

The analysis assumed that the studies are exchangeable in the sense that the investigators would be willing to assign each of the patients in the studies to any of the interventions.

A random-effects NMA was conducted with the baseline treatment being defined as usual care.

The studies presented data in terms of the number of patients who had an event (i.e. all-cause mortality, all-cause hospitalisation and HF-related hospitalisation). To account for the variation in follow-up between studies,⁸⁶ it was assumed that the data arose according to a Poisson process for each trial arm, with a constant event rate, λ_{ik} , for arm k in study i , so that T_{ik} , the time until an event occurs in arm k of study i , is distributed exponentially such that:

$$T_{ik} \sim \text{Exp}(\lambda_{ik}) \quad (1)$$

Therefore, the probability that there are no events by time f_i in arm k of study i (i.e. the survivor function of an exponential distribution) is:

$$S(f_i) = P(T_{ik} > f_i) = 1 - F(f_i) = e^{-\lambda_{ik} f_i} \quad (2)$$

Then for each study, i , p_{ik} , the probability of an event in arm k of study i after follow-up time f_i , can be written as:

$$P_{ik} = 1 - P(T_{ik} > f_i) = 1 - e^{-\lambda_{ik} f_i} \quad (3)$$

which is time dependent.

Therefore, the event rate, λ_{ik} , was modelled using the complimentary log-log link function such that:

$$\begin{aligned} \theta_{ik} &= \text{cloglog}(p_{ik}) \\ &= \ln(-\ln(1 - p_{ik})) \\ &= \ln(-\ln(1 - [1 - \exp(-\lambda_{ik} f_i)])) \\ &= \ln(-\ln[\exp(-\lambda_{ik} f_i)]) \\ &= \ln(-(-\lambda_{ik} f_i)) = \ln(\lambda_{ik} f_i) \\ &= \ln(\lambda_{ik}) + \ln(f_i) \\ &= \mu_i + \delta_{i,bk} + \ln(f_i) \end{aligned} \quad (4)$$

where $\delta_{i,bk}$ are the treatment effects of interest and are also the log-HRs relative to the baseline treatment.

This model assumes that the hazards for each intervention are constant irrespective of follow-up. Although this is a strong assumption, it is preferable to assuming that the follow-up has no impact on the number of events that are accumulated over time.