CHET Analytics
CENTER FOR HEALTH + TECHNOLOGY

UNIVERSITY of ROCHESTER

Ancillary Analytical Services
Case Studies Highlights

Model-Based Clinical Trial Enrichment:
Predicting Fast Progressors in Parkinson's disease

Problem

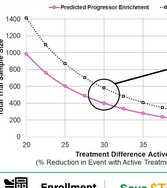
Clinical trials in Parkinson's Disease often face challenges with large sample sizes and lengthy durations to detect meaningful changes.

CHET Value Add

Using our predictive models, we can significantly **reduce the required sample size and reduce follow-up times** for clinical trials by enriching the enrollment with patients likely to experience rapid disease progression.

Our model predicts:

- **15% to 30% Reduction in Sample Size** by focusing on patients more likely to reach meaningful endpoints.
- **Patient Enrollment Savings** resulting in dozens to 100s of fewer participants compared to traditional target enrollment in most clinical trials.



EXAMPLE

30% treatment difference requires **400** participants instead of **600**

33.33% Reduction in Sample Size!

Enrollment Savings

Save $Thousands+ in operating costs by reducing sample size requirements

Biostatistical Services:
Case Study #1

2CARE

Coenzyme Q10 in Huntington's Disease

The largest therapeutic clinical trial to date in Huntington disease

- 608 research participants
- 46 clinical sites in the US, Canada and Australia

Roche · UCL · Huntington Study Group · Massachusetts General Hospital · CHDI · University of Rochester

Problem

A pharmaceutical company wanted to identify an **improved measure of clinical progression** in early Huntington disease (HD) using existing observational & interventional clinical trial data.

CHET Value Add

Leveraging our experience with existing HD studies and statistical expertise,

➡ **A composite measure was identified that characterized clinical progression better than individual symptom domain outcomes.**

Results & Impact

- This measure has been used as an outcome in clinical trials investigating potentially disease-modifying therapies, allowing a more sensitive measure of clinical change over current outcomes.
- Use of this measure in clinical trials results in smaller sample size estimates.

Biostatistical Services - Pharmacology:
Case Study #2

ACTG Study A5386

Broadly Neutralizing Antibody Therapy for HIV Treatment and Cure

Phase 1 clinical trial to induce HIV-1 control

- Up to 46 research participants living with HIV-1
- Two novel antibody drugs with long half-lives given in combination for the first time to adults living with HIV
- Goal is to stop antiretroviral therapy and test whether study compounds can control HIV infection.
- NCT04340596

ACTG
Advancing Clinical Therapeutics Globally (formerly AIDS Clinical Trials Group)

Problem

Unknown exposure-response profile of investigational agents required advanced translational PK/PD modeling and simulation to **determine appropriate timing of antiretroviral treatment interruption**.

CHET Value Add

Leveraging data from animal studies and healthy human subject studies to predict PK/PD profiles of two novel broadly neutralizing antibodies,

➡ **PK profiles were modeled and used to predict appropriate timing of antiretroviral treatment interruptions to maximize safety and potential to see efficacy.**

Results & Impact

- PK/PD modeling and simulation findings incorporated into the study design of the trial protocol.
- PK/PD modeling and simulations correctly predicted exposure profiles and continues to aid in the interpretation of study findings.

Biostatistical Services:
Case Study #3

DATATOP

Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism

One of the largest and longest prospective controlled studies of therapeutic interventions in Parkinson's disease

- 800 research participants
- 28 clinical sites in the US and Canada

UCSF
University of California San Francisco

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

Problem

An academic neurologist wanted to **determine if an association existed** between vitamin B12 deficiency and clinical progression in early Parkinson disease (PD).

CHET Value Add

Leveraging our expertise with existing PD studies and deep statistical knowledge,

➡ **We identified a trial dataset to examine the relationship between serum B12 levels and disease progression.**

Results & Impact

- Additional work involved analyses based on B12 levels in cerebral spinal fluid and current work includes analyses to determine associations in contemporary, similarly designed clinical trials.
- These combined results support a future study in early PD to determine whether B12 supplementation alters disease progression in a trial setting.

Biostatistical Services:
Case Study #4

2CARE

Coenzyme Q10 in Huntington's Disease

- 608 research participants
- 46 clinical sites in the US, Canada and Australia

CARE-HD

Co-Enzyme Q10 and Remacemide: Evaluation in Huntington's Disease

- 347 research participants
- 22 clinical sites in the US and Canada

CREST-E

Creatine Safety, Tolerability, & Efficacy in Huntington's Disease

The largest, longest duration, and highest dose study of creatine in Huntington's disease to date. (To date as of the conduct of the study).

- 553 research participants
- 47 clinical sites in the US, Canada, Australia, and New Zealand

Rowan University · Cooper University Health Care · FOX FAMILY FOUNDATION

Problem

An academic neurologist wanted to **extend prior methodology of suicidality risk factors** in early Huntington disease (HD) to additional clinical trials.

CHET Value Add

Leveraging our expertise with existing PD studies and deep statistical knowledge,

➡ **Similar statistical analyses were conducted across multiple existing studies and relationships of interest for several variables were observed.**

Results & Impact

- Several baseline demographic and time-dependent Unified HD Rating Scale (UHDRS) variables were associated with suicidality across 3 large HD clinical trials.
- It may be possible to better monitor or predict suicidality risk in HD clinical trials by using these variables in a more structured way, perhaps as a UHDRS-based subscale.

Biostatistical Services:
Case Study #5

PRESTO

Parkinson's Rasagiline: Efficacy and Safety in Treatment of OFF

A Multicenter, US and Canada, Double Blind, Randomized, Placebo-Controlled, Parallel Group Study, for the Efficacy, Tolerability and Safety of Rasagiline Mesylate in Levodopa Treated Parkinson's Disease Patients with Motor Fluctuations.

This study evaluated safety, tolerability, and efficacy of rasagiline in levodopa-treated participants with motor fluctuations.

- 472 research participants
- 57 clinical sites in the US and Canada

SEESAW

Safety and Efficacy of Entacapone Study Assessing Wearing-off

This study demonstrates that entacapone is effective in increasing "on" time in levodopa-treated Parkinson's disease patients experiencing motor fluctuations.

- 205 research participants
- 18 clinical sites in the US and Canada

Problem

A therapeutics company wanted to **quantify therapeutic benefit** in advanced stage Parkinson disease (PD)

CHET Value Add

Leveraging our proficiency in existing PD studies and statistical expertise,

➡ **We identified two trials to determine the efficacy of treatment based on time with dyskinesia.**

Results & Impact

These findings will further quantify the therapeutic benefit of treatment, particularly in advanced stage PD, and help to guide future trial designs.