CSRC 2nd Annual Think Tank on Prevention of Sudden Cardiac Death in the Young

The Importance of Knowing Normal: Industry Perspective

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Pediatric Capabilities

Eli Lilly and Company

Which industry and why?

- Device manufacturers? Of what?
  - ECG machines?
  - Echocardiograms?
  - MRIs?
  - CT scans?
  - Lab test machines?
  - To incorporate as “norms” in devices?
- Biopharmaceutical industry?
  - To study efficacy or safety of drugs/biologics?
- Sports/athletic equipment manufacturers?
  - To improve design, enhance protection?
- Others?

What is “normal” for industry?

- Want “normals” to be “normal,” whatever that is…
  - Within Normal Limits (WNLs) often refers to between 5th percentile and 95th percentile of the entire population
  - But…sometimes interested in subpopulations, which may differ from each other and from the entire population. Examples:
    - patients with various diseases/conditions or subgroups (cancer: leukemia)
    - musicians (string instruments: violins)
    - athletes (soccer, gymnastics, football, track & field: sprinter, marathon runner, pole vaulter, hammer or discus hurdler)
- **Industry wants a well defined, reproducible “normal” population that is relevant to (experimental) population of interest**
  - For example: biopharmaceutical companies usually study asthma drugs/biologics in patients with asthma, not in athletes (though some athletes may have asthma)

What are industry perspectives on studying “normal”?

- Must have **clearly stated objectives** for a study of “normals”
- **Objectives must have “value”** to justify the study ethically
- Must **design the study based on the objectives**, not other things
  - cart goes after the horse
- Operational considerations
  - Must be able to **consistently and reproducibly** identify “normal” individuals
  - Must plan for **large enough sample** to achieve objectives
  - **For pediatric studies, must consider impact of development** on objectives, sample size, data collected, planned analyses
  - Must conduct study using **consistent and reproducible** methods
  - Depending on objectives, appropriate clinical outcomes must be defined, identified, recorded for individuals in a **consistent and reproducible** way
  - Data must be captured and stored in a **consistent and reproducible** manner that allows for intended analysis

So…

- What are the objectives of what is being proposed?
- What “value” do the objectives have?
- Forgetting everything else, how would an “ideal” study be designed to achieve the objectives?
  - Would compromises to ideal study to allow analysis of existing clinical data still achieve the desired objectives and have same value?