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Reference values for peak flow and FEV_1 variation in healthy schoolchildren, using home spirometry.

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Abstract

Rationale: Current reference values for diurnal peak flow variation in healthy children (median 8.2%; 95th centile 31%) are so high that considerable overlap exists with asthmatic children. These values have been obtained with written peak flow diaries, which are unreliable.

Objective: To obtain reliable reference values of peak flow variation and forced expiratory volume in the 1st second (FEV_1) variation in healthy schoolchildren using home spirometry with electronic data storage.

Methods: Two-hundred-and-four healthy schoolchildren (100 boys), 6-16 years of age, measured peak flow and FEV_1 twice daily for two weeks using an electronic home spirometer. Variation of peak flow and FEV_1 were calculated as diurnal amplitude as a percentage of the day's mean.

Main results: Mean peak flow variation was 6.2% (95%CI 5.8 to 6.7%; 95th centile 12.3%) and mean FEV_1 variation was 5.7% (95%CI 5.4 to 6.1%; 95th centile 11.8%).

Conclusions: Using home spirometry with electronic data storage, healthy schoolchildren show considerably less peak flow and FEV_1 variation than previously reported with written peak flow diaries. Being the 95th centiles of the distributions in healthy children, we suggest using 12.3% for peak flow variation and 11.8% for FEV_1 variation as cut-off values for disease when using home spirometry.

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Introduction

Home monitoring of peak expiratory flow (PEF) is advocated in international guidelines for the management of asthma in children and adults.[1] Because PEF values are highly variable between patients, the patient's personal best value and diurnal variation of PEF are used in asthma guidelines, rather than age and sex dependent reference values for PEF levels.[2-5]

Studies have shown a strong correlation between airway hyperresponsiveness and diurnal PEF variation in children with asthma.[6;7] Therefore, variation of PEF is considered to be a measure of asthma severity,[1;2] and a diurnal variation of PEF above 15 to 20% is considered 'increased'. There is, however, only limited evidence to support this cut-off point.[1;2;8;9] The only reference values for PEF variation published have been obtained using mechanical PEF-meters with written diaries and showed high levels of PEF variation in healthy children, with a median of 8.2% and a 95th centile as high as 31%.[9] As a result, PEF variation is regarded to be of limited use to diagnose asthma in children.[1]

More recently, it was shown that PEF registrations using written PEF diaries yield unreliable data and electronic registrations were advocated.[10-12] Because the previously published reference values of PEF variation were obtained using written PEF diaries,[9] it is likely that these are unreliable. Children show high adherence to electronic home spirometry and perform these measurements in a technically correct manner.[13-15] We hypothesized that diurnal variation of lung function in healthy schoolchildren obtained by electronic home spirometry would be lower than values recorded by unreliable written diaries of measurements from mechanical devices. Therefore, we designed this study to obtain new reference values for PEF variation

and of FEV_1 variation in healthy schoolchildren, using such a home spirometer with electronic data storage under field conditions.

Methods

We recruited healthy peers, 6-16 years of age, of children with asthma visiting our outpatient clinic. Children were excluded if they had 1) a recent or chronic disease of the respiratory tract, or a history of chronic respiratory disease; 2) a history of severe respiratory disease e.g. congenital lung disease, hospitalization for pneumonia or surgery of the thorax; 3) systemic disease with direct or indirect influence on the respiratory tract e.g. neuro-muscular disorders; 4) other chronic or acute disease with influence on the respiratory tract; 5) use of inhaled corticosteroids, bronchodilators or other medicines influencing the respiratory tract or 6) household exposure to tobacco smoke.[16]

In order to obtain PEF and FEV_1 variation data from different age groups and sexes, we intended to include four groups of at least 50 children each: boys aged 6 to 11 years, boys aged 12 to 16 years, girls aged 6 to 11 years and girls aged 12 to 16 years. The total number of 200 participants was preset empirically, based on previously published normative data studies concerning respiratory disease in childhood.[17-20] The age groups were formed to represent elementary school versus secondary school children.

At the start of the study, children performed flow-volume curves at our pulmonary function laboratory on a Jaeger Masterlab pneumotachograph (Erich Jaeger, Würzburg, Germany) following ATS/ERS guidelines for measuring lung function.[5] Children were excluded if FEV_1 was below 80% of the predicted value or the flow-volume curve had an abnormal shape.[5;21]

After inclusion, patients were instructed how to use the electronic home spirometer (Koko Peak Pro, Ferraris, Louisville, Colorado, USA).[1;5] This portable home spirometer has been designed to measure PEF and FEV_1 under field conditions without the need for repeated calibrations. It has been validated using a precision waveform generator demonstrating its agreement with performance standards as recommended by international guidelines,[5;22] as well as in children with asthma in the same age group.[23] Patients were instructed to perform three forced expiratory flow maneuvers twice daily at home between 6AM and 10AM and between 6PM and 10PM throughout a 2-week study period. All instructions were given by the same experienced technician, encouraging the children to obtain optimal lung function values and at least one parent attended the instruction session. Patients were instructed to achieve PEF as rapidly as possible and to continue the maneuver for at least 2 seconds. An integrated quality check warned the user when a cough was detected, the blow was not long enough, or there was a slow start. The device then showed an exclamation mark and children were asked to repeat their measurements. During analyses, measurements were only accepted if forced vital capacity exceeded FEV_1. The device automatically stored the highest of the three correctly performed PEFs on a microchip, along with the accompanying FEV_1, labelled with the time and date of the measurement.

After the 2-week study period, the device was returned and all registrations were downloaded on a PC. Adherence to home spirometry measurements was expressed as the %days with two usable recordings (one recording in the morning and one in the evening).[24] Diurnal variation of PEF (L/min) and of FEV_1 (L) was expressed as the absolute amplitude (maximum-minimum) as a percentage of the day's absolute mean (ampl%mean) and day-to-day variation of PEF and FEV_1 was

expressed as the absolute amplitude (maximum-minimum) of the morning measurements as a percentage of their absolute mean (ampl%mean).[25] All data were analyzed using PRISM™ (GraphPad Software, San Diego, California, USA) for Windows™ version 3.00 applying standard parametric and non-parametric tests as appropriate.[26] This study was approved by the hospital ethics review board and study subjects and parents gave written informed consent. The reference values for PEF and FEV_1 variation obtained in this population of healthy schoolchildren were compared to values of PEF and FEV_1 variation over a 2-wk period obtained in a sample of asthmatic schoolchildren published previously.[14] The home spirometer used, the instructions and procedures of recording PEF and FEV_1 at home, and the analysis of data were identical between that study and the present one.

Results

Two-hundred-and-five healthy children, aged 6 to 16 years, were included in this study. After inclusion, one child was excluded because of an abnormal lung function and flow-volume curve (FEV_1 < 80%predicted and curve concavity) at the start of the study, despite absence of respiratory symptoms. Each predefined group consisted of at least 50 children, with a minimum number of 13 children per age (yrs). Characteristics of these groups are shown in table 1.

	♀ 6-11 yrs	♂ 6-11 yrs	♀ 12-16 yrs	♂ 12-16 yrs
Number of participants (n)	51	50	53	50
Age (years)	8.4 ± 1.7	8.8 ± 1.6	13.8 ± 1.4	13.7 ± 1.1
FEV_1 pneumotachograph (% pred)	105.0 ± 11.9	103.9 ± 12.2	106.1 ± 10.9	98.5 ± 11.1
FVC pneumotachograph (% pred)	98.2 ± 11.1	98.9 ± 11.1	98.3 ± 11.4	92.8 ± 10.2
MEF_{50} pneumotachograph (% pred)	90.7 ± 20.3	88.7 ± 18.5	99.7 ± 19.2	93.7 ± 20.7

Table 1. Characteristics of the four age/sex groups (see text for details; mean±SD). FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; MEF_{50}: mean expiratory flow at 50% of the maneuver.

The median adherence to home spirometry was 86%, with no significant difference between the groups and a small, but statistically significant difference between the first and the last week for the total study group (87 vs 82%; $p<0.0001$). The mean PEF variation (and 95th centile) and the mean FEV_1 variation (and 95th centile) for the four groups are shown in tables 2 and 3, for diurnal and day-to-day variation respectively.

	vPEF (ampl%mean)			$vFEV_1$ (ampl%mean)		
Age/sex groups	mean	95%CI	95^{th} centile	mean	95%CI	95^{th} centile
♀ 6-11 yrs (n=51)	7.3	6.4-8.2	12.3	6.1	5.4-6.8	11.8
♂ 6-11 yrs (n=50)	6.9	6.1-7.7	10.4	6.6	5.8-7.4	9.8
♀ 12-16 yrs (n=53)	5.8	5.0-6.7	12.2	5.2	4.5-5.9	8.5
♂ 12-16 yrs (n=50)	4.9	4.3-5.6	8.0	5.1	4.3-6.0	10.1
All children (n=204)	6.2	5.8-6.7	12.3	5.7	5.4-6.1	11.8

Table 2. Reference values for diurnal variation of PEF (vPEF) and FEV_1 ($vFEV_1$) using home spirometry with electronic data storage.

	day-to-day PEF variability (ampl%mean)			day-to-day FEV_1 variability (ampl%mean)		
Age/sex groups	mean	95%CI	95^{th} centile	mean	95%CI	95^{th} centile
♀ 6-11 yrs (n=51)	7.3	6.1-8.4	12.2	7.1	5.7-8.7	13.2
♂ 6-11 yrs (n=50)	6.8	6.1-7.6	11.3	7.0	6.0-7.9	11.3
♀ 12-16 yrs (n=53)	5.8	5.1-6.5	8.7	5.3	4.7-6.0	8.6
♂ 12-16 yrs (n=50)	5.2	4.4-5.9	9.5	4.8	3.9-5.7	8.7
All children (n=204)	6.3	5.8-6.7	12.2	6.1	5.5-6.5	11.3

Table 3. Reference values for day-to-day variability of morning PEF and FEV_1 using home spirometry with electronic data storage.

Children 6-11 years of age had statistically significantly higher variations of PEF (95%CI for difference 0.9 to 2.5%; $p<0.0001$) and FEV_1 (95%CI for difference 0.5 to 2.0%; $p=0.002$) than children 12-16 years of age. There were no statistically significant differences in variation of PEF or FEV_1 between boys and girls, nor

between the first and the last week of measurements. Figures 1a and 1b show the diurnal variation of PEF and FEV_1 per year of age and illustrate the slightly decreasing variation of PEF with increasing age. Both PEF and FEV_1 variation were independent of height and weight. Self-reported atopy was only present in 6 children. Exclusion of these 6 children did not change the outcome. None of the children had a variation of PEF or FEV_1 above 20%. The overall mean diurnal PEF variation for healthy children aged 6-16 years was 6.2% (95%CI 5.8 to 6.7%; 95^{th} centile 12.3%), and the overall mean diurnal FEV_1 variation was 5.7% (95%CI 5.4 to 6.1%; 95^{th} centile 11.8%). The mean absolute difference between the morning and evening PEF was 18.9 L/min (95%CI 17.7 to 20.2; SD 9.0 L/min), and the mean absolute difference between the morning and evening FEV_1 0.13 L (95%CI 0.12 to 0.14; SD 0.07). The diurnal differences per age group are presented in table 4.

	Difference in PEF (L/min)			Difference in FEV_1 (L)		
Age/sex groups	mean	95%CI	SD	mean	95%CI	SD
♀ 6-11 yrs (n=51)	16.4	14.8-18.0	5.6	0.10	0.09-0.11	0.04
♂ 6-11 yrs (n=50)	17.5	15.4-19.7	7.7	0.12	0.11-0.14	0.06
♀ 12-16 yrs (n=53)	23.5	19.9-27.1	13.0	0.16	0.13-0.18	0.08
♂ 12-16 yrs (n=50)	18.2	16.5-19.8	5.8	0.14	0.12-0.17	0.09

Table 4. Mean differences between the morning and evening PEF (PEF) and FEV_1 (FEV_1) using home spirometry with electronic data storage. SD (standard deviation).

Seventy-six percent of all healthy children had morning PEFs lower than evening PEF, suggesting a similar circadian rhythm as is seen in asthmatic children.[27]

However, only 48% of the healthy children had lower morning than eveningFEV1 values.

The previously published asthmatic group consisted of 36 well-controlled asthmatic children (25 boys) with a mean age of 10.4 years. [14] In all children, the diagnosis was confirmed by a pediatric pulmonologist, and all were using maintenance treatment with inhaled corticosteroids. Their lung function characteristics are shown in table 5.

Table 5. Characteristics of 36 asthmatic children

logPD_{20}-methacholine (µg)	1.98 (1.28-2.91)
FEV_1 (% pred)	99.1 ± 12.6
FVC (% pred)	98.0 ±8.6
MEF_{50} (% pred)	79.7 ± 21.7

Tabel 5. Values are presented as mean ± SD, or as median and inter-quartile range for PD_{20}. FEV_1: forced expiratory volume in one second; PD_{20}-methacholine: provocative dose of methacholine causing a 20% fall in FEV_1; FVC: forced vital capacity; MEF_{50}: mean expiratory flow at 50% of the maneuver.

Figure 2 shows the differences in PEF and FEV_1 variation between the well-controlled asthmatic children of the previously conducted study and the present data of the healthy children. The differences were statistically significant for both diurnal PEF variation ($p=0.001$) and diurnal FEV_1 variation ($p<0.0001$), with mean differences of 1.4% (95%CI 0.3 to 2.5%) and 2.7% (95%CI 1.6 to 3.8), respectively. There was considerable overlap between the healthy children and the well-controlled

asthmatics for both variables (figure 2). The range of mean diurnal PEF variation and diurnal FEV_1 variation in the asthmatic group was 3.5-24.3 (ampl%mean) and 2.8-26.4 (ampl%mean) for PEF and FEV_1, respectively, in the first two weeks of the study. Twenty-four asthmatic children (62%) showed a diurnal PEF variation above 12.3% or diurnal FEV_1 variation above 11.8%; the overall 95^{th} centile of the healthy group of schoolchildren, in any given week of the total study period of 3-months.

Discussion

This study shows that, using home spirometry, healthy children have substantially lower variation of lung function than previously described with mechanical PEF meters.[9] Because the previously described reference values were obtained using unreliable written PEF diaries,[10;11] the present study used validated home spirometers with electronic data storage, generating more reliable reference values of variation of PEF and FEV_1.[12] There were no differences between boys and girls. Although younger children had significantly higher levels of variation of PEF and FEV_1 than older children (table 2; figures 1), we considered this difference too small and too varying to be clinically relevant. Because PEF and FEV_1 variation were not dependent on height or weight, and the influence of age was negligible, we pooled all data from the participating children into a single reference value of variation of lung function for all ages and sexes. Only two subjects (<1%) showed registrations of PEF or FEV_1 variation above 15%, and none above 20%. The day-to-day variability data showed similar results, also lower than those previously published,[9] showing the stability of lung function measurements throughout the study. We propose to use the 95^{th} centiles from our present study as new reference values for diurnal variation of

lung function in schoolchildren when using home spirometry under field conditions: 12.3% for PEF variation and 11.8% for FEV_1 variation.

The reference values of PEF and FEV_1 variation in healthy schoolchildren were significantly lower than the values for PEF and FEV_1 variation recorded in a group of asthmatic schoolchildren with chronic persistent, but clinically stable, asthma (figure 2). This suggests that home spirometry might be a useful diagnostic tool to differentiate asthmatics from non-asthmatic children. However, it should be emphasized that these results were obtained in selected groups of clearly healthy children on the one hand and children with a firm diagnosis of chronic persistent asthma who were diagnosed and followed up in a specialized clinic on the other. Whether home spirometry will be a useful tool to rule out or diagnose asthma in children with non-specific chronic respiratory symptoms remains to be evaluated in a separate study.

Some limitations of our study need to be discussed. Firstly, our study population was not a random population sample. For practical reasons, we recruited healthy school children by asking asthmatic children to approach healthy peers to participate. By applying strict exclusion criteria, which have proven to be useful in selecting healthy subjects to obtain reference values of lung function,[16] our selection of healthy children should be representative of healthy non-asthmatic children. The application of these strict exclusion criteria precludes examining the influence of passive smoke exposure on our reference values. In studies using mechanical PEF meters and written diaries, diurnal PEF variation was up to 10% higher in children exposed to tobacco smoke.[28] Although this suggests that variation of PEF and FEV_1 recorded by home spirometry may be higher in healthy

children of smoking parents than the values we report, this should be substantiated by further studies. Due to the low prevalence of atopy in our study cohort we were unable to examine its influence on PEF and FEV_1 variation in a meaningful way.

Secondly, the reference values are obtained using only one type of portable home spirometer. It is possible that the use of a different device may have rendered different results. It is unlikely, however, that this is clinically relevant. All home spirometers are designed for the same purpose, namely measuring lung function under field conditions, without the need for repeated calibrations. All comply with ATS/ERS guidelines and have to be validated using computer-generated waveforms.[5] Although small differences between measurements obtained with home spirometers and hospital pneumotachographs have been found,[23;29-31] maneuver reproducibility in home spirometry has been shown to be acceptable for a reliable calculation of variation in lung function.[13;23] In addition, though there is increasing evidence that younger children are able to exhale their complete VC in less than a second,[32] the younger children in our study showed that they could perform reliable FEV_1 measurements during the instruction sessions and only a maximum of 2 measurements per child were excluded from analyses for this reason (data not shown). Furthermore, the children were warned by the device during the measurements when a blow was to short and then repeated the measurement correctly. Therefore, it is likely that our reference values for PEF and FEV_1 variation are also applicable with other home spirometers.

Finally, the technical quality of the forced expiratory maneuver was only checked during the instruction session at the start of the study and was not assessed at home. However, as mentioned above, a quality check is integrated into the home

spirometer, warning the user, with an exclamation mark on the screen, if a maneuver is incorrectly performed. More importantly, other studies have shown that children generate high quality lung function values with home spirometry under field conditions after careful instructions.[13;15] This was also the case in the present study. They recorded two usable recordings on more than 85% of days and showed no deterioration of PEF and FEV_1 variation over time. Furthermore, these reference values will be used under similar circumstances in clinical practice. Therefore, we are confident that the reference values obtained for PEF and FEV_1 variation are of high quality and can be used in clinical practice and research.

To our knowledge, ours are the first reference values published for variation of both PEF and FEV_1 using home spirometry with electronic data storage. Because FEV_1 is considered to reflect the patency of intrathoracic airways more reliably than PEF and is less effort dependent,[2;5] FEV_1 may well be a more useful measure of lung function monitoring in children than PEF. Although monitoring lung function at home is advocated in guidelines on the long-term management of asthma, studies have consistently shown that such home monitoring of lung function and modifying long-term treatment accordingly does not improve asthma control or outcome.[33-36] As a result, we would not encourage the use of our reference values in asthma self-management. We do believe, however, that our results support the hypothesis that home spirometry might be used as a *diagnostic* tool for childhood asthma in children with chronic wheeze, cough, or dyspnoea, when history, physical examination and office spirometry are insufficient to make or exclude the diagnosis reliably. This hypothesis will have to be tested in a study specifically designed to that end. The use of PEF diaries to distinguish asthmatic from non-asthmatic children has been largely abandoned because previous studies showed almost complete overlap in PEF

variation between asthmatic children [6;7] and healthy children, with a 95th centile as high as 31% for PEF variation in healthy children.[9] It is now highly likely that these reference values were spuriously high because they were obtained using unreliable written PEF diaries. If we compare our reference values for PEF and FEV_1 variation to levels of such variation in well controlled asthmatic children using an electronic home spirometer as monitoring tool, there is much less overlap in variation of lung function between healthy children and children with asthma, even when the latter were using inhaled corticosteroids.[10;13;14] For example, in our previously published study of well-controlled asthmatic children using inhaled corticosteroids, 62% had a PEF variation above 12.3% during any given week in a 3-month study period, using the same home spirometer,[14] despite (near) normal lung function (table 5). Given the fact that inhaled corticosteroids reduce PEF variation considerably,[6;7] it is highly likely that even more symptomatic asthmatic children will show variation of lung function above our reference values when they are not using inhaled corticosteroids. Prospective studies, however, are needed to examine the diagnostic value of home spirometry to identify asthma in children in whom history and physical examination are insufficiently helpful to rule asthma in or out as the cause of chronic respiratory symptoms.

In conclusion, the 95th centiles of variation of PEF and FEV_1 in healthy schoolchildren, using home spirometers with electronic data storage, are 12.3% and 11.8%, respectively. This is considerably lower than reference values for PEF variation previously reported with mechanical meters and written diaries, and reduces the amount of overlap between healthy and asthmatic children. Further prospective

studies are needed to investigate whether home spirometry could be a useful diagnostic tool for childhood asthma.

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Figure legends

Figure 1ab: Variation of PEF (1a) and FEV_1 (1b) are reasonably consistent in the different age groups with a trend towards a lower variation of PEF with the older children (1a). Single reference values for variation of PEF and of FEV_1 are possible. Bars represent the mean values; error bars represent the 95% confidence interval. The dotted line represents the overall mean.

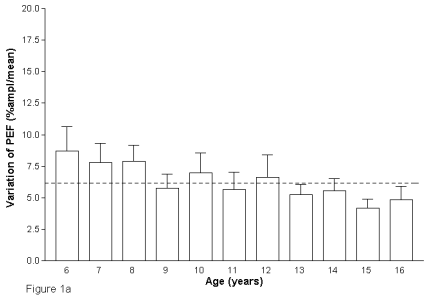


Figure 1a

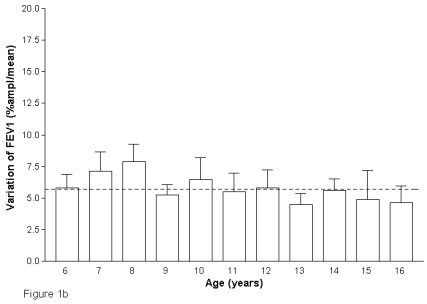
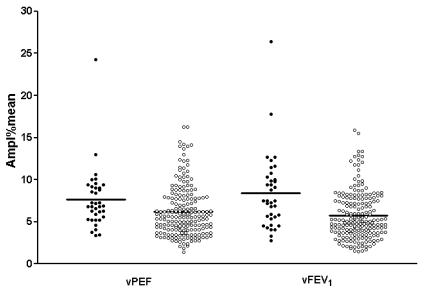


Figure 1b

Figure 2: Variation of PEF and FEV_1 in asthmatic children (closed circles) and healthy children (open circles). Although the means of both groups are statistically different for PEF and FEV_1, there is a considerable overlap between healthy children and well controlled asthmatics. Line represents the mean values.


30
25
20
15
10
5
0
Ampl%mean
vPEF
vFEV1