- Dolan CM, Fraher KE, Bleecker ER, et al, for the TENOR Study Group. Design and baseline characteristics of the epidemiology and natural history of asthma: Outcomes and Treatment Regimens (TENOR) study: a large cohort of patients with severe or difficult-to-treat asthma. Ann Allergy Asthma Immunol 2004; 92: 32–39.
- 2 Chung KF, Godard P, Adelroth E, et al. Difficult/therapy-resistant asthma: the need for an integrated approach to define clinical phenotypes, evaluate risk factors, understand pathophysiology and find novel therapies. ERS Task Force on Difficult/Therapy-Resistant Asthma. European Respiratory Society. Eur Respir J 1999; 13: 1198–208.
- 3 Chipps BE, Szefler SJ, Simons FE, et al. Demographic and clinical characteristics of children and adolescents with severe or difficult-to-treat asthma. J Allergy Clin Immunol 2007; 119: 1156–63.
- 4 Bracken M, Fleming L, Hall P, et al. Results of nurse-led home visits for children with difficult asthma. Thorax 2007; 62 (suppl 111): A21–22.
- Warner JO. Review of prescribed treatment for children with asthma in 1990. BMJ 1995; 311: 663-66.
- 6 Kam JC, Szefler SJ, Surs W, Sher ER, Leung DY. Combination of IL-2 and IL-4 reduces glucocorticoid receptor binding affinity and T-cell response to glucocorticoids. J Immunol 1993; 151: 3460-66.
- 7 Nimmagadda SR, Szefler SJ, Spahn JD, Surs W, Leung DY. Allergen exposure decreases glucocorticoid receptor binding affinity and steroid responsiveness in atopic asthmatics. Am J Respir Crit Care Med 1997; 155: 87–93.
- 8 Langley SJ, Goldthorpe S, Craven M, Woodcock A, Custovic A. Relationship between exposure to domestic allergens and bronchial hyperresponsiveness in non-sensitised, atopic asthmatic subjects. Thorax 2005; 60: 17–21.

- 9 Chinn S, Heinrich J, Antó JM, et al. Bronchial responsiveness in atopic adults increases with exposure to cat allergen. Am J Respir Crit Care Med 2007; 176: 20–26
- 10 Chaudhuri R, Livingston E, McMahon AD, Thomson L, Borland W, Thomson NC. Cigarette smoking impairs the therapeutic response to oral corticosteroids in chronic asthma. Am J Respir Crit Care Med 2003; 168: 1308–11.
- 11 Tomlinson JE, McMahon AD, Chaudhuri R, Thompson JM, Wood SF, Thomson NC. Efficacy of low and high dose inhaled corticosteroid in smokers versus non-smokers with mild asthma. Thorax 2005; 60: 282–87
- 12 Suntharalingam G, Perry MR, Ward S, et al. Cytokine storm in a phase 1 trial of the anti-CD28 monoclonal antibody TGN1412. N Engl J Med 2006; 355: 1018–28.
- 13 Saglani S, Nicholson AG, Scallan M, et al. Investigation of young children with severe recurrent wheeze: any clinical benefit? Eur Respir J 2006; 27: 29–35.
- 14 Global Allergy and Asthma European Network. http://www.ga2len.net (accessed Aug 13, 2008).
- WHO. Global Alliance Against Chronic Respiratory Diseases. http://www. who.int/gard/en (accessed Aug 13, 2008).
- 16 Leckie MJ, ten Brinke A, Khan J, et al. Effects of an interleukin-5 blocking monoclonal antibody on eosinophils, airway hyper-responsiveness, and the late asthmatic response. Lancet 2000; 356: 2144-48.
- 17 Berry MA, Hargadon B, Shelley M, et al. Evidence of a role of tumor necrosis factor alpha in refractory asthma. N Engl J Med 2006; 354: 697–708.

## The coming of age of asthma guidelines

The first international asthma guidelines meeting was held in Toronto almost 20 years ago and the consensus conclusions from this meeting were published the following year.1 Since then, many national and international groups have developed asthma guidelines as evidence-based documents.<sup>2,3</sup> For what purpose and for whom are these documents intended? The intended audience and outcomes are seldom stated explicitly by the authors of quidelines, but it is widely assumed that the documents are written to inform primary-care physicians, who care for most asthma patients, and that the intended result is to improve the outcomes of asthma management. This common failure to identify the target audience and intended outcomes might explain why the guidelines so often fail to meet the hopes of their authors.

An early innovation of the Canadian Asthma Guidelines group was to introduce the concept of asthma control as a pragmatic outcome measure after office-based treatment and as a decision-making tool, which suggests a strategic approach to asthma management that has since been widely incorporated, clarified, and refined by subsequent guideline documents. Despite widespread adoption by academic specialists, translating this consensus knowledge into improved practice patterns and outcomes has been unsuccessful.<sup>4</sup> The latest and

largest study to document our failure to improve asthma control outcomes in primary practice has been the Personal Practice Assessment Program, in more than 350 Canadian primary-care settings where physicians surveyed the asthma control status of more than 10 000 patients. Of the surveyed patients, 59% were considered uncontrolled. These uncontrolled patients were six times more likely to have an unscheduled health-care visit, almost four times more likely to seek care in an emergency department, and twice as likely to be admitted to hospital for out-of-control disease, compared with their controlled counterparts.

Such suboptimum outcomes probably reflect several management recommendations that are more often neglected than implemented. Despite universal recommendations that the diagnosis of asthma requires an objective measurement of lung function to show airway variability (ie, an increased bronchodilator response to a fast-acting  $\beta$  agonist), spirometry is seldom used in primary practice and methacholine challenge remains almost unknown. Environmental assessment and educational interventions are commonly neglected. Treatment remains over-reliant on high doses of inhaled corticosteroids and the introduction of combination inhaler therapy (inhaled corticosteroid plus a long-acting bronchodilator in a single inhaler) is often delayed



inappropriately.<sup>6</sup> Despite recurrent controversy,<sup>78</sup> we now have more than 10 years experience to confirm long-acting  $\beta$  agonists are the first choice add-on therapy to inhaled corticosteroids for patients who are not adequately controlled with low doses of inhaled corticosteroid. Combination therapy is safe and cost effective, and should be prescribed in a single inhaler to avoid the possibility of treating asthma with a long-acting  $\beta$  agonist alone.<sup>9</sup> Action plans to guide the self-management of exacerbations are also seldom discussed and even less often committed to writing.

How has the academic respiratory community responded to these findings? A casual review of recent guidelines and guideline discussions shows that considerable effort has been expended to grade the levels of evidence on which guideline recommendations are based.10 These efforts are replete with acronyms, workshop reports, and further guidelines on evaluating and grading the evidence used in guidelines. Although clearly of importance to scholars that their academic rigour is on display in the guidelines, it is less clear (and seems unlikely) that busy practitioners have failed to implement guideline recommendations because they have doubts about the evidence on which recommendations are based. Instead, it seems more plausible that the harried general practitioner omits spirometry because the measurement is not readily available, is too costly, has not been explained clearly, or requires more time to arrange and evaluate than is available (or seems available) in a busy office.

Against this background, ever more elegant grading schemes for weighing the academic evidence must seem akin to medieval scholars debating how many angels can dance on the head of a pin. Fortunately, the obvious needs of the overburdened primary practitioner have not gone unnoticed by those who propose writing guidelines. Increasingly, there is awareness that those who are to be guided by guidelines must be an integral part of the guideline development process from the outset. Indeed, the implementations of quidelines are more and more to be viewed as an integral part of the quideline process and not an afterthought once the recommendations have been published. A new-found focus on practical and implementable recommendations is welcome. At about 20 years of age, the guidelines might be leaving behind their self-absorbed and selfindulgent teenage years to arrive at a sensible and achievable goal—the widespread adoption of simple and practical measures to improve asthma control and reduce preventable asthma disability.

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- 1 Hargreave FE, Dolovitch J, Newhouse MT, et al. The assessment and treatment of asthma: a conference report. J Allergy Clin Immunol 1990; 85: 1098–111.
- 2 Bateman ED, Hurd SS, Barnes PJ, et al. Global strategy for asthma management and prevention: GINA executive summary. Eur Respir J 2008; 31:1/3-78
- 3 British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma: a natonal clinical guideline. May, 2008. http://www.sign.ac.uk/pdf/sign101.pdf (accessed Aug 8, 2008).
- 4 Graham ID, Logan J, Harrison MB, et al. Lost in knowledge translation: time for a map? J Contin Educ Health Care Prof 2006; 26: 13–24.
- 5 Chapman KR, Boulet LP, Rea RM, et al. Suboptimal asthma control: prevalence, detection and consequences in general practice. Eur Respir J 2008; 31: 320–25.
- 6 Ernst P, McIvor A, Ducharme FM, et al. Safety and effectiveness of long-acting inhaled β-agonist bronchodilators when taken with inhaled corticosteroids. Ann Intern Med 2006: 145: 692–94.
- 7 Martinez FD. Safety of long-acting beta-agonists—an urgent need to clarify the air. N Engl J Med 2005; 353: 2637–39.
- 8 Salpeter SR, Buckley NS, Ormiston TM, et al. Meta-analysis: effect of long-acting β-agonists on severe asthma exacerbations and asthma related deaths. Ann Intern Med 2006; 144: 904–12.
- 9 McIvor RA, Pizzichini E, Turner MO, et al. Potential masking effects of salmeterol on airway inflammation in asthma. Am J Respir Crit Care Med 1998; 158: 924–30.
- 10 Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report from an American College of Chest Physicians task force. Chest 2006: 129: 174-81.