Asthma is a respiratory disease characterised by episodes of obstruction of the airways which are reversible by medication. Severe asthma is the most difficult-to-treat type as it usually refractory to most treatments and requires combinations of high doses of ICS/LABA and additional oral medication to control symptoms. [1, 2, 3] Studies have shown that the majority of severe asthmatic patients have high numbers of eosinophils present in their airway tissue which is believed to be important in the pathology of the disease [4, 5]. As a result, biological therapies which target immunoglobulin E (IgE) have been used in the recent years to treat severe asthmatic patients.

Objectives
- This Bayesian network meta-analysis (NMA) aimed at assessing the relative efficacy and safety of monoclonal antibodies and a tyrosine-kinase inhibitor for severe or uncontrolled asthma based on studies identified via a systematic literature review.

Methods
- Bayesian NMAs were conducted based on a systematic literature review. Methods were in line with NICE guidelines [6, 7].
- Outcomes of interest included asthma control questionnaire (ACQ) score, asthma exacerbations and discontinuations due to adverse events (AE).
- Networks of evidence were based on treatment- and dose-specific nodes except for masitinib for which results were published only for placebo doses.
- Separate analyses were conducted at 16 weeks (±4 weeks), 26 weeks (±4 weeks) and 52 weeks (±4 weeks).
- Relative efficacy was evaluated based on absolute differences [8] or odds-ratios (OR), Bayesian pairwise probabilities (P, i.e. probability to perform better) and ranking of treatments based on the surface under the cumulative ranking (SUCR(8). The thresholds 90% and 85% were chosen to indicate a smaller and larger effect, respectively [9].
- To assess heterogeneity, the I² statistic was calculated for each pairwise comparison. Heterogeneity was suspected if I² was higher than 50% [10].
- Vague prior distributions were used to produce results derived by the data.
- The selection of using a fixed or random effects model was based on the Deviance Information Criterion (DIC), which measures the relative goodness of fit between models [11].

Results
- The systematic literature review led to the inclusion of 8 trials reporting results at 16 weeks (±4 weeks), 6 trials at 26 weeks (±4 weeks) and 3 trials at 52 weeks (±4 weeks). Treatments assessed were omalizumab, lebrikizumab, mepolizumab and masitinib.
- The limited reported data in the study publications [12, 13] led to restricted networks at 16 weeks (7 trials) and 26 weeks (5 studies) (figures 1a and 1b). The network at 26 weeks is reported in figure 1c.
- The DIC associated with the fixed effect model was lower than the DIC associated with the random effects model for all the outcomes and times of assessment, except for the discontinuations due to AE at 26 weeks for which the random effects model was selected.

Discussion
- Few trials were included in each analysis resulting in broad credible intervals. Two trials assessed mepolizumab but the study by Ayars et al. [13] did not report the same outcomes than others included studies. A single trial was included assessing lebrikizumab [14] and only one trial assessed masitinib, which was a small trial with less than 50 patients in total [15].
- Two trials [16, 17] were identified as potential sources of heterogeneity in the analyses of exacerbations at 16 weeks and discontinuations due to AE at 26 weeks respectively and were excluded as part of sensitivity analysis. Based on these results, omalizumab had a higher risk of discontinuations due to AE compared to placebo (OR=4.48, P=0.06).

Conclusions
- The network meta-analysis of asthmatic treatments suggested that omalizumab had greater ACQ score reductions at 52 weeks than mepolizumab 75mg and 750mg but was comparable to mepolizumab 250mg. Active treatments were comparable regarding asthma exacerbations and discontinuations due to AE.

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References