Original articles

Can peak expiratory flow measurements reliably identify the presence of airway obstruction and bronchodilator response as assessed by FEV$_1$ in primary care patients presenting with a persistent cough?

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Abstract
Background—In general practice airway
obstruction and the bronchodilator re-
sponse are usually assessed using peak
expiratory flow (PEF) measurements. A
study was carried out in patients present-
ing with persistent cough to investigate to
what extent PEF measurements are reli-
able when compared with tests using
forced expiratory volume in one second
(FEV$_1$) as the measure of response.
Methods—Data (questionnaire, physical
examination, spirometry, PEF) were col-
lected from 240 patients aged 18–75 years,
not previously diagnosed with asthma or
chronic obstructive pulmonary disease
(COPD), who consulted their general
practitioner with cough of at least two
weeks duration. The relationship between
low PEF (PEF < PEFpred − 1.64RSD) and
low FEV$_1$ (FEV$_1$ < FEV$_1$pred − 1.64RSD)
was tested. A positive bronchodilator
response after inhaling 400 µg salbutamol
was defined as an increase in FEV$_1$ of ⩾9%
predicted and was compared with an
absolute increase in PEF with cut off
values of 40, 60, and 80 l/min and ΔPEF %
baseline with cut off values of 10%, 15%,
and 20%.
Results—Forty eight patients (20%) had
low FEV$_1$, 86 (35.8%) had low PEF, and 32
(13.3%) had a positive bronchodilator
response. Low PEF had a positive predic-
tive value (PPV) for low FEV$_1$ of 46.5% and
a negative predictive value (NPV) of 95%.
ΔPEF of ⩾10%, ⩾15%, or ⩾20% baseline
had PPVs of 36%, 52%, and 67%, respec-
tively, and ΔPEF of ⩾40, ⩾60, and ⩾80 l/
min in absolute terms had PPVs of 39%,
45%, and 57%, respectively, for ΔFEV$_1$
⩾9% predicted; NPVs were high (88–93%).
Conclusions—Although PEF measure-
ments can reliably exclude airway ob-
struction and bronchodilator response,
they are not suitable for use in the assess-
ment of the bronchodilator response in
the diagnostic work up of primary care
patients with persistent cough. The clini-
cal value of PEF measurements in the
diagnosis of reversible obstructive airway
disease should therefore be re-evaluated.
(*Thorax* 1999;**54**:1055–1060)

Many reports have emphasised the importance
of measuring peak expiratory flow (PEF) in
general practice. It has been reported to be
useful in establishing a diagnosis of asthma and
has been widely adopted for monitoring
patients with asthma.[1–4] In the consulting room
PEF is used for diagnostic purposes to identify
reversible airflow limitation and it is applied at
home to assess peak flow variability. PEF
measurements might reliably replace forced
expiratory volume in one second (FEV$_1$) in
general practice since the correlation of PEF
values with FEV$_1$ values has been found to be
high.[5–7] However, restrictions must be applied
because PEF measurements are more effort
dependent than FEV$_1$ and may therefore
underestimate the degree of airway
obstruction.[1]

Up to the present time almost all studies on
the bronchodilator response have been per-
formed using FEV$_1$ measurements. The use of
PEF meters has also been recommended for
the same purpose in general practice but has
only been investigated in one study.[8] This
study, performed in adults with asthma and
chronic obstructive pulmonary disease
(COPD), showed that an increase in PEF of
60 l/min indicated a clinically significant im-
provement. The global consensus and the
international consensus consider an increase of
15% in PEF from baseline as indicative of
asthma, whereas others state that an improve-
ment in PEF of ⩾20% of the initial value
should establish a diagnosis of asthma.[2 4]

However, none of these statements has been validated.

The aim of this study was to investigate to what extent PEF measurements reliably identify the presence of airway obstruction and a positive bronchodilator response as assessed by FEV_1. It is obvious that, in general practice where spirometers are generally unavailable, PEF measurements would be particularly useful. We therefore investigated patients presenting in general practice with persistent cough who had no previous diagnosis of pulmonary disease. This study is part of a larger project, the results of which have been published elsewhere.[9][10]

Methods

PATIENTS

The study took place between November 1993 and January 1995 in a primary health care centre manned by six general practitioners (GPs) serving a catchment area of 12 000; 8450 subjects aged 18–75 years were registered and their mean age and sex distribution matched that of the rest of the country.

We studied consecutive consultations of patients who presented with a troublesome cough that had lasted for at least two weeks, but who had no known pre-existing pulmonary disease. Patients with a previous diagnosis of asthma or COPD were excluded, as were pregnant patients and those with cardiovascular disease or concomitant pulmonary disease.[9] To ensure that all subjects with a cough of at least two weeks duration had been included, records of every patient in the practice were checked using the GP's computerised register. Subjects were seen by the investigator on the same day as they attended their GP. Once a patient had been admitted to the study any subsequent episode of coughing for two weeks or more was not investigated.

Informed consent was obtained from all the participants and the study was approved by the medical ethics committee of Leiden University.

MEASUREMENTS

Ventilatory function was measured using a turbine spirometer (Microlab 3300, Sensormedics Ltd Rochester, UK). Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and peak expiratory flow (PEF) were measured until three reproducible recordings (with a difference of less than 5%) were obtained, of which the highest was used in the analysis. Reference values of FEV_1, FVC, and PEF were those of the European Respiratory Society.[3][11] The bronchodilator response was assessed 15 minutes after inhaling 400 µg salbutamol by a spacer device (Volumatic, GlaxoWellcome, The Netherlands).

DEFINITIONS

The bronchodilator response was expressed as an increase in FEV_1 to the predicted value:

$$\Delta FEV_1 \text{ \% pred} = (FEV_{1post-BD} - FEV_{1pre-BD})/FEV_1 \text{ predicted} \times 100\%$$

The expressions in bronchodilator response of PEF investigated were (1) absolute increase ($PEF_{post-BD} - PEF_{pre-BD}$) and (2) increase in PEF to the baseline value (($PEF_{post-BD} - PEF_{pre-BD}$)/$PEF_{pre-BD} \times 100$). A positive bronchodilator response was considered to be present if FEV_1 improved by $\geq 9\%$ of the predicted value after inhalation of 400 µg salbutamol.[11–13] Airway obstruction was defined as $FEV_1 < FEV_1$pred − 1.64RSD (low FEV_1).[9] Obstruction as assessed by PEF was defined as PEF < PEFpred − 1.64RSD (low PEF).[5][9]

STATISTICAL ANALYSIS

Data for this study were analysed using SPSS 4.0 (SPSS Inc, Chicago, Illinois, USA). Normal distributions of FEV_1 and PEF were inspected visually by probability plots. Correlations between PEF and FEV_1 were calculated for their absolute values before and after inhaling 400 µg salbutamol. The relationship between "low" PEF (test) and "low" FEV_1 (reference) was studied using χ^2 tests.

Pearson correlation coefficients between bronchodilator response in PEF (for different expressions) and bronchodilator response in FEV_1 as % predicted FEV_1 after inhaling a bronchodilator (400 µg salbutamol) were calculated. The relationship between ΔFEV_1 and ΔPEF was investigated by calculating sensitivity, specificity, and predictive values for several cut off values. Absolute increases in PEF of 40, 60, and 80 l/min after 400 µg salbutamol were compared with ΔFEV_1 of 9% predicted, the "reference". The same procedures were performed taking different cut off values (10%, 15%, and 20%) of ΔPEF % baseline in relation to the "reference" ΔFEV_1 of $\geq 9\%$ predicted. In the Netherlands this cut off value is recommended to indicate a positive bronchodilator response both by the Dutch College of General Practitioners and the Dutch Society of Pulmonologists. Since there is no universal agreement for the cut off value of significant ΔFEV_1, we also studied the ΔPEF measures against the following recommended ΔFEV_1 measurements: (1) ΔFEV_1 absolute ($FEV_{1\ post-BD} - FEV_{1pre-BD}$) ≥ 200 ml[14]; (2) $\Delta FEV_1 \geq 12\%$ predicted and 200 ml[11]; and (3) $\Delta FEV_1 \geq 15\%$ to baseline and 200 ml.[15] Finally, receiver operating characteristic (ROC) curves were generated against ΔPEF % baseline and ΔPEF absolute using the above mentioned cut off values for ΔFEV_1 as the gold standard.

Table 1 Characteristics of patients (n=240)*

Men (%)	40.4
Age (years)	44.9 (15.9)
Median (range) pack years	2.1 (0–65.0)
FEV_1 (% predicted)	91.3 (17.9)
PEF (l/min)	394.8 (122.9)
PEF (% pred)	84.8 (19.0)
FEV_1/FVC (%)	78.8 (8.9)
ΔFEV_1 (% predicted)	3.7 (4.7)
$\Delta FEV_1 \geq 9\%$ predicted (n, %)	32, 13.3
$\Delta FEV_1 \geq 200$ ml absolute (n, %)	63, 26.3
$\Delta FEV_1 \geq 12\%$ predicted and 200 ml (n, %)	11, 4.6
$\Delta FEV_1 \geq 15\%$ baseline and 200 ml (n, %)	15, 6.3
$FEV_1 < FEV_1$pred − 1.64RSD (n, %)	48, 20
PEF < PEF pred − 1.64RSD (n, %)	86, 35.8

*All values are expressed as mean (SD) unless stated otherwise. FEV_1 = forced expiratory volume in one second; PEF = peak expiratory flow; FVC = forced vital capacity; RSD: residual standard deviation.
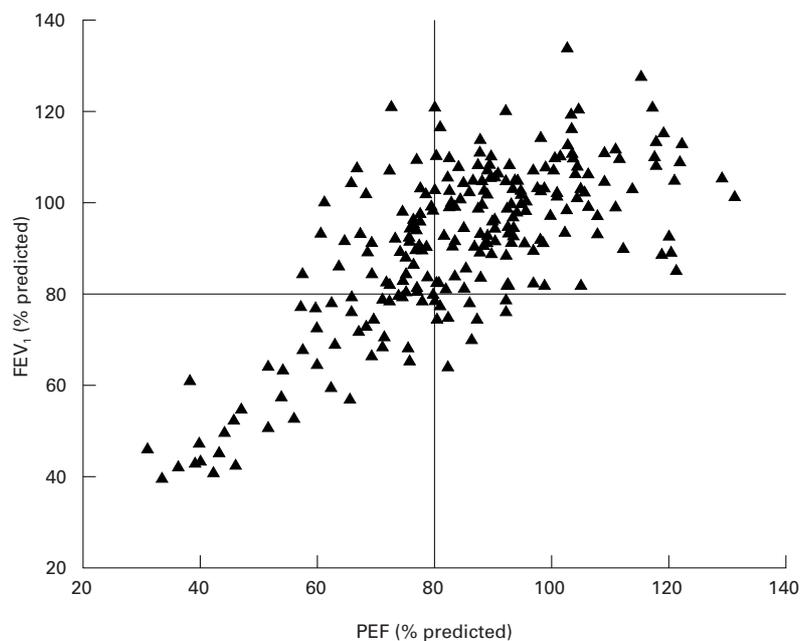
Figure 1   Relationship between predicted values of PEF and FEV$_1$ in the population.

Table 2   Relationship between airway obstruction as assessed by FEV$_1$ and PEF

	$FEV_1 < FEV_1\ pred - 1.64RSD$	$FEV_1 \geqslant FEV_1\ pred - 1.64RSD$	Total
PEF < PEFpred − 1.64RSD	40	46	86
PEF ⩾ PEFpred − 1.64RSD	8	146	154
Total	48	192	240

p = 0.0001 (χ^2 test).

Results

During the study period 256 subjects had a cough lasting for at least two weeks and met the inclusion criteria. Sixteen subjects refused to enter the study. Those participating in the study (n = 240) did not differ in age and sex from the rest of the study group (n = 16). Table 1 shows the characteristics of the patients. Men were under-represented in the study. There was no significant difference in ventilatory function and age between sexes. Airway obstruction as assessed by FEV$_1$ (low FEV$_1$) was found in 48
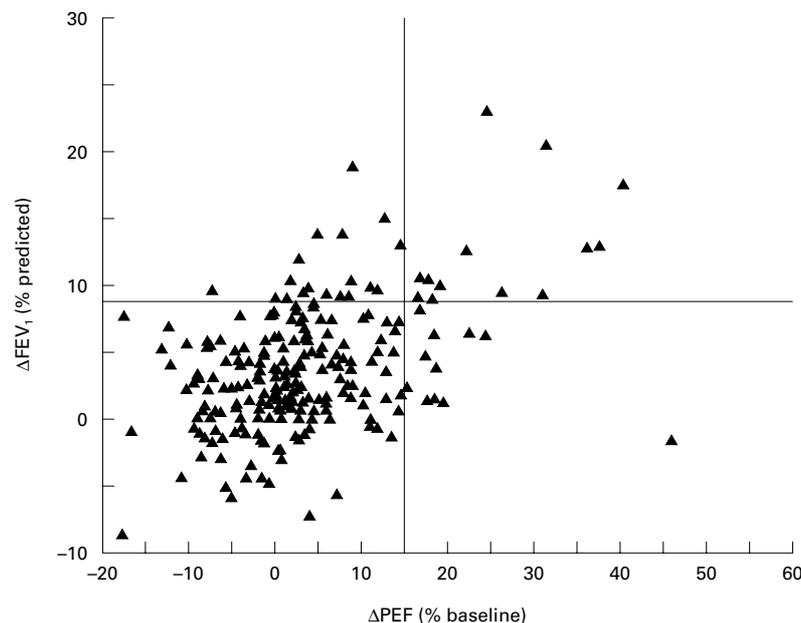
subjects (20%) and a positive bronchodilator response as assessed by FEV$_1$ ranged from 11 subjects (4.6%) when a cut off value of ΔFEV$_1$ of ⩾12% predicted and 200 ml absolute increase was used to 63 subjects (26.3 %) when the cut off value used was ΔFEV$_1$ absolute ⩾200 ml.

The correlation between absolute values of FEV$_1$ and PEF was high ($r = 0.82$, $p<0.001$ before bronchodilation, $r = 0.80$, $p<0.0001$ after bronchodilation). Figure 1 shows the relationship between the predicted values of FEV$_1$ and PEF before bronchodilation and table 2 shows the relationship between low PEF and low FEV$_1$. More patients had a low PEF (n = 86, 35.8%) than a low FEV$_1$ (n = 48, 20%). Forty six of the 86 patients with a low PEF value (53.5%) did not have a low FEV$_1$. Eight patients with low FEV$_1$ did not have obstructive disease according to their PEF values. The sensitivity of a low PEF in relation to a low FEV$_1$ was 83.3%, the specificity was 76%, positive predictive value (PPV) 46.5%, and negative predictive value (NPV) 94.4%.

BRONCHODILATOR RESPONSIVENESS

Correlations between ΔPEF % baseline and absolute ΔPEF with ΔFEV$_1$ % predicted were $r = 0.43$ and $r = 0.32$, respectively ($p<0.001$). Figure 2 shows the scatter between ΔFEV$_1$ % predicted and ΔPEF % baseline.

Figure 3 shows ROC curves using different expressions of ΔFEV$_1$ cut off at different levels against ΔPEF % baseline and ΔPEF absolute. Table 3 shows the test qualities of both ΔPEF absolute with increases of 40, 60, and 80 l/min as cut off values and ΔPEF % baseline with improvements of 10%, 15%, and 20% as cut off values after 400 μg salbutamol in relation to (1) ΔFEV$_1$ % predicted with a cut off value of 9%, (2) ΔFEV$_1$ absolute with a cut off value of 200 ml, (3) ΔFEV$_1$ cut off at an increase of 12% predicted and 200 ml absolute, and (4) ΔFEV$_1$ cut off at an increase of ⩾15% to baseline and 200 ml. Specificities and NPVs were high but sensitivities and PPVs were low. The highest PPV (83%) was found for ΔPEF % baseline with a cut off value of 20% in relation to ΔFEV$_1$ absolute with a cut off value of 200 ml.

Discussion

The study shows that, in patients who attend their GP with persistent cough, there is a considerable lack of agreement between PEF and FEV$_1$ values in assessing airway obstruction and bronchodilator response. Although most patients with a "normal" PEF did not have airway obstruction, there were far more patients with airway obstruction as assessed by PEF than by FEV$_1$ in this study population. There was a lack of agreement between the bronchodilator response as assessed by ΔFEV$_1$ and different expressions of bronchodilator response as assessed by PEF. For example, ΔPEF absolute with a cut off value of 60 l/min and ΔPEF % baseline with cut off values of 15% and 20%, as recommended in the literature, had low sensitivities and PPVs but high specificities and NPVs in relation to ΔFEV$_1$ ⩾9% predicted.

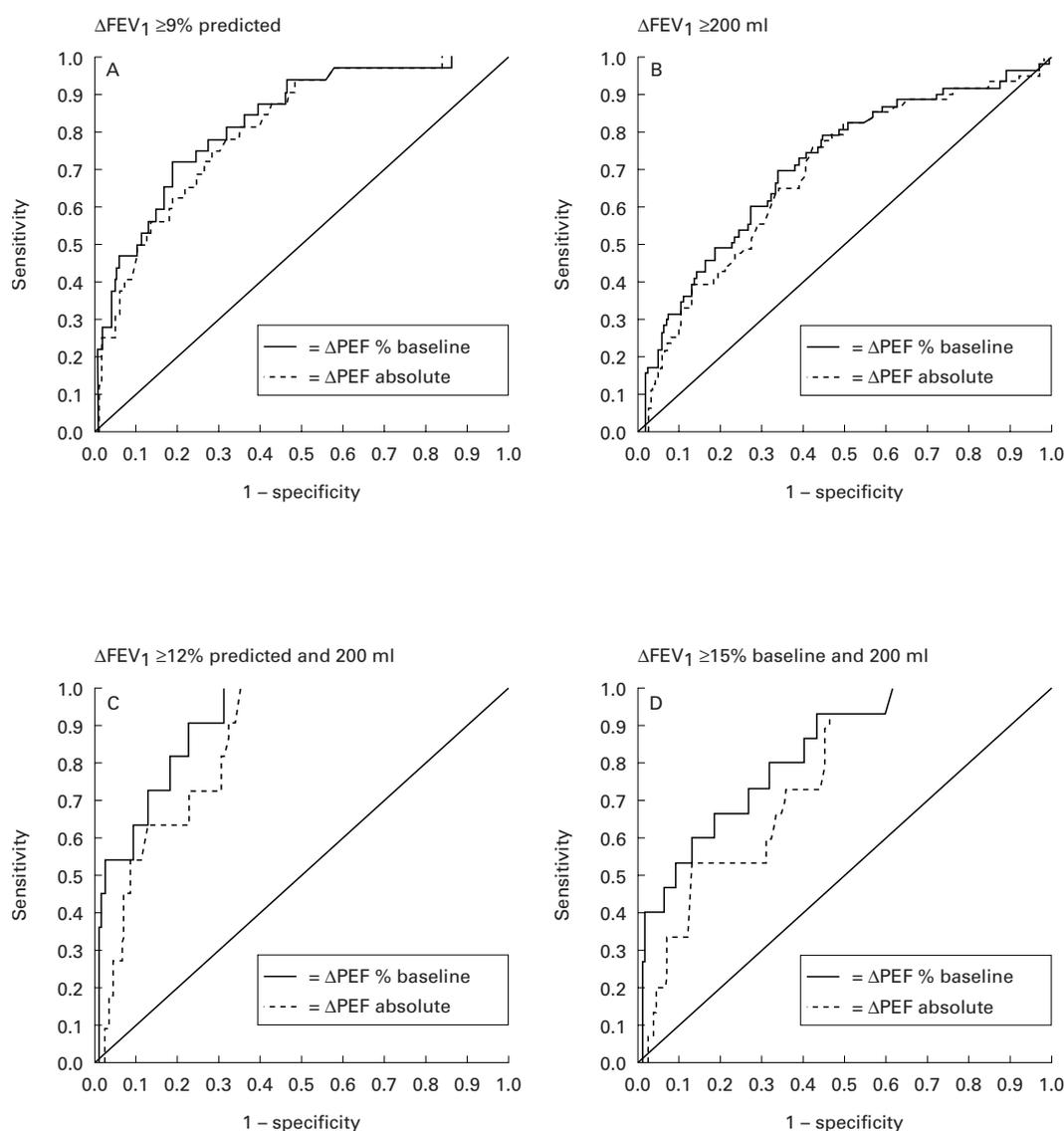*Figure 2   Relationship between ΔPEF % baseline and ΔFEV$_1$ % predicted*

Figure 3   ROC curves using different expressions of ΔFEV₁ cut off at different levels as the standard against ΔPEF % baseline and ΔPEF absolute.

Also, when using different expressions and cut off values for ΔFEV₁, PPVs remained low while NPVs remained high.

Thus, in the diagnostic work up of primary care patients presenting with persistent cough, PEF can reliably exclude airway obstruction when normal PEF values are present. Otherwise it is an unreliable tool, especially for assessment of the bronchodilator response.

More patients had low PEF values than low FEV₁ values in this study population. We measured PEF and FEV₁ with a turbine meter which might provide a systematic underestimation of PEF by mass inertness.[5] However, this is not very likely because PEF and FEV₁ values assessed by the Micro Medical turbine spirometer used in this study are in agreement with the values obtained with pneumotachometers.[16] Besides, the advantage of assessing ventilatory function with a turbine spirometer is that it measures both PEF and FEV₁ during the same forced exhalation. Another explanation might be that the reference values of PEF are less reliable than those of FEV₁. We feel that the most likely explanation is that PEF and FEV₁ were assessed during an

unstable phase of the patient—that is, during a coughing period. Since PEF is more effort dependent than FEV₁, this may have resulted in more subjects having a low PEF value.

A single PEF measurement is of limited value in assessing airflow limitation but it may sometimes suffice to exclude the presence of airway obstruction at the time of measurement.[5] Our study confirms this statement: the presence of low PEF had a low PPV for airway obstruction (low FEV₁) whereas the absence of low PEF made airway obstruction unlikely. In other words, PEF testing to assess airway obstruction has the properties to be a good screening test (high specificities and NPVs) but it was of less clinical value as a diagnostic test (requiring high sensitivity and high PPVs) because of the low PPV.

The correlations between changes in PEF and FEV₁ after inhaling 400 µg salbutamol were only weak to moderate. This is in accordance with studies showing a weak correlation between changes in FEV₁ and PEF after bronchodilation and after bronchoconstriction.[7] It seems likely that PEF and FEV₁ respond in a different way to changes in the mechanical

Table 3 Test qualities of different ways of expressing a positive bronchodilator response with PEF measurements (ΔPEF absolute with cut off values of 40, 60, and 80 l/min and ΔPEF % baseline with cut off values of 10%, 15%, and 20%) in relation to different references as assessed by spirometric tests (n = 240)

Δ PEF measurements	Sensitivity	Specificity	PPV	NPV
(A) $\Delta FEV_1 \geq 9\%$ predicted				
≥10% baseline	56	85	36	93
≥15% baseline	44	94	52	92
≥20% baseline	25	98	67	90
≥40 l/min	53	87	39	92
≥60 l/min	28	95	45	90
≥80 l/min	13	99	57	88
(B) $\Delta FEV_1 \geq 200$ ml absolute				
≥10% baseline	41	86	52	81
≥15% baseline	27	94	63	78
≥20% baseline	16	99	83	77
≥40 l/min	35	88	50	79
≥60 l/min	18	95	55	76
≥80 l/min	6	98	57	75
(C) $\Delta FEV_1 \geq 12\%$ predicted and 200 ml absolute				
≥10% baseline	73	82	16	98
≥15% baseline	42	93	37	93
≥20% baseline	29	98	58	93
≥40 l/min	64	84	16	98
≥60 l/min	36	93	20	97
≥80 l/min	9	97	14	96
(D) $\Delta FEV_1 \geq 15\%$ baseline and 200 ml				
≥10%baseline	60	82	18	97
≥15% baseline	47	91	26	96
≥20% baseline	40	97	50	96
≥40 l/min	53	84	18	96
≥60 l/min	27	93	20	95
≥80 l/min	7	97	14	94

PPV = positive predictive value; NPV = negative predictive value.

qualities of the airways as caused by a bronchodilator.

The presence of a positive reversibility test in addition to respiratory symptoms is considered to be a key factor in diagnosing airway obstruction (asthma)[17 18] so general practitioners are interested in the precision of the PPV (rarely false positives) of the different recommended measurements of ΔPEF.

The European Respiratory Society (ERS) states that an increase in PEF of 60 l/min is a clinically significant improvement.[5] This statement was based on one study of 73 adults known to have asthma or COPD[8] in which an absolute increase in PEF measured with a mini-Wright spirometer was compared with an increase in FEV_1 % predicted with a cut off value of 9%. In contrast, we have found that, using the same dose and bronchodilating agent (salbutamol 400 μg) but in a different population, this cut off value has a low PPV. We therefore conclude that this cut off value is not suitable for use in assessing a significant bronchodilator response during a coughing episode in patients not previously known to have asthma or COPD.

In recent guidelines it is stated that an increase in PEF of 15% or 20% from baseline after bronchodilation is a clinically significant improvement.[2–4] These statements are not based on studies but are probably derived from FEV_1 measurements. In the current study none of these proposed expressions corresponded sufficiently with an increase in FEV_1 of ≥9% predicted which is considered to be a clinically significant response and is recommended in several papers.[12 13] The use of ≥9% FEV_1 % predicted as the reference value with which to compare other tests for bronchodilator response may be open to question. Every cut off value is arbitrary because acute reversibility of airway obstruction to a bronchodilator is a continuous variable rather than a dichotomous trait.[12] However, a cut off value for ΔFEV_1 of 9% predicted has been found to be useful and valid for measuring the bronchodilator response, both in separating asthma from COPD and because it is not dependent on the initial FEV_1, and it is now the accepted cut off value in The Netherlands.[12 13] Furthermore, PPVs to assess the bronchodilator response were also low with other cut off values recommended by the ERS and BTS ($\Delta FEV_1 \geq 12\%$ predicted or 15% baseline in combination with 200 ml[11 15] or an absolute increase in FEV_1 of 200 ml[14]).

One may argue that the use of any cut off value might result in a loss of power and precision. However, it is commonly used by doctors since most medical action is dichotomous—to operate or not to operate, to initiate treatment or not.[19]

The findings of this study might have implications in general practice for the assessment of airway obstruction and the bronchodilator response in the diagnostic work up of asthma and COPD. If a patient has a low PEF, conclusions about the presence or absence of airway obstruction cannot be made. Further investigation such as spirometric testing is necessary before the general practitioner can decide which treatment is the most appropriate. In the absence of a low PEF further investigation is not necessary. In this analysis all the expressions of bronchodilator response by PEF studied showed high NPVs and high specificities in relation to a positive bronchodilator response (good screening test) but the diagnostic properties were poor (low sensitivity, low PPV). Thus, testing of the bronchodilator response by PEF should be replaced by FEV_1 measurements in the diagnosis of reversible airway disease. As a consequence, general practitioners should be better trained in spirometric testing than at present to ensure that quality controls are performed according to international guidelines.

In conclusion, general practitioners should be cautious in interpreting low PEF values and bronchodilator response assessed by PEF in patients presenting with a troublesome cough. The lack of agreement with FEV_1 values raises the question whether PEF measurements are of sufficient clinical value in assessing airway obstruction and bronchodilator responsiveness.

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