A NATURAL HISTORY STUDY TO COMPARE TREATMENTS

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New treatments are often evaluated in clinical trials in which they are compared to existing treatments. However, sometimes a situation occurs in which a new treatment, approved based on clinical trials, needs to be further evaluated. For example, a treatment may be approved in several countries but not in others, and a natural history study where the treatment is approved, comparing the new treatment to the standard treatment, may be helpful in increasing the understanding and depth of knowledge regarding the new treatment. Because clinical trials have by design a self-selecting sample, a natural history study may be considered more representative of the disease population. However, in order for such a study to be useful, one needs to account for the different exposures to the two treatments. Furthermore, if the primary analysis approach is survival analysis, special care needs to be taken in defining study entry time, which is an artificial construct in absence of a clinical trial structure. We provide an example in a study of time to cardiac events in patients with thalassemia major treated with one of two medications, deferoxamine or deferiprone. All patients started on deferoxamine and 30% switched at some point to deferiprone. 41% of those switched back to deferoxamine. The analysis shows that one can consider the various biases that may occur in a natural history study and provide valid results that extend the results of the clinical trials to compare the treatments.