Using fractional exhaled nitric oxide to guide step down treatment decisions in asthma patients: a systematic review and individual patient data meta-analysis

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Aim: To assess the value of fractional exhaled nitric oxide (FeNO) in guiding step down treatment decisions in patients with asthma.

Method: We searched Medline and Medline In Process (OvidSP) [1946-], EMBASE (OvidSP)[1974-], Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley) and Web of Science Core Databases (Web of Science, Thomson Reuters) until 7th November 2016 with no language restrictions. We included studies which recruited patients aged 12 years and over with clinician-diagnosed asthma maintained on low or medium dose inhaled corticosteroids (ICS) in whom FeNO was measured before stepping down ICS.

To examine the relationship between FeNO and acute exacerbations, we performed multi-level mixed-effects logistic regression accounting for within-study clustering, age and sex. We calculated net benefit values across a range of risk thresholds, comparing our model with "step down all patients" and "step down none" strategies. For risk thresholds where our model showed net benefit over these strategies, we calculated observed exacerbation risks with 95% confidence intervals (CI).

Results: Eight studies met our inclusion criteria. We obtained individual participant data from seven studies (393 participants, 44 with an acute exacerbation [11.2%]). There was no significant association between FeNO and acute exacerbations (adjusted Odds Ratio 1.01, 95% CI 1.00-1.02, P=0.163). However, the net benefit of this model was greater than "step down all patients" and "step down none" strategies when baseline exacerbation risk was 8-18% (Figure 1). Observed exacerbation risk was 1.5-2 times higher in patients whose predicted risk was greater than or equal to risk thresholds within this range (Figure 2).

Conclusion: Using FeNO to guide step down treatment decisions is more beneficial than stepping down treatment in all or no patients in asthma populations where baseline exacerbation risk is 8-18%. Clinicians should consider reducing treatment in patients whose predicted risk is below the baseline population risk.

Declaration of Interest:

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