Cutting-edge technologies and strategies – using real world data

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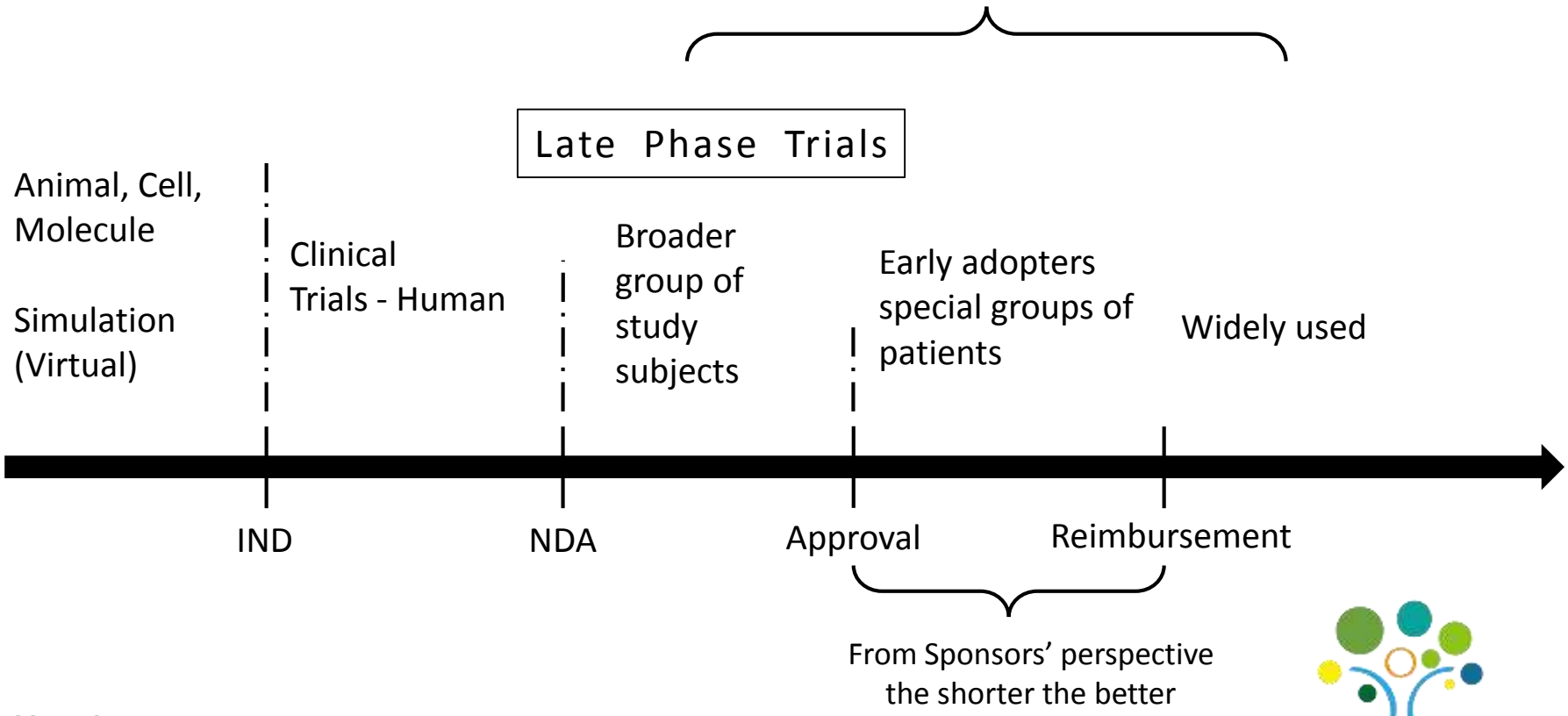
Conflict of Interest disclosure

- Deputy Chair, Drug Safety Committee, Taiwan FDA
- Under a grant from the Ministry of Health and Welfare to NTU Hospital, I provide free consultation to private companies in Taiwan to promote the biotechnology industry
- I conduct public domain research sponsored by medical product companies

Different types of data

Experimental / Research Center settings
- Efficacy
- Short term safety

Real World setting
- Effectiveness
- Safety
- Value ($$$)



www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm

- Real world data (RWD) and real world evidence (RWE) are playing an increasing role in health care decisions.
- FDA uses RWD and RWE to monitor postmarket safety and adverse events and to make regulatory decisions.
- The health care community is using these data to support coverage decisions and to develop guidelines and decision support tools for use in clinical practice.
- Medical product developers are using RWD and RWE to support clinical trial designs (e.g., large simple trials, pragmatic clinical trials) and observational studies to generate innovative, new treatment approaches.
- The 21st Century Cures Act, passed in 2016, places additional focus on the use of these types of data to support regulatory decision making.

www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm

- Real world ***data*** are the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. For example …
  - Electronic health records (EHRs)
  - Health insurance claims and billing activities
  - Product and disease registries
  - Patient-related activities in out-patient or in-home use settings
  - Health-monitoring devices

www.fda.gov/ScienceResearch/SpecialTopics/RealWorldEvidence/default.htm

- Real world ***evidence*** is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD *(I added the following.)*
  - Randomized at individual level
  - Randomized at group level (cluster randomized trial)
  - Non-randomized / observational

Viewpoint

August 22/29, 2017

Multidimensional Evidence Generation and FDA Regulatory Decision Making

Defining and Using "Real-World" Data

Jonathan P. Jarow, MD[1]; Lisa LaVange, PhD[1]; Janet Woodcock, MD[1]

» Author Affiliations

JAMA. 2017;318(8):703-704. doi:10.1001/jama.2017.9991

www.raps.org/Regulatory-Focus/News/2016/05/11/24929/Califf-Leveraging-Real-World-Evidence-is-Top-Programmatic-Priority-for-FDA/?sthash.oewL4dWs.mjjo

Califf: Leveraging Real World Evidence is 'Top Programmatic Priority' for FDA

Posted 11 May 2016

By Michael Mezher

The "top programmatic priority" for the US Food and Drug Administration (FDA), under Commissioner Robert Califf, is to leverage real world evidence from the healthcare system to inform FDA decision making, he told participants at the Food and Drug Law Institute's annual conference last week.

While Califf said his first priority as commissioner is to strengthen FDA's workforce, that stronger workforce will be critical to achieving FDA's goals in specific program areas such as real world evidence.

Specifically, Califf said he wants to see FDA develop a system for "[real world] evidence generation that can meet the demands of the next few decades."

- “Rather than primarily relying on randomized controlled trials, Califf said he sees well-designed pragmatic studies as a way of generating high quality evidence.”
- ‘ "Prospectively designed registries and cohort studies in the context of clinical practice are highly valuable, and randomized trials conducted in the context of clinical practice, often called a pragmatic clinical trial may be the most important source of knowledge in the future," he said.’

N Engl J Med 2016; 375: 2293-7

SOUNDING BOARD

Real-World Evidence — What Is It and What Can It Tell Us?

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Gerald J. Dal Pan, M.D., M.H.S., Gerry W. Gray, Ph.D., Thomas Gross, M.D., M.P.H.,
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Peter W. Marks, M.D., Ph.D., Melissa A. Robb, B.S.N., M.S., Jeffrey Shuren, M.D., J.D.,
Robert Temple, M.D., Janet Woodcock, M.D., Lilly Q. Yue, Ph.D., and Robert M. Califf, M.D.

- Experimental setting vs. Real-World setting
- Randomized and non-randomized studies

JAMA 2012; 308: 1906-13

- Using Taiwan Health insurance data

ONLINE FIRST

Association Between Nucleoside Analogues and Risk of Hepatitis B Virus–Related Hepatocellular Carcinoma Recurrence Following Liver Resection

Chun-Ying Wu, MD, PhD, MPH
Yi-Ju Chen, MD, PhD
Hsiu J. Ho, PhD
Yao-Chun Hsu, MD, MS
Ken N. Kuo, MD
Ming-Shiang Wu, MD, PhD
Jaw-Town Lin, MD, PhD

Context Tumor recurrence is a major issue for patients with hepatocellular carcinoma (HCC) following curative liver resection.

Objective To investigate the association between nucleoside analogue use and risk of tumor recurrence in patients with hepatitis B virus (HBV)–related HCC after curative surgery.

Design, Setting, and Participants A nationwide cohort study between October 2003 and September 2010. Data from the Taiwan National Health Insurance Research Database. Among 100 938 newly diagnosed HCC patients, we identified 4569 HBV-related HCC patients who received curative liver resection for HCC between Oc-

JAMA 2017; 318: 1250-9

- Using Taiwan health insurance data

Research

JAMA | Original Investigation

Association Between Use of Non–Vitamin K Oral Anticoagulants With and Without Concurrent Medications and Risk of Major Bleeding in Nonvalvular Atrial Fibrillation

Shang-Hung Chang, MD, PhD; I-Jun Chou, MD; Yung-Hsin Yeh, MD; Meng-Jiun Chiou, MSc; Ming-Shien Wen, MD; Chi-Tai Kuo, MD; Lai-Chu See, PhD; Chang-Fu Kuo, MD, PhD

Using Taiwan health insurance data

Comparative Effectiveness and Safety of Dabigatran and Rivaroxaban in Atrial Fibrillation Patients

Chao-Lun Lai, MD, PhD; Ho-Min Chen, MS; Min-Tsun Liao, MD; Ting-Tse Lin, MD; K. Arnold Chan, MD, ScD

Background—We aimed to examine the comparative effectiveness and safety between dabigatran and rivaroxaban in atrial fibrillation patients.

Methods and Results—We conducted a population-based, retrospective, new-user cohort study based on the National Health Insurance claims database in Taiwan. Adult atrial fibrillation patients who initiated dabigatran (N=10 625) or rivaroxaban (N=4609) between June 1, 2012 and May 31, 2014 were identified as the overall population. A propensity score was derived using logistic regression to model the probability of receipt of rivaroxaban as a function of potential confounders. Altogether, 4600 dabigatran users were matched with 4600 rivaroxaban users to create a propensity score–matched population. The marginal proportional hazards model was applied among the propensity score–matched population as the primary analysis, and the proportional hazards model with adjustment of the quintiles of the propensity score among the overall population was used as the secondary analysis. Rivaroxaban users had a higher risk of all-cause death than dabigatran users (hazard ratio 1.44, 95%CI 1.17-1.78 in the primary analysis and hazard ratio 1.47, 95%CI 1.23-1.75 in the secondary analysis). Rivaroxaban users also possessed a higher risk of gastrointestinal hemorrhage needing transfusion than dabigatran users in the primary analysis (hazard ratio 1.41, 95%CI 1.02-1.95), but the difference diminished in the secondary analysis (hazard ratio 1.20, 95%CI 0.92-1.56). The risks of ischemic stroke, acute myocardial infarction, arterial embolism/thrombosis, and intracranial hemorrhage were similar between the 2 groups.

Conclusions—Rivaroxaban therapy was associated with a statistically significant increase in all-cause death compared with dabigatran therapy in atrial fibrillation patients. (***J Am Heart Assoc*. 2017;6:e005362. DOI: 10.1161/JAHA.116.005362.)**

2015; 5: e006450

Open Access Research

BMJ Open

Epidemiology of psoriasis and palmoplantar pustulosis: a nationwide study using the Japanese national claims database

Kiyoshi Kubota,[1,2] Yukari Kamijima,[1,2] Tsugumichi Sato,[1,3] Nobuhiro Ooba,[1,4] Daisuke Koide,[5] Hajime Iizuka,[6] Hidemi Nakagawa[7]

Environmental Health and Preventive Medicine 2017; 22: 51

STUDY PROTOCOL Open Access

Analysis of the evidence-practice gap to facilitate proper medical care for the elderly: investigation, using databases, of utilization measures for National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB)

Takeo Nakayama[1*], Yuichi Imanaka[2], Yasushi Okuno[3], Genta Kato[4], Tomohiro Kuroda[5], Rei Goto[6,11], Shiro Tanaka[7], Hiroshi Tamura[5], Shunichi Fukuhara[8], Shingo Fukuma[8], Manabu Muto[9], Motoko Yanagita[10], Yosuke Yamamoto[8] and on behalf of BiDAME: Big Data Analysis of Medical Care for the Elderly in Kyoto

Ongoing collaboration with Kyoto U

N Engl J Med 2016; 374: 1145-54

ORIGINAL ARTICLE

A Multicenter Observational Study of Incretin-based Drugs and Heart Failure

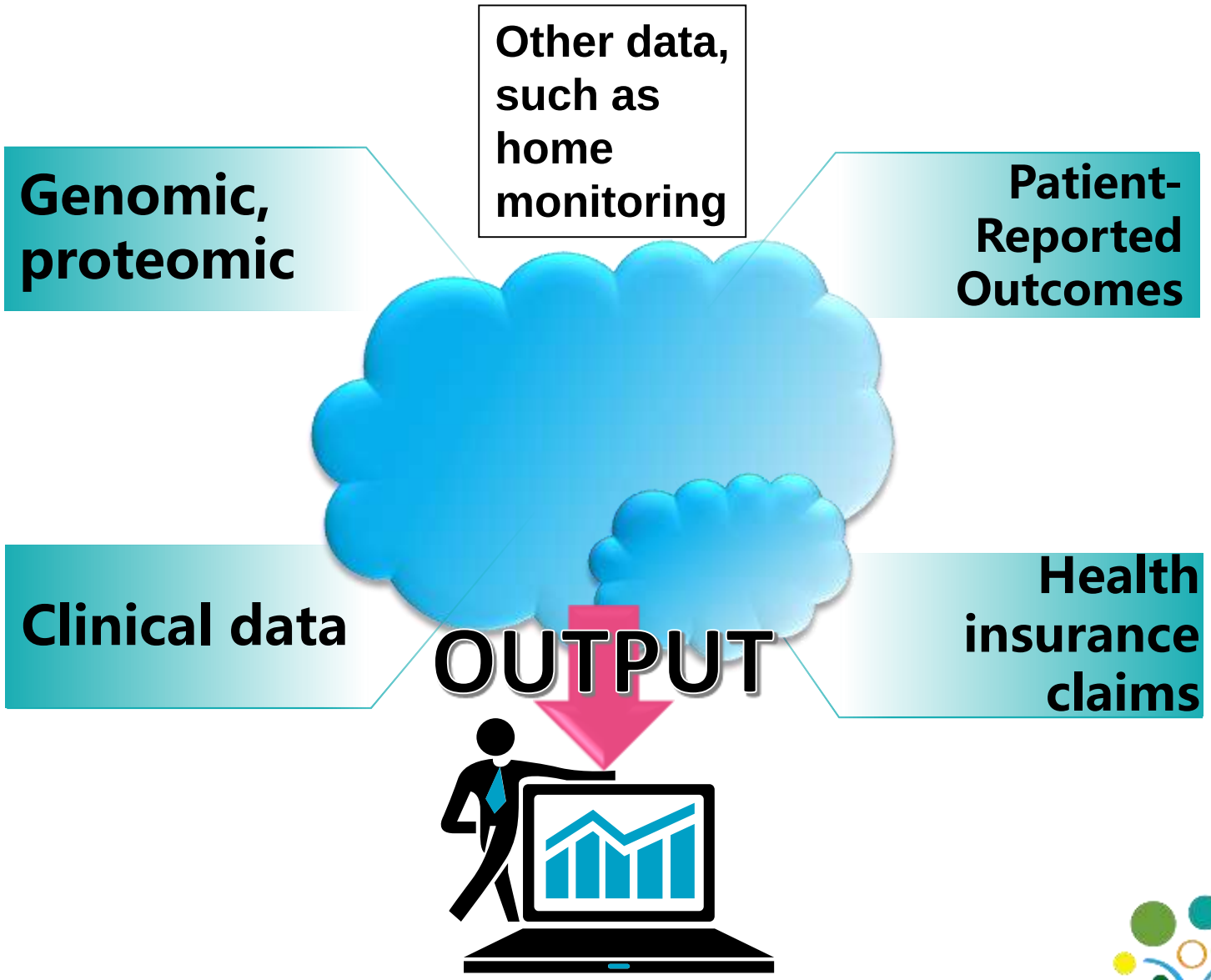
Kristian B. Filion, Ph.D., Laurent Azoulay, Ph.D., Robert W. Platt, Ph.D., Matthew Dahl, B.Sc., Colin R. Dormuth, Sc.D., Kristin K. Clemens, M.D., Nianping Hu, M.D., Ph.D., J. Michael Paterson, M.Sc., Laura Targownik, M.D., M.S.H.S., Tanvir C. Turin, M.D., Ph.D., Jacob A. Udell, M.D., M.P.H., and Pierre Ernst, M.D., for the CNODES Investigators*

- Canada-CNODES: Alberta, Manitoba, Ontario(>65y/o),and Saskatchewan
- United Kingdom - Clinical Practice Research Datalink (CPRD), electronic medical records
- United States- MarketScan (health insurance claims)

Big Data, a very popular term these days … but the concept is not new …

- "We call this the problem of big data." – Cox & Ellsworth (National Aeronautics and Space Administration, USA) 1997
  - Datasets too big for existing hardware and software to handle
- Gaining "insight" from "data" is different from simply collecting "big data"
  - Epidemiologists have been doing it for years …

It is happening now …



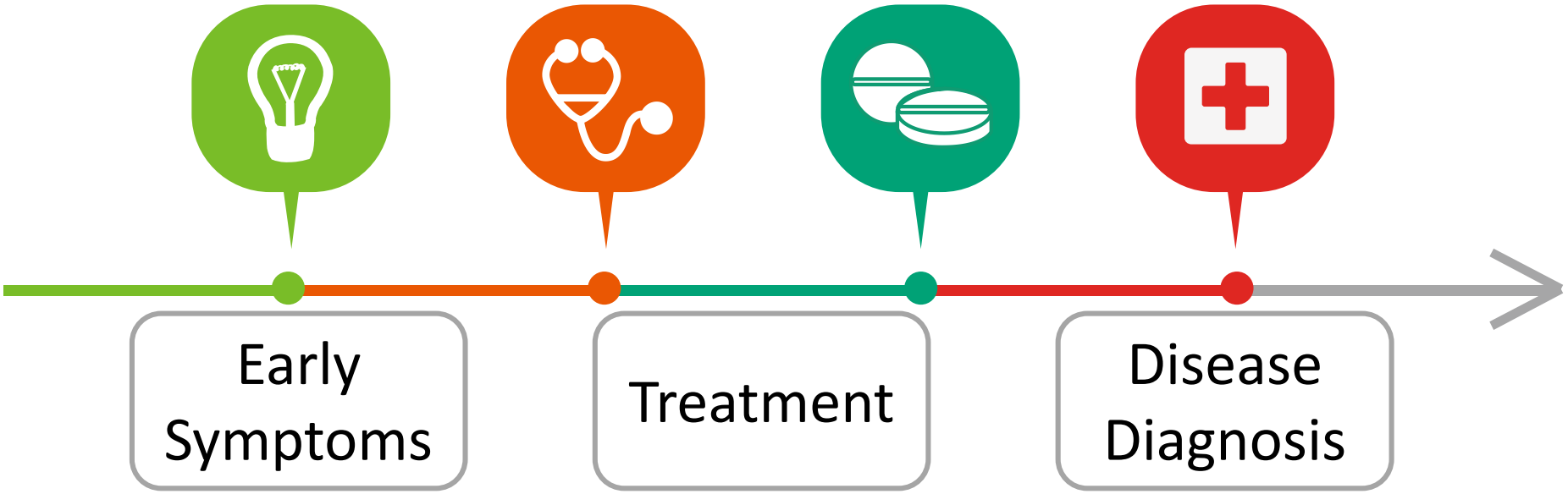
The Economist, May 6, 2017

Regulating the internet giants

The world's most valuable resource is no longer oil, but data

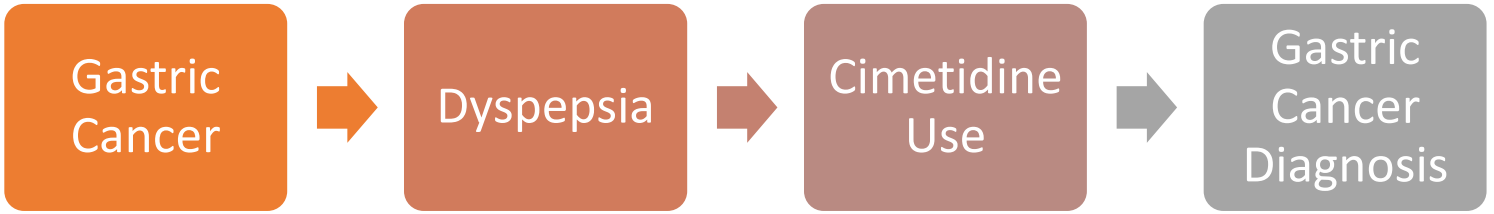
The data economy demands a new approach to antitrust rules

How to analyze and interpret the data is most important – the central role of observational research methods



Apparent (but spurious) association between treatment and disease in non-randomized studies

For example (protopathic bias)



Epidemiology 1990; 1: 251-4

Cimetidine Use and Gastric Cancer

Mary Catherine Schumacher,[1] Susan S. Jick,[2] Hershel Jick,[2] and Andrew D. Feld[3]

- A case control study
  - For cimetidine, odds ratio = 2.3 (95% CI = 0.8-6.9)
  - For antacid, odds ratio = 1.9 (95% CI = 1.0-3.7)
- "Although a causal relation between gastric cancer and cimetidine is possible, the similarity of the findings for cimetidine and antacids lends support to other explanations."

In summary

- A lot of real world health data are available
- How to linked and utilize them?
- Methods (observational / epidemiology)
- Personnel and skillset

- Will provide solid evidence to improve healthcare

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