KU DEPARTMENT OF
BIOSTATISTICS & DATA SCIENCE
The University of Kansas Medical Center

DRIVE: Daily Route Investigation Via an Efficient Bayesian Adaptive Trial Design

Database Management Plan

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1. Randomization

This trial is structured with a response-adaptive randomization (RAR) design. In the initial interim, involving 8 participants, we implemented a fixed allocation ratio of 2:1:1 (Plaza:Rainbow:Stateline). In subsequent interims at 16, 24, and the final analysis at 33, additional participants are selectively randomized into the most successful route. To facilitate our adaptive design, we adopted a block size of 4, ensuring that the control arm (Plaza) is consistently assigned to at least one drive.

1.1. Initial Phase

The randomization for the initial interim was executed by the data managers through R statistical software version 4.3.0, utilizing the R package 'randomizeR.' To ensure reproducibility, a specific seed has been established during program execution. In this first interim, comprising 8 driving times, Plaza will be randomly assigned to four drives, while the comparator arms each receive two drives.

1.2. Interim 1, 2 & Final Phase

The randomization list for the subsequent interims and the final analysis phase will be generated using the 'Analysis' tab of the FACTS software, based on data collected in the preceding interim. The data analysis team will be tasked with producing the blinded randomization list and subsequently delivering it to the data managers.

1.3. Rerandomizing Routes for Drop-out Days

In the event of a dropout during a specific interim, Dr. Gajewski will be reassigned to the same route once the original randomization list for that interim is depleted. If there are multiple dropouts, a randomized list for the routes affected by the dropouts will be uploaded prior to sending the data for interim analysis. The data managers will assume the responsibility of re-randomizing the routes that have been dropped out.

2. Utilizing R Shiny to Deliver Randomized Route of the Day and Trigger REDCap record for the Day

We have streamlined the delivery of randomized routes and data collection by implementing a custom R Shiny app. This app generates the randomization list for the initial interim. For each succeeding interim, a distinct randomization list is generated through FACTS by the data analysis team and subsequently uploaded to the app following the data analysis of the preceding interim. The data managers are responsible for both developing the R Shiny app and undertaking the task of unblinding the blinded randomization list produced by the analysis team. This cycle of repeatedly generating randomization list and uploading to the app for the upcoming interim repeats until data for the final analysis is collected. In the event of a dropout, we replace the data with a new driving time for the same dropped out route prior to interim data analysis.

To ensure app security, Dr. Gajewski receives a unique 4-digit passcode for each interim, known only to him, the data managers, and the protocol team. While other team members can access the app, they are unable to view the randomization list without the correct passcode. The app interface is user-friendly; Dr. Gajewski simply navigates to the app link (https://sreejatadutta.shinyapps.io/RandomizationApp_Test1/), enters the passcode, and the app generates the randomized route for the day. The app also triggers a new record in the REDCap database, which further triggers a survey link for Dr. Gajewski to complete upon reaching the office and obtaining all necessary driving time information (see Section 3 for details).

Moreover, the app is designed to prevent the display of different randomization lists on the same day. Each time Dr. Gajewski enters the correct passcode, the app prompts the same route as indicated for the first time and no new REDCap record is generated. In addition to updating the REDCap database, the app synchronizes with a Google Sheet containing daily information

about the randomized route, sunrise, and record_id from REDCap. For each interim, a counter file is maintained to track the number of times Dr. Gajewski has driven within that interim.

In the event of any app outage, the backup plan is that, prior to the commencement of an interim, the data managers provide Dr. Gajewski with a backup contact whom he can contact whenever he has any questions or issues on the randomized route. The data managers are tasked with fixing the randomization app and initiating a new record in case there is a problem.

3. DRIVE Trial REDCap Database

3.1. Introduction

The DRIVE Trial REDCap Database is designed to house the study data of the DRIVE Trial. There are two forms in the database: Other Info and Survey. The Other Info form captures the data generated by the randomization R Shiny app, including Record ID, date of commute, time of sunrise, route randomized, and an email address field, as well as the starting time of first meeting of the day that requires manual data entry. Dr. Gajewski's email address is used by default for the email address field, so the REDCap system will send him an email invitation to enter the trial data in the Survey form. Email reminders will be sent up to two times if Dr. Gajewski has not responded by three hours. After Dr. Gajewski has completed a survey form, an email notification will be sent to the data managers for confirmation. At the end of each study week or interim, the data managers enter the starting time of the first meeting of the day, identify and resolute data issues, and export the blinded data to the Analysts.

3.2. Data Management and Quality Control

To identify and resolve data issues, we use the 'Data Quality' application in REDCap. At the end of each study week or interim, the data managers run a quality control report, identify, and resolve any data issues. The Data Managers will contact Dr. Gajewski to clarify his survey response if necessary.

3.3. Blinded Items and Data Export Policy

The routes randomized and driven on should remain blinded after the DSMB has reviewed the final blinded analysis. Therefore, the database access is restricted to the principal investigator (PI) and co-investigators (Co-Is) of the protocol and data management teams. Additionally, the data will be exported with the routes blinded, at the end of each interim and at the end of the study.

Table 1. DRIVE Trial REDCap database use access.

User Role: Name Initials	Co-I (Data Manager): SD, XS	Co-I (Protocol; API): KY	Co-I (Protocol): GM
Project Design and Setup	Y	Y	N
User Rights	Y	Y	N
Data Viewing Rights	View and edit	View and edit	Read only
Data Export Rights	Identifier removed fields	Identifier removed fields	No access
Survey Distribution Tools	Y	Y	N
Alerts & Notifications	Y	Y	N
Add/Edit/Organize Reports	Y	Y	Y
Stats & Charts	Y	Y	Y
Data Import Tool	Y	Y	N
Logging	Y	Y	Y
Data Quality (create/edit rules)	Y	N	N
Data Quality (execute rules)	Y	N	N
API Export	N	Y	N
API Import/Update	N	Y	N
Create Records	Y	Y	N
Rename Records	Y	Y	N
Delete Records	Y	N	N

Note: KY maintains the API token.

SD – Sreejata Dutta; XS – Xiaosong (Fred) Shi; KY – Kate Young; GM – Geethanjalee Mundunkotuwa

4. Update in V2

We changed the backup plan for randomization.