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Developing a surrogate endpoint for AIDS clinical trials

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When it comes to the process of developing new treatments, the choice of an endpoint is crucial because this endpoint will be used to assess the effects of the treatments. However the most sensitive endpoint is difficult to use in a clinical trial because the measurement of the true endpoint can be costly and difficult to measure. Therefore the most feasible solution is to replace the true endpoint by another endpoint termed "surrogate endpoint" which can be measured earlier and more frequently.

Although there are some limitations, *CD4* cell count and viral loads are used in majority of AIDS clinical trials as surrogate endpoints. Therefore, the current study was intended on developing a surrogate endpoint for Acquired Immune Deficiency Syndrome (AIDS) based on a combination of variables. This study was based on a published dataset and consists of 16 variables measured on 1151 Human Immunodeficiency Virus (HIV) infected patients. Through the Log Rank test, variables *CD4*, *Karnofsky score* and age were identified as potential candidates for surrogate. The behaviors of those variables with respect to survival were further analyzed using Kaplan-Meier plots. Conventional statistics like sensitivity, specificity and attributable proportion were calculated to evaluate the suitability for surrogacy which suggests on its own *CD4* is the best to use as a surrogate. However a model with a combination of variables named score consisting of *CD4*, *Karnofsky score* and age yielded positive results in log rank test and conventional statistics was designed. Sensitivity of score was 0.78, specificity 0.62, attributable proportion 0.98. Score was also successful in identifying the difference between the two treatments. Validation of the score model using Prentice's criteria fulfilled all four criterions of Prentice suggesting that the model is accurate. The Prentice's criteria were also well validated for *CD4* yet, it is important to note that the newly developed surrogate endpoint score was better than *CD4* with respect to all four criteria. Sensitivity and the attributable proportion values of score were higher compared to *CD4*. Therefore, by considering all these facts, it can be concluded that the newly developed surrogate endpoint score is better than *CD4* to be used in AIDS clinical trials.