A Time to Event Approach for Standard of Care Meta-Analysis in HCV Trials

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Abstract

The current consensus on use of antiviral drugs in chronic HCV is based on observational studies with shorter follow-up (SFU) of up to 72 weeks or on a few landmark randomized trials, and as such there is no robust evidence on the relative efficacy of a new generation HCV polymerase inhibitors (PIs) and IFN. In this study we present results from a nonparametric meta-analytic estimation of sustained virological response (SVR) for the new class of drugs with the aim to provide new evidence on the relative cost-effectiveness of the new drugs compared to existing therapy.

Introduction

Hepatitis C virus (HCV) is a blood-borne virus that causes chronic liver disease, selecting an estimated 290 million people worldwide and no effective vaccine for its prevention. The high rate of incidence and proportion of patients who progress to cirrhosis or hepatocellular carcinoma is largely due to viral persistence. The mainstay of HCV treatment has been combination therapy with PEGylated interferon (peg-IFN) and ribavirin (RBV). With the advent of more potent direct acting antiviral (DAA) agents, the goal of curing chronic HCV is rapidly becoming achievable. Patients treated with combination therapy with DAA agents and RBV show higher rates of sustained virological response (SVR) compared to previous regimens. However, while DAA agents are highly effective, they are associated with a high cost that requires the development of meta-analytic evidence to support their continued use. A Time to Event Approach for Standard of Care Meta-Analysis in HCV Trials

Data

In order to use the data reported in both formats and prepare the data for analysis, we performed a few steps with the final goal being producing a pooled model for sustained virological response (SVR) for patients treated with the different drugs. First, we identified the available data in each format. The model used in the final format is based on the one described in the first format, but for the second form, we used the data in the form of patient level data, which allows for a more comprehensive analysis of the patient data. The model used in the first form was based on the one described in the first format, but for the second form, we used the data in the form of patient level data, which allows for a more comprehensive analysis of the patient data.

Model

Table 1 shows the distribution of the proportion of patients with SVR at each time point. As we can see, the distribution of the proportion of patients with SVR is not uniform across all time points. However, the distribution of the proportion of patients with SVR at each time point remains relatively consistent across time. The proportion of patients with SVR at each time point is shown in the second format.

Appendix: General derivation of modeling approach


Figure 1: Plot of the estimated proportion of patients with SVR at each time point. The estimated proportion of patients with SVR is shown in the second format.

Figure 2: Results: Predictive distribution for hypothetical patients.

Conclusions

The model was fit using WinBUGS (MCMC) and a Markov Chain Monte Carlo (MCMC) algorithm. We use the estimated parameters to make predictions about the expected efficacy of the new drugs compared to existing therapy. As we can see, the distribution of the proportion of patients with SVR is not uniform across all time points. However, the distribution of the proportion of patients with SVR at each time point remains relatively consistent across time. The proportion of patients with SVR at each time point is shown in the second format.

Appendix: General derivation of modeling approach

Aggregated WHR probability

Table 1 shows the distribution of the proportion of patients with SVR at each time point. As we can see, the distribution of the proportion of patients with SVR is not uniform across all time points. However, the distribution of the proportion of patients with SVR at each time point remains relatively consistent across time. The proportion of patients with SVR at each time point is shown in the second format.


References


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