

[Group A]/[Group B] or, alternatively, to calculate the ratio of hazards for [Group B]/[Group A] (22,23).

The term “hazard” refers to the probability that an individual, under observation in a clinical trial at time  $t$ , has an event at that time (24). It represents the instantaneous event rate for an individual who has already survived to the time “ $t$ .”

The two arms of a clinical trial can be compared by way of the hazard ratio and the P value. The following serves as a starting point for defining hazard ratio and P value, as it applies to two curves in a Kaplan–Meier plot. The hazard ratio is a measure of the magnitude of the difference between the two curves in the Kaplan–Meier plot, while the P value measures the statistical significance of this difference. These two definitions serve only as starting points for our present goal in arriving at correct definitions. The following are the correct definitions. The numerical value of the hazard ratio expresses the relative hazard reduction achieved by the study drug compared to the hazard reduction by the control treatment. The numerical value can be a fraction of 1.0 or it can be greater than 1.0. For example, a hazard ratio of 0.70 means that the study drug provides 30% risk reduction compared to the control treatment (25). A hazard ratio of exactly 1.0 means that the study drug provides zero risk reduction, compared to the control treatment. The P value gives the probability of observing an event by chance alone, if the null hypothesis is true. The P value expresses the probability of observing a difference as extreme as that observed, if in fact the null hypothesis is true (26). If the P value from the study results is smaller than the alpha value, it is concluded that the observed difference is unlikely to be from chance, and that it arose from the treatment used in the clinical trial.

A Kaplan–Meier plot can be used to plot results from only one group. The Kaplan–Meier plot can also be used to plot results from two groups, for example study drug group and control group. The Kaplan–Meier plot can also be used for data from more than two groups. But a hazard ratio is used to represent the relative difference between only two groups. Please also note that when the hazard ratio is used as a measure for the difference between two survival curves (on one Kaplan–Meier plot), the hazard ratio can be calculated from data collected from the entire study period or, alternatively, from an early time interval or from a late time interval (27). According to Dr. Harvey Motulsky (28) the hazard ratio is only meaningful if you assume that the hazard ratio is the same at all time points.

<sup>22</sup> Machin D, Cheung YB. *Survival Analysis: A Practical Approach*. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc.; 2006;62.

<sup>23</sup> Crowley J. *Handbook of Statistics in Clinical Oncology*. New York, NY: Marcel Dekker; 2001;541.

<sup>24</sup> Duerden M. *What are Hazard Ratios? What is...? Series*. Hayward Medical Communications, Hayward Group, Ltd.; 2009;8.

<sup>25</sup> Kane RC. The clinical significance of statistical significance. *The Oncologist*. 2008;13:1129–1133.

<sup>26</sup> Kane RC. The clinical significance of statistical significance. *The Oncologist*. 2008;13:1129–1133.

<sup>27</sup> Kestenbaum B. *Epidemiology and Biostatistics: An Introduction to Clinical Research*. New York, NY: Springer; 2009;227–228.

<sup>28</sup> Motulsky H. E-mail of May 9, 2011.