

The paradox of adult asthma control: “Who’s in control anyway?”

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Surveys of Canadian patients with asthma and their physicians consistently report satisfaction with asthma management; however, when objective indicators are used, these same surveys also observe very poor levels of asthma control. The reasons for this apparent discrepancy, with an emphasis on the factors influencing adherence to therapy, are explored in the present review. Clues to the identification of patients at risk of dying from asthma and an approach to difficult asthma are discussed.

Key Words: *Adherence; Asthma; Asthma control*

Despite an increasing prevalence of asthma, death from asthma in Canada is reported to be decreasing (1). On the other hand, despite that clinical trials of asthma medications consistently demonstrate positive results as measured by reduced frequency of exacerbations, fewer symptoms and improved quality of life (2,3), national and international surveys continue to indicate that the majority of adults with asthma have poorly controlled disease (4-6). What is the explanation for this apparent paradox of asthma control?

Several years ago, the landmark survey ‘Asthma in Canada’ (5) indicated that notwithstanding the availability of excellent asthma medications and management strategies, 57% of Canadians with asthma had failed to meet the Canadian Thoracic Society definition of asthma ‘control’ (Table 1) (7). The situation has hardly improved, because the recent The Reality of Asthma Control (TRAC) study of 893 patients with asthma indicated that 53% of the patients still had poorly controlled asthma (4). Also recently completed is the Global Asthma Physician and Patient (GAPP) survey (6), in which over 1700 adult patients with asthma (102 Canadians) and over 1700 physicians (100 Canadians) from 16 countries were interviewed, and the results were again depressing. Although the survey observed that most Canadian physicians felt that they were managing asthma in a manner consistent with the Canadian Asthma Consensus Guidelines (7), nearly 40% of the patients with asthma continued to experience limitations to their daily activities due to asthma, and 56% stated that they had required unscheduled

Le paradoxe de la maîtrise de l’asthme chez l’adulte : qui est maître de la situation, d’ailleurs?

D’après des enquêtes, les patients asthmatiques et les médecins traitants, au Canada, sont généralement satisfaits de la maîtrise de l’asthme; cependant, lorsqu’on utilise des indicateurs objectifs, on constate, dans ces mêmes enquêtes, que le degré de maîtrise de l’asthme est très faible. Les raisons de l’apparente contradiction, notamment les facteurs qui influent sur l’observance thérapeutique, font l’objet du présent examen. Il sera aussi question d’indices facilitant le repérage des patients susceptibles de succomber à l’asthme et d’une approche du traitement de l’asthme rebelle.

contact with a health care professional because of asthma, including calls to the doctor (19%), clinical visits (19%), emergency department visits (18%) and hospitalizations (4%). A consistent and puzzling observation is that all of these surveys suggest that both patients and their physicians seem to be unaware that there is a problem. For example, in the TRAC study, in which only 47% of patients with asthma met the Canadian definition of ‘control’, 97% of patients and 88% of their primary care physicians reported that the asthma was in fact well-controlled (4).

Thus, it appears that there is a significant and persisting disconnection between the excellent tools at our disposal for managing asthma and our success in achieving control over asthma for the majority of our patients. At least two questions come to mind. Is this apparent sorry state of affairs in fact true, and if so, why? On the other hand, is it possible that the reality of asthma control is actually better than our surveys tell us, and if that is indeed the case, why can we not see the truth? Perhaps the problem lies in the currently accepted asthma guideline definition of ‘control’, which, although logical, is completely arbitrary. Implicit in this definition, is the tacit assumption that it is acceptable, or even normal, for people with asthma to have symptoms from time to time, and even to have occasional (albeit ‘mild’) exacerbations; that is the nature of the disease, it cannot be cured and perfect control simply is not possible for most patients. While this opinion can be debated, it is nevertheless what the majority of both patients and physicians seem to believe.

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TABLE 1
Criteria for determining whether asthma is controlled, according to the Canadian Asthma Consensus Guidelines*

Daytime symptoms fewer than four days per week
Nighttime symptoms fewer than one night per week
Normal physical activity
Mild, infrequent exacerbations
No absenteeism due to asthma
Fewer than four doses per week of a fast-acting beta ₂ -agonist as needed†
Forced expiratory volume in 1 s or peak expiratory flow at 90% of their personal best or greater
Diurnal variability in peak expiratory flow of less than 10% to 15%

*Adapted from reference 7; †Apart from one dose per day before exercise

It is important to emphasize that control over asthma and asthma severity are largely independent issues. So-called mild asthma (as defined by near-normal lung function) can be associated with severe asthma exacerbations when patients fail to follow good asthma management practices (8), and even severe asthma (as defined by poor lung function) can be well-controlled for the majority, with due diligence to standard asthma management strategies and drugs (2,3). The TRAC study, for example, observed that the degree of asthma control did not predict the risk of an asthma flare-up because 95% of 'uncontrolled' and 82% of 'controlled' asthmatics experienced a period of worsening asthma symptoms during the preceding year (4).

Notwithstanding the potentially misleading 'optics' of asthma control, there must be a real problem, because surveys consistently demonstrate a high prevalence of unscheduled contact with physicians due to asthma problems (4-6). I find this fact and its apparent acceptance by patients and physicians as being 'normal' to be quite troublesome because it suggests an attitude of low expectations for what is achievable in asthma control with modern asthma management strategies. It is encouraging that in one insightful study, patients' satisfaction with asthma care fell by almost one-half once they were shown the asthma symptom management goals outlined in international asthma guidelines (9). In a recent Canadian study (10), physician awareness of the asthma control goals was improved with the simple practice of incorporating a stamp showing the control criteria into the patient's clinical chart.

Additional possible reasons for poor asthma control are listed in Table 2. The refractory nature of the disease despite good adherence to standard treatment is an issue for only a minority of people with asthma, usually older individuals who have had poorly managed asthma for years and now have 'remodelled' airways with fixed airflow obstruction (11-13). We do not as yet have perfect asthma medications, but modern therapeutics are capable of controlling asthma for the vast majority of patients, and new innovations, such as the combination of a long-acting beta₂-agonist (LABA) with a powerful inhaled corticosteroid (ICS) (2,3), anti-immunoglobulin E therapy (14), or the use of old or newer theophyllines (15,16), may provide additional help for some patients. While access to several different brands of asthma medication permits more choice, competing corporate agendas

TABLE 2
Potential reasons for failure to achieve satisfactory asthma control

Refractory nature of the disease
Limitations of current treatments
Limited access to health care professionals
Confusing corporate agendas
Poor adherence with standard asthma management plans
Poor patient or health care professional communication
Low patient or health care professional expectations
Poor access to asthma education

("My drug is better than yours") can be counterproductive by obscuring the real issues at hand, or by introducing an element of confusion for the physician over which asthma management strategy is best. Limited access to physicians, in general, may be a problem leading to poor asthma control in some cases, but, at least in theory, intelligent and effective asthma control can be practised from either the walk-in clinic or the emergency department.

Probably the biggest impediment to achieving superior control over asthma at the moment is nonadherence with effective and readily available asthma management strategies, and both patients and health care professionals must share the blame. That nonadherence can have devastating consequences for some patients with asthma is clearly demonstrated by the many studies that consistently demonstrate an association between death from asthma and low levels of adherence with recommended asthma therapy (17-22). This is especially true for patients who are considered to be 'at risk' for severe asthma and asthma death (18,23-25). However, what is perhaps even more surprising is that many patients seem to be able to effectively control their asthma despite quite low adherence levels (22,26-28).

Nonadherence in asthma management is well-documented (29-33), and although nonadherence applies to both the non-pharmacological (allergen avoidance, cessation of smoking) and the pharmacological aspects of asthma management, nonadherence with asthma medications is the best studied. Objective measures of adherence such as electronic monitoring of inhaler use suggest that common levels of adherence to controller medication, such as ICSs, are between 60% and 80% of the prescribed dose, taken on 50% to 60% of days prescribed (30,34).

Nonadherence has many causes, the most important being related to poor communication, low expectations for what is achievable and limited access to asthma education. Nonadherence due to medication expense is usually not a major issue because even simple, low-cost ICSs will work if taken appropriately. When access to high-end expensive drugs is really necessary, there is usually some way to work around the dilemma for truly financially compromised individuals. Nonadherence in relation to medication delivery method is much discussed, but has been extremely difficult to clearly document. There is emerging evidence, however, that the time-honoured assumption that preference for a specific inhaler will lead to improved adherence with therapy (35,36) may have some validity. In this regard, both improved adherence and asthma outcome have been shown to be associated with the

use of a breath-actuated pressurized metered dose inhaler compared with a standard 'press-and-inhale' pressurized metered dose inhaler (37), and also with patients using combination inhalers for asthma compared with those given the same drug components but in two concurrent inhalers (38,39).

While oral medication may be preferred by some patients, and higher adherence rates have been observed for oral compared with inhaled therapy (40), long-term data are not available on the consequences (good or bad) of this approach, and there are many caveats to oral asthma therapy. For example, one recent study comparing a leukotriene receptor antagonist with an ICS as initial therapy for newly diagnosed asthma demonstrated significantly better adherence with the leukotriene receptor antagonist over nine months, but this had no effect on the degree of asthma control (40). Once-daily medication regimens promote better adherence, but symptom outcomes have generally been found to be poorer for patients using these regimens (41).

Although ICSs are generally safe when used at recommended doses, patient concern over side effects from ICSs has been consistently identified with poor adherence (42-44). In the recent GAPP survey, fear of ICS side effects was noted to be the most significant factor leading to patient dissatisfaction with current asthma therapy (6). Both patients and physicians were concerned about short-term, local (oropharyngeal) and long-term, systemic (osteopenia, cataracts) side effects of current ICSs. It is possible that newer ICSs with the potential for minimal side effects, such as the once-daily prodrug ciclesonide (45,46), may obviate these fears and facilitate better adherence with asthma therapy and thus lead to improved control. It will be interesting to observe whether ciclesonide use in asthma will affect the current trend toward using combination inhalers (LABA plus ICS) for all people with asthma, regardless of asthma severity.

Adherence or nonadherence is not simply a black or white phenomenon. Nonadherence, for example, has been broadly categorized into 'nonintentional' nonadherence (forgetting or lack of understanding), reasoned or 'intentional' nonadherence (testing or pragmatism), or an unwillingness to accept or identify oneself as asthmatic (denial) (47). Nonintentional nonadherence includes both forgetting to take asthma medications and mixing up which inhalers do what (eg, relievers versus controllers). In some cases, this reflects coexisting psychological morbidity, or simply an underlying troubled life, which requires specialized attention (25). Forgetting to take inhalers is also more likely to occur when symptoms are absent or minimal. Probably the bulk of nonintentional nonadherence can be reversed with better patient education, but effecting this solution continues to be problematic (48). When surveyed, Canadian primary care physicians acknowledge the need for more patient education, but consistently identify several valid barriers to this, including not enough time, lack of training, lack of materials and lack of community resources (49). In the GAPP survey, for example, 30% of Canadian patients stated that asthma management was never discussed by their physicians (6). The topic of delivering asthma education in Canada has recently been reviewed, with an emphasis on the helpful role of certified asthma educators (29,50). Unfortunately, there are probably not enough certified asthma educators and other health care educators, or at least they are not being used effectively, because according to the GAPP survey, the majority (86% to 88%) of both patients and

physicians believed that the individual with the primary responsibility for asthma education was the treating physician (6). Clearly, more work needs to be performed by our health authorities to facilitate and improve access to asthma educators.

More controversial is the issue of intentional or reasoned nonadherence. This is a provocative issue for health care professionals, either because they worry that this behaviour will lead to worsening or even fatal asthma, or because it may be seen by some as a challenge to their authority as the directors of what is in the best interests of the patient; the "who's in control?" phenomenon. Many, if not most, patients self-manage their asthma in some fashion, and often this involves taking 'drug holidays'. Some of these individuals can be characterized as 'testers', whose medication use fluctuates because they test to see whether they still need it, while others are 'pragmatists' who use medication intermittently because they feel that they have developed a satisfactory management plan that does not require taking medication continuously. Data from the TRAC study indicate that 94% of patients surveyed expressed a willingness to take more control of managing their asthma with guidance from their physicians (4). While this is a good thing, we must take very good care to ensure that patients are aware of, and demand, the degree of asthma control that is achievable with the modern approach to asthma care.

Intentional nonadherence can be either successful or unsuccessful. This issue was addressed in a recent primary care study by Greaves et al (22) comparing asthma outcomes in three groups of patients: those taking regular (as prescribed) ICSs; those taking regular ICSs but at lower than prescribed doses; and those taking their ICSs only when prompted by symptoms. Patients were classified as 'mild-to-moderate' if they required only low doses of ICSs (200 µg to 800 µg per day of beclomethasone or equivalent) to 'control' their asthma, or 'moderate-to-severe' if they required higher doses of ICSs plus a LABA for control. For patients with mild-to-moderate disease (the majority of patients seen in the primary care setting), quality of life was good and the need for unscheduled visits to the doctor was minimal, regardless of the way in which medications were taken.

In another trial exploring the safety of intermittent versus daily ICSs in patients with so-called 'mild persistent' asthma, at one year the ICS group had fewer symptoms, better pre-bronchodilator forced expiratory volume in 1 s and reduced sputum eosinophils than the control group, but there were no differences in postbronchodilator forced expiratory volume in 1 s, quality of life or asthma exacerbations (51). Indeed, most patients with low adherence tend to be less symptomatic than patients with high adherence, and medication adherence increases as symptoms escalate, confirming that symptom-based dosing is a successful strategy for many patients with asthma, especially those with milder disease.

The Canadian Asthma Consensus Guidelines emphasize the value of regular reassessment of all asthma patients, with regularly scheduled appointments to review the true level of asthma control, the role of asthma triggers, inhaler technique, comorbidities and adherence to the agreed management plan (7). Regularly scheduled reassessment of asthma control will also help physicians and educators be aware that a certain degree of intentional nonadherence to round-the-clock drug dosing is a fact of life for many patients, and to identify individuals for whom this practice is successful and those for whom it is not. Intentional nonadherence, or in this case 'permissive'

TABLE 3
'Difficult' asthma checklist

Under treatment?	ICS prescribed and taken? Other anti-inflammatories (LTRA, theophyllines)? Role for anti-immunoglobulin E therapy?
Poor adherence?	Too many drugs or drug regimen too complex? Confusion over identity of inhalers? Poor understanding of rationale for ICS? No perceived immediate benefit to ICS? Fear of ICS side effects? Unwillingness to take medications in general? Poor inhaler technique? Drugs too expensive?
Unidentified exacerbating factors and comorbidities?	Continued smoking? Continued allergen exposures? Occupational exposures? Drugs (beta-blockers, salicylates, ACE inhibitor, etc)? Gastroesophageal reflux disease?
Corticosteroid-resistant asthma?	No response to oral corticosteroid trial? Neutrophils predominate in sputum (specialist referral)?
Corticosteroid-dependent asthma?	Oral corticosteroids necessary? Prophylaxis versus steroid side effects
Fixed airflow obstruction?	Treat as for chronic obstructive pulmonary disease? Consider additional nonpharmacological therapy (eg, rehabilitation)?
Incorrect diagnosis?	Upper airway obstruction? Other?

ACE Angiotensin-converting enzyme; ICS Inhaled corticosteroid; LTRA Leukotriene receptor antagonist

nonadherence, will only work if it is deemed to be safe. Physicians will more likely accept this form of 'collaborative self-management' that empowers patients to take more control over medication dosage if they are confident that patients will not be harmed, over both the short term (symptoms and exacerbations) and the long term (airway remodelling leading to fixed obstruction). The long-term effects of potential airway remodelling are the most difficult to predict (11,13). We suspect, but have not been able to prove, that at least for some patients, obsessive use of ICSs (and possibly other anti-inflammatory medications) is essential to prevent, or at least to modulate, long-term irreversible lung damage. Those likely to be at greatest risk for remodelling are patients who are almost continuously symptomatic and who will likely be continuously taking medications anyway. If regularly scheduled reassessment of asthma control occurs, these persistently symptomatic individuals can usually be readily identified, and they should be referred to an asthma specialist. An initial approach to the asthmatic patient who is persistently symptomatic despite apparently good asthma management is outlined in the 'difficult' asthma checklist shown in Table 3.

An important requirement for successful asthma self-management is to ensure that the patient knows when and how to respond to increasing symptoms by increasing the dose of ICS, or in some cases, by reinstating ICS use if these drugs have been temporarily stopped. In my opinion, this requires that an individualized written action plan be collaboratively

developed by the patient, the physician and an asthma educator if available, as part of a comprehensive asthma self-management plan. Although methodological limitations have made it difficult for some systematic reviews to clearly demonstrate that action plans alone lead to improved asthma outcomes (52), there is now undeniable evidence that a written action plan is a key element for successful collaborative self-management in asthma (26,53-57). Action plans reduce the likelihood of unintentional nonadherence (forgetting) by providing clear written guides for medication use both when asthma is well-controlled and when symptoms escalate. Action plans also help promote successful intentional nonadherence by requiring that patients and health care professionals agree to certain individualized treatment goals, and by reinforcing what can be achieved with modern asthma therapy. In addition, action plans facilitate improved communication and highlight the value of regularly scheduled reassessment of asthma control.

Action plans also have the potential to stabilize asthma control in the difficult situation of denial (both the patient's and the physician's denial). Canadian data confirm that simply handing out an action plan alone, without educational discussion, is not effective in improving asthma control (56). There is also good evidence that mere verbal action plans are inadequate because the OR for death from asthma has been shown to be four times lower with a written compared with a verbal asthma action plan (58). Sadly, the TRAC study confirms that Canadian health care professionals are woefully underusing asthma action plans (4). Forty-four per cent of patients with asthma surveyed had no action plan at all, and only 17% of patients had a written asthma action plan. However, when an asthma action plan was provided, 86% of patients used it when needed. There are many examples of simple action plans available (<www.asthmaguidelines.com/downloads.html>; <www.lung.ca>; <www.bc.lung.ca>), some supplied by industry, and all of them can add a level of confidence and safety to asthma management, especially when they are used as part of a collaborative self-management plan for asthma.

Achieving good control over asthma is not nearly as simple as it seems, and when we ponder the question, "who's in control anyway?", we must acknowledge that perhaps for the majority of patients with asthma, medication adherence levels as low as 60% are not only the reality, but that for most, this level of adherence seems to be good enough (26). On the other hand, for some patients, nonadherence is clearly dangerous, because individuals who practise unsuccessful, intentional nonadherence are more likely to have asthma attacks and even die from asthma (17,18,23,25). Clearly, we need to know how to identify and to distinguish between these two types of patients. In addition, from time to time, some patients will likely move from being able to practise successful intermittent adherence to requiring regular adherence and vice versa. I believe that this sends the message that rather than concentrating on poor patient adherence with its pejorative implications, we should focus our efforts on patients who can be recognized as being 'at risk' for poor asthma outcomes, such as patients who frequently miss appointments, have frequent attacks and frequent unscheduled visits for asthma, or have made significant lifestyle alterations because of poorly controlled asthma symptoms (Table 4) (59). Perhaps also, there would be less confusion and more effective preventive maintenance, if instead of labelling patients with asthma as being 'mild' or 'severe', or as having nebulously defined 'mild intermittent' or

'mild persistent' asthma, we were to concentrate on the 'at risk' individuals and target them for more regular follow-up with individualized asthma action plans. We also need a logical approach to the problem of 'difficult asthma' that does not merely involve shifting drugs.

Ultimately, we will need to answer the important question of whether relatively asymptomatic, low levels of ongoing airway inflammation will inevitably lead to irreversible airflow obstruction due to remodelling. This is important because the link between inflammation and poor asthma control, which is defined clinically, is not entirely obvious (60). Some patients for example, appear to be in complete clinical remission, but have signs of persisting airway inflammation (61). In the future, perhaps more widespread use of induced sputum analysis (62,63) and improvements in the monitoring of surrogate markers of airway inflammation, such as exhaled nitric oxide (64), will help us to better understand the remodelling problem and launch an era of truly preventive therapy for asthma.

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TABLE 4
Features identifying the 'at risk' asthmatic patient*

Asthma severity
Previous near-fatal asthma or hospitalization for asthma in the past year
Frequent unscheduled contacts (telephone, clinic, emergency department)
Frequent oral corticosteroids
Pattern of sudden attacks
Significant lifestyle alterations because of asthma
Psychosocial profile
Frequent missed appointments
Self-discharge from hospital
Continued smoking
Alcohol or drug abuse
Psychosis or depression
Denial
Learning difficulties
School, employment or financial problems
Social isolation or domestic distress

*Adapted from reference 59

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