4. **Reddel HK,** Taylor DR, Bateman ED, *et al*. An Official American Thoracic Society/European Respiratory Society Statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. *Am J Respir Crit Care Med* 2009;**180**:59—99.
5. **Frey U,** Suki B. Complexity of chronic asthma and chronic obstructive pulmonary disease: implications for risk assessment, and disease progression and control. *Lancet* 2008;**372**:1088—99.
6. **Bateman ED,** Bousquet J, Busse WW, *et al*. Stability of asthma control with regular treatment: an analysis of the Gaining Optimal Asthma controL (GOAL) study. *Allergy* 2008;**63**:932—8.
7. **Zhang J,** Yu C, Holgate ST, *et al*. Variability and lack of predictive ability of asthma end-points in clinical trials. *Eur Respir J* 2002;**20**:1102—9.
8. **Reddel HK.** Peak flow monitoring in clinical practice and clinical asthma trials. *Curr Opin Pulm Med* 2006;**12**:75—81.
9. **Frey U,** Brodbeck T, Majumdar A, *et al*. Risk of severe asthma episodes predicted from fluctuation analysis of airway function. *Nature* 2005;**438**:667—70.
10. **Thamrin C,** Zindel J, Nydegger R, *et al*. Predicting future risk of asthma exacerbations by using individual conditional probabilities. *J Allergy Clin Immunol* 2011;**127**:1494—502.e3.
11. **Taylor DR,** Town GI, Herbison GP, *et al*. Asthma control during long term treatment with regular inhaled salbutamol and salmeterol. *Thorax* 1998;**53**:744—52.
12. **Wenzel SE,** Barnes PJ, Bleecker ER, *et al*. A randomized, double-blind, placebo-controlled study of tumor necrosis factor-alpha blockade in severe persistent asthma. *Am J Respir Crit Care Med* 2009;**179**:549—58.
13. **Peng CK,** Havlin S, Stanley HE, *et al*. Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series. *Chaos* 1995;**5**:82—7.
14. **Thamrin C,** Stern G, Strippoli MP, *et al*. Fluctuation analysis of lung function as a predictor of long-term response to beta2-agonists. *Eur Respir J* 2009;**33**:486—93.
15. **Bateman ED,** Bousquet J, FitzGerald M, *et al*. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;**31**:143—78.
16. **Juniper E,** O'Byrne P, Guyatt G, *et al*. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;**14**:902—7.
17. **Juniper EF,** Guyatt GH, Epstein RS, *et al*. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992;**47**:76—83.
18. **Thomas M,** Kay S, Pike J, *et al*. The Asthma Control Test (ACT) as a predictor of GINA guideline-defined asthma control: analysis of a multinational cross-sectional survey. *Prim Care Respir J* 2009;**18**:41—9.
19. **Orr LC,** Fowler SJ, Lipworth BJ. Relationship between changes in quality of life and measures of lung function and bronchial hyper-responsiveness during high-dose inhaled corticosteroid treatment in uncontrolled asthma. *Am J Respir Med* 2003;**2**:433—8.
20. **Carranza Rosenzweig JR,** Edwards L, Lincourt W, *et al*. The relationship between health-related quality of life, lung function and daily symptoms in patients with persistent asthma. *Respir Med* 2004;**98**:1157—65.
21. **Siroux V,** Boudier A, Anto JM, *et al*. Quality-of-life and asthma-severity in general population asthmatics: results of the ECRHS II study. *Allergy* 2008;**63**:547—54.
22. **Juniper E,** Svensson K, O'Byrne P, *et al*. Asthma quality of life during 1 year of treatment with budesonide with or without formoterol. *Eur Respir J* 1999;**14**:1038—43.
23. **Juniper EF,** Wisniewski ME, Cox FM, *et al*. Relationship between quality of life and clinical status in asthma: a factor analysis. *Eur Respir J* 2004;**23**:287—91.
24. **Haldar P,** Pavord ID, Shaw DE, *et al*. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 2008;**178**:218—24.
25. **Forno E,** Fuhlbrigge A, Soto-Quiros ME, *et al*. Risk factors and predictive clinical score for asthma exacerbations in childhood. *Chest* 2010;**138**:1156—65.
26. **Chanez P,** Wenzel SE, Anderson GP, *et al*. Severe asthma in adults: what are the important questions? *J Allergy Clin Immunol* 2007;**119**:1337—48.
27. **Stern G,** de Jongste J, van der Valk R, *et al*. Fluctuation phenotyping based on daily fractional exhaled nitric oxide in asthmatic children. *J Allergy Clin Immunol* 2011;**128**:293—300.

Journal club

Does the addition of high-dose vitamin D_3 reduce the period of time required for the treatment of pulmonary tuberculosis?

This double-blind randomised placebo control trial investigated the addition of four doses of 2.5 mg of vitamin D_3 to intensive phase antimicrobial therapy (isoniazid, rifampicin, pyrazinamide and ethambutol) for tuberculosis and the effect upon culture conversion rates. Time to conversion was measured at 14, 28, 42 and 56 days compared with placebo with intensive antimicrobial therapy. The primary outcome was also characterised with respect to the expression of vitamin D_3 genotypes *Tak*1 and *Fok*1.

The authors recruited one hundred and forty-six patients from 10 NHS London Trusts, of which one hundred and twenty-six were included. The median age of the patients was 30.6 years. The authors demonstrated a reduced median culture time in the vitamin D_3 group of 36 days (95% CI 31.8 to 40.2) compared with the placebo group of 43.5 days (95% CI 36.5 to 50.5). Subgroup analysis of the *Taq*1 and *Fok*1 vitamin D receptor types showed that patients homozygous for the *Taq*1 polymorphism had reduced time to culture conversion.

In conclusion, the addition of vitamin D_3 to intensive anti-tuberculosis treatment did not confer a significant advantage compared with placebo in the time taken for sputum culture conversion except in individuals who were homozygous for the *Taq*1 polymorphism. Investigation of this gene interaction and its possible clinical advantage is therefore warranted.

► Martineau AR, Timms PM, Bothamley GH, *et al*. High-dose vitamin D_3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: a double-blind randomised controlled trial. *Lancet* 2011;**377**:242—50.

Jessica Reed

Correspondence to Dr Jessica Reed, FY1, South Tees Hospitals NHS Trust, Middlesbrough, UK; jessica.reed@nhs.net

Published Online First 28 March 2011

Thorax 2011;**66**:1042. doi:10.1136/thoraxjnl-2011-200114