Biostatistician's Perspective:

Roles in Observational Studies, Electronic Health Records & Big Data

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Disclosures

- No financial conflicts of interest
- *Director,* Biostatistics, Epidemiology, Research Design (BERD) Core (UL1 RR025767)
- *Director,* Biomedical Informatics Core, Clinical Translational Science Award (UL1 RR025767)
- *Director*, Biostatistics Shared Resource, Cancer Therapy & Research Center, University of Texas Health Science Center at San Antonio (P30 CA054174)
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Disclosures

- I am really an epidemiologist raised by a pack of biostatisticians.
  - Therefore, I am bipolar, so take everything I say with a grain of salt.

Three Domains

Observational Studies

Electronic Health Records

Big Data

- Not orthogonal
- Cut across disciplines
- Cut across units

Observational Research

- Covers research that isn't interventional
- Standard biostatistics stuff:
  - Hypothesis formation
  - Sample size/feasibility
  - Monitoring (quality)
  - Analysis
  - Reporting

Observational Research (continued)

- Observational designs are deployed when randomized clinical trial (RCT) designs are not possible or not ethical
  - More potential for bias to creep in
  - More complex designs and analysis approaches are needed to minimize bias; i.e., more biostatistical involvement

Observational Research: Team

- Epidemiologists
- Biostatisticians
- Other public health experts
- Clinical and translational scientists

Observational Research: Considerations

+ *Omic-specific groups too small to run RCTs*
+ *“Free” plentiful data from sources like EHRs*
+ *Pivotal for the design of future RCTs*
– *Non-existent or poor quality data*
– *Less weight of evidence*

- Increasing reliance on observational data for precision medicine
- Need ontologies for observational studies beyond *ClinicalTrials.gov*
  – Meta-study data repositories

EHR Research

- Building and beginning to exploit EHR repositories
- Research employs mostly observational designs but increasing use of cluster randomized designs (pragmatic trials), and potential for individual RCT designs
  - Being pushed rapidly by PCORnet and the PCORI-CDRNs

EHR Research: Disciplines

- Medical informatics
- Health IT
- Computer science
- Clinical / applied epidemiology
- Biostatistics
- Health services research
- Medical domain expertise
- Bioethics

EHR Research: Trends

- Informatics focus has been on building repository infrastructure, just starting to shift to analytics and development of decision support tools
- Toward a Common Data Model?
  - i2b2/SHRINE vs. Mini-Sentinel Distributed Database
- Realization of the IOM's *Learning Healthcare System*


BIG
DATA
ALSO
TOOLS
DISK
TARGET
APPLIED
SENSOR
MAY
EXAMPLES
SHARED
DEFINITION
CURRENT
MOVING
RECONSIDER
WITHIN
EVERY
ZETTABYTES
PRACTITIONERS
CAPTURE
THOUGHT
BUSINESS
INTERNET
DISTRIBUTED
SETS
GENOMICS
DESCRIBING
RADIO-FREQUENCY
COMPLEXITY
MANAGEMENT
TERABYTES
CASE
ABILITY
PETABYTES
INCLUDE
ETC
ELAPSED
SYSTEMS
TOLERABLE
SIZE
STORAGE
MPP
PARALLEL
SAN
QUALITIES
SINCE
MASSIVELY
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SEARCH
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NETWORKS
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LARGER
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SOCIAL
INDEXING
CITATION
USE
SET
CONNECTOMICS
ORGANIZATIONS
RELATIONAL

Big Data Research: Subdomains

- -Omics research
- Administrative database research
- Electronic Health Record (EHR) research

Big Data: Biostatistical Considerations

- Often requires complex modeling approaches and validation methods
- Missing data challenges
- Computational platform constraints
- Sample size issues for -omics studies
  - Many variables, few cases
  - Linkage with whole human data

Big Data: Concerns

Paradigm shift with the ever-increasing generation and availability of data, going:

From: **Hypotheses** in search of **Data**

To: **Data** in search of **Hypotheses**

- Missing or inappropriately structured data elements; e.g., the EHR may miss:
  - Dose schedule, dose intensity, AUC, dose modifications, patient PK/PD characteristics

Big Data: Concerns (continued)

- Systematic biases in big data sources only get amplified, not attenuated.

Need extremely tight integration of clinical and translational researchers with bioinformaticians, IT experts, biostatisticians and epidemiologists.

Transdisciplinary Approach to Big Data

Type	Disciplines	Biostatistical Considerations
-Omics	Bioinformatics	Experimental design, modeling (time series and nested effects); Linkage for clinical annotation
Administrative	Health Services Research, Applied Epidemiology, Public Health, Medical Informatics	Debiasing observational data; Missing data; Propensity scores; Secular changes in coding for longitudinal datasets
EHR	Medical Informatics, Health IT, Clinical domain experts, Finance, Psychometrics	Cohort assembly; Deciphering EHR entries (defining incident cases); Missing data; PROs

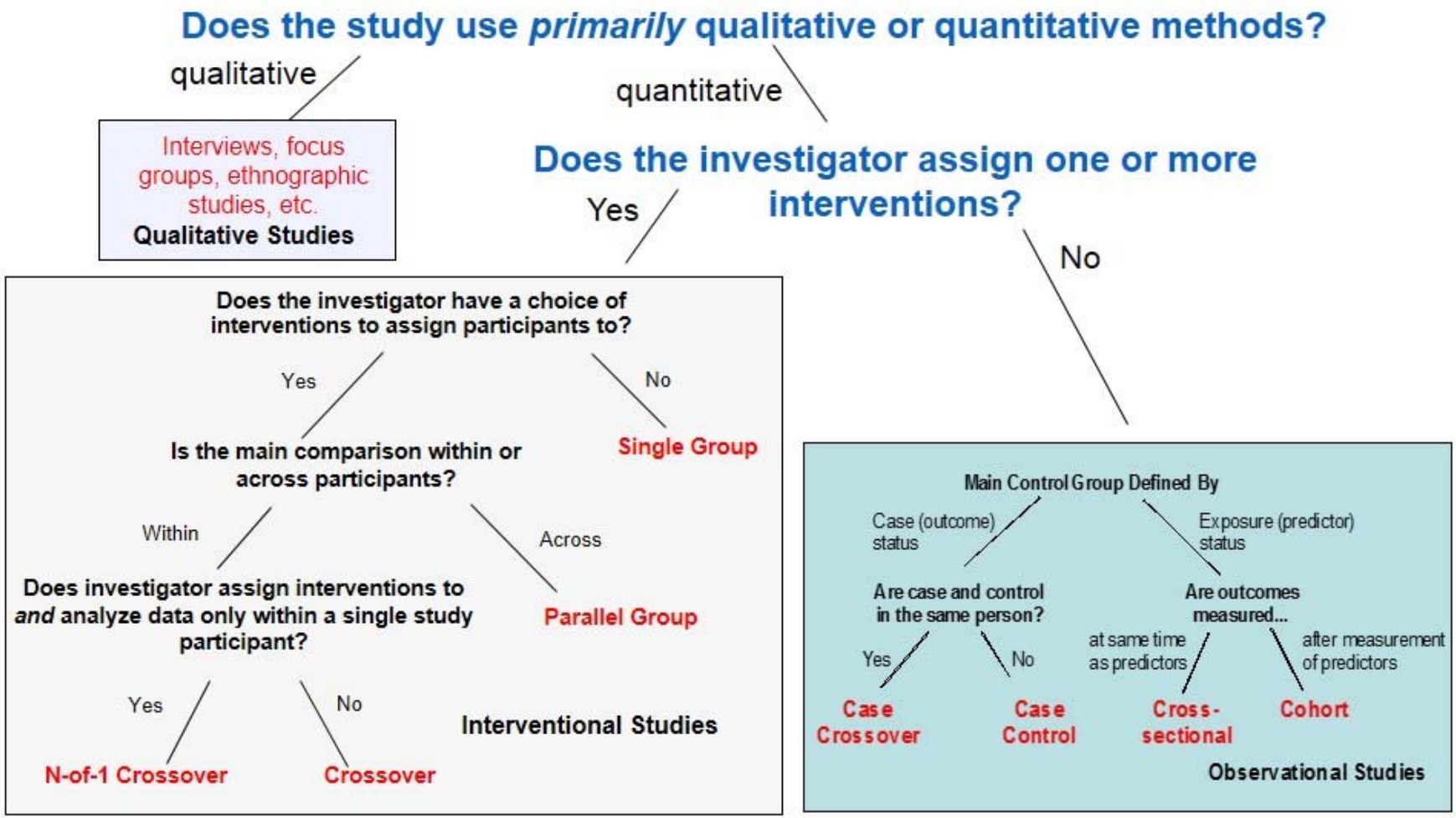
Examples Illustrating the Need for a Transdisciplinary Approaches

- Oncology of Clinical Research (OCRe)
- IOM's *Learning Healthcare System*

Ontology of Clinical Research (OCRe)

- Goal is to develop common taxonomy and vocabularies to standardize the storage of study information (meta-study data)
- Elements:
  - Study design type
  - Interventions/exposures
  - Participants
  - Outcomes
  - Statistical analyses

OCRe Study Design Topology



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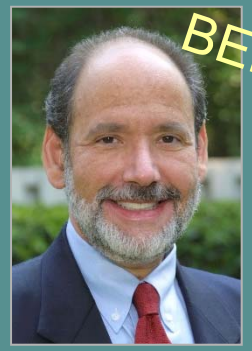

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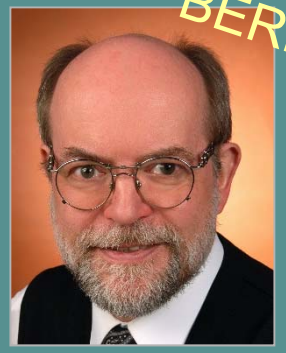

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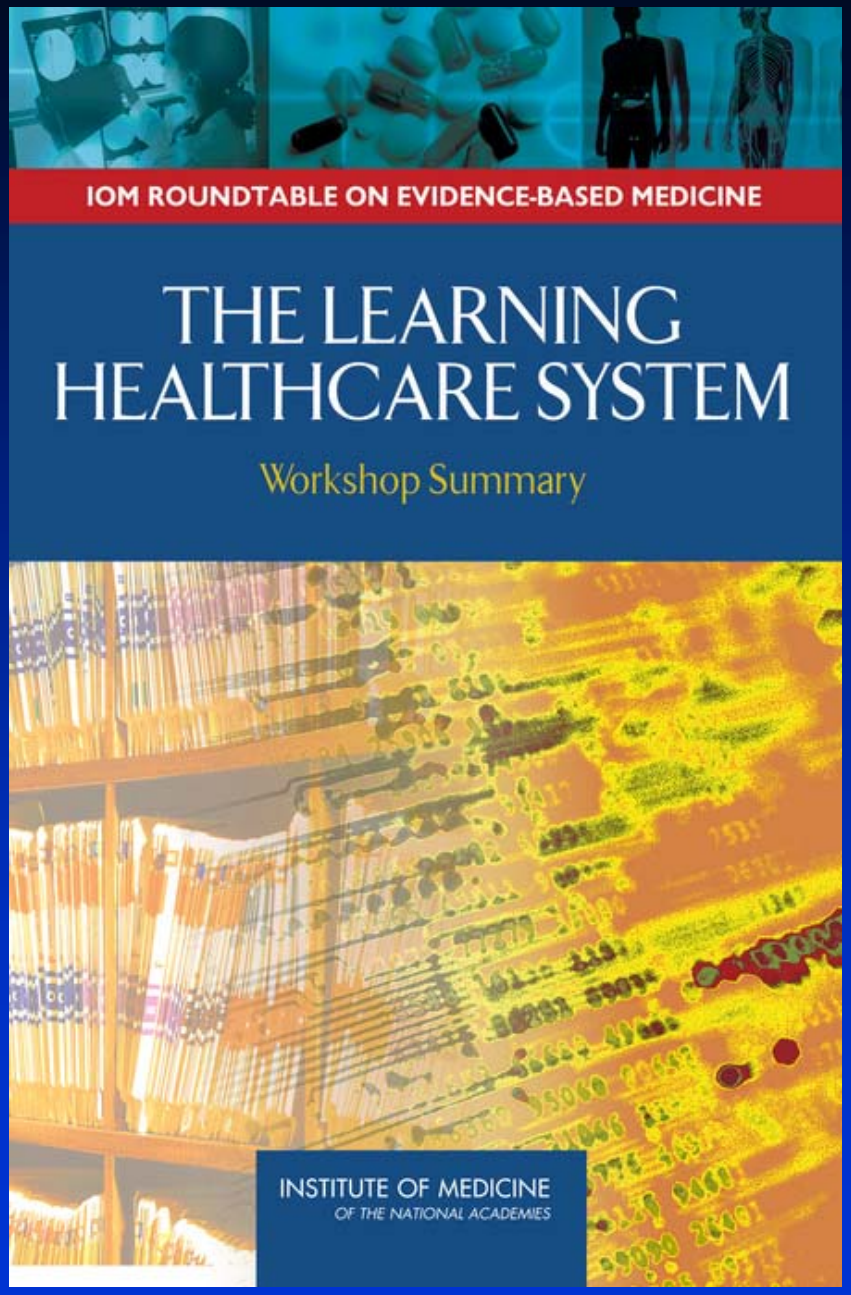
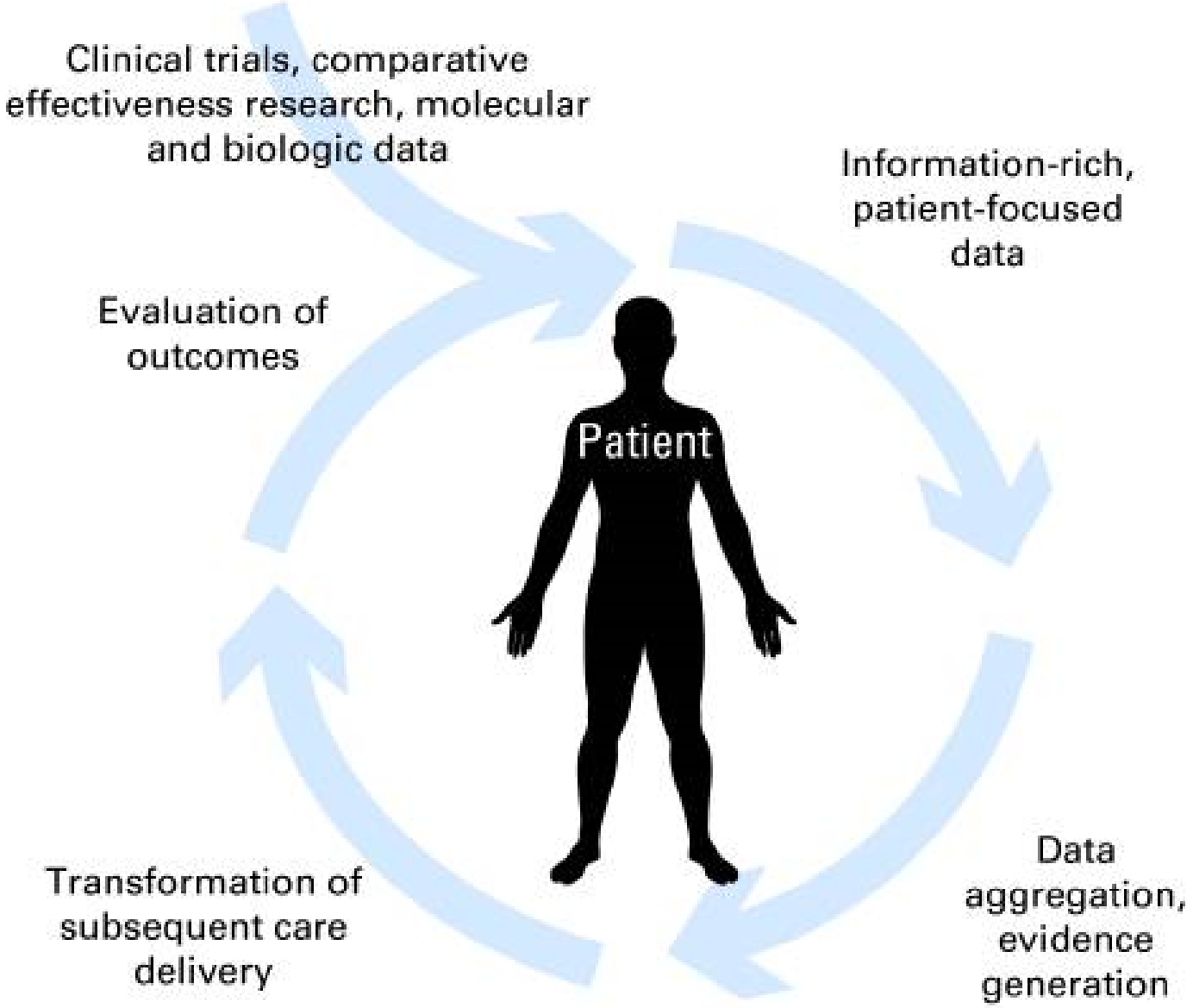


National Research Council. *The Learning Healthcare System: Workshop Summary (IOM Roundtable on Evidence-Based Medicine)*. Washington, DC: The National Academies Press, 2007

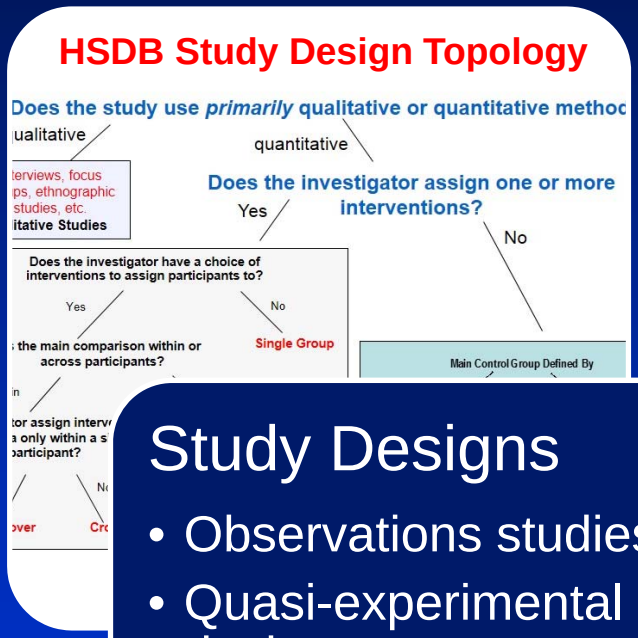
Learning Healthcare System

The learning healthcare system refers to the cycle of turning health care data into knowledge, translating that knowledge into practice, and creating new data by means of advanced information technology.

Learning Health Care System Process



Gathering Data to Make Decisions



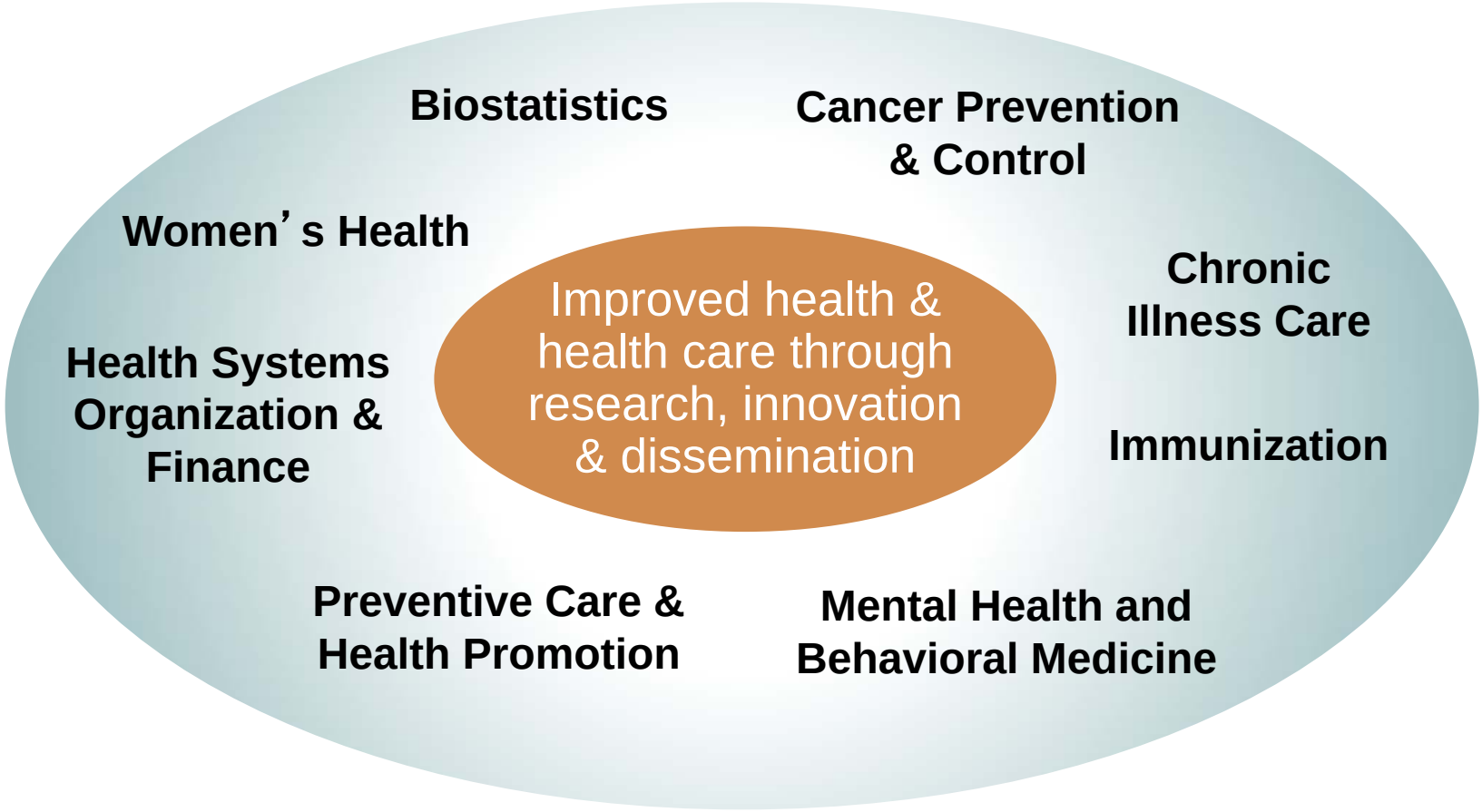
Study Designs

- Observations studies
- Quasi-experimental designs
- Cluster randomized clinical trials
- Individual randomized clinical trials

End Products

- Clinical practice guidelines
- Roadmaps / Critical pathways
- Decision support tools
- Automated EHR recommendations

Primary areas of research focus



Summary

- Hard to imagine having research success without close interactions between biostatistics and other disciplines
- Trend is toward more transdisciplinary research
- Developing *Learning Healthcare Systems* will put this to the penultimate test

Transdisciplinary Research Secrets of Success

- Ability to be able to step outside your skin
- Genuine desire to understand the fundamental principles of other disciplines
- Flexible thinking to reimagine dogmatic or unquestioned concepts within your own discipline
- Desire to have the combined effort be much greater than the sum of the parts

Transdisciplinary Research Secrets of Success (continued)

- Proximity is 9/10s of the law; i.e., it sure helps to have diverse discipline experts in close proximity
  - Maybe even develop transdisciplinary units/programs that transcend traditional:
    - Divisions
    - Departments
    - Centers / Institutes
    - Universities
    - Hospitals

Thank you