OUTCOMES RESEARCH USING A LEARNING HEALTH SYSTEM: PROMISE & PITFALLS

Richard L. Tannen, M.D.
University of Pennsylvania Perelman School of Medicine
KFF director of Medical research
• 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 the 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

GPRD = RCT

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

| GPRD = RCT | 6 | GPRD ≠ RCT | 8 |

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

| Comparison          | GPRD  = RCT | GPRD-PERR  = GPRD | 6     | 8                        | GPRD  ≠ RCT | GPRD-PERR  ≠ GPRD | 7     | 8                        |
## RELIABILITY OF GPRD-PERR

<table>
<thead>
<tr>
<th>GPRD-PERR = RCT</th>
<th>11 / 14</th>
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<tr>
<td>GPRD-PERR ≠ RCT</td>
<td>3 / 14*</td>
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*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

RCT = GPRD

||

GPRD-PERR

UNIDENTIFIED CONFOUNDING
PRESENT

RCT ≠ GPRD

|| ≠

GPRD-PERR
• 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

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 CONFOUINDING”. (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

[Graph showing comparisons between RCT and GPRD for various conditions such as Myocardial Infarction, CABG/PTCA, and Stroke across different studies including SYST EUR, 4S, HOPE, EUROPA, WHI INTACT, and WHI UTERUS.]
Summary of RCT versus GPRD Replications with PERR correction

- MYOCARDIAL INFARCTION
  - SYST EUR
  - 4S
  - HOPE
  - EUROPA
  - WHI INTACT UTERUS
  - WHI HYSTERECTOMY

- CABG/PTCA

- STROKE
UNIDENTIFIED CONFOUNDING
NOT PRESENT

RCT = GPRD

||

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GPRD-PERR