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# Disease control in general practice patients with asthma Hanneke A.H. Wijnhoven. Didi M.W. Kriocement I.I.

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#### **KEYWORDS**

Respiratory symptom; PEF variability; FEV<sub>1</sub>; Disease control; Asthma

Summary Objectives: To examine asthma control in conjunction with medication use in asthma patients from general practice. To determine features of patients with inadequately controlled asthma.

Methods: A cross-sectional study was performed among 661 adult asthma patients recruited from general practice. Disease control was defined by: (1) respiratory symptoms; (2) forced expiratory volume in 1 s ( $FEV_1$ )% predicted; (3) PEF variability; and (4) the use of  $\beta$ 2-agonists. Medical treatment was categorised according to the step-care therapy rules following the 1997 guideline of the Dutch College of General Practitioners (DDGP).

Results: Of the 661 asthma patients studied, 262 (40%) had a good disease control, 84 (13%) a mildly reduced, 235 (36%) a moderately reduced, and 80 (12%) had a poor disease control. Of the 399 patients (60%) inadequately controlled, in 292 patients (44%) adequate control might be achieved by changing treatment, in 99 patients (15%) adequate control might not completely be achieved by changing treatment, and 8 (1%) were already maximally treated. Compared to patients with a good disease control, patients inadequately controlled were usually older, less educated, younger at onset of pulmonary complaints, and in addition had more severe dyspnea and poorer health-related quality of life (HRQoL).

*Conclusion*: Using our criteria, a substantial proportion of asthma patients primarily treated in general practice is not adequately controlled. Assessing patients' disease control together with the level of medical treatment may help to gain insight into the effectiveness of current disease management.

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#### Introduction

A recent multinational survey showed that asthma control is sub-optimal for many people in Western

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Europe [1]. In this study, we examine the level of disease control in an asthma population recruited from Dutch general practices. The level of disease control was related to the amount of asthma medication used in order to estimate how many of the inadequately controlled patients might benefit from changing treatment. In addition, features of patients not adequately controlled were examined in order to create a risk-profile of use for the general practitioner.

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## Methods

The study has a cross-sectional design. An extensive description of the study population and methods of measurements can be found elsewhere [2]. A short description of patients and measurements will be given here.

## Patients

General practices in three regions of The Netherlands selected all patients registered with a diagnosis of asthma and COPD [2]. For the present study, from the total group of asthma and COPD patients included in the longitudinal study, asthma patients were selected, using the 1997 diagnostic guidelines of the Dutch College of General Practitioners (DDGP) [3]. Asthma was defined as: (1) a pre-forced expiratory volume in 1 s (FEV<sub>1</sub>)% predicted  $\geq$ 80%; or (2) a combination of a pre-percentage of the predicted FEV<sub>1</sub> (FEV<sub>1</sub>% predicted) <80%, a reversible obstruction ( $\geq$ 9% of predicted), and a post-FEV<sub>1</sub>% predicted >80% [2].

#### Measurements

Forced expiratory volume in 1 s was measured according to ATS criteria [4] before (pre-FEV<sub>1</sub>) and after (post-FEV<sub>1</sub>) administration of a bronchodilator [2]. FEV<sub>1</sub> was expressed as a percentage of the predicted FEV<sub>1</sub> using the adult predicted normals of the European Community for Coal and Steel [5].

A 2-week diary chart, including questions on respiratory symptoms, use of bronchodilators, and peak flow assessment, was handed out to the patient to be completed at home. Peak expiratory flow (PEF) was measured every morning and evening three times in standing position with the 'Personal Best Peak Flow meter' (Respironics Inc., Pittsburgh, USA). Each day, the single best morning and evening PEF were noted on the diary chart. Variability in PEF was expressed as the mean diurnal (within-day) PEF variation [(highest PEF - lowest PEF)/[(morning PEF + lowest PEF)/[(morning PEevening PEF)/2]  $\times$  100, averaged over 14 days]. Each day, the patient also recorded whether the past day and night were disturbed by pulmonary complaints. In the morning, the patient had to record if, in the past night, he or she had woken up due to pulmonary complaints (yes or no). In the evening, the patient had to record if, during the day, he or she had skipped school or work or had been restricted in daily activities due to pulmonary complaints (yes or no). Additionally, patients recorded the number of times bronchodilators had been used in the past 24 h. For all scores calculated, data were extrapolated in case of missing data when at least 10 days provided valid data.

Medication use was assessed by asking patients which kind of medication they used and in which dose they used this medication. The amount of medical treatment was then categorised according to the stepped-care therapy rules of the 1997 guidelines of the DCGP for the treatment of asthma [6]. This stepped-care therapy recommends which kind of medication should be used according to the severity of the disease (Table 2). Compliance with the use of inhaled anti-inflammatory agents was assessed by means of a three-item checklist. Patients were considered non-compliant if they in the last 3 months ever: (1) forgot using their medication; (2) stopped using their medication because they felt better; (3) used less medication than prescribed because they felt better. Inhalation technique (sufficient or insufficient) was scored by means of a short three-item version of the validated, inhalerspecific checklist of the Dutch Asthma Foundation [7].

Health-related quality of life (HRQoL) was measured using the disease specific *Quality Of Life in Respiratory Illness Questionnaire (QOL-RIQ)* [8]. It comprises 55 items, categorised under seven subscales and an overall score. For every item, patients are asked to answer, on a seven-point Likert-type scale, to what degree they are bothered by pulmonary complaints (from 1: not bothered at all, to 7: very much bothered).

Information was obtained on age (years), age at onset of pulmonary complaints (years), gender, and educational level (low, medium, high) [2]. Co-morbidity was defined present if the patient reported any other chronic disease (such as diabetes mellitus, hypertension, cardiovascular disease, stroke, arthritis, or malignancies). Cigarette smoking habits were defined by assessing smoking status (never, former, current). Allergy was defined present by a positive Phadiatop test (Pharmacia AB, Uppsala, Sweden) [9].

The degree of dyspnea (no dyspnea, dyspnea when in a hurry, dyspnea when walking with others on flat ground, having to stop for breath when walking alone on flat ground or dyspnea in rest) was assessed using the Dutch version of Medical Research Council (MRC) questionnaire [10]. In addition, information was obtained on: (1) wheezing (never, ever, most days and nights); (2) chronic cough (present, not present); and (3) sputum production (present, not present) [2].

#### Assessment of asthma control

We used: (1) respiratory symptoms during day and night [11,12], (2) FEV<sub>1</sub>% predicted [11,12], (3) PEF variability [11], and (4) the use of  $\beta$ 2-agonists [12] to define disease control. Categorisation into dif-

ferent levels of disease control was done separately for each criterion and for all criteria together using the worst categorisation [12]. The worst categorisation means for example that when a patient has good disease control according to the FEV<sub>1</sub>, PEF variability, and day- and night-time symptoms, but

 Table 1
 Level of disease control: classification rules (adopted from NAEPP Expert Panel Report II [1] and Colice et al. [12]).

|   | Symptoms <sup>a</sup>           | Night-time<br>symptoms [1] | FEV <sub>1</sub> %<br>predicted | PEF variability<br>[1] (%) | $\beta$ 2-agonist use [1]                               |
|---|---------------------------------|----------------------------|---------------------------------|----------------------------|---|
| Good disease control<br>Mildly reduced<br>disease control | ≤4 days<br>>4 days,<br><14 days | ≤1 night<br>2 nights       | ≥80<br>≥80                      | <20<br>20—30               | On $\leq$ 4 days<br>>0 uses on >4 days,<br>but <14 days |
| Moderately reduced<br>disease control                     | 14 days                         | >2 nights,<br><8 nights    | >60- <u>&lt;</u> 80             | >30                        | >0 uses on 14 days,<br>but ≤2 uses on at<br>least 1 day |
| Poor disease control                                      | 14 days                         | $\geq$ 8 nights            | ≤60                             | >30                        | >2 uses on each of the 14 days                          |

<sup>a</sup> Per 2 weeks.

| Table 2 | Level of | disease | control | according | to | 'worst | category' | vs. | medical | treatment. |  |
|---------|----------|---------|---------|-----------|----|--------|-----------|-----|---------|------------|--|
|         |          |         |         |           |    |        |           |     |         |            |  |

| Disease control       | Medical treatment according to the step-care therapy rules [9] |  |   |  |  |  |
|-----------------------|--|--|---|--|--|--|
|                       | Step 0   | Step 1:<br>Short-acting<br>β2-agonists if<br>necessary | Step 2 <sup>a</sup> : Low<br>dose [2] inhaled<br>corticosteroids or<br>cromoglycine | Step 3 <sup>a</sup> : (1) High<br>dose <sup>b</sup> inhaled<br>corticosteroids;<br>or (2) moderate<br>dose <sup>b</sup> inhaled<br>corticosteroids<br>and long-acting<br>β2-agonists | Step $4^a$ : (1) High<br>dose <sup>b</sup> inhaled<br>corticosteroids<br>combined with<br>long-acting<br>$\beta$ 2-agonists or<br>ipratropiumbro-<br>mide; or (2) oral<br>steroids |  |
| Good <sup>c</sup>     | Wrongly labeled<br>as asthma                                   | Mild intermittent disease severity                     | Mild persistent<br>disease severity   | Moderate<br>persistent<br>disease severity   | Severe persistent disease severity   |  |
| Mildly reduced        | Undertreatment<br>by one dose level                            | Undertreatment<br>by one dose level                    | Undertreatment<br>by one dose level   | Undertreatment<br>by one dose level  | Adequate control<br>cannot be<br>achieved  |  |
| Moderately<br>reduced | Undertreatment<br>by two dose<br>levels                        | Undertreatment<br>by two dose<br>levels                | Undertreatment<br>by two dose<br>levels   | Undertreatment<br>by one dose<br>levels/adequate<br>control cannot be<br>achieved  | Adequate control<br>cannot be<br>achieved  |  |
| Poor                  | Undertreatment<br>by three dose<br>levels                      | Undertreatment<br>by three dose<br>levels              | Undertreatment<br>by two dose<br>levels/adequate<br>control cannot be<br>achieved   | Undertreatment<br>by one dose<br>levels/adequate<br>control cannot be<br>achieved  | Adequate control<br>cannot be<br>achieved  |  |

<sup>a</sup> Including short-acting  $\beta$ 2-agonists if necessary.

 $^{b}$  For beclometason and budesonide, low dose was 200–400  $_{\mu}g$  2 dd, moderate dose was 400–800  $_{\mu}g$  2 dd, and high dose was  $>800 \,_{\mu}g$  2 dd. For fluticason, low dose was 100–250  $_{\mu}g$  2 dd, moderate dose was 250–500  $_{\mu}g$  2 dd, and high dose was  $>500 \,_{\mu}g$  2 dd.

<sup>c</sup> In case of adequate disease control (mild intermittent), the amount of medical treatment indicates global disease severity (mild intermittent trough severe persistent).

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#### Statistical analyses

Data were analysed using the statistical package SPSS.7.5. Classification rules for describing the level of disease control can be found in Table 1. The level of disease control was cross-tabulated with the amount of medical treatment (true-use). which was categorised according to the step-care therapy rules of the DCGP-guideline [6] (Table 2): 2 With this cross-tabulation, we were able to classify disease severity in patients with adequate disease control, identify patients not adequately treated (separated in patient in which adequate control may be achieved by changing treatment and patients in which adequate control might not be achieved by changing treatment), and identify patients with inadequate disease control despite maximum treatment.

Determinants of the following patient groups were examined (reference group: good asthma control using anti-asthma medication): (1) good asthma control not using anti-asthma medication; (2) inadequate control, adequate control may be achieved by changing treatment; (3) inadequate control, adequate control might not be achieved. Determinants were examined using bivariate and multivariate multinomial logistic regression techniques with patient groups as the dependent variable and demographic and asthma characteristics as the independent variables. Since HRQoL is rather an outcome measure than a determinant, its association with patient groups was examined bivariately but it was not included in the multivariate model.

# Results

A total of 2047 patients with asthma or COPD were selected by the general practitioners. Of them, 722 (mean age, 43 years; 50% male) refused to participate, leaving 1325 patients (mean age, 46 years; 44% male). Another 13 patients were excluded because they did not perform the pulmonary function test. Of the 1312 patients left, 963 were defined as asthma patients. After exclusion of all missing data, 661 patients were included in the present study. Patients excluded due to missing data appeared to be younger (mean age, 41 years) than patients included (mean age, 45 years). No differences were found regarding gender, pulmonary function and medical treatment (Table 3), although excluded patients tended to have a lower level of medical treatment (P = 0.08).

Table 4 describes the level of disease control in the study population according to classification rules presented in Table 1. When the worst classification was used, 262 (39.6%) asthma patients appeared to have a good disease control, 84 (12.7%) a mildly reduced, 235 (35.6%) a moderately reduced, and 80 (12.1%) a poor disease control. A poor correlation was found between individual variables in categorising the level of disease control. Cohen's kappa's [13] ranged from 0.01 to 0.15, indicating poor agreement (data not shown). We found that the use of  $\beta$ 2-agonists and night-time symptoms

| Characteristics                                | Asthma patients included $(n = 661)$ | Asthma patients excluded ( $n = 302$ ) | <i>P</i> -value |
|--|--------------------------------------|--|-----------------|
| Age (years)                                    | 45 (15)                              | 41 (15)                                | 0.002           |
| Male gender                                    | 38                                   | 42                                     | 0.37            |
| Prebronchodilator FEV <sub>1</sub> % predicted | 95.9 (14.9)                          | 96.3 (13.9)                            | 0.66            |
| Medical treatment <sup>b</sup>                 |                                      |  |                 |
| Step 0   | 21.3                                 | 24.7                                   | 0.08            |
| Step 1   | 18.2                                 | 19.7                                   |                 |
| Step 2, corticosteroids when necessary         | 12.2                                 | 18.0                                   |                 |
| Step 2   | 37.2                                 | 27.0                                   |                 |
| Step 3   | 9.7                                  | 9.7                                    |                 |
| Step 4   | 1.4                                  | 1.0                                    |                 |

**Table 3** Characteristics of all asthma patients selected (n = 963) separately for patients included (n = 661) and patients excluded (n = 302) due to missing data<sup>a</sup>.

<sup>a</sup> Data are presented as % or mean (S.D.).

<sup>b</sup> Excluding four patients using long-acting  $\beta$ 2-agonists only.

|   | Symptoms [1]                       | Night-time<br>symptoms [1]           | FEV <sub>1</sub><br>predicted | PEF<br>variability                | β2-agonist<br>use                      | Worst<br>category                     |  |
|---|------------------------------------|--------------------------------------|-------------------------------|-----------------------------------|--|---------------------------------------|--|
| Good disease control<br>Mildly reduced<br>disease control<br>Moderately reduced | 608 (92.0)<br>43 (6.5)<br>10 (1.5) | 439 (66.4)<br>52 (7.9)<br>126 (19.1) | 577 (87.3)<br>81 (12.3)       | 644 (97.4)<br>13 (2.0)<br>4 (0.6) | 369 (55.8)<br>108 (16.3)<br>140 (21.2) | 262 (39.6)<br>84 (12.7)<br>235 (35.6) |  |
| disease control<br>Poor disease control   |                                    | 44 (6.7)                             | 3 (0.5)                       |                                   | 44 (6.7)                               | 80 (12.1)                             |  |
| General Praction Prohibility  |                                    |                                      |                               |                                   |  |                                       |  |

**Table 4** Level of disease control: number of asthma patients (n = 661).

were most dominant in determining the level of disease control. Cohen's kappa was 0.63 for use of  $\beta$ 2-agonists versus the level of disease control, 0.50 for night-time symptoms, and it ranged from 0.02 to 0.26 for the other variables (data not shown).

In Table 5, one can see the level of disease control according to the worst categorisation in conjunction with the level of medical treatment as described in Table 2. It appeared that 262 (39.6%) patients had good disease control, 292 (44.2%) were not adequately treated, but by changing treatment adequate control may be achieved, 99 (15.0%) were not adequately treated, but adequate control might not completely be achieved by changing treatment, and 8 (1.2%) were considered as patients in which adequate control can not be achieved since they did not have good disease control despite maximum treatment. Of the 262 patients with good disease control, 100 (38.2%) did not use any medication according to the stepped-care therapy rules for asthma. Furthermore, 49 (18.7%) were treated according to step 1, 110 (42.0%) according to step 2, 6 (2.3%) according to step 3, and 1 (0.4%) according to step 4.

groups are studied both bivariately and multivariately. Patients with good disease control not using any anti-asthma medication did not statistically significantly differ from patients with good disease control using anti-asthmatic medication, on a wide variety of characteristics, except for that they were more often male  $(OR = 1.64 \ (0.99 - 2.71))$ (data not shown). Compared to patients with good asthma control using anti-asthmatic medication (Table 7), patients not adequately controlled were (independently) older, less well educated, younger when their pulmonary complaints started, and had a more severe dyspnea grade. In addition, they had poorer HRQoL (Table 6). Furthermore, wheezing most days and nights was more often found in patients who might gain most from changing treatment when compared to patients with good asthma control. Patients in whom adequate control might not be achieved by changing treatment more often presented with sputum production when compared to patients with good disease control and, although not statistically significant (P = 0.06), they were less often ex-smokers than 'never smokers'.

| Table 5           | Level of disease control according to 'w | vorst category' vs. medica | al treatment: number of asthma patients |
|-------------------|--|----------------------------|---|
| ( <i>n</i> = 661) | ).                                       |                            |   |

| Disease control                    | Medical treatment     |                 |                         |                       |                |  |  |
|------------------------------------|-----------------------|-----------------|-------------------------|-----------------------|----------------|--|--|
|                                    | Step 0                | Step 1          | Step 2ª                 | Step 3                | Step 4         |  |  |
| Good disease control               | 100 <sup>c</sup>      | 49 <sup>c</sup> | 73 (+33) <sup>c</sup>   | 6 <sup>c</sup>        | 1 <sup>c</sup> |  |  |
| Mildly reduced disease control     | 3 <sup>d</sup>        | 25 <sup>d</sup> | 32 (+12) <sup>d</sup>   | 10 <sup>d</sup>       | 2 <sup>f</sup> |  |  |
| Moderately reduced disease control | 28 <sup>d</sup>       | 35 <sup>d</sup> | 100 (+27) <sup>d</sup>  | 39 <sup>e</sup>       | 6 <sup>f</sup> |  |  |
| Poor disease control               | <b>9</b> <sup>d</sup> | 11 <sup>d</sup> | 40 (+11) <sup>b,e</sup> | <b>9</b> <sup>e</sup> | 0 <sup>f</sup> |  |  |

<sup>a</sup> Corticosteroids used 'when necessary' are considered as Step 2 care, but are showed separately in parenthesis. <sup>b</sup> Of these patients, eight use corticosteroid when necessary and three use long-acting  $\beta$ 2-agonists only.

<sup>c</sup> n = 262.

<sup>d</sup> *n* = 292.

<sup>e</sup> *n* = **99**.

 $^{f} n = 8.$ 

 
 Table 6
 Bivariate multinomial logistic regression analyses with different groups according to disease control and
 medical treatment (see Tables 2 and 5) as the dependent variable (good asthma control is reference group) and characteristics as the independent variables.

|   | Patient groups (reference group: good asthma control)                                  |   |  |  |  |
|---|--|---|--|--|--|
|   | Inadequate disease control:<br>change in treatment required;<br>OR (95% CI), $n = 292$ | Inadequate disease control:<br>adequate control might not be<br>achieved; OR (95% CI), $n = 99$ |  |  |  |
| Age ≥45 years (reference: <45 years)<br>Male gender (reference: female)   | 2.14 (1.44–3.19)<br>0.90 (0.60–1.33)   | 3.50 (2.07–5.91)<br>0.79 (0.47–1.33)  |  |  |  |
| Educational level<br>Low (reference: high)<br>Medium  | 5.06 (2.02–12.68)<br>1.38 (0.91–2.09)  | 12.41 (4.51–34.13)<br>1.57 (0.87–2.84)  |  |  |  |
| Co-morbidity<br>Present (reference: not present)<br>Missing   | 1.31 (0.86–1.98)<br>0.78 (0.33–1.84)   | 2.14 (1.25–3.66)<br>2.61 (1.03–6.60)  |  |  |  |
| Smoking status<br>Ex (reference: never smoker)<br>Current<br>Missing  | 1.04 (0.65–1.65)<br>1.49 (0.89–2.48)<br>0.86 (0.39–1.91)                               | 0.67 (0.35–1.29)<br>1.53 (0.81–2.89)<br>1.41 (0.56–3.54)  |  |  |  |
| Presence of chronic cough<br>(reference: not present)<br>Presence of sputum production<br>(reference: not present)              | 1.50 (1.00–2.26)<br>1.56 (1.02–2.40)   | 2.35 (1.40–3.95)<br>2.61 (1.53–4.44)  |  |  |  |
| Wheeze<br>Ever (reference: never)<br>Most days/nights   | 1.51 (0.89–2.58)<br>3.61 (1.69–7.70)   | 1.03 (0.52–2.02)<br>2.91 (1.17–7.19)  |  |  |  |
| Dyspnea<br>Grade 1 (reference: Grade 0)<br>Grade 2<br>Grade 3   | 1.50 (0.95–2.39)<br>2.00 (0.91–4.37)<br>3.59 (1.96–6.60)                               | 2.04 (1.05–3.93)<br>2.80 (1.00–7.82)<br>8.09 (3.90–16.81)                                       |  |  |  |
| Allergy<br>Present (reference: not present)<br>Missing  | 0.79 (0.52–1.20)<br>0.43 (0.21–0.85)   | 0.40 (0.24–0.69)<br>0.34 (0.14–0.84)  |  |  |  |
| Age at onset of pulmonary<br>complaints ≥26 years<br>(reference: <26 years)   | 0.93 (0.63–1.36)   | 1.16 (0.70–1.92)  |  |  |  |
| Compliance <sup>a</sup><br>Not compliant (reference: compliant)<br>Missing  | 1.14 (0.65–1.98)<br>1.10 (0.65–1.87)   | 0.51 (0.28–0.95)<br>0.12 (0.06–0.25)  |  |  |  |
| Inhalation technique <sup>b</sup><br>Poor (reference: good)<br>Missing  | 1.17 (0.63–2.19)<br>1.35 (0.89–2.04)   | 1.72 (0.78–3.79)<br>1.71 (0.99–2.97)  |  |  |  |
| HRQoL <sup>c</sup><br>Poor, score $\geq$ 13 (reference: score <13)<br>Missing<br>Odds Ratios (ORs) are presented ( $n = 653$ ). | 4.05 (2.63–6.23)<br>2.22 (1.11–4.45)   | 6.21 (3.45–11.17)<br>3.71 (1.53–9.04)   |  |  |  |

Odds Ratios (ORs) are presented (n = 653). <sup>a</sup> Assessed for use of inhaled corticosteroids or cromoglycates only.

 $^{\rm b}\,{\rm Not}$  assessed in the northwest of The Netherlands.

<sup>c</sup> A higher score means poorer HRQoL.

**Table 7** Multivariate multinomial logistic regression analyses with different groups according to disease control and medical treatment (see Tables 2 and 5) as the dependent variable (good asthma control is reference group) and characteristics as the independent variables<sup>a</sup>.

|   | Patient groups (reference group: good asthma control)                                  |   |  |  |  |
|---|--|---|--|--|--|
|   | Inadequate disease control:<br>change in treatment required;<br>OR (95% CI), $n = 292$ | Inadequate disease control:<br>adequate control might not be<br>achieved; OR (95% CI), $n = 99$ |  |  |  |
| Age $\geq$ 45 years (reference: <45 years)                                  | 2.30 (1.38–3.85)   | 3.57 (1.63–7.82)  |  |  |  |
| Educational level<br>Low (reference: high)<br>Medium                        | 2.86 (1.06-7.72)<br>1.36 (0.87-2.11)   | 9.20 (2.64–32.06)<br>1.16 (0.58–2.31)   |  |  |  |
| Smoking status<br>Ex (reference: never smoker)<br>Current<br>Missing        | -<br>-<br>-  | 0.46 (0.21–1.03)<br>1.49 (0.68–3.25)<br>1.12 (0.35–3.55)  |  |  |  |
| Presence of sputum production<br>(reference: not present)                   | -  | 2.30 (1.20-4.40)  |  |  |  |
| Wheeze<br>Ever (reference: never)<br>Most days/nights                       | 1.62 (0.91–2.87)<br>2.76 (1.39–7.15)   |   |  |  |  |
| Dyspnea<br>Grade 1 (reference: Grade 0)<br>Grade 2<br>Grade 3               | 1.41 (0.86–2.29)<br>1.40 (0.61–3.21)<br>2.94 (1.55–5.58)                               | 1.64 (0.78–3.44)<br>0.84 (0.24–2.92)<br>6.51 (2.84–14.96)                                       |  |  |  |
| Age at onset of pulmonary<br>complaints ≥26 years<br>(reference: <26 years) | 0.53 (0.33–0.87)   | 0.35 (0.16–0.74)  |  |  |  |

Odds Ratios (ORs) are presented (n = 653).

<sup>a</sup> No association is found with age, co-morbidity, chronic cough, allergy, complianc, inhalation technique. HRQoL is not included in the multivariate model.

#### Discussion

This study proposes a model to define the level of disease control in adult asthma patients in conjunction with the level of medical treatment, in order to assess which patients are inadequately controlled and which of these patients might benefit from changing treatment. Applying this model to asthma patients from Dutch general practices participating in an observational study on the course of asthma, it appeared that a substantial proportion of asthma patients was inadequately controlled. Approximately 60% had mildly reduced to poor disease control, of whom 73% might benefit from changing treatment, while only 2% were already maximally treated. Compared to patients with good disease control, patients inadequately controlled were usually older, less well educated, younger at onset of pulmonary complaints, and in addition had more severe dyspnea and poorer health-related quality of life.

Since no consensus exists on the assessment of disease control, we used the classification rules of the Expert Panel Report II [11]. Although these classification rules are not validated, they are widely accepted for categorising disease severity. Despite the fact that the Expert Panel Report II did not include the use of  $\beta$ 2-agonists, we, as well as others [12,14,15], believe that this variable is a relevant marker of disease control. As explained well by Colice et al. [12], as asthma worsens, patients could either experience more troublesome symptoms or use  $\beta$ 2-agonists more regularly. Furthermore, excessive use of  $\beta$ 2-agonists combined with under-use of corticosteroids is found to result in greater asthma related morbidity [15,16]. The model used to define disease control in this study (combining several parameters and then using the worst categorisation) maximises the identification of treatment inadequacy. So although treatment might have partly been effective in terms of improvement of some parameters, it is regarded as

inadequate until all parameters are improved. Like Colice et al. [12], we found a poor correlation between individual variables in categorising the level of disease control in asthma patients, supporting the fact that all variables are important for categorisation of disease control. The poor association between pulmonary function and respiratory symptoms in asthma patients [2], furthermore supports the assumption that all aspects of disease control should be taken into account in the assessment of disease control. A patient with normal pulmonary function who has severe respiratory complaints? to the extent that he or she regularly awakes at night and/or is forced to refrain from his or her normal activities, should not be regarded as well controlled based on pulmonary function alone. However, whether or not the model we used to define disease control is too strict, implying that the number of patients inadequately treated is overestimated, is for the reader to decide.

A part (15%) of the asthma patients included in this study appeared to have good disease control while they did not use anti-asthma medication. These patients did not differ, besides the fact that they were more often male, from asthma patients with good asthma control using anti-asthma medication. It is possible that some patients are falsely labelled as asthma; however, since asthma is characterised by periodical complaints, it seems more likely that these patients had no complaints at the time of data collection.

The finding that a substantial proportion of patients with asthma may be inadequately controlled is supported by others in various countries and time periods [1,14,17–20]. Selection bias may have affected our results in two ways. Firstly, excluded patients tended to use less medication than included patients. It seems, therefore, likely that participating patients were less healthy than not participating patients, thus resulting in an overestimation of the number of patients inadequately controlled. Secondly, it is possible that participating practices were more motivated to provide good care for their patients, resulting in an underestimation of the number of inadequately controlled patients in the general population.

Besides global disease severity and level of medical treatment, other factors such as patients' compliance with the use of medication, inhalation technique, and patients' behaviour in avoiding environmental exposure, influence the level of disease control in asthma patients. Bivariate analyses show that compliant patients are more often patients in which adequate control might not be achieved as concluded by the large discrepancy between medication use and disease control. Dekker et al. [21] found that compliant patients had daily symptoms more often than non-compliant patients. A plausible explanation is that the presence of symptoms motivates patients to be more compliant. However, this study uses self-report of compliance which may well provide an overestimation of compliance [22]. Hypothesising that over-estimating compliance is related to over-reporting medication use might explain why compliant patients have inadequate disease control despite the fact that they report that they use medication.

Under-reporting of symptoms may be a reason why asthma patients are not adequately controlled. In a large survey in Europe [1] it was found that approximately 50% of asthma patients who reported severe persistent symptoms considered their asthma to be completely or well controlled. Consequently, a physician should take an active role in assessing symptoms of asthma, instead of waiting for them to be spontaneously mentioned [23]. It should, however, be noted that some patients may have preferred to accept symptoms at the level at which they are experienced rather than take additional treatment. In addition, some patients may previously have tried more intensive treatment and found it inadequate. Patient's dissatisfaction with asthma treatment is found to be associated with poor disease control, problems with the process of care, and problems related to patients' belief in their medication. More personal care may improve satisfaction and also disease control [24].

It is thought that anywhere between 1 and 15% of asthma patients have severe asthma responding poorly to anti-asthmatic drugs [25]. This is in accordance with results from our study; 8 (1.2%) patients had poorly controlled asthma despite maximal treatment and an additional 99 (15%) patients were defined as under-treated patients in which adequate control might not be achieved by increasing treatment.

The level of disease control may determine, in conjunction with other patient factors, the healthrelated quality of life (HRQoL) of a patient. This is confirmed in our analyses as HRQoL is strongly associated with the inadequate control. Also others [26] found disease control in asthma patients to be associated with HRQoL.

The finding that older age is associated with inadequate control of asthma, might be explained by the finding that older patients generally have a more blunted perception of their pulmonary obstruction [27–29]. In addition, Weiner et al. [29] report that particularly older patients with long-standing disease had less pulmonary complaints irrespective of the level of pulmonary obstruction. This supports our finding that a younger age at onset of pulmonary complaints is associated with inadequate control after adjusting for other variables such as age. The fact that reporting more severe dyspnea was associated with inadequate control is not really surprising, but it does support the use of a short validated questionnaire to assess dyspnea as a sensitive instrument to identify patients with inadequate asthma control. The finding that patients with a lower educational level are more often inadequately controlled is in accordance with Watts et al. [30] who found that asthma patients in the lower social class were less likely to fill their prescriptions compared to other groups, possibly due to financial difficulties, disagreement with diagnosis, or lack of understanding. Poorer environmental conditions or reduced capability of adequate self-management might be additional explanations.

In conclusion, a substantial proportion of asthma patients primarily treated in general practice were inadequately controlled according to our criteria. Assessing patients' disease control together with the level of medical treatment may help to gain insight into the effectiveness of current disease management. Improving disease control in asthma patients is likely to improve the health-related quality of life of these patients.

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