Estimating the Best Commute: Adaptive Trial Design and Execution

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FACTS Working Group
9/1/2023
9/15/2023 (slide 18)
9/22/2023 (slide 18)

Note

- Most of these images come from me
- However, Richard Kinai or Jiawai Duan contributed some

Introduction

- The use of adaptive designs in clinical trials has been increasing due to its flexibility and efficiency gains, besides being more ethical as they assign fewer subject to treatment arms with inferior outcomes [1][2].

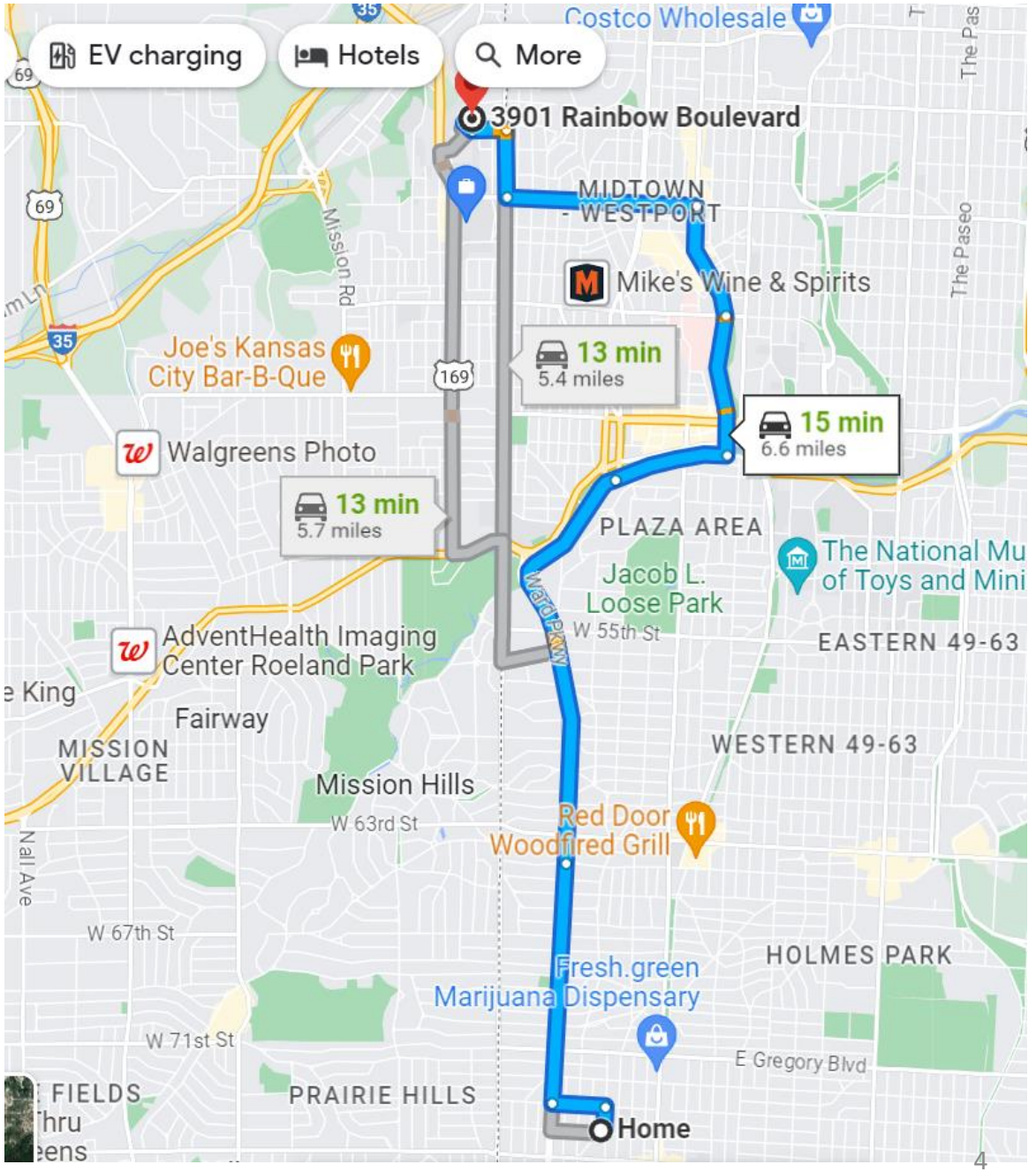
- Their use is gradually being extended to other areas to capture the already realized benefits [1][3][4].

- Reducing the amount of time spent driving from home to work can help maximize productivity in the work place.

- This study utilizes adaptive designs to determine the optimal driving route from Dr. Gajewski's home to his work place at KUMC.

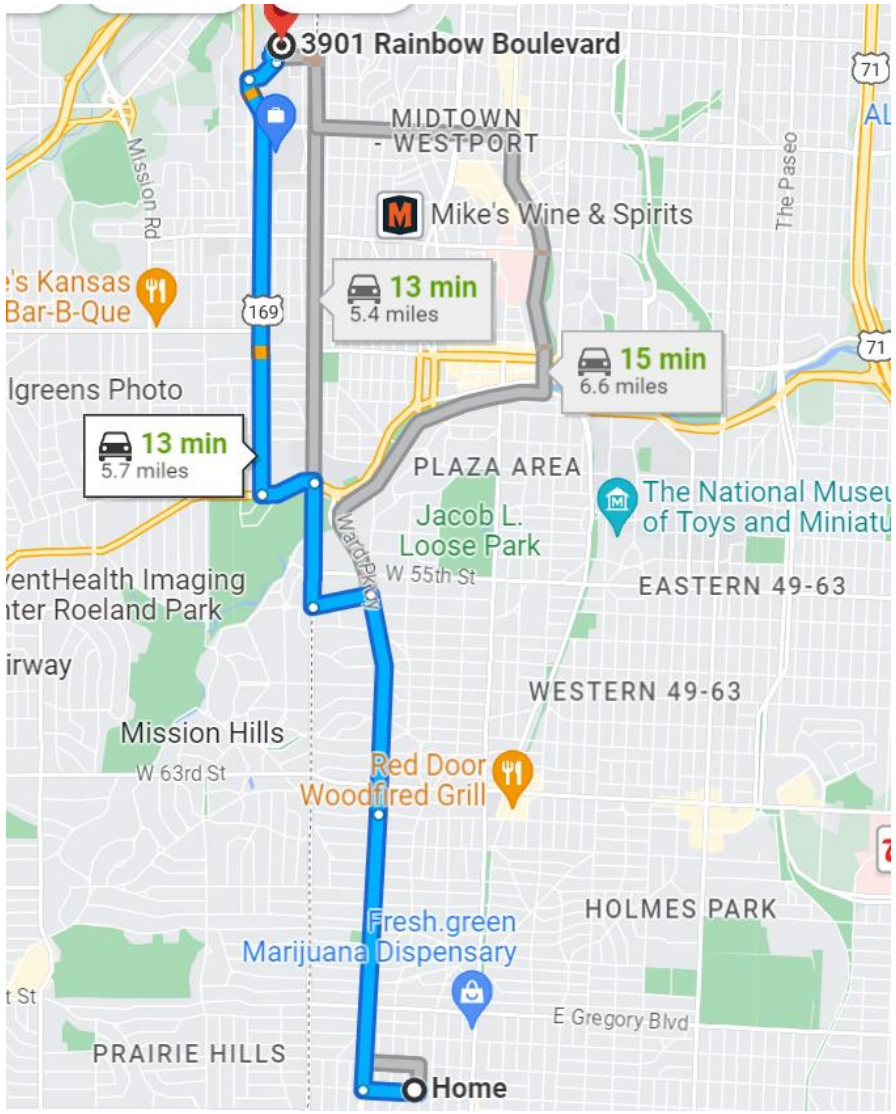
Plaza Route (Control)

- Three lanes (faster speed)
- Aesthetic (goes through Plaza)
- First route when moving to KC
- Indirect (slow?)



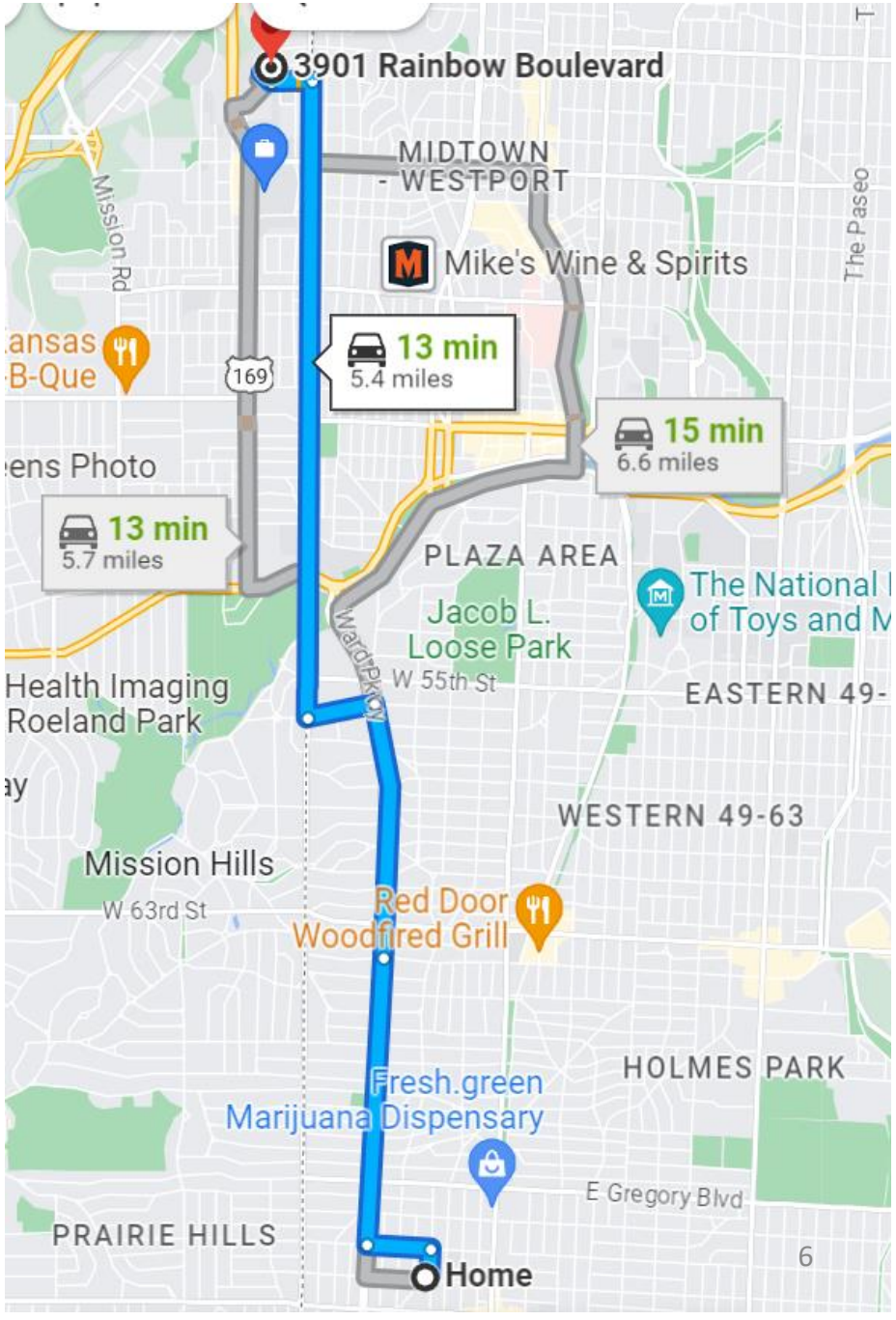
New route 1: Rainbow

- Two lanes
- Faster speed
- Direct



New route 2: Stateline

- Straight
- Direct
- One lane (slower?)



I want to see if there is a better route than Plaza

Arm	Route
1	Plaza (Control)
2	Rainbow
3	Stateline

Assumptions

Arm	Route	Data Source	Average Driving Time (μ_j)
1	Plaza (Control)	Google maps	15 minutes
2	Rainbow	Google maps	13 minutes
3	Stateline	Google maps	13 minutes

$\sigma \sim 1.2$ minutes (preliminary data)

Fixed Design (Strawman)

- 1:1:1 Allocation
- One analysis
- Compare two new arms to control
- Type I error 2.5%, 1-sided, Bonferroni (2.5%/2=1.25%)
- 90% power -> 11/group (n=33)
- Will take about 6.5 weeks to implement (1 driver, 5 times/week)

Can we do better? Adaptive Design Choices?

- Prior?
- Randomization? Response Adaptive Randomization
- What's the optimal allocation control?
- Interim analyses? How many?
- Success and futility rule?
- Can we do better in the average number of drives, time, better route?

Goal

- Design, conduct, and analyze this study.
- Write-up for a journal (*Journal of Statistics and Data Science Education*), all of us co-authors
- Need a Principal Investigator (PI) (Naima Alam)
  - Leads the project, manages timelines, and works with Co-Investigators
  - Works with notes taker to have good notes
  - Responsible for leading the final write-up
- Need milestone co-I (co-Investigators)
- Who's in?

Milestones/Products

1) Design (FACTS) (co-I: Elena)
2) Protocol (co-I: Geeth/Kate)
3) Statistical Analysis Plan (Geeth/Kate)
4) Data Capturing (RedCAP and a Shiny App for Randomization) (Sreejata/Fred)
5) Analysis (Kaustubh/JZ)
6) Paper (PI)

Milestone 1: Design

- Each of you, with a partner, come up with a new design
  - Pair a rookie user with a veteran user of FACTS
  - FACTS, Core Design, Continuous
- Calculate operating characteristics under various virtual subject responses (VSR)
- Accrual (drive all workdays)
- Endpoint (Driving time immediate)
- When you have your design in FACTS:
  - S:\Biostats\BIO-STAT\BISR\FACTS Working Group\FACTS code\Case Study 22 Optimal Driving Route
  - Have done by September 15
  - Each will present brief overview, then we vote which one to build off of

Virtual Subject Responses (VSR): Average Driving Time

Arm	Route	Null	Expected	One Best
1	Plaza (Control)	15 minutes	15 minutes	15 minutes
2	Rainbow	15 minutes	13 minutes	13 minutes
3	Stateline	15 minutes	13 minutes	14 minutes

$\sigma \sim 1.2$ minutes

Procedure

- This will be our primary agenda for the FACTS Working Group until done
- If it is a slow meeting day, will have presentations on other topics from Working Group members

Questions

Appendix: Alternate

- 2 x 2 factorial design
  - Route: Stateline vs. Rainbow
  - Elevator: Wescoe vs. Orr Major
  - Interesting: no interaction expected!!!!!
- Endpoint: home-to-office travel time
- Which one does the group prefer???
  - Three arms best driving (questionable control)
  - Four arms 2 x 2 factorial design

Initial Designs

Team	Type of Design	Comments
DIAS	Adaptive (RAR, three interims, success/futility), EMAX and Independent, deterministic accrual!!! Fixed allocation for control	No dose structure no EMAX (over parameterized) Independent model good, modify variance prior
Lauren&Elena	Comparative (no control), adaptive (arm dropping), fixed sample size, drops an arm immediately. Always dropped control	Prior needs fixing N(0,10) to N(13,10), variance prior needs fixing (prior sample size say .1) The arm dropping is good, but let other have a chance to be dropped I think they are comparing two active arms against each other, which is not a goal Optimistic prior
TheStarFish	"weeks" means "days" Adaptive (RAR, power .7, aggressive), control is not fixed allocation it allocates with the best	Type I error needs to be lowered to .025; match the block size with the interim, Not a lot of early sample size savings. Allows one to choose among the active routes in addition to better than control. Optimistic prior
JZ	Fixed	Fixed design with success criteria 1:1:1 allocation. "delta=1 min" decision making criteria (non-zero)
Byron	Two RAR's	

Elena: for our next meeting we need you and your team to evaluate the designs above and give a recommendation of a final desig to Naima with a 2-page rationale (by Oct 13). Naima will present and discuss the next steps (Elena can present too).