Sharing Clinical Trial Data: Challenges and a Way Forward

Use Case: Population Data

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Issues of Interoperability & Platform Usability in Cancer Prevention Trials

• Insufficient data standardization and collection
  • Standardized questionnaires not used
  • Behavioral data often not collected
  • mHealth data – how to incorporate?
  • No systematic collection of exposures, concomitant medications

• External validity of trial sample
  • Under-representation of women & minorities
  • Genetics
  • SES, insurance status & other demographics

• Safety assessments & pooling across trials to strengthen signals
  • Affected by governance structures of trials
Insufficient data standardization and collection

Example: Tobacco use

- Tobacco
  - 1st modifiable behavioral risk factor identified, 1964¹
  - Remains significant risk factor today
    - ~20% of cancer cases, 29% of cancer deaths²
  - Negatively affects cancer outcomes³
    - ↑ SPTs, treatment toxicity, & morbidity
    - ↓ survival time, treatment efficacy, & QoL

Assessment in Clinical Trials (2012)⁴
- 29% of Cooperative Group trials assessed any form of tobacco use at enrollment
  - 4.5% assessed during F/U
  - 2.5% assessed SHS at enrollment & 0.6% at F/U
  - None assessed pt. interest in quitting at any point
- When captured, not standardized

Cancer Patient Tobacco Use Questionnaire (C-TUQ) published by NCI-AACR Task Force (2016)⁵
- Allows for harmonization across trials

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External validity of trial samples

Example: Minority recruitment to clinical trials

Barriers to Recruitment
- Less trust in health care system
- SES factors – lack of insurance
- Language
- Lack of awareness / access

U.S. Cancer Center Strategies to Increase Recruitment
- Organizational commitment to diversity
- Partnerships btw faculty & community docs
- Institutional presence in community
  - Community advisory boards
  - Lay community “ambassadors”
  - Transparency in sharing research findings
- Provider recommendation (most influential)
- Engage patient in trial participation decision-making
- Earn trust of patient
- Ensure availability of culturally appropriate, ethnicity-specific materials

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Safety assessments & pooling across trials to strengthen signals

Example: Celecoxib & the Cross-Trial Safety Analysis

• APC Trial (2005)¹
  • Celecoxib 200 mg BID, 400 mg BID, or placebo for colorectal adenoma prevention (2005)
  • Safety signal detected: ↑ CVD events 2-3x

• Celecoxib stopped in APC & 5 other trials
  • PreSAP, ADAPT, MA27, CDME, & Celecoxib/Selenium Trial

• Individually, too few events in each trial to determine relationship between coxib dose or pretreatment CVD status & drug-associated CVD risk

Cross-Trial Safety Analysis (2008)²

• Patient-level pooled analysis of adjudicated data from 6 RCTs (7,950 patients)

• Challenges
  • Different baseline data collected in each trial
  • Clearly determined risks associated with celecoxib use in relation to baseline CVD risk
  • Answered questions that couldn’t be answered from single trial

Hazard of Serious CV Events Considering Celecoxib Regimen & Baseline CV Risks in Six Trials

The Cross-Trials Safety Analysis

Baseline Risk – Dose Regimen
Interaction p = 0.034

Solomon et al., Circulation 2008
Thank you