

Abdominal Imaging and HCC Risk

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February 12, 2020

We have restricted our dataset to adult UCSF patients diagnosed with HCV who, prior to the start of follow up (ie. as of 12/31/14) had no cirrhosis and no HCC. (n = 1905) For those who had been in the system prior to 2015, historical data back to 2011 was used to calculate their FIB-4 score at the beginning of follow up (ie. by the end of 2014), for those who did not yet have those data, the FIB-4 score in 2014 was imputed using the median value.

- **Sex.** This is a dichotomous variable, with two categories (male, female), as UCSF has not been capturing other gender categories within Epic.
- **Race.** This is a categorical variable, which we have recategorized into White, Black/African American, Latinx, and Other for ease of analysis.
- **SES.** We are using insurance type (Medi-Cal, or not Medi-Cal) as a marker of SES status, which is again a dichotomous variable.

The table below displays the demographic breakdown of the sample.

| Demographic | Category | n | % |
|------------------|------------------------|------|-------|
| Sex | Male | 1064 | 55.9% |
| | Female | 841 | 44.1% |
| Race/ethnicity | Black/African American | 297 | 15.6% |
| | Latinx | 264 | 13.9% |
| | White | 944 | 49.6% |
| | Other | 378 | 19.8% |
| | Unknown | 22 | 1.2% |
| SES (Payor type) | Medi-Cal | 286 | 15% |
| | Not Medi-Cal | 1570 | 82.4% |
| TOTAL | | 1905 | 100% |

Here, $Y(t)$ is an indicator variable describing whether or not the patient has been diagnosed with HCC by time t ; as such, it deterministically jumps to 1 and remains there once an individual has become ill.

Causal Question: How would the counterfactual probability of getting HCC differ by the end of the 5 year follow up under an intervention to get abdominal imaging at least once a year every year for four years?

The target causal parameter is $\psi^F(\mathcal{P}_{U,X}) = E_{U,X}(Y_{\bar{a}=1(5)} - Y_{\bar{a}=0(5)})$

the average treatment effect on HCC diagnosis in year 5 assuming that all patients had abdominal imaging every year for the 4 prior years ($Y_{\bar{a}=1}$), compared to HCC outcomes in year 5 if all patients did NOT have abdominal imaging at any time point during the preceding four years ($Y_{\bar{a}=0}$).

When testing our estimators against a simulation of 100,000 patients roughly matching the variable distribution of our observed dataset, here is how they performed:

| | G-Comp | IPTW | TMLE |
|------|---------|----------|---------|
| Bias | 0.00396 | 0.249134 | 0.00729 |

| | G-Comp | IPTW | TMLE |
|----------|---------|----------|---------|
| Variance | 0.00001 | 0.02397 | 0.00077 |
| MSE | 0.00003 | 0.086037 | 0.00082 |

Ultimately, implementing *tmle* with *Super Learner* on our observed data produced the following estimates for the risk difference of developing HCC in year 5 when receiving abdominal imaging at least once per year for the 4 preceding years, compared to not receiving abdominal imaging during that time, when controlling for the number of hepatology or primary care visits, FIB-4 score, sex, race, and SES was:

| G-Comp (95% CI) | IPTW (95% CI) | TMLE (95% CI) |
|----------------------|----------------------|----------------------|
| 1.179 (1.148, 1.274) | 1.226 (1.171, 1.318) | 1.234 (1.183, 1.313) |

If we use the G-computation estimate, this means that over the five years under study, patients with no cirrhosis at baseline were 1.2% less likely to develop HCC by year 5 when they had abdominal imaging each year for the 4 previous years, compared to patients who had no abdominal imaging, when controlling for liver cirrhosis, number of primary care or hepatology visits, sex, race, and SES. **This represents a number needed to treat (NNT) of 83** : for every 83 people who receive annual abdominal imaging despite no evidence of cirrhosis at baseline, 1 case of HHC could be prevented over 5 years.