Risk Boundaries in BP Assessment

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BP Risk Boundaries

- Description and development
- Application
  - When is a given degree of CV risk ‘too much’ for a given population?
  - How should risk boundaries be used in drug development?

BP Risk Boundary

- Shape of the curve for CV risk as a function of change in BP
  - Foundation of the discussion today
    - Based in, and made possible by, the extensive outcomes data available for effects of changes in BP
  - Date-driven, populational
    - Size of database allows us to examine changes in overall risk for some other risk factors (e.g., age, sex, smoking status)
  - Focus is on optimizing the ability of a given tool to predict CV risk (individual or populational)
    - Individual tools/databases (Framingham, Prospective Studies Group)
    - What aspects of BP matter?

How to Use BP Risk Boundaries

- Second task for today: how do we use these risk boundaries in drug development?
- Issues
  - Approval decision
  - What to measure
  - Threshold for concern

Uses of Risk Boundaries in Drug Development: Approval Decision

- Application of these risk curves to decide when a CV risk (linked to BP elevation) is ‘too much’ for a given level of benefit in a given population
  - Starts with understanding data on risk for CV events based on given BP effect in the population
  - Informed by personal/societal factors
  - Complicated by the observation that the effects on BP we’re interested in here are too small to measure in a routine office visit
  - A benefit-risk calculation

Uses of Risk Boundaries in Drug Development: Threshold of Concern

- What effect of a drug under development should we be able to detect/exclude as a part of drug development?
  - Focused in part to the magnitude of the effect (1, 3, 5, 7 mmHg…..)
  - Also potentially focused on particular aspects of BP measurement (systolic, mean, trough…)

Conclusion: Role of BP Risk Boundaries in Drug Development

- Date on change in BP and populational CV risk allows for linkage between small effects on BP and outcome in large populations and some subpopulations with discrete additional risks
- Issues for today:
  - Development of best tools to characterize risk
  - Tolerable level of risk (how much BP increase matters and in what populations)
  - How to apply risk boundaries thoughtfully to BP assessment during drug development