Pragmatic Solutions for Pragmatic Problems: Examples from the STOP CRC Trial

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The speaker has no conflicts to disclose relative to this presentation.
Overview

- Focus more broadly on statistical issues posed by pragmatic trials rather than specific issues posed by analysis of EMR data per se.
- Most issues are nonetheless related to our use of EMR data in one way or another.
Strategies and Opportunities to STOP Colorectal Cancer in Priority Populations: the STOP CRC Study

Gloria Coronado, KPCHR, Portland, OR
Beverly Green, GHCCHS, Seattle, WA
Tim Burdick, OCHIN, Portland, OR
Coronado et al., (BMC Cancer. 2014; 14: 55)
STOP CRC Primary Objective

Test the effectiveness of automated EMR-driven strategies to raise CRC screening rates in safety-net clinics
STOP CRC Design

- Cluster randomized trial
  - Intervention delivered at clinic level

- 26 federally qualified health clinics that are part of OCHIN network
  - Share common EMR platform – EPIC
  - Part of 8 larger networks
  - 334-2619 (mean=1150) qualifying patients per clinic

- EMR used to drive system-level intervention
STOP CRC Intervention - 1

- Each month, lists of individuals eligible for CRC screening automatically generated from EMR
  - No FOBT or FIT in past 12 months
  - No sigmoidoscopy in past 4 years
  - No colonoscopy in past 9 years
  - No Hx of CRC, renal failure, or inflammatory bowel disease
  - Active clinic patient (visit w/i past 12 months)
  - Aged 50-74 years

- Recruitment continues for 1 yr for main analysis
STOP CRC Intervention - 2

- Clinics work the lists in whatever manner best fits with their internal workflows
- Actual “intervention” consists of prescribed sequence of proactive outreach efforts, including mailed FIT kits
STOP CRC Outcome

**Individual level**
- Completion of FIT kit within 12 months of initially being flagged for screening
- Not same as 12 mos from initial outreach

**Clinic level**
- % targeted patients who complete a FIT kit
- Identify comparable target population for usual care clinics
Statistical Issues

- Randomization process
Randomization Challenges

- Small number of clinics increases risk of imbalance in one or more important factors
  - Network, clinic size, %Hispanic, %urban

- Options
  - Simple randomization
  - Stratified randomization
  - Constrained randomization

- Leveraged homogeneity of clinics within networks
Statistical Issues

- Randomization process
- Calculating sample size
Sample Size for CRTs

- Need to adjust for intraclass correlation (ICC)
  - How to calculate for binary outcomes?
  - Limited in #clinics we could use, and for relatively fixed #clinics design effect increases with increasing clinic size
  - Good news is that power for subgroup analyses is similar to overall power

- Degrees of freedom determined by #clinics and not #subjects

- Change from initial 3-arm trial to 2-arm trial
Statistical Issues

- Randomization process
- Calculating sample size
- Data validation
Data Validation - 1

- Do we accurately capture inclusion criteria?
  - Is end-user database fully reflective of what is in the EMR?
    - (e.g., info in text fields not coded)
  - Does EMR capture full patient experience?
    - patients may seek care from multiple clinics concurrently
    - 10-year eligibility history may not be complete

- Do we accurately capture outcome data?
  - Same issues involved, but validation more tractable.
Data Validation - 2

- Chart Audits
  - Positive and negative predictive value for eligibility

- Comparison vs. Care Oregon Medicaid database
  - Se, Sp, PPV, NPV
  - 1-yr FIT/FOBT, 5-yr sigmoidoscopy, & 10-yr colonoscopy

- Separately for each clinic

- Actively working with clinics to improve data capture and documentation
Statistical Issues

- Randomization process
- Calculating sample size
- Data validation
- Unit of analysis
Unit of Analysis

- Primary interest on clinic rather than patient
  - Want to weight clinics equally, despite varying Ns

- Structure primary dataset as proportion of responders in each of 8 age-gender-race categories and weight by relative distribution
  - Weights clinics equally while generating correct clinic means

- Doesn’t provide a unified approach that would accommodate other covariates. Ideas?
Statistical Issues

- Randomization process
- Calculating sample size
- Data validation
- Unit of analysis
- Choice of primary outcome
Choice of Primary Outcome

- Proportion of targeted individuals who return a FIT kit vs. each clinic’s HEDIS score
  - Former is more direct measure of intervention impact, but ultimately HEDIS is more policy relevant metric
  - HEDIS timeframe doesn’t coincide with intervention rollout
  - HEDIS calculation somewhat problematic given lack of defined population, though rules exist

- Sustainability of intervention effect could be biased based on how target popn defined
Statistical Issues

- Randomization process
- Calculating sample size
- Data validation
- Unit of analysis
- Choice of primary outcome
- Adapting to change inherent in pragmatic nature of the design
Adapting to Change - 1

- Staggered rollout planned for Feb 2014
- External incentives generated demand for common starting point
- As it turns out, clinics weren’t really ready to start
- Influx of new patients generated by ACA and high leadership turnover at some sites has led to delays in scheduling visits that cause some patients to no longer meet visit requirements for eligibility, yet still in analysis sample
Adapting to Change - 3

- Magnitude of problem varies from clinic to clinic
- No way to mimic problem for control clinics since rollout process is not specified as part of protocol
- Considering a sensitivity analysis that excludes all individuals not still eligible as of July, 2014
  - Pros: treats treatment and control clinics the same
  - Cons: would ignore results of early outreach efforts at some intervention clinics.
- Thoughts on other options welcome
Summary

- Pragmatic clinical trials can pose some unique challenges not typically encountered in traditional RCTs
  - Often use cluster randomized designs
    - implications for power and analysis
    - choice of randomization strategy
  - Increased emphasis on data validation
  - Need to deal with lack of design control that is inherent in many PCTs