

varieties of cognitive illusions that can hamper human judgement.¹⁴ A prediction rule has no such illusions.

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Is once enough? Understanding the preferences of COPD and asthma patients for once- versus twice-daily treatment

See linked article by Price *et al.* on pg 161

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Once-daily treatments are sometimes perceived to be the 'holy grail' in terms of promoting adherence. The idea that a simple once a day administration regime will foster adherence is certainly beguiling, but the research evidence is more nuanced. A number of systematic reviews^{1,2} and a recent meta-analysis³ have addressed the relationship between adherence and dose frequency, and their findings do indeed suggest an inverse gradient between dose frequency and adherence. The meta-analysis by Coleman and colleagues³ was methodologically more advanced and focused on oral dosage forms where adherence was assessed by electronic monitoring. The overall finding was that patients with long-term conditions (including three studies of patients with asthma) are more

adherent to once-daily oral regimes than more frequent dosing – and adherence was significantly higher for once- versus twice-daily regimes. This contrasts with the Claxton¹ and Saini² reviews which found that once-daily treatment was associated with significantly higher adherence than treatment three or four times a day, but found no significant differences between once- and twice-daily regimes overall.

However, we should be cautious about extrapolating these findings to a prescription of once-daily maintenance therapy for all patients with asthma and COPD. Although the aforementioned reviews¹⁻³ are well designed, they are inevitably limited by the fact that they draw on heterogeneous studies. Moreover, differences in adherence between once- versus twice-daily regimes, although statistically significant in the Coleman review,³ were relatively small; the percentage of doses taken was 93.0% (95% CI 91.2 to 94.7%) versus 85.6% (95% CI 82.5 to 88.8%), respectively. These findings are similar to those obtained by Price and colleagues in their 12-week open-label study of 1,233 patients with asthma randomised to receive once-daily versus twice-daily dosing of mometasone fumarate administered by dry powder inhaler;⁴ adherence was significantly higher with once-daily dosing, but adherence was high across the study and the difference between the dosing regimens was small (93.3% vs. 89.5%) – indicating that twice-daily dosing was not a significant barrier for most patients in the study. Nevertheless, research to date seems to be consistent with the 2008 UK National Institute for Health and Clinical Excellence (NICE) Medicines Adherence Guidelines

– i.e. that although a simple treatment regime can help with adherence, this single measure alone is unlikely to guarantee adherence.⁵

Yet in real-life practice, adherence rates tend to be much lower than they are in clinical trials, with 50% adherence rates being much more typical in asthma.^{6,7} The commonsense approach might therefore be to default to a once-daily dosing regimen, if available, on the grounds of patient convenience. This may be acceptable if costs are equivalent. However, if the once-daily formulation is more expensive, then the cost-effectiveness of routine once-daily prescribing becomes more difficult to justify, with a greater need to tailor the regime to patient need. Systematic reviews of interventions to support adherence have consistently found that single strategy interventions, applied uniformly, are rarely effective.^{8,9} Rather, the prescription and associated support should be tailored to the needs of the individual patient, addressing specific perceptual and practical factors influencing the patient's motivation and ability to adhere to treatment.¹⁰ Some patients may be very happy with a twice-daily regimen, and may even prefer the idea of receiving a dose of their medication twice rather than once a day. Other patients may prefer once-daily and may be more adherent because there are fewer opportunities to forget. This may be particularly relevant for patients receiving multiple therapies for co-morbid conditions where reducing polypharmacy may be a priority.

Unfortunately, few studies have systematically explored patient preferences for once- versus twice-daily regimens. The paper by Price and colleagues¹¹ in this issue of the *PCRJ* provides a welcome exception. In this large retrospective cohort study of 5869 patients with asthma (n=3,731) and COPD (n=2,138), they examined patients' preferences for once-daily controller therapy and whether these expressed preferences were associated with demographic factors (age, gender), clinical factors (disease severity, asthma control and COPD exacerbations), and/or patients' beliefs about their treatment (using the Necessity Concerns Framework). Approximately half of the patients expressed a preference for once-daily dosing. Preferences were not associated with age or gender or with severity of the disease and frequency of exacerbations for COPD. However, preferences were associated with asthma control, reported adherence, and patients' beliefs about controller therapy ('perceived necessity', and their concerns about its potential adverse consequences).

Preference for once-daily dosing was associated with lower reported adherence in both asthma and COPD.¹¹ However, we cannot simply conclude that patients' adherence would improve if their preferences were met, since the correlates of patient preference provide a complex picture that is difficult to interpret. For example, patients with asthma, who expressed a preference for once-daily treatment, had significantly better asthma control but were also more likely to doubt their personal need for the treatment (lower necessity beliefs). At first sight, this might seem counter-intuitive. One might expect a preference for once-daily dosing to be associated with low adherence and poor control (e.g. '*It is difficult for me to manage twice a day and I often forget a dose*'). However, this finding is consistent with previous studies of patients' perception of the necessity of controller therapy where doubts about the need for regular treatment

were linked to the perception and experience of asthma symptoms; those who experienced fewer symptomatic episodes were significantly less likely to perceive a personal need for regular controller treatment ('*No symptom: no asthma*').^{12,13} Doubts about treatment necessity were associated with non-adherence, since patients who perceived themselves to be better controlled thought they could manage with less medication.¹³ This view has a 'commonsense logic', but may be mistaken if good control is consequent on using the medication. In the Price *et al.* study,¹¹ good control may be linked to doubts about the continuing need for treatment influencing preferences for once-a-day in the belief that 'I can get away with less treatment'. It is interesting to note that for patients with COPD, the perception of high treatment necessity was more common, and high need was associated with once-daily dosing because this was perceived as easier to manage. For patients with COPD, symptoms are more constant, thus reinforcing perceptions of the necessity of treatment on a daily basis.

Although the paper by Price *et al.*¹¹ has several limitations – for example, we do not know how many people who expressed a preference for once-daily treatment were already receiving once-daily treatment – it is a valuable addition to the literature. We should make more use of this type of large, naturalistic study of patients' perceptions and experiences to inform the development of products and support ('reverse translation'). The findings of this study reinforce the principle that decisions about dosage frequency (once versus twice a day) should be considered in the light of patients' beliefs about the prescription (e.g. necessity and concerns) and their preferences. The key is to tailor the medication and dose frequency to the needs of the individual and to identify and address perceptual and practical barriers to optimum use. For some patients, once-daily dosing might be helpful in achieving this. But once-daily dosing is not a panacea for non-adherence, and we need to identify those patients who will benefit most from once-daily versus twice-daily treatment.

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Assessment of COPD in primary care: new evidence supports use of the DOSE index

See linked article by Rolink *et al.* on pg 169

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Recent modifications of the GOLD recommendations emphasise the importance of assessing symptoms or health status, in addition to lung function and exacerbation frequency, in order to produce a more comprehensive view of the COPD patient.¹ There is, however, a difficult challenge in finding a convenient way of evaluating COPD in primary care where the majority of COPD patients are managed. In fact, the usefulness of the new GOLD categories in primary care has been debated.²

The article by Rolink and colleagues³ in this issue of the *PCRJ* shows that the recently described DOSE index is predictive of change in health status measured by the Clinical COPD Questionnaire (CCQ). This finding increases the potential value of the DOSE index, which has

already demonstrated its clinical usefulness.

The MRC scale is a well-known instrument for estimating the important symptom of dyspnoea due to physical activity in COPD patients. In a study from 2002, the MRC scale was shown to be a more effective predictor of mortality than lung function in COPD.⁴ However, the multisystem complexity of COPD has resulted in a requirement for comprehensive instruments that can take into account several aspects of the disease. The term health status covers not only symptoms but the broader influence of disease on daily activities and wellbeing.⁵ The St George's Respiratory Questionnaire (SGRQ), a disease-specific instrument originally developed to evaluate health status,⁶ is often used in clinical trials as a gold standard for evaluating health-related quality of life (HRQL) in respiratory diseases. As HRQL reflects the general impact of a disease on a patient's wellbeing, the terms HRQL and health status are very closely related and often used synonymously.

However, the SGRQ is an extensive instrument that can be time-consuming to complete, making it inconvenient to use in clinical practice. More recently, shorter instruments have been developed. In 2005, the CCQ was introduced as a convenient instrument for measurement of health status; it includes ten items about symptoms, emotional dysfunction and limitations of physical activity.⁷ It correlates well with the SGRQ, with the Chronic Respiratory Questionnaire (CRQ), and the generic instrument Short form-36 (SF-36),^{7,8} and is practical to use in primary care.⁹ In 2009, the COPD Assessment Test (CAT) was developed, and this includes eight items on symptoms, activities and other impacts of COPD on health status.¹⁰ In the most recent GOLD update, both the CAT and CCQ scores are recommended for clinical evaluation of health status in COPD patients.¹

In primary care, there is clearly a need for simple tools which can present as much clinically relevant information on the disease as efficiently as possible. Jones and colleagues developed the Dyspnoea, Obstruction, Smoking and Exacerbation (DOSE) index with a view to combining information relevant for both clinical management and assessment of disease severity.¹¹ Other multidimensional instruments, like the BODE index (BMI, Obstruction, Dyspnoea and Exercise capacity)¹² and the ADO index (Age, Dyspnoea and Obstruction),¹³ also