

Social Determinants and EHR Data: Analytic Decision Support

Harold P. Lehmann MD PhD

The PaTH Clinical Data Research Network



Patrick Ryan, Observational Health Data Sciences and Informatics (OHDSI) Overview, 5/14/14

Pioglitazone and bladder cancer: a propensity score matched cohort study

Li Wei, Thomas M. MacDonald

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BMJ

BMJ 2012;344:e3645 doi: 10.1136/bmj.e3645 (Published 31 May 2012)

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BJCP May 2012: "In this study population, pioglitazone does not appear to be significantly associated with an increased risk of bladder cancer in patients with type 2 diabetes."

RESEARCH

WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Pioglitazone is mainly used in combination with diet and exercise and other anti-diabetic medications to treat type 2 diabetes mellitus.
- Long term use of pioglitazone (as part of therapy) may be associated with an increased risk of bladder cancer.

WHAT THIS STUDY ADDS

- In this study population, pioglitazone does not appear to be significantly associated with an increased risk of bladder cancer in patients with type 2 diabetes.

The use of pioglitazone and the risk of bladder cancer: a propensity score matched case-control study

BMJ May 2012: "The use of pioglitazone is associated with an increased risk of incident bladder cancer among people with type 2 diabetes."

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ORIGINAL CONTRIBUTION

JAMA

Oral Fluoroquinolones and Risk of Retinal Detachment

Mahyar Elminan, PharmD, MSc (epi)
Farzin Forooghian, MD, MSc, FRCSC
James M. Brophy, MD, PhD, FRCPC
Steven T. Bird, PharmD
David Maberley, MD, MSc, FRCSC

Context Fluoroquinolone use is associated with numerous case reports of ocular safety, particularly retinal detachment.
Objective To examine the risk of developing a retinal detachment in patients taking oral fluoroquinolones.
Design, Setting, and Population Retrospective cohort study in British Columbia, Canada.

April 2012: "Patients taking oral fluoroquinolones were at a higher risk of developing a retinal detachment"

associated with a wide array of adverse events such as dysglycemia,¹ cardiac arrhythmia,² and neuropsychiatric events.³ Fluoroquinolones also have been linked to several forms of ocular toxicity such as corneal perforations,⁴ optic neuropathy,⁵ and retinal hemorrhages.⁶ In 2011, the label for gemifloxacin was updated to include hemorrhage,⁶ which includes retinal hemorrhage that was reported during postmarketing surveillance. A class-wide warning for fluoroquinolones also has been issued for tendon rupture,⁷ which raises concerns for the effect of these drugs on connective tissue in the eye. Animal studies also provide evidence for retinal degeneration with use

a higher risk of developing retinal detachment. The adjusted rate ratio (ARR), 4.0 vs 0.2% of controls; ARR, 6.1% of controls; ARR, 1.1% of controls. The absolute risk in person-years (number needed to harm) was 1.1. There was no evidence of association between retinal detachment and β -lactam or β -agonists (ARR, 0.95 [95% CI, 0.53 to 1.71]).

Conclusion Patients taking oral fluoroquinolones had a higher risk of developing retinal detachment.

JAMA. 2012;307(13):1414-1419.

through the destructive effects of these drugs on collagen and elastin.⁸ Collagen fibers play a key role in the structure of

Research

Original Investigation

Association Between Oral Fluoroquinolone Use and Retinal Detachment

Björn Pasternak, MD, PhD; Henrik Svanström, MSc; Mads Melbye, MD, DrMedSci; Anders Hviid, MSc, DrMedSci

JAMA

IMPORTANCE A recent study of ophthalmologic patients found a strong association between fluoroquinolone use and retinal detachment. Given the prevalent use of fluoroquinolones, this could, if confirmed in the general population, translate to many excess cases of retinal detachment that are potentially preventable.

Oral fluoroquinolone use is associated with an increased risk of retinal detachment.

OBJECTIVE A nationwide, register-based cohort study in Denmark linked data on participant characteristics, filled prescriptions, and hospitalizations to identify associations between oral fluoroquinolone use and cases of retinal detachment with surgical treatment (scleral buckling, vitrectomy, or pneumatic retinotomy). The cohort included 748 702 episodes of fluoroquinolone use (660 572 [88%] in current users and 88 130 [12%] in past users).

MAIN RESULTS The risk of incident retinal detachment was higher in current users of fluoroquinolones compared with nonusers. The risk was not significantly increased in past users. The risk of retinal detachment was not significantly increased in current users of fluoroquinolones compared with nonusers.

RESULTS A total of 566 cases of retinal detachment occurred, of which 465 (82%) were rhegmatogenous detachments; 72 in fluoroquinolone users and 494 in control nonusers. The crude incidence rate was 25.3 cases per 100 000 person-years in current users, 18.9 in recent users, 26.8 in past users, and 24.8 in distant users compared with 19.0 in nonusers. Compared with nonuse, fluoroquinolone use was not associated with a significantly increased risk of retinal detachment: the adjusted RRs were 1.29 (95% CI, 0.53 to 3.13) for current use;

Dec 2013: "Oral fluoroquinolone use was not associated with increased risk of retinal detachment"

- ← Editorial page 2151
- ← JAMA Patient Page 2212
- ← Supplemental content at jama.com

Challenge

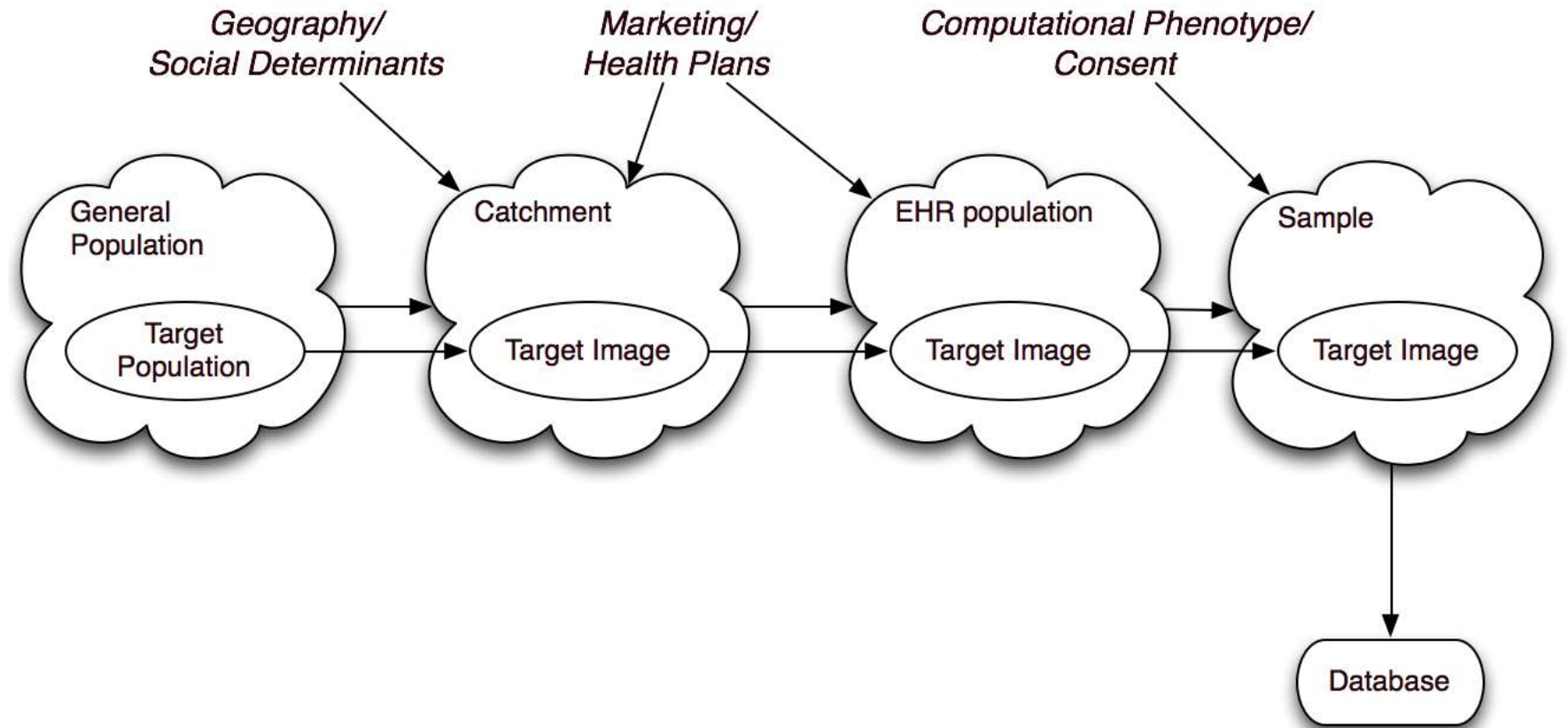
“ How do I convince hard-boiled researchers that our results are as trustworthy and believable as the best epidemiological data?

➤ Dan Ford



<http://skepticwiki.org/>

Where's the Population?

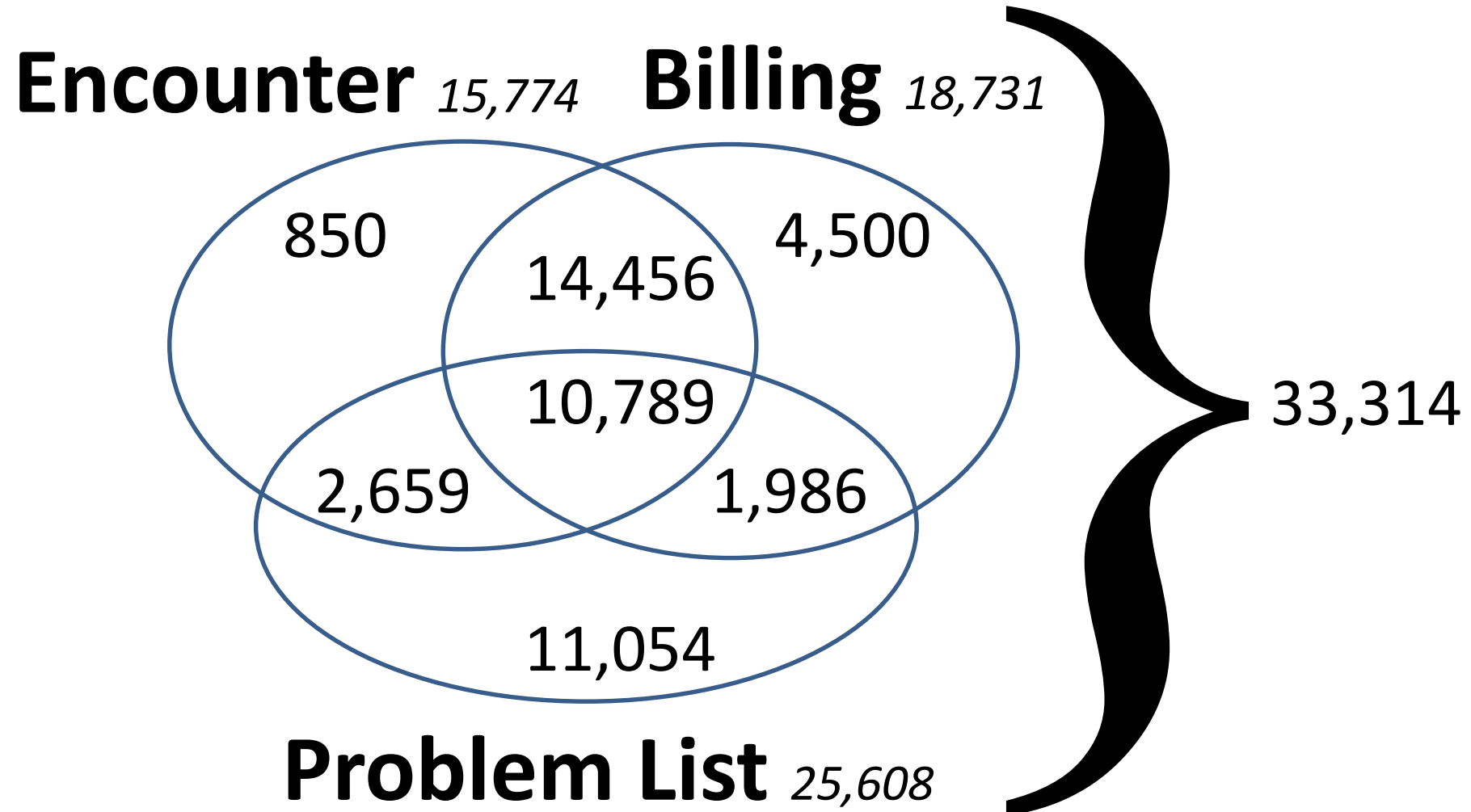


Sen A, et al. GIST 2.0: A scalable multi-trait metric for quantifying population representativeness of individual clinical studies. *J Biomed Inform.* 2016 Oct;63:325-336.

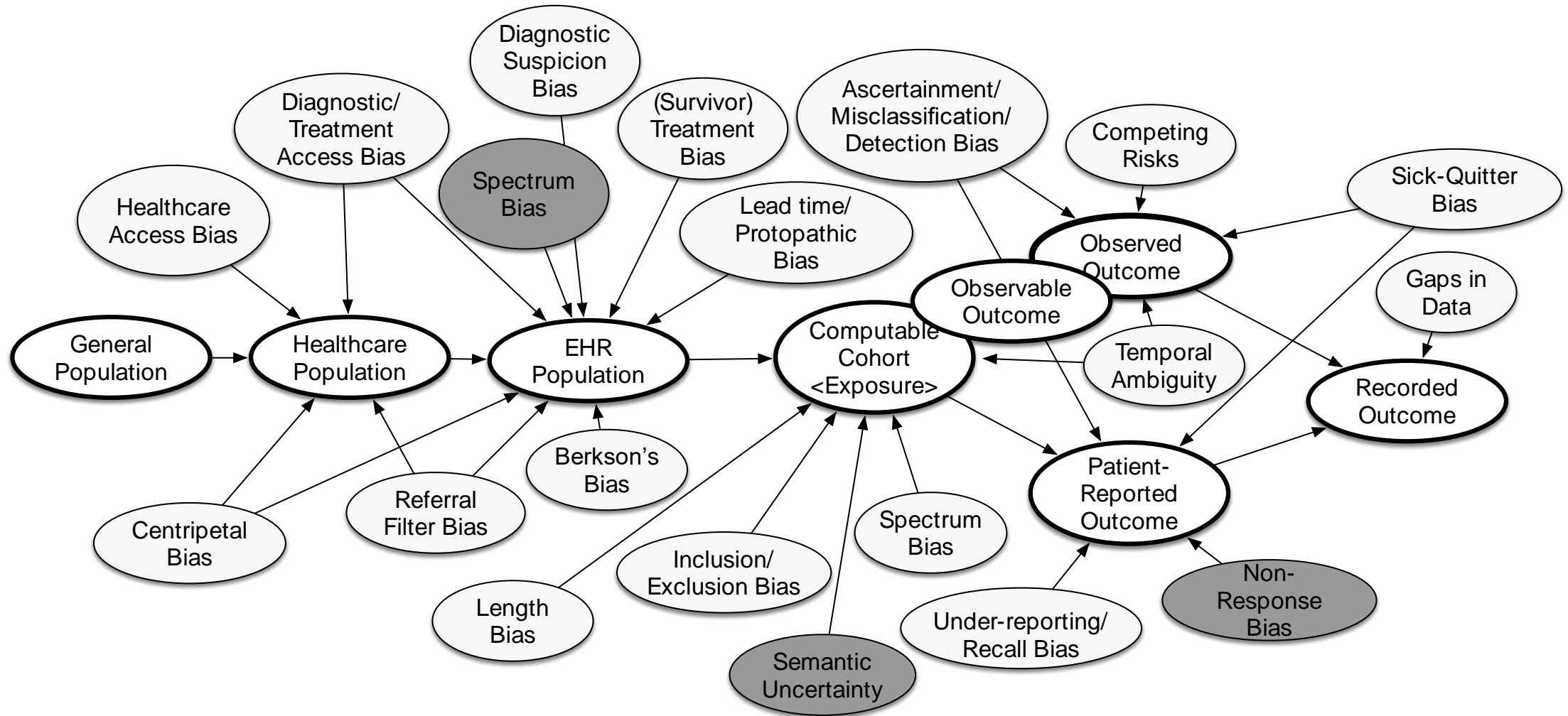
What's the "diagnosis"?

The case of atrial fibrillation

- Do all the fields with the same name mean the same thing?



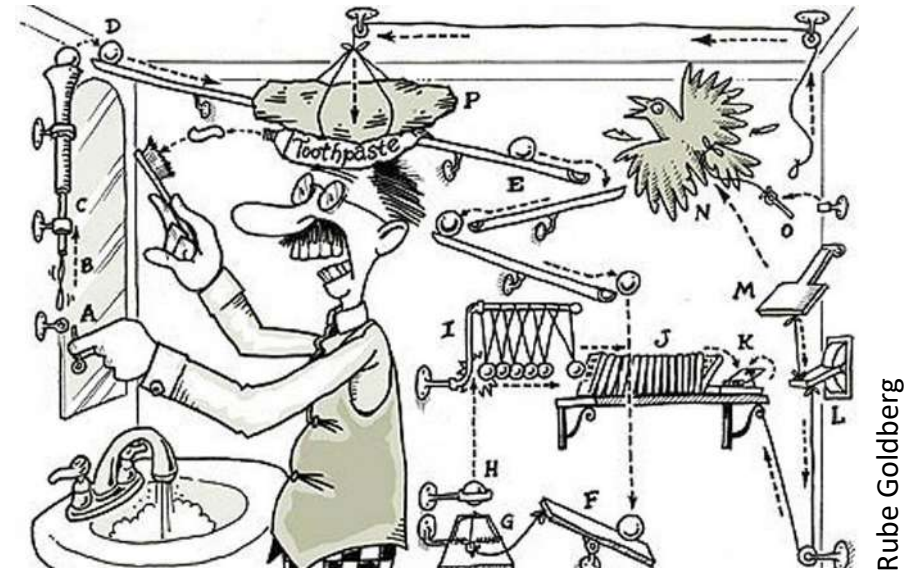
Some Potential Biases



Amateur Analysts

3. Amateur analysts

- Too many analysts to train them all at the level we want
 - MACRA, eCQM, Pop Health, PMI, ...
- Analyses are the most complicated
- No funds for proper statistical analysis
- Statistical-analytic decision support is needed
- We need to convert methodological knowledge into computer-readable form

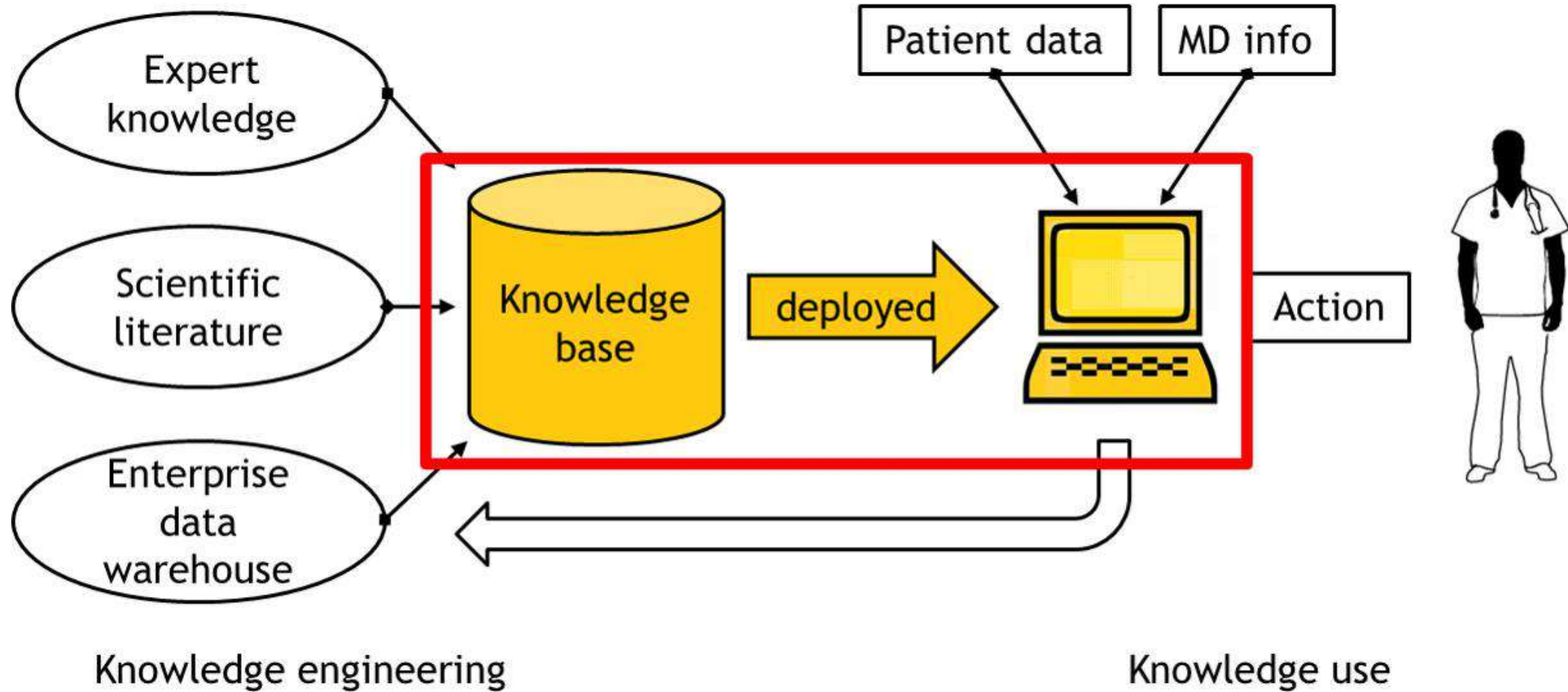


Rube Goldberg

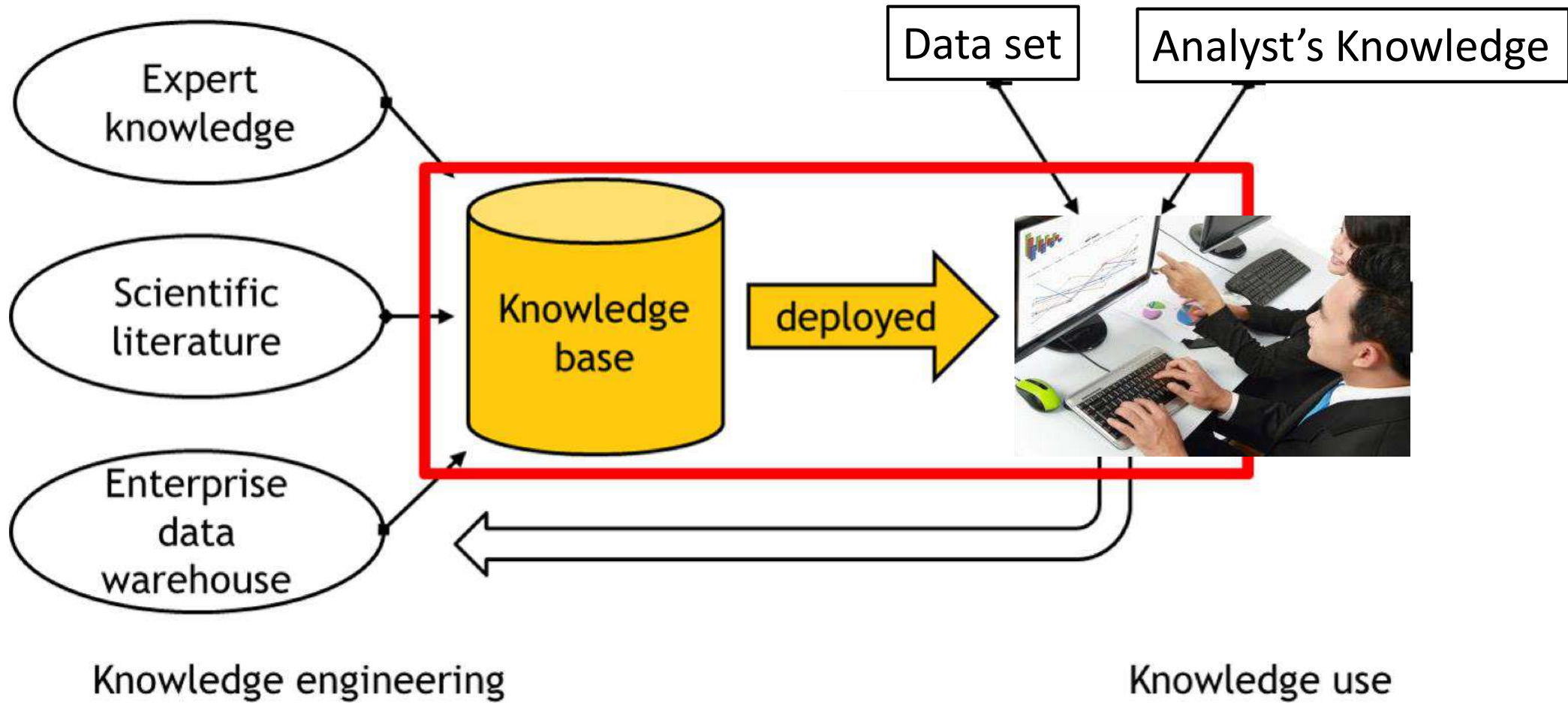
“According to the McKinsey report, the United States will need an **additional 140,000 to 190,000 data science experts** with “deep analytical skills,” plus 1.5 million managers capable of using data analytics in decision making.



Decision Support Cycle



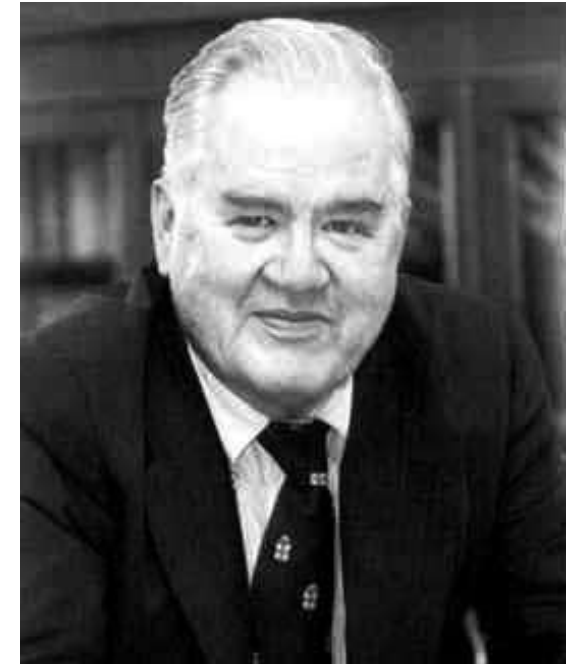
Decision Support Cycle



Intelligent Assistance and Data Analysis

“By 1995 or so, the largest single driving force in guiding general work on data analysis and statistics [will be] to understand and improve data-analytic expert systems...”

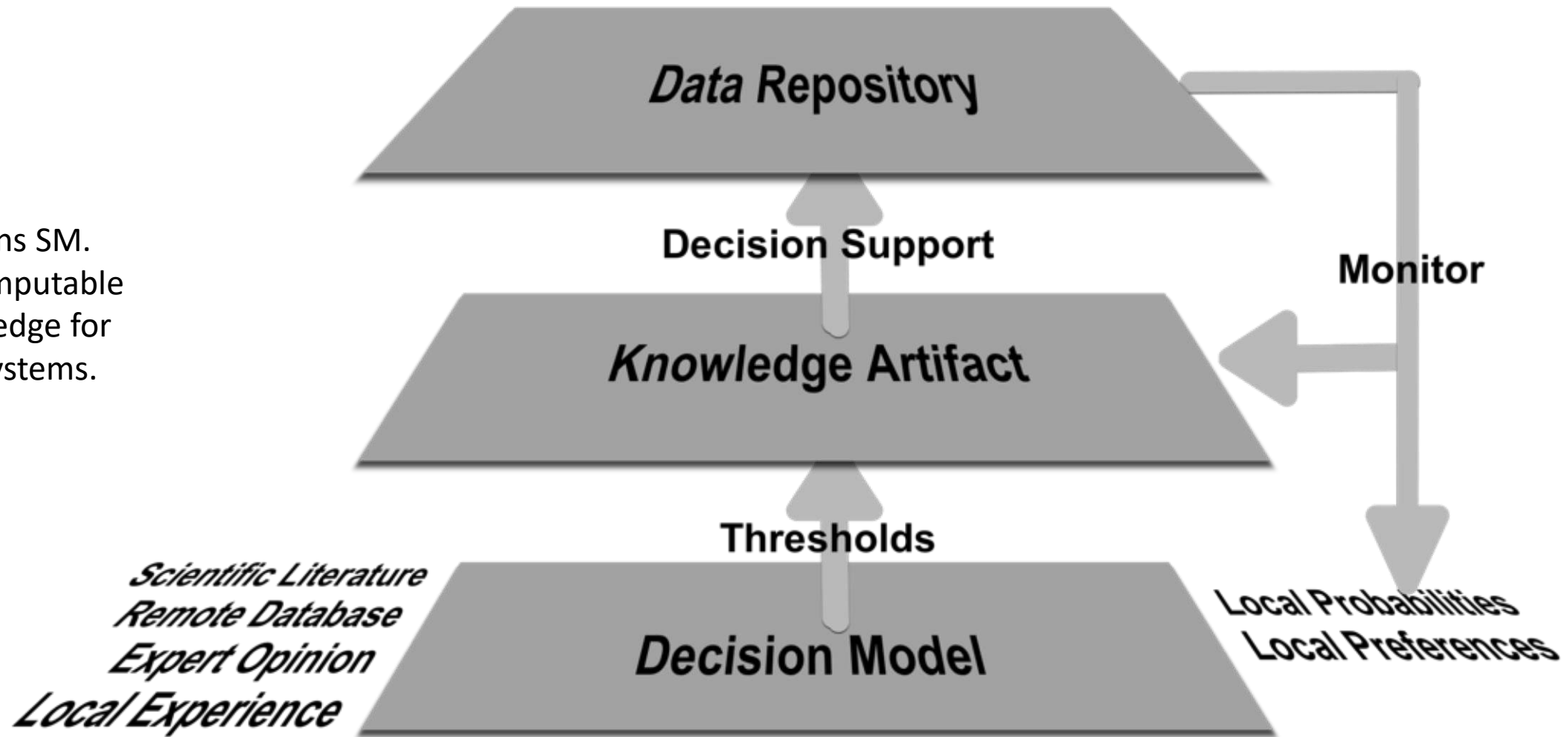
➤ John Tukey, 1986



Early History

- 1983: Nedler: Front-end system (for GLIM)
- 1984: Gale, Pregiborn: REX: Advise on linear regression
- 1985: Hahn defines levels of intelligence: simple computerized answering→automated statistical consulting
- 1988: Duijsens: PRINCE helps naïve users formulate analysis options
- 1988: Oldford & Peters: DINDE: graphical environment tracks steps
- 1989: Chowdury: MAXITAB for inexperienced users for data analysis and interpretation
- 1994: Silvers et al.: PROPHET: Beyond Anova
- Silvers, 1994

Knowledge Cycle



Lehmann HP, Downs SM.
Desiderata for Computable
Biomedical Knowledge for
Learning Health Systems.
Learn Heal Syst.
2018;e10065:1–9.

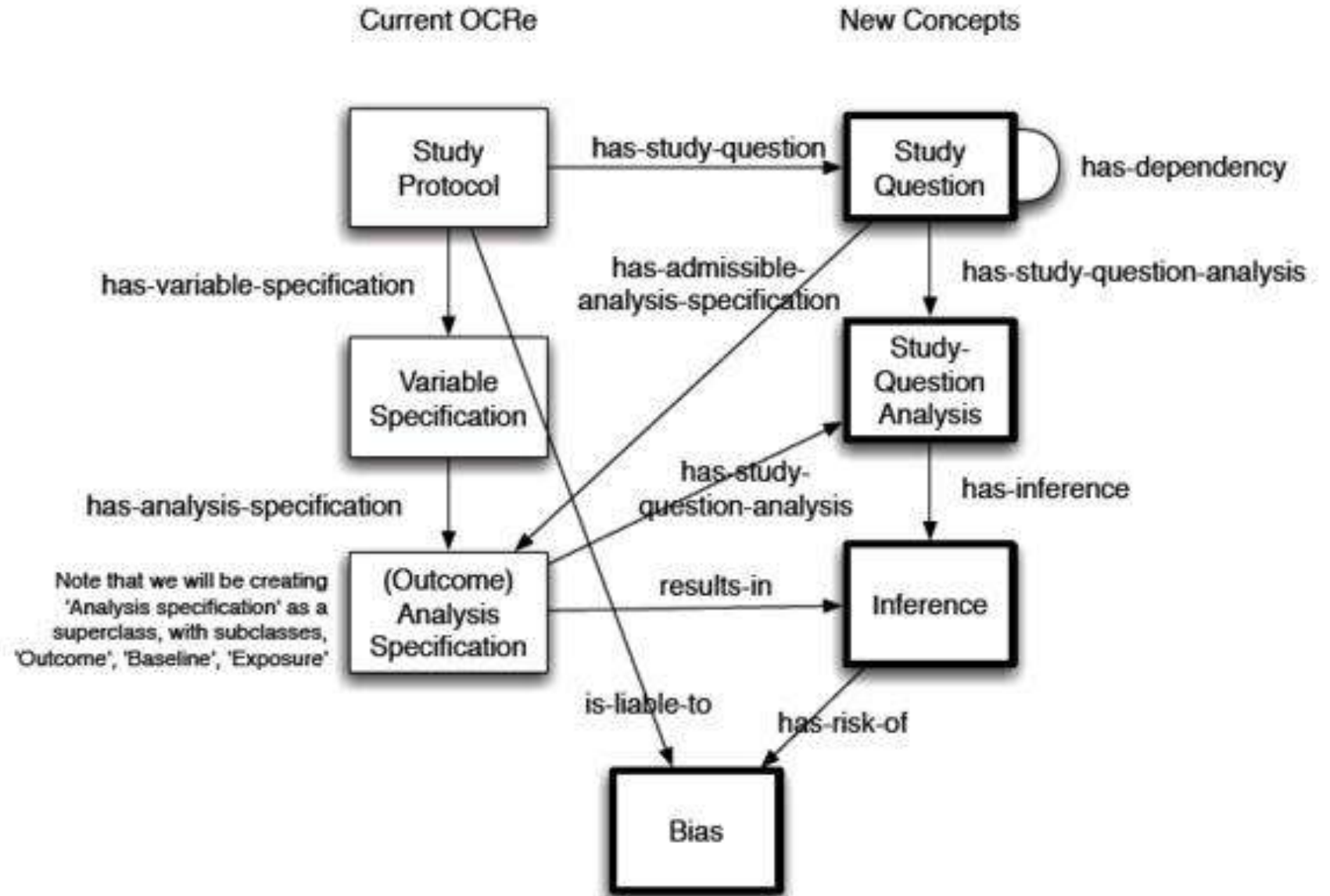
Desiderata for Computable Biomedical Knowledge for Learning Health Systems

Lehmann HP, Downs SM. Desiderata for
Computable Biomedical Knowledge for
Learning Health Systems. Learn Heal Syst.
2018;e10065:1–9.



Desiderata	Development Work to Be Done
1. Discrimination	<ul style="list-style-type: none"> Measures that take clinical thresholds into account^{70,71} Elicitation and articulation of those thresholds Methods for recalculating local discrimination
2. Local Recalibration	<ul style="list-style-type: none"> Application of calibration based on thresholds¹⁷
3. Thresholds & Local Preferences	<ul style="list-style-type: none"> Elicitation, articulation of preferences Local calculation of thresholds
4. Explanation	<ul style="list-style-type: none"> Deployment
5. Monitoring	<ul style="list-style-type: none"> Choose variables based on value of information⁷²
6. Debiasing	<ul style="list-style-type: none"> Creation and curation of debiasing models Application of debiasing models
7. Generalizability	<ul style="list-style-type: none"> Calculation of distance⁶² Adding to the Knowledge Artifact the meta data required to choose the calculation
8. Semantic Uncertainty	<ul style="list-style-type: none"> Derivation of the epistemic confidence interval
9. Findable	<ul style="list-style-type: none"> Articulation of the full ontology required to index a Knowledge Artifact at all its multiple levels Tagging KO with that ontology
10. Other Commandments as necessary and proper	<ul style="list-style-type: none"> Continuous monitoring and improvement of these desiderata

Ontology for Biases: Extensions to OCRE



H Lehmann, T Darden, G Williams. 2014.
Unpublished.

To Do

- Methodology for the analysts
- Knowledge tools to store the knowledge
- Knowledge tools to apply the knowledge
- Combine JH/PaTH/Israeli expertise

