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Clinical Tools to Assess Asthma Control in Children

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abstract

Asthma affects an estimated 7 million children and causes significant health care and disease burden. The most recent iteration of the National Heart, Lung and Blood Institute asthma guidelines, the Expert Panel Report 3, emphasizes the assessment and monitoring of asthma control in the management of asthma. Asthma control refers to the degree to which the manifestations of asthma are minimized by therapeutic interventions and the goals of therapy are met. Although assessment of asthma severity is used to guide initiation of therapy, monitoring of asthma control helps determine whether therapy should be maintained or adjusted. The nuances of estimation of asthma control include understanding concepts of current impairment and future risk and incorporating their measurement into clinical practice. Impairment is assessed on the basis of frequency and intensity of symptoms, variations in lung function, and limitations of daily activities. "Risk" refers to the likelihood of exacerbations, progressive loss of lung function, or adverse effects from medications. Currently available ambulatory tools to measure asthma control range are subjective measures, such as patient-reported composite asthma control score instruments or objective measures of lung function, airway hyperreactivity, and biomarkers. Because asthma control exhibits short- and long-term variability, health care providers need to be vigilant regarding the fluctuations in the factors that can create discordance between subjective and objective assessment of asthma control. Familiarity with the properties, application, and relative value of these measures will enable health care providers to choose the optimal set of measures that will adhere to national standards of care and ensure delivery of high-quality care customized to their patients.

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INTRODUCTION

Guidelines from the National Heart, Lung and Blood Institute for the diagnosis and management of asthma, and the Global Initiative for Asthma Control, revolve around the yardstick of evaluation of the severity of asthma and attainment of control to guide initiation and

adjustment of therapy.[1,2] Numerous studies have confirmed the inadequacy of asthma control in the United States.[3,4]

The domains of severity and control can be assessed in terms of impairment (frequency and intensity of symptoms, variations in lung function, and limitations of daily activities) and future risk (likelihood of exacerbations, progressive loss of lung function, or adverse effects from medications). Asthma can be considered to be well controlled if symptoms are present twice a week or less; rescue bronchodilator medication is used twice a week or less; there is no nocturnal or early awakening; there are no limitations of work, school, or exercise; and the peak flow (PEF)/forced expiratory volume in 1 second (FEV_1) is normal or at the personal best. Asthma control can be further classified as well controlled, not well controlled, and very poorly controlled as elegantly laid out in the National Heart, Lung and Blood Institute Expert Panel Report 3 (EPR3).[1] Asthma can be considered not well controlled if symptoms are present more than 2 days a week or multiple times on 2 or fewer days per week; rescue bronchodilator medication is used more than 2 days per week; nighttime awakenings are 2 times a month or more; there is some limitation of work, school, or exercise; and the PEF/FEV_1 is 60% to 80% of personal best/predicted, respectively. Asthma is classified as very poorly controlled if symptoms are present throughout the day; rescue bronchodilator medication is used several times per day; nighttime awakenings are more than 1 time a week; there is extreme limitation of work, school, or exercise; and the PEF/FEV_1 is less than 60% of personal best/predicted, respectively.

The keystone of asthma management is the achievement and maintenance of optimal asthma control. However, to date, there is no universally recognized gold standard measure of asthma control that can accurately capture both patient-reported domains of impairment and risk and objective measures of lung function. The tools available in a clinical practice setting can be classified as subjective ("patient reported") and objective ("physiologic and inflammatory measures"). A judicious combination of measures from each category may be needed to optimally assess asthma control.

SUBJECTIVE MEASURES

Subjective measures of asthma control include (1) detailed history taking, (2) use of composite asthma control scores, and (3) quality-of-life measures (used mainly in research settings).

History

Assessment of asthma control in the health care provider's office starts with the history. Detailed information should be sought on patient-centered outcomes (such as asthma exacerbations in the past year and the limitations asthma imposes on the patient's daily activities including sports and play), sleep disturbance, medication use (both daily controller and reliever medication), adherence to therapy, and comorbidities/factors that may complicate care.[5]

Composite Asthma Scores

Patient-reported composite asthma control score instruments are attempts to capture the multidimensional nature of asthma control in a single numerical value. This enables the degree of asthma control to be compared across encounters. More than 17 composite instruments, each with at least 1 published validated study, are available.[6] These instruments have comparable content and have been designed to measure asthma disease activity over a period of 1 to 4 weeks. Notably, none of them have been validated to assess an acute exacerbation (Table 1). Therefore, from a pediatric emergency medicine perspective, caution should be taken when using composite asthma score instruments during an acute exacerbation, as is typically encountered in the emergency department setting.

The commonly used validated tools are the Asthma Control Test (ACT),[7] the Childhood Asthma Control Test C-ACT,[8] and the Asthma Control Questionnaire (ACQ).[9] The ACT contains 5 items, with a recall window of 4 weeks. The C-ACT is for use in children 4 through 11 years of age and consists of 4 pictorial items and 3 verbal items that are scored by the children and parents, respectively. It has been reported that children tend to assess their asthma control to be significantly lower than their parents do. The Asthma Control Questionnaire (ACQ) contains 6 items with a recall window of 1 week, supplemented by percentage of predicted FEV_1 measurement. The Test for Respiratory and Asthma Control in Kids (TRACK)[10] is a 5-question caregiver-completed questionnaire that determines respiratory control in children 0 to 5 years of age with symptoms consistent with asthma. Another less commonly used instrument is the Asthma Therapy Assessment Questionnaire (ATAQ), a 20-item parent-completed questionnaire exploring several domains, with 4 questions relating to symptom control and primarily used in research.[11,12]

Individual instruments contain 3 to 10 questions, and scoring varies by instrument (Table 1). Four instruments have established cutoff values for uncontrolled versus controlled asthma (ACQ, ACT, C-ACT, and TRACK), and 2 have cutoffs for identifying poorly controlled asthma (ACT and ATAQ). Because these cutoffs have been defined

TABLE 1 Age-Specific Asthma Control Tools and Their Properties

Age	Instrument
0–4 y	TRACK
5–11 y/older children	Asthma Quiz, ATAQ for Children and Adolescents, Breathmobile Assessment of Asthma Control, Asthma Control in Children, Functional Severity of Asthma Scale, C-ACT, and Pediatric Asthma Control Tool
12 y and older	ACT and ACQ
18 y and older	Asthma Control and Communication Instrument, ATAQ, Seattle Asthma Severity and Control Questionnaire, and 30-Second Asthma Test
Comments	Other asthma questionnaires include the Asthma Quiz for Kidz, the 23-item/13-item Pediatric Asthma Quality of Life Questionnaire (PAQLQ)/Mini-PAQLQ, the Pediatric Quality of Life Inventory, the Asthma Routines Questionnaire, and the Pediatric Asthma Control and Communication Instrument
Tool	Properties
ACT (5-item questionnaire)	Composite, numeric score (up to 25)
	MCID 3 points
	Controlled >19
	Poorly controlled ≤15
C-ACT (7-item questionnaire)	4 filled out by child, 3 questions by parent/caregiver
	Composite numeric score (up to 27)
	MCID 2 points
	Controlled >19
ACQ (7 items: 6 questionnaire, and 1 FEV_1)	Composite numeric score (up to 6)
	MCID 0.5 points
	Controlled >19
ATAQ (4-item questionnaire in the control dimension; overall 20 questions)	Composite numeric score (up to 4)
	MCID: none established
	Controlled (0); not well controlled (1–2), poorly controlled (3–4)
TRACK (5-item questionnaire)	Composite numeric score (up to 100)
	MCID: 10
	Controlled (≥80)

Adapted from Cloutier et al.[6] MCID, minimally clinically important difference.

at a population level, they may not be accurate for an individual patient. Tracking the numerical and categorical responses over time for each individual patient may prove to be more helpful than looking at cutoff values alone. For instance, if a patient reports frequent nocturnal awakenings, following the response to that particular question may help individualize attainment of control. The minimal clinically important differences or temporal differences in scores that indicate clinical significance have been determined for a few of the instruments (ACQ, ACT, C-ACT, and TRACK[6,13]; Table 1). Three of the instruments (ACQ, ACT, and TRACK) have been validated in Spanish-speaking groups.[14–16] The ACQ and ACT have been validated for use as self-administered instruments in person, at home, by telephone, and by Internet tracking.[6,17]

Poor asthma control, as measured by the commonly used composite scores, is associated with reduced lung function and elevated exhaled nitric oxide fraction[5,18] (discussed later in the article). Studies have shown that changes in these composite scores reflect changes in the overall clinical assessment of asthma control by physicians and the need to step-up therapy.[19] However, a recent study showed that the degree of asthma control, as assessed by these tools, changes over time and shows variable concordance with the risk of exacerbations.[12]

Despite being fairly well validated, these scores share drawbacks that limit their usefulness in clinical practice.[6] Although the short recall window facilitates reliable recollection of recent asthma events, it fails to represent the fluctuations in control. Children may be excellently controlled during one season and then have poor control during another. In addition, asthma exacerbations can occur in children with good short-term asthma control.[20] Exacerbations, an important component of the impairment domain of asthma control, are not covered in the ACT, C-ACT, and ACQ but are assessed in the TRACK and the Composite Asthma Severity Index.[21,22]

Quality of Life

A range of pediatric asthma quality-of-life instruments have been developed, encompassing the impact of asthma on children's or their parents' lives.[23] The instruments have been validated but are time-intensive to fill out and are therefore not routinely used in clinical practice.

OBJECTIVE MEASURES

Currently available objective measures of asthma control include (1) assessment of lung function, (2) evaluation of airway

TABLE 2 Objective Measures of Asthma Control

Spirometry	Measured by ATS/ERS guidelines and using NHANES-3 normative values. Serial measures should be performed at the same time each day, if possible (Indicate whether bronchodilator was withheld before test.)
	Standardized methodology and equipment (ATS/ERS guidelines)
	Performed in a clinic/laboratory setting under the supervision of a qualified technician
	Can be performed by children >5 y (in general) under guidance of trained personnel
	Portable and handheld devices available for use in the field/home settings
	FEV_1 report:
	Percent predicted values (at baseline and at any other time point, if applicable)
	Changes over the course of evaluation:
	Percent change from baseline in the absolute value
	Absolute change from baseline (in milliliters)
	Change from baseline in the percent predicted value
	FEV_1/FVC report:
	Ratio of absolute values (at baseline and at any other time point, if applicable)
	Changes over the course of evaluation:
	Absolute change from baseline in the value of the ratio
	Change from baseline in the percent predicted value
Bronchodilator reversibility (prebronchodilator and postbronchodilator spirometry)	1. Withhold bronchodilator before the measure (12–24 h for long-acting β-2-agonists or anticholinergics; 4–6 h for short-acting β-agonists)
	2. Administer 4 separate puffs of albuterol (90 mg of albuterol base/puff) with spacer at 30-s intervals between puffs, followed by spirometry after 15 min
	Report:
	Prebronchodilator and postbronchodilator FEV_1 (expressed as percent predicted)
	Percent change from prebronchodilator to postbronchodilator in the absolute value of FEV_1
	Absolute change in FEV_1 from prebronchodilator to postbronchodilator (in milliliters)
PEF	PEF is a measure of maximum instantaneous expiratory
	Can be self-administered on a daily basis and results recorded manually or electronically to obtain day-to-day or within-day variability
	Percent predicted values (NHANES-3 normative values)
	When measured with a peak flowmeter, PEF is usually expressed in units of L/min; in contrast, when PEF is measured with spirometry systems, it is usually expressed in units of liters/second
	Percent change from baseline in the absolute values over the course of evaluation
	Absolute change from baseline over the course of the evaluation (in liters/minute)
	Variability (diurnal amplitude as a percentage of the day's mean)

Adapted from Tepper et al.[24]

hyperresponsiveness, and (3) biomarkers.

Assessment of Lung Function

Peak Flow

The PEF is defined as the highest instantaneous expiratory flow achieved during a maximal forced expiratory maneuver starting at total lung capacity.[24] PEF variability is the degree to which the PEF varies among multiple measurements performed over time (Table 2). The management of acute exacerbations has traditionally been guided by PEF measurements. However, the correlation between PEF and FEV_1 worsens in asthmatic patients with airflow limitation. Also, although reference to normal PEF values is important, the "personal best" value, and the trend of change in individual patients, is of greater value in managing their asthma.[24]

The advantages of PEF are that it is easier to perform than a spirometric maneuver and it is measurable with a relatively small and inexpensive instrument. Thus, PEF may be suitable for individual testing at home, at school, and in patients who are poor perceivers of their degree of airway obstruction. It may help prevent delayed treatment in underperceivers and excessive use of services in overperceivers.

Many concerns regarding PEF have been described, with the primary ones being that the results are highly variable even when performed well, limiting its utility in the diagnosis and management of asthma. Parents and child should be appropriately trained on use, but there is no gauge of effort, and it gives no information regarding the site of airflow obstruction. It cannot distinguish obstructive from restrictive ventilatory impairment. PEF meters from different manufacturers may show different results, and the "personal best" measurements may change with growth and degree of asthma control. Adherence to PEF monitoring is a challenge[25] and is often the reason it is not widely used in clinical practice. Overall, PEF monitoring alone has not been shown to be more effective than symptom monitoring on influencing asthma outcomes[26] and is no longer recommended.[1]

Spirometry

Measurement of spirometric indices of lung function, such as the FEV_1,

forced vital capacity (FVC), and FEV_1/FVC ratio, are an integral part of the assessment of asthma severity, control, and response to treatment.[1,2] They have been shown to be associated with the risk of asthma attacks in children.[27] Children with chronic airway obstruction have been reported to be less likely to perceive dyspnea than those with acute obstruction.[28] The EPR3, therefore, recommends performing office-based spirometry every 1 to 2 years and more frequently if clinically indicated in children 5 years or older with asthma.[1] However, only 20% to 40% of primary care providers use lung function measurements in asymptomatic asthmatic patients, and up to 59% of pediatricians never perform lung function tests.[29]

Normal values for spirometry are well established and are based on height, age, sex, and race/ethnicity of the healthy US population. Spirometric measures are highly reproducible within testing sessions in approximately 75% of children older than 5 to 6 years of age. Guidance on performing spirometry in an office setting and coding for asthma visits have been described.[30] The forced expiratory maneuver may be displayed as a flow-volume loop. Guidelines regarding interpretation of the primary measures (FEV_1, FVC, and the FEV_1/FVC ratio) are well outlined in the EPR3.[1,31] Of note, most automatic interpretations of the spirometry report fail to comment on the FEV_1/FVC ratio, an important parameter that, in children, is normally 85% predicted or greater.[1] Forced expiratory flow between 25% and 75% of vital capacity (FEF25–75) may reflect obstructive changes that occur in the small airways of children with asthma. However, FEF25–75 is considered to be of secondary importance because it is not specific and is highly variable (effort dependent).

Reduced spirometric measures are associated with symptom severity, reduced quality of life, and poor asthma outcomes.[24] However, individual patients, particularly children, may have misleadingly normal spirometry results, despite frequent or severe symptoms. An analysis of 2728 children between 4 and 18 years of age attending a tertiary care facility showed that the majority of asthmatic children had FEV_1 values within normal ranges.[32]

Spirometry, by itself, is not useful in establishing the diagnosis of asthma because airflow limitation may be mild or absent, particularly in children. In other words, if the spirometry result is normal, it does not rule out asthma. Variability of airflow obstruction over time and the response to treatment, when clinically relevant, can aid in the diagnosis and assessment of asthma control.

Although there are organizations that are attempting to integrate spirometry results into the electronic health record with varying degrees of success, the most commonly used approach at this time is to scan the printed spirometry result into the electronic health record.

Prebronchodilator and Postbronchodilator Spirometry (Bronchodilator Reversibility)

Bronchodilator reversibility testing helps determine the presence and magnitude of reversible airflow limitation.[24] Baseline spirometry is performed and repeated after administration of bronchodilator test agents (eg, 15 minutes after 4 inhalations of albuterol). Change in FEV_1 is the most common parameter followed because the value of reversibility in other measurements is less established (eg, FEV_1/FVC or FEF25–75).

The most widely used definition of "significant" bronchodilator response is that of the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines for interpretation of spirometry and consists of an improvement in FEV_1 greater than 12% and 200 mL.[33] Other parameters that have been used in children include a 9% to 10% increase in percent predicted FEV_1.[24]

Bronchodilator reversibility testing, although not specific, is useful for confirming the diagnosis of asthma. Increased bronchodilator reversibility correlates with increased asthma severity. Bronchodilator reversibility is diminished in patients with well-controlled asthma as well as those with narrowing or remodeling of the airways. Annual assessment of prebronchodilator and postbronchodilator FEV_1 might help identify children at risk for developing progressive decline in airflow.[34]

Recent Advances in Monitoring PEF and Spirometry

Advances in home-based airflow monitoring include the use of electronic, handheld devices with easily downloadable recordings of multiple PEF or FEV_1 point measures with software that facilitates easy use and interpretation.[35] The availability of these instruments for routine clinical use is limited at this time.

Impulse Oscillometry

Impulse oscillometry assesses airflow resistance and bronchodilator response in younger children. Measurement of airway resistance is a direct indicator of airway caliber with increased resistance indicating narrowing of airways. It is used largely as a research tool and is only available in a few centers.[24]

Airway Hyperresponsiveness

A major characteristic of asthma is the variability in bronchial tone in response to a variety of stimuli. Airway hyperresponsiveness (AHR) may be assessed by bronchial

provocation tests. Bronchial provocation tests may be performed with agents such as methacholine or stimuli such as physical exercise.[24,28,36] A positive test result for AHR is indicated by a 20% reduction in FEV_1 after inhalation of a methacholine dose of 8 mg/mL or less. A negative test suggests a diagnosis other than asthma. A reduction in FEV_1 of at least 10% during exercise testing is taken as a sign of exercise-induced bronchoconstriction. These tests take approximately 2 hours and require trained personnel to perform them. In general, evidence does not support the routine assessment of AHR in the clinical management of asthma control.[28]

Biomarkers

Apart from exhaled nitric oxide measurements, the role and usefulness of noninvasive biomarkers in routine clinical practice for monitoring inflammation in children with asthma is undefined. Sputum eosinophilia, exhaled breath condensates, and urinary leukotrienes are used as tools primarily in research studies.[28,37]

Exhaled Nitric Oxide

The fractional concentration of nitric oxide in exhaled air (FENO) is a quantitative measure of airway nitric oxide, an endogenously produced gaseous mediator that is an indirect marker of airway inflammation. The joint ATS/ERS guideline for the measurement of FENO is the current standard.[38,39] The testing is noninvasive, reproducible, easy to perform in patients (including children), feasible to measure in ambulatory clinical settings, and has no risk to patients.[40,41]

FENO is generally accepted as a marker of eosinophilic airway inflammation. Individuals with asthma have been reported to have elevated levels of FENO, but because FENO is also related to atopy, elevated levels may be seen in atopic individuals without asthma. Although FENO levels overlap among healthy, atopic, and asthmatic cohorts, in general, the upper value of normal is 25 ppb. It has been suggested that a clinically important decrease of FENO is a change of 20% for values greater than 50 ppb or a change of 10 ppb for values less than 50 ppb.[38] Studies in children suggest that FENO correlates with severity and with asthma control.[42] FENO reduces in a dose-dependent manner with corticosteroid treatment[43] and has been shown to increase with deterioration in asthma control.[44] The value of additional FENO monitoring in children whose asthma is appropriately managed using guideline-based strategies is unproven,[28,45–47] and insurance payment for this test varies by geographic location. Nevertheless, some asthma specialists have adopted the use of FENO as an adjunct ambulatory clinical tool for measuring airway inflammation and serial monitoring asthma control in individual patients with difficult-to-control asthma.

Assessing Asthma Control in Children Younger Than 5 Years

In children younger than 5 years, it is recommended that both symptom control and future risk be monitored.[2] The risk domain is assessed by historical review of exacerbations with need for oral steroid. Validated measures to assess asthma control in this age group include the TRACK (0–5 years) and the C-ACT in children (4–11 years) of age.

Children younger than 5 years are typically unable to perform spirometry; hence, confirmation of the diagnosis of asthma is challenging in this age group. Recurrent wheezing occurs in a large proportion of these children, typically with viral infections. A therapeutic trial of regular controller therapy (for 1–3 months) may often be necessary to evaluate response and maintenance of control.

Assessment of risk profiles using tools such as the asthma predictive index (API) may be helpful in predicting the likelihood of recurrent wheezing in school-age children. One study showed that children with a positive API had a fourfold to 10-fold greater chance of developing asthma at 6 through 13 years of age than those with a negative API, and 95% of children with a negative API remained free of asthma.[48] The modified API suggests that the diagnosis of asthma in young children with a history of more than 3 episodes of wheezing is more likely if they meet 1 major or 2 minor criteria.[49] Major criteria include a parent with asthma, physician diagnosis of atopic dermatitis, or sensitization to aeroallergens (positive skin or allergen-specific immunoglobulin E test results). Minor criteria include the presence of food allergies or sensitization to milk, egg, and peanut; blood eosinophil counts greater than 4%; or wheezing apart from colds.[49]

SUMMARY

Recent advances in measuring lung function, biomarker profiles, adherence, utilization and outcomes data, and development of validated questionnaires have made ongoing assessment and monitoring of asthma control a reality. Following is a schema of suggested measures that may be used in routine ambulatory monitoring of asthma control in clinical practice.

Initial Consultation

- The encounter between patient and health care provider may involve critical and empathetic listening to the patient and accurate elicitation of symptoms

as indicators for asthma control, aided by validated asthma control tools such as the C-ACT/ACT. A complete environmental and social history should be obtained to evaluate for triggers.[50]

- Airway obstruction and AHR can be assessed by measuring prebronchodilator and postbronchodilator FEV_1. Some specialists may consider evaluation of airway inflammation by using FENO to be useful.
- Education and training regarding asthma and its management can be provided, taking into consideration the patient's personal preference and goals while creating an individualized action plan.
- Action strategies can be based on either symptoms or objective criteria, such as by monthly monitoring of the age-specific, validated asthma control instrument, or in individualized circumstances, by daily electronic FEV_1 or conventional peak flow monitoring at home.

Subsequent Visits

- Symptom scores with validated control instruments and FEV_1 can be monitored at subsequent visits along with serial health care utilization data to tailor the medication dose to degree of asthma control. The risk domain is validated by a history of systemic steroid prescription, emergency department visits, or hospitalizations.
- In individuals whose FENO was elevated at the initial visit and shows variation in response to therapy, repeat FENO monitoring may be considered.
- Education regarding asthma triggers, review of inhaler techniques, assessment and reinforcement of adherence, treatment of comorbidities (eg, gastroesophageal reflux, sinusitis, obesity), and encouragement and fortification of the collaborative provider-patient relationship can be provided at each follow-up visit.
- The need for continued assessment or reassessment by a pediatric allergist or pulmonologist can be considered when faced with challenges in attaining optimal asthma control.
- Information on appropriate coding for the asthma management tools and services provided can be found in the Asthma Coding Fact Sheet at the following link: https://www.aap.org/asthmacodingfacts heets.

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ABBREVIATIONS

ACT: Asthma Control Test
ACQ: Asthma Control Questionnaire
AHR: airway hyperresponsiveness
ATAQ: Asthma Therapy Assessment Questionnaire
ATS/ERS: American Thoracic Society/European Respiratory Society
C-ACT: Childhood Asthma Control
EPR3: Expert Panel Report 3
FENO: fractional exhaled nitric oxide
FEV_1: forced expiratory volume in 1 second
FEF25–75: forced expiratory flow between 25% and 75% of vital capacity
FEV_1/FVC ratio: ratio of forced expiratory volume in 1 second to forced expiratory volume
FVC: forced expiratory volume
PEF: peak flow
TRACK: Test for Respiratory and Asthma Control in Kids

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