Appendix E. Additional details of the network meta-analysis

E.1 Methods of the network meta-analysis

We first define the Bayesian network meta-analysis (NMA) statistical models used to synthesize transformed outcomes, on the log hazard scale, from each randomized controlled trial (RCT). The link functions to connect these models to the different data summaries are then presented. The same statistical models are used for crisis, hospitalization days, adverse events, and serious adverse events but the link functions vary depending on what data is reported by each RCT (see main text for outcomes analyzed). The NMA models are in line with the recommendations of the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) technical support documents (TSD), in particular NICE DSU TSD 2. OpenBUGS code is provided for each outcome in appendix **B.4**.

For all random parameters (i.e. μ and d.) vague $Normal(0, 0.001)$ priors were used.

Fixed-effects network meta-analysis model

When the available evidence consists of a network of multiple pairwise comparisons (i.e. AB-trials, AC-trials, BC-trials, etc.) the standard fixed effects model for NMA can be specified as follows:

$$\theta_{jk} = \begin{cases} \mu_{jb} & \text{if } k = b \\ \mu_{jb} + d_{bk} = \mu_{jb} + d_{Ak} - d_{Ab} & \text{if } k > b \end{cases} \tag{3}$$

$$d_{AA} = 0$$

There are k treatments labelled as A, B, C, etc., and treatment A is taken to be the reference treatment for the analysis. μ_{jb} is the (transformed) outcome in study j on 'baseline' treatment b which will vary across studies. d_{bk} is the fixed effect of treatment k relative to 'baseline treatment' b. d_{bk} are identified by expressing 0them in terms of the reference treatment A: $d_{bk} = d_{Ak} - d_{Ab}$ with $d_{AA} = 0$.

Random-effects network meta-analysis model

$$\theta_{jk} = \begin{cases} \mu_{jb} & \text{if } k = b \\ \mu_{jb} + \delta_{jbk} & \text{if } k > b \end{cases} \tag{4}$$

$$\delta_{jbk} \sim Normal(d_{bk}, \sigma^2) = Normal(d_{Ak} - d_{Ab}, \sigma^2)$$

$$d_{AA} = 0$$

δ_{jbk} is the trial-specific treatment effect of k relative to treatment b. These trial-specific effects are drawn from a random-effects distribution: $\delta_{jbk} \sim N(d_{bk}, \sigma^2)$ Again, the pooled effects, d_{bk}, are identified by expressing them in terms of the reference treatment A. The heterogeneity σ^2 is assumed constant for all treatment comparisons. (A fixed effect model is obtained if σ^2 equals zero.)