INTRODUCTION
In the context of Health Technology Assessment (HTA) and reimbursement decision-making across Europe, several comparators may be relevant to the assessment of a new drug in accordance with current clinical practice and previous recommendations. Hence, Network Meta-Analysis (NMA) is commonly used to answer such a decision problem as it allows the simultaneous comparison of multiple treatments of interest by synthesising relevant evidence. NMA combines both the direct and indirect evidence from randomised studies forming a connected network of evidence to produce an ‘internally coherent’ set of effect estimates for each treatment of interest relative to every other. However, there are many circumstances under which networks of evidence may be ‘disconnected’; i.e. treatments are not linked via at least one common comparator, and NMA cannot be conducted. In the case of Rheumatoid Arthritis (RA), most biologic therapies have only been investigated as first-line treatment options and only 4 RCTs were identified in a literature review for biologics in second-line use.

DATA
A systematic literature review was undertaken to identify RCTs that evaluated biologic therapies for RA as second-line treatment regimens. The scope of the review was restricted to licenced biologic therapy that had undergone at least one HTA in Europe by January 2015. The outcome of interest was Disease Activity Score (DAS) remission at 6 months. A total of 4 trials investigating second-line biologics were included in the analysis. Figure 1 shows the RCT network with 1 of the 4 trials disconnected from the other 3. RWE was obtained from two European Registries, the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry and the British Society of Rheumatology Biologics Register (BSRBR). After applying the inclusion criteria used in the trials and data cleaning only 50 patients were included from the Swiss registry and 1353 from the BSRBR. The inclusion of this data expanded the network, as well as, connected the disconnected RCT network.

Methods
A number of NMA's were conducted (using MCMC in WinBUGS) on the risk difference scale which included; fixed and random effects of only RCTs, both RCTs and registries (accepted at "face-value") and the RCTs with the registry data down-weighted (using a power transform prior approach). To down-weight the registry data we raise the log-likelihood of the binomial distribution to a power α, where 0 ≤ α ≤ 1. So if we let rki be the number of remissions and nki be the total number of patients in arm k of study i then the log-likelihood of the registry data is as follows:

\[
\log L(r_{ki}) = \log \binom{n_{ki}}{r_{ki}} \frac{1}{\alpha} \left(1 - \exp\left(-\frac{\alpha}{\alpha + 1} r_{ki}\right)\right)^{\alpha}
\]

Where α = 0 discounts the registry data completely and α = 1 accepts the registry data at "face-value". Initially a NMA was performed using only the connected RCT data (top half of figure 1). Then the impact that the registry data had, by connecting the network, on the results was evaluated. An inconsistency model was also evaluated for all networks to ensure the NMA consistency assumption remained valid within all networks, especially when registry data were added.

Results
A fixed effect NMA was chosen for all models due to the size of the network, the number of patients, and only a small reduction in the Deviance Information Criterion (DIC) when using a random effects compared to fixed effect NMA model.

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Figure 3 - Forest plot of treatment risk difference vs MTX for all 3 NMAs

Figure 4 - Risk difference power prior results for each treatment (vs MTX)