# MEDIATION ANALYSIS

To investigate the role of time to treatment in explaining disparities in cancer survival

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### Introduction

- Increasing differences in cancer survival among ethnic groups.
- Stage at diagnosis does not account for all the racial survival disparity.



Figure1 Diagram of Causal Relationship

### **Objectives**

- Decompose the effect of Race on cancer survival.
- Evaluate the effect of **Time to Treatment** adjusted by stage at diagnosis.



Figure1 Diagram of Causal Relationship

### **Data and Methods**

### Study Population

- Non-Hispanic White and non-Hispanic Black patients diagnosed with colorectal cancer
- Dagnosed above the age of 18
- Followed up for seven years since the date of diagnosis
- Data Resources
  - Cancer Care Outcomes Research and Surveillance(CanCORS) cohort study
  - Exposures (X) race, gender, income, education
  - <u>Mediator (T)</u> time to treatment (in month), which is log transformed
  - <u>Outcome (Y)</u> indicator of five year survival

### **Data and Methods**



Figure1 Diagram of Causal Relationship

# **Mediation Analysis**

- Mediator Modeling
  - AFT model  $\log(T_i) = \beta_0 + \beta_1 \operatorname{race}_i + \beta_2 \operatorname{stage}_i + \beta_3 \mathbf{X} + \epsilon_m$
- Outcome Modeling
  - Logistic model  $logit[P(Y_i = 1)] = \theta_0 + \theta_1 race_i + \theta_2 T_i + \theta_3 race_i * T_i + \theta_4 stage_i + \theta_5 X$
- Effect Decomposition
  - Average causal mediation effects (ACME)
  - Average direct effects (ADE)

## **Mediation Analysis - Mediator Modeling**



Figure2 KM Estimates of Time to Treatment

- Stage I and II patients white patients are more likely to receive early treatment than black patients.
- Stage III and IV patients no significant racial disparity in treatment waiting time.
- Potential Race/Stage Interaction

### **Mediation Analysis - Mediator Modeling**

#### AFT model with Weibull assumption

 $\log(T_i) = \beta_0 + \beta_1 \operatorname{race}_i + \beta_2 \operatorname{stage}_i + \beta_3 \operatorname{race}_i * \operatorname{stage}_i + \beta_4 X + \epsilon_m$ 

- Results
  - 5.4% 8.2% longer treatment waiting time for black patients vs. white patients in early diagnosis.
  - No significant racial difference in treatment waiting time for patients diagnosed at stage III and IV.



Figure3 Fitted Probability of Time to Treatment

### **Mediation Analysis - Outcome modeling**



Figure4 Fitted Posterior Probability of Five-year Survival

- Non-linear Effects The probability of 5-year survival declines with the prolongation of Time to Treatment within 18 months of diagnosis.
- Racial Disparity The effect of mediator is potentially modified by race with a overall higher survival probability in white patients than black patients

### **Mediation Analysis - Outcome modeling**

#### Logistic model with Degree-3 Polynomial

 $logit[P(Y_i = 1)] = \theta_0 + \theta_1 race_i + \theta_2 T_i + \theta_3 T_i^2 + \theta_4 T_i^3 + \theta_5 race_i * T_i + \theta_6 stage_i + \theta_7 race_i * stage_i + \theta_8 X$ 

- Results
  - 70.5% 84.3% odds of 5-year survival for black patients vs. white patients with treatment receipt at T=1.
  - 68.5% 82.0% odds of 5-year survival for black patients vs. white patients with treatment receipt at T=2.



Figure5 Estimated Coefficients for Exposures

# **Mediation Analysis - Effect Decomposition**

Exposure	Effect	Estimate	CIlower	CIupper	p-value
race	ACME	0.0010	-0.0031	0.01	0.42
	ADE	-0.0568	-0.1130	-0.01	0.02 *
gender	ACME	-0.0053	-0.0097	0	0.04 *
	ADE	0.0530	0.0174	0.08	<2e-16 ***
income	ACME	-0.0017	-0.0054	0	0.42
	ADE	0.0778	0.0285	0.12	<2e-16 ***
age	ACME	-0.0007	-0.0079	0	0.78
	ADE	0.0098	-0.0264	0.06	0.6

\*Nonparametric bootstrap simulation was performed for variance estimation

Figure6 Mediation Analysis with Estimation of ACMEs and ADEs

ACMEs

Only significant in gender

#### ADEs

Significant in race, gender and income

# **Discussion**

### Achievement

- Parametrized the distribution of time to treatment and survival outcome
- Quantified the mediation effect of time to treatment in explaining survival disparities

### Limitation

- Predictive power of mediation analysis was limited by insufficient black patients.
- Confounders were not fully identified (e.g. health status)
- Improvement
  - Allow for time-dependent effects of survival probability and time to treatment
  - Consider multiple mediators (e.g. stage of diagnosis)