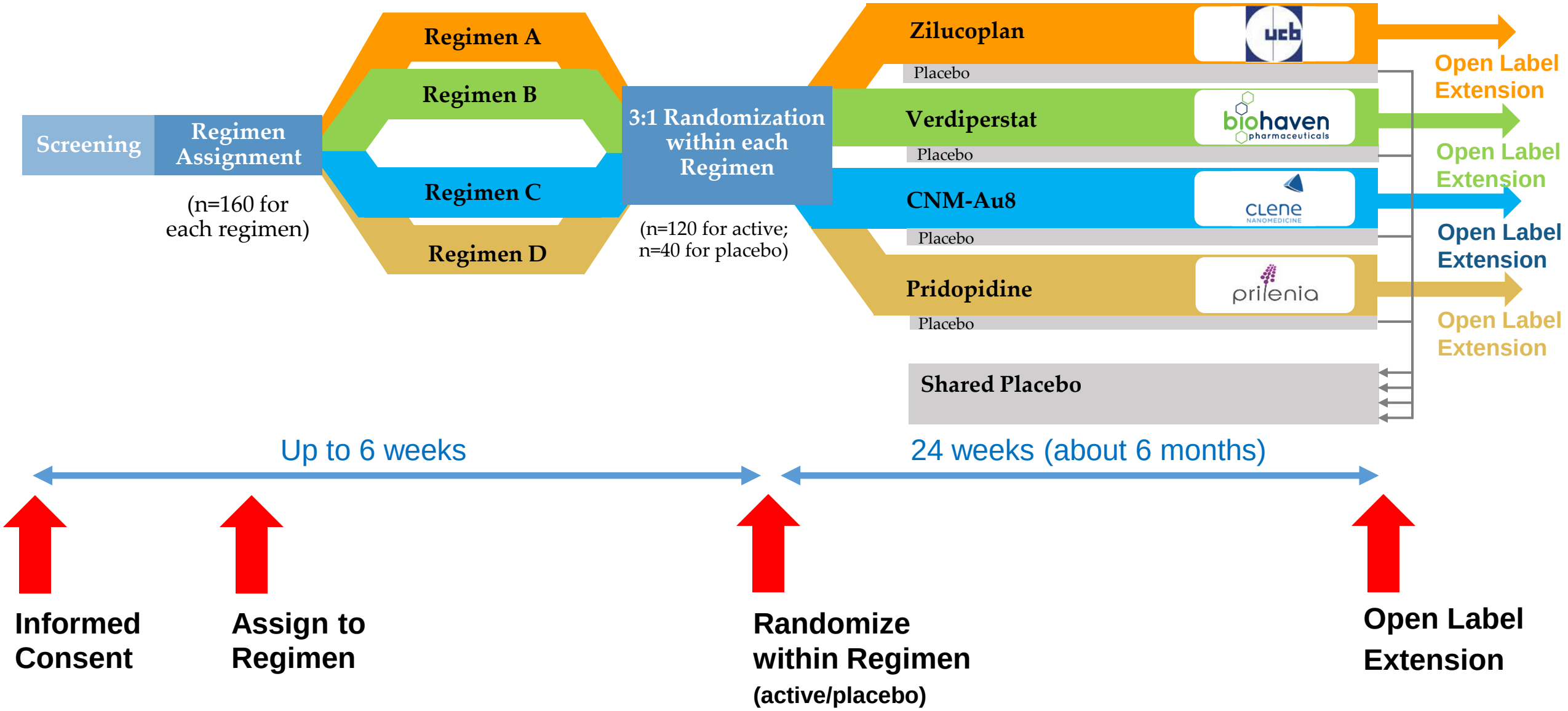
HEALEY ALS Platform Trial

Weekly Q&A – Nov 4, 2021

Perpetual Adaptive Trial
Shared Placebo; Randomization Ratio 3:1
Open Label Extension (OLE) offered



HEALEY ALS Platform Trial
Enrollment Updates (as of November 4, 2021)

- **851** individuals with ALS signed informed consent
- **675** individuals were assigned to a regimen
- **605** individuals were randomized within a regimen (active or placebo)
- **263** have entered the Open Label Extension (OLE)

- **160** individuals were randomized within Regimen A
- **167** individuals were randomized within Regimen B
- **161** individuals were randomized within Regimen C
- **117** individuals were randomized within Regimen D

Guest Speakers

Robert Glanzman, MD, FAAN
Chief Medical Officer
Clene Nanomedicine, Inc.

Michael Hotchkin
Chief Development Officer
Clene Nanomedicine, Inc.

Lori Chibnik, PhD, MPH
Assistant Professor & Biostatistician
Harvard TH Chan School of Public Health & MGH

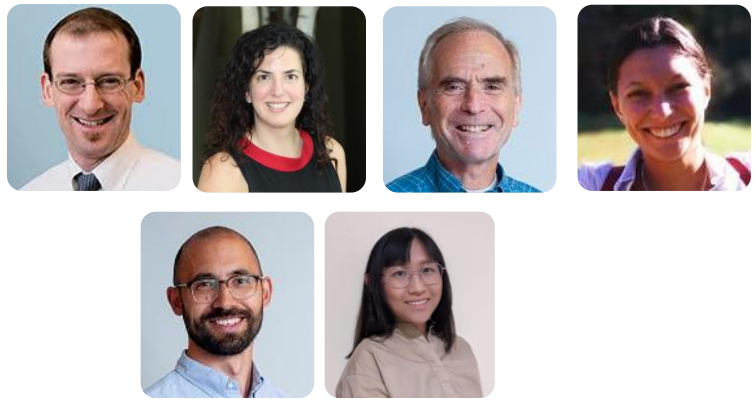
Guest Speakers

James Berry, MD, MPH
Regimen C, Co-Lead Investigator
Massachusetts General Hospital

Nicholas Maragakis, MD
Regimen C, Co-Lead Investigator
Johns Hopkins University

Trial Statisticians

MGH Biostatistics



Eric Macklin, PhD; Lori B. Chibnik, PhD, MPH; Douglas Hayden, PhD; Marie-Abele Bind, PhD; James Chan, MA; PoYing Lai, MS

HARVARD MEDICAL SCHOOL

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

MASSACHUSETTS GENERAL HOSPITAL

Berry Consultants

Michelle Detry, PhD; Melanie Quintana, PhD; Ben Saville, PhD; Matteo Vestrucci, PhD

Berry Consultants
Statistical Innovation

INTRODUCTION TO BIOSTATISTICS WEBINAR SERIES

Impetus

- Curated questions from
  - Past webinars
  - Facebook sessions and AMA
  - Emailed questions

What determined n=160 as the magic number for each regimen?

How does the platform randomization work given that there are 3 drugs that have over 200 patients enrolled, the placebo, and now Pridopidine is new with just 1 patient?

For the next round, will the current placebo data be combined with that to be acquired in the next round?

One of the slides mentioned a non-statistically significant difference. Can you explain that please, since you were so positive on the positive results.

If someone re-randomizes into a second regimen, is it possible then could be randomized into placebo 2x?

How come trials are set up in a way to “prove statistical significance”, but even when they are deemed “positive”, they are not “significant” ENOUGH for the FDA?

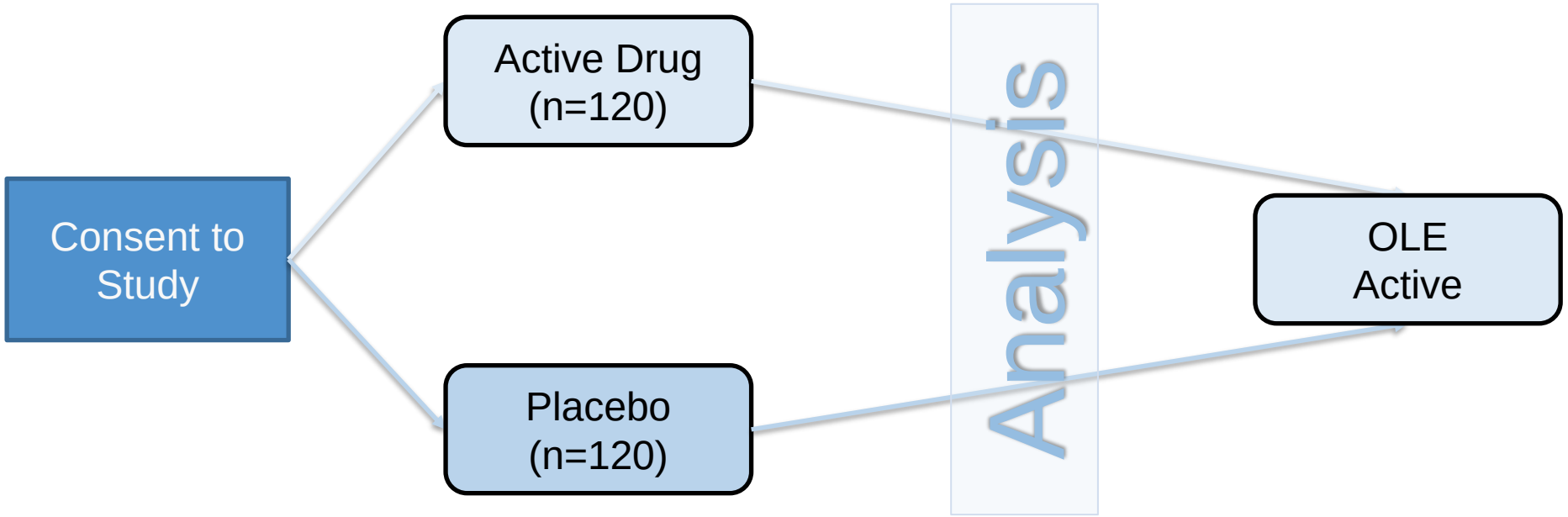
How are deaths included in the statistical analysis of adverse consequences if the death is from ALS and not trial complications?

Can you explain to people how the FDA's statistical penalty works for manufacturers who decide to do an interim analysis and how you or a manufacturer decides if they will be doing those in the Healey trials?

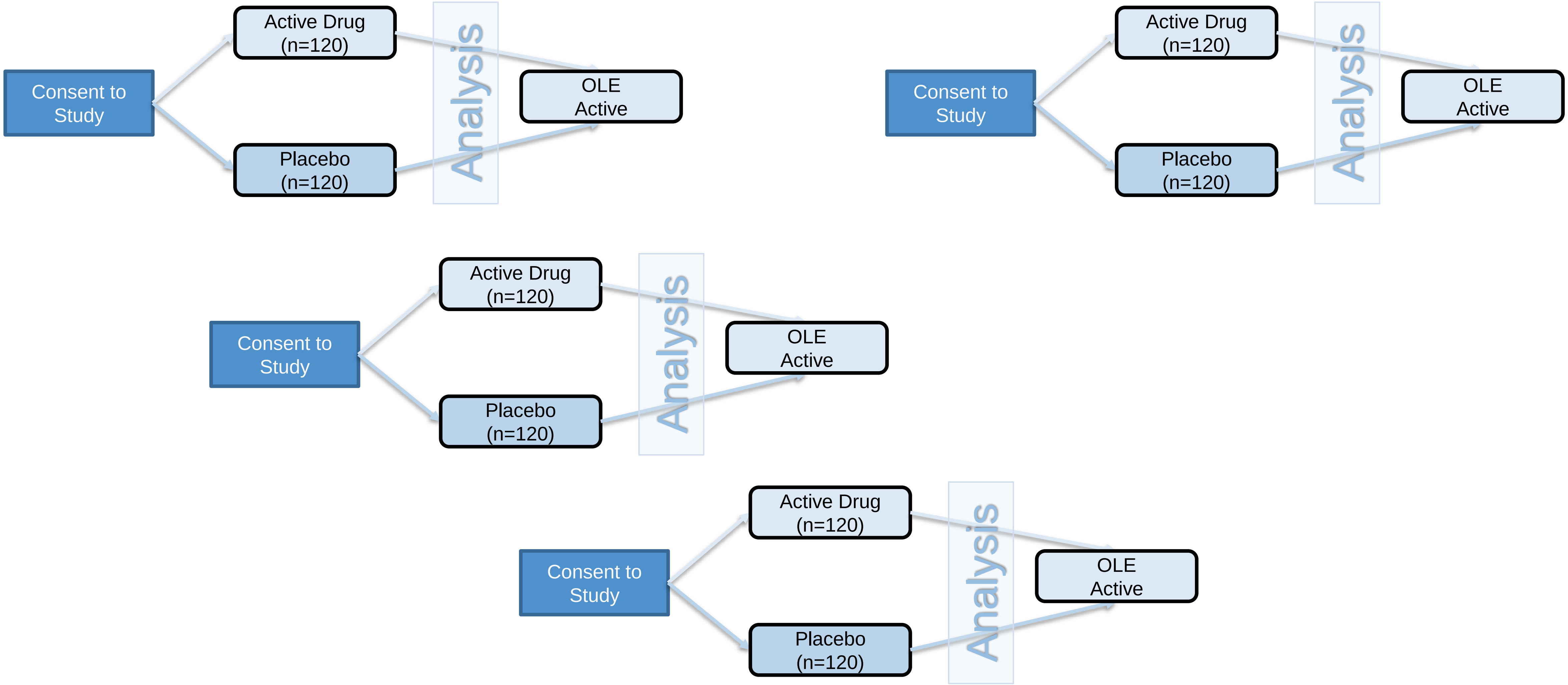
TO THINK LIKE A BIOSTATISTICIAN

ALS PLATFORM TRIAL THROUGH THE EYES OF A STATISTICIAN

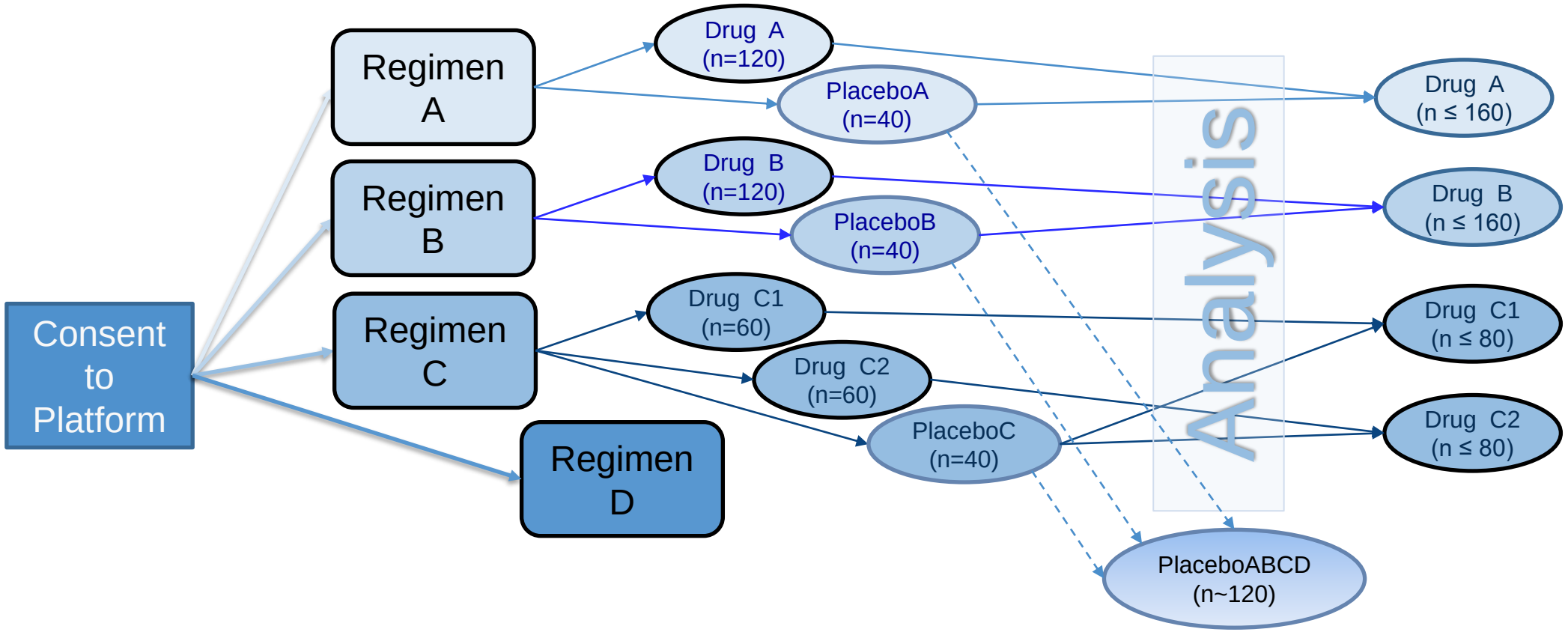
Generic Clinical Trial



Generic Clinical Trials



Healey ALS Platform trial



unblinded unblinded blinded *unblinded*

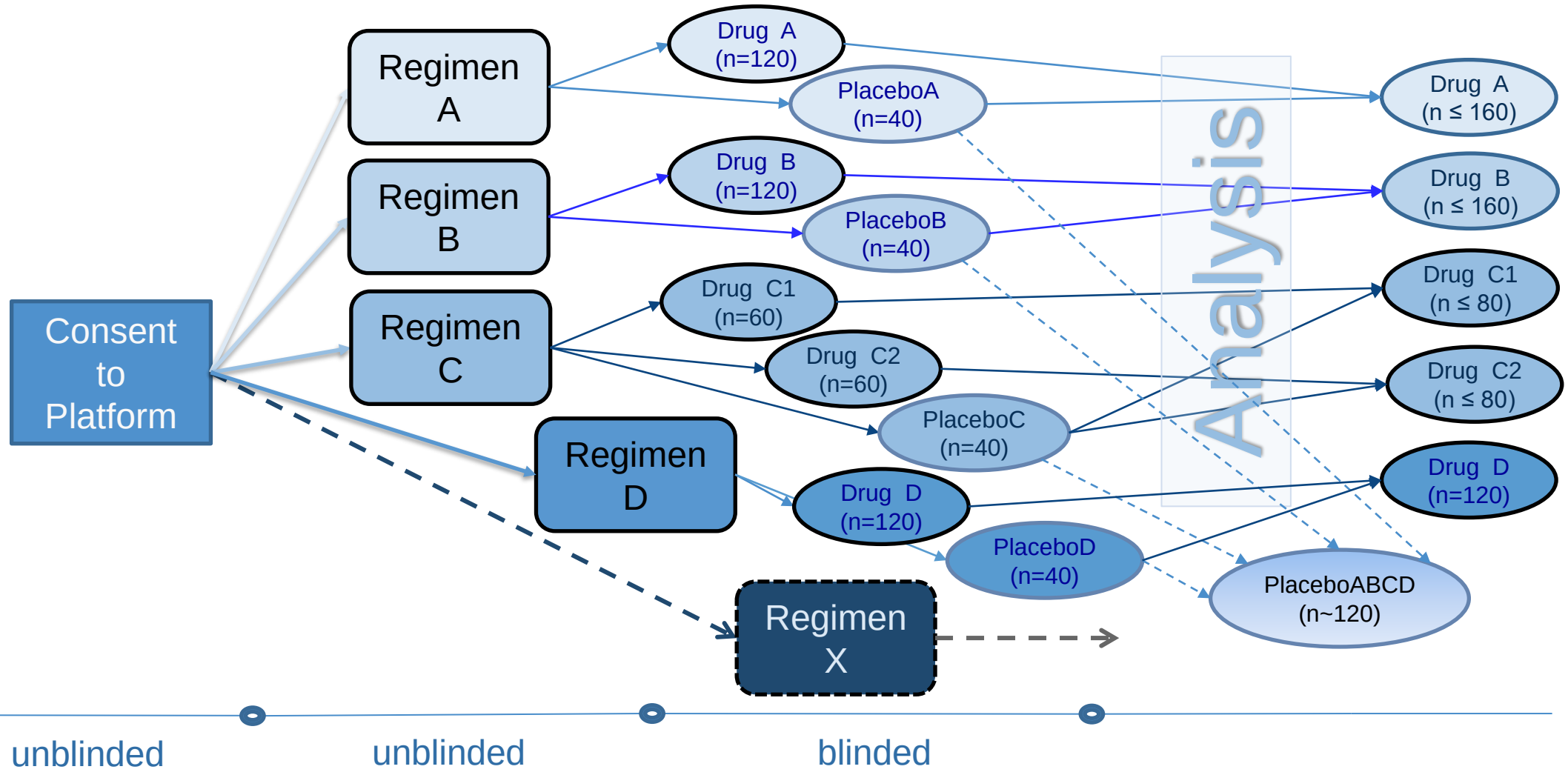
Healey ALS Platform trial

Study design

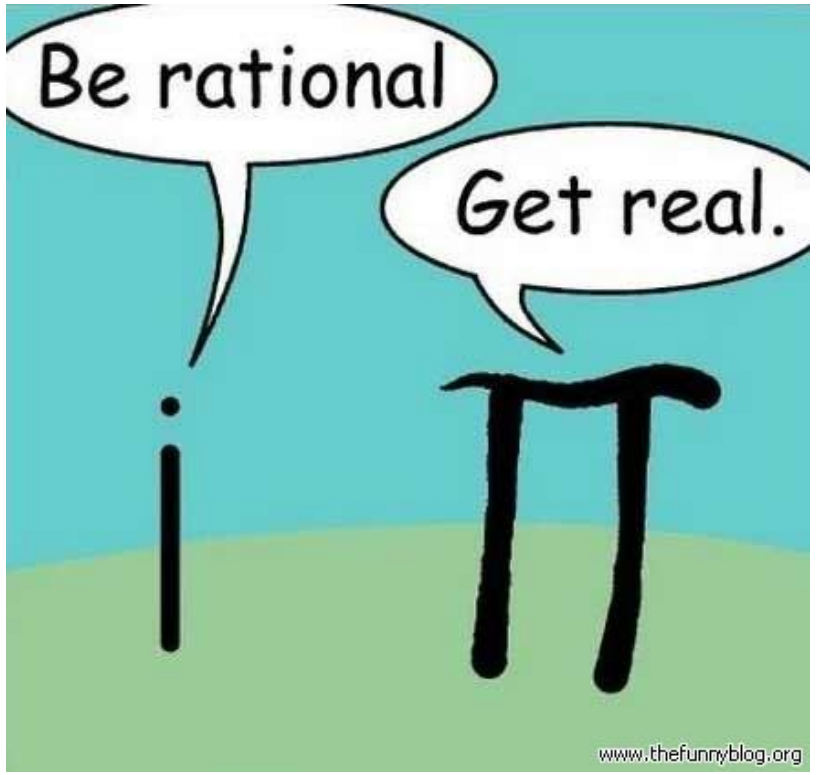
'clinically meaningful' results

Sample Size

Randomi-zation



Questions?



Planned topics

- Why and when Placebos are important
- Statistical Significance
- Randomization
- Determining optimal sample sizes
- Statistical tests used in ALS clinical trials and how they are modified for a platform design
- The statistics behind biomarkers discovery and use