

Embedding Interventions into Cohort Studies: Need, Duty, Innovation

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I Scientific Workshop of Latin American Population Cohorts

Quinamávida Hotsprings Linares, Chile

April 5, 2018



Epidemiologic Studies

“Good epidemiologic studies progress from descriptive to analytical to experimental epidemiology and then to studies of effectiveness leading to prevention programs.”

Lewis Kuller, Am J Epidemiol 1999; 150: 897-903



But...

- One level of evidence
- One type of study design
- Regression or rediscovery of previously described findings
- Lack of systematic approach to acquiring new knowledge to reach a goal of improving public health and preventive medicine
- Little incremental knowledge or uncertain validity

Kuller L, Am J Epidemiol 1999; 150: 897-903

Sorlie P et al., Am J Epidemiol 2012; 175: 597-601

Also...

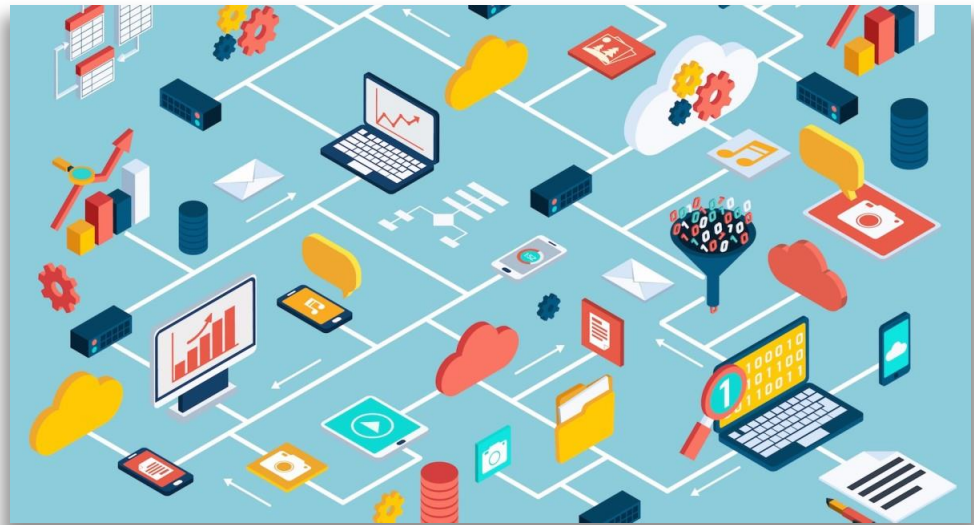
- Participation of individuals from minority groups in observational studies
- Little transformation or translation of observational findings into interventions or preventive medicine
- Value to communities



Alternative Models

Registries, Big Data

- Evaluate specific disease outcomes, processes and infrastructure of patient care.
- Real-world patients and can include very large cohorts at less expense.
- Large populations of well-characterized patients.
- Hypothesis-generating
- Safety signals for rare events.



Alternative Models

Registries, Big Data - Limitations



- Lack of a biorepository
- Disease-specificity that may render them less valuable for primary prevention trials
- Need to link to administrative data (e.g., demographic, health insurance)
- Potential need for additional data collection
- Challenging requirements for statistical methodologies.

Cost-effective Alternatives

Cohort Studies

- Leverage and even consolidate existing infrastructures
 - Consortia of existing cohorts – banks of data, biospecimens
 - Consortia on best practices – methods, policy
- Cross-collaborations among existing cohort studies
- Large health-care databases
- Determine how best to use (electronic) medical records



Cost-effective Alternatives

Cohort Studies

- Decentralize examinations by:
 - Seeing participants in their homes using standardized protocols
 - Employing efficient examination operations
 - Consider creating cohorts within established clinical care settings, depending on the research question.



Why to embed interventions into observational studies?

- There is a need for more rapid translation from observation to intervention.
- Interventions may be started in a more timely manner if embedded into an observational study.
- Hybrid design
 - Embedding an intervention within an observational study
 - Joint observational and clinical trial components into a single study design
- Value of gained information to the community
- Ethical questions

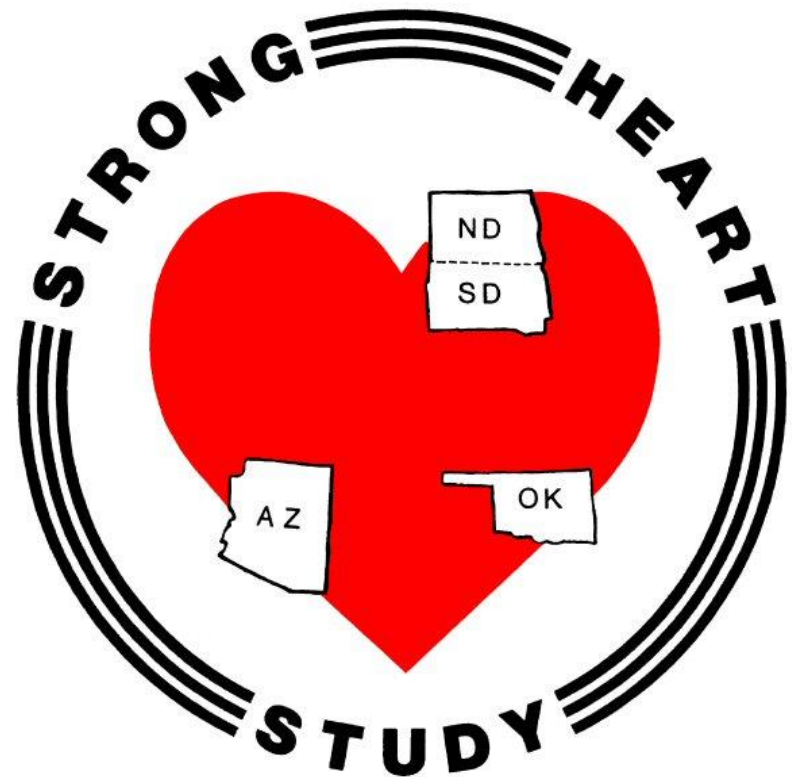
Why to embed interventions into observational studies?

- Embedding an intervention into an observational study may enhance generalizability.
- Great efficiencies of established cohort studies
 - Well characterized and engaged population
 - Preexisting procedures for follow-up and retention
 - Infrastructure
 - Clinical trials experts need to be included in the team

The Strong Heart Study

The Stop Atherosclerosis in Native Diabetics Study (SANDS)

- Cohort study of American Indians living in four States
 - N = 4,549
 - Ages: 45-74 y at baseline
- SANDS
 - Randomized clinical intervention (n = 500)
 - Compare CV outcomes of two different interventions in individuals with diabetes and no underlying CVD.
 - Lowering BP and LDL-cholesterol to standard target levels versus more intense lowering.



The Strong Heart Study

The Stop Atherosclerosis in Native Diabetics Study (SANDS)

- Three years of intervention
- Both groups experienced decreased rates of CIMT progression.
- The group randomized to more strict BP and LDL-cholesterol levels demonstrated regression of the CIMT.



The Jackson Heart Study

The Health Promotion Study

- African Americans in Jackson, Mississippi.
 - N = 5,249
 - Ages = 21-94 years
- The Health Promotion Study
 - Feasibility
 - Pilot study comparing yoga versus regular walking, and counseling
 - High interest among participants
 - High eligibility and enrollment



Timing of the intervention



- The state of the science should set the timing for the introduction of the interventions.
- Time is critical.
- Testing interventions related to a new risk factor or involving a new technology should be done early enough before the treatment or new technology of interest are widely adopted.

Questions to consider before embedding interventions

- Is the cohort the right population to test the hypothesis?
- Is the intervention/randomization brought at the right time?
- Could the proposed outcomes be assessed in the cohort?
- Are there any ethical concerns?



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