. E. Freas M. R. Wallace A. S. Kempe A. Gelfand E. W. and Liu A. H. (2004). "Successful school-based intervention for inner-city children with persistent asthma." J Asthma 41(4): 445-53
294	Berg, J., D. R. Wahlgren, et al. (2004) "Latino children with asthma: rates and risks for medical care utilization." J Asthma 41(2): 147-57.
113	Berger, W. E. Legorreta A. P. Blaiss M. S. Schneider E. C. and et al. (2004). "The utility of the Health Plan Employer Data and Information Set (HEDIS) asthma measure to predict asthma-related outcomes." Annals of Allergy, Asthma, & Immunology (93(6), p. 538-45).
242	Birnbaum, H. G., W. E. Berger, et al. (2002) "Direct and indirect costs of asthma to an employer." J Allergy Clin Immunol 109(2): 264-70.
163	Blixen, C. E. Education C. Tilley B. Havstad S. and Zoratti E. (1997). "Quality of life, medication use, and health care utilization of urban African Americans with asthma treated in emergency departments." Nursing Research 46(6): 338-341
93	Bloom, B. and Dey A. N. (2006). "Summary health statistics for U.S. children: National Health Interview Survey, 2004." Vital Health Stat 10(227): 1-85.
292	Borker, R., A. Emmett, et al. (2005) "Determining economic feasibility of fluticasone propionate-salmeterol vs montelukast in the treatment of persistent asthma using a net benefit approach and cost-effectiveness acceptability curves." Ann Allergy Asthma Immunol

<u>ID</u>	<u>Citation</u>
86	Boyd, B. J. (1997). The Effects of Community-Based Pharmaceutical Care Services on Asthma-Related Health Care Expenditures, Utilization, and Quality of Life, THE UNIVERSITY OF TEXAS AT AUSTIN.
105	Carroll, K. N. Griffin M. R. Gebretsadik T. Shintani A. Mitchel E. and Hartert T. V. (2005). "Racial differences in asthma morbidity during pregnancy." Obstet Gynecol 106(1): 66-72.
129	Castro, M. Zimmermann N. A. Crocker S. Bradley J. Leven C. and Schechtman K. B. (2003). "Asthma intervention program prevents readmissions in high healthcare users." Am J Respir Crit Care Med 168(9): 1095-9.
103	2005). "Reducing childhood asthma through community-based service delivery--New York City, 2001-2004." MMWR Morb Mortal Wkly Rep 54(1): 11-4.
353	Cisternas, M. G., P. D. Blanc, et al. (Jun 2003). "A comprehensive study of the direct and indirect costs of adult asthma." J Allergy Clin Immunol 111(6): 1212-8.
97	Cloutier, M. M. Hall C. B. Wakefield D. B. and Bailit H.(2005). "Use of asthma guidelines by primary care providers to reduce hospitalizations and emergency department visits in poor, minority, urban children." J Pediatr 146(5): 591-7.
42	Cooper, W. O. and Hickson G. B.(2001). "Corticosteroid prescription filling for children covered by Medicaid following an emergency department visit or a hospitalization for asthma." Arch Pediatr Adolesc Med 155(10): 1111-5.
27	David, C. (2004). "Preventive therapy for asthmatic children under Florida Medicaid: changes during the 1990s." J Asthma 41(6): 655-61.
112	(2005). Chronic care for low-income children with asthma: strategies for improvement. Research in action ;; issue no. 18; AHRQ Publication ;; no. 05-0073;; U.S. Dept. of Health and Human Services, Agency for Healthcare Research and Quality: 11 p. : ill. ; 28 cm.
47	Diaz, T. Sturm T. Matte T. Bindra M. Lawler K. Findley S. and Maylahn C.(2000). "Medication use among children with asthma in East Harlem." Pediatrics 105(6): 1188-93.
266	Ebrahim, N.(2004) The pharmaco-economic impact of non-adherence to the standard treatment guidelines for the treatment of asthma in community primary health care centres in the Cape Metropolitan Area, University of the Western Cape (South Africa): 105.

<u>ID</u>	<u>Citation</u>
117	Ebrahim, N. (2004). The pharmaco-economic impact of non-adherence to the standard treatment guidelines for the treatment of asthma in community primary health care centres in the Cape Metropolitan Area, University of the Western Cape, South Africa: 105.
52	Eggleston, P. A. Malveaux F. J. Butz A. M. Huss K. Thompson L. Kolodner K. and Rand C.S. (1998). "Medications used by children with asthma living in the inner city." Pediatrics 101(3 Pt 1): 349-54.
202	Eisner, M. D., E. H. Yelin, et al. (2002) "The influence of chronic respiratory conditions on health status and work disability." Am J Public Health 92(9): 1506-13.
219	Eroglu, G. E., F. A. Rabito, et al. (2002) "Mortality from asthma in children and young adults in Louisiana." Ann Allergy Asthma Immunol 89(2): 191-4.
165	Evans, D. Mellins R. Lobach K. Ramos-Bonoan C. Pinkett-Heller M. Wieseemann S. Klein I. Donahue C. Burke D. Levison M. Levin B. Zimmerman B. and Clark N. (1997). "Improving care for minority children with asthma: professional education in public health clinics." Pediatrics 99(2): 157-64.
82	Farber, H. J. Johnson C. and Beckerman R. C. (1998). "Young inner-city children visiting the emergency room (ER) for asthma: Risk factors and chronic care behaviors." Journal of Asthma 35(7): 547-552.
49	Finkelstein, J. A. Barton M. B. Donahue J. G. Algatt-Bergstrom P. Markson L. E. and Platt R. (2000). "Comparing asthma care for Medicaid and non-Medicaid children in a health maintenance organization." Arch Pediatr Adolesc Med 154(6): 563-8.
104	Getahun, D. Demissie K. and Rhoads G. G. (2005). "Recent trends in asthma hospitalization and mortality in the United States." J Asthma 42(5): 373-8.
322	Guilbert, Theresa W.; Morgan, Wayne J.; Zeiger, Robert S.; Mauger, David T.; Boehmer, Susan J.; Szeffler, Stanley J.; Bacharier, Leonard B.; Lemanske, Robert F. Jr.; Strunk, Robert C.; Allen, David B.; Bloomberg, Gordon R.; Heldt, Gregory; Krawiec, Marzena; Larsen, Gary; Liu, Andrew H.; Chinchilli, Vernon M.; Sorkness, Christine A.; Taussig, Lynn M.; Martinez, Fernando D. "Long-Term Inhaled Corticosteroids in Preschool Children at High Risk for Asthma" NEJM Volume 354(19), 11 May 2006, pp 1985-1997.

<u>ID</u>	<u>Citation</u>
121	Halterman, J. S. Szilagyi P. G. Yoos H. L. Conn K. M. Kaczorowski J. M. Holzhauer R. J. Lauver S. C. Neely T. L. Callahan P. M. and McConnochie K. M. (2004). "Benefits of a school-based asthma treatment program in the absence of secondhand smoke exposure: results of a randomized clinical trial." Arch Pediatr Adolesc Med 158(5): 460-7.
147	Harish, Z. Bregante A. C. Morgan C. Fann C. S. Callaghan C. M. Witt M. A. Levinson K. A. and Caspe W. B. (2001). "A comprehensive inner-city asthma program reduces hospital and emergency room utilization." Ann Allergy Asthma Immunol 86(2): 185-9.
46	Hartert, T. V. Togias A. Mellen B. G. Mitchel E. F. Snowden M. S. and Griffin M. R. (2000). "Underutilization of controller and rescue medications among older adults with asthma requiring hospital care." J Am Geriatr Soc 48(6): 651-7.
254	Heaton, P. C., J. J. Guo, et al. (2006) "Analysis of the effectiveness and cost benefit of leukotriene modifiers in adults with asthma in the Ohio Medicaid population." J Manag Care Pharm 12(1): 33-42.
166	Homer, C. J. Szilagyi P. Rodewald L. Bloom S. R. Greenspan P. Yazdgerdi S. Leventhal J. M. Finkelstein D. and Perrin J. M. (1996). "Does quality of care affect rates of hospitalization for childhood asthma?" Pediatrics 98(1): 18-23.
4	Huse, D. M. Russell M. W. Weiss S. T. and Hartz S. C. (2000). "Anti-inflammatory therapy reduces total costs of asthma care compared with bronchodilation: the Asthma Outcomes Registry." Am J Manag Care 6(9): 1045-50.
367	Janson, S. L., J. V. Fahy, et al. (Dec 1 2003). "Effects of individual self-management education on clinical, biological, and adherence outcomes in asthma." Am J Med 115(8): 620-6.
5	Johnson Ae Yin M and Berg (2003). "Utilization and financial outcomes of an asthma disease management program delivered to Medicaid members: results of a three-group comparison study." Disease Management & Health Outcomes 11(7): 455-65.
61	Johnson, A. Berg G. Fleegler E. and Sauerbrun M. (2005). "A matched-cohort study of selected clinical and utilization outcomes for an asthma care support program." Disease Management 8(3): 144-54.
236	Lenhardt, R, et al. (2003) "Trends in emergency department asthma care in metropolitan Chicago: results from the Chicago Asthma Surveillance Initiative." Chest 124(5), p. 1774-80.

<u>ID</u>	<u>Citation</u>
359	Lozano, P., J. A. Finkelstein, et al. (Jan 2003). "Asthma medication use and disease burden in children in a primary care population." Arch Pediatr Adolesc Med 157(1): 81-8.
149	Lurie, N. Bauer E. J. and Brady C. (2001). "Asthma outcomes at an inner-city school-based health center." J Sch Health 71(1): 9-16.
257	Luskin, A., D. Bukstein, et al. (2005) "Asthma rescue and allergy medication use among asthmatic children with prior allergy prescriptions who initiated asthma controller therapy." Ann Allergy Asthma Immunol 95(2): 129-36.
229	Maier, W. C., H. M. Arrighi, et al. (1998) "The impact of asthma and asthma-like illness in Seattle school children." J Clin Epidemiol 51(7): 557-68.
10	Markovitz, B. P. and Andresen E. M. (2006). "Lack of insurance coverage and urgent care use for asthma: a retrospective cohort study." BMC Public Health 6: 14.
143	Marosi, A. and Stiesmeyer J. (2001). "Improving pediatric asthma patient outcomes by incorporation of effective interventions." J Asthma 38(8): 681-90.
79	McConnochie, K. M. Russo M. J. McBride J. T. Szilagyi P. G. Brooks A. M. and Roghmann K. J. (1999). "Socioeconomic variation in asthma hospitalization: excess utilization or greater need?" Pediatrics 103(6): e75.
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