Title Slide Title

First Last

University of North Carolina at Chapel Hill

THE DATE

UNC
GILLINGS SCHOOL OF
GLOBAL PUBLIC HEALTH

Overview

1. Background: Motivation
2. Methods
3. DNA Damage Repair Subtyping
4. Discussion

Background

- Talk about your motivation

Background: Motivation

Dr. Corey Kalbaugh

Dr. Melina Kibbe

Dr. Edward Bahnson

1. Scientific Study
2. Clinical Trial
3. Observational Study

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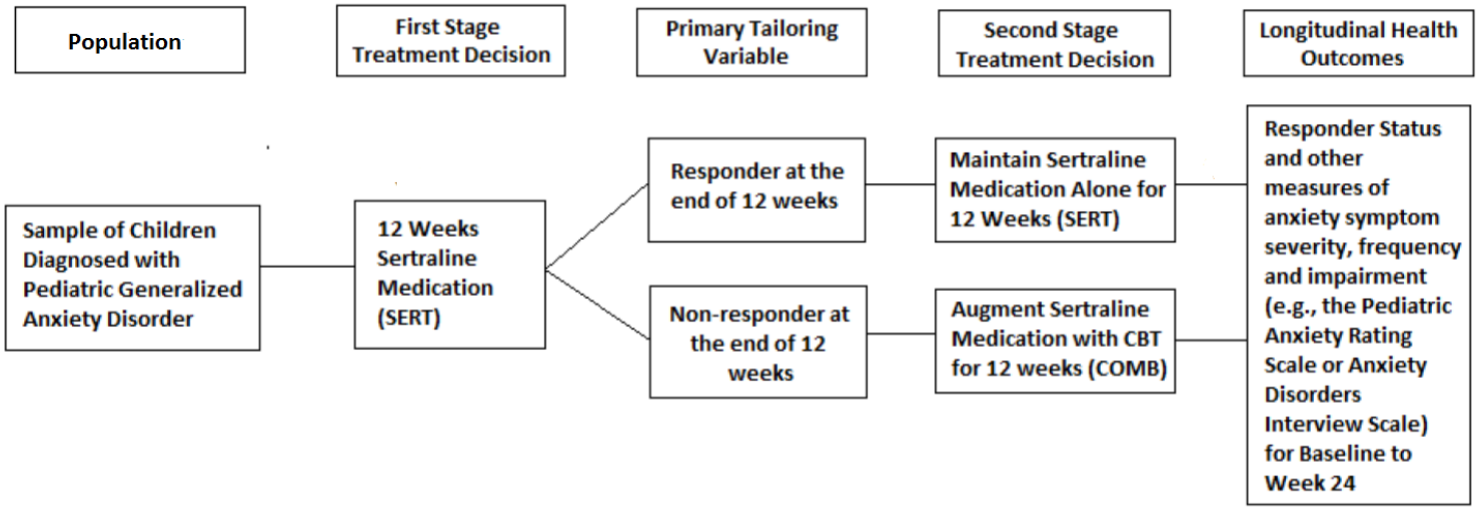
Dynamic Treatment Regimes

- A sequence of decision rules that assigns treatment based on some covariates or *tailoring variables*[1]
- One decision per intervention stage
- *Optimal* DTRs maximize some clinical outcome(s) of interest



[1] Alimirall, Compton, Gunlicks-Stoessel, Duan, and Murphy 2012

Addressing the Clinical Aim

"Identify the optimal dosage regimen of SFN supplementation that achieves the best functional outcome with and **without** additional tailoring variables."

Outcomes

- Tolerance
- 6-Minute Walking Distance

Covariates

- SFN Supplementation
- Dosing
- Diabetic Status
- Demographics
- Blood Work
- Biomarkers

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DNA Damage Repair (DDR) Motivation

- Given that Platinum-based chemotherapies act by damaging DNA, it is assumed that tumor cells that have better repair efficiencies.

Data

- There are RNA-Seq samples for 376 cases in the available data for the TCGA-OV project. We will restrict the sample to only those with clinical data available.
- The DNA Damage Response (DDR) gene set was retrieved from the Gene Ontology Consortium. It contains 830 genes of which 808 appear in the TCGA samples.
- Conclusion, Summary, Limitations, Future Work

Preprocessing Considerations

- Dimensionality Reduction: Distance measures in high-dimensional spaces.
- Normalization - Variance Stabilizing Transformation (DESeq2)
  Assume that the number of reads in sample j that are assigned to gene i can be modeled by a negative binomial (NB) distribution, $K_{ij} \sim NB(\mu_{ij}, \sigma_{ij}^2)$
- Low counts

Discussion

- Conclusion, Summary, Limitations, Future Work

References

1. Almirall, D., Compton, S. N., Gunlicks-Stoessel, M., Duan, N., and Murphy, S. A. (2012). "Designing a Pilot Sequential Multiple Assignment Randomized Trial for Developing an Adaptive Treatment Strategy". In: *Statistics in Medicine* 31.17, pp. 1887–1902.
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6. Zhao, Y. (2015) "Reinforcement Learning Applications in Clinical Trials". In: *Adaptive Treatment Strategies in Practice: Planning Trials and Analyzing Data for Personalized Medicine*. Ed. by M. Kosorok and E. Moodie. SIAM. Chap. 17.