Objective: To determine whether lung function alters asthma severity based on symptom history in asthmatic adolescents.

Design: Data on asthma symptoms and lung function were collected from adolescents randomly selected from the general population.

Setting: Five schools from the central Wellington, New Zealand, area during 2003 to 2005.

Participants: Two hundred twenty-four secondary school students aged 13 to 17 years (asthmatic, 118; non-asthmatic, 106).

Main Exposures: Asthma questionnaire and lung function testing.

Main Outcome Measures: Distribution of asthmatic adolescents in each severity class based on symptoms, lung function, or a combination of both.

Results: Median values for all spirometric parameters for asthmatic adolescents, apart from forced expiratory volume in the first second of expiration (FEV₁)/forced vital capacity (FVC), were in the normal range. Distribution of severity (based on symptoms and β₂-agonist use with adjustment for regular inhaled corticosteroid use) was 48.3%, mild; 28.8%, moderate; and 22.9%, severe asthma. For severity based on percentages of predicted FEV₁ and predicted forced expiratory flow, midexpiratory phase (FEF₂₅₋₇₅%) and FEV₁/FVC, the percentages were 89.8%, 86.4%, and 63.5%, mild; 9.3%, 10.2%, and 18.6%, moderate; and 0.9%, 3.4%, and 17.8%, severe asthma, respectively. When percentages of predicted FEV₁ or predicted FEF₂₅₋₇₅% or FEV₁/FVC were added to symptom severity, 6.8%, 5.1%, and 16.9% of asthmatic adolescents were reclassified into another severity group, respectively.

Conclusions: The majority of asthmatic adolescents have normal lung function despite experiencing significant asthma symptoms. Adding FEV₁/FVC to symptom history changes the distribution of severity; however, both percentages of predicted FEV₁ and FEF₂₅₋₇₅% have little added effect in assessing asthma severity in adolescents.

Arch Pediatr Adolesc Med. 2008;162(12):1169-1174
FEV\textsubscript{1}/FVC has been included together with percentage of predicted FEV\textsubscript{1}. It remains unclear as to whether an assessment of lung function aids in determining asthma severity, particularly in the child and adolescent age groups. Including spirometry adds significant extra work for the already busy practitioner, and indeed, it has been shown that PEF is more commonly used by general practitioners rather than spirometry to assess asthma severity. We have conducted a study investigating asthma disease severity in a random general population sample of asthmatic adolescents to determine whether adding spirometric parameters (percentage of predicted FEV\textsubscript{1}, FEV\textsubscript{1}/FVC, and percentage of predicted FEF\textsubscript{25%-75%}) to a disease severity classification system based solely on symptom frequency and \(\beta_2\)-agonist use alters the assessment of disease severity sufficiently to justify its use.

### METHODS

#### SUBJECT RECRUITMENT

Subjects were recruited from 5 schools that had participated in the Wellington International Study of Asthma and Allergies in Childhood (ISAAC) Phase III survey of asthma symptom prevalence. These schools were chosen because of their proximity to the study center. Potential asthmatic adolescents (n=224) and nonasthmatic adolescents (n=595) were identified from the ISAAC Phase III study from their response to the question “Have you had wheezing or whistling in the chest in the past 12 months?” From this group, 136 asthmatic adolescents and 134 nonasthmatic adolescents consented to participate in a further study. At the study visit, a further questionnaire based on the ISAAC Phase III questionnaire and including additional questions on medication use for the 12-month and 2-week period prior to the clinic visit was completed. Final assignment to asthmatic or nonasthmatic status was determined from this questionnaire. Asthmatic adolescents had a history of wheezing or whistling in the chest in the last 12 months and/or any asthma medication use in the last 12 months. Nonasthmatic adolescents had no current wheeze, no history of asthma, no nocturnal cough in the last 12 months apart from that associated with a cold or chest infection, and no asthma medication use in the past 12 months. Sixteen subjects were excluded because they did not meet the definitions for asthma or nonasthma either because of a history of asthma but no current symptoms or an ambiguous response to the relevant questions. A further 8 subjects were excluded because they were unable to be contacted after indicating a willingness to participate in the study, 11 were unable to perform adequate spirometry, and 11 were excluded because of medication use, such as \(\beta_2\)-agonist, within 6 hours prior to spirometry.

The study visit was deferred if subjects had had an acute exacerbation of asthma or respiratory tract infection in the previous 4 weeks. Subjects with chronic illnesses other than asthma were ineligible. School decile rating was used as a proxy for socioeconomic status, ranging from 1-10, with a rating of 10 equating to the highest socioeconomic group.

Ethical approval for the study was obtained from the Wellington Ethics Committee (00/03/010). Written consent was obtained from school principals and from each child in the study and their parents.

#### SPIROMETRY

Lung function was measured as the best of 3 reproducible forced expiratory maneuvers (EasyOne Spirometer; ndd Medizintechnik AG, Zurich, Switzerland). The spirometer was calibrated daily with a 3-L calibration syringe (Hans Rudolph, Inc, Kansas City, Missouri). Predicted values for lung function parameters were determined using the National Health and Nutrition Examination Survey III prediction equations.

### SYMPTOM AND LUNG FUNCTION CLASSIFICATION OF SEVERITY

Asthma symptoms were classified as mild, moderate, or severe based on the NAEPP EPR-3 guidelines. This included frequency of wheezing attacks, nocturnal symptoms, and frequency of \(\beta_2\)-agonist use in the last 2 weeks preceding the study visit (unadjusted symptom severity) (Table 1). Adjustment was made for regular inhaled corticosteroid (ICS) use by moving the severity level up one step (ie, mild to moderate and moderate to severe [ICS-adjusted symptom severity]). For asthma severity using percentage of predicted FEV\textsubscript{1}, FVC, and PEF, mild asthma was defined as 80% or more; moderate asthma, as 60% or more and less than 80%; severe asthma, less than 60%; for percentage of predicted FEF\textsubscript{25%-75%}, mild, moderate, or severe asthma was defined as 65% or more, 50% or more and less than 65%, and less than 50%, respectively; and for FEV\textsubscript{1}/FVC, mild, moderate, or severe asthma was defined as 80% or more, 75% or more and less than 80%, and less than 75%, respectively, using the NAEPP ERP-3 guidelines cutoff points.

#### DATA ANALYSIS

All analyses were carried out using SAS (SAS Institute Inc, Cary, North Carolina). Lung function was expressed as median values and interquartile range. Comparisons between groups were made using the \(\chi^2\) test and Fisher exact test. The Wilcoxon rank sum test was used to determine significant differences between nonparametric data. A \(\kappa\) value was calculated to assess the agreement between tests. A \(P\) value of <.05 was considered significant.

### RESULTS

#### SUBJECT DEMOGRAPHICS

There was no significant difference in the distributions of the asthmatic adolescents and nonasthmatic adolescents by age (mean, 14.9 and 15.1 years, respectively), sex (26% and 32%, female, respectively), or ethnicity (81% and 83%, European, respectively). This study included...
subjects attending schools with decile ratings ranging from 5 to 10 (ie, lower socioeconomic groups [school decile 1-4] were not included). There was no difference in the distribution of asthmatic adolescents and nonasthmatic adolescents in school decile rating. Five percent of asthmatic adolescents were smokers compared with 1% of nonasthmatic adolescents. Just more than half (52.5%) of asthmatic adolescents reported ICS use at some time; however, only 24% reported regular ICS use. Of the 118 asthmatic adolescents included in the study, 89% responded positively to the question “Have you ever had asthma?”

BASELINE SPIROMETRY

For the nonasthmatic adolescents, the percentages of predicted FEV1 and FVC values were all very close to 100% (Table 2), suggesting that the reference values from the National Health and Nutrition Examination Survey were appropriate for use in New Zealand adolescents.10 Asthmatic adolescents had significantly lower percentages of predicted values for FEV1 and FEF25%-75%, and lower values for FEV1/FVC than nonasthmatic adolescents but not for percentages of predicted FVC and PEF (Table 2). The median values for asthmatic adolescents for all spirometric parameters, apart from FEV1/FVC, were in the normal range (ie, for percentages of predicted FEV1, FVC, and PEF, ≥80%; for percentage of predicted FEF25%-75%, ≥65%) (Table 2). For the complete asthmatic group and all levels of asthma severity, FEV1/FVC was less than 85%, the value given as normal for FEV1/FVC in the NAEPP EPR-3 guidelines for this age group.

SEVERITY AND LUNG FUNCTION

The median values for FEV1/FVC and for percentage of predicted FEF25%-75% were significantly lower in the severe asthmatic adolescents compared with the mild asthmatic adolescents (Table 2). There were no significant differences among the 3 symptom severity groups for percentage of predicted FEV1, percentage of predicted FVC, and percentage of predicted PEF and no significant differences between moderate and severe asthmatic adolescents for all spirometric parameters.

Table 2. Spirometry Results for Asthma Symptom Severity Groups, Asthmatic and Nonasthmatic

<table>
<thead>
<tr>
<th></th>
<th>Mild (n = 57)</th>
<th>Moderate (n = 34)</th>
<th>Severe (n = 27)</th>
<th>Asthma (n = 118)</th>
<th>Nonasthma (n = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, % predicted</td>
<td>96.9 (18.5)</td>
<td>97.8 (14.5)</td>
<td>95.8 (18.3)</td>
<td>96.9 (17.1)</td>
<td>101.2 (15.1)</td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>98.7 (18.8)</td>
<td>100.2 (18.7)</td>
<td>101.6 (13.0)</td>
<td>99.3 (16.5)</td>
<td>100.4 (17.9)</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>84.3 b (9.3)</td>
<td>83.1 (8.7)</td>
<td>78.5 (10.5)</td>
<td>83.2 c (10.5)</td>
<td>86.0 (9.1)</td>
</tr>
<tr>
<td>FEF25%-75%, % predicted</td>
<td>90.4 b (26.8)</td>
<td>87.5 (32.2)</td>
<td>75.8 (41.3)</td>
<td>86.5 c (32.0)</td>
<td>100.9 (26.8)</td>
</tr>
<tr>
<td>PEF, % predicted</td>
<td>100.6 (19.1)</td>
<td>106.1 (23.3)</td>
<td>96.0 (19.9)</td>
<td>100.6 (22.4)</td>
<td>101.1 (20.0)</td>
</tr>
</tbody>
</table>

Abbreviations: FEF25%-75%, forced expiratory flow, midexpiratory phase; FEV1, forced expiratory volume in the first second of expiration; FVC, forced vital capacity; PEF, peak expiratory flow rate.

a P < .01 asthma vs nonasthma.
b P < .05 mild asthma vs severe asthma.
c P < .001 asthma vs nonasthma.

ASTHMA SEVERITY DISTRIBUTION

Using the adjusted symptom severity definition, 48.3% of asthmatic adolescents had mild, 28.8% had moderate, and 22.9% had severe symptoms (Table 3). Without adjustment for regular ICS use, the distribution was 54.2%, mild, 36.4%, moderate, and 9.3%, severe. The distribution of severity based on percentage of predicted FEV1 alone was mild, 89.8%; moderate, 9.3%; and severe, 0.9%; on FEV1/FVC was mild, 63.3%; moderate, 18.6%; and severe, 17.8%; and on percentage of predicted FEF25%-75% was mild, 86.4%; moderate, 10.2%; and severe, 3.4% (Table 3). When lung function was added to the adjusted symptom severity distribution, percentage of predicted FEV1 or FEF25%-75% caused little change in distribution, with only 6.8% and 5.1% of asthmatic adolescents changing severity, respectively. Adding percentage of predicted FEV1 or FEF25%-75% to the unadjusted symptom severity caused a change in severity for 7.6% and 4.1% of asthmatic adolescents, respectively. The change in distribution was much greater for FEV1/FVC, with 16.9% of subjects changing severity for the adjusted symptom severity and 22.9%, for the unadjusted symptom severity. Combining both percentage of predicted FEV1 and FEV1/FVC caused a change in severity for 20.3% of asthmatic adolescents for the adjusted symptom severity and 26.3% for the unadjusted severity. κ Values were calculated to assess the agreement between the severity classifications. There was no agreement with symptom severity and percentage based on predicted FEV1 (κ = -0.04 for adjusted ICS severity and -0.08 for unadjusted severity) or on percentage of predicted FEF25%-75% (κ = 0.02 for adjusted ICS severity and 0.09 for unadjusted severity) and minimal agreement with FEV1/FVC (κ = 0.18 for adjusted ICS severity and 0.14 for unadjusted severity).

The disparities between the classification of asthma severity based on symptoms and that based on percentage of predicted FEV1 and percentage of predicted FEF25%-75% lie mainly in subjects with moderate and severe symptom classification having an FEV1 of 80% or more predicted or FEF25%-75% of 65% or more predicted. Specifically, 91.2% (31 of 34) of subjects with moderate symptom severity (adjusted for ICS use) had mild asthma ac-
In this study, we found that in the large majority of asthmatic adolescents in this group recruited from the general population lung function was within the normal range, apart from FEV1/FVC, where median values for all levels of asthma severity were less than 85%. In determining disease severity, a single assessment of percentage of predicted FEV1 or percentage of predicted FEF25%-75% added little further information to the severity classification obtained using symptom questionnaire responses. In contrast, adding FEV1/FVC to asthma symptoms altered the distribution of severity for 17% of subjects. For severity distribution based on all these 3 lung function parameters, there was minimal agreement with that based on asthma symptoms and β2-agonist use with and without adjustment for ICS use.

This study recruited a random sample of asthmatic adolescents and nonasthmatic adolescents from the general population rather than from subspecialty clinics. The findings of this study are therefore directly relevant to the general population and in particular to the use of spirometry in assessment and management of asthma in adolescents in general practice. The findings may not be applicable to a population of asthmatic adolescents attending specialty clinics, where asthma symptoms and lung function are likely to be more severe than in this population. However, lung function has also been found to be normal in the majority of students recruited from tertiary care asthma clinics, suggesting that lung function is normal in the young asthmatic population throughout all levels of asthma severity. Similarly, a mismatch between asthma symptoms and lung function in adolescents with more severe asthma has been found, suggesting this finding is also true in general for young people with asthma.

In a cross-sectional population where a proportion of subjects are using medication to control their symptoms, classification of asthma severity should also include intensity of treatment, particularly ICS use. Regular ICS use is likely to reduce asthma symptom frequency and categorize an individual with milder asthma than is actually the case. However, we also conducted our analyses without making an adjustment for regular ICS use (ie, using symptom frequency and β2-agonist use only in the definition of asthma symp-
tom severity). Naturally, fewer subjects were classified as having severe asthma with this classification (mild, 54%; moderate, 36%; and severe, 9%). The effect of adding the lung function parameters to symptom severity was greater for FEV1/FVC, with 22.9% of asthmatic adolescents reclassified as having more severe asthma, minimal change for percentage of predicted FEV1, and less for percentage of predicted FEF25%-75%. Combining percentage of predicted FEV1 with FEV1/FVC resulted in a 26.3% change in severity as compared with a 20.3% change using the symptom severity adjusted for regular ICS use. The overall conclusion, therefore, that adding either percentage of predicted FEV1 or percentage of predicted FEF25%-75% to symptom severity causes minimal change in severity classification, is not altered by adjusting for regular ICS use in this study.

It may be argued that some of our subjects did not have asthma because we did not use a physician diagnosis of asthma to determine asthmatic status. Rather, we defined subjects as having current asthma based on a self-report of wheeze in the preceding 12 months. Using only a physician diagnosis of asthma excludes a significant proportion of the population with wheezing symptoms. This was shown in a large study of children aged 12 to 14 years, where 17% of children with current asthma-like symptoms did not have a diagnosis of asthma.1 The ISAAC questionnaire, on which the questionnaire used in this study was based, has been shown to have both a high sensitivity and specificity for physician-diagnosed asthma. Another study of asthma diagnosis in New Zealand has shown a similarly high sensitivity and specificity for wheezing in the last 12 months for a diagnosis of asthma.13 Although it is possible that we have included some subjects without asthma as asthmatic adolescents, the survey instrument we used to identify those with asthma has been shown to have sufficiently high sensitivity and specificity to be used with confidence for this purpose.

It is possible that asthma severity has been misclassified because of inaccurate recall of symptoms by our subjects. We based our severity classification on both short-term recall (symptoms and B2-agonist use in the preceding 2 weeks), as is recommended in the NAEPP EPR-3 guidelines, and long-term recall (symptoms in the preceding 12 months). Long-term recall is likely to be inaccurate, particularly for recall of symptom frequency. However, using only 2 weeks’ recall would not take into account the inherent variability of asthma symptoms that results in individuals with asthma having changes in severity over time. In an analysis of five 12-week asthma trials in pediatric subjects, it was found that subjects frequently moved between severity groups. We therefore elected to combine both short- and long-term recall of symptoms to determine symptom severity.

In a large study of 2 cohorts of children aged between 8 and 11 years, Stout et al14 found that approximately one-third of children were reclassified with higher asthma severity when FEV1 was added to symptom frequency to assess asthma severity. This contrasts with our finding that using percentage of predicted FEV1 does little to change severity classification as determined by symptoms. In the Stout et al study, asthma was defined as a physician diagnosis of asthma and either a history of asthma symptoms or at least 1 hospitalization or at least 2 urgent care visits in the previous 6 months. We used a definition of asthma based on a self-reported history of current wheeze, and although the majority of subjects in our study appeared to have a previous asthma diagnosis, it is likely that our subjects had milder asthma than those in the Stout et al study. However, the unadjusted symptom severity distribution in our study was similar to that in the more severe cohort in the Stout et al study, where 57.4% of subjects had mild intermittent or persistent asthma and 42.6% of subjects had moderate or severe asthma. There was a difference between the 2 studies in the numbers of subjects demonstrating abnormal lung function (ie, a predicted FEV1 < 80%), with 10.2% of subjects in our study and 16.7% and 28.2% in cohort 1 and cohort 2 of the Stout et al study, respectively. This suggests that overall lung function was better in our subjects and this likely accounts for the different effect of adding percentage of predicted FEV1 to symptom severity in both studies.

Of the lung function parameters, only FEV1/FVC and percentage of predicted FEF25%-75% showed any significant difference in asthma groups based on symptom severity (Table 2). Similar results have been found in other studies of lung function in children. The authors of one of these studies have suggested that these parameters have greater sensitivity in measuring airflow obstruction and should be assessed when spirometry is performed. FEF25%-75% measures the average flow rate over the middle 50% of the FVC and is said to be more sensitive than FEV1 in detecting small-airway obstruction. However, we found that adding percentage of predicted FEF25%-75% to asthma symptoms resulted in little change in severity classification and that there was also no agreement between asthma symptom severity and percentage of predicted FEF25%-75%. In addition to this, percentage of predicted FEF25%-75% demonstrates high variability, making its use for monitoring asthma progression difficult. These results suggest that percentage of predicted FEF25%-75% is not a useful tool for assessing asthma severity in this age group.

The median value for FEV1/FVC was less than 85%, the value defined as the cutoff for normality in the NAEPP EPR-3 guidelines for this age group, for the asthmatic population, and also for each symptom severity group. For the nonasthmatic group, the median value was 86%. These results suggest that a level of 85% for FEV1/FVC may be overestimating the number of young people with asthma with airflow obstruction. The value of 85% is taken from the National Health and Nutrition Examination Survey control data for this age group. Because the percentage of predicted FEV1 and FVC values for nonasthmatic adolescents in this study were all very close to 100%, suggesting that the reference values from the National Health and Nutrition Examination Survey were appropriate for use in New Zealand adolescents, it also suggests that a ratio of 85% for FEV1/FVC is appropriate for use in this study. In the large National Jewish Medical and Research Center study of lung function in children, the average value for the FEV1/FVC ratio was approximately 77% for males and 83% for females. This group of children was recruited from a tertiary specialist cen-

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ter and therefore is likely to have had more severe asthma than the group in our study. The American Thoracic Society/European Respiratory Society task force has recommended using the fifth percentile of predicted values rather than set cutoff values for the FEV1/FVC ratio to define obstructive lung disease. It is particularly important for younger and older adults, because the set cutoff ratio of 70% has been found to misclassify a significant number of subjects in these age groups. It may also be appropriate to apply this criterion to defining airway obstruction in adolescents rather than using the set cutoff ratio of 85%.

In conclusion, in the vast majority of asthmatic adolescents, a single measure of percentage of predicted FEV1 or percentage of predicted FEV1/FVC adds little extra information to that obtained from a symptom history in assessing asthma severity. FEV1/FVC, however, does appear to add value to this assessment, suggesting that this parameter should be used in determining asthma severity in adolescents.

Accepted for Publication: May 6, 2008.

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Author Contributions: Dr van Dalen had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: van Dalen, Pearce, and Douwes. Acquisition of data: van Dalen, Harding, Parkin, Cheng, and Douwes. Analysis and interpretation of data: van Dalen, Cheng, Pearce, and Douwes. Drafting of the manuscript: van Dalen, Pearce, and Douwes. Critical revision of the manuscript for important intellectual content: van Dalen, Harding, Parkin, Cheng, Pearce, and Douwes. Statistical analysis: van Dalen, Cheng, Pearce, and Douwes. Obtained funding: Pearce and Douwes. Administrative, technical, and material support: Harding and Parkin. Study supervision: van Dalen, Pearce, and Douwes. Financial Disclosure: None reported.

Funding/Support: This project was supported by project grants from the Health Research Council of New Zealand and Lotteries Health Research. Dr van Dalen is supported by a postdoctoral fellowship from Massey University. Dr Douwes is supported by a Sir Charles Hercus Fellowship from the Health Research Council of New Zealand.

Additional Contributions: We wish to thank Ian St George, MD, FRACP, FRNZCGP, and Wallace Farquhar, MBCChB, for their facilitation and support of this project. We are particularly grateful to all the students who participated so willingly in this study and to their parents who encouraged their participation.

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