Statistical methods - Monte Carlo simulation

The data collected for each patient was used in the calculations of a predictive scoring system, to make an individual risk of death prediction for that patient. For VV ECMO patients the RESP score was used for predictive scoring, while for VA ECMO patients the SAVE score was used. The primary intention was to compare whether the number of deaths observed in the series of patients differs from the expected number of deaths from the predictive models. This was done using Monte Carlo simulation.

Monte Carlo simulation

Repeated simulation was used to generate a probability distribution of the expected number of deaths from which the 95% confidence limits are determined. This was done by running a large number of simulations. The observed number of deaths was compared to this expected distribution.

For a series of patients, each patient was indexed (). Each patient had a predicted risk of death () of between 0 and 1, which did not vary between simulations. simulations were modelled (indexed by ). In each simulation an individual patient may either live () or die (). A Bernoulli trial was performed by random assignment of outcome such that . In practice this was programmed by randomly assigning a number between 0 and 1, then treating the patient as a non-survivor () if the number assigned was ≤ and a survivor () if the number assigned is > . The number of deaths in that simulation was , where .

Let be any of the values that can hold, so that . The number of instances of each value of counted over the simulations was , so that , and

The proportion of the total simulations that had a given number of deaths was

This provided a discrete distribution and the probability distribution function (pdf) of the total number of deaths of the n patients was approximated by plotting against . The precision of this estimate depended on the size of .

**Determining 95% confidence limits**

The two tailed 95% confidence intervals were estimated from the pdf generated by the simulations. The cumulative probability at a given value of was

Values of with < 0.025 were treated as being below the lower 95% confidence interval (.

In order to establish the upper 95% confidence interval ( the cumulative probability from the upper end of the distribution was used

Values of with < 0.025 were treated as being the .

If the observed number of deaths lay outside the 95% confidence limits, it was considered to be significantly different from the number of deaths expected from the predictive scoring system.

This approach avoids assumptions about the anticipated pdf. It is suited to relatively small numbers of patients and the discrete nature of the data.

**Number of simulations required**

This Monte Carlo technique has been used as a numerical method to generate a robust estimate of the pdf. The precision of this approximation increases with the number of simulations. To decide whether the pdf was sufficiently precise, an a priori precision was declared, then improvement in approximation (error reduction) with increasing number of simulations was documented.

The primary purpose of generating the probability distribution was to find the number of deaths that would be outside the 95% confidence intervals, so the primary focus was ensuring that the 95% confidence intervals were sufficiently trustworthy and reproducible. To achieve, this it was necessary to determine that enough simulations had been conducted.

To test the data generated by any N simulations

1. N simulations were replicated 1 000 times, to give 1 000 distributions.
2. For each given number of deaths () this gave 1 000 estimates of the probability of that number of deaths .
3. For each of the 1 000 distributions the highest below the and the lowest above the were calculated. N was deemed insufficient if these values were not identical for all 1 000 distributions.