

ONLINE SUPPLEMENT:

Table 4a. Performance characteristics of all action points based solely on Symptoms.

The action point ‘nocturnal awakening’ was considered positive whenever a patient had awoken due to asthma symptoms; ‘appearance of any symptoms’ was positive whenever a patient had experienced any breakthrough symptoms; ‘severe symptoms’ whenever the composite symptom score was two or more, or yes in case of nocturnal awakening. The action points based on SD are positive whenever the result of a composite symptom score was higher than respectively 1, 2, or 3 standard deviations from a mean symptom score calculated from data obtained during the run in period.

<i>Action point criteria</i>	Definition exacerbation	Early diagnosis (days)	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC	NNT
<i>Nocturnal awakening</i>	Symptoms PEFs	2.5	83.9	86.3	86.3	0.85	26
	Use of prednisone	2.6	77.6	86.7	86.6	0.82	16
<i>Appearance of any symptoms</i>	Symptoms PEFs	5.4	100	42.0	42.4	0.71	94
	Use of prednisone	5.2	97.7	42.3	42.9	0.70	57
<i>Severe symptoms</i>	Symptoms PEFs	3.0	90.8	79.5	79.6	0.85	36
	Use of prednisone	3.2	91.2	79.9	80.0	0.86	21
<i>Symptom</i>	Symptoms PEFs	3.6	95.4	77.3	77.4	0.86	38

<i>score >1SD</i>	Use of prednisone	3.4	91.8	77.7	77.8	0.85	23
<i>Symptom score >2SD</i>	Symptoms PEFs	2.9	88.5	86.3	86.3	0.87	24
	Use of prednisone	2.7	76.9	86.6	86.5	0.82	17
<i>Symptom score >3SD</i>	Symptoms PEFs	2.7	74.7	90.9	90.8	0.83	19
	Use of prednisone	2.6	61.9	91.1	90.8	0.77	14

Table 4b. Performance characteristics of action points based solely on Peak Flow.

‘PEF 2 days 85% of personal best’ was considered positive whenever PEF was lower than 85% of the personal best PEF on two consecutive days; ‘PEF % of personal best’ whenever PEF was lower than the designated percentage of that patients personal best PEF score; ‘PEF SD’ whenever PEF was lower than respectively 1, 2, or 3 standard deviations from the mean PEF obtained during the run in period.

<i>Action point criteria</i>	Definition of exacerbation	Early diagnosis (days)	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC	NNT
<i>PEF 85% pb on 2 consecutive days</i>	Symptoms PEFs	4.4	87.4	78.8	78.8	0.83	38
	Use of prednisone	3.7	82.3	79.0	79.1	0.81	24
<i>PEF <80% pb</i>	Symptoms PEFs	4.4	94.3	80.4	80.5	0.87	33
	Use of prednisone	3.5	87.1	80.6	80.7	0.84	21
<i>PEF <70% pb</i>	Symptoms PEFs	2.9	90.8	93.9	93.9	0.92	11
	Use of prednisone	2.6	61.2	93.9	93.5	0.78	10
<i>PEF <60% pb</i>	Symptoms PEFs	1.0	78.2	98.7	98.6	0.88	3
	Use of prednisone	1.2	38.1	98.7	98.0	0.68	4
<i>PEF <1SD †</i>	Symptoms PEFs	4.4	95.4	71.3	71.4	0.83	49

	Use of prednisone	3.7	87.1	71.5	71.6	0.79	32
<i>PEF <2SD †</i>	Symptoms PEFs	3.3	89.7	85.3	85.3	0.87	26
	Use of prednisone	2.5	76.9	85.5	85.4	0.81	18
<i>PEF <3SD †</i>	Symptoms PEFs	2.7	70.1	92.6	92.5	0.81	17
	Use of prednisone	2.6	54.4	92.8	92.3	0.74	13

Table 4c. Performance characteristics of all action points that combined thresholds for both Symptoms and PEF, where *both* thresholds were reached on the same day. For example ‘symptoms 1SD and PEF 80%’ was positive whenever the composite symptom score was higher than 1 standard deviation from the mean symptom score *and* PEF was lower than 80% of that patients personal best. For a further description see table 4a and 4b.

<i>Action point criteria</i>	Definition of exacerbation	Early diagnosis (days)	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC	NNT
<i>Symptoms >1SD and PEF <80% pb</i>	Symptoms PEFs	2.6	89.7	92.1	92.1	0.91	14
	Use of prednisone	2.3	77.6	92.4	92.2	0.85	10
<i>Symptoms >2SD and PEF <70% pb</i>	Symptoms PEFs	1.4	80.5	98.3	98.2	0.89	4
	Use of prednisone	1.4	47.6	98.3	97.7	0.72	4
<i>Symptoms >2SD and PEF <60% pb</i>	Symptoms PEFs	0.3	67.8	99.6	99.4	0.84	2
	Use of prednisone	0.5	30.6	99.5	98.7	0.65	2

<i>Symptoms >3SD and PEF 60% pb</i>	Symptoms PEFs	0.3	55.2	99.8	99.5	0.77	2
	Use of prednisone	0.5	23.1	99.7	98.8	0.61	2
<i>Appearance of symptoms and PEF <80% (NAEPP)</i>	Symptoms PEFs	3.9	94.3	83.3	83.4	0.89	28
	Use of prednisone	3.1	85.0	83.5	83.6	0.84	18
<i>Appearance of symptoms and PEF <70% pb</i>	Symptoms PEFs	2.7	90.8	94.4	94.4	0.93	10
	Use of prednisone	2.4	60.5	94.4	94.1	0.78	9
<i>Appearance of severe symptoms and PEF <70% pb</i>	Symptoms PEFs	1.6	81.6	97.4	97.3	0.90	6
	Use of prednisone	1.6	51.0	97.5	97.0	0.74	5
<i>Nocturnal awakening and PEF <70% pb</i>	Symptoms PEFs	1.3	75.9	98.1	97.9	0.87	5
	Use of prednisone	1.2	44.2	98.1	97.5	0.71	5

<i>Symptoms >1SD and PEF >1SD</i>	Symptoms PEFs	2.6	92.0	89.0	89.0	0.90	19
	Use of prednisone	2.7	75.5	89.2	89.1	0.82	14
<i>Symptoms >2SD and PEF >2SD</i>	Symptoms PEFs	1.8	81.6	95.5	95.4	0.89	9
	Use of prednisone	1.8	60.5	95.6	95.2	0.78	7
<i>Symptoms >3SD and PEF >3SD</i>	Symptoms PEFs	1.7	56.3	97.9	97.7	0.77	6
	Use of prednisone	2.1	41.5	98.0	97.4	0.70	5

Table 4d. Performance characteristics of action points that used a Time Window for thresholds of Symptoms and PEF. For example ‘7 day timeframe 2SD symptoms, 70% personal best PEF’ was positive whenever the composite symptom score was higher than two standard deviations above the mean symptom score on a certain day and the PEF result was lower than 70% of that patients personal best PEF on that day, or on any of the preceding or following seven days.

TIME WINDOW							
<i>Action point criteria</i>	Definition of exacerbation	Early diagnosis (days)	Sensitivity (%)	Specificity (%)	Accuracy (%)	AUC	NNT
<i>3 day timeframe Symptoms 2SD PEF <70% pb</i>	Symptoms PEFs	3.4	81.6	97.7	97.6	0.90	5
	Use of prednisone	2.6	51.0	97.6	97.1	0.74	5
<i>7 day timeframe Symptoms 2SD PEF <70% pb</i>	Symptoms PEFs	4.1	85.1	97.2	97.1	0.91	6
	Use of prednisone	3.5	54.4	97.2	96.7	0.76	5

Table 5a. Symptom score used in developmental dataset [8]. Each symptom was scored between 0 and 1. Zero meant that symptom was not experienced, and 1 was the maximum score for that symptom. For symptoms scored between 0-3, i.e. chest tightness, we adjusted results (0=0, 1=0.33, 2=0.66, 3=1). B2-usage was scored as 0 when no ‘reliever’ medication was used; 0.16 for 1 or 2 puffs; 0.33 for 3 or 4; 0.5 for 5-8; 0.66 for 9-12; 0.83 for 13-16; and 1 for >16 uses of reliever medication per day. Nocturnal awakening scored 0 if it had not occurred that day and 1 if the patient had awoken due to symptoms.

Symptom	Score
Morning and evening chest tightness	0-1
Morning and evening cough	0-1
Nocturnal awakening	0-1
Sputum production	0-1
Exercise limitations	0-1
B2-usage	0-1
Total daily composite symptom score	0-6

Table 5b. Symptom score in the validation dataset [9]. Symptoms were scored between 0 - 5. 0 = no symptoms, 1 = symptoms for one short period, 2 = symptoms for two or more short periods, 3 = symptoms most of the time that did not affect normal daily activities, 4 = symptoms most of the time that did affect normal daily activities, and 5 = symptoms so severe as to disrupt daily activities. This score between 0 and 5 was recalculated between 0-3 (i.e. 0=0, 1=0.6, 2=1.2, 3=1.8, 4=2.4, 5=3). Nocturnal awakening and B2-usage were scored similarly as in the development dataset (see description Table 5a).

Symptom	Score
Limitations and symptoms	0-3
Nocturnal awakening	0-1
B2-usage	0-1
Total daily composite symptom score	0-5

