Project ECHO Revisited: Propensity Score Analysis And HCV Treatment Outcomes

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Abstract: Propensity score analysis is a statistical approach to reduce bias often present in non-randomized observational studies. In this paper we use this method to re-analyze data from a study that assessed whether patients receiving HCV treatment from providers in Project ECHO had different clinical outcomes than patients treated by specialists from an academic medical center (UNM HCV clinic) but in which treatment assignment was not randomized. We modeled the best estimated probability of treatment assignment, and then assess differences overall SVR and SVR in patients with genotype 1 infection by treatment arm using Stabilized Inverse Probability of Treatment Weights (SIPTW). Results show that after adjustment for SIPTW, HCV treatment outcomes were significantly better for the ECHO patients compared to the UNM HCV clinic patients. Higher proportions of patients treated by primary care providers achieved SVR and SVR with genotype 1 compared to those treated at UNM HCV clinic with 15.1% and 16.3% absolute differences, respectively. These results indicate that previously published results (showing no differences) were biased, and resulted in an underestimation of the treatment effect of ECHO on HCV treatment.

Keywords: propensity scoring, ECHO, hepatitis C virus, treatment

Introduction

A prospective cohort study from 2004 through 2008, conducted by Arora et al.1 comparing HCV treatment outcomes in patients treated for hepatitis C virus (HCV) infection at specialty clinics in an academic medical center (University of New Mexico (UNM)) and patients treated by primary care providers in Project ECHO showed no differences in sustained viral response (SVR) between the groups. A total of 57.5% (84 of 146) of patients treated at UNM HCV clinic achieved SVR and 58.2% (152 of 261) patients treated at ECHO sites achieved SVR. The difference in the proportion achieving SVR was 0.7 percentage points (95% confidence interval (CI); -9.2 to 10.7; P=0.89). Among patients with HCV genotype 1 infection, SVR was 45.8% (38 of 83 patients) at the UNM HCV clinic and 49.7% (73 of 147 patients) at ECHO sites (P=0.57). The impact of these results was significant as they showed that complex interferon-based HCV treatment could be effectively delivered outside of specialty care using a telehealth knowledge dissemination model. The ECHO (Extension for Community Healthcare Outcomes) model, developed as a platform to deliver complex specialty medical care and improve access of minorities and underserved populations to best practice care through an educational model of team-based interdisciplinary development - worked.1

This study’s limitations, however, were evident and discussed. As with many observational studies of clinical care, this was not a randomized trial; in a randomized...
Despite large differences on their measured covariates in this observational study, we reduced the common support and balance assumptions were satisfied for this problem. Specifically, the SIPTWs exhibited similar distributions and the distributions of propensity scores between the two treatments completely overlapped between the two treatments with means close to one (ECHO: M=1.0, SD=0.8; UNM HCV clinic: M=1.2, SD=4.7), suggesting no misspecification of the used model.11

Our results show that after adjustment for SIPTW, HCV treatment outcomes were significantly better for the ECHO patients compared to the UNM HCV clinic patients (Table 1). Higher proportions of patients treated by primary care providers achieved SVR and SVR with genotype 1 compared to those treated at UNM HCV clinic with 15.1% and 16.3% absolute differences, respectively.

Discussion
Our results indicate that by using propensity scoring with measured covariates in this observational study, we reduced
bias and achieved improved precision of the difference in HCV treatment results for HCV infection in ECHO compared to UNM HCV clinic patients. And importantly, the results show that patients treated by ECHO providers had significantly better outcomes than those treated by specialty providers at the academic medical center. These results indicate that previously published results (showing no differences) were biased, and resulted in an underestimation of the treatment effect of ECHO on HCV treatment. Analyses to further explore the sources of this bias showed three factors that primarily contributed to the direction of the adjusted findings: male sex, creatinine levels and white blood cell count. For example, there were many more males in ECHO (72%) than in UNM (45%) and males had a somewhat lower SVR rate; this is a selection bias that artificially caused ECHO to have a lower SVR rate than would have been observed in a randomized clinical trial.

This analysis benefitted from a large enough sample size (406 patients: 261 were treated at ECHO sites and 146 were treated at UNM HCV clinic) to implement inverse probability weighting. While there are several strategies to building the multiple logistic regression models to calculate the propensity scores, we used strategy which utilizes a non-parsimonious model as recommended by most authors.\textsuperscript{2,12–18} We had similar findings with better outcomes in ECHO patients when we used a parsimonious model using methods described by Shadish et al.,\textsuperscript{14} wherein 19 covariates and factors were used instead of 27. This previously published study is an important example of how propensity scoring can (and should) be used in statistical analysis in applied medicine, where treatment assignment is not randomized. Further these results confirm previous findings showing that the ECHO model is an effective way to deliver HCV treatment to underserved communities. This research in this study was conducted when interferon-based treatment was standard of care and treatment success rates were much lower than with current direct-acting antiviral (DAA) treatments, which are effective in over 95% of patients.\textsuperscript{19} As the ECHO model has now been expanded into new clinical areas and populations and with the new highly effective DAA treatment, ongoing evidence will still be needed to measure effectiveness and impact. Using propensity scoring for

Table 1 HCV Treatment Outcomes By ECHO Vs. UNM HCV Clinic: Original Analyses Vs. Analyses Adjusted For SIPTW

|                        | Unadjusted (Previous Analysis) | Adjusted By SIPTW* |
|------------------------|-------------------------------|--------------------|
|                        | ECHO | UNM HCV clinic | P-value | ECHO | UNM HCV Clinic | p-Value |
| Proportion with SVR    | 58.2% | 57.5% | 0.890 | 58.1% | 43.0% | 0.003 |
| Proportion of patients with HCV genotype 1 with SVR | 49.7% | 45.8% | 0.572 | 48.2% | 31.9% | 0.008 |

Note: *Stabilized Inverse Probability of Treatment Weight.
further observational analyses has important potential provide unbiased and better estimates of these outcomes.

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