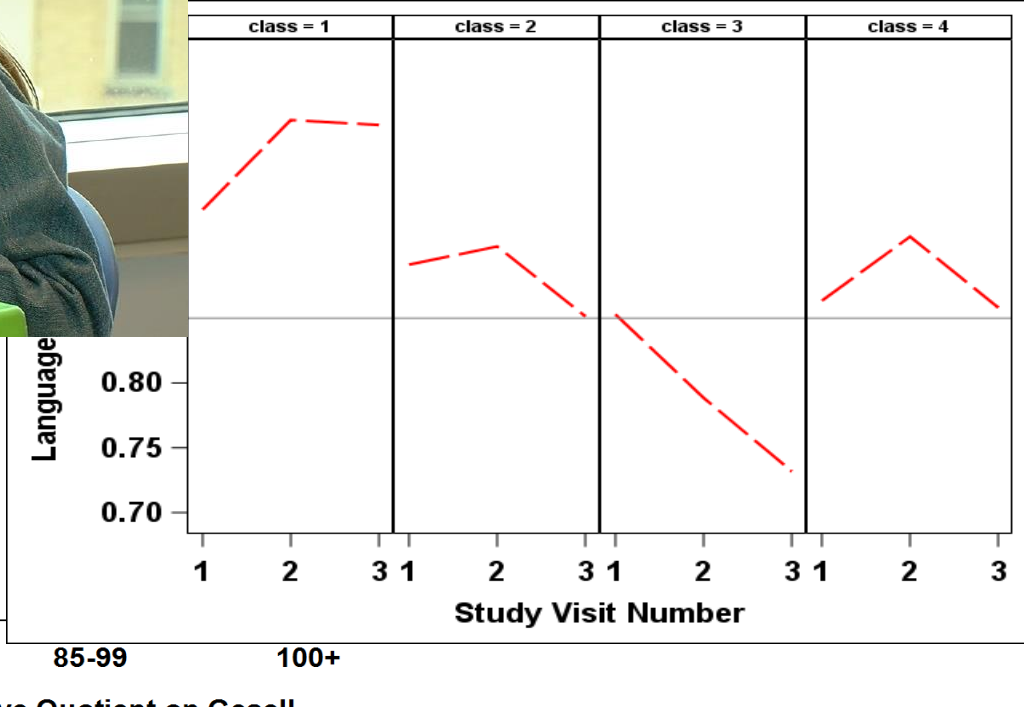
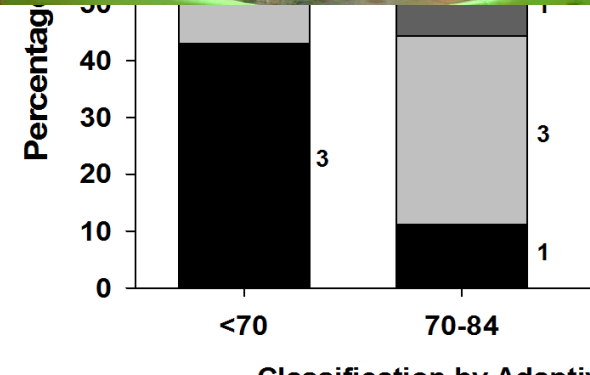
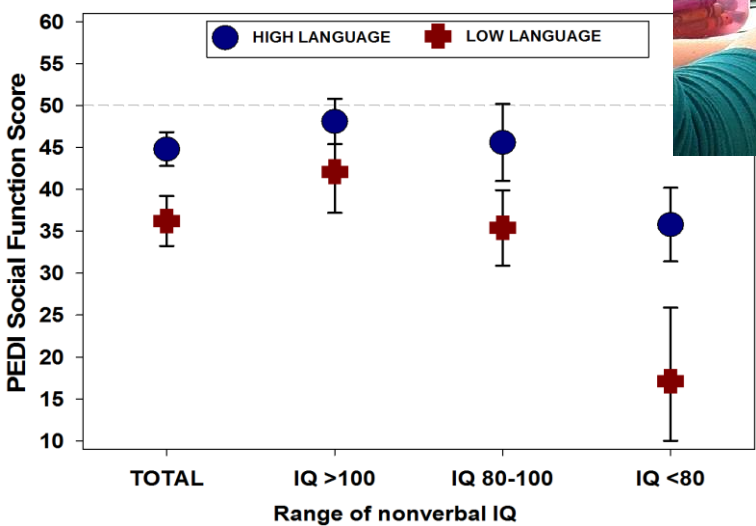
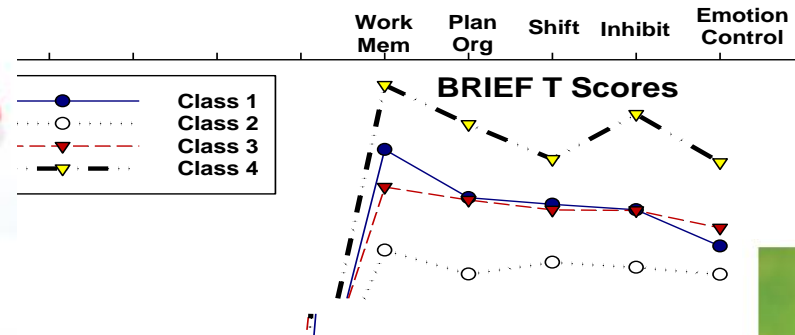
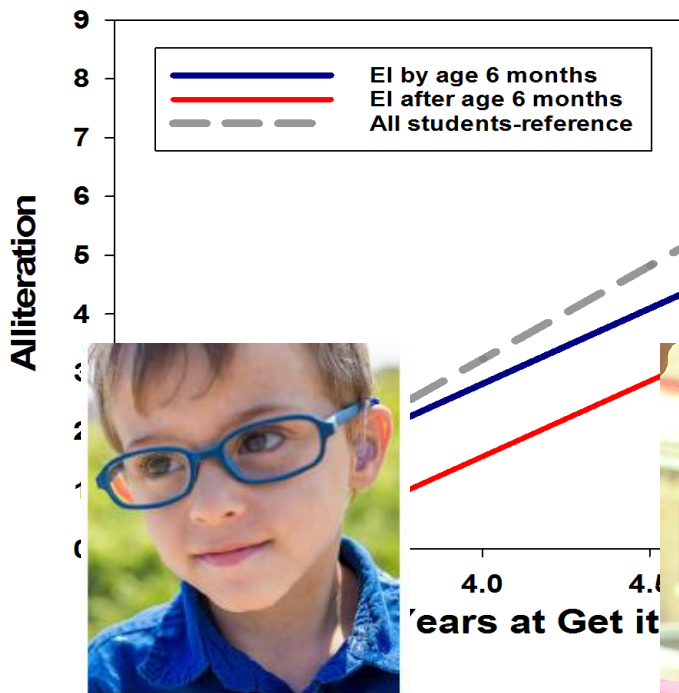


Leveraging data for surgical research: Research in the right place in the right way

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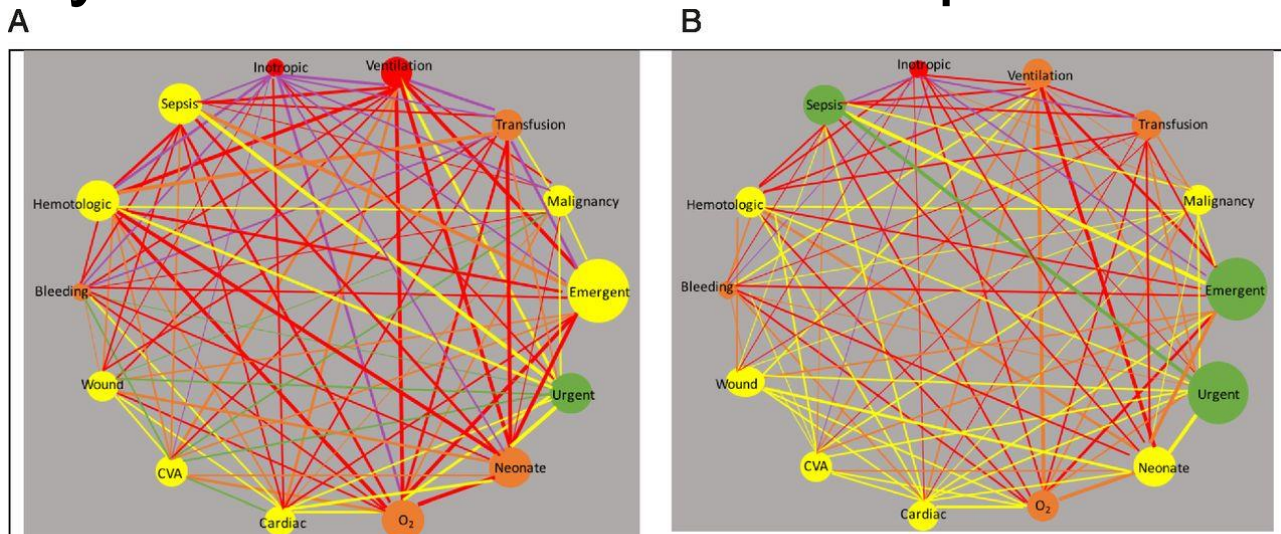
What we'll be discussing

- Introduction to importance of conversation
- Difficulties in conducting research in surgical field
- Discussion of alternatives – using data sources
 - Medical records (electronic and otherwise)
 - Registries
 - Large-volume databases
- Examples
- Summary

Why is this dialogue important

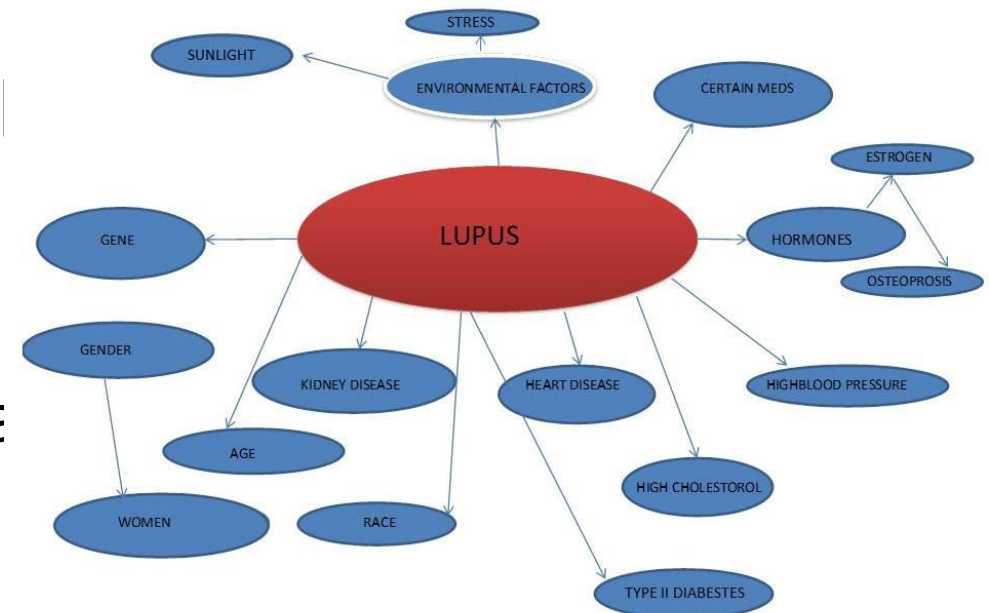
- Health care (and humans) part of a complex nonlinear chaotic system with inconsistent “predictive” relationships

Morris 2013



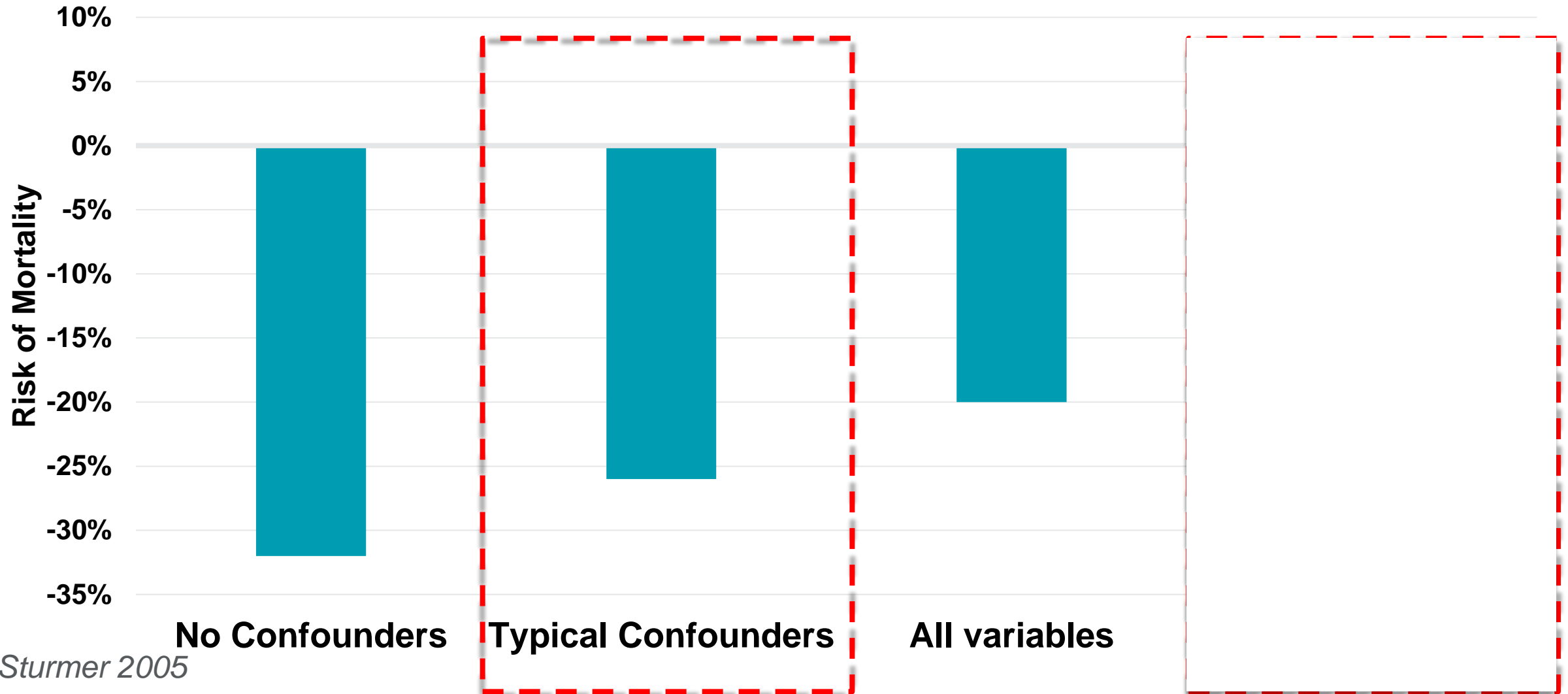
(left) and White (right) children

<u>Node Size: Prevalence of Condition (%)</u>	<u>Node Color: Risk of Condition (%)</u>	<u>Edge Thickness: Prevalence of Comorbid Condition (%)</u>	<u>Edge Color: Risk of comorbid Condition (%)</u>
Size 1: 0–1	Green: 0–1	Size 1: 0.0–0.1	Green: 0–1
Size 2: 1–5	Yellow: 1–5	Size 2: 0.1–0.5	Yellow: 1–5
Size 3: 5–10	Orange: 5–10	Size 3: 0.5–1.0	Orange: 5–10
Size 4: 10–100	Red: 10–100	Size 4: 1.0 <100	Red: 10–25
			Purple: 25–100



Confounding Can Harm

Mortality Risk associated with NSAID, Hospitalized Patients ≥ 65 years



Why is this dialogue important



- Health care (and humans) part of a complex nonlinear chaotic system with inconsistent “predictive” relationships
- Morris 2013*
- What we do [in research] should make a difference
 - Incorrect results can cause harm
 - It is difficult to make the effects “go away”
 - Incorrect results do not always have to seem “large” to have an impact
 - **We are all biased**



**Objective of surgical outcomes research –
assess the effectiveness, appropriateness,
and costs of surgical care
questions researchers seek to address.”**

Anyanwu & Treasure, 2004



Difficulties with research in surgical field



- Case series are a favored method of clinical investigation
- Bias and confounding by indication
- Lack of adequate controls
- **Barriers to Surgical RCTs (“gold standard”)**
 - Surgical patients more heterogeneous
 - Skill level differences=difficult to generalize to wider community
 - Referrer, patient, & surgeon preference for “new” as better
 - Unplanned cross-over/inability to apply blinding
 - Ethical considerations
- Often surgical patients have “rare” disorders (sample size remains problematic)
- Data woes

Leverage what is available



Start where you are.

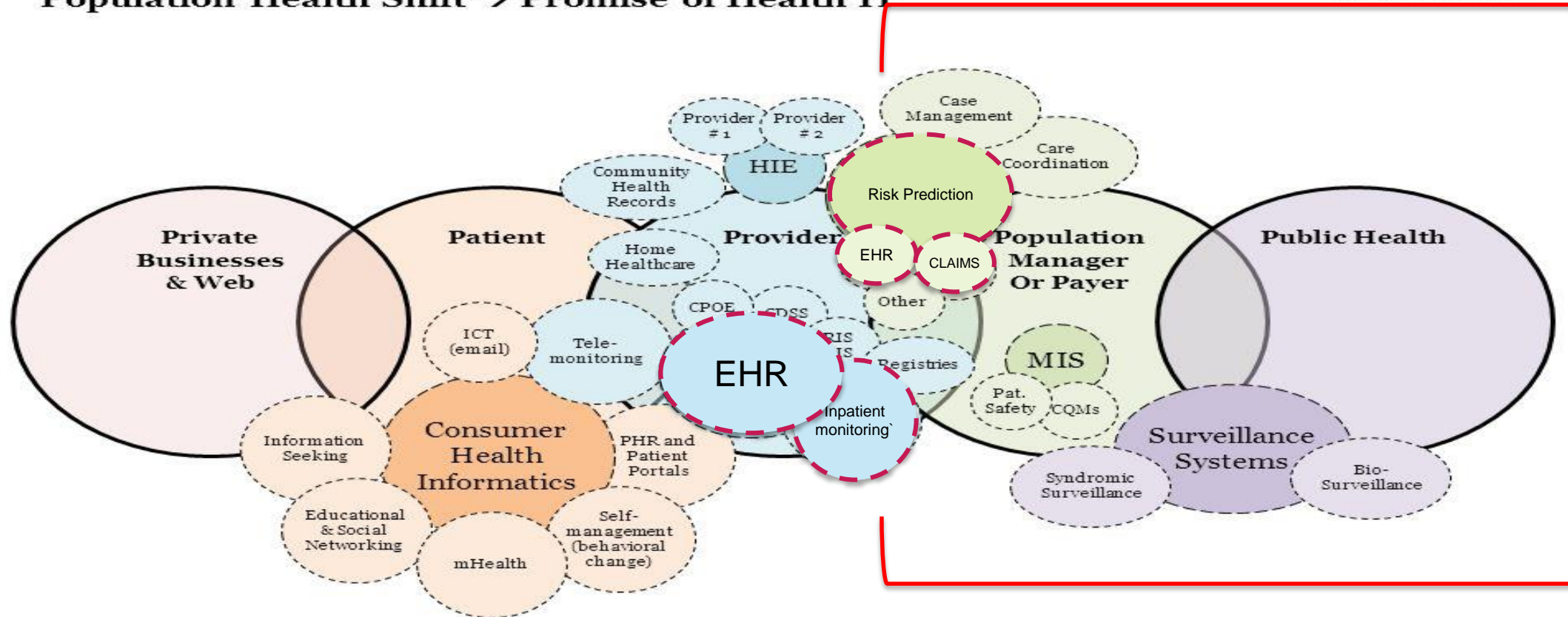
Use what you have.

Do what you can.

Leverage what is available-DATA

Population Health Shift → Promise of Health IT

Copyright Hadi Kharrazi



Population health stakeholders and health IT platforms/tools

Leverage what is available



- Health and medical records (electronic or otherwise)
- Registries
 - Primary data collection
 - Transferred data from existing sources
- Contextual data
 - Linking to vital records, emerging technologies, environmental data, biobanks expands opportunities to improve outcomes
- Administrative databases
- National surveys

How to choose a database/data source?



- What is my research question
 - Is it descriptive vs. analytic?
 - Does it have a clear testable hypothesis?
- What is my hypothesis
 - What is the **appropriate study design**?
 - Who is my target population?
 - Who are my comparison groups?
 - Is time a factor?
 - Is my outcome well defined?
- Which database will have data that I need?
- How are the data captured and defined?
 - Will the database allow me to test my hypothesis?
 - Will I be able to address confounding and effect modification?
- What are the limitations I face with the database I have chosen?
 - How will the limitations impact my interpretation of the results (bias)
 - Are my results generalizable to my actual target population?

What do I need to also consider in my database?



- **Comprehensiveness** describes completeness of records of patient care events and information relevant to individual
 - Record contains demographic data, administrative data, health risks and health status, patient medical history, current management of health conditions, and outcomes data
 - The more comprehensive the database, the more current and more sensitive information is likely to be
- **Inclusiveness** refers to which populations in a geographic areas are included
 - The more inclusive the more it approaches 100% coverage of population intended
 - Most databases are designed to include only subsets of population

Study Design Always Matters!!!



- Unfortunately, poorly designed RCTs are considered “superior”
McCulloch, 2002
- Case control studies should be contemplated
 - Low incident outcomes – maximize sample size
 - *35% of surgical articles identified as CC studies were “true” CC design*
Milhailovic, 2005
- Cohort studies often used for EHR and large-volume databases
 - Large sample sizes
 - Large volume of data
 - Historical data often available

Great Opportunities to Harness EHR



- Quality improvement/improved safety purposes
- Public health initiatives (Facilitate surveillance)
- Recruiting for prospective studies/clinical trials
- Replicating results of randomized controlled trials (CER)
- Conduct "Big Data" research (Rich data to study disease progress, health disparities, clinical outcomes, treatment effectiveness)
- Practice precision medicine to improve patient outcomes
- Can be linked to contextual data using geographic information systems (GIS) and combined with self-reported data to address questions about complex networks of causation

But it is complicated



- Medical Records ARE DESIGNED FOR CLINICAL CARE, NOT RESEARCH
 - Not structured in a way that facilitates research
- Conceptual idea of clinical process does not translate to how data are captured in the record
- Many different ways to document same piece of information
 - Workflow used to collect data often dictates where those elements are stored in reporting database
 - Most researchers lack understanding of these workflows
- Quality of results then depend on how question is asked, skill of analyst

Poor Data Quality



- Quality variable due to differences in measurement, recording, information systems, and clinical focus
- Data entry errors (Reported as high as 26.9%) *Goldberg 2008*
 - Medication discrepancies common
 - Pull forward/copy forward
 - “Adjacency” errors with medical records
- Data coding, standardization, extraction
 - Free text narrative; Inconsistent terms, phrases, abbreviations; Billing purposes; Diagnostic codes may be recorded for detection or “rule out” purposes
- Context dependent
 - Same elements deemed high quality for one use and poor quality for different use

Incomplete Data



- Due to fragmentation of healthcare systems
 - Patients moving between systems for special referrals or emergency care
- Due to “poor”/inaccurate documentation (on the part of patients and healthcare providers)
 - Lack essential information such as treatment outcomes
- Sick patients often have more data
 - Non-random missing
- Complete information about patient vs. complete information about patient’s encounter
- ***It is difficult to interpret gaps in care***

Examples in the literature



- 30-40% of patients have clinical visits across multiple institutions *Bourgeois 2010; Finnell 2011*
- 55% of clinical research studies supplemented with non-EHR sources of data
 - 40% supplemented with patient-reported data *Thiru 2003; Dean 2009;*
- 49% of patients with ICD-9 pancreatic cancer did not have corresponding pathology documentation (incomplete or incorrect) *Botsis 2010*

“Sicker” Have More Data



Figure 5. Average number of days with data per patient by ASA class. For both medication orders and laboratory results, all ASA Classes are significantly different except for Classes 1 and 2.

Sicker have more complete data

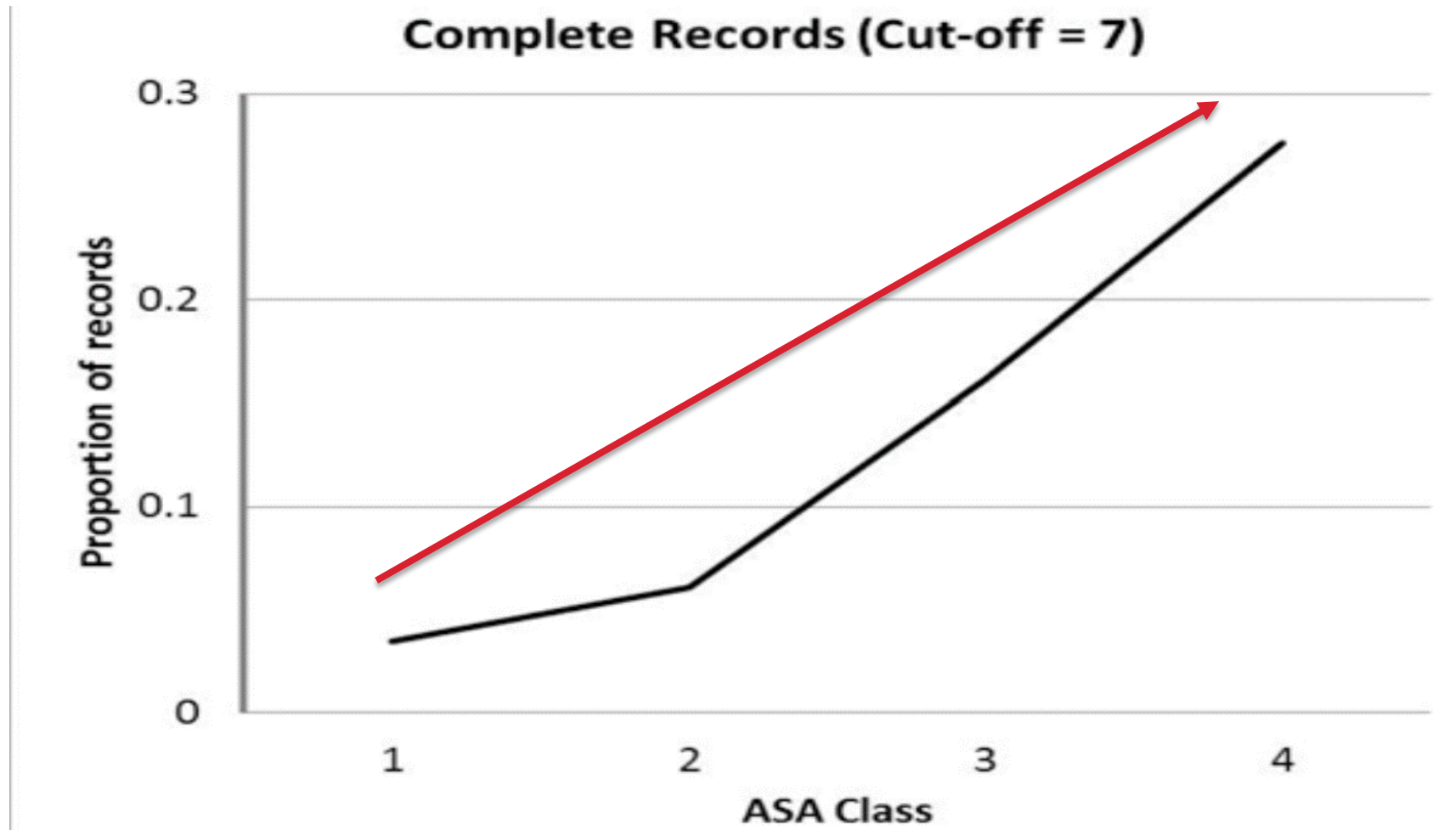


Figure 4. Complete records by ASA Class where complete records are those having at least seven values in each of the two categories (medication orders and laboratory results).

Patient/Clinical/Disease/Outcome Registries

NCBI: Glicklich et al, AHRQ 2014



- Should be designed and evaluated with respect to their intended purpose(s)
- 4 major purposes
 - Describing natural history of disease
 - Determining clinical and/or cost-effectiveness
 - Assessing safety or harm
 - Measuring or improving quality of care
- *Society of Thoracic Surgeons (STS) (Cardiac and Thoracic)*

Rare disease registry



- Specific objectives include
 - To connect affected patients, families, and clinicians
 - To learn the natural history, evolution, risk, and outcomes of specific diseases
 - To support research on genetic, molecular, and physiological basis of rare diseases
 - To establish a patient base for evaluating drugs, medical devices, and orphan products
- Multi-national/multi-institutional collaborations to combine data

Registry Design

NCBI: Glicklich, 2014



Construct	Relevant questions
Research question	What are the clinical and/or public health questions of interest
Resources	What resources, in terms of funding, sites, clinicians, and patients are available for the study
Exposures and outcomes	How do the clinical questions of interest translate into measurable exposures and outcomes
Data sources	Where can the necessary data elements be found
Study Design	What types of design can be used to answer the questions or fulfill the purpose
Study population	What types of patients are needed for study? is a comparison group needed? How should patients be selected for study?
Sampling	How should the study population be sampled, taking into account the target populations and study design
Study size and duration	For how long should data be collected and for how many patients
Internal and external validity	<u>What are the potential biases?</u> What are the concerns about generalizability of the results (external validity)

Large-Volume Databases



- Increased use in surgical research
- Can include all patients or a predefined sample of patients from a broad (national) or narrow (state) geographic area, and are composed of patient-encounter records from more than one specialty or procedure
- Contain more generalized information-provide macro-level contributions
- Used to develop perioperative risk stratification tools, assess postop complications, calculate costs, evaluate trends in field (descriptive epidemiology), etc

Why use large-volume databases?



- Efficacy studies (i.e., RCTs) in the surgical field are extremely difficult
- Investigation of rare disease states and uncommon complications
- Facilitate studies analyzing surgical procedure variation
 - By region, gender, age, ethnicity SES, comorbidities, insurance-type, institution-type
- Examination of temporal trends for management of specific surgical procedure
- Develop preoperative and postoperative risk stratification protocols for given procedure

Classification of LV Databases

Administrative

Derived from
payments/claims

- HCUP (NIS, KID, SID)
- PHIS
- NHDS*
- Medicare/Medicaid
- Discharge Abstract Database (DAD)
- Canadian Institute of Health Information DB

Billing info

Clinical

Derived from patient
information

- NSQIP
- SEER
- ACTUR
- NTDB
- CanCORS
- NCDB

Patient info

Survey

Derived from
surveys/questionnaires/
patient information

- MEPS
- NCHS (NHIS, NHANES, NAMCS, NSAS, NHAMCS, NHCS-NHDS*)

Participant info

Large-volume database caveats



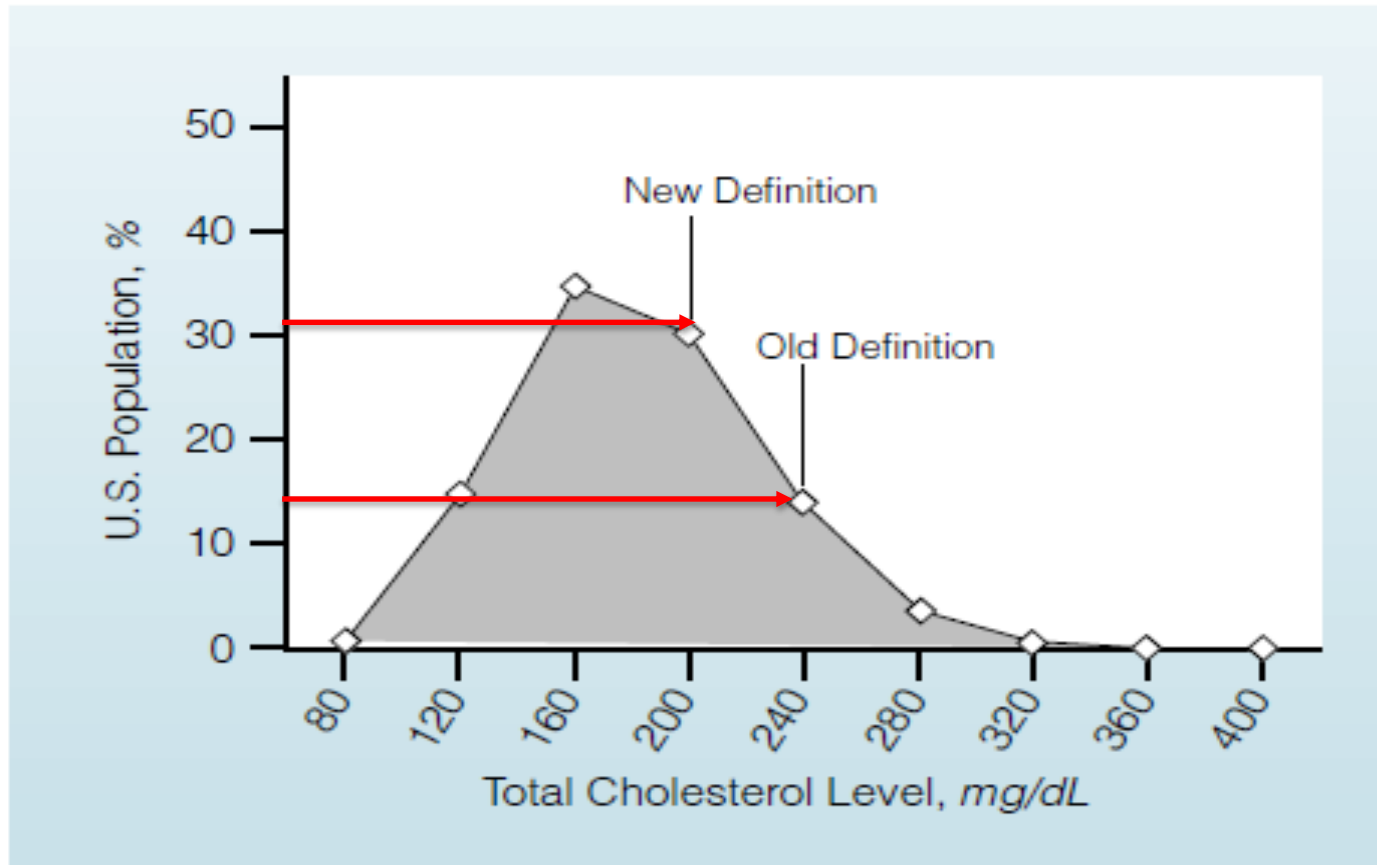
- Selection bias
 - Patients who are captured are not necessarily representative
 - Present for inpatient procedures
- Information bias
 - Sicker patients have more data and more complete data
 - Different settings capture data differently (accuracy and precision)
- Time-dependent bias
 - Survivor bias (those who die before procedure are often not captured)
- Clinical vs. Statistical significance
 - Large sample sizes will increase likelihood of finding something not meaningful
 - Reporting CI helps provide better understanding of significance

Common Limitations



- **THE PURPOSE OF COLLECTING ADMINISTRATIVE DATA IS NOT RESEARCH**
 - Majority of databases are dependent on ICD/CPT codes
 - To isolate comorbidities, diagnoses, procedures, complications
 - May be only valid for certain diagnoses, procedures, complications
 - Extraction of codes often comes from insurance claims or hospital-level records which may be influenced by reimbursement strategies or coded by nonmedical team
 - Inconsistencies across regions/providers
 - **Changes in definitions over time influence findings**

Definition changes alter prevalence estimates



NHANES survey data

FIGURE 4. Distribution of total serum cholesterol levels for the U.S. adult population and two definitions for hypercholesterolemia.

Surgery specific databases

- Healthcare Cost & Utilization Project (HCUP)
 - Pediatric Health Information System (PHIS)
 - National Inpatient Sample
- National Surgical Quality Improvement Program (NSQIP)
- Medical Expenditure Panel Survey (MEPS)
- National Trauma Data Bank (NTDB)
- National Survey of Ambulatory Surgery (NSAS)
- National Hospital Ambulatory Medical Care Survey (NHAMCS)
- Surveillance, Epidemiology, and End Results (SEER)
- Canadian Institute for Health Information
- National Physician Database Metadata
- Private Databases

- Canada has some of the most comprehensive and high-quality administrative health data in the world
 - Universal health insurance registries
 - Comprehensive coverage of inpatient and outpatient services
 - Linkage of databases via unique personal identifiers within provinces and territories

Quan et al, 2012
- Canadian Institute for Health Information
 - Maintains 27 pan-Canadian databases, provides education, reporting tools, strategies for uses
 - Largest: Discharge Abstract Database
 - National db of administrative, clinical, demographic info relating to all separations from acute care institutions (75% of all inpatient discharges)

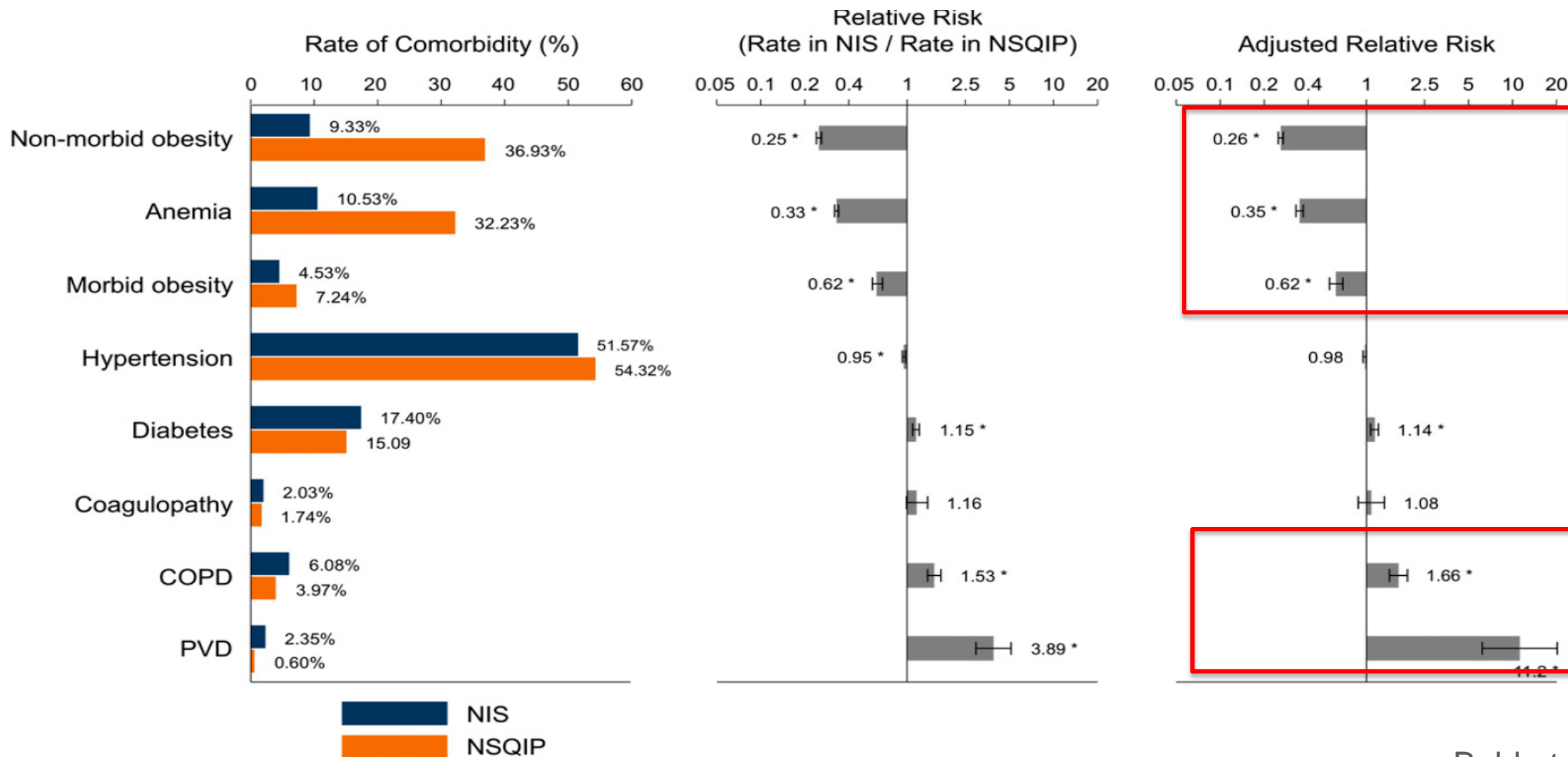
Lucyk et al, 2015

Survey Databases

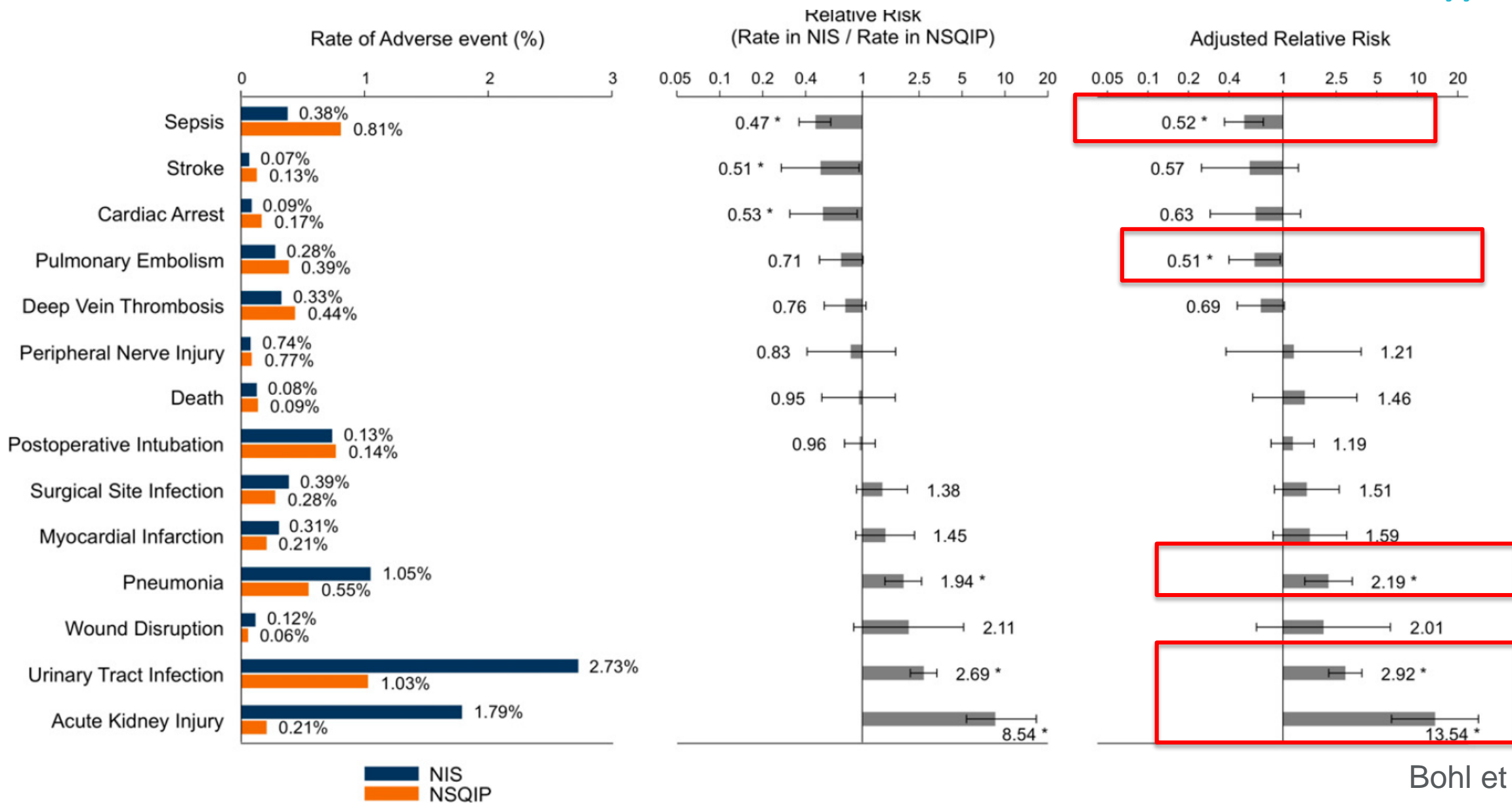


- Use of large-volume databases for surgical research allows for better understanding of perioperative complications, temporal trends, risk stratification, and cost-analysis
 - Can be very useful for effectiveness research (but not efficacy research)
 - Track trends over time to evaluate changes in population health, including prevalence of any number of conditions
- Use complex sampling design
 - Allows for over-sampling of certain populations
- Sampling requires weights to be calculated that take into account survey nonresponse, oversampling, post-stratification, and sampling error
- Some surveys over-sample different groups

Tale of 2 databases: NIS vs. NSQIP



Tale of 2 databases: NIS vs. NSQIP



Tale of 2 databases: KID vs. Peds NSQIP



TABLE 2. Complications of nonsyndromic craniosynostosis operations

Complication	KID	Peds NSQIP	p Value*	Selected Literature†
Infection	0.2%	0.8%	<0.001	0%–8%
Wound disruption	0.2%	0.5%	<0.001	0%–4%
Seizures	0.7%	0.8%	0.412	0%–0.8%
Cardiac event	0.5	0.3%	0.025	0.4%–2.2%
Stroke/intracranial bleed	0.4%	0.5%	0.291	0.3%–1.2%
Blood transfusion	36%	64%	<0.001	1.7%–100%
Sepsis	1%	0%	1.000‡	0.1%

Tale of 2 databases: KID vs. Peds NSQIP



TABLE 3. Identification of complications

Complication	KID (ICD-9 code)	Peds NSQIP (clinical variable)
Infection	320.0–322.9, 324.0–324.9, 998.5, 998.59, 682.0, 682.8–682.9, 686.8–686.9, 410.0–411.9, 411, 412, 417, 418, 419, 730.00, 730.08–730.09, 730.90, 730.98–730.99	Superficial incisional surgical site infection, deep incisional surgical site infection
Wound disruption	998.3, 998.31–998.32	Wound disruption
Seizures	780.3, 780.39	Seizure occurrence
Cardiac complication	997.1	Cardiac arrest requiring cardiopulmonary resuscitation
Stroke/intracranial hemorrhage	998.1, 998.11–998.12, 432.1	Cerebrovascular accident/stroke or intracranial hemorrhage
Blood transfusion	990.1–990.7	Occurrence of transfusion
Sepsis	381.0–384.9, 380–389, 995.90–995.94	Occurrence of sepsis

Future and Continuing Developments

- Increased use of sophisticated statistical methods and coding algorithms
 - Methods for text fields, methods for causal inference, addressing bias
- Improved capture of social and behavioral data
 - Supplementing EHR with direct patient reported data
- Better standardization to allow linkage and merging across health centers.
 - Need to fill “gaps” in data
- Linkage to vital records, emerging technologies, environmental data, biobanks to expand opportunities to improve outcomes
- Require close collaborations with clinicians AND clinical researchers AND methodologists

In Summary

- Many alternatives to RCTs
- Many alternatives to case series
- Appropriate study design is vital to achieving the closest “truth” possible
- Involve methodologist EARLY
 - Understand study design, power and statistical analysis, interpretation, methods for causal inference and addressing bias and confounding
 - *How do I create a relationship with one??*

Always Remember



- Research should be driven by the important questions and the need for knowledge to improve
- Consider the most appropriate database for the research question at hand
- Consider the most appropriate study design for the research question at hand!!

Thank you

- <https://www.nlm.nih.gov/hsrinfo/datasites.html>
- <https://www.facs.org/quality-programs/acs-nsqip>
- https://www.cdc.gov/nchs/nsas/nsas_questionnaires.htm
- <http://www.cdc.gov/nchs/nhis.htm>
- www.cdc.gov/nchs/nhanes.htm
- <https://meps.ahrq.gov/mepsweb/>
- www.hcup-us.ahrq.gov/kidoverview.jsp
- <http://www.childhealthdata.org/learn/NS-CSHCN>
- <http://www.cdc.gov/nchs/slait/cshcn.htm>
- <https://www.childrenshospitals.org/programs-and-services/data-analytics-and-research/pediatric-analytic-solutions/pediatric-health-information-system>
- www.entnet.org
- <http://www.disabilitystatistics.org/sources-rehab.cfm>