



Predictors of asthma control: what can we modify?

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Purpose of review

One strategy to improve asthma control is to identify risk factors for uncontrolled asthma in epidemiologic studies and then consider those risk factors as potential targets for intervention. This article reviews predictors of impairment based on validated tools and predictors of severe asthma exacerbations.

Recent findings

Indirectly modifiable risk factors for poor asthma control include older age in adults, lower socioeconomic status, and poor perception of dyspnea. Modifiable risk factors for poor asthma control include allergy triggers, low adherence, comorbidities, absence of specialty care, and various aspects of asthma self-management education.

Summary

Intervention strategies are suggested for predictors that are directly or indirectly modifiable. It is hoped that attention to these factors will improve asthma control and reduce the burden of disease.

Keywords

asthma control, asthma exacerbations, asthma impairment, asthma risk, predictors, validated asthma control tools

INTRODUCTION

In spite of advances in the field, most population surveys show that asthma remains inadequately controlled in 40% or more of patients [1,2,3^a,4^a]. One strategy to improve asthma control is to identify risk factors for uncontrolled asthma in epidemiologic studies and then consider those risk factors as potential targets for intervention. Ideally, the efficacy and effectiveness of those interventions would be confirmed in randomized controlled trials.

Asthma control has been defined to encompass two domains: impairment and risk. Impairment is the frequency and intensity of symptoms and functional limitations the patient is experiencing currently or has recently experienced [5]. Risk includes the risk of future adverse events, especially asthma exacerbations [5]. Studies addressing predictors of asthma control have generally evaluated either impairment or exacerbations, but not both.

The literature addressing asthma impairment has used various definitions of asthma control. Many of the studies have used validated asthma control tools to assess impairment. This review is limited to studies that have used validated tools to assess asthma impairment as those tools provide a standardized approach to measure impairment in epidemiologic studies.

As this review focuses on studies that use asthma control tools to define impairment, it is useful to review the characteristics of these tools. Asthma control tools have been defined as single questionnaires (with or without physiologic measures) designed to measure the multidimensional construct of asthma control, which comprises more than just asthma symptoms and frequency of rescue therapy use [6]. Validation information for at least 17 different asthma control score instruments have been published, with the Asthma Control Test (ACT) and Asthma Control Questionnaire (ACQ) being the most extensively used and validated [6]. The content of all of the validated asthma control score instruments is similar and includes symptom frequency, rescue therapy use, nocturnal symptoms or interference with sleep, and activity limitation [6].

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KEY POINTS

- Predictors of asthma impairment and risk include nonmodifiable demographic factors and asthma severity.
- Modifiable predictors of asthma impairment include smoking, obesity, low adherence, comorbidities (rhinitis, sinusitis, reflux, anxiety–depression), and absence of specialty care.
- Additional modifiable predictors of asthma risk include allergy triggers, absence of an action plan, lack of self-management education, incorrect inhaler technique, and environmental tobacco smoke exposure.
- Addressing these modifiable risk factors should improve asthma control.

Exacerbations have been defined in the most recent national guidelines as episodes of increased asthma requiring systemic corticosteroids [5]. However, the most common outcomes in population studies addressing risk factors for exacerbations have been asthma emergency department (ED) visits or hospitalizations, which generally represent more severe exacerbations that can be more consistently and specifically identified in population studies. This review is thus limited to studies in which exacerbations have been defined as ED visits or hospitalizations for asthma.

Although asthma impairment and asthma risk are considered two separate domains of asthma control, there are data suggesting they are related to each other. For example, we have recently studied this relationship in 2680 Southern California Kaiser Permanente patients [7]. These patients completed a questionnaire by mail in the fall of 2007 that included the ACT and a history of exacerbations in the prior year. Relationships were assessed between subsequent exacerbations during 2008, captured using administrative data, and baseline ACT and exacerbation history. Both the ACT and

prior exacerbations were related to subsequent exacerbations in bivariate analyses and were independently related in multivariable analyses considering both predictors (Table 1). Because current impairment is related to future risk, we have identified risk factors for poorly controlled asthma in this review as those related to either impairment, risk, or both.

PREDICTORS OF IMPAIRMENT

Two representative studies have evaluated predictors of asthma impairment. We studied 570 adults aged 35 and older from Colorado Kaiser Permanente who completed a mailed questionnaire containing the ACT to define uncontrolled asthma (score < 20) and various self-reported potential risk factors (Table 2) [8]. Of the demographic risk factors assessed, lower education and lower income, but not age, sex, or race/ethnicity, were related to the likelihood of uncontrolled asthma. Four comorbidities (smoking, elevated BMI, concomitant diagnosis of chronic obstructive pulmonary disease (COPD), and reflux disease) increased the risk of uncontrolled asthma. In bivariate analyses, disease severity as assessed by oral corticosteroids in the past four weeks or asthma hospitalization in the past year were related to an increased risk of uncontrolled asthma based on impairment, but not management characteristics such as regular inhaled corticosteroid use, possession of a written action plan, and regular specialist care. In multivariate analysis (Table 3), independent predictors of ACT score included (in order of strength of contribution to the observed variability) oral corticosteroid requirement in the prior month, coexistent COPD, lack of regular specialist care, higher BMI, gastroesophageal reflux disease, nonwhite race and low income. It is of interest that regular specialist care did not emerge as a predictor in unadjusted analysis. This is probably because specialists manage patients with more severe asthma and more comorbidities, and the role of specialist care in improving outcomes could

Table 1. Relationship of impairment, as measured by Asthma Control Test, to subsequent risk (exacerbations)^a

2007 Predictor	2008 Exacerbations		
	Bivariate: proportion with exacerbations		Multivariable: OR (95% CI) for exacerbations
	Predictor present	Predictor absent	
ACT ≤ 16	31.4%**	20.0%	1.3 (1.1–1.5)
Prior exacerbation	33.7%**	14.6%	2.2 (1.9–2.5)

ACT, Asthma control test; CI, confidence interval; OR, Odds ratio.
^aData from Schatz *et al.* [7].
***P* < 0.0001.

Table 2. Predictors of impairment (Asthma Control Test less than 20) in US study: bivariate analyses^a

Predictor category	Significant relationship (<i>P</i> value)	No significant relationship
Demographic characteristics	Education (<i>P</i> = 0.0002)	Age
	Income (<i>P</i> = 0.0002)	Sex
		Race/ethnicity
Comorbidities	Smoking (<i>P</i> = 0.003)	Allergy/sinus disease
	BMI (<i>P</i> < 0.0001)	
	COPD (<i>P</i> < 0.0001)	
	Reflux (<i>P</i> = 0.0006)	
Severity	Oral corticosteroids in past 4 weeks (<i>P</i> < 0.0001)	–
	Hospitalization past year (<i>P</i> = 0.0009)	
Management characteristics	–	Regular inhaled corticosteroids
		Written action plan
		Regular asthma specialist care

COPD, chronic obstructive pulmonary disease.

^aData from Schatz *et al.* [8].

only be identified when adjusting for these factors (Table 3).

The other study [9] that identified a number of predictors of asthma impairment was a larger European internet-based survey study of 2337 adults aged 18 and older from France, Germany, Italy and the United Kingdom. The survey included the ACT, validated adherence questions (Morisky Medication Adherence Scale), and various other self-reported predictors. Demographic characteristics associated with asthma impairment based on ACT included older age and less education (Table 4). Comorbidities that increased the risk of uncontrolled asthma were obesity and smoking, as in the United States study described above, as well as depression. Various markers of asthma severity

and increased utilization increased the risk, as did reduced self-reported medication adherence. Duration of asthma did not increase the risk of uncontrolled asthma in this study.

Besides predictors identified in these two studies, other predictors of asthma impairment demonstrated in other studies include female sex, coexistent rhinitis or sinusitis, low vitamin D levels, and limited language proficiency. All identified predictors of asthma impairment are listed in Table 5 (10–62).

PREDICTORS OF EXACERBATIONS

A number of predictors of exacerbations are similar to those identified for impairment, such as older age, female sex, lower socioeconomic status (SES) (education and income), minorities, limited language proficiency, increased disease severity, low adherence, smoking, obesity, rhinitis, sinusitis, reflux, anxiety–depression, and absence of specialty care (Table 5). In addition, certain risk factors unique to exacerbations have been identified, such as low perception of dyspnea, pregnancy, diabetes, allergy sensitization or triggers, absence of an action plan, incorrect use of inhalers, lack of self-management education, and environmental tobacco smoke exposure (Table 5).

INTERVENTIONS

Some of the risk factors identified cannot be modified, such as certain demographic characteristics, disease severity (including prior exacerbations), and some comorbidities (diabetes, pregnancy) (Table 5). In this case, only increased surveillance

Table 3. Predictors of impairment (Asthma Control Test score) in US study: significant predictors in multivariable analyses^a

Variable	Partial <i>R</i> square ^b	<i>P</i> value
Oral steroid	0.10	<0.0001
COPD	0.05	<0.0001
No specialist care	0.02	0.006
Higher BMI	0.02	0.01
Reflux disease	0.01	0.02
Nonwhite race	0.01	0.04
Low income	0.01	0.04

COPD, chronic obstructive pulmonary disease.

^aData from Schatz *et al.* [8]. All predictors in Table 2 offered as candidate predictors in step-wise linear regression.^bHigher number indicates more contribution to prediction.

Table 4. Predictors of impairment (ACT < 20) in European study^a

Predictor category	Significant relationship (<i>P</i> value)	No significant relationship
Demographic characteristics	Older age (<i>P</i> < 0.001) Less education (<i>P</i> < 0.001)	Sex Marital status
Comorbidities	Smoking (<i>P</i> = 0.003) Obesity (<i>P</i> < 0.0001) Depression (<i>P</i> < 0.001)	–
Severity and utilization	Higher asthma severity classification (<i>P</i> < 0.001) Number of provider visits past 6 months (<i>p</i> , 0.001) ED visits past 6 months (<i>P</i> < 0.001)	–
Other	Reduced adherence (<i>P</i> = 0.015)	Duration of asthma

ED, emergency department.

^aData from Demoly *et al.* [9].**Table 5. Summary of predictors of asthma impairment or risk identified in the literature**

Predictor	References for predictors		Comment
	Impairment (validated tools)	Risk (ED visits or hospitalizations)	
Not modifiable			Increased surveillance
Women	[10–15]	[16]	
Minorities	[17–19]	[16,20]	
Increased disease severity	[10,19,21–23]	[16,20,24–28]	
Prior exacerbations	[8,9]	[16,20,26,29–34]	
Diabetes	–	[35]	
Pregnancy	–	[35]	
Indirectly modifiable			
Older age (adults)	[15,23,36]	[37,38]	Consider cognitive or physical impairment in management
Lower socioeconomic status	[18,19,21,23,39–41]	[16,20,33]	Environmental or educational intervention
Low perception of dyspnea	–	[16]	Home PEFr monitoring
Modifiable			
Smoking	[17,19,21,23,39,42–44]	[16,44,45]	
Obesity	[10,15,19,23,46,47]	[16,35,48,49]	
Allergy sensitivity/trigger	–	[16,31]	
Low adherence	[24,39]	[50,51]	
Rhinitis	[14,52,53]	[16,28,54]	
Sinusitis	[18]	[38]	
Reflux	[18,19,55]	[16,35]	
Anxiety/depression	[15,23,56–58]	[16,35]	
Low vitamin D	[59]	–	
Limited language proficiency	[60]	[60]	
Absence of specialty care	[19,61]	[16]	
Absence of action plan	–	[16,33]	
Incorrect use of inhaler	–	[16]	
Lack of self-management education	–	[16,32]	
Environmental tobacco smoke exposure	–	[16,62]	

PEFR, peak expiratory flow rate.

and optimal use of standard therapy can be recommended to improve asthma control.

Other risk factors are not directly modifiable, but may be indirectly modifiable in that characteristics potentially associated with the risk factor may be addressed in spite of not being able to influence the risk factor itself. For example, management that takes into account cognitive or physical disabilities (e.g. choices of educational techniques, monitoring regimen, or inhaler devices) may reduce asthma impairment and risk in older individuals. Educational or environmental interventions may increase the likelihood of achieving control in lower SES patients. Home peak flow monitoring may reduce the risk of exacerbations in patients with low perception of dyspnea.

The remaining risk factors appear to be at least potentially modifiable. It should be recognized, though, that these predictors were identified in observational studies and that these types of associations do not prove cause and effect relationships. Some of the recommended interventions have been shown to be effective in randomized controlled trials. However, most of the other identified modifiable risk factors still seem to be worth addressing, pending confirmation of their efficacy or effectiveness in randomized controlled trials.

Interventions suggested by the modifiable risk factors identified in this review can be summarized in various categories (Table 6). Of course, regular visits and assessment of control (both impairment

and risk) are necessary to determine that control is being achieved and maintained. Self-management education and a written action plan should improve asthma control. Optimal controller therapy is an important aspect of achieving asthma control, including assuring optimal inhaler technique, adherence assessment, and improvement of adherence, if needed. Effective management of a number of comorbidities has been shown to or should reduce asthma impairment and risk. Addressing allergy triggers by environmental control and/or immunotherapy and specialty care have been shown to improve asthma control. Reducing environmental tobacco smoke exposure appears to be worth doing, although efficacy data from randomized controlled trials are lacking. Further studies will be necessary to show that normalizing vitamin D levels improve asthma control.

SUMMARY

In summary, a number of predictors of uncontrolled asthma (impairment and/or risk domains) have been identified in epidemiologic studies. Most of these predictors are potentially indirectly or directly modifiable. Attention to these factors should improve asthma control and reduce the burden of disease.

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Conflicts of interest

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REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 333).

1. Fuhlbrigge A, Reed ML, Stempel DA, *et al.* The status of asthma control in the US adult population. *Allergy Asthma Proc* 2009; 30:529–533.
 2. Mintz M, Gilsenan AW, Bui CL, *et al.* Assessment of asthma control in primary care. *Curr Med Res Opin* 2009; 25:2523–2531.
 3. Haselkorn T, Chen H, Miller DP, *et al.* Asthma control and activity limitations: insights from the Real-world Evaluation of Asthma Control and Treatment (REACT) study. *Ann Allergy Asthma Immunol* 2010; 104:471–477.
- This is a recent population-based survey of asthma control.
4. Liu AH, Gilsenan AW, Stanford RH, *et al.* Status of asthma control in pediatric primary care: results from the pediatric Asthma Control Characteristics and Prevalence Survey Study (ACCESS). *J Pediatr* 2010; 157:276–281.
- This is a recent population-based survey of asthma control in children.
5. National Asthma Education and Prevention Program Expert Panel Report 3. Guidelines for the diagnosis and management of asthma. Summary Report 2007. *J Allergy Clin Immunol* 2007; 120:S93–S138.
 6. Cloutier MM, Schatz M, Castro M, *et al.* Asthma outcomes: Composite scores of asthma control. *J Allergy Clin Immunol* 2012; 129 (3 Suppl):S24–S33.

Category	Intervention
Surveillance and education	Follow-up visits with assessment of control
	Home peak flow monitoring if indicated
	Self-management education
Pharmacologic management	Action plan
	Optimal controller therapy
	Consider physical or cognitive impairment
Comorbidities	Optimize inhaler technique
	Adherence assessment and improvement if needed
	Address smoking, obesity, rhinitis, sinusitis, reflux, anxiety/depression
Other	Address allergy triggers (environmental control, immunotherapy)
	Reduce environmental tobacco smoke exposure
	Specialty care

7. Schatz M, Zeiger RS, Yang S-J, *et al*. The relationship of asthma impairment determined by psychometric tools to future asthma exacerbations. *Chest* 2012; 141:66–72.
8. Schatz M, Mosen DM, Kosinski M, *et al*. Predictors of asthma control in a random sample of asthmatic patients. *J Asthma* 2007; 44:341–345.
9. Demoly P, Paggiaro P, Plaza V, *et al*. Prevalence of asthma control among adults in France, Germany, Italy, Spain and the UK. *Eur Respir Rev* 2009; 18:105–112.
10. Laforest L, Van Ganse E, Devouassoux G, *et al*. Influence of patients' characteristics and disease management on asthma control. *J Allergy Clin Immunol* 2006; 117:1404–1410.
11. Lee JH, Haselkorn T, Chipps BE, *et al*. Gender differences in IgE-mediated allergic asthma in the epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) study. *J Asthma* 2006; 43:179–184.
12. Braido F, Balardini I, Ghiglione V, *et al*. Sleep disturbances and asthma control: a real life study. *Asian Pac J Allergy Immunol* 2008; 26:27–33.
13. Rodrigo GJ, Arcos JP, Nannini LJ, *et al*. Reliability and factor analysis of the Spanish version of the Asthma Control Test. *Ann Allergy Asthma Immunol* 2008; 100:17–22.
14. Braido F, Baiardini I, Balestracci S, *et al*. Does asthma control correlate with quality of life related to upper and lower airway real life study. *Allergy* 2009; 64:937–943.
15. Di Marco F, Verga M, Santus P, *et al*. Close correlation between anxiety, depression, and asthma control. *Respir Med* 2010; 104:22–28.
16. Schatz M. Outcome measures in asthma management. In: Pawanker R, Holgate ST, Rosenwasser LJ, editors. *Allergy frontiers: diagnosis and health economics*. Tokyo: Springer, 2009, p. 507.
17. LeNoir M, Williamson A, Stanford RH, Stempel DA. Assessment of asthma control in a general population of asthmatics. *Curr Med Res Opin* 2006; 22:17–22.
18. Peters SP, Jones CA, Hasselkorn T, *et al*. Real-world Evaluation of Asthma Control and Treatment (REACT): findings from a national web-based survey. *J Allergy Clin Immunol* 2007; 119:1454–1461.
19. Schatz M, Mosen DM, Kosinsky M, *et al*. Predictors of asthma control in a random sample of asthmatic patients. *J Asthma* 2007; 44:341–345.
20. Walsh-Kelly CM, Kelly KJ, Drendel AL, *et al*. Emergency department revisits for pediatric acute asthma exacerbations. *Ped Emerg Care* 2008; 24:505–510.
21. de Vries MP, van den Bemt L, Lince S, *et al*. Factors associated with asthma control. *J Asthma* 2005; 42:659–665.
22. Mehuys E, Bortel LV, Annemans L, *et al*. Medication use and disease control of asthmatic patients in Flanders: a cross-sectional community pharmacy study. *Respir Med* 2006; 100:1407–1414.
23. Lim KG, Patel AM, Naessens JM, *et al*. Flunking asthma? When HEDIS takes the ACT. *Am J Manag Care* 2008; 14:487–494.
24. Meng Y-Y, Babey SH, Brown ER, *et al*. Emergency department visit for asthma: the role of frequent symptoms and delay in care. *Ann Allergy Asthma Immunol* 2006; 96:291–297.
25. Federico MJ, Wamboldt FS, Carter R, *et al*. History of serious asthma exacerbations should be included in guidelines of asthma severity. *J Allergy Clin Immunol* 2007; 119:50–56.
26. Miller MK, Lee JH, Miller DP, Wenzel SE. Recent asthma exacerbations: a key predictor of future exacerbations. *Respir Med* 2007; 101:481–489.
27. Kwong KYC, Morpew T, Scott L, *et al*. Asthma control and future asthma-related morbidity in inner-city asthmatic children. *Ann Allergy Asthma Immunol* 2008; 101:144–152.
28. Brandao HV, Cruz CS, Pinheiro MC, *et al*. Risk factors for ER visits due to asthma exacerbations in patients enrolled in a program for the control of asthma and allergic rhinitis in Feira de Santana, Brazil. *J Bras Pneumol* 2009; 35:1168–1173.
29. Mudd K, Bollinger ME, Hsu VD, *et al*. Pharmacy fill patterns in young children with persistent asthma. *J Asthma* 2006; 43:597–600.
30. Miller MK, Lee JH, Blanc PD, *et al*. TENOR risk score predicts healthcare in adults with severe or difficult-to-treat asthma. *Eur Resp J* 2006; 28:1145–1155.
31. Osborne ML, Pedula KL, O'Hollaren M, *et al*. Assessing future need for acute care in adult asthmatics: the profile of asthma risk study: a prospective health maintenance organization-based study. *Chest* 2007; 132:1151–1161.
32. To T, Wang C, Dell S, *et al*. Risk factors for repeat adverse asthma events in children after visiting an emergency department. *Ambul Pediatr* 2008; 8:281–287.
33. Ungar WJ, Paterson JM, Gomes T, *et al*. Relationship of asthma management, socioeconomic status, and medication insurance characteristics to exacerbation frequency in children with asthma. *Ann Allergy Asthma Immunol* 2011; 106:17–23.
34. Rabito FA, Carlson J, Holt EW, *et al*. Cockroach exposure independent of sensitization status and association with hospitalizations for asthma in inner-city children. *Ann Allergy Asthma Immunol* 2011; 106:103–109.
35. Guo JJ, Tsai K, Kelton CML, *et al*. Risk of serious asthma exacerbations associated with long-acting beta agonists among patients with asthma: A retrospective cohort study. *Ann Allergy Asthma Immunol* 2011; 106:214–222.
36. Talreja N, Baotist AP. Effect of age on asthma control: results from the National Asthma Survey. *Ann Allergy Asthma Immunol* 2011; 106:24–29.
37. Laumann JM, Bjornson DC. Treatment of Medicaid patients with asthma: comparison of treatment guidelines using disease-based drug utilization review methodology. *Ann Pharmacother* 1998; 32:1290–1294.
38. Bavec S, Celik G, Demirel YS, Misirligil Z. Risk factors associated with hospitalizations for asthma attacks in Turkey. *Allergy Asthma Proc* 2003; 24:437–442.
39. Starobin D, Bargutin M, Rosenberg I, *et al*. Asthma control and compliance in a cohort of adult asthmatics: first survey in Israel. *IMAJ* 2007; 9:358–360.
40. Al-Jahdali HH, Al-Hajjaj MS, Alanezi MO, *et al*. Asthma control assessment using asthma control test among patients attending 5 tertiary care hospitals in Saudi Arabia. *Saudi Med J* 2008; 29:714–717.
41. Jones CA, Bender BG, Haselkorn T, *et al*. Predicting asthma control using patient attitudes toward medical care: the REACT study. *Ann Allergy Asthma Immunol* 2009; 102:385–392.
42. Schatz M, Zeiger RS, Drane A, *et al*. Reliability and predictive validity of the Asthma Control Test administered by telephone calls using speech recognition technology. *J Allergy Clin Immunol* 2007; 119:336–343.
43. Chauhuri R, McSharry C, McCoard A, *et al*. Role of symptoms and lung function in determining asthma control in smokers with asthma. *Allergy* 2008; 63:132–135.
44. Eisner MD, Iribarren C. The influence of cigarette smoking on adult asthma outcomes. *Nicotine Tob Res* 2007; 9:53–56.
45. Sharma HP, Matsui EC, Eggleston PA, *et al*. Does current asthma control predict future healthcare use among black preschool-aged inner-city children? *Pediatrics* 2007; 120:e1174–e1181.
46. Lavoie KL, Bacon SL, Labrecque M, *et al*. Higher BMI is associated with worse asthma control and quality of life but not asthma severity. *Respir Med* 2006; 100:648–657.
47. Mosen DM, Schatz M, Magid DJ, Camargo CA. The relationship between obesity and asthma severity and control in adults. *J Allergy Clin Immunol* 2008; 122:507–511.
48. Vargas PA, Perry TT, Robles E, *et al*. Relationship of body mass index with asthma indicators in Had Start children. *Ann Allergy Asthma Immunol* 2007; 99:22–28.
49. Peters AT, Klemens JC, Haselkorn T, *et al*. Insurance status and asthma-related healthcare utilization in patients with severe asthma. *Ann Allergy Asthma Immunol* 2008; 100:301–307.
50. Balkrishnan R, Christensen DB. Inhaled corticosteroid nonadherence and immediate avoidable medical events in older adults with chronic pulmonary ailments. *J Asthma* 2000; 37:511–517.
51. Williams LK, Pladevall M, Hugo X, *et al*. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 2004; 114:1288–1293.
52. Braido F, Baiardini I, Balestracci S, *et al*. The relationship between asthma control and quality-of-life impairment due to chronic cough: a real-life study. *Ann Allergy Asthma Immunol* 2008; 101:370–374.
53. Vandenplas O, Dramaix M, Joos G, *et al*. The impact of concomitant rhinitis on asthma-related quality of life and asthma control. *Allergy* 2010; 65:1290–1297.
54. Ponte EV, Franco R, Nascimento HF, *et al*. Lack of control of severe asthma is associated with co-existence of moderate-to-severe rhinitis. *Allergy* 2008; 63:564–569.
55. Cheung TK, Lam B, Lam KF, *et al*. Gastroesophageal reflux disease is associated with poor asthma control, quality of life, and psychological status in Chinese asthma patients. *Chest* 2009; 135:1181–1185.
56. Lavoie KL, Bacon SL, Barone S, *et al*. What is worse for asthma control and quality of life: Depressive disorders, anxiety disorders, or both? *Chest* 2006; 130:1039–1047.
57. Laforest L, Van Ganse E, Devouassoux G, *et al*. Factors influencing dispensing of psychotropic medications in patients with asthma: a community pharmacy-based survey. *Ann Allergy Asthma Immunol* 2008; 100:230–236.
58. Vieira AA, Santoro IL, Dracoulakis S, *et al*. Anxiety and depression in asthma patients: impact on asthma control. *J Bras Pneumol* 2011; 37:13–18.
59. Chinellato I, Piazza M, Sandri M, *et al*. Vitamin D serum levels and markers of asthma control in Italian children. *J Pediatr* 2011; 158: 437–441.
60. Wosniwsky JP, Kattan M, Evans D, *et al*. Assessing the relationship between language proficiency and asthma morbidity among inner-city asthmatics. *Med Care* 2009; 47:243–249.
61. Laforest L, Van Ganse E, Devouassoux G, *et al*. Management of asthma in patients supervised by primary care physicians or by specialists. *Eur Respir J* 2006; 27:42–50.
62. Gerald LB, Gerald JK, Gibson L, *et al*. Changes in environmental tobacco smoke exposure and asthma morbidity among urban school children. *Chest* 2009; 135:911–916.