II. DEFINITIONS AND FORMULAS

The following definitions and formulas are used to calculate the hazard ratio (29).

O_1 is the observed number of deaths at time t for group 1.

O_2 is the observed number of deaths at time t for group 2.

E_1 is the expected number of deaths at time t for group 1, where this expectation is based on the number of deaths occurring in this group for the immediately previous time point (the time just before time t).

E_2 is the expected number of deaths at time t for group 2, where this expectation is based on the number of deaths occurring in this group for the immediately previous time point (the time just before time t).

E_1 is calculated from the following formula (Eq. (1)):

$$E1 = \sum \left[\frac{[(r_{1i})(d_i)]}{r_i} \right] \tag{1}$$

E_2 is calculated from the following formula (Eq. (2)):

$$E2 = \sum \left[\frac{[(r_{2i})(d_i)]}{r_i} \right] \tag{2}$$

The term r_{1i} is the number of subjects alive and not censored in group 1, just before time t_i.

The term r_{2i} is the number of subjects alive and not censored in group 2, just before time t_i.

The term r_i, which appears in the denominator, means: $r_{1i} + r_{2i}$. In other words, r_i is the total number of subjects alive in both groups and not censored, just before time t.

The term d_i is the total number of subjects who died at time t_i, in both groups combined. In other words, $d_i = d_{1i} + d_{2i}$.

The symbol $\sum$ (summation sign) indicates the addition over each time of death up to and including time t. The summation sign indicates that the following calculation must be made. Assume that the clinical study has six time periods. This type of clinical study can be represented by a Kaplan-Meier plot where each curve has six points.

The hazard ratio is calculated from the following formula (Eq. (3)) (30):

$$h = \frac{[O_1 / E_1]}{[O_2 / E_2]} \tag{3}$$

[29] Machin D, Gardner MJ. Calculating confidence intervals for survival time analyses. *Brit Med J.* 1988;296:1369–1371.
[30] Machin D, Gardner MJ. Calculating confidence intervals for survival time analyses. *Brit Med J.* 1988;296:1369–1371.