

OUTCOMES RESEARCH USING A LEARNING HEALTH SYSTEM: PROMISE & PITFALLS

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- More than a decade ago, similar to Joe Kanter, we had the vision that a robust electronic amalgamation of patient health records had the potential to **TRANSFORM FUTURE HEALTHCARE.**
- Therefore we embarked on an investigative strategy to **determine whether this strategy was feasible.**
- **SHORT ANSWER: INDEED IT IS**

RANDOMIZED CONTROLLED TRIAL STUDIES (RCTs)

- **RCTs are the most reliable method for outcomes research**, i.e. **to determine whether a therapy really works**, because randomization produces treated and untreated groups that are similar.
- **RCTs suffer from many constraints** including:
 - cost,
 - long duration to obtain results,
 - **RESTRICTION** that their results apply only to the specific population studied in the RCT.
- For example, **RCT findings typically cannot be extrapolated reliably** to determine:
 - whether **women and men**, or whether **all age groups** respond in the same fashion,
 - how patients in the real world who do not fit the characteristics of the RCT population will respond.

Non-Randomized (Observational) Studies

- Non-randomized studies using amalgamated healthcare data can overcome the RCT constraints; **however**, the treated and untreated populations typically **exhibit different characteristics**.
- Sophisticated **statistical analytical techniques** can **reliably** overcome identified differences in characteristics of the treated and untreated groups.
- However, if crucial differences in characteristics are not identifiable (“Unidentified Confounding”) **INCORRECT RESULTS WILL RESULT.**

RECENT LAY PRESS ARTICLE

- On its front page, the [Wall Street Journal](#) (5/3/2012) reports on the increase in observational studies, despite that fact that these studies, according to some researchers, produce findings that are not as reliable as controlled studies.
- In contrast to this report, our recent studies, published 3 years ago in BMJ, describe a [new method that surmounts this problem.](#)

RIGOROUS EXAMINATION OF EMR DATABASE POTENTIAL

- Replicate previously performed RCTs using the data from an EMR database, except for “RANDOMIZATION”.
- **VALIDITY of database outcome results** were assessed by comparison with the RCT results, which were presumed to reflect correct answers.

KEY FEATURES – UK GPRD

- Approximately **10M patient records**
- **Representative sample** of entire UK population
- All healthcare centralized in GP record, so **all key patient health events are captured**
- Complete **longitudinal record** of care
- Includes **All medications prescribed**, so comprehensive treatment record

COMPARISON GPRD to RCT RESULTS

Cardiovascular outcomes (Myocardial Infarction, Stroke or Coronary Revascularization) from 5 different RCT's were analyzed.

GPRD = RCT	6	GPRD ≠ RCT	8
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Different results presumably due to “Unidentified Confounding”

NEW METHOD TO OVERCOME “UNIDENTIFIED CONFOUNDING”

- Developed a **new statistical method (PRIOR EVENT RATE RATIO [PERR])** to address “Unidentified Confounding”
- PERR can **assess the validity of RESULTS** by comparison with standard analytical techniques
- PERR also can **produce reliable RESULTS**, similar to the RCT

COMPARISON of GPRD-PERR vs GPRD (standard analysis)

ASSESSMENT OF VALIDITY

GPRD = RCT	6	GPRD \neq RCT	8
GPRD-PERR = GPRD	6	GPRD-PERR \neq GPRD	7

RELIABILITY OF GPRD-PERR

GPRD-PERR = RCT	11 / 14
GPRD-PERR \neq RCT	3 / 14*

*When the GPRD-PERR differed from the RCT , it was always more similar to the RCT than the GPRD (standard analysis)

SUMMARY - PERR

UNIDENTIFIED CONFOUNDING
NOT PRESENT

UNIDENTIFIED CONFOUNDING
PRESENT

RCT = GPRD

RCT \neq GPRD

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GPRD- PERR

GPRD-PERR

PROOF OF PRINCIPLE

- Our studies demonstrate **PROOF OF PRINCIPLE:**
 - A properly constructed large **LEARNING HEALTH SYSTEM** can produce **RELIABLE** answers to **OUTCOMES RESEARCH**
 - **IT CAN TRANSFORM HEALTHCARE**

REFERENCES

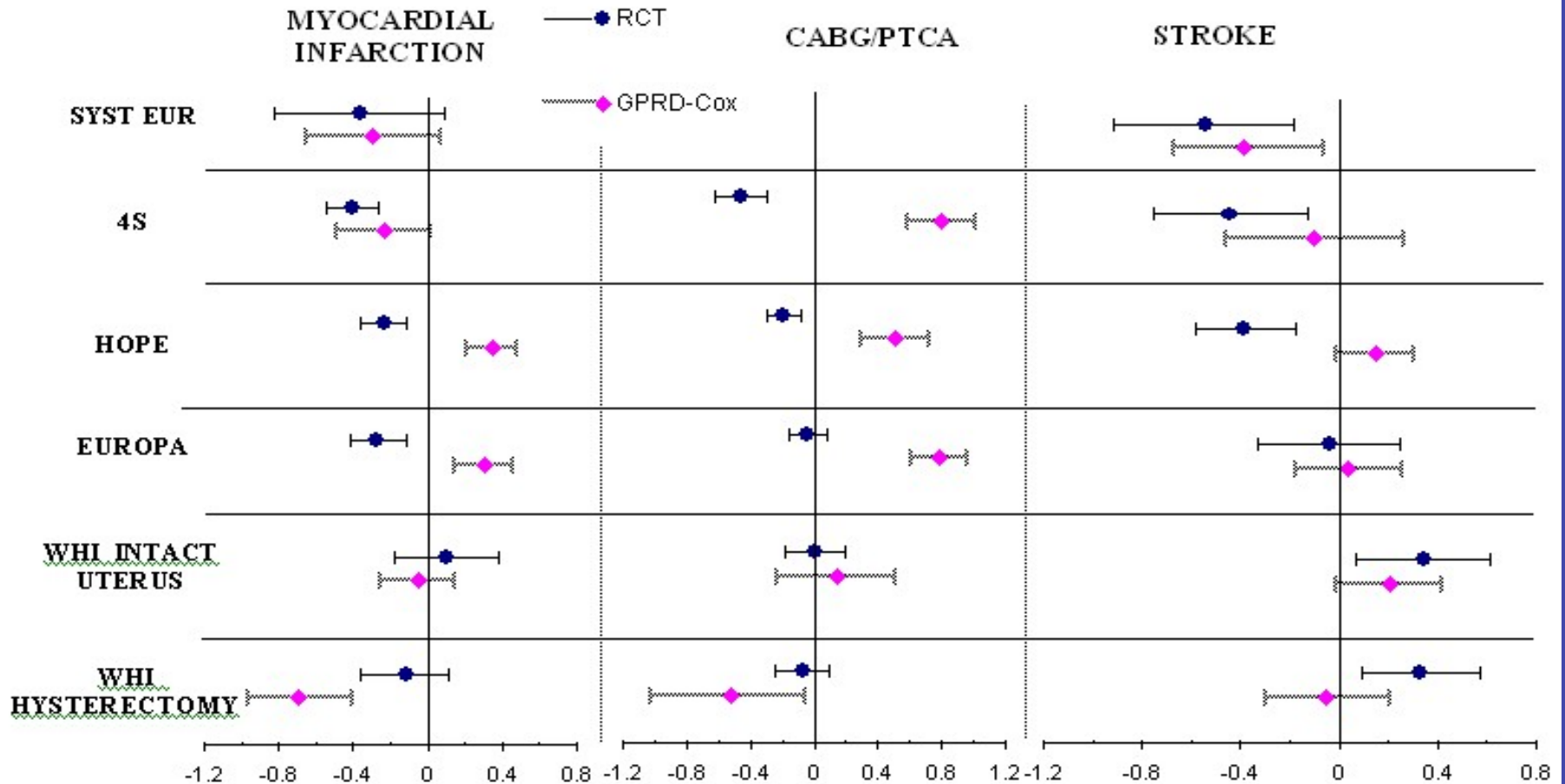
1. Tannen RL, Weiner MG, Xie D. Use of primary care electronic medical record database in drug efficacy research on cardiovascular outcomes: comparison of database and randomized controlled trial findings. [BMJ](#) 2009, 338; b81
2. Yu M, Xie D, Wang X, Weiner MG, Tannen RL. Prior event rate ratio adjustment: numerical studies of a statistical method to address unrecognized confounding in observational studies. [Pharmacoepidemiology and Drug Safety](#) 2012; 21(S2): 60–68

FUTURE CHALLENGES

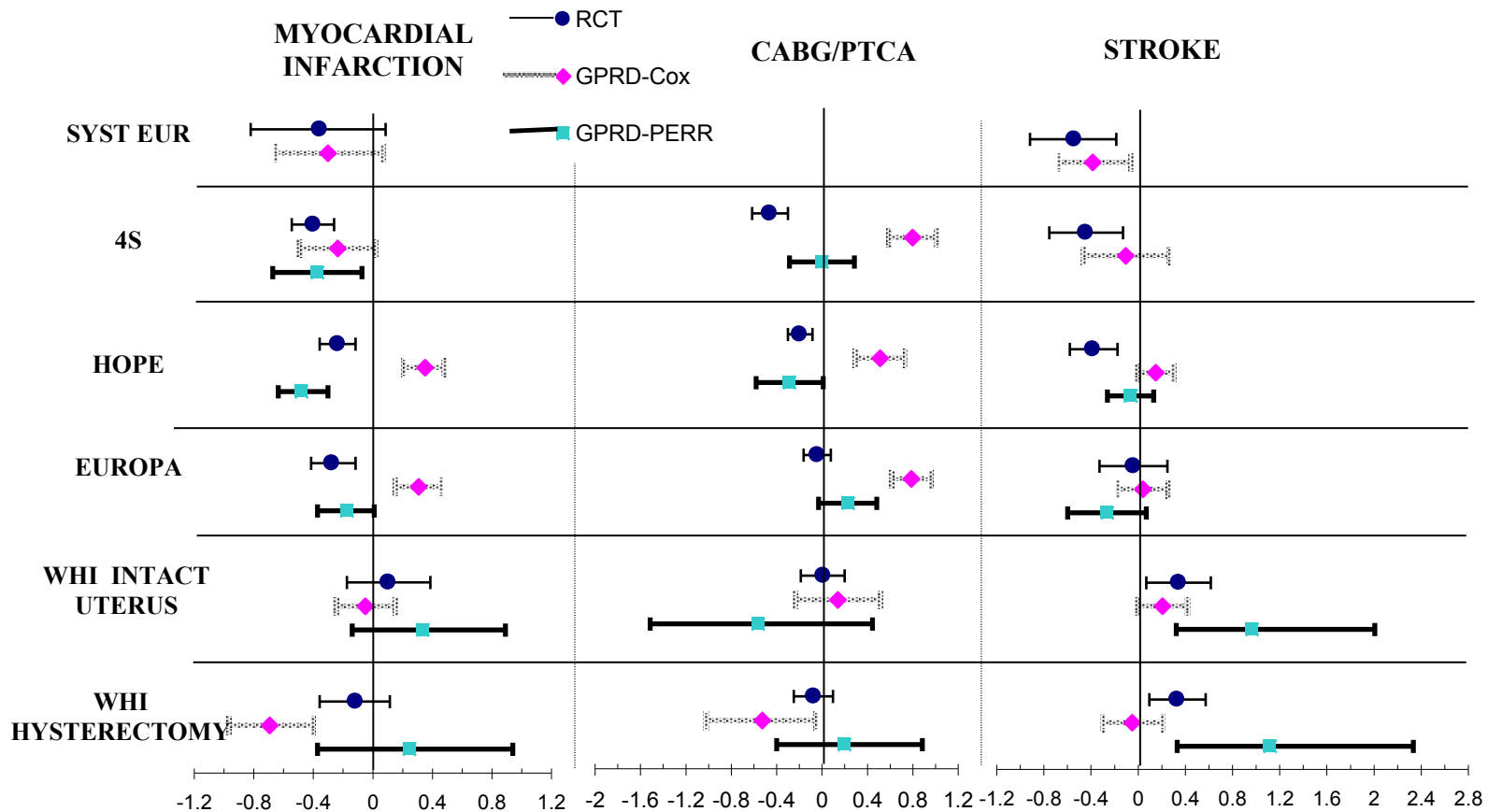
What are the future challenges?

- Implement a sufficient large information set in the US to facilitate **OUTCOME STUDIES** (we project that **50+ million patient records** are needed).
- Demonstrate rigorously that this “Database” can yield reliable answers to **Outcomes Research**
- Develop additional methodologies to address “**UNIDENTIFIED CONFOUDING**”. (Our studies demonstrate such methods can be developed, but **OUR METHOD** will not be applicable to all health issues)

SUMMARY of RCT versus GPRD REPLICATIONS



Summary of RCT versus GPRD Replications with PERR correction



UNIDENTIFIED CONFOUNDING
NOT PRESENT

RCT = GPRD

|| ||

GPRD- PERR

UNIDENTIFIED CONFOUNDING
PRESENT

RCT \neq GPRD

|| \neq

GPRD-PERR