

Cost-effectiveness of school-based asthma screening in an urban setting

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Background: Much has been done to promote population-based childhood asthma screening; however, concerns remain regarding its cost-effectiveness.

Objectives: To conduct a cost-effectiveness analysis of school-based asthma screening strategies.

Methods: A 5 health state Markov approach (symptom-free, symptom, exacerbation recovery, emergency department, and hospitalization day) was used to evaluate school-based screening in a simulated population of urban elementary-age school children. Two questionnaire and 2 multistage strategies incorporating spirometry or spirometry with exercise testing were evaluated from the societal perspective by using 365 daily cycles. The outcome was 2006 dollars per quality-adjusted life year (QALY).

Results: The most efficient strategy identified children with previously diagnosed but poorly controlled asthma at a cost of \$150,000 per QALY (95% CI, \$65,800-\$318,000). Uncertainty surrounding the cost-effectiveness estimate was primarily a result of the symptom day preference weight estimate (44%), the probability of confirmation after screening (17%), the adequacy of asthma control in the population (9%), and the estimated treatment effect on symptoms (6%). Screening generated an additional 21 symptom-free day equivalents per child identified with previously diagnosed but not well controlled asthma and led to \$85.55, \$12.36, and \$2.58 in additional screening, daily treatment, and indirect costs and \$5.01 less in emergency department and hospitalization costs. **Conclusion:** Population-based asthma screening is not cost-effective at \$50,000 per QALY and has only a 20% chance of being cost-effective at \$100,000 per QALY. The most efficient

approach is to screen for previously diagnosed but poorly controlled asthma. Linking screening with better treatment, and long-term adherence strategies might yield future cost-effective approaches. (J Allergy Clin Immunol 2010;125:643-50.)

Key words: Asthma, screening, case detection, childhood asthma, cost-effectiveness, quality of life, economic analysis, Markov modeling

Asthma is a common chronic condition of childhood that is associated with significant morbidity and excess health care use, particularly in minority, low-income, urban populations.^{1,2} In the United States, asthma-related expenditures for school-age children exceed \$2 billion annually and are almost equally divided between direct and indirect costs.³ Population-based asthma screening has been promoted to improve disease recognition and control.⁴⁻⁶ Questionnaire-based strategies are relatively easy to administer but are plagued by high false-positive rates that generate unnecessary referrals to community physicians.⁷⁻¹¹ Augmenting questionnaires with lung function testing improves accuracy but is resource-intensive.¹²⁻¹⁶ Because the trade-off between improved accuracy and higher costs has not been systematically investigated, the preferred screening strategy is uncertain.

Additional concerns raise doubts about the magnitude of expected benefits from screening. Few parents have positive results confirmed after screening.^{17,18} Many children do not receive inhaled corticosteroids when needed.¹⁹⁻²² Many children are not adherent even when they are prescribed.²³⁻²⁵ These factors reduce the potential benefits of screening and are often of greatest concern in populations with high disease burden. On the basis of these concerns, a recent American Thoracic Society workgroup called for evidence demonstrating the cost-effectiveness of population-based asthma screening.²⁶ We answer this call by evaluating the cost-effectiveness of 4 school-based asthma screening strategies in a simulated population of urban, primarily black, elementary-age school children.

METHODS

A cost-effectiveness analysis of school-based asthma screening in a simulated population of urban, low-income, minority school children was undertaken from the societal perspective. Although the analysis is generalizable to most urban settings, specific inputs reflect the characteristics of the Birmingham City School System in Birmingham, Ala, where enrollment was 95% African American and 80% of children were eligible for subsidized lunches.²⁷ Four mutually exclusive screening strategies were compared against the status quo of no screening over the course of 1 year while accounting for daily costs and health outcomes. The primary outcome was 2006 dollars per quality-adjusted life-year (QALY). The estimates used in this analysis (eg, screening sensitivity and specificity, prevalence, treatment effects, and so forth) were obtained from readily available secondary sources (published studies, government reports, public databases, and so forth; Table I). The only exception was screening costs, which were provided by the authors based on their previous implementation of these screening methodologies.^{13,14}

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Abbreviations used

ACT: Asthma Control Test
ASFD: Asthma symptom-free day
BQ: Broad Questionnaire
ED: Emergency department
ICER: Incremental cost-effectiveness ratio
MSwET: Multi-Stage with Exercise Testing
MSwSP: Multi-Stage with Spirometry
NQ: Narrow Questionnaire
PAHOM: Pediatric Asthma Health Outcome Measure
QALY: Quality-adjusted life year

The Narrow Questionnaire (NQ) strategy identified children with previously diagnosed, not well controlled asthma based on report of a previous diagnosis, asthma medication use in the past year, and a score ≥ 19 on the Asthma Control Test (ACT).^{28,29} The Broad Questionnaire (BQ) strategy extended the NQ strategy by also identifying children with undiagnosed asthma based on report of respiratory symptoms (wheezing, night awakenings, or early morning symptoms) in children without a previous diagnosis. The Multi-Stage with Spirometry (MSwSP) strategy added basic spirometry for children with respiratory symptoms to improve the accuracy of the BQ. Impaired lung function was determined by a FEV₁/forced vital capacity ratio $< 80\%$ of predicted. The Multi-Stage with Exercise Testing (MSwET) strategy added submaximal exercise testing for symptomatic children with normal spirometry. Abnormal submaximal exercise testing was determined by a $\geq 15\%$ decline in FEV₁ or a $\geq 25\%$ decline in forced expiratory flow over 25% to 75% of forced expiratory volume.

A decision tree was used to assign children to possible screening outcomes on the basis of prevalence,^{1,7-16} the probability of a previous asthma diagnosis,⁸⁻¹⁵ the probability of asthma control at the time of screening in those previously diagnosed,²⁸⁻³⁰ and the sensitivity and specificity of the applicable screening strategy¹³ (Fig 1). The sensitivity and specificity reflect the strategies' ability to detect undiagnosed asthma in children who did not report a previous diagnosis and did not report asthma medication use in past year. These two questions were assumed to be 100% sensitive and 100% specific for previously diagnosed asthma. The tree was also used to determine whether screening would result in treatment changes based on the probability that parents confirmed the screening result,^{17,18} physicians provided guideline concordant treatment,¹⁹⁻²² and children were adherent to controller medication.²³⁻²⁵ Last, the tree accounted for differences in the distribution of asthma severity between children identified by screening (less severe) and those identified in the community (more severe).^{8,13} A more detailed decision tree can be found in the Online repository (Fig E1).

Children were assigned to 1 of 3 treatment conditions: no benefit, partial benefit, or full benefit. Children with undiagnosed asthma or previously diagnosed but not well controlled asthma who were missed by screening or who did not seek confirmation were assigned to the no benefit condition. Children who had their positive screening result confirmed by a physician but who did not receive guideline concordant care or who did not adhere to controller medication were assigned to the partial benefit condition. Compared with the no benefit condition, the partial benefit condition was associated with 20% fewer emergency department (ED) visits and, hospitalizations, and 15% fewer symptom days. This magnitude of benefit was comparable to pre-post differences observed in control groups or less effective treatment arms in the clinical trials used to establish the treatment effect of the full benefit condition in the paragraph below.

Children who received guideline concordant care and who were fully adherent to controller medication were assigned to the full benefit condition. Compared with the no benefit condition, the full benefit condition was associated with 60% fewer ED visits³¹⁻³⁵ and hospitalizations^{31-33,35} and 55% fewer symptom days.^{33,36-40} Guideline concordant care was conceptually viewed as treatment appropriate for severity and control status as outlined in the 2007 National Asthma Education and Prevention Program guidelines.²

TABLE I. Estimates (range) and sources for model inputs

	Point estimate (range)	References
Epidemiologic factors		
Prevalence	.15 (.10-.20)	1,7-16
Symptom days (per year)*	189 (136-240)	33,36-40
Hosp (per 1,000 person-yr)*	61 (20-102)	31-33,35
ED visits (per 1,000 person-yr)*	211 (141-282)	31-35
Behavioral factors		
Postscreen MD visit	.30 (.15-.45)	17,18
Medication adherence	.60 (.40-.80)	23-25
Health system factors		
Controlled if previously diagnosed	.60 (.45-.75)	28-30
Probability undiagnosed asthma	.30 (.10-.50)	8-15
Guideline concordant care	.60 (.40-.80)	19-22
Treatment reductions		
Symptoms (partial)	.15 (0-.30)	33,36-40
Symptoms (full)	.55 (.40-.70)	33,36-40
ED visits (partial)	.20 (0-.40)	31-35
ED visits (full)	.60 (.50-.70)	31-35
Hospitalizations (partial)	.20 (0-.40)	31-33,35
Hospitalizations (full)	.60 (.50-.70)	31-33,35
Sensitivity†		
ACT	.70 (.67-.73)	28,29
BQ	.64 (.59-.69)	13
MSwSP	.36 (.31-.41)	13
MSwET	.45 (.40-.50)	13
Specificity†		
ACT	.73 (.70-.76)	28,29
BQ	.60 (.55-.65)	13
MSwSP	.97 (.95-.99)	13
MSwET	.97 (.95-.99)	13
Preference weights		
ASFD	1.0 (.98-1.0)	49
Symptomatic	.90 (.84-.96)	49
Recovery	.70 (.64-.76)	49
ED	.43 (.37-.49)	49
Hospitalization	.06 (.01-.11)	49
Conversion factors‡		
Symptoms to mild	1.25 (.875-1.625)	64
Symptoms to moderate	1.50 (1.05-1.95)	64
Symptoms to severe	2.0 (1.4-2.6)	64
ED visit to mild	4 (3-5)	64-66
ED visit to moderate	6 (4-8)	64-66
ED visit to severe	12 (8-16)	64-66
Hosp to mild	4 (3-5)	64-66
Hosp to moderate	8 (6-10)	64-66
Hosp to severe	16 (12-20)	64-66
Severity (previous)		
Intermittent	.40 (.44-.34)	8,13
Mild	.36 (.40-.30)	8,13
Moderate	.20 (.14-.28)	8,13
Severe	.04 (.02-.08)	8,13
Severity (undiagnosed)		
Intermittent	.54 (.60-.50)	8,13
Mild	.24 (.28-.20)	8,13
Moderate	.20 (.11-.26)	8,13
Severe	.02 (.10-.04)	8,13
Screening costs		
Questionnaire	\$25,825 (\$18,525-\$33,350)	Authors
MSwSP (incremental)	\$19,725 (\$9,850-\$29,575)	Authors
MSwET (incremental)	\$7,550 (\$3,775-\$11,350)	Authors

(Continued)

TABLE I. (Continued)

	Point estimate (range)	References
MD visit (postscreen, direct)	\$98 (\$68-\$123)	19,20,58
Indirect costs		
Caregiver daily wage	\$100 (\$50-\$150)	50
School absence day	\$45 (\$25-\$65)	27
Caregiver transportation	\$10 (\$5-\$15)	51
Medication costs		
Daily cost full to partial	0.50 (0.30-0.80)	Author estimate
Daily cost full to no	0.10 (0-0.20)	Author estimate
Budesonide inhaler	\$103 (\$52-\$155)	53-55
Albuterol inhaler	\$26 (\$13-\$39)	53-55
Salmeterol	\$83 (\$41-\$124)	53-55
Prednisone (14 d)	\$10 (\$5-\$15)	53-55
MD visit (routine, direct)	\$54 (\$27-\$81)	58
Acute care costs		
Hospital day (direct)	\$1,200 (\$900-\$1,500)	42,43,56
ED visit (direct)	\$350 (\$175-\$525)	43,57

ACT, Asthma Control Test; Hosp, hospitalization; MD, medical doctor; Prev, previously.

*Weighted mean for previously diagnosed asthma within no benefit group.

†NQ assumed to be 100% specific and sensitive.

‡Factors applied to baseline rates of intermittent asthma.

Markov models were used to account for daily changes in health status of varying severity, duration, and costs.⁴¹ Five health states were modeled: asthma symptom-free day (ASFD), symptom days, exacerbation recovery days, ED visits, and hospitalization days (Fig 2 and Fig E2). Children started in either the ASFD or symptom day states on the basis of asthma severity and assigned treatment condition. Children could transition freely between the ASFD and symptom day states but could only experience ED visits or hospitalizations from the symptom state. The ED visit state represented visits that did not result in hospitalization.⁴² Transition out of the ED state was mandatory after 1 day. The hospitalization state was modeled to have an average and maximum length of stay of 2.5 and 7 days, respectively.^{43,44} The exacerbation recovery state was modeled to have a duration of 14 days during which there was an increased risk of ED visits and hospitalizations.⁴⁵

Base rates for symptom days, ED visits, and hospitalizations were 189 per year,^{33,36-40} 211 per 1000 person-years,³¹⁻³⁵ and 61 per 1000 per-years,^{31-33,35} respectively, for children with previously diagnosed asthma assigned to the no benefit condition. Rates were subsequently adjusted to account for asthma severity, treatment assignment, and method of diagnosis (Table II). Base rates for ED visits, hospitalizations, and symptom days for children with undiagnosed asthma were 70%, 70%, and 30% lower, respectively, to account for lower burden of symptoms and less frequent health care use observed in previous studies.⁴⁶⁻⁴⁸

Each health state was associated with a daily preference weight and cost. The preference weight represented the desirability of that health state on an interval scale bounded by 0 (death) and 1 (perfect health). The weights were derived from the Pediatric Asthma Health Outcome Measure (PAHOM).⁴⁹ The daily cost for each health state included direct and indirect asthma-related costs. Indirect costs accounted for lost caregiver wages,⁵⁰ school absence days,²⁷ and transportation⁵¹ costs.

Costs for the ASFD, symptom day, and exacerbation recovery day included daily medication costs and routine physician visits throughout the year (Table III). Many acceptable combinations of medication choices existed; however, to simplify the model and to examine the lowest possible daily treatment cost, we limited the choices in the model to those obtainable from Alabama Medicaid.⁵² Children were assigned medications based on their modeled severity and the national guidelines.² Children with intermittent asthma

took only short-acting albuterol as needed (<2 puffs twice a week). Children with mild and moderate persistent asthma had 200 µg/d and 400 mcg/d budesonide, respectively, added to as-needed albuterol. Children with severe persistent asthma took 800 mcg/d budesonide and salmeterol. Symptom and recovery days were associated with increased use of albuterol (2 puffs per day), and recovery days were also associated with daily prednisone use.

Medication costs were based on average wholesale drug prices⁵³ adjusted for Medicaid discounts, Medicaid year-end rebates, and dispensing fees.^{54,55} The direct costs of an ED visit and a hospitalization day were \$350 and \$1200, respectively.^{42,43,56,57} Each encounter was also associated with indirect costs on the day of the encounter and subsequent convalescence (eg, school absence days and lost caregiver wages).⁴⁵ The costs associated with the full benefit condition were 100% of the calculated costs, whereas the costs of the partial benefit and no benefit conditions were 50% and 10%, respectively. These adjustments reflected lower adherence and subsequently lower medication costs.

Screening costs were provided by the authors (Table I). Screening was modeled to occur at a single grade level including approximately 2500 children. Both questionnaire strategies had identical costs that included administrative oversight (45%), personnel (31%), teacher incentives (13%), transportation (9%), and supplies (1%). Incremental costs associated with spirometry included personnel (38%), program administration (33%), missed class time (16%), and spirometer depreciation, maintenance, and supplies (12%). Incremental costs associated with exercise testing included personnel (87%) and additional spirometers (13%). Costs to confirm the screening result were based on the May 2006 Alabama Medical Fee Schedule⁵⁸ and included a physician visit, various diagnostic procedures,^{19,20} and 1 albuterol inhaler. Indirect costs were also included (one-half day school absence, lost caregiver wage, and transportation). Costs for routine physician visits during the simulation were slightly lower because of lower visit fees and fewer diagnostic procedures performed.

TreeAge Pro 2008 was used to conduct the analysis with a Monte Carlo simulation and probabilistic sampling (10,000 iterations).⁵⁹ Additional methodologic details are provided in this article's Methods section of the Online Repository at www.jacionline.org.

Human subjects

No human subjects were involved in this research. The research was approved for exemption by the Institutional Review Board of the University of Alabama at Birmingham.

RESULTS

The status quo was the least costly and least effective option. The NQ was the most efficient option but was not cost-effective. The mean incremental cost-effectiveness ratio (ICER) of the NQ was \$151,000 per QALY, with 95% of iterations falling between \$65,800 and \$318,000 and 21% falling below \$100,000. The BQ had a mean ICER of \$312,000 per QALY, with 95% of iterations falling between \$120,400 and \$735,800. Both the MSwSP and MSwET options were more costly and less effective than the BQ. Because of this, these options were dominated, meaning that they were inferior to the other available options, and by convention their costs and outcomes are not reported. The acceptability curve is shown in Fig 3. Table E3 in the Online repository presents the costs and outcomes associated with each strategy and Figure E3 displays the cost-effectiveness graph.

The NQ generated 21 additional symptom-free day equivalents per year per child correctly identified as having previously diagnosed, but not well controlled asthma (1 quality-adjusted life-day = 10 symptom days, ~2.5 ED days, or ~1 hospital day). The BQ generated an additional 3 symptom-free day equivalents per child correctly identified as having undiagnosed asthma. The costs per child screened, including physician confirmation costs, were \$86, \$218, \$224, and \$246 for the NQ, BQ, MSwSP, and



Sensitivity analysis demonstrated that 3 variables accounted for 90% of the total model uncertainty: symptom day preference weight (54%), prevalence (23%), and baseline rate of symptom days (15%). When sensitivity analysis was limited to a comparison of the NQ and the status quo, 4 variables accounted for 75% of the uncertainty: the symptom day preference weight (44%), the probability that parents would confirm screening results (17%), the adequacy of asthma control in the population (9%), and the

Population-based childhood asthma screening is not cost-effective at \$50,000 per QALY and is unlikely to be cost-effective

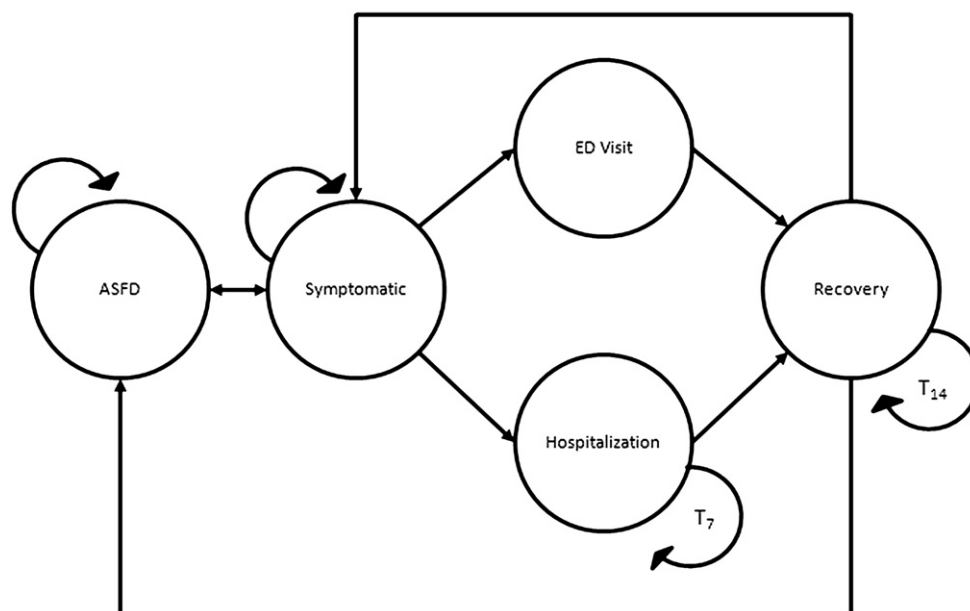


FIG 2. Asthma health states (T7: tunnel state, 7 days duration; T14: tunnel state, 14 days duration).

TABLE II. Symptom days (per year), ED visits, and hospitalizations (per 1000 person-years) for children with previously diagnosed asthma by severity and treatment assignment

Severity	Symptom days			ED visits			Hospitalizations		
	Full	Partial	None	Full	Partial	None	Full	Partial	None
Intermittent	87	146	165	24	48	60	6	12	15
Mild persistent	105	172	193	96	192	240	24	48	60
Moderate persistent	122	195	217	144	288	360	48	96	120
Severe persistent	153	234	255	288	576	720	96	192	240
Weighted mean	103	169	189	84	169	211	24	49	61

at \$100,000 per QALY. However, it is possible to envision scenarios in which strengthening the links among screening, treatment, and long-term adherence might make screening cost-effective at a threshold of \$100,000 per QALY. If the more stringent threshold of \$50,000 per QALY is used, it is much more difficult to envision such a scenario. Sensitivity analysis provides guidance for which changes could create more favorable screening conditions. For example, increasing the number of children who are evaluated after screening and improving their adherence to controller medication (behavioral factors) would yield a mean ICER of \$98,000 per QALY. More certainty is also needed regarding the true valuation of the symptom day, which estimates how harmful respiratory symptoms are to a child's quality of life. Given that there are scenarios in which screening could approach cost-effectiveness, it is understandable why asthma screening has been controversial.

A number of important conclusions can be drawn from this analysis. First, the optimal screening strategy is to only seek out children with previously diagnosed but not well controlled asthma. Screening for undiagnosed asthma is problematic for 2 reasons. First, screening generates many false-positive results that require significant resources to confirm. Second, identifying children with undiagnosed asthma will yield only modest benefits because they already experience relatively infrequent symptoms

TABLE III. Daily direct medical costs (annualized) in 2006 dollars for ASFD health state by severity and treatment assignment

Severity	Full treatment (\$)	Partial treatment (\$)	No treatment (\$)
Severe persistent	5.36 (1957)	2.68 (978)	.54 (196)
Moderate persistent	1.43 (522)	.72 (261)	.14 (52)
Mild persistent	.72 (261)	.36 (131)	.07 (26)
Intermittent	.20 (72)	.10 (36)	.02 (7)

and health care use. Even when health care use is assumed to be equivalent between children with diagnosed and undiagnosed asthma, the NQ remains the most efficient strategy. This finding was true under all modeled conditions. This unexpected finding is contrary to the prevailing wisdom that identifying undiagnosed asthma is an important screening objective. Our findings suggest that current community-based diagnosis appears to identify children whose asthma can be treated cost-effectively. Focusing on other determinants of poor asthma control (eg, access to care or better adherence) may be a better use of scarce resources.

The opportunity to engage schools as champions of screening by leveraging fewer school absence days also appears unlikely. For schools to break even under the reference case assumptions, screening would have to prevent 26 school absence days per child identified with previously diagnosed but not well controlled asthma who was evaluated by a physician. Under the best case scenario, screening would still have to prevent 3.5 school absences per year to break even, which is almost twice the excess school absences per year in children with asthma.⁶⁰ If screening is to be undertaken, it appears that it will have to be a societal priority.

The potential for cost savings from improved recognition and treatment of asthma also appears illusory as increases in daily medication costs overwhelm the relatively small savings from fewer ED visits and hospitalizations. This finding appears to be generalizable to asthma interventions that yield benefits by improving treatment adherence. Even with large treatment

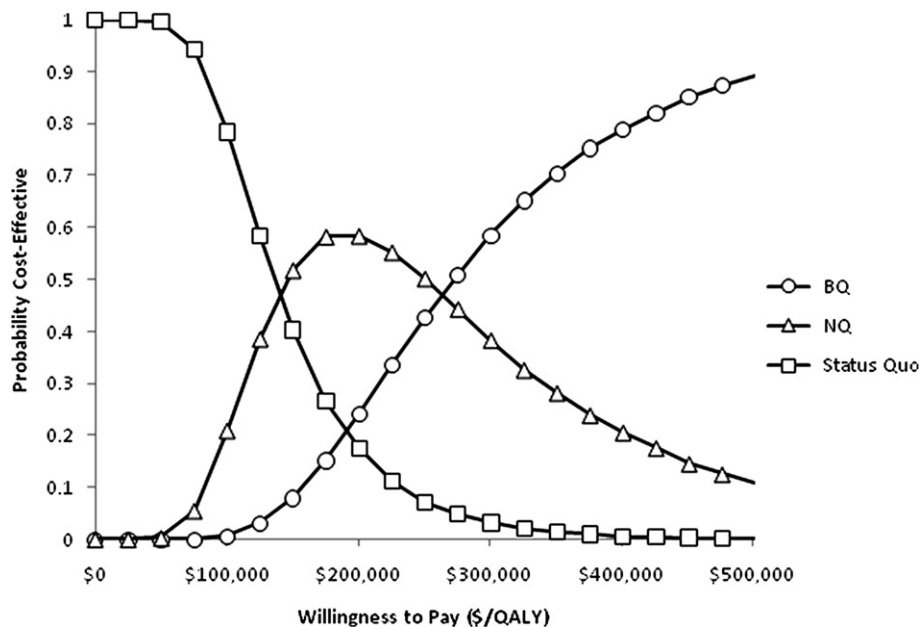


FIG 3. Acceptability curve.

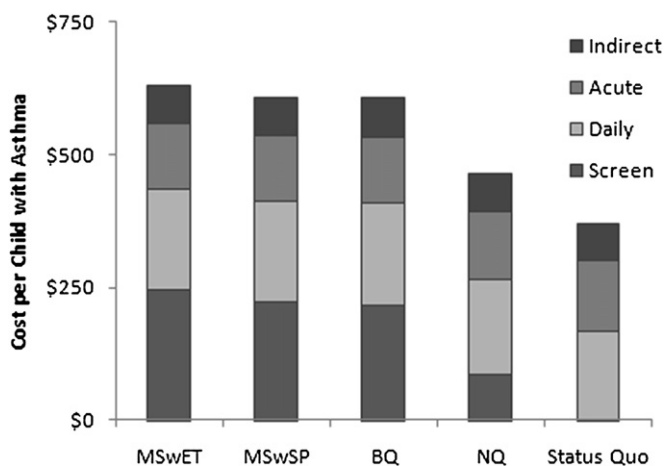


FIG 4. Distribution of total costs (2006 dollars) per child with asthma.

effects, the lower unit costs of medications spread over a large number of children outweigh the savings from fewer but costlier acute care events concentrated among a minority.

The importance of the symptom day versus acute care visits to screening cost-effectiveness is also unexpected. The preference weight for the symptom day used in this analysis, .90 (range, .84-.96), means that a symptom day was worth 90% of a symptom-free day. Lower weights for the symptom day preference weight were associated with more cost-effective outcomes because treatment yielded a corresponding larger benefit.

The symptom day preference weight was derived from the PAHOM, a multiattribute measure that used a standard gamble approach to derive utility-based preference weights for various asthma health states. The health states were based on impairments across 3 dimensions: symptoms, activity limitation, and/or emotional impairment.⁴⁹ Various combinations of impairments produced 10 possible health states, and 3 to 4 of them could have

reasonably characterized a symptom day in our analysis (eg, moderate symptoms with activity limitation but no emotional impairment versus days with both). Because each of the PAHOM's 10 health states was associated with its own unique preference weight, several PAHOM states were combined and averaged to create the single weight used in our analysis. It is possible that our simple approach did not accurately capture the true valuation of the symptom day.

We have previously presented data from a small sample of children ($N = 81$) that demonstrated a correlation of -0.77 between the PAHOM and the Juniper Asthma Control Questionnaire.⁶¹ In addition, the mean PAHOM score for children with well controlled asthma was 0.99, and for children with uncontrolled asthma, it was 0.89, 0.85, and 0.84 at Asthma Control Questionnaire scores of >0.75 , 1.25, and 1.50, respectively. This provided suggestive evidence that the symptom day preference weight used in this analysis was reasonable. However, a larger, more systematic study is needed to confirm this. The weights were also derived from a small population of adults ($N = 94$) from the Seattle, Wash, area and may not have been generalizable to the population in our analysis.⁴⁹

Our novel use of PAHOM weights in conjunction with daily Markov modeling allowed us to identifying the importance of the symptom day preference weight to the cost-effectiveness of asthma screening.⁶² Our approach extends the work of Price and Briggs⁶³ and demonstrates the importance of short cycle lengths when modeling chronic conditions with high symptom burden. Although ED visits and hospitalizations are costly and severe, symptom days may be more important drivers of cost-effectiveness because of their frequency. For relatively asymptomatic conditions, daily modeling may not be desirable. However, it may be necessary for chronic conditions such as asthma, for which symptoms are frequent and debilitating.

Several limitations should be acknowledged. First, the use of preference weights could be problematic and these results should be interpreted cautiously.⁶² A second limitation is the reliance on

TABLE IV. Probabilistic sampling outcomes of reference case, alternative best case scenarios, and overall best case scenario

Scenario	2006 Dollars per QALY gained		
	Low estimate (2.5%)	Estimate (mean)	High estimate (97.5%)
Reference case	65,800	150,700	318,000
Optimal QALD weights	47,700	90,700	171,000
Optimal epidemiologic factors	50,000	108,800	227,000
Optimal health system	59,000	121,900	234,400
Optimal behavioral factors	45,900	93,800	181,300
Optimal treatment effect	42,900	91,200	184,900
Optimal screening costs	54,900	118,900	243,800
Best case	11,200	12,800	14,800

QALD, Quality-adjusted life day.

secondary data. Ideally, cost-effectiveness analysis should be performed prospectively as part of a randomized trial; however, the need to follow a large sample of children over time while capturing daily symptom, medication use, and health care use data makes such a trial economically unfeasible.⁴¹ In the absence of a large trial, reliance on secondary data analyses is inevitable. Last, the generalizability of our results outside the simulated population of urban, primarily black elementary-age school children is uncertain. However, we believe that the unique combination of high asthma prevalence, high rates of undiagnosed asthma, poor access to health care, and high nonadherence rates makes this population an ideal setting to conduct school-based asthma screening. It is difficult to envision how screening in other populations with lower prevalence, better recognition, and better treatment could be more cost-effective. Our model is robust to a wide range of assumptions, suggesting that the importance of any single variable appears small, with the exception of the symptom day preference weight.

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Key messages

- School-based asthma screening is unlikely to be cost-effective.
- Screening children with previously diagnosed asthma at risk of poor control is the most efficient approach.
- Strengthening links among screening, treatment, and long-term adherence would make future screening approaches more cost-effective.
- The asthma symptom day is the most important driver of cost-effectiveness in this model.

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The purpose of this Online Repository is to provide cost-effectiveness specialists with important details omitted from the printed article because of space constraints. It may also be useful for those without previous background in cost-effectiveness analysis because it also provides more explanation regarding the choice of specific inputs and their ranges. Unfortunately, some duplication of material is inevitable

METHODS

A cost-effectiveness analysis of school-based asthma screening in a simulated population is undertaken from the societal perspective. The inputs used in the model are representative of a population of urban, low-income, minority school children from the Birmingham City School System in Birmingham, Ala.^{E1} In 2006, this system included 42 elementary schools, had 160 teachers and 2500 students per grade level, and spent \$7800 per child for 175 days of instruction. Four mutually exclusive screening strategies are compared against the status quo of no screening. The time frame is 1 year, and the cycle length is 1 day. The outcome is 2006 dollars per QALY gained. No discounting of costs or health outcomes is modeled because of the short time horizon. Data are derived from the literature except screening costs, which are provided by the authors.

Screening methodologies

The screening methodologies have been previously described.^{E2,E3} The Asthma Control Test (ACT) was not part of the original screening designs because the NQ was not intended to be a independent screening strategy; however, the addition of the ACT to assess control in those with previously diagnosed asthma is reasonable. The NQ is assumed to be 100% sensitive and specific for previously diagnosed asthma. This decision was made because there is no easy way to confirm or disprove a self-report of a previous asthma diagnosis. In addition, the purpose of the NQ is to identify children with poor asthma control who already have access to asthma care. The sensitivity and specificity estimates for the BQ, MSwSP, and MSwET strategies differ from those found in the original article because the original article determined these test characteristics using all children with asthma (previously diagnosed and undiagnosed). For this analysis, children with previously diagnosed asthma (responded yes to NQ) were not considered. The test characteristics used here reflect only the strategies' ability to detect undiagnosed asthma.

Decision tree

A more detailed decision tree is provided (Fig E1). From left to right, the tree predicts the screening result based on prevalence,^{E2-E12} the probability that children with asthma have been previously diagnosed,^{E2,E3,E6-E9,E11,E12} the probability their asthma is controlled if they are diagnosed,^{E13-E15} and the sensitivity and specificity of the various strategies. Next, the tree estimates the likelihood that the child's treatment status will change after screening based on the probability that parents will confirm the screening result,^{E16,E17} the probability that physicians will provide guideline concordant treatment,^{E18-E21} and the probability that children will be adherent to the treatment regimen.^{E22-E24} Last, the tree accounts for the distribution of asthma severity by diagnostic method (previously diagnosed vs newly diagnosed) because children identified by screening have, on average, less severe asthma than those diagnosed by physicians in the community.^{E2,E6}

Children who successfully complete these 3 steps are assigned to receive the full benefit offered by guideline concordant care. The effect sizes for the full and benefit conditions represent the magnitude of improvement seen in randomized controlled trials of inhaled corticosteroid (ICS) use. The partial benefit condition models either the placebo effect or the less effective treatment option in trials depending on the type of control group. The no benefit condition is based on baseline rates when a washout period is used. Children are assigned to 1 of 3 treatment conditions: no benefit, partial benefit, and full benefit. Children who are undiagnosed or who are diagnosed but not well controlled are assigned to no benefit. Children who are evaluated by a physician after screening but do not receive guideline concordant care or do not fully adhere are assigned to partial benefit, where they experience 20%

fewer ED visits, hospitalizations, and symptom days than children in the no benefit condition. Children who receive guideline concordant care and are fully adherent are assigned to full benefit, where they experience 60% fewer ED visits^{E25-E29} and hospitalizations^{E25-E27,E29} and 55% fewer symptom days^{E27,E30-E34} than children in the no benefit condition.

Ultimately, children with asthma are assigned to 1 of 24 Markov models in which costs and outcomes are simulated after accounting for asthma severity (intermittent and mild, moderate, or severe persistent), treatment benefit (none, partial, or full) and diagnostic source (screening or previously diagnosed). Children without asthma have their screening costs and health outcomes assigned in the decision tree itself.

Markov models

Markov models are state transition models that are well suited to simulate asthma-related costs and outcomes because asthma is characterized by frequent and abrupt changes in health status of varying severity, duration, and costs.^{E35} Five mutually exclusive health states are modeled: ASFD, symptom day, exacerbation recovery day, ED visit, and hospitalization day (Fig E2). Deaths are not modeled because of their rarity and the short duration of the simulation.^{E4}

On day 1, children are assigned to either the ASFD or symptom states on the basis of assigned severity and treatment benefit after screening. As the simulation progresses, children transition to other states based on predefined transition pathways and probabilities. Allowed pathways are depicted by arrows exiting the health states. A curved arrow indicates the possibility of remaining in that state for multiple cycles, and a curved arrow with a numbered box represents a tunnel state of the specified duration in days.

Children may transition between the ASFD and symptom days, but may experience an ED visit or hospitalization only from the symptom state. The ED visit state represents only those visits that do not result in a hospitalization, because visits that do are often not reported independently of the hospitalization.^{E36} Transition out of the ED visit is mandatory after 1 cycle. The hospitalization state is a tunnel state with an exponentially declining probability of remaining hospitalized to achieve an average and maximum length of stay of 2.5 and 7 days, respectively.^{E37,E38} The exacerbation recovery state is a tunnel state of 14 days maximum duration during which there is a fixed and increased risk of repeat ED visit or hospitalization.^{E39}

Base rates for symptom days, ED visits, and hospitalizations are 189 per year,^{E27,E30-E34} 211 per 1000 person-years,^{E25-E29} and 61 per 1000 person-years,^{E25-E27,E29} respectively, for children with previously diagnosed asthma assigned to no benefit. Rates are subsequently adjusted to account for asthma severity, treatment assignment, and method of diagnosis. Base rates for ED visits, hospitalizations, and symptom days for children with undiagnosed asthma are 70%, 70%, and 30% lower, respectively.^{E40-E42}

Each health state is associated with a daily health outcome (quality-adjusted life-day [QALD]) and a daily cost (2006 dollars). The health outcome for each state is derived from the PAHOM, which used a standard gamble approach to define utility-based preference weights for clinically relevant asthma health states on an interval scale bounded by 0 (death) and 1 (perfect health).^{E43} The daily health outcomes and costs are summed over 365 cycles.

The daily cost for each health state includes direct and indirect asthma-related costs. The cost of an ED visit is \$350 in direct and \$369 in indirect costs.^{E37,E44} The cost of a hospitalization day is \$1200 in direct and \$150 in indirect costs.^{E36,E37,E45} Indirect costs account for lost caregiver wages for women of all races between the ages of 35 and 44 years,^{E46} school absence days,^{E1} and transportation^{E47} costs associated with the encounter and subsequent convalescence. Larger indirect costs are associated with the ED visit and the last hospitalization day to account for additional school absence days after the encounter.^{E39}

Daily costs for the ASFD, symptom day, and exacerbation recovery day include daily medication costs and routine physician direct and indirect costs. The medications considered include those consistent with guideline concordant therapy^{E48} and with the Alabama Medicaid Agency formulary^{E49}: short-acting β -agonists (albuterol), long-acting β -agonists (salmeterol), ICSs (budesonide), and oral corticosteroids (prednisone). In this analysis, children with intermittent asthma are modeled to take only short-acting β -agonists. Children with mild and moderate persistent also take low-dose (200 μ g/d)

and medium-dose (400 mcg/d) ICSs, respectively. Children with severe persistent asthma take high-dose (800 mcg/d) ICSs and long-acting β -agonists. The symptom day costs also account for increased use of albuterol, and the recovery day also incorporates increased albuterol use and a course of oral prednisone. Direct medication costs are based on average wholesale drug prices^{E50} adjusted for direct Medicaid discounts, annual Medicaid rebates to the state, dispensing fees to reflect the cost to the Alabama Medicaid program, and patient copayments.^{E51,E52}

Screening costs

Screening is modeled as being provided by a third-party vendor with the necessary expertise, equipment, and administrative oversight. Costs are estimated using a microcosting technique based on information provided by the authors. Screening occurs at a single grade-level including approximately 2500 children, and screening costs are considered fixed. All children are expected to complete screening, and all caregivers are expected to receive results. The costs of conducting both questionnaire strategies are the same.

The costs associated with the questionnaire include administrative oversight (45%), personnel (31%), teacher incentives (13%), transportation (9%), and supplies (1%). Administrative oversight includes 0.15 full-time equivalent health care supervisor at an annual wage of \$78,370.^{E53} Incentives of \$20 per teacher are included to maximize compliance. Administering the questionnaire is estimated to require approximately 400 hours of respiratory therapist time at an hourly wage of \$20.89.^{E53} Transportation costs include four 30-mile round trips per school at \$0.49 per mile for each of the 42 elementary schools. No school absence time is needed to complete the parental questionnaire.

The costs associated with spirometry include personnel (38%), program administration (33%), missed class time (16%), and spirometer depreciation, maintenance, and supplies (12%). A single respiratory therapist augmented by 2 medical assistants (\$12.03 hourly wage) can complete spirometry in approximately 200 hours.^{E53} An additional 0.10 full-time equivalent of administrative oversight is modeled to organize and supervise spirometry. Spirometry is estimated to result in 1 hour of missed classroom time per child at \$6.43 per hour (\$45/d).^{E1} Supplies include disposable mouthpieces (\$1.80) and nose clips (\$0.80). The capital costs of spirometers are not considered; however, depreciation (10% per year), periodic calibration, and annual maintenance costs are. The costs associated with exercise testing include 1 additional respiratory therapist and medical assistant (87%) and additional spirometers (13%). No additional missed classroom time is necessary because of efficiencies associated with group testing.

The direct costs of medical confirmation of the screening result are estimated at \$98 and include the physician visit, diagnostic procedures, and 1 albuterol inhaler. Direct medical costs are based on the May 2006 Alabama Medical Fee Schedule.^{E54} Diagnostic procedures include spirometry, chest radiographs, sinus radiographs, and skin testing. Costs of these procedures are discounted to reflect that not all children will receive all them.^{E18,E19} Indirect costs include one-half day of lost caregiver wages, one 10-mile round-trip transportation, and one-half day school absence. The direct costs of routine physician visits in the daily treatment costs are lower (\$54) than those for confirmation because visit fees are lower and diagnostic procedures are fewer.

The software used is TreeAge Pro 2008 (TreeAge Software, Inc, Williams-town, Mass), and the analysis is conducted with a Monte Carlo simulation and probabilistic sampling.^{E55} All distributions are triangular. One-way deterministic sensitivity analysis is performed over the specified range of input values. Probabilistic sampling is again used to evaluate various alternative best case scenarios using groups of related variables. A best case scenario is also conducted with all major inputs forced to their most favorable position.

RESULTS

Screening outcomes are reported in Table E2. The status quo is the least costly and least effective option (Table E3). The Narrow Questionnaire is the most cost-effective option with a mean ICER of \$151,000 per QALY and a slightly lower median ICER of \$136,000 per QALY. The distribution of ICERs demonstrates that 95% fall between \$65,800 and \$318,000 and 21% fall below

\$100,000 per QALY. The BQ option has a higher mean ICER of \$312,000 per QALY with 95% of ICERs falling between \$120,400 and \$735,800. Both the MSwSP and the MSwET options are dominated because they are more costly and less effective than the BQ (Fig E3).

Total costs and QALDs are presented in Table E3. From this table, one notices that the NQ is the most cost-effective option, with an ICER of \$127,000 per QALY gained. The BQ option is not dominated either, but its ICER is higher, \$252,000. The ICERs in Table E3 are on average lower than those presented using the probabilistic outcomes (main outcome and Table IV in main text). The ICERs in Table E3 are calculated as the mean incremental cost divided by the mean incremental outcome,

$$\sum \Delta \text{costs} / N / \sum \Delta \text{QALDs} / N$$

When each trial's incremental cost and outcome are linked

$$\sum (\Delta \text{costs} / N / \Delta \text{QALDs}) / N$$

as they are for the probabilistic outcomes, the mean is \$150,700, and the median is \$136,000. Table E3 outcomes are more closely aligned with the median rather than mean outcomes.

One-way deterministic sensitivity analysis results between the NQ and the status quo are presented in Table E1 and graphically represented by a Tornado diagram (Fig E4). These ICERs are comparable to those in Table E1. Four variables account for 75% of the total uncertainty in the model (risk percent). One variable alone, the symptom day preference weight, accounts for 44% of the uncertainty. The probability that parents will obtain physician confirmation of the screening result (17%), the probability that asthma is controlled at the time of screening (9%), and the estimated symptom reduction expected from full benefit (6%) account for another 31%. Each variable, when forced to its most favorable position, is associated with an ICER <\$100,000. When the symptom day preference weight is <.872, the ICER is <\$100,000.

Sensitivity analysis is repeated with individual cost elements aggregated by category: screening (screening plus postscreen physician confirmation), daily treatment (medication costs and direct costs of physician visits), acute care (direct ED and hospital costs), and indirect costs (Fig E5). Doing so demonstrates that screening costs contribute more to model uncertainty. This finding must be interpreted cautiously because screening costs and costs of postscreen physician visits are independent. Lowering the cost of the NQ would have no impact on the probability of parents seeking confirmation of the result. However, it does raise intriguing questions about how to combine the 2 to achieve overall lower screening costs.

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FIG E1. Decision tree.

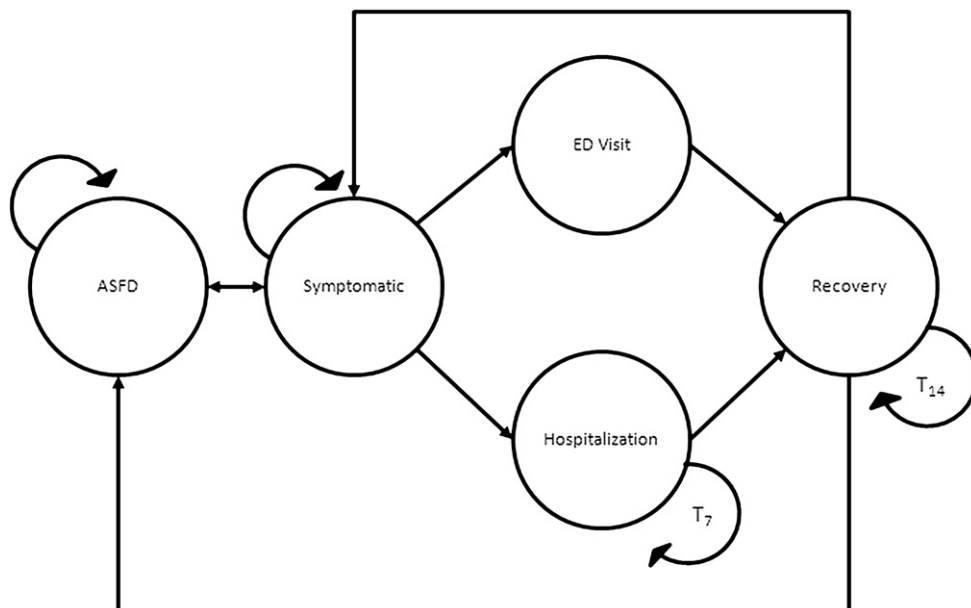


FIG E2. Asthma health states (T7: tunnel state, 7 days duration; T14: tunnel state, 14 days duration).

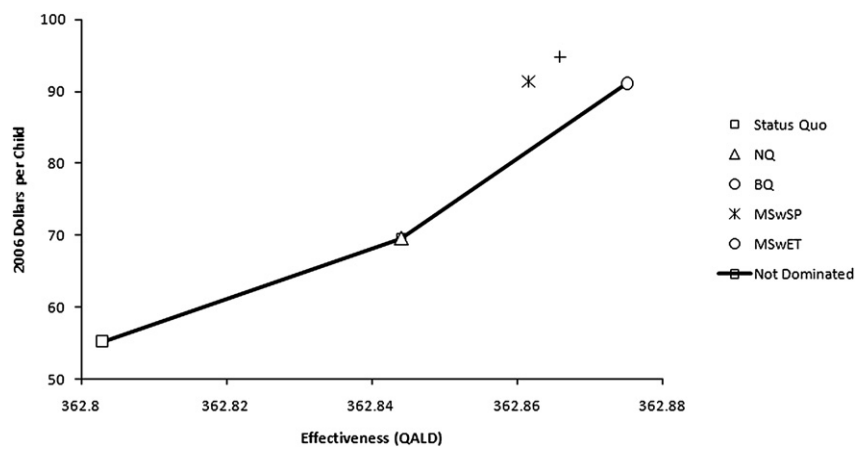


FIG E3. Reference case cost-effectiveness graph.

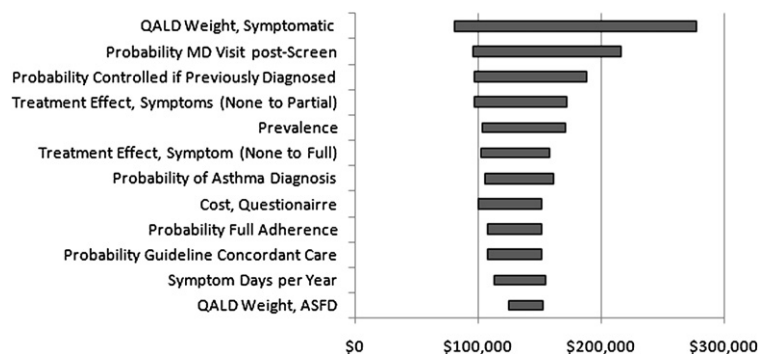


FIG E4. Tornado diagram (\$/QALY): NQ vs *status quo*. MD, Medical doctor.

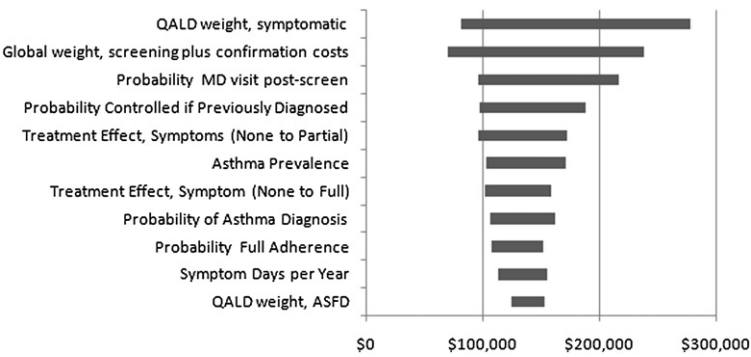


FIG E5. Tornado diagram (\$/QALY): NQ vs status quo using aggregated costs. *MD*, Medical doctor.

TABLE E1. Estimates (range), sensitivity analysis results (NQ vs status quo), risk percent and references for selected variables

	Point estimate (range)	(\$/QALY)		Risk* (%)	References
		Low	High		
Epidemiologic factors					
Prevalence	.15 (.10-.20)	103,300	171,600	5	E2-E12
Symptom days†	189 (136-240)	113,800	155,500	2	E27,E30-E34
Hosp (per 1000 person-yrs)†	61 (20-102)	120,700	131,600	<1%	E25-E27,E29
ED visits (per 1000 person-yrs)†	211(141-282)	123,500	128,700	<1%	E25-E29
Behavioral factors					
Postscreen MD visit	.30 (.15-.45)	95,800	217,000	17	E16,E17
Medication adherence	.60 (.40-.80)	107,800	152,200	2	E22-E24
Health system factors					
Control if prev diagnosed	.60 (.45-.75)	97,600	188,600	9	E13-E15
Prev diagnosed if asthma	.70 (.50-.90)	106,000	162,000	4	E2,E3,E6-E9,E11,E12
Guideline concordant care	.60 (.40-.80)	107,800	152,200	2	E18-E21
Treatment reductions					
Symptoms (partial)	.15 (0 -.30)	96,800	172,400	6	E27,E30-E34
Symptoms (full)	.55 (.40-.70)	102,300	158,700	4	E27,E30-E34
ED visits (partial)	.20 (0 -.40)	122,500	129,700	<1%	E25-E29
Hospitalizations (partial)	.20 (0 -.40)	122,800	129,400	<1%	E25-E27,E29
ED visits (full)	.60 (.50-.70)	124,900	127,200	<1%	E25-E29
Hospitalizations (full)	.60 (.50-.70)	125,000	127,000	<1%	E25-E27,E29
Sensitivity‡					
ACT	.70 (.67-.73)	122,000	130,400	<1%	E13,E14
BQ	.64 (.59-.69)	NA§	NA	NA	E2
MSwSP	.36 (.31-.41)	NA	NA	NA	E2
MSwET	.45 (.40-.50)	NA	NA	NA	E2
Specificity					
ACT	.73 (.70-.76)	125,100	126,911	<1%	E13,E14
BQ	.60 (.55-.65)	NA	NA	NA	E2
MSwSP	.97 (.95-.99)	NA	NA	NA	E2
MSwET	.97 (.95-.99)	NA	NA	NA	E2
Preference weights					
Symptomatic	.90 (.84-.96)	81,500	277,800	44	E43
ASFD	1.0 (.98-1.0)	124,900	153,400	1	E43
Recovery	.70 (.64-.76)	122,800	129,500	<1%	E43
ED	.43 (.37-.49)	125,800	126,300	<1%	E43
Hospitalization	.06 (.01-.11)	126,000	126,100	<1%	E43
Conversion factors					
Symptoms to mild	1.25 (.875-1.625)	122,400	133,300	<1%	E56
Symptoms to moderate	1.50 (1.05-1.95)	124,700	129,400	<1%	E56
ED visit to moderate	6 (4-8)	125,200	126,900	<1%	E56-E58
ED visit to mild	4 (3-5)	125,200	126,800	<1%	E56-E58
Hosp to moderate	8 (6-10)	125,200	126,800	<1%	E56-E58
Hosp to mild	4 (3-5)	125,300	126,800	<1%	E56-E58
Hosp to severe	16 (12-20)	125,700	126,300	<1%	E56-E58
ED visit to severe	12 (8-16)	125,700	126,300	<1%	E56-E58
Symptoms to severe	2.0 (1.4-2.6)	126,000	126,400	<1%	E56
Severity (previous)#					
Intermittent	.40 (.44-.34)				E2,E6
Mild	.36 (.40-.30)				E2,E6
Moderate	.20 (.14-.28)				E2,E6
Severe	.04 (.02-.08)				E2,E6
Severity (undiagnosed)		126,400	126,900		
Intermittent	.54 (.60-.50)				E2,E6
Mild	.24 (.28-.20)				E2,E6
Moderate	.20 (.11-.26)				E2,E6
Severe	.02 (.10-.04)				E2,E6
Screening costs					
Questionnaire	\$25,825 (18,525-33,350)	100,200	152,100	3	Authors
MSwSP (incremental)	\$19,725 (9,850-29,575)	NA	NA	NA	Authors
MSwET (incremental)	\$7,550 (3,775-11,350)	NA	NA	NA	Authors
MD visit (postscreen, direct)	\$98 (68-123)	122,300	129,000	<1%	E18,E19,E54

(Continued)

TABLE E1. (Continued)

	Point estimate (range)	(\$/QALY)		Risk* (%)	References
		Low	High		
Indirect costs					
Caregiver wage	\$100 (50-150)	122,000	130,000	<1%	E46
School absence day	\$45 (25-65)	124,400	127,600	<1%	E1
Caregiver transportation	\$10 (5-15)	125,100	126,900	<1%	E47
Medication costs					
Daily cost full to partial	.50 (.30-.80)	121,200	133,300	<1%	NA
Daily cost full to no	.1 (0-.20)	122,200	129,900	<1%	NA
Budesonide inhaler	\$103 (52-155)	122,200	129,800	<1%	E50-E52
Albuterol inhaler	\$26 (13-39)	124,300	128,000	<1%	E50-E52
Salmeterol	\$83 (41-124)	125,100	126,900	<1%	E50-E52
Prednisone (14 d)	\$10 (5-15)	126,000	126,100	<1%	E50-E52
MD visit (routine, direct)	\$54 (27-81)	124,500	127,500	<1%	E54
Acute care costs					
Hospital day (direct)	\$1,200 (900-1,500)	124,900	127,200	<1%	E36,E37,E45
ED visit (direct)	\$350 (175-525)	125,000	127,000	<1%	E37,E44

Hosp, Hospitalization; MD, medical doctor; Prev, previous; NA, not applicable.

*Percent contribution to total model uncertainty; only contributions $\geq 1\%$ shown.

†Weighted mean for children within no treatment group.

‡Sensitivity of NQ assumed to be 100% specific and sensitive.

§Variables not contained within subset of NQ versus BQ analysis.

||Factors applied to baseline rates of intermittent asthma.

#Sensitivity analysis of severity performed as a group in sensitivity analysis.

TABLE E2. Screening outcomes for 2500 children under reference case assumptions

Screening method*	Previously diagnosed, not controlled				
	TP	FP	TN	FN	PPV
ACT	74	43	115	32	63%
BQ	72	850	1275	41	8%
MSwSP	41	64	2061	72	39%
MSwET	51	64	2061	62	44%

FN, False negative; FP, false positive; PPV, positive predictive value; TN, true negative; TP, true positive.

*NQ assumed to be 100% sensitive and specific for previously diagnosed asthma.

TABLE E3. Costs (2006 dollars), health outcomes, and incremental cost-effectiveness ratios for reference case analysis

Methodology	Cost (\$)	Incr cost (\$)	Effectiveness (QALD)*	Incr effect (QALD)	ICER (\$/QALY)
<i>Status quo</i>	55.29	0	362.803	0	0
NQ	69.62	14.32	362.844	.04	127,020†
BQ	91.11	21.49	362.875	.03	251,850†
MSwSP	91.35	Dominated	362.862	Dominated	Dominated
MSwET	94.80	Dominated	362.866	Dominated	Dominated

Incr, Incremental.

*Per child screened.

† $\sum \Delta \text{costs} / N / \sum \Delta \text{QALDs} / N$.