Linking Electronic Health Records & Insurance Claims Data for Clinical Research:
Opportunities and Challenges

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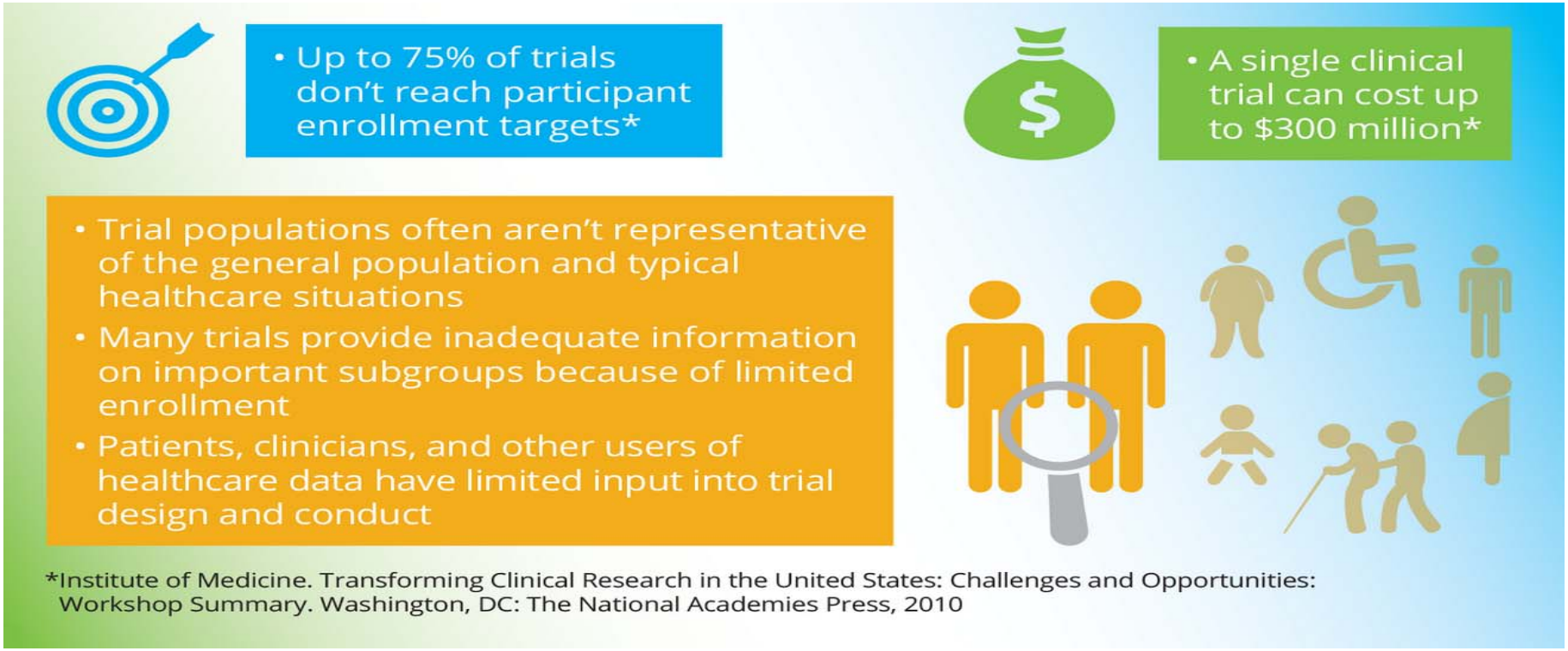
Challenges to the classic randomized clinical trial



Big data with linkage potential

- Electronic Medical Records
  - Single system, multi-system
- Insurance claims
  - Medicare, Medicaid, Commercial
- Registries (e.g. SEER)
- Primary data
  - Patient reported outcomes
  - Research-specific assessments
- Lab data, imaging, pathology
- Genomic data
- Aggregate data from geographical units
  - Air pollution, water quality
  - Weather (heat waves)
  - SES
- Wearables
  - Fit bit, smart phone apps
- Social media, internet searches, purchases (pregnancy tests)

Motivating examples

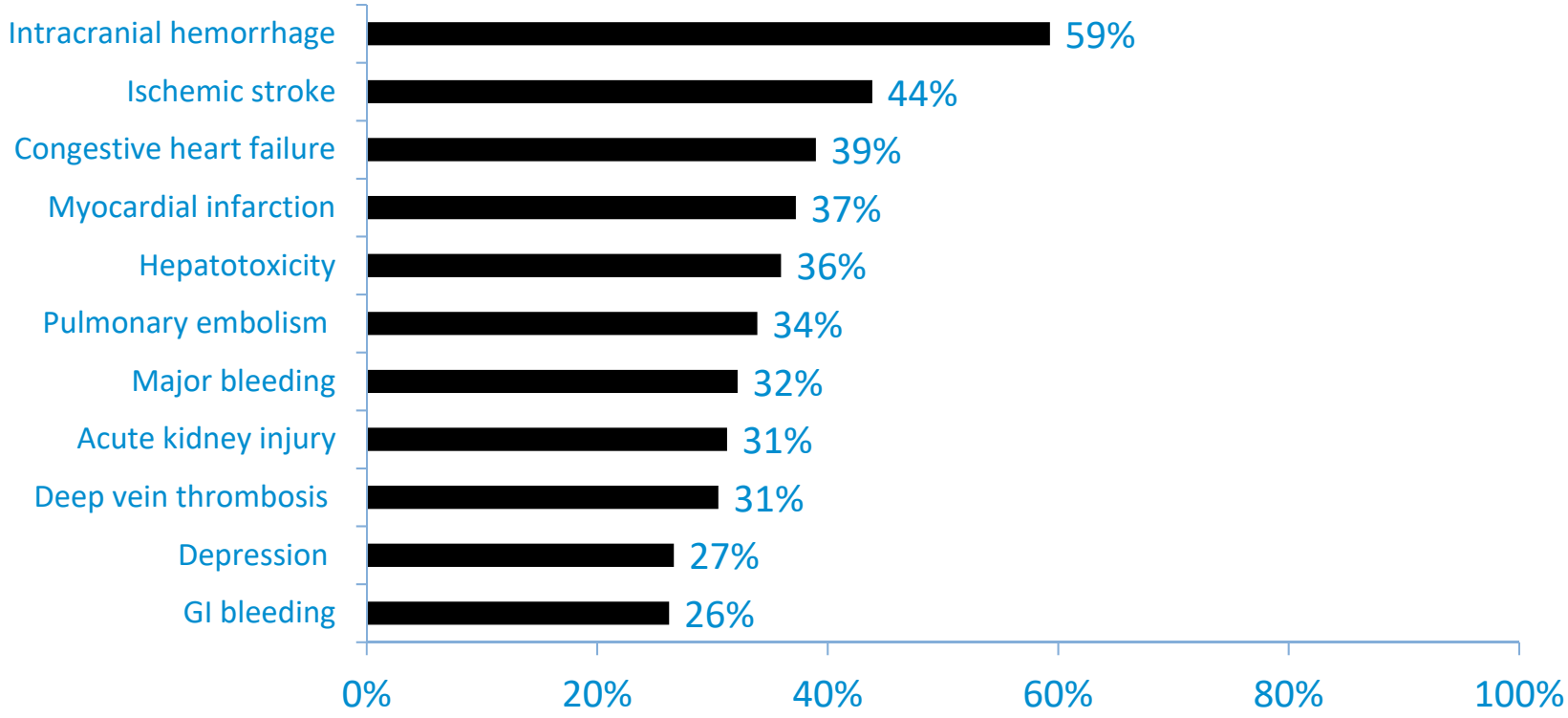
- 81 vs 325mg aspirin and CVD outcomes and GI bleed as major endpoints
- Long term outcomes after bariatric surgery including all-cause mortality
- Risk of cancer between two antidiabetic medications
- Effects of anti-emetics on pregnancy outcomes
- Receipt of recommended care postpartum among moms of medically fragile infants vs. well newborns
- Healthcare utilization among children with autism

Following patients through time and space

Identifying the right population

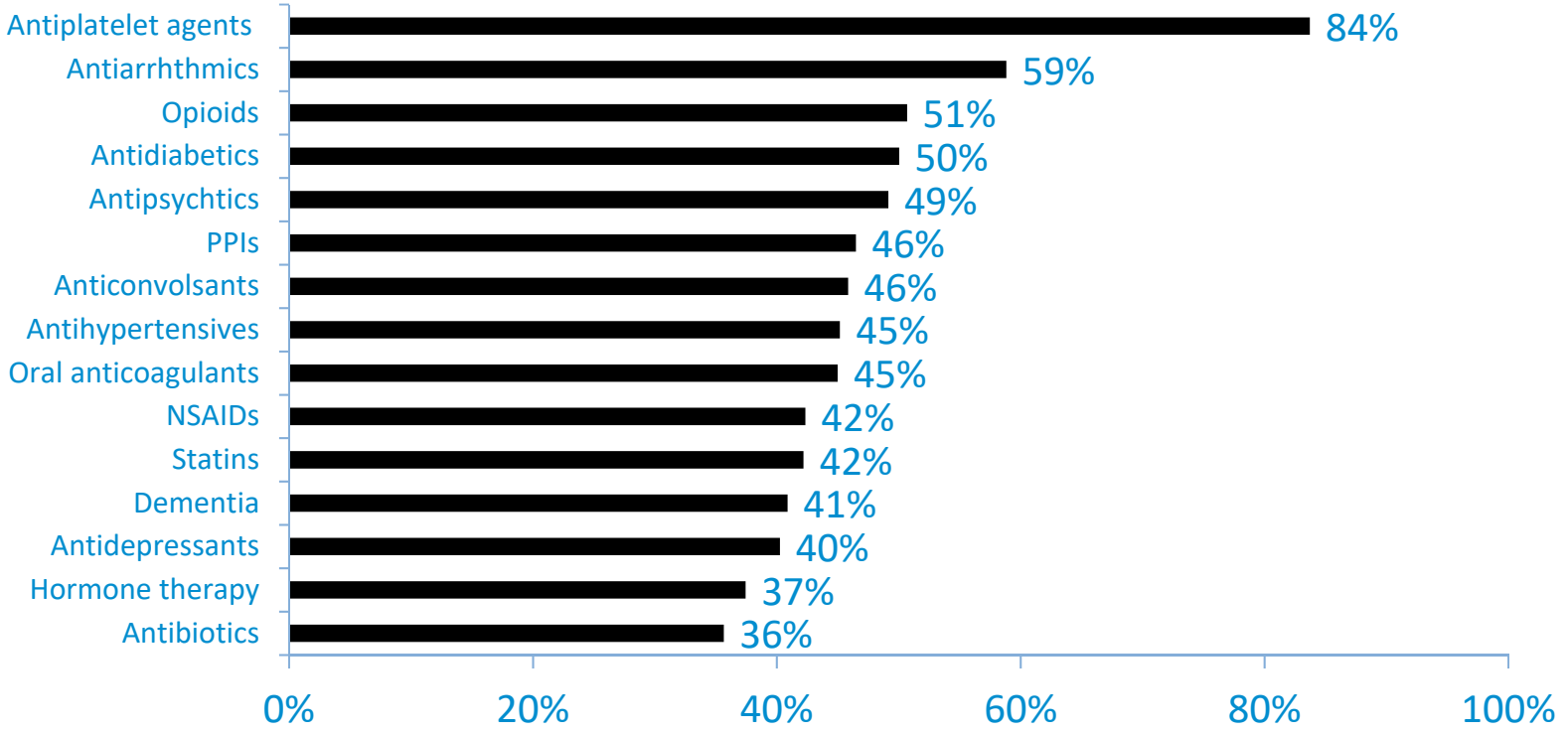
- Equipoise
- Assessing inclusion & exclusion criteria
  - Indicated for treatment
  - Not already treated (e.g. new users)
  - Not contraindicated (e.g. CKD, pregnancy)
  - No history of the outcome (e.g. prevalent cancers)

Conditions: Single EHR vs. EHR+claims



Source: (Lin et al., 2018)

Medications: Single EHR vs EHR+claims

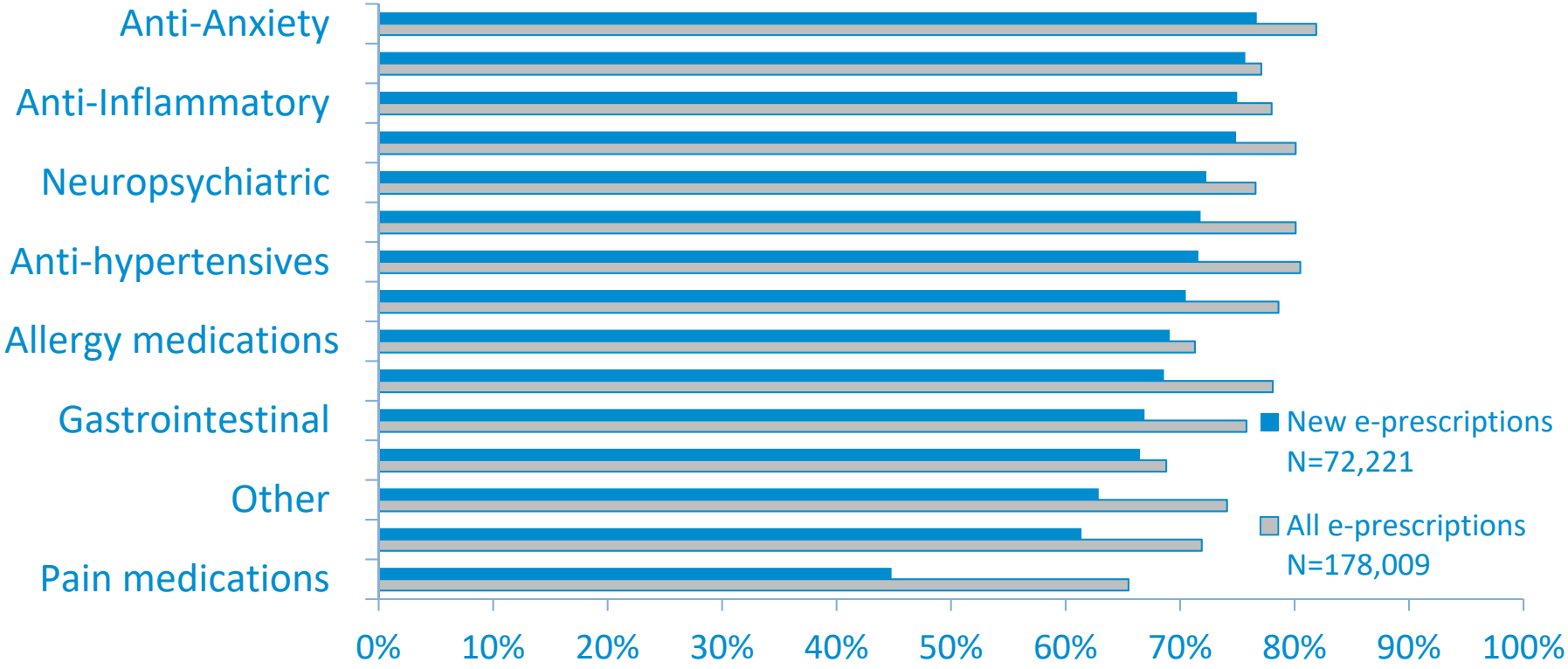


Source: (Lin et al., 2018)

Treatments

- Medications
  - Prescribed vs filled vs ingested
  - Inpatient vs outpatient vs OTC
  - Use over time (adherence, persistence)
- Devices
  - General (CPT) vs specific (UDI, serial number)
  - Placed, revised, removed

Fraction of EMR prescription medications actually filled



Source: (Fischer et al., 2018)

Outcomes

- Verifying presence of health outcomes
  - Labs, imaging, pathology, clinical notes
- Across care settings
  - Urgent care vs usual provider vs hospital
- Across health systems
  - Mobile populations
- Identifying patients in the risk set (denominator)
  - Restricting to loyal patients vs insurance enrollment dates
- Identifying competing events (e.g. mortality)

Risk factors (potential confounders)

- Clinical details
  - BMI, BP, lab results, smoking status, renal function
- Timing
  - Before or after exposure (lipid tests and statin exposure)
  - Recent vs distal (MI, cancer)
- Presence vs severity
  - Type 2 diabetes dx code vs HbA1c
  - Heart failure dx code vs. ejection fraction
  - Cancer dx vs pathology and stage

To link or not to link

Assess feasibility

- Conditions for use
  - DUA
  - Limitations on linkage
  - Data security requirements, access
- Available identifiers or linkage keys
  - Quality, completeness, uniqueness

Assess the potential gains

- Population overlap
  - Sufficient to be valuable
  - Consistently identifiable to avoid double/triple counting some patients or events
  - Consider selection

Scientific value

- Key data made possible only through linkage
- Data quality
  - Accuracy, completeness, differences in coding practice
- More valid, robust, or precise inference
  - Gold standard or alloy
- One time use vs. future research potential
  - NDI

Governance

- Review process for use of the data
- Requirements for data security
- DUA and limits to linkage
- Patient consent, IRB review

Costs

- Data costs
  - Server / disk space
- Personnel, training
  - Server admin
  - Honest broker
- Complexity, time

Linkage Execution

- Cleaning, standardizing, normalizing
- Linkage approach
  - Probabilistic vs deterministic
- Linkage conduct
  - Investigator, one of the original data holders, or honest broker
- Evaluation and validation of record linkage
  - Gold standard available?
- Reporting results

Linking EHR and Claims Data @ UNC

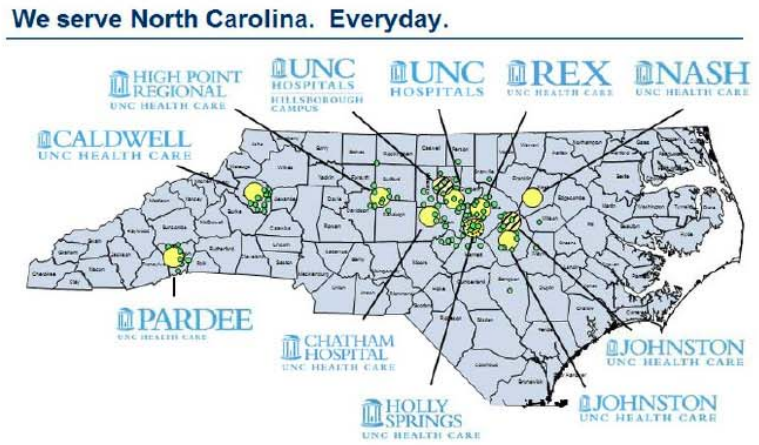
UNC's EMR Warehouse: CDW-H

- The Carolina Data Warehouse for Health
- Aggregate of electronic health record data collected in UNCHCS, live as of 2009
- Data on ~5+ M unique patients, 800K+ continuous, expanding with UNCHCS
- Additional hospitals added as they "go live" with Epic
  - If it's in Epic (or was in WebCIS), it's in the CDW-H.
- Data collection dates back to:
  - July 2004: Hospital Billed Data
  - July 2008: Physician Billed Data
  - April 2014 : Epic Systems Data

Our pre-Epic, homegrown EMR

CDW-H: Not just Chapel Hill

- UNC Health Care System includes hospitals and clinics across North Carolina
- Epic roll-out started in April, 2014



Practice	Epic live date
UNC Hospitals and outpatient	April 4, 2014
UNC Faculty Physicians	April 4, 2014
Chatham Hospital	April 4, 2014
UNC Physicians Network West	April 4, 2014
Rex Healthcare and outpatient	June 20, 2014
UNC Physicians Network East	June 20, 2014
Caldwell Memorial, outpatient only	May 5, 2015
Johnston Health, outpatient only	May 5, 2015
High Point Regional, outpatient only	May 5, 2015
Johnston Health Hospitals	May 21, 2016
High Point Regional Hospital	May 21, 2016
Caldwell Memorial Hospital	June 18, 2016
Pardee Hospital and outpatient	June 18, 2016

i2b2 at UNC

- Self-service, web-based query tool which researchers can pull back deidentified data (counts) from the CDW-H
- Launched in March 2015, used by 600+ users at UNC (and growing) to perform data queries preparatory to research
- i2b2@UNC Requirements:
  - UNC-Chapel Hill faculty, staff, or student with an active ONYEN (ID and password)
  - Attendance at Introduction to i2b2 Training
  - Online training now available
  - https://tracs.unc.edu/index.php/services/informatics-and-data-science/i2b2

Claims data at UNC

- NC TraCS, Epidemiology, Gillings Innovation Lab, and the Sheps Center support access to a variety of claims data sources:
  - Marketscan national commercial claims data (2000-2017)
  - 20% national random sample of FFS Medicare claims (2006-2016)
  - 100% of UNCHCS Medicare FFS patient claims linkable with EMR data
    - ~275K people (2015-2016)
  - NC Medicaid data (100%) ~7 years, updated regularly
  - NC BCBS data (100%) ~7 years, updated regularly
  - SEER-Medicare-Part D
  - NC state discharge data (includes ED, surgery center)

Insurance claims linkable to UNC EHR data

	Medicare	NC Medicaid	BCBSNC
Population	FFS Medicare (~20% <65); seen in UNCHS 2014-2017	Low income; pregnant women	Privately insured, <65
Years of claims	2015 – 2016 (2006 – 2014 for ~10%) Annual updates	1/2011 – 6/2018 Quarterly updates	1/2003 – 9/2018 Quarterly updates
Total n	280k	2.4m (2018)	475k (2018)
Approvals required	CMS (reuse)	CCQI / NC DMA	CCQI / BCBCNC
Identifiers used for linkage	HIC (Medicare ID), (birthdate, gender)	Name, birthdate, SSN, zipcode	Name, birthdate, SSN, zipcode; procedure(s)
Linkage execution	CMS (existing crosswalk)	NC DMA	Honest broker (UNC's Sheps Center)

Stage 1 – Ask the experts

- Consult with **TraCS CER/BERD** regarding
  - Appropriate data sources
  - Feasibility (including timelines, anticipated sample size)
  - Study design
  - Analytic plan
- Consult with **Sheps Center** re: linkage process as well as expectations, costs, and timeline for honest broker data linkage work
- Consult w/ **TraCS Bioinformatics** re: cost of data extraction from CDW-H

Stage 2 - Approvals

- UNC Institutional Review Board

- In parallel, prepare applications for permission to use CDW-H and claims data source(s) from:
  - CDW-H oversight (UNC EHR data)
  - ResDAC / CMS (Medicare)
  - CCQI / NC DMA (NC Medicaid)
  - CCQI / BCBSNC (BCBSNC)
- Submit once IRB approval granted

Stage 3 – Primary cohort identification

- Computable phenotype (algorithm) to be applied to structured data
  - Validated method when possible
- Key data elements needed for linkage, claims extraction
  - Study-specific ID
  - Identifiers (name, insurance type, insurance number, birthdate, zip code, sex)
  - Index date (clinical event, treatment, calendar time)
- EHR-derived data on exposure, outcome, patient characteristics extracted by TraCS analyst

Stage 4 - Linkage

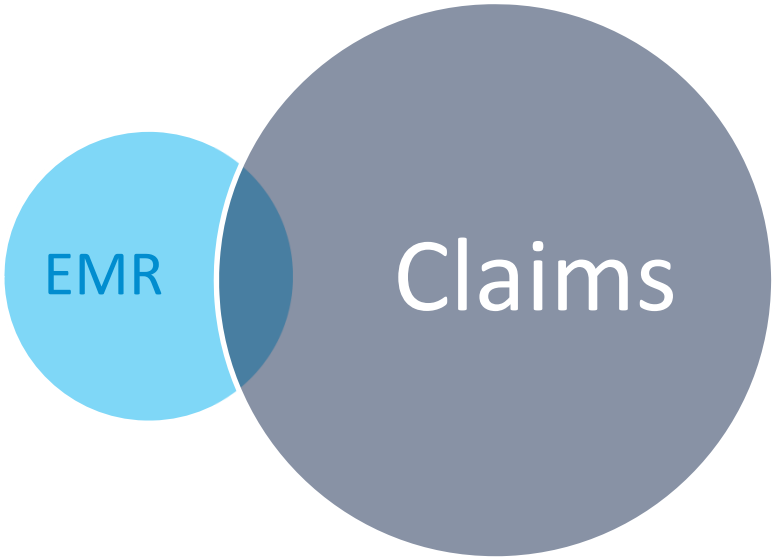
- NC Medicaid
  - Identifiers provided to NC DMA
  - Crosswalk between encrypted Medicaid ID and Study ID returned to honest broker at Sheps
  - Claims for linked individuals extracted and provided to research team in project-specific work space on Sheps secure server
- BCBSNC
  - Identifiers provided to honest broker at Sheps along with any 'blocking' criteria to limit the pool of potential matches
  - Claims for linked individuals extracted and provided to research team in project-specific work space on Sheps secure server
- Medicare
  - Patids provided to Medicare programmer
  - Relevant claims extracted and provided in project-specific work space on Sheps secure server.

Stage 5 – Actual research (finally)!

- EHR and claims-derived data placed in project-specific folder within Sheps secure server
- Study's analytic programmer creates analytic cohort
- Investigator or statistical programmer conducts analysis
- Present, publish, and improve public health
- Remember to cite UNC's CTSA

Study population options

1. Only those that link (overlap)
   - Akin to ‘complete case’ analysis
   - Smallest n
   - Consider potential biases
2. Claims + partial EMR (gray)
   - Population-based cohort with enhanced ascertainment of clinical details in a subset
3. EMR + partial claims (blue)
   - Health-system based cohort with enhanced ascertainment of outcomes, adherence, co-morbid conditions in a subset



Methods for analyzing partial data

- Sensitivity analysis in subset with full data
  - May differ due to same biases that affect the 'complete case' analysis
- Quantitative bias analysis
  - Conduct the main analysis in the primary data
  - Adjust results using estimates of sensitivity / specificity (possibly differential) from the linked sample
- Multiple imputation
  - Requires outcomes in the subsample to perform well
- Propensity score calibration
  - Does not require outcome in the subsample
  - Surrogacy assumption needed

Care4moms

- Comparing access to routine post-partum visit and other recommended healthcare services between mothers of medically fragile infants (NICU >3 days) vs those with well babies
- Deliveries (n=6849) at UNC hospital, 7/2014 - 6/2016
- Linkage to claims data attempted for n=1687
- Context-based blocking (delivery during the relevant time period) and fuzzy matching on combinations of first and last name
- Linkage rate 97%

Bariatric surgery

- Comparison of surgical approaches to treat obesity
- Primary outcomes
  - Change in BMI, improvement in diabetes, reoperation, hospitalization, death

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ORIGINAL RESEARCH | 4 DECEMBER 2018

Comparative Effectiveness and Safety of Bariatric Procedures for Weight Loss: A PCORnet Cohort Study FREE

*David Arterburn, MD, MPH; Robert Wellman, MS; Ana Emiliano, MD; Steven R. Smith, MD; Andrew O. Odegaard, PhD, MPH; Sameer Murali, MD; Neely Williams, MDiv; Karen J. Coleman, PhD; Anita Courcoulas, MD, MPH; R. Yates Coley, PhD; Jane Anau, BS; Roy Pardee, JD, MA; Sengwee Toh, ScD; Cheri Janning, RN, BSN, MS; Andrea Cook, PhD; Jessica Sturtevant, MS; Casie Horgan, MPH; Kathleen M. McTigue, MD, MPH, MS; for the PCORnet Bariatric Study Collaborative **

- Linkage to claims to identify subsequent operations and hospitalizations up to 5 years later
- Results using linked claims pending

Take home messages

- Both EHR and claims data have important gaps that can lead to substantial bias in estimated treatment effects
- Combining complementary data from EHR + claims often strengthens studies that would otherwise rely on a single data domain
- Benefits need to be weighed against costs (time, funding, complexity)
- Encourage early discussions to assess both

Questions

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Request a consultation with CER/BERD at
https://tracs.unc.edu/index.php/consultation

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Challenges in claims-centric clinical research

- Unmeasured risk factors (e.g. BMI, smoking status)
- Poorly measured disease severity (e.g. HbA1c, ejection fraction), indications (e.g. depression), contra-indications (renal impairment; allergies; pregnancy)
- Unobservable periods (e.g. medications administered during inpatient stay)
- Inability to conduct chart review to verify cases

Challenges in EHR-centric clinical research

- Missing medications / comorbid conditions from encounters outside of the health system
  - Esp when longitudinal follow-up is needed
- Person-time at risk poorly defined
- Health-system specific practices
  - Protocols that dictate treatment
- Selected patient population
  - Tertiary care hospital vs community hospital
  - Public (accepts Medicaid patients) vs Private (avoids Medicaid insured when possible)

The CDW-H Data Model

- The CDW-H contains data in all of the following domains (and more), BUT no master dictionary:
  - Patient demographics
  - Encounter details
  - Diagnoses
  - Procedures
  - Providers
  - Patient vitals
  - Lab tests
  - Medications
  - Orders
  - Notes
  - Charges and Payors
  - Surgery
  - Labor and delivery
  - Medical and social history
  - Patient-reported data
  - Custom data elements