American Thoracic Society Documents

An Official ATS Workshop Report: Issues in Screening for Asthma in Children

Lynn B. Gerald, Marianna M. Sockrider, Roni Grad, Bruce G. Bender, Leslie P. Boss, Stanley P. Galant, Jorrit Gerritsen, Christine L. M. Joseph, Robert M. Kaplan, Julie A. Madden, Joan M. Mangan, Greg J. Redding, Diana K. Schmidt, Christina D. Schwindt, Virginia S. Taggart, Lani S. Wheeler, Kristin N. Van Hook, Paul V. Williams, Barbara P. Yawn, and Bulend Yuksel, on behalf of the ATS Ad Hoc Committee on Issues in Screening for Asthma in Children

This Official American Thoracic Society (ATS) Workshop Report was approved by the ATS Board of Directors, September 2006

CONTENTS

INTRODUCTION

Some national health organizations advocate screening entire communities for pediatric asthma. They do so for the following reasons: asthma is associated with an early childhood onset; it is one of the most common chronic diseases in children; it is a common reason for school absences, which are a factor in poor school performance; and it is the leading cause of hospitalization in childhood (1–5). In addition, some children are undiagnosed and many are undertreated (6–11). Much of the morbidity associated with asthma is largely preventable with proper treatment (12); therefore, the desire to implement asthma screening in the population is quite natural.

Proc Am Thorac Soc Vol 4. pp 133–141, 2007
DOI: 10.1513/pats.200604-103ST
Internet address: www.atsjournals.org

Although population screenings for asthma make sense in theory, recent analyses of existing asthma screening methods and health outcomes concluded that the benefits of population-based asthma screening are unproven (13, 14). Despite the lack of clear evidence of benefit, some organizations continue their advocacy of population-based asthma screening (15–19). In 2005, the Behavioral Science and Pediatric Assemblies of the American Thoracic Society convened a multidisciplinary panel of experts to review the existing literature and to attempt to answer the question of whether population-based asthma screening programs for children are warranted at this time. Before the workshop, participants were assigned topics for which they reviewed the literature and prepared presentations. Topics included the following: (*1*) a review of the World Health Organization criteria for population-based screening (*see* Table 1), (*2*) experiences with the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, (*3*) experiences with several National Heart, Lung, and Blood Institute (NHLBI)–funded school-based asthma screening studies, (*4*) experience with asthma screening/case detection in Europe, (*5*) the Breathmobile experience, and (*6*) the experiences of one of the American College of Asthma, Allergy, and Immunology–funded school-based asthma screening study sites. Additional topics presented addressed the impact of false positives and false negatives, and where asthma might fit into the continuum of childhood chronic diseases that may benefit from screening/case detection. After the presentations, much discussion ensued, and opinions/recommendations were formulated based on group consensus. The methodology for the literature review was left to each presenter's discretion; additional evidence from the literature was offered in the discussion. After the meeting, the participants were invited to submit their findings in writing to the organizers. Each participant had an opportunity to review and comment on the symposium proceedings before submission of the document. This document summarizes the group's findings and recommendations.

PROCEEDINGS

Participants began the workshop by carefully reviewing the terminology used to describe the process of identifying children with asthma. "Screening" refers to a process used to identify individuals with disease but who are in a preclinical (asymptomatic) state. In contrast, "case detection" identifies individuals with disease who are symptomatic but undiagnosed. Therefore, the term *case detection* most accurately describes the methods that are currently used and advocated in the asthma screening literature (13). Even though the term *case detection* best

TABLE 1. WORLD HEALTH ORGANIZATION CRITERIA FOR ASSESSMENT OF SCREENING PROGRAMS

1. The condition must be an important public health problem.
2. The natural history of the disease state should be understood.
3. There should be a recognizable latent or early symptomatic stage.
4. There should be accepted treatment for patients with recognized disease, and there should be an agreed-upon policy for treatment, including whom to treat.
5. Facilities for diagnosis and treatment should be available.
6. There should be a suitable screening test or examination.
7. The screening test should be acceptable to the population.
8. The cost of screening (including diagnosis and treatment) should be economically balanced.
9. Screening should be continuous.

describes current methods, this semantic argument should not overshadow the most important, underlying question: whether asthma screening or case detection is advisable at this time.

The current state of the art for asthma case detection and its relevant outcomes were evaluated by workshop participants using the World Health Organization's criteria (*see* Table 1) for scientifically acceptable population-based screening (13). This document presents the findings of the group as they relate to each of these criteria.

1. THE CONDITION MUST BE AN IMPORTANT HEALTH PROBLEM

The high prevalence of asthma and the cost of disease to society clearly attest to its importance as a public health problem. Studies indicate that the prevalence of undiagnosed asthma in children ranges from 3 to 20% (6, 20–23). Furthermore, the prevalence of undertreatment in persistent asthma is high (8–11, 24–26). Certain high-risk subgroups within the population may have even higher rates of undiagnosed and undertreated asthma and therefore may benefit more from case detection programs (*see* section 8). Before undertaking asthma case detection, it is important to estimate the prevalence of undiagnosed and/or undertreated asthma in the targeted population. This panel acknowledges that childhood asthma is an important health condition; however, the panel cannot unequivocally recommend implementation of widespread population-based asthma case detection programs. Although there is evidence to suggest that case detection programs may be beneficial in settings with a high prevalence of undiagnosed and/or undertreated asthma (27), such programs should be weighed against expenditures for other programs that also provide important public health benefits. Even if one were to identify a case of undertreated asthma, there is no certainty that the patient would then have access to and/or receive optimal therapy (*see* section 4).

Bottom line: Although asthma is an important public health problem, the probability of undiagnosed and/or undertreated asthma in the target population should be sufficiently great to justify the expense.

2. THE NATURAL HISTORY OF THE DISEASE STATE SHOULD BE UNDERSTOOD

Asthma likely consists of multiple phenotypes, each with its own unique natural history (1, 4, 28). However, reliable markers to fully differentiate among the phenotypes are not clinically available. In addition, the current state of medical practice is unable to identify children who are in a preclinical stage. It is also unclear whether early intervention in a preclinical stage would improve the natural history of the disease. Even in patients with known asthma, the nature of progression, if any, in mild, moderate, and severe asthma is not clear. It is also unknown whether treatment can reverse progression of the disease (29–32). In toddlers with a history of wheezing, fluticasone propionate, although controlling symptoms, does not alter the course of asthma (33). Thus, it appears that even beginning treatment at age 2 or 3 years is too late to alter the course of asthma. If early intervention could improve the natural history of asthma, it is possible that case detection would need to occur in very early life, because it appears that many of the asthma phenotypes are likely to be firmly established by the time children are school-aged. An exception to this may be found in asthma phenotypes that first express themselves during adolescence (34). It is at least reassuring to know, however, that inhaled steroids can control disease even in toddlers; thus, even though the treatment does not alter the natural history of asthma, one could argue for case detection even in that age group to potentially reduce morbidity from the disease.

Bottom line: No evidence exists that early intervention with treatments currently available alters the natural history of asthma.

3. THERE SHOULD BE A RECOGNIZABLE LATENT OR EARLY SYMPTOMATIC STAGE

Because a latent (preclinical) phase of asthma has not been identified and no biomarkers exist to reliably identify asymptomatic patients, classic screening *per se* is not possible. Furthermore, even when asthmalike symptoms appear for the first time, particularly in infancy, they do not reliably predict a future asthma diagnosis (5). The same problems exist with clinical tools that have been developed to identify asthma in toddlers with recurrent wheezing (35, 36); it is not possible to accurately identify prospectively which toddlers will develop asthma. Furthermore, the definition of "early symptomatic stage" in asthma is unclear; one may have had symptoms for many years without realizing their significance. Trials of aggressive allergen avoidance in early life have yielded modest reductions in some asthma symptoms in toddlers (37, 38) and school-aged children (39, 40). Cetirizine treatment of infants with atopic dermatitis who were sensitized to house dust mite or grass pollen has been associated with reduced risk of developing asthma (41). Other potential risk factors for asthma development include obesity and viral illnesses; to date, no clinical trials have been performed to document that avoidance of these conditions can alter the natural history of asthma onset. Thus, we have no clear-cut mechanism to reliably identify presymptomatic individuals with asthma. Efforts to reduce asthma onset in "high risk" children have yielded at best modest results for very high cost, and potentially impacted only on those with an atopic phenotype. However, when programs are viewed from the case detection perspective, the criterion that a preclinical phase must exist does not necessarily apply.

Bottom line: No preclinical state for asthma has been reliably identified.

4. THERE SHOULD BE ACCEPTED TREATMENT FOR PATIENTS WITH RECOGNIZED DISEASE, AND THERE SHOULD BE AN AGREED-UPON POLICY FOR TREATMENT, INCLUDING WHOM TO TREAT

Various widely accepted guidelines exist for the treatment of asthma (the NHLBI-EPR2 guidelines [http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf], the various other national guidelines [http://www.sign.ac.uk/guidelines/published/support/guideline63/download.html, http://www.nationalasthma.org.au/html/management/home/index.asp], and the GINA guidelines [Global Initiative for Asthma] [http://www.ginasthma.com/GuidelinesResources.asp]). Unfortunately, even with these guidelines,

undertreatment of asthma is a common problem (8, 24–26, 42); therefore, the benefit of case detection programs will be partially offset by difficulty in obtaining effective treatment for those children identified. This problem may be most pronounced in the very populations in which case detection would be most beneficial (vulnerable populations with high prevalence of undiagnosed asthma). Lessons learned from several asthma intervention programs suggest that it is difficult to engage primary care physicians to improve the quality of asthma care (22, 26, 43). However, another study providing intensive asthma education for physicians and allied health staff in a public health department setting demonstrated modest improvements in the provision of asthma education and the prescription of asthma controller medications for patients with persistent asthma (44–46). The feasibility of reproducing these programs for all or even most primary care physicians is unknown.

Bottom line: Although accepted treatments for asthma exist, undertreatment is still common; therefore, additional work is needed before this criterion is met.

5. FACILITIES FOR DIAGNOSIS AND TREATMENT SHOULD BE AVAILABLE

Case detection for any disease without assured access to follow-up diagnostic and treatment services makes it unlikely that improved health outcomes will result from the activity. Current evidence suggests that identifying and referring patients with probable asthma to a health care provider is insufficient to improve rates of appropriate asthma care. One recent study, conducted in a relatively affluent community with adequate physician coverage, demonstrated that less than one-third of children who were referred to care after being identified with undertreated asthma were actually seen by a physician (26). Other studies have attempted to overcome this problem by locating health care providers within or very near the schools themselves or by transporting the children to the health care providers (47–55). Although these options may be effective in improving care, they are not currently available in a majority of schools or communities and require significant resources to establish and maintain. Another limitation of some of these approaches is that medical care should be available on a consistent basis, not just limited to a one-time visit to confirm a diagnosis or "tune up" care. Ideally, medical care would also include access to asthma specialists who can provide comanagement for children with moderate to severe asthma. It must be noted that, even in areas where reliable follow-up care is readily available, it is unclear whether these providers can handle a rapid influx of large numbers of children who may need to be evaluated for possible asthma as a result of population-based case detection programs. Until these shortcomings can be addressed, the potential positive impact of population-based case detection programs cannot be fully realized. For this reason, case detection programs should not be implemented in communities where reliable linkages to appropriate asthma care are unavailable.

Bottom line: Many communities lack facilities where reliable follow-up asthma care is readily available for those who are identified with the disease.

6. THERE SHOULD BE A SUITABLE SCREENING TEST OR EXAMINATION

Before the adoption of a specific tool for identifying asthma in a given population, the key stakeholders should carefully consider the primary purpose of the intervention (i.e., identifying undiagnosed children vs. undertreated children, or both) and should identify a tool that will be valid in the population of interest. Most asthma case detection in children has been performed at public schools; however, children who attend private school, who are home schooled, or who are absent on the day of case detection activities can be missed. In a study in a relatively affluent community that included private schools, the response rate for the initial surveys was higher than in those studies that only included public schools; however, the follow-up rates did not differ (26). Furthermore, asthma may not be considered a priority by all school systems. Schools should be viewed as equal partners with full buy-in if school-based case detection programs are to be successful in the long run. Finally, no case detection technique is perfect; ultimately, a health care provider should be available to confirm or refute the diagnosis, and to provide appropriate care for the child who is identified with the disease.

There is no existing instrument that can reliably identify presymptomatic children with asthma. Therefore, existing surveys are case detection instruments (to identify symptomatic children) that are based on the diagnostic criteria set by the National Asthma Education and Prevention Program (NAEPP [the NHLBI-EPR2 guidelines]), GINA, and others. These surveys generally include 2 to 16 questions presented to parents, but some are also presented to children who are able to report their own symptoms (56). Published reports of some of these instruments' performance are provided in Table 2. These instruments are not directly comparable in that they were tested in different populations and used different gold standards for the validation procedure.

When evaluating the accuracy of these instruments, consideration should be given to the interaction between prevalence and positive predictive value. A diagnostic tool's positive predictive value is increased in high-prevalence settings and decreased in low-prevalence settings. The studies in Table 2 were conducted in populations where the asthma prevalence ranged from 25 to 50%. Therefore, one would predict that these instruments would not perform as well when used in the general population where asthma prevalence is lower (57). The differences observed in performance of the various instruments relate in part to the combination of items used to define a positive screen. Case detection instruments that are most likely to be valuable are those that are brief with high sensitivity and specificity.

Other important issues impact on the feasibility and reliability of survey methodology for population-based case detection. Certainly, the availability of adequate financial resources is critical. In addition, case detection may impact classroom time if surveys are conducted with children or children perform pulmonary function as part of the case detection program. The age of the child dictates whether surveys should be sent only to parents versus relying on self-reporting by children in the classroom to narrow the focus of parental survey or further evaluation. The most widely used survey to assess asthma prevalence has been the ISAAC questionnaire, which is available in print and video formats (58–60). The ISAAC has had multiple translations and its items are designed to be given across cultures. Concordance between the written and video ISAAC survey tools has been modest and criteria for how many scenes a child must identify to be considered a positive responder to the video tool have varied among studies. In addition, ISAAC is designed to measure prevalence of asthma and allergy symptoms, not to detect individuals in need of treatment.

Because asthma is a disease characterized by episodes of airflow obstruction that are often reversible (NAEPP definition, 1997), objective measures of lung function and bronchial hyperresponsiveness (BHR) are commonly included in case detection programs. These measures have been used to confirm positive survey responses, thereby reducing false positives. Detection of obstruction during baseline lung function testing is frequently assessed by measuring peak flow or by obtaining spirometry. When obstruction is present, a 12% response of peak flow or

TABLE 2. SENSITIVITY AND SPECIFICITY OF SCHOOL SURVEYS FOR CASE DETECTION

Study	n	No. of Items	Sensitivity	Specificity	Gold Standard
Bansal and colleagues (2001) (Ref. 76)	244	2	0.97	0.97	Physician specialist review of clinical data
Frank and colleagues (1999) (Ref. 77)	157	5	0.23–0.70	0.91–0.99	Physician evaluation
Fuso and colleagues (2000), video (Ref. 78)	106	5	0.75	0.87	Physician specialist evaluation
Fuso and colleagues (2000), written (Ref. 78)	106	4	0.87	0.73	Physician specialist evaluation
Galant and colleagues (2004) (Ref. 25)	401	3,7	0.63–0.83	0.88	Physician specialist evaluation
Gerald and colleagues (2004) (Ref. 57)	2,738	5	0.88	0.58	Physician specialist evaluation
Glasgow and colleagues (2001) (Ref. 79)	180	5	0.92	0.76	Physician specialist evaluation
Gruchalla and colleagues (2003) (Ref. 80)	300	8	0.64	0.11	Positive methacholine challenge test
Jones and colleagues (2004) (Ref. 48)	675	7	0.87	0.84	Physician specialist evaluation
Redline and colleagues (2003) (Ref. 81)	107	5	0.80	0.75	Physician specialist evaluation
Sockrider and colleagues (2001) (Ref. 56)	350	9	0.79–0.81	0.94–0.95	Medical record evaluation or clinical phone interview
Wolf and colleagues (1999) (Ref. 82)	81	5	0.75	0.81	Physician specialist evaluation

FEV_1 to bronchodilator strongly suggests the presence of asthma. Both peak flow and spirometry are effort dependent, and typically require a child to be at least 6 years of age to perform consistently. Lung function testing methods for those younger than 6 years are not yet widely available. Single measures of spirometry and peak flow measurement may miss a considerable number of children with asthma, because lung function fluctuates and is frequently normal if children are not symptomatic at the time of testing. Challenge studies to detect BHR may also be negative in some cases of asthma, and BHR is not specific for asthma. Thus, relying solely on these measures of lung function may result in false negatives. In addition, such studies are costly and not practical for large-scale case detection (61). Measurements of markers of inflammation in exhaled breath condensate are showing promise as a noninvasive method to detect asthma presence and disease activity, but considerable work needs to be done before they are ready to be used as a screening or case detection tool (62). Technological advancements in asthma testing have not yet provided a reliable tool to replace survey methodology.

Bottom line: Survey methodology appears to be the most cost-effective method to carry out case detection activities. Several tools show promise.

7. THE SCREENING TEST SHOULD BE ACCEPTABLE TO THE POPULATION

Available evidence suggests that existing case detection methods involving questionnaires, physiologic testing, or both are likely to be acceptable to the general population. High questionnaire return rates (75–98%) documented in most population-based studies suggest that asthma questionnaires are widely acceptable to the population. However, many studies suggest that it is necessary to provide incentives to obtain high response rates; this practice greatly increases the cost of asthma case detection programs. One program reported that over three-quarters of parents in an inner-city elementary school system consented to physiologic testing of their children (78–84% consenting to spirometry and a modified exercise challenge [57]); thus, these tests would likely be acceptable to the population at large. As newer algorithms and tests become available, their acceptability will have to be assessed.

Bottom line: Tests likely to be used for case detection appear to be acceptable to the population.

8. THE COST OF SCREENING (INCLUDING DIAGNOSIS AND TREATMENT) SHOULD BE ECONOMICALLY BALANCED

Targeting Those for Case Detection to Maximize Economic Balance

Because population-based case detection is expensive, there should be convincing evidence that children identified with asthma by case detection benefit as a result of having been recognized. For asthma case detection to be cost-effective, asthma should cause considerable morbidity in the population being examined and the population should contain a sufficiently large number of individuals who are undiagnosed or whose asthma is not well controlled (to maximize the positive predictive value as discussed earlier). In a population that contains a sufficiently large number of undiagnosed individuals, it is also important to consider how disease severity is distributed among those undiagnosed and whether or not identifying children will result in their accessing care. Some recent studies have indicated that children with undiagnosed asthma have less severe asthma than those who have a current diagnosis (22, 57), whereas others have found a high prevalence of persistent disease among the undiagnosed. Researchers have also demonstrated significant symptoms among those diagnosed with persistent disease (25, 63, 64). In fact, a recent study in Arkansas indicated that 98% of students with asthma were identified by parent-reported physician diagnosis of asthma alone, indicating a low prevalence of undiagnosed disease in that community (64). Furthermore, those with a current asthma diagnosis had greater morbidity than those without a current diagnosis. Thus, in some areas, children with significant symptoms may have already sought care. If this is true, then case detection may only identify children with mild asthma for whom treatment, while perhaps benefiting the individual, may have little public health impact. Furthermore, simply identifying children with asthma may not improve health outcomes (7), given that they may or may not receive further evaluation and care for their newly identified disease (26). This is at least partly explained by the fact that many of the children identified will never come to the attention of their health care provider or the formal medical system. The possibility that case detection may only identify those with mild asthma and may not result in improved care for children identified suggests that the decision to perform case detection should be considered in the context of how available resources might be better used to improve other competing health problems.

It is likely that those groups experiencing the greatest morbidity and mortality would benefit most from case detection programs. Morbidity and mortality from asthma disproportionately affect low-income minority communities (65). Asthma exacerbation prevalence is highest in children aged 5 to 14 years and in African Americans (65). Bloomberg and colleagues found hospital readmissions for childhood asthma to be more common in African Americans who were either self-paying or who had Medicaid insurance; prior admission was the most specific predictor of subsequent admission (66). Conversely, whites may be at greater risk for asthma death during sports; individuals with even mild disease may be at risk as well (67, 68). In addition, a

review of 51 pediatric asthma deaths over a 3-year period beginning May 1, 1986, in Victoria, Australia, demonstrated that one-third of these deaths occurred in individuals who had a previous history of mild asthma (69). One study found that children with asthma have 1.7 times the risk of having a learning disability, and children with asthma from families with incomes below $20,000 had twice the odds of grade failure (3). However, in the overwhelmingly white, relatively affluent school system of Rochester, Minnesota, asthma had no impact on school performance (70). Furthermore, in a cohort of relatively affluent children with mild or moderate asthma, the disease did not impact on neurocognitive functioning (71).

The data are insufficient to conclusively identify those who would most benefit from asthma case detection. It would appear that, when considering morbidity factors, inner-city, low-income minority children in elementary or junior high school should be targeted, because this is the group in which some benefit to case identification has been identified (27). However, children in these areas are those most likely to have limited access to appropriate care, and the primary problem limiting the impact, to date, of case detection programs on asthma outcomes has been the lack of reliable follow-up medical care. Thus, the workshop participants believe that the current priority goal should be to identify children with moderate to severe persistent asthma who are either undiagnosed or those who are diagnosed but are still experiencing significant symptoms, when linkage to appropriate care can be assured. Furthermore, given the risk of death to those with asthma who participate in sports, carefully looking for asthma in preparticipation physical examinations is important. In settings where access to reliable follow-up care and resources to implement programs are available, case detection programs may have benefit, especially given the observation that earlier treatment of asthma in children (72) and adults (73) is associated with higher lung function. Again, the costs should be carefully weighed against competing public health needs.

Impact of False Positives

Before considering instituting universal asthma case detection programs, the risk of false positives should be considered. False positives as a result of asthma case detection programs can be stressful for families and overburden health care providers with unnecessary referrals. Even though positive evaluations do not always (or even usually) equate to diagnoses of asthma, the confusion and concern they engender are significant. Therefore, false-positive evaluations need to be minimized. When case detection is done in a multistage process, the number of false positives is reduced, but cost and impact on the school system increase, so there is a trade-off (21). Furthermore, as mentioned above, targeting populations with expected high disease prevalence can reduce the number of false positives identified by a case detection procedure.

Impact of False Negatives

In addition to false positives, screening or case detection programs run the risk of false negatives. Most case detection procedures have had high sensitivity, with few false negatives. In a recent validation study of a multistage case detection procedure, the false-negative rate varied from 3.3 to 18% depending on the questionnaire that was used (57). Roughly half of the false negatives represented children with mild intermittent asthma, with the remainder divided almost evenly between mild and moderate persistent asthma (57). Continuous screening or case detection could potentially reduce the likelihood of false negatives; further studies are needed to assess this.

Cost/Benefit

In considering the costs versus the benefits of a case detection procedure, one should consider the outcomes shown in Figure 1. Table 3 presents a list of direct and indirect costs that workshop participants identified as associated with asthma case detection programs. The costs of a case detection program include the costs of the program itself such as school staff time, student time away from class, health care provider time, additional correspondence, and records; the costs of evaluation of those who test positive; the costs of treatment for those who are diagnosed; and the costs of false negatives. The costs of health care in treated and untreated individuals include preventive care for those treated (medications, visits, peak flow meters, spacers, transportation to/from visits, time off work/school) and adverse health outcomes in those who are treated and untreated.

In considering costs, one should also consider the opportunity costs, or the forgone opportunities, when resources are used to support a particular decision. For example, resources that are spent on identifying children with undiagnosed asthma are resources that are not available for treatment of the disease or for identification of other diseases or conditions. In addition, the costs and benefits may differ by disease severity.

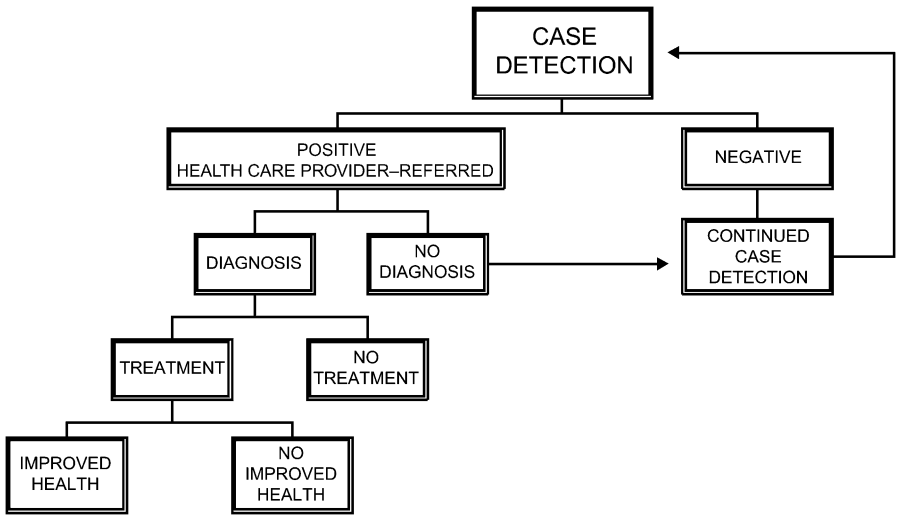

Figure 1. Costs associated with school-based case detection.

TABLE 3. COSTS ASSOCIATED WITH SCHOOL-BASED CASE DETECTION

Cost for Testing

- Preparation for case detection: determine who, how, etc.
  - Determining whether to screen or detect probable cases and which method to use
    - Spirometry with or without exercise testing
    - Questionnaire
      - Child or parent
      - Long or short
      - Written self-administered, interview, or video-guided
  - Approaching institutions
    - Obtaining approval of school board
    - Obtaining approval of individual school administration
  - Obtaining parental consents, distribution and collection
    - Staff or volunteer time to distribute and collect parental consent
    - Use of incentives to improve response rates
      - Staff incentives
      - Parental or child incentive
  - Matching consents with students
  - Moving and monitoring students from class to s/c site if not in classroom
- Actual case detection event
  - Student time away from academics, physical activity, or arts
  - Staff or volunteer time to conduct, distribute, collect, collate
  - Supply costs
    - Equipment supplies
    - Reproduction costs of instruments/questionnaires
    - Child incentives
- After case detection
  - Scoring test/survey
  - Determining which students require further evaluation
  - Communicating results to parents/students
  - Determining which students obtained further evaluation
  - Calculating follow-up rate
  - Determining which students had positive evaluations
  - Calculating case detection rate
  - Conduct periodic reevaluation? How often?
- Evaluation of positive tests
  - Student and parent time away from school/work
  - Transportation to medical evaluation
  - Health care providers, support staff, and equipment (including spirometers)
    - Reviewing school documentation
    - Conducting evaluation
    - Documenting and reporting evaluation to school
    - Missed appointments/rescheduling

Cost of Results

- Cost of false positive
  - Unnecessary evaluation costs
  - Anxiety or fear due to possibility of having disease
  - Believing that positive test means disease diagnosis (could be compounded by periodic reevaluation)
  - Home treatment of nondisease with over-the-counter medications
- Cost of false negative
  - Inappropriate reassurance
  - Delay in seeking medical care
  - Loss of resources: reidentification of children with a previous diagnosis of asthma
- Privacy issues and confidentiality
  - Health Insurance Portability and Accountability Act (HIPAA)
  - Family Educational Rights and Privacy Act (FERPA)

TABLE 4. OUTCOME MEASURES* FOR SCHOOL-BASED CASE DETECTION PROGRAMS

Population-based levels (including surveillance)

- Rates of emergency department visits
- Rates of hospitalization
- Mortality
- Prevalence
  - Ever
  - Active or "current"

Student academic performance

- Absenteeism (% attendance)
- Letter grades by academic subject
- Standardized measures/test results
- Participation in physical education
- Participation in extracurricular activities
  - Group bus travel to other sites
  - Sports activities
  - Music, playing wind instruments or singing

Individual student asthma control/level of burden (includes parent/caregiver burden)

- Unscheduled asthma visits
  - Office
  - Urgent care
  - Emergency department
  - Hospitalization
- Level of symptoms
  - Daytime
  - Nighttime
- Absenteeism (this is already listed under student academic performance)
  - School
  - Work
- Quality of life
  - Student
  - Parent or care giver
- Frequency of modified/minimal physical or social activity?
- Self-efficacy
  - Student
  - Parent

Student's personal interface with health care professions

- Asthma action plan present in school
- Change in medication for those with undertreated asthma
- New asthma diagnosis for those with unrecognized asthma
- Follow-up visits with physician completed after screening or case identification "concerns"

* It is best to use validated and standardized measures for all outcomes when such measures exist.

In conclusion, to determine the cost-effectiveness of a case detection procedure, we should consider who we are finding, how much it costs to find them, and what the implications are for health outcomes of those who are found as well as the implications for those who are not found. To date, no studies examining the cost-effectiveness of asthma case detection programs have been conducted.

Health and Functional Outcomes

Studies of case detection programs should provide evidence of patient outcomes that are important enough to the individual patients or to public health to justify the expenditures involved in time and opportunity, and social costs. Neonatal screening for cystic fibrosis coupled with aggressive medical management from the time of diagnosis has been associated with improved nutritional status and long-term growth (74), reduced acquisition of *Pseudomonas aeruginosa*, and improved survival (75). In asthma, there is reason to believe that a combination of early and accurate diagnosis, and suitable management and appropriate monitoring, could result in positive health outcomes by preventing the serious physical and psychosocial morbidity and mortality related to asthma. To date, mixed health outcomes have been documented following case detection activities in schools, ranging from modest improvements in functional status (25, 27, 49) to no changes in health status (7, 26). However, it is important to recognize that it is not the case detection activities *per se* that improve the asthma outcomes but rather the intervention activities within these programs, just as is the case with neonatal screening for cystic fibrosis.

Table 4 lists outcome measures that workshop participants believe should be considered for future evaluation of case detection

procedures. These range from individual-level to population-based outcomes. At the outset, it is appropriate and prudent to measure process outcomes (examples include the number of students with asthma who receive education on the disease, or number of students participating in case detection programs) as these assess the effectiveness of program implementation. Ultimately, however, effective implementation of interventions should result in change that can be measured with impact/outcome measures, including adoption of policies or legislation as well as health, quality of life, and school performance improvements. Thus, although process outcomes are important to measure at the outset, the effectiveness of any case detection program should ultimately be assessed by measures of reduction in disease morbidity, at the individual and the population levels.

Bottom line: There are insufficient data to state whether or not asthma case detection is economically balanced.

9. SCREENING SHOULD BE CONTINUOUS

Each year, new children join the ranks of school-aged and children who previously had no signs or symptoms of asthma identifiable by case detection questionnaires develop asthma. Therefore, case detection cannot be a one-time event.

Bottom line: Once appropriate case detection methods are identified, further studies will be required to assess the appropriate frequency for continued case detection.

SUMMARY

The workshop participants concluded that, at this time, the adoption of population-based asthma case detection programs is unwarranted given the lack of evidence of improvement in health outcomes as a result of case detection. It is important to note, however, that there are advocates for nationwide asthma screenings. One such ongoing effort is sponsored by the American College of Allergy, Asthma, and Immunology; on their website, the chair of their screening effort states, "We believe the nationwide screenings help raise awareness about asthma and the fact that the disease doesn't have to lead to major lifestyle compromises. By informing people about the symptoms of asthma and by offering free screenings and consultation by an allergist, we can help improve quality of life for children and adults with asthma" (http://www.acaai.org/public/lifeQuality/nasp/nasp.htm, accessed August 15, 2006). The actual health outcomes of these screenings, however, are unclear. Although such voluntary programs in community settings may have value, the external validity of their outcomes is limited by self-selection of the individuals choosing to be screened.

The participants of this workshop believe that limited case detection programs may be appropriate in areas where there is a high prevalence of undiagnosed asthma and where newly identified patients have functional access to consistent, high-quality asthma care. Methods to identify children with significant asthma symptoms may also be appropriate. The use of case detection methods to identify children with undiagnosed asthma may be a worthy future goal. However, before this panel can recommend widescale case detection, a number of issues should be addressed:

1. Health care systems should be adapted to deliver care that optimizes health outcomes in populations that are difficult to reach through our traditional health care delivery mechanisms. The goal is to guarantee timely access to asthma care consistent with existing guidelines and access to education to improve daily self-management. Access to health behavior experts and social workers will be important to address psychosocial and health literacy issues which impact on adherence and health outcomes.
2. The primary site of asthma case detection should be the primary care clinician's office. Clinicians should be attentive to respiratory symptoms and reports of morbidity or missed school days among children. If populations are identified that are not reached by primary care, then alternative methods should be developed for other sites (possibly schools, community centers, or youth-serving organizations). In some settings, it may be prudent to combine asthma case detection with other case detection procedures that identify other common, chronic diseases, such as vision screening for myopia.
3. Tools should be refined to identify those who would benefit most from further assessment and treatment for undiagnosed and/or undertreated asthma.
4. Identification of a preclinical state for asthma may allow for true screening and treatment to prevent the onset of the disease. A better understanding of the different asthma phenotypes and their natural history is needed to help inform the nature, timing, and possibly the setting of ideal asthma case detection or screening programs.
5. The cost-effectiveness of asthma case detection programs should be examined.

Until these issues are addressed, parents, school personnel, and primary health care providers should be attentive to respiratory symptoms in children. Given that public health resources within communities and schools are very limited, current efforts should seek to identify and intervene with those children who are experiencing significant morbidity from respiratory symptoms. This targeted use of resources should include connection to proper medical care to have an impact on asthma morbidity.

This ATS workshop report was developed by an *ad hoc* subcommittee of the ATS Behavioral Science and the Pediatrics Assemblies.

Members of the Writing Committee are as follows:
Lynn B. Gerald, Ph.D., M.S.P.H.
Marianna M. Sockrider, M.D., Dr.P.H.
Roni Grad, M.D.

Workshop participants are as follows:
Lynn B. Gerald, Ph.D., M.S.P.H. (*Co-Chair*)
Marianna M. Sockrider, M.D., Dr.P.H. (*Co-Chair*)
Bruce G. Bender, Ph.D.*
Leslie P. Boss, Ph.D., M.P.H.
Stanley P. Galant, M.D.
Jorrit Gerritsen, M.D., Ph.D.
Roni Grad, M.D.
Christine L. M. Joseph, Ph.D.
Robert M. Kaplan, Ph.D.*
Julie A. Madden, M.A.
Joan M. Mangan, Ph.D., M.S.T.
Greg J. Redding, M.D.
Diana K. Schmidt, M.P.H.
Christina D. Schwindt, M.D.
Virginia S. Taggart, M.P.H.
Kristin N. Van Hook, M.D., M.P.H.
Lani S. Wheeler, M.D.
Paul V. Williams, M.D.
Barbara P. Yawn, M.D., M.Sc.
Bulend Yuksel, M.D.

*Participated in project but not present at the workshop.

Conflict of Interest Statement: L.B.G. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. M.M.S.

has participated as a speaker in scientific meetings or courses organized and financed by Genentech and Novartis pharmaceutical companies; she has grant funding from Genentech for asthma epidemiologic studies (TENOR and EXCELS). B.G.B. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. L.P.B. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. S.P.G. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. J.G. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. R.G. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. C.L.M.J. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. R.M.K. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. J.A.M. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. J.M.M. does not have a financial relationship with a commercial entity with an interest in the subject matter of this manuscript. G.J.R. has received money from AstraZeneca, Merck, and MedImmune Inc. for lectureships and consultations, and has received a research grant from MedImmune, but these do not relate to the subject of this manuscript. D.K.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. C.D.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. V.S.T. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. K.N.V.H. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. L.S.W. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. P.V.W. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript. B.P.Y. received $4,000 for advisory board attendance for Schering-Plough in 2006 and $3,500 for advisory board attendance for AstraZeneca in 2007; she received a $150,000 grant for an investigator initiated project on step up and step down therapy in asthma from Schering-Plough. B.Y. received lecture fees from MSD, from 2006 to 2007 ($1,500) and AstraZeneca, in 2005 ($1,000).

Acknowledgment: The authors acknowledge the technical assistance of Ms. Lindsey McGinnis and Ms. Irene Lynn for their assistance in the preparation of this manuscript.

References

1. Kelley CF, Mannino DM, Homa DM, Savage-Brown A, Holguin F. Asthma phenotypes, risk factors, and measures of severity in a national sample of US children. *Pediatrics* 2005;115:726–731.
2. Bonilla S, Kehl S, Kwong KYC, Morphew T, Kachru R, Jones CA. School absenteeism in children with asthma in a Los Angeles inner city school. *J Pediatr* 2005;147:802–806.
3. Fowler MG, Davenport MG, Garg R. School functioning of US children with asthma. *Pediatrics* 1992;90:939–944.
4. Martinez FD. Development of wheezing disorders and asthma in preschool children. *Pediatrics* 2002;109:362–367.
5. Morgan WJ, Stern DA, Sherrill DL, Guerra S, Holberg CJ, Guilbert TW, Taussig LM, Wright AL, Martinez FD. Outcome of asthma and wheezing in the first 6 years of life. *Am J Respir Crit Care Med* 2005;172:1253–1258.
6. Joseph CLM, Foxman B, Leickly FE, Peterson E, Ownby D. Prevalence of possible undiagnosed asthma and associated morbidity among urban schoolchildren. *J Pediatr* 1996;129:735–742.
7. Yawn BP, Wollan P, Scanlon PD, Kurland M. Are we ready for universal school-based asthma screening? An outcomes evaluation. *Arch Pediatr Adolesc Med* 2002;156:1256–1262.
8. Riekert KA, Butz AM, Eggleston PA, Huss K, Winkelstein M, Rand CS. Caregiver-physician medication concordance and undertreatment of asthma among inner-city children. *Pediatrics* 2003;111:e214–e220.
9. Halterman JS, Yoos HL, Kaczorowski JM, McConnochie K, Holzhauer RJ, Conn KM, Lauver S, Szilagyi PG. Providers underestimate symptom severity among urban children with asthma. *Arch Pediatr Adolesc Med* 2002;156:141–146.
10. Halterman JS, Aligne CA, Auinger P, McBride JT, Szilagyi PG. Inadequate therapy for asthma among children in the United states. *Pediatrics* 2000;105:272–276.
11. Eggleston PA, Malveaux FJ, Butz AM, Huss K, Thompson L, Kolodner K, Rand CS. Medications used by children with asthma living in the inner city. *Pediatrics* 1998;101:349–354.
12. Schwartz J, Gold D, Dockery DW, Weiss ST, Speizer FE. Predictors of asthma and persistent wheeze in a national sample of children in the United States: association with social class, perinatal events and race. *Am Rev Respir Dis* 1990;142:555–562.
13. Boss LP, Wheeler LS, Williams PV, Bartholomew LK, Taggart VS, Redd SC. Population-based screening or case detection for asthma: are we ready? *J Asthma* 2003;40:335–342.
14. Yawn BP. Asthma screening, case-identification and treatment in school-based programs. *Curr Opin Pulm Med* 2006;12:23–27.
15. American College of Allergy, Asthma, and Immunology. Nationwide Asthma Screening Program. Available from: http://www.acaai.org/public/lifeQuality/nasp/nasp.htm (accessed March 17, 2006).
16. Blaiss M. School-based asthma and allergy screening initiative. American Academy of Asthma, Allergy, and Immunology eNews (accessed September 29, 2004).
17. Chapman JA, Ford L, Miles RM, Storms WW, Winder JA. An idea bearing fruit. *Ann Allergy Asthma Immunol* 2000;85:89.
18. Aminian AM. Life quality test and nationwide screening program increase asthma awareness. *Ann Allergy Asthma Immunol* 2000;85:434.
19. Miles R. Four pilot projects completed for school-based allergy and asthma screening. *Ann Allergy Asthma Immunol* 2003;90:461.
20. Hahn DL, Beasley JW. Diagnosed and possible undiagnosed asthma: a Wisconsin research network (WReN) study. *J Fam Pract* 1994;38:373–377.
21. Gerald LB, Redden D, Feinstein R, Hains C, Erwin S, Turner-Henson A, Hemstreet MP, Brooks CM, Bailey WC. A multi-stage asthma screening procedure for elementary school children. *J Asthma* 2002;39:29–36.
22. Clark NM, Brown R, Joseph CLM, Anderson EW, Liu M, Valerio MA, Gong M. Issues in identifying asthma and estimating prevalence in an urban school population. *J Clin Epidemiol* 2002;55:870–881.
23. Lee T, Brugge D, Francis C, Fisher O. Prevalence among inner-city Asian American schoolchildren. *Public Health Rep* 2003;118:215–220.
24. Lewis TC, Robins TG, Joseph CLM, Parker EA, Israel BA, Rowe Z, Edgren KK, Salinas MA, Martinez ME, Brown RW. Identification of gaps in the diagnosis and treatment of childhood asthma using a community-based participatory research approach. *J Urban Health* 2004;81:472–488.
25. Galant SP, Crawford LJR, Morphew T, Jones CA, Bassin S. Predictive value of a cross-cultural asthma case-detection tool in an elementary school population. *Pediatrics* 2004;114:e307–e316.
26. Yawn BP, Wollan P, Scanlon PD, Kurland M. Outcome results of a school-based screening program for undertreated asthma. *Ann Allergy Asthma Immunol* 2003;90:508–515.
27. Joseph CLM, Havstad S, Anderson EW, Brown R, Johnson CC, Clark NM. Effect of asthma intervention on children with undiagnosed asthma. *J Pediatr* 2005;146:96–104.
28. Martinez FD, Godfrey S. Wheezing disorders in the preschool child. New York: Martin Dunitz; 2003.
29. Wahn U; ETAC Study Group. Allergic factors associated with the development of asthma and the influence of cetirizine in a double-blind, randomised, placebo-controlled trial: first results of ETAC. *Pediatr Allergy Immunol* 1998;9:116–124.
30. The Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. *N Engl J Med* 2000;343:1054–1063.
31. Zeiger RS, Szefler SJ, Phillips BR, Schatz M, Martinez FD, Chinchilli VM, Lemanske RF Jr, Strunk RC, Larsen G, Spahn JD, *et al.* Response profiles to fluticasone and montelukast in mild-to-moderate persistent childhood asthma. *J Allergy Clin Immunol* 2006;117:45–52.
32. Pauwels RA, Pedersen S, Busse WW, Tan WC, Chen YZ, Ohlsson SV, Ullman A, Lamm CJ, O'Byrne PM. Early intervention with budesonide in mild persistent asthma: a randomised, double-blind trial. *Lancet* 2003;361:1071–1076.
33. Guilbert TW, Morgan WJ, Mauger DT, Boehmer SJ, Szefler SJ, Bacharier LB, Lemanske RF, Strunk RC, Allen DB, Bloomberg GR, *et al.* Long-term inhaled steroids in preschool children at high risk for asthma. *N Engl J Med* 2006;354:1958–1997.
34. Guerra S, Wright AL, Morgan WJ, Sherrill DL, Holberg CJ, Martinez FD. Persistence of asthma symptoms during adolescence: role of obesity and age at the onset of puberty. *Am J Respir Crit Care Med* 2004;170:78–85.
35. Castro-Rodríguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med* 2000;162:1403–1406.
36. Guilbert TW, Morgan WJ, Zeiger RS, Bacharier LB, Boehmer SJ, Krawiec M, Larsen G, Lemanske RF Jr, Liu A, Mauger DT, *et al.* Atopic characteristics of children with recurrent wheezing at high risk for the development of childhood asthma. *J Allergy Clin Immunol* 2004;114:1282–1287.
37. Peat JK, Mihrshahi S, Kemp AS, Makrs AS, Tovey ER, Webb K, Mellis CM. Three-year outcomes of dietary fatty-acid modification and house dust mite reduction in the Childhood Asthma Prevention Study. *J Allergy Clin Immunol* 2004;114:807–813.

38. Schonberger HJAM, Dompeling E, Knottnerus JA, Maas T, Muris JWM, van Weel C, van Schayck CP. The PREVASC Study: the clinical effect of a multifaceted educational intervention to prevent childhood asthma. *Eur Respir J* 2005;25:660–670.
39. Arshad SH, Bateman B, Matthews SM. Primary prevention of asthma and atopy during childhood by allergen avoidance in infancy: a randomized controlled study. *Thorax* 2003;58:489–493.
40. Chan-Yeung M, Ferguson A, Watson W, Dimich-Ward H, Rousseau R, Lilley M, Dybuncio A, Becker A. The Canadian Childhood Asthma Primary Prevention Study: outcomes at 7 years of age. *J Allergy Clin Immunol* 2005;116:49–55.
41. Warner JO; ETAC Study Group. A double-blinded, randomized, placebo-controlled trial of cetirizine in preventing the onset of asthma in children with atopic dermatitis: 18 months' treatment and 19 months' posttreatment follow-up. *J Allergy Clin Immunol* 2001;108:929–937.
42. Rand CS, Butz AM, Kolodner K, Huss K, Eggleston P, Malveaux F. Emergency department visits by urban African American children with asthma. *J Allergy Clin Immunol* 2000;105:83–90.
43. Halterman JS, McConnochie K, Conn KM, Yoos HL, Callahan PM, Neely TL, Szilagyi PG. A randomized trial of primary care provider prompting to enhance preventive asthma therapy. *Arch Pediatr Adolesc Med* 2005;159:422–427.
44. Evans D, Mellins R, Lobach K, Ramos-Bonoan C, Pinkett-Heller M, Wiesemann IK, Donahue C, Burke D, Levison M, Levin B, *et al.* Improving care for minority children with asthma: Professional education in public health clinics. *Pediatrics* 1997;99:157–164.
45. Clark NM, Gong M, Schork A, Evans D, Roloff D, Hurwitz M, Maiman L, Mellins RB. Impact of education for physicians on patient outcomes. *Pediatrics* 1998;101:831–836.
46. Bonner S, Zimmerman BJ, Evans D, Irigoyen M, Resnick D, Mellins RB. An individualized intervention to improve asthma management among urban Latino and African-American families. *J Asthma* 2002; 39:167–179.
47. Webber MP, Carpiniello KE, Oruwariye T, Yungtai L, Burton WB, Appel DK. Burden of asthma in inner-city elementary schoolchildren: do school-based health centers make a difference? *Arch Pediatr Adolesc Med* 2003;157:125–129.
48. Jones CA, Morphew T, Clement LT, Kimia T, Dyer M, Li M, Hanley-Lopez J. A school-based case identification process for identifying inner city children with asthma: the Breathmobile Program. *Chest* 2004;125:924–934.
49. Jones CA, Clement LT, Hanley-Lopez J, Morphew T, Kwong KY, Lifson F, Opas L, Guterman JJ. The Breathmobile program: structure,implementation, and evolution of a large-scale, urban, pediatric asthma disease management program. *Dis Manage* 2005;8:205–222.
50. Lurie N, Bauer EJ, Brady C. Asthma outcomes at an inner-city school-based health center. *J Sch Health* 2001;71:9–16.
51. Adams EK, Johnson V. An elementary school-based health clinic: can it reduce Medicaid costs? *Pediatrics* 2000;105:780–788.
52. Guo JJ, Jang R, Keller KN, McCracken AL, Pan W, Cluxton RJ. Impact of school-based health centers on children with asthma. *J Adolesc Health* 2005;37:266–274.
53. Webber MP, Hoxie A-ME, Odlum M, Oruwariye T, Lo Y, Appel D. Impact of asthma intervention in two elementary school-based health centers in the Bronx, New York City. *Pediatr Pulmonol* 2005;40:487–493.
54. Anderson ME, Freas MR, Wallace AS, Kempe A, Gelfand EW, Liu AH. Successful school-based intervention for inner-city children with persistent asthma. *J Asthma* 2004;41:445–453.
55. Liao O, Morphew T, Amaro S, Galant SP. The Breathmobile: a novel comprehensive school-based mobile asthma care clinic for urban underprivileged children. *J Sch Health* 2006;76:313–319.
56. Sockrider MM, Tortolero SR, Bartholomew LK, Markham CM, Abramson SL, Fernandez M, Parcel GS. Pilot study of a screening questionnaire for asthma. *Pediatric Asthma, Allergy & Immunology* 2001;15:15–24.
57. Gerald LB, Grad R, Turner-Henson A, Hains C, Tang S, Feinstein R, Wille K, Erwin S, Bailey WC. Validation of a multistage asthma case-detection procedure for elementary school children. *Pediatrics* 2004; 114:e459–e468.
58. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, Mitchell EA, Pearce N, Sibbald B, Stewart AW, *et al.* International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483–491.
59. Asher MI, Weiland SK. The International Study of Asthma and Allergies in Childhood (ISAAC). *Clin Exp Allergy* 1998;28:52–66.
60. Ellwood P, Asher MI, Beasley R, Clayton TO, Stewart AW. The International Study of Asthma and Allergies in Childhood (ISAAC): phase three rationale and methods. *Int J Tuberc Lung Dis* 2006;9:10–16.
61. Pattemore PK, Asher MI, Harrison AC, Mitchell EA, Rea HH, Stewart AW. The interrelationship among bronchial hyperresponsiveness, the diagnosis of asthma, and asthma symptoms. *Am Rev Respir Dis* 1990; 142:549–554.
62. Moeller A, Kielbasa B. Exhaled breath condensate and other markers in exhaled air. In: Hammer J, Eber E, editors. Pediatric pulmonary function testing. Basel, Switzerland: Karger;2005. pp. 190–202.
63. Clark NM, Brown R, Joseph CLM, Anderson EW, Liu M, Valerio MA. Effects of a comprehensive school-based asthma program on symptoms, parent management, grades and absenteeism. *Chest* 2004;125: 1674–1679.
64. Vargas PA, Magee JS, Bushmiaer M, Simpson PM, Jones CA, Feild CR, Jones SM. School-based asthma case finding: the Arkansas experience. *J Sch Health* 2006;76:223–226.
65. Mannino DM, Homa DM, Akinbami LJ, Moorman JE, Gwynn C, Redd SC. Surveillance for asthma: United States, 1980–1999. *MMWR Morb Mortal Wkly Rep* 2002;51:1–13.
66. Bloomberg GR, Trinkaus KM, Fisher EB Jr, Musick JR, Strunk RC. Hospital readmissions for childhood asthma: a 10-year metropolitan study. *Am J Respir Crit Care Med* 2003;167:1068–1076.
67. Becker JM, Rogers J, Rossini G, Mirchandani H, D'Alonzo GE Jr. Asthma deaths during sports: report of a 7-year experince. *J Allergy Clin Immunol* 2004;113:264–267.
68. Greiling AK, Boss LP, Wheeler LS. A preliminary investigation of asthma mortality in schools. *J Sch Health* 2005;75:286–290.
69. Robertson CF, Rubinfeld AR, Bowes G. Pediatric asthma deaths in Victoria: the mild are at risk. *Pediatr Pulmonol* 1992;13:95–100.
70. Silverstein MD, Mair JE, Katusic SK, Wollan PC, O'Connell EJ, Yunginger JW. School attendance and school performance: a population-based study of children with asthma. *J Pediatr* 2001;139:278–283.
71. Annett RD, Aylward EH, Lapidus J, Bender BG, DuHamel T. Neurocognitive functioning in children with mild and moderate asthma in the childhood asthma management program. *J Allergy Clin Immunol* 2000; 105:717–724.
72. Agertoft L, Pedersen S. Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children. *Respir Med* 1994;88:373–381.
73. Selroos O, Pietinalho A, Lofroos AB, Riska H. Effect of early vs. late intervention with inhaled corticosteroids in asthma. *Chest* 1995;108: 1228–1234.
74. Farrell PM, Kosorok MR, Rock MJ, Laxova A, Zeng L, Lai HC, Hoffman G, Laessig RH, Splaingard ML; Wisconsin Cystic Fibrosis Neonatal Screening Study Group. Early diagnosis of cystic fibrosis through neonatal screening prevents severe malnutrition and improves long-term growth. *Pediatrics* 2001;107:1–13.
75. Lai HCJ, Cheng Y, Cho H, Kosorok MR, Farrell PM. Association between initial disease presentation, lung disease outcomes, and survival in patients with cystic fibrosis. *Am J Epidemiol* 2004;159:537–546.
76. Bansal A, Farnham JM, Crapo RO, Hughes DC, Jensen RL, Cannon-Albright LA. A simple diagnostic index for asthma. *Clin Exp Allergy* 2001;31:756–760.
77. Frank TL, Frank PI, McNamee R, Wright T, Hannaford P, Morrison J, Hirsch S, Pickering CA. Assessment of a simple scoring system applied to a screening questionnaire for asthma in children aged 5-15 yrs. *Eur Respir J* 1999;14:1190–1197.
78. Fuso L, de Rosa M, Corbo GM, Valente S, Forastiere F, Agabiti N, Pistelli R. Repeatability of the ISAAC video questionnaire and its accuracy against a clinical diagnosis of asthma. *Respir Med* 2000;94: 397–403.
79. Glasgow NJ, Ponsonby AL, Yates RE, McDonald T, Attewell R. Asthma screening as part of a routine school health assessment in the Australian capital territory. *Med J Aust* 2001;174:384–388.
80. Gruchalla RS, Gan V, Roy L, Bokovoy J, McDermott S, Lawrence G, Hynan L, Luckett P. Results of an inner-city school-based asthma and allergy screening pilot study: a combined approach using written questionnaires and step testing. *Ann Allergy Asthma Immunol* 2003;90: 491–499.
81. Redline S, Larkin EK, Kercsmar C, Berger M, Siminoff LA. Development and validation of school-based asthma and allergy screening instruments for parents and students. *Ann Allergy Asthma Immunol* 2003;90:516–528.
82. Wolf RL, Berry CA, O'Connor T, Coover L. Validation of the Brief Pediatric Asthma Screen. *Chest* 1999:116(Suppl):224S–229S.