

The Uneven Future of Evidence-Based Medicine

Ida **Sim** MD, PhD

Professor of Medicine, UCSF

Co-Director, Biomedical Informatics, CTSI

Co-Founder, Open mHealth



*Open mHealth is a project of the Tides Center, funded by
Robert Wood Johnson Foundation*



Thanks!

- Russ Altman, Stanford University
- Lisa Bero, University of Sydney
- Julian Elliott, Monash University
- Steve Goodman, Stanford University
- Jeremy Grimshaw, Ottawa Health Research Institute
- Santosh Kumar, University of Memphis
- Chris Mavergames, Cochrane Collaboration
- Susan Murphy, University of Michigan

- Diverse Data Meeting, Cochrane, Oct 3, 2015



*Open mHealth is a project of the Tides Center, funded by
Robert Wood Johnson Foundation*





Cochrane
Library

Trusted evidence.
Informed decisions.
Better health.

Intervention Review

Antibiotics for acute laryngitis in adults

Ludovic Reveiz^{1,*}, Andrés Felipe Cardona² **Database Title**

The Cochrane Library

Editorial Group: [Cochrane Acute Respiratory Infections Group](#)

Published Online: 23 MAY 2015

Assessed as up-to-date: 16 DEC 2014

DOI: 10.1002/14651858.CD004783.pub5

Authors' conclusions

"Antibiotics do not appear to be effective in treating acute laryngitis when assessing objective outcomes."

About 22,700,000 results (0.28 seconds)

What Is MS? : National Multiple Sclerosis Society

www.nationalmssociety.org/What-is-MS ▾ National Multiple Sclerosis Society ▾
The cause of MS is still unknown – scientists believe the disease is triggered by as-yet-
unidentified environmental factor(s) in a person who is genetically ...
[Multiple Sclerosis FAQs](#) - [What Causes MS?](#) - [Definition of MS](#) - [Who Gets MS?](#)

Multiple Sclerosis (MS) Overview

www.webmd.com/multiple-sclerosis
Multiple sclerosis affects 2.5 million people in the United States. Get in-depth multiple sclerosis information, including:
[Symptoms of MS](#) - [Symptoms & Types](#)

Multiple sclerosis - Mayo Clinic

www.mayoclinic.org/.../multiple-sclerosis/.../con-20026689 ▾ Mayo Clinic ▾
There's no cure for multiple sclerosis. However, treatments can help speed recovery from attacks, modify the course of the disease and manage symptoms.

Multiple sclerosis - Wikipedia, the free encyclopedia

https://en.wikipedia.org/wiki/Multiple_sclerosis ▾ Wikipedia ▾
Multiple sclerosis (MS), also known as disseminated sclerosis or encephalomyelitis disseminata, is a demyelinating disease in which the insulating covers of ...

In the news

Melatonin Linked to Seasonal Relapses of Multiple Sclerosis

Scientific American - 2 days ago

Multiple sclerosis (MS) relapses are known to swing with the seasons. Scientists have

Multiple sclerosis

Also called: MS

ABOUT SYMPTOMS TREATMENTS

"The information has been checked
by medical doctors at Google and the
Mayo Clinic for accuracy"¹

...d, but treatment may help
...nd medications that suppress the
...an help with symptoms and slow
...on.

Prescription

Steroids: Methylprednisolone by injection or by mouth (Medrol)

Other treatments: Fingolimod (Gilenya), Natalizumab by injection, Mitoxantrone by injection, Interferon beta-1b by injection, Interferon beta-1a by injection, Glatiramer by injection (Copaxone), Azathioprine

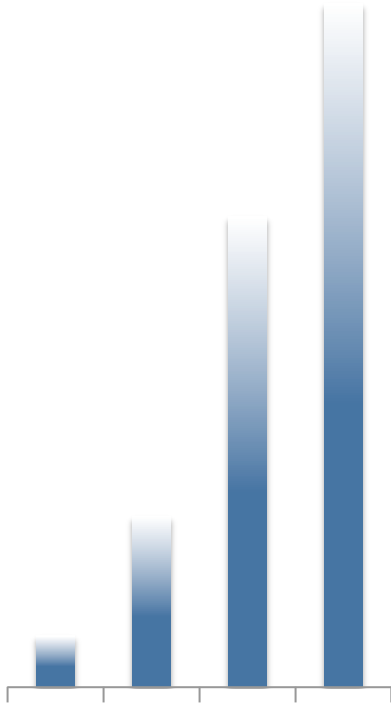
Also common

Lifestyle: Physical exercise

Therapies: Support group

Other treatments: Peginterferon beta-1a

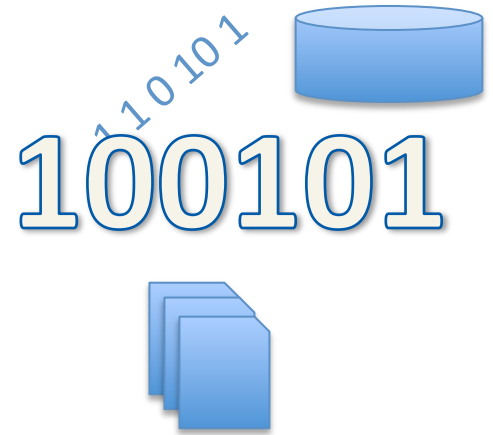
Big Data



Volume



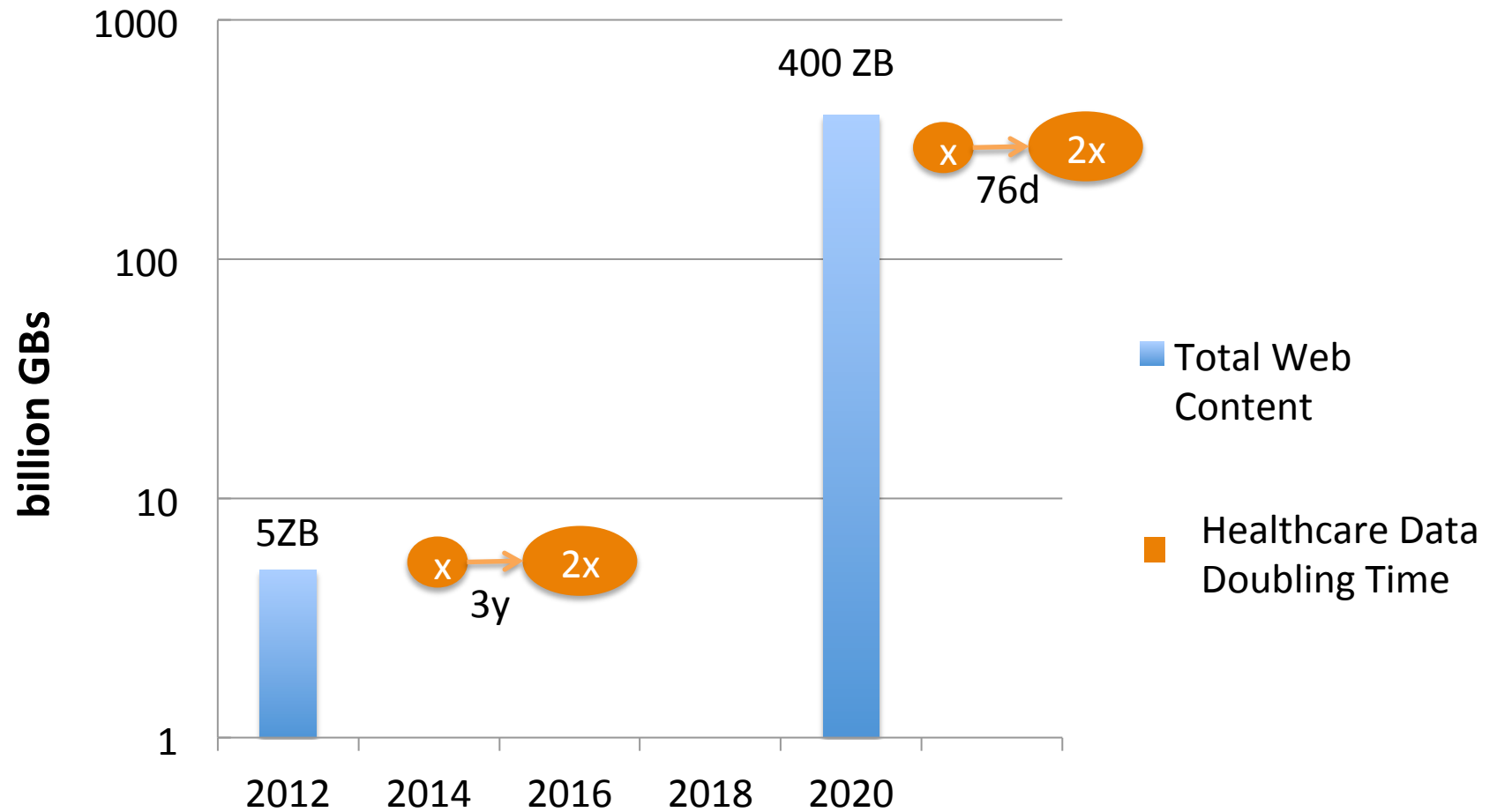
Velocity



Variety

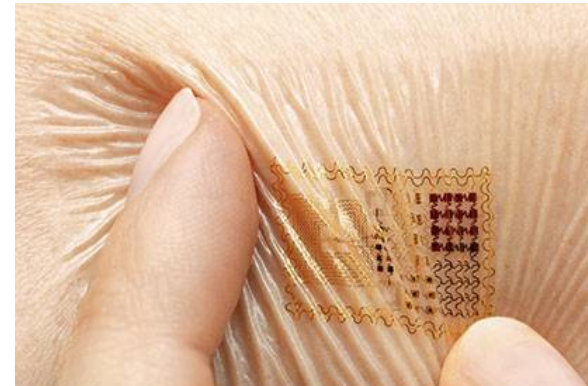
[illegible]

Velocity

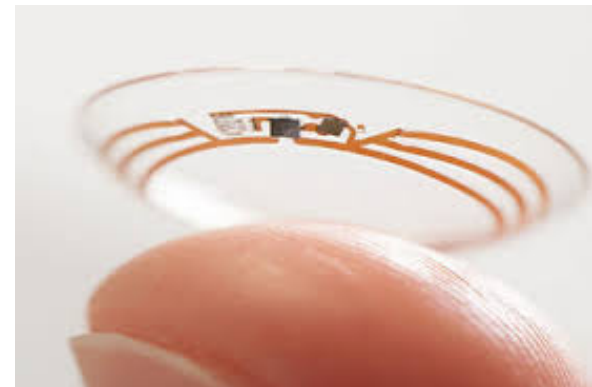


Variety (physiology)

- increasing ability to passively sense biophysiological parameters



MC10 BioStamp sensor



Google Lens

Variety (behavior)

- new field of "emotion analytics"



Affectiva
MIT Media Lab spin off

Variety (built environment)

- the Internet of Things are sensors to our physical environment
 - 25 billion things now
 - 75 billion by 2020



Proactive Health Lab, Intel



Array of Things,
City of Chicago

Variety of Data

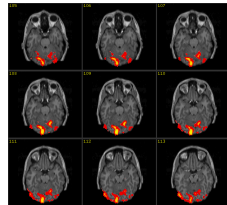
EHR data

clinical trial data

public health data

claims data

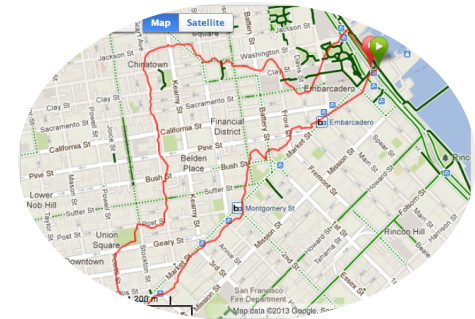
survey data



Internet of Things



Instagram



Traditional

Non-traditional

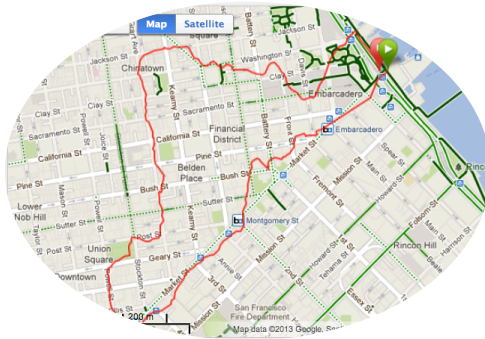
Variety of Data

Hypothetical Relational Database Model

PubID	Publisher	PubAddress
03-4472822	Random House	123 4th Street, New York
04-7733903	Wiley and Sons	45 Lincoln Blvd, Chicago
03-4859223	O'Reilly Press	77 Boston Ave, Cambridge
03-3920886	City Lights Books	99 Market, San Francisco

AuthorID	AuthorName	AuthorBDay
345-28-2938	Haile Selassie	14-Aug-92
392-48-9965	Joe Blow	14-Mar-15
454-22-4012	Sally Hemmings	12-Sept-70
663-59-1254	Hannah Arendt	12-Mar-06

ISBN	AuthorID	PubID	Date	Title
1-34532-482-1	345-28-2938	03-4472822	1990	Cold Fusion for Dummies
1-38482-995-1	392-48-9965	04-7733903	1985	Macrame and Straw Tying
2-35921-499-4	454-22-4012	03-4859223	1952	Fluid Dynamics of Aqueducts
1-38278-293-4	663-59-1254	03-3920886	1967	Beads, Baskets & Revolution



Structured



EHR document

Semi-structured



Unstructured

Faster, larger, *different* studies



The ADAPTABLE trial will compare two common aspirin dosages.



325 mg



81mg

The study will be large and will involve patients across the U.S.

20,000

patients living with heart disease will use a daily aspirin dose of either 81 mg or 325 mg.

The ADAPTABLE Aspirin Study





WIKIPEDIA
The Free Encyclopedia

[Main page](#)

[Contents](#)

[Featured content](#)

[Current events](#)

[Random article](#)

[Donate to Wikipedia](#)

[Wikipedia store](#)

Interaction

[Help](#)

[Create account](#)  [Not logged in](#) [Talk](#) [Contributions](#) [Log in](#)

Article [Talk](#)

Read

[Edit](#)

[View history](#)



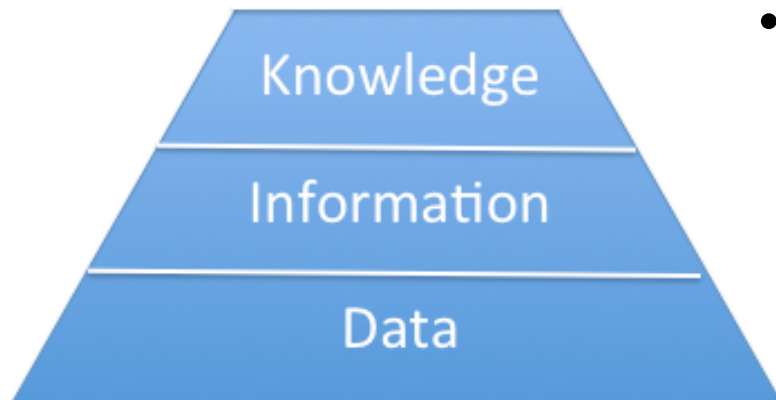
Data driven

From Wikipedia, the free encyclopedia

Data driven means that progress in an activity is compelled by [data](#), rather than by [intuition](#) or [personal experience](#). It is often labeled as the business jargon for what scientists call evidence based decision making. This often refers to:

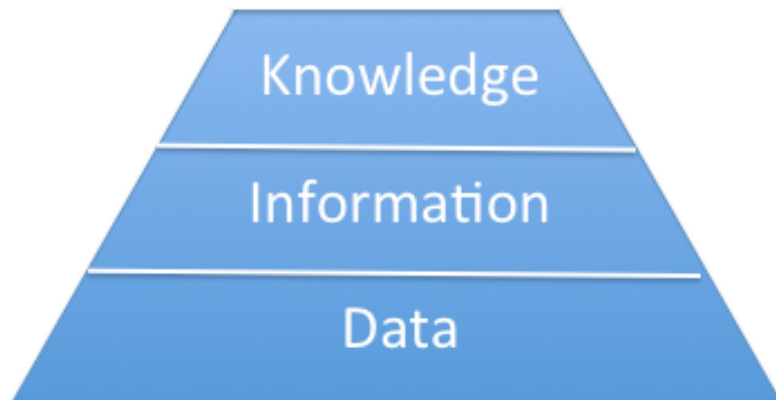
- [Data-driven programming](#)
- [Data-driven journalism](#)
- [Data-driven testing](#)
- [Data driven learning](#)
- [Data-driven science](#)

Data – Information - Knowledge



- Data
 - raw observations, objective facts
- Information
 - data in meaningful context
- Knowledge
 - understanding about the world
 - explicit, codifiable (e.g. Wikipedia, guideline)
 - tacit, not codifiable (e.g. expertise)
 - also process knowledge, i.e., riding a bike
 - useful for explaining, predicting, and guiding future action

D-I-K Example



- Data
 - HgbA1C value 10.1%
- Information
 - occurred last Thursday
 - 10.1% is above normal
- Knowledge
 - high HgbA1C occurs in diabetes
 - associated with higher risk for cardiovascular outcomes
- Evidence?

Evidence : basis for a claim of knowledge

Evidence : data + "study" design + analysis



big, non-traditional data

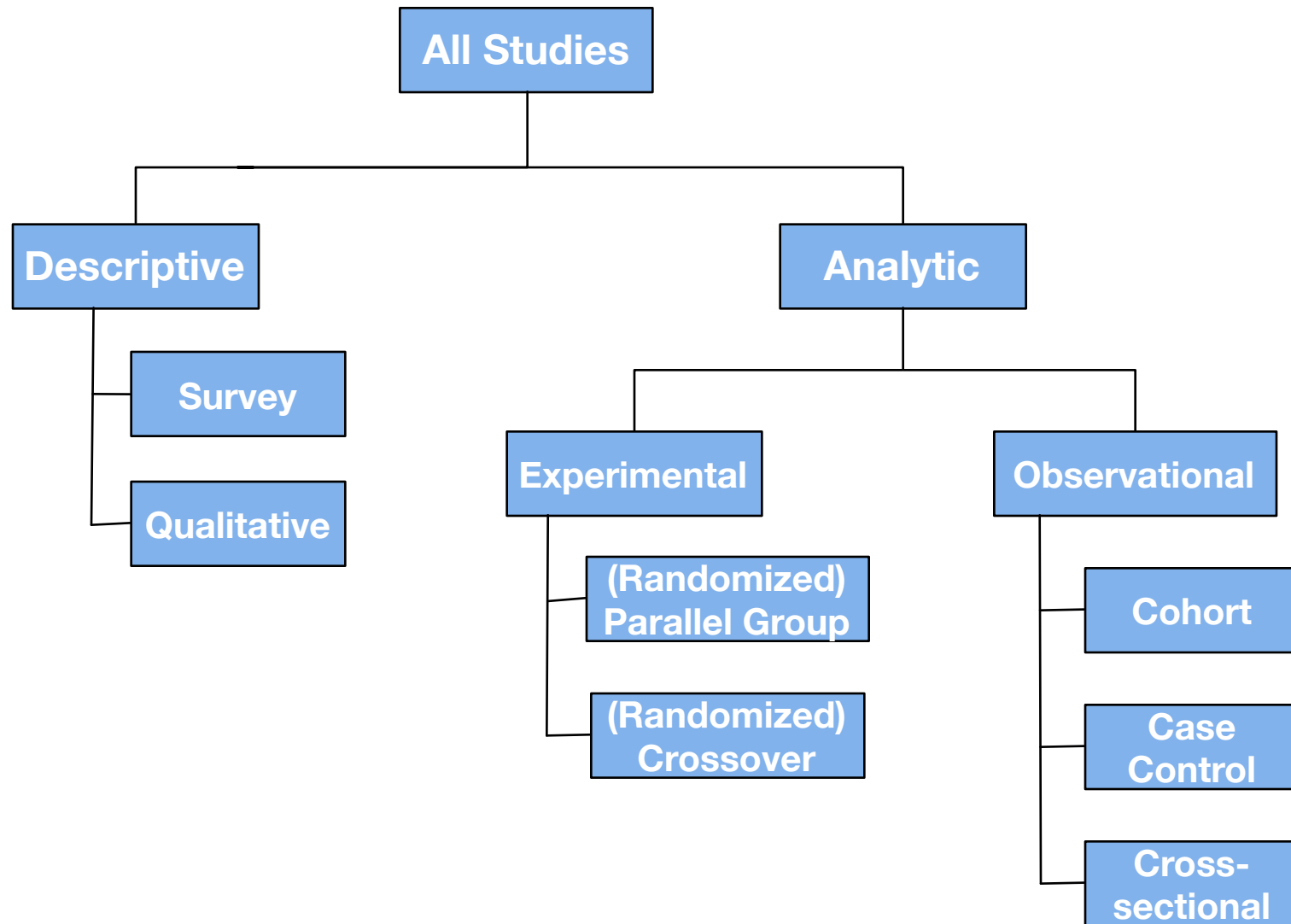


new machine
learning methods

“The future is already here – it's just not evenly distributed.”

William Gibson

The Uneven Future of EBM



Opinions About HPV Vaccination: Traditional Survey

Asian Pac J Cancer Prev. 2012;13(5):2369-78.

A multi-center survey of HPV knowledge and attitudes toward HPV vaccination among women, government officials, and medical personnel in China.

Zhao FH¹, Tiggelaar SM, Hu SY, Zhao N, Hong Y, Niyazi M, Gao XH, Ju LR, Zhang LQ, Feng XX, Duan XZ, Song XL, Wang J, Yang Y, Li CQ, Liu JH, Liu JH, Lu YB, Li L, Zhou Q, Liu JF, Xu LN, Qiao YL.

Table 5. Reasons for and against HPV vaccination

	General Female Population		Healthcare Providers		Government Officials	
	Urban	Rural	Urban	Rural	Urban	Rural
Reasons for willingness to be vaccinated, multiple answers allowed (number, %)						
	N=3,661	N=5,358	N=284	N=338	N=280	N=372
Self-benefit	2,678 (73.1)	4,165 (77.7)	235 (82.7)	273 (80.8)	213 (76.1)	283 (76.1)
Benefit to other youth	542 (14.8)	912 (17.0)	24 (8.5)	67 (19.8)	55 (19.6)	100 (26.9)
Fear of cervical cancer	1,992 (54.4)	3,503 (65.4)	171 (60.2)	228 (67.5)	163 (58.2)	247 (66.4)
Fear of genital warts	483 (13.2)	944 (17.6)	69 (24.3)	111 (32.8)	48 (17.1)	93 (25.0)
Fear of HPV infection	1,383 (37.8)	1,590 (29.7)	142 (50.0)	173 (51.2)	120 (42.9)	163 (43.8)
Fear of having been infected with HPV	272 (7.4)	290 (5.4)	31 (10.9)	59 (17.5)	33 (11.8)	35 (9.4)
Reasons against willingness to be vaccinated, multiple answers allowed (number, %)						
	N=1,100	N=1,561	N=70	N=68	N=72	N=39
Belief in low self-risk	302 (27.5)	598 (38.3)	23 (32.9)	14 (20.6)	17 (23.6)	14 (35.9)
Limited usage to date	434 (39.5)	353 (22.6)	31 (44.3)	32 (47.1)	21 (29.2)	14 (35.9)
Belief that vaccination is risky	563 (51.2)	489 (31.3)	49 (70.0)	42 (61.8)	52 (72.2)	26 (66.7)
Doubt of vaccine efficacy	365 (33.2)	326 (20.9)	39 (55.7)	37 (54.4)	32 (44.4)	17 (43.6)
Doubt of source of vaccine	164 (14.9)	160 (10.2)	12 (17.1)	10 (14.7)	14 (19.4)	3 (7.7)
Expense of vaccine	226 (20.5)	579 (37.1)	9 (12.9)	14 (20.6)	9 (12.5)	8 (20.5)
Other	87 (7.9)	144 (9.2)	2 (2.9)	2 (2.9)	0 (0.0)	0 (0.0)

Opinions About HPV Vaccination: Using "Non-traditional" Data

PLoS One. 2015 Jun 8;10(6):e0129587. doi: 10.1371/journal.pone.0129587. eCollection 2015.

Understanding Public Perceptions of the HPV Vaccination Based on Online Comments to Canadian News Articles.

Feinberg Y¹, Pereira JA¹, Quach S¹, Kwong JC², Crowcroft NS³, Wilson SE⁴, Guay M⁵, Lei Y¹, Deeks SL⁴; Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Program Delivery and Evaluation Group.

- Non-traditional, unstructured data
 - keyword search of all Canadian newspapers → 71 articles
 - 3073 comments from 1198 individuals
- Manual qualitative analysis
 - thematic analysis
 - sentiment analysis (positive, negative, neutral)

Opinions About HPV Vaccination: Using "Non-traditional" Data

PLoS One. 2015 Jun 8;10(6):e0129587. doi: 10.1371/journal.pone.0129587. eCollection 2015.

Understanding Public Perceptions of the HPV Vaccination Based on Online Comments to Canadian News Articles.

Feinberg Y¹, Pereira JA¹, Quach S¹, Kwong JC², Crowcroft NS³, Wilson SE⁴, Guay M⁵, Lei Y¹, Deeks SL⁴; Public Health Agency of Canada/Canadian Institutes of Health Research Influenza Research Network (PCIRN) Program Delivery and Evaluation Group.

Table 2. Sentiment of articles and sentiment of majority of comments.

		Sentiment of Articles		
		Positive	Negative	Neutral
Sentiment of majority of comments	Positive	32	2	6
	Negative	15	7	3
	Equal	5	0	1
	Total	52	9	10

Opinions About HPV Vaccination: "Non-traditional" Data and Machine Analytics

Adv Exp Med Biol. 2011;696:181-90. doi: 10.1007/978-1-4419-7046-6_18.

Predicting individual affect of health interventions to reduce HPV prevalence.

Corley CD¹, Mihalcea R, Mikler AR, Sanfilippo AP.

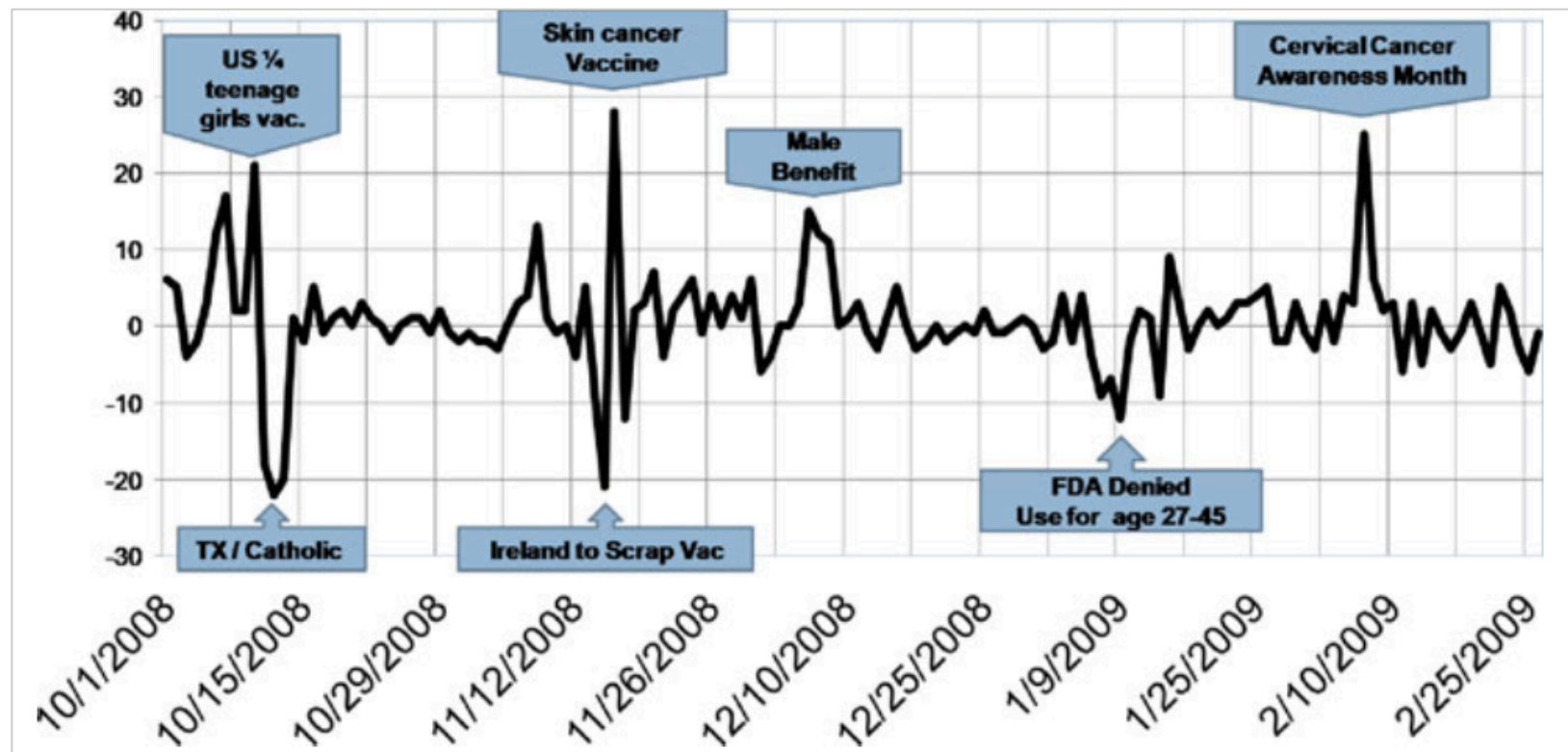
- Non-traditional data
 - scanned 130 million English language blogs and media items
 - identified 9,656 HPV-related posts over 7 months in 2008-9
- Machine learning
 - manually labeled set: 157 blog posts as positive or negative sentiment
 - training set: 1000 posts
 - supervised learning: support vector machine (SVM) method
 - overall accuracy of 70%
- SVM classifier run on remaining 8500+ posts

Opinions About HPV Vaccination: "Non-traditional" Data and Machine Analytics

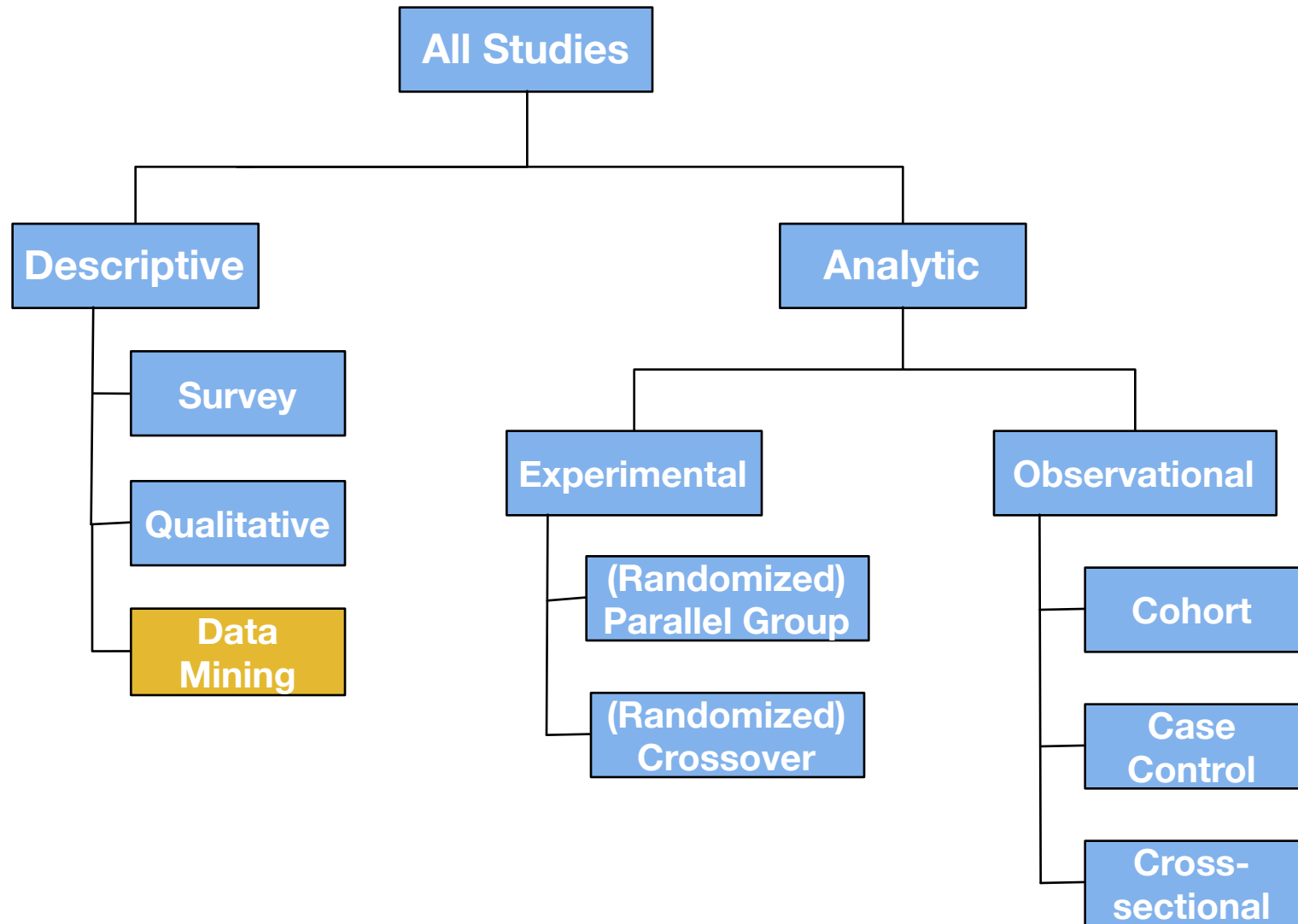
Adv Exp Med Biol. 2011;696:181-90. doi: 10.1007/978-1-4419-7046-6_18.

Predicting individual affect of health interventions to reduce HPV prevalence.

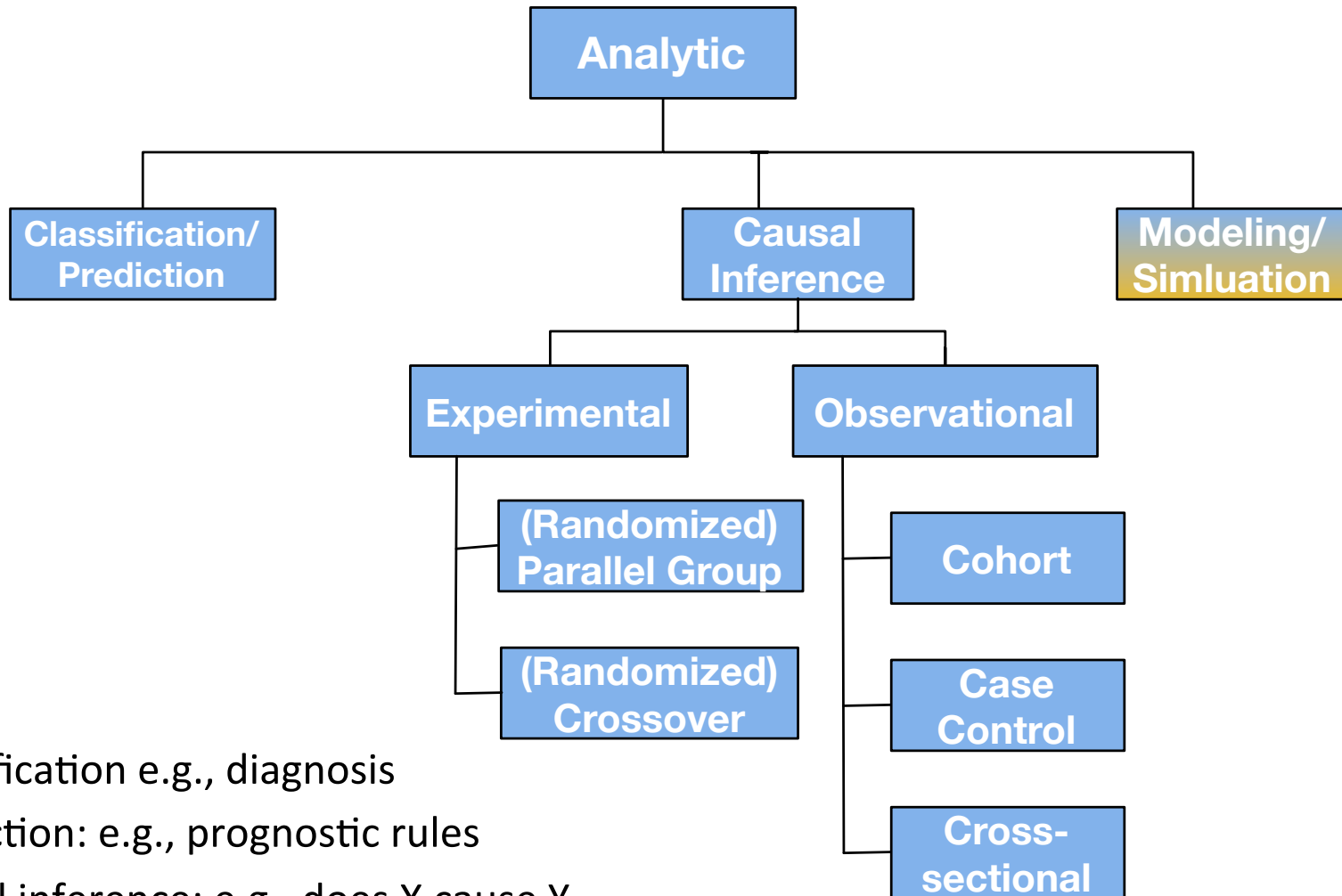
Corley CD¹, Mihalcea R, Mikler AR, Sanfilippo AP.



Descriptive Study Designs: Add Data Mining



Analytic Intent



- Classification e.g., diagnosis
- Prediction: e.g., prognostic rules
- Causal inference: e.g., does X cause Y
- Explanation, modeling, simulation – biomedical, implementation

Examples of Analytic Studies

Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured		
Causal Inference	Semi-structured		
	Unstructured		

N Engl J Med. 2011 Nov 10;365(19):1758-9. doi: 10.1056/NEJMp1108726. Epub 2011 Nov 2.

Evidence-based medicine in the EMR era.

Frankovich J¹, Longhurst CA, Sutherland SM.

Results of Electronic Search of Patient Medical Records (for a Cohort of 98 Pediatric Patients with Lupus) Focused on Risk Factors for Thrombosis Relevant to Our 13-Year-Old Patient with Systemic Lupus Erythematosus.*

Outcome or Risk Factor	Keywords Used to Conduct Expedited Electronic Search	Prevalence of Thrombosis	Relative Risk (95% CI)
Outcome — thrombosis	"Thrombus," "Thrombosis," "Blood clot"		
Thrombosis risk factor			
Heavy proteinuria (>2.5 g per deciliter)			
Present at any time	"Nephrosis," "Nephrotic," "Proteinuria"		
Present >60 days	"Urine protein"		
Pancreatitis	"Pancreatitis," "Lipase"		
Antiphospholipid antibodies	"Aspirin"		

N Engl J Med. 2011 Nov 10;365(19):1758-9. doi: 10.1056/NEJMp1108726. Epub 2011 Nov 2.

Evidence-based medicine in the EMR era.

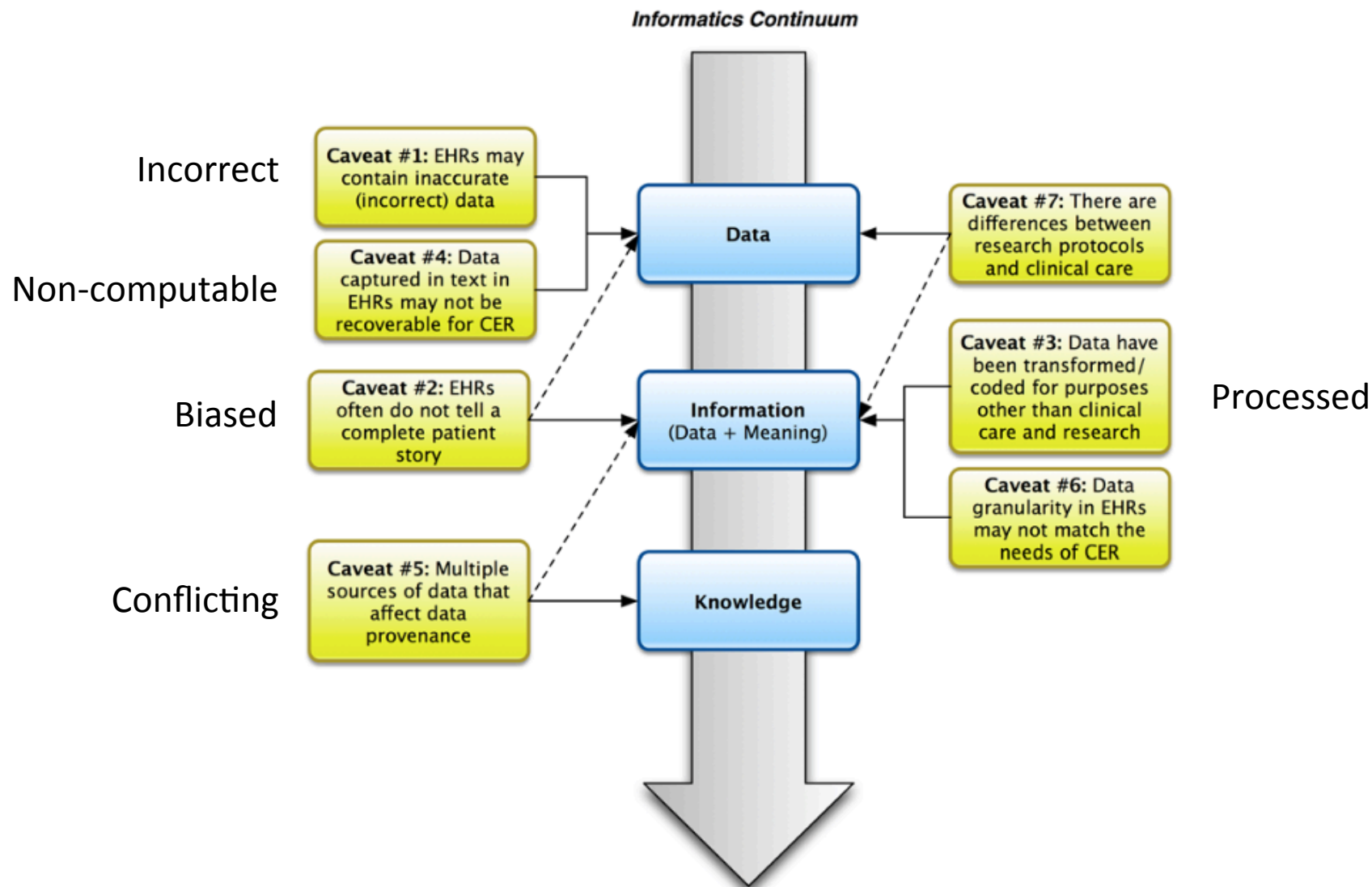
Frankovich J¹, Longhurst CA, Sutherland SM.

Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured	"Grab and go"	Classical or Bayesian Statistics
Causal Inference	Semi-structured		
	Unstructured		

- data challenges
 - quality of EHR data
 - quality of data processing (e.g., NLP)

Caveats for the use of operational electronic health record data in comparative effectiveness research.

Hersh WR¹, Weiner MG, Embi PJ, Logan JR, Payne PR, Bernstam EV, Lehmann HP, Hripcsak G, Hartzog TH, Cimino JJ, Saltz JH.



N Engl J Med. 2011 Nov 10;365(19):1758-9. doi: 10.1056/NEJMp1108726. Epub 2011 Nov 2.

Evidence-based medicine in the EMR era.

Frankovich J¹, Longhurst CA, Sutherland SM.

Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured	"Grab and go"	Classical or Bayesian Statistics
Causal Inference	Semi-structured		
	Unstructured		

- data challenges
 - quality of EHR data
 - quality of data processing (e.g., NLP)
- analysis challenges
 - providing epi/biostats expertise via a [patients like mine](#) button
 - how to combine near real-time EHR data with published evidence



Predicting Depression via Social Media. De Choudhury, M et al. Proceedings of the Seventh International AAAI Conference on Weblogs and Social Media, p 128-137.

Total number of users	476
Total number of Twitter posts	2,157,992
Mean number of posts per user over the entire 1 year period	4,533.4
Variance of number of posts per user over the entire 1 year period	3,836
Mean number of posts per day per user	6.67
Variance of number of posts per day per user	12.42

Table 1: Statistics of Twitter data of study cohort.

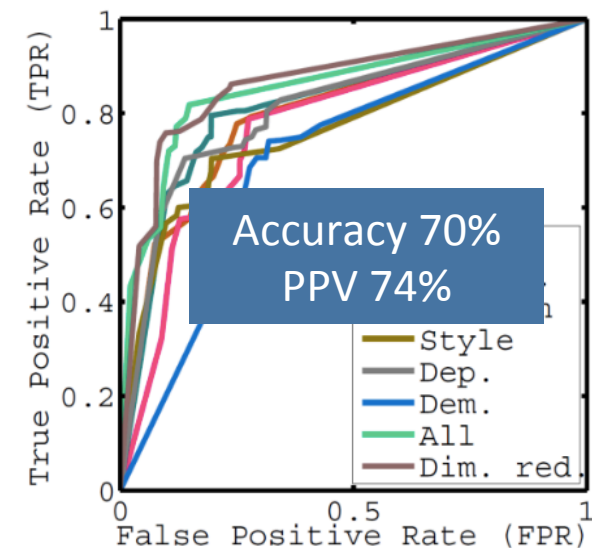


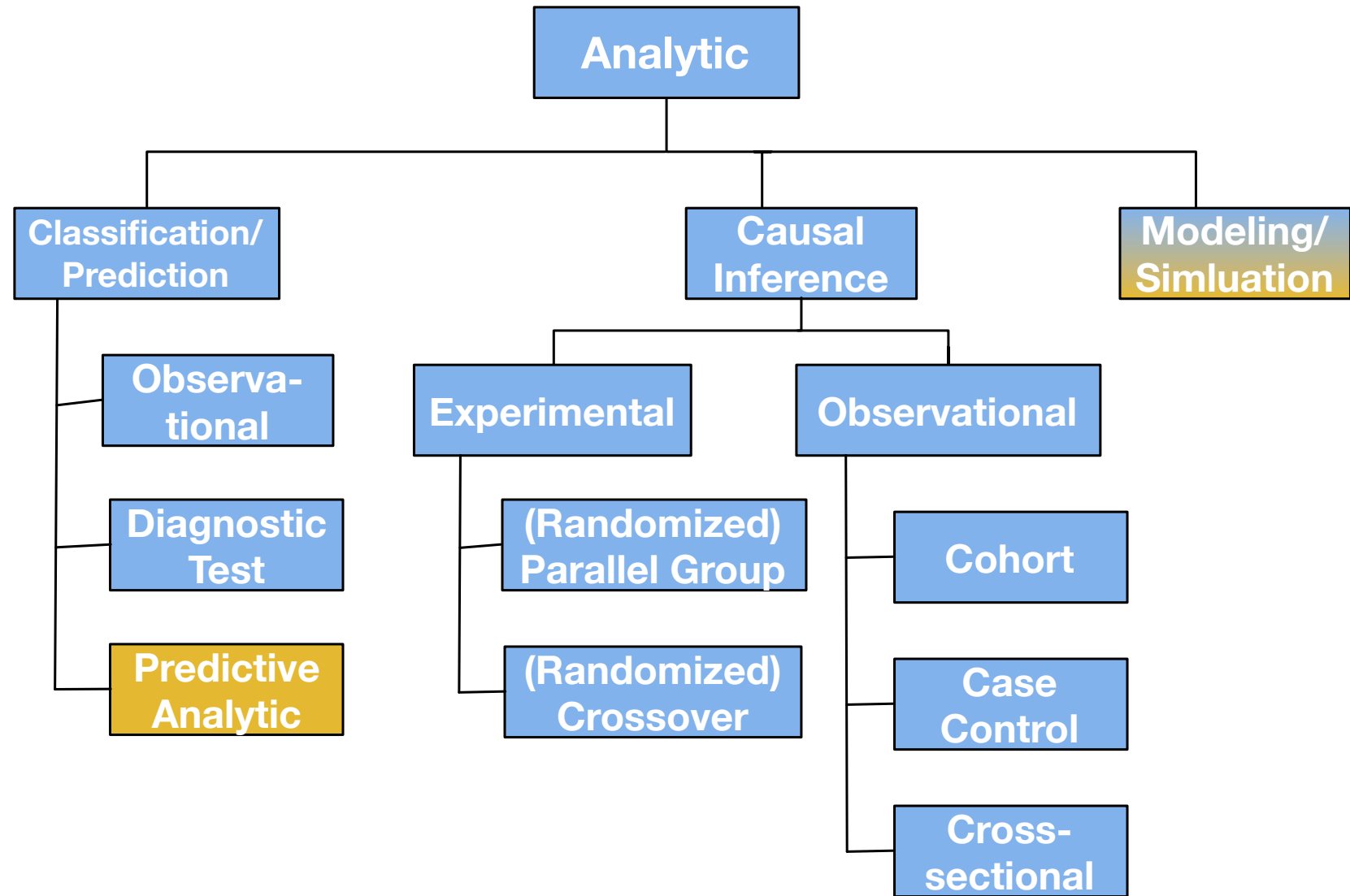
Figure 4. Receiver Operating Characteristic (ROC) curves in predicting labels of users. Each curve corresponds to a model trained on a particular feature type.



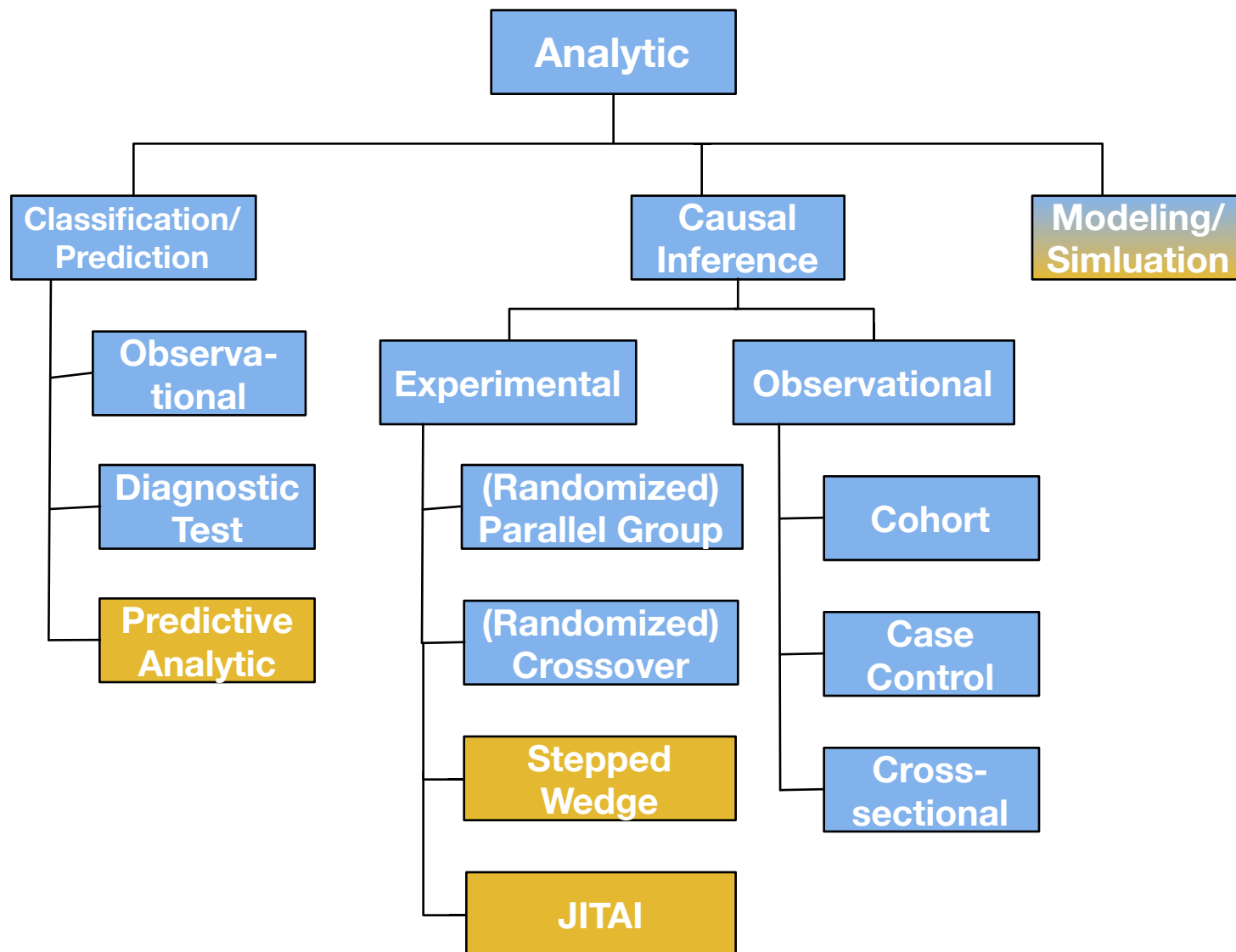
Predicting Depression via Social Media. De Choudhury, M et al. Proceedings of the Seventh International AAAI Conference on Weblogs and Social Media, p 128-137.

Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured	"Grab and go"	Classical or Bayesian Statistics
Causal Inference	Semi-structured		NLP, SVM, automated sentiment and affect analysis...
	Unstructured		

Classification/Prediction Study Designs



Technology-Enabled Experimental Studies

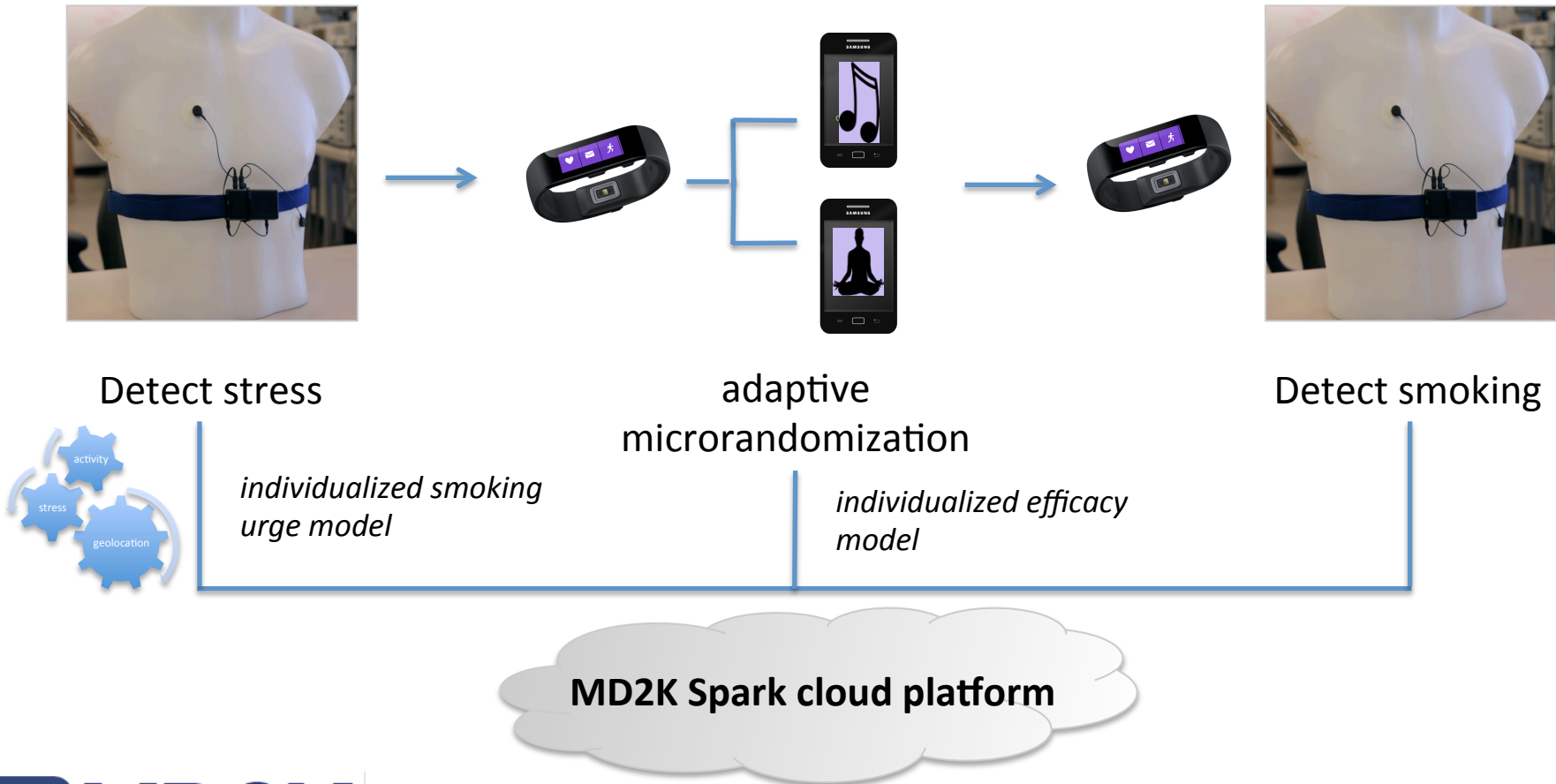


Staying Quit – A JITAI Study

Just-in-time Adaptive Intervention

- P: smokers who have just quit
- I: just-in-time stress reduction
- C: usual care
- O: time to first lapse, rate of relapse

Staying Quit – A JITAI Study



Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured	"Grab and go"	Classical or Bayesian Statistics
Causal Inference	Semi-structured	JITAI with micro- randomization	Machine learning
	Unstructured		

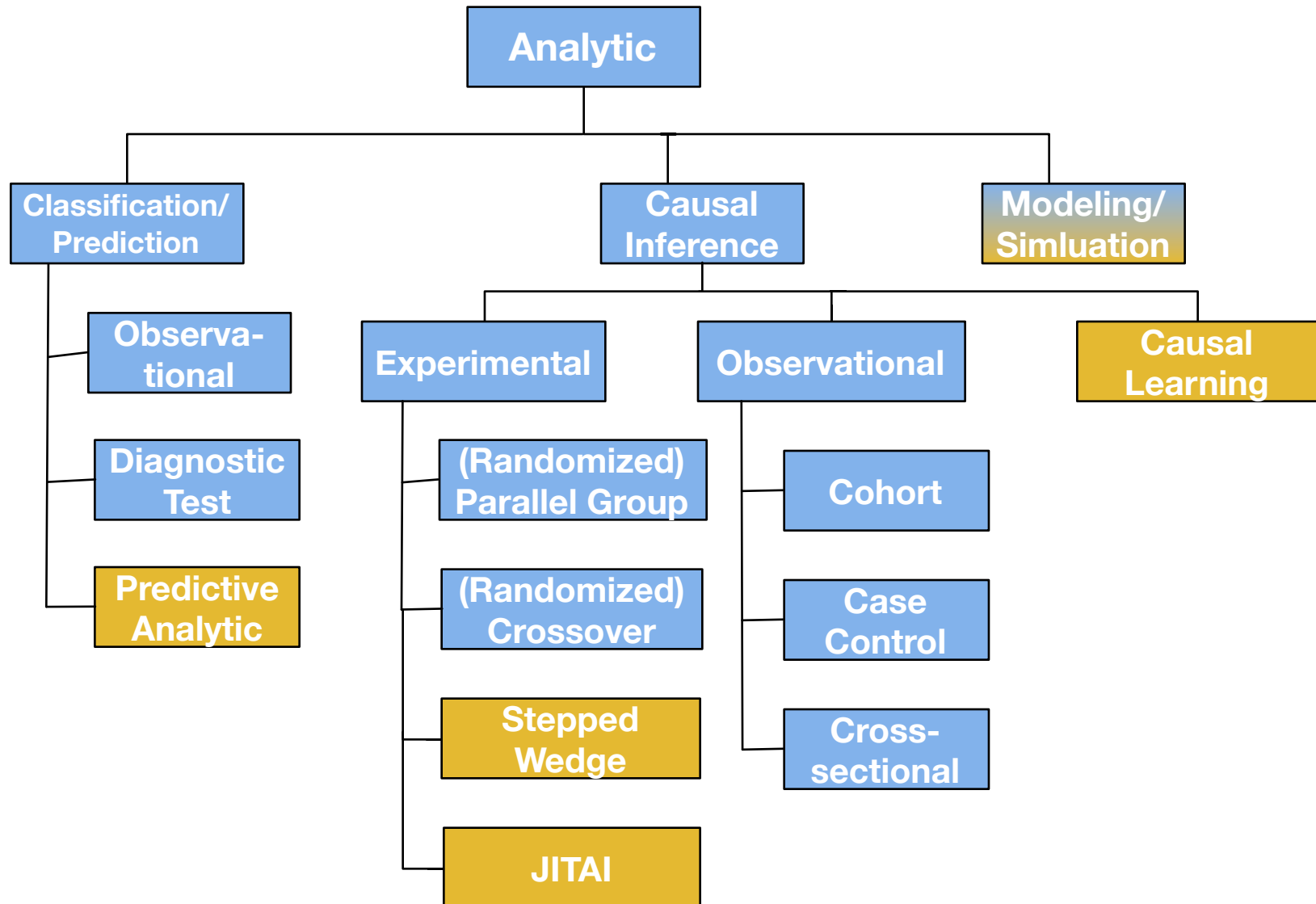
- Team includes engineers, behavioral psychologists, biostatisticians, data scientists, computer scientists
- MD2K platform to be freely downloadable, for running other JITAI studies
- Enabling rigorous testing of sensor-driven complex behavioral interventions



Advancing biomedical discovery and improving health through mobile sensor big data

*Cornell Tech ♦ Georgia Tech ♦ U. Memphis ♦ Northwestern ♦ Ohio State ♦ Open mHealth ♦
Rice ♦ UCLA ♦ UC San Diego ♦ UC San Francisco ♦ UMass Amherst ♦ U. Michigan*

Machine Learning for Causality



Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population.

Shah NH¹, LePendur P¹, Bauer-Mehren A¹, Ghebremariam YT², Iyer SV¹, Marcus J³, Nead KT⁴, Cooke JP², Leeper NJ⁴.

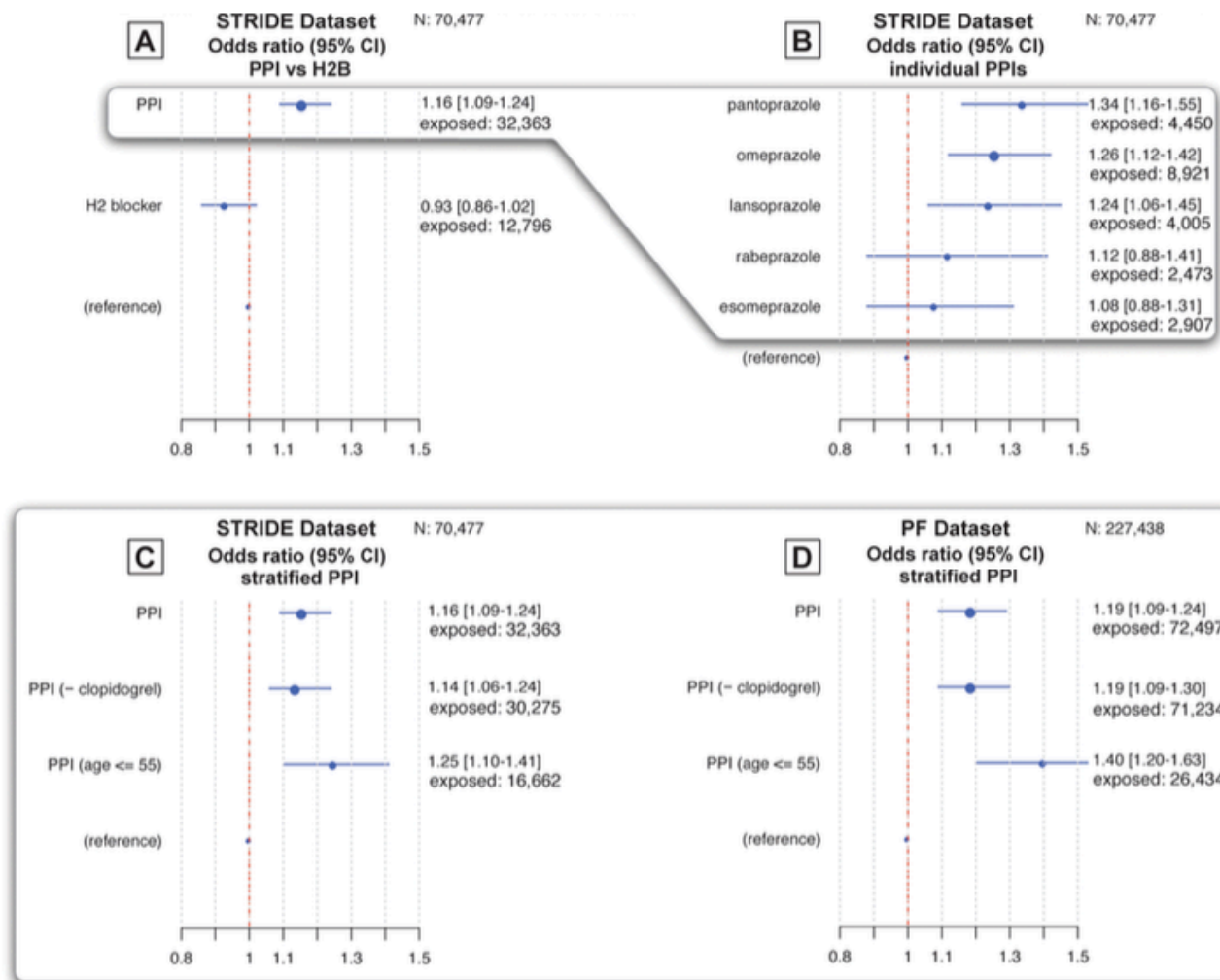


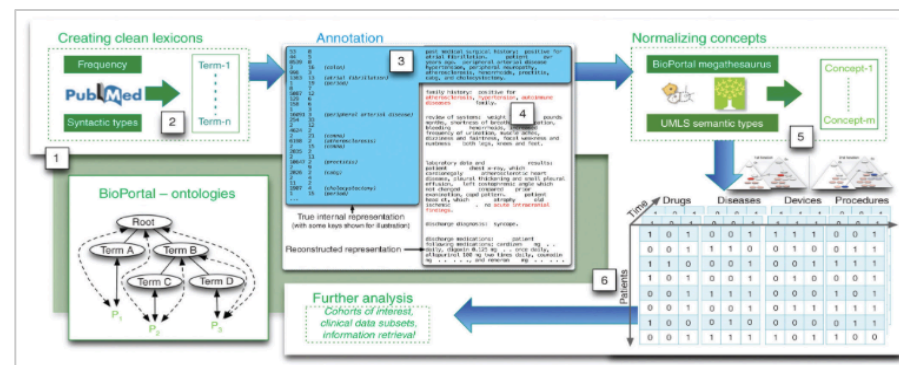
Fig 1. PPI use is associated with an increased risk for MI, regardless of age or clopidogrel use. No association is identified

Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population.

Shah NH¹, LePendur P¹, Bauer-Mehren A¹, Ghebremariam YT², Iyer SV¹, Marcus J³, Nead KT⁴, Cooke JP², Leeper NJ⁴.

EHR	Patients	Encounters	ICD-9 Diagnoses	Prescriptions	Unstructured Notes
Stanford	1.8 m	19 m	35 m		11 m
Practice Fusion	1.1 m		5.5 m	6.8 m	5.5 m

- MI case finding (n=1503): GenePAD study and independently verified
- Pharmacovigilance data mining pipeline:



Clin Pharmacol Ther. 2013 Jun;93(6):547-55. doi: 10.1038/clpt.2013.47.

- previously validated with 97.5% sensitivity and 39% specificity

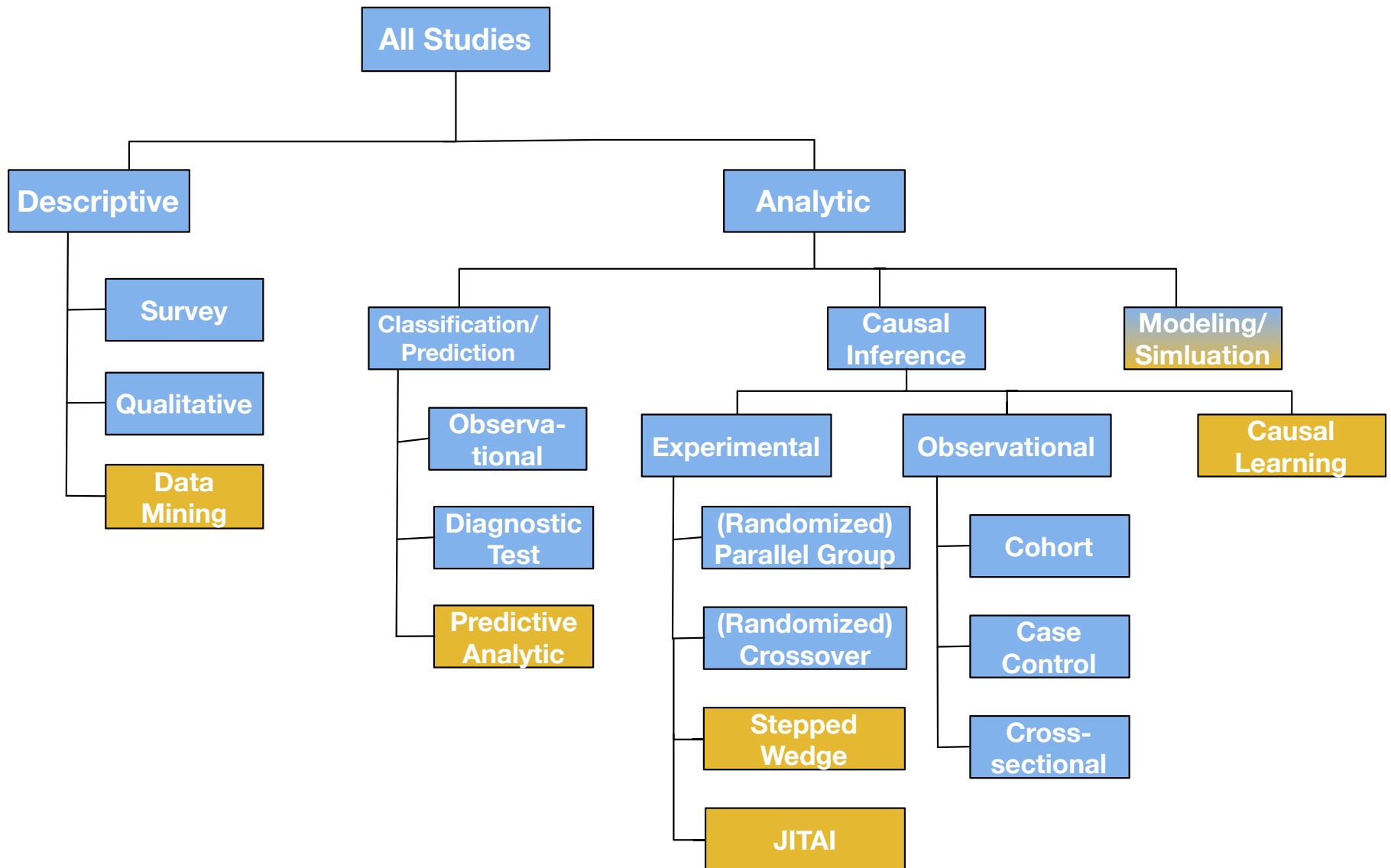
Proton Pump Inhibitor Usage and the Risk of Myocardial Infarction in the General Population.

Shah NH¹, LePendur P¹, Bauer-Mehren A¹, Ghebremariam YT², Iyer SV¹, Marcus J³, Nead KT⁴, Cooke JP², Leeper NJ⁴.

Analytic Intent	Data Source	"Study" Design	Analytic Method
Classification/ Prediction	Structured	"Grab and go"	Classical or Bayesian Statistics
Causal Inference	Semi-structured	Pharmacovigilance workflow	Pharmacovigilance pipeline
	Unstructured		

- Can anticipate more studies from reusable analytic platforms (e.g., MD2K JITAI) and pipelines (e.g., Stanford pharmacovigilance)
 - each with their own risks of bias

Putting it All Together: Blue and Orange Boxes





Deep Learning Cognitive Systems



THE DINOSAURS	NOTABLE WOMEN	OXFORD ENGLISH DICTIONARY	NAME THAT INSTRUMENT	BELGIUM	COMPOSERS BY COUNTRY
\$200	\$200	\$200	\$200	\$200	\$200
\$400	\$400	\$400	\$400	\$400	\$400
\$600	\$600	\$600	\$600	\$600	\$600
\$800	\$800	\$800	\$800	\$800	\$800
\$1000	\$1000	\$1000	\$1000	\$1000	\$1000

Jeopardy! TV Game Show

<http://www.ibm.com/analytics/watson-analytics/>



"Dr. Watson"

- Supervised and unsupervised learning
 - ingested textbooks, PubMed, took board exam questions, solved NEJM cases
 - with Memorial Sloan Kettering: analyzed 605,000 pieces of medical evidence, 2 m pages of text from 42 medical journals, assisted by 14,700 clinician hours
- Offering individualized oncology treatment advice
 - based on EHR data and "a synthesis of updated guidelines and published research" (including Cochrane reviews)
 - provides users with evidence trail
- Now partnering with Epic

EBM in a Box?

- "Watson and Epic software could ... **intelligently assist doctors and nurses by providing relevant evidence from the worldwide body of medical knowledge**. Providers will be able to share patient-specific data with Watson in real time, within workflows, allowing Watson to bring forth critical evidence from medical literature and case studies that are most relevant to the patient's care"

<http://www-03.ibm.com/press/us/en/pressrelease/46768.wss>

Two Cultures

Evidence-based Medicine

1. Emphasis of empirical evidence over expert judgment, and research over authority
2. Evidence must be appraised and synthesized with methodological rigor

Data Science

1. Emphasis of empirical observation via data
2. "More data is better than better data"
3. Trust in algorithms

Two Epistemological Approaches

Evidence-based Medicine

- Frequentist, hypothesis-testing
- Internal validity is paramount: "best" evidence should be the main basis for decisions
- Decisions often narrowly framed: does this drug work?

Data Science

- Data-driven rather than hypothesis-testing
- External validity is more highly valued ("patients like mine")
- Decisions are personal, iterative, and contingent, involving tradeoffs and uncertainty (Bayesian, decision-theoretic)

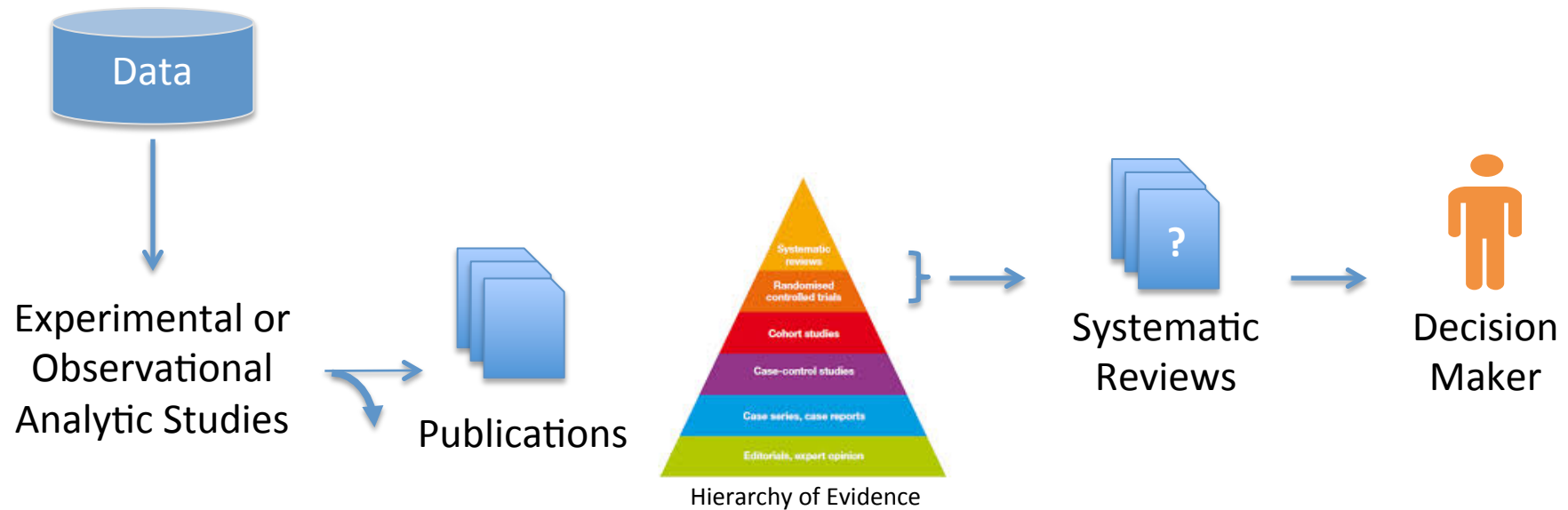
Potential Paths into Uneven Future

1. Focus on improving today's EBM
2. Incorporate studies that use big and non-traditional data and machine analytics
3. Pursue a synergy of EBM and data science



"We gather and summarize the best evidence from research to help you make informed choices about treatment"

EBM Pipeline



A Synergy?

Data and Information

Description
Classification/Prediction
Causal Inference
Modeling/Simulation

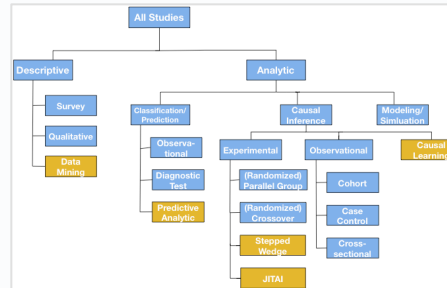


Decision
Maker(s)

*personalized, just-in-time,
predictive decision support*

Evidence from Many Study Types

Data and Information



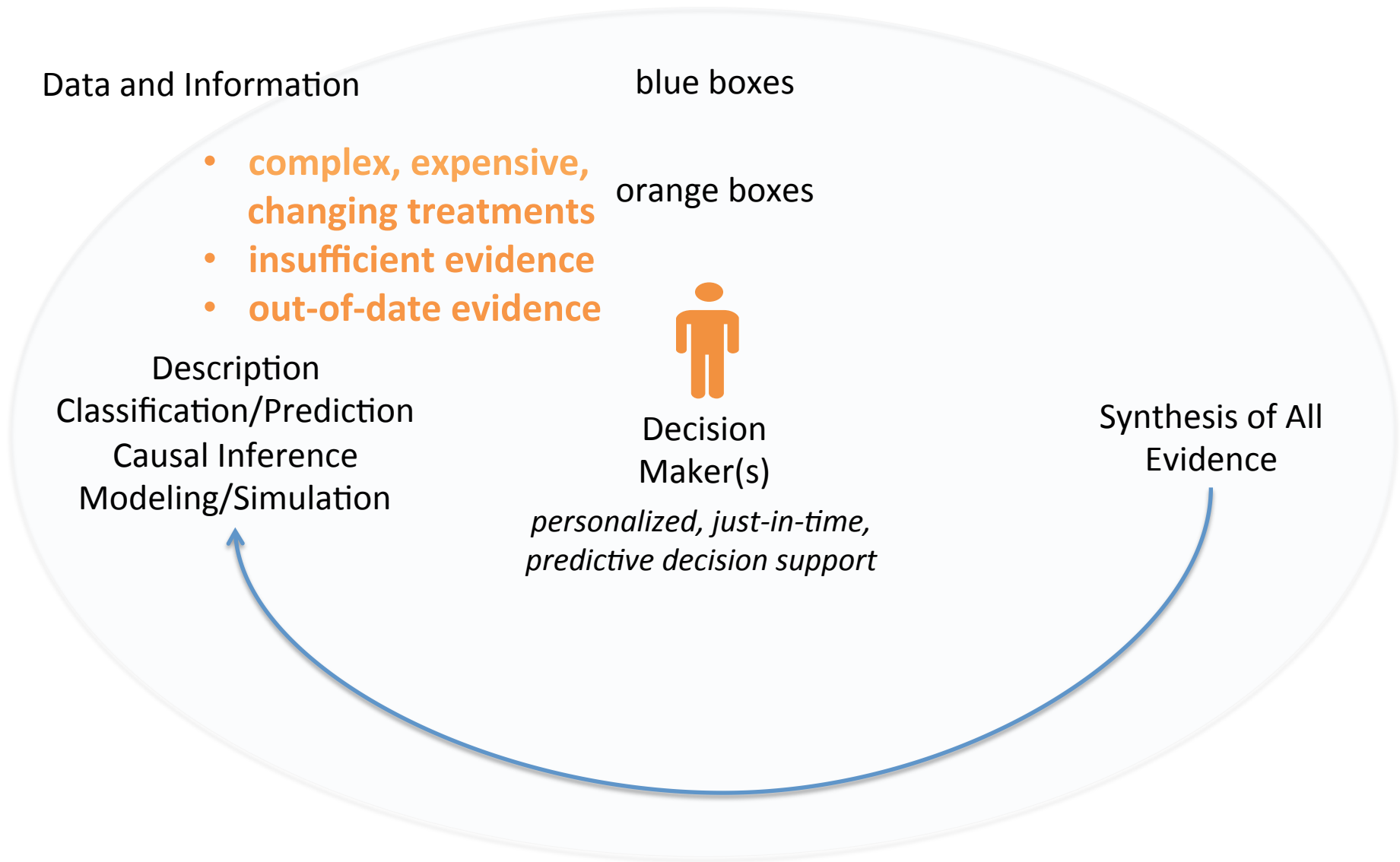
Decision
Maker(s)

*personalized, just-in-time,
predictive decision support*

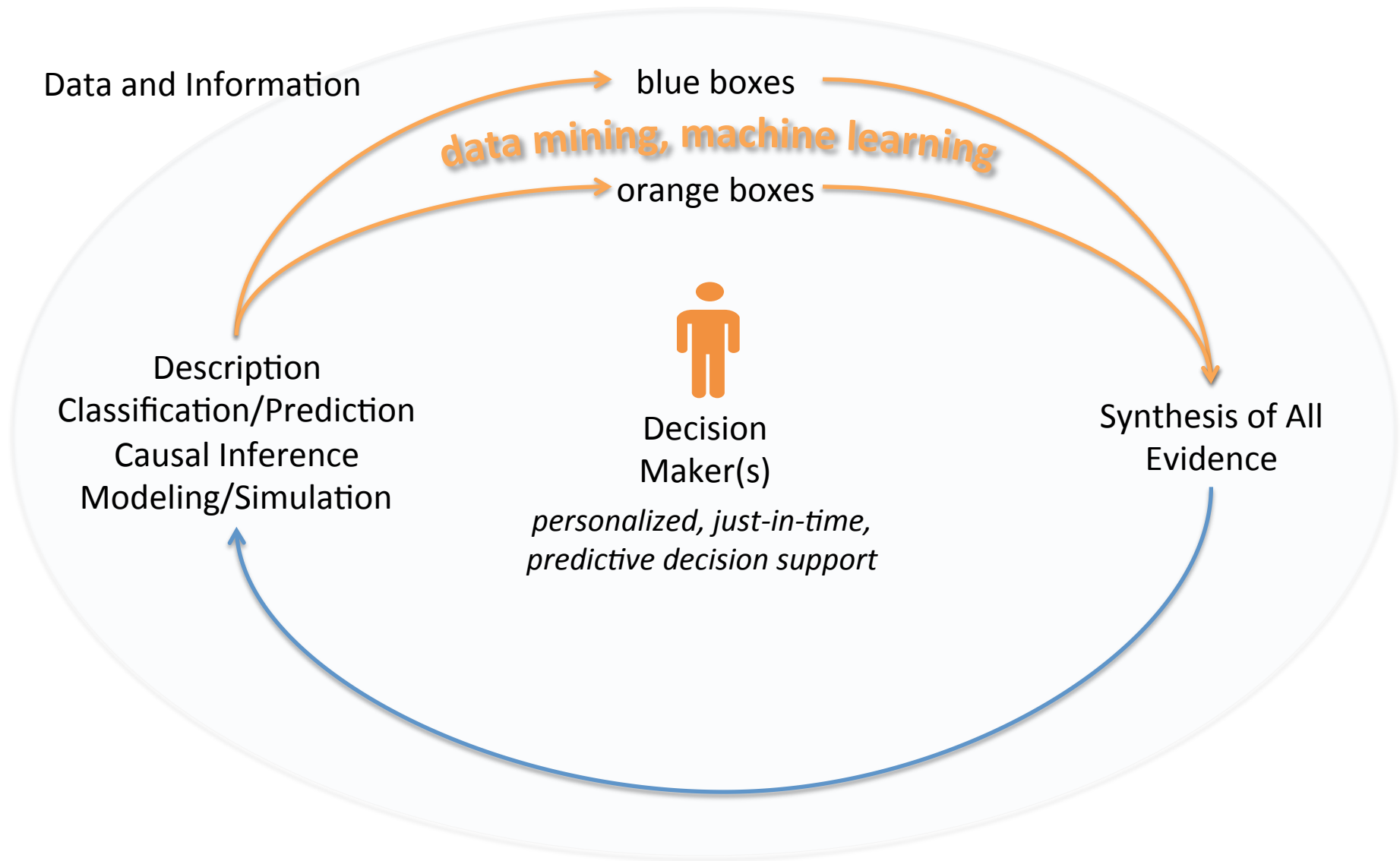
Description
Classification/Prediction
Causal Inference
Modeling/Simulation

Synthesis of All
Evidence

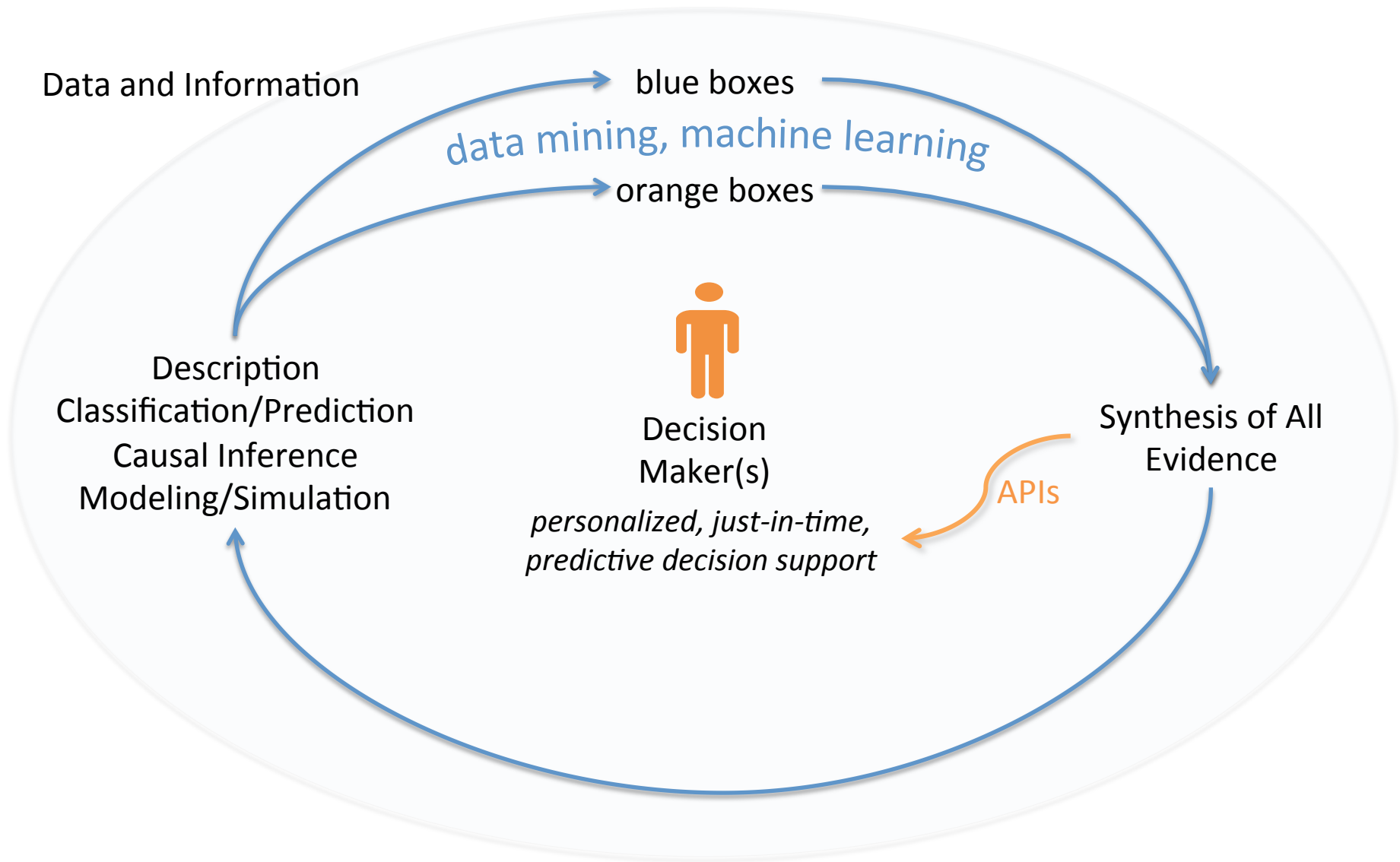
Need New Evidence?



Data-Driven Research Design

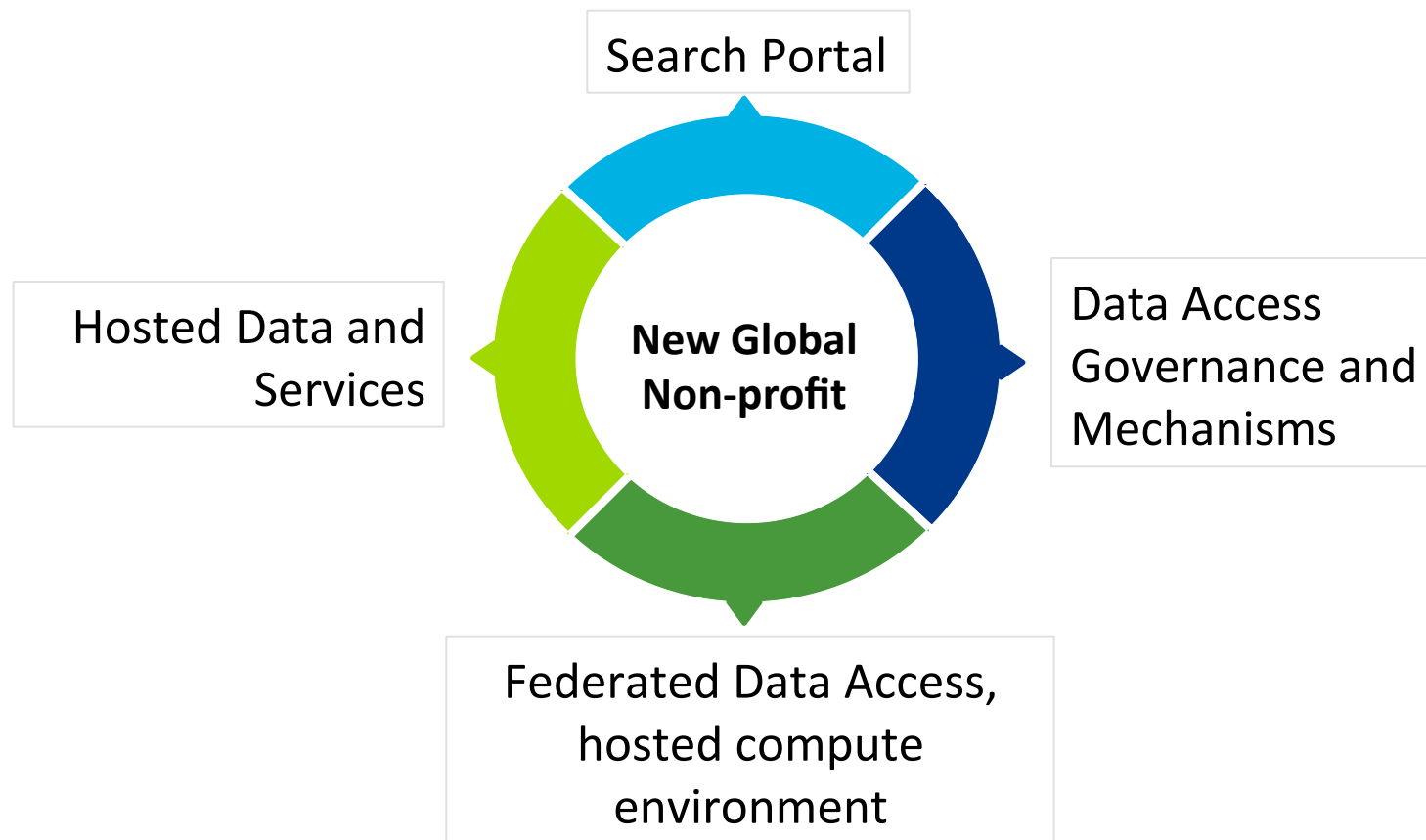


Evidence as a Service

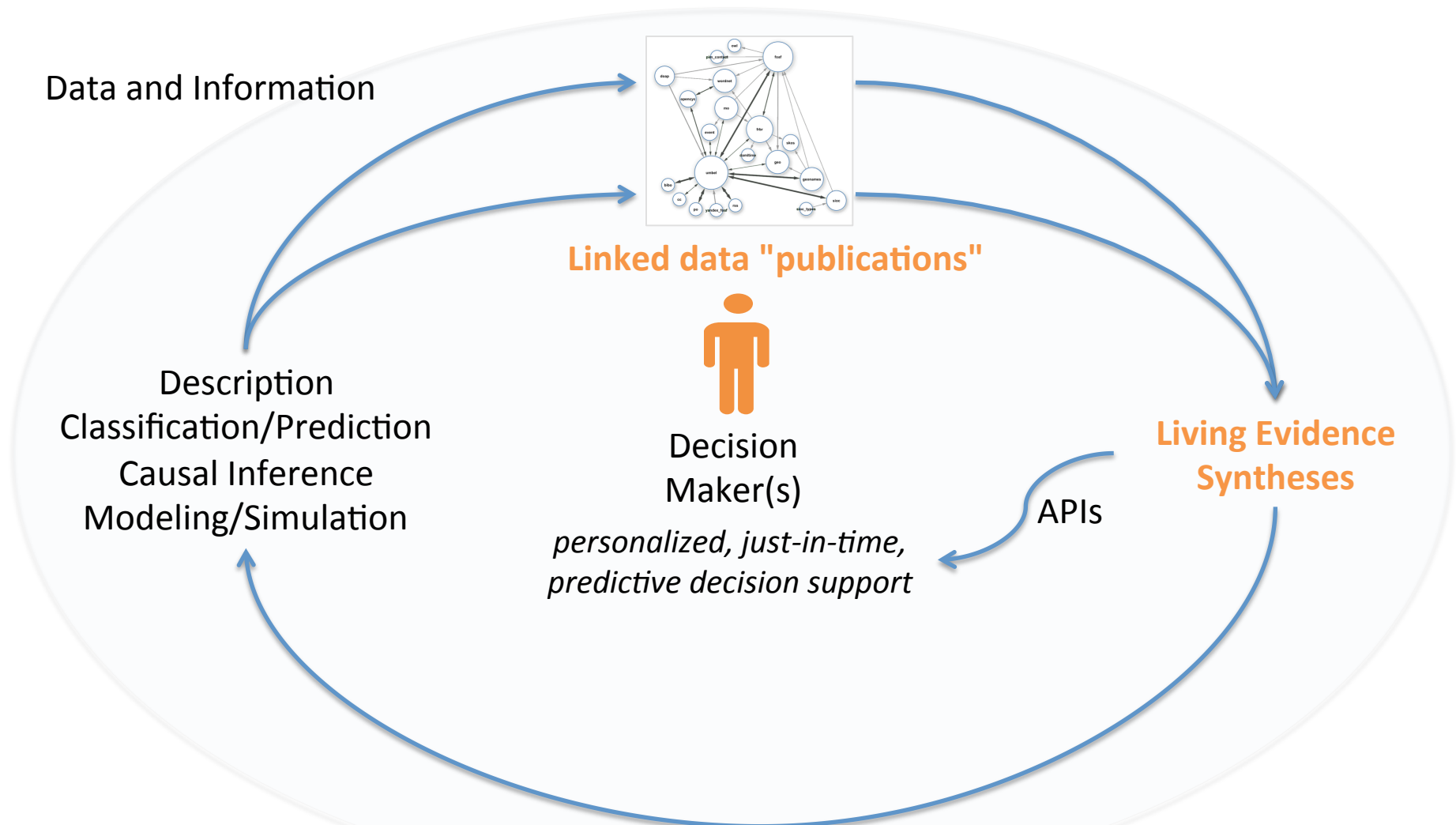


Global Platform for Sharing IPD

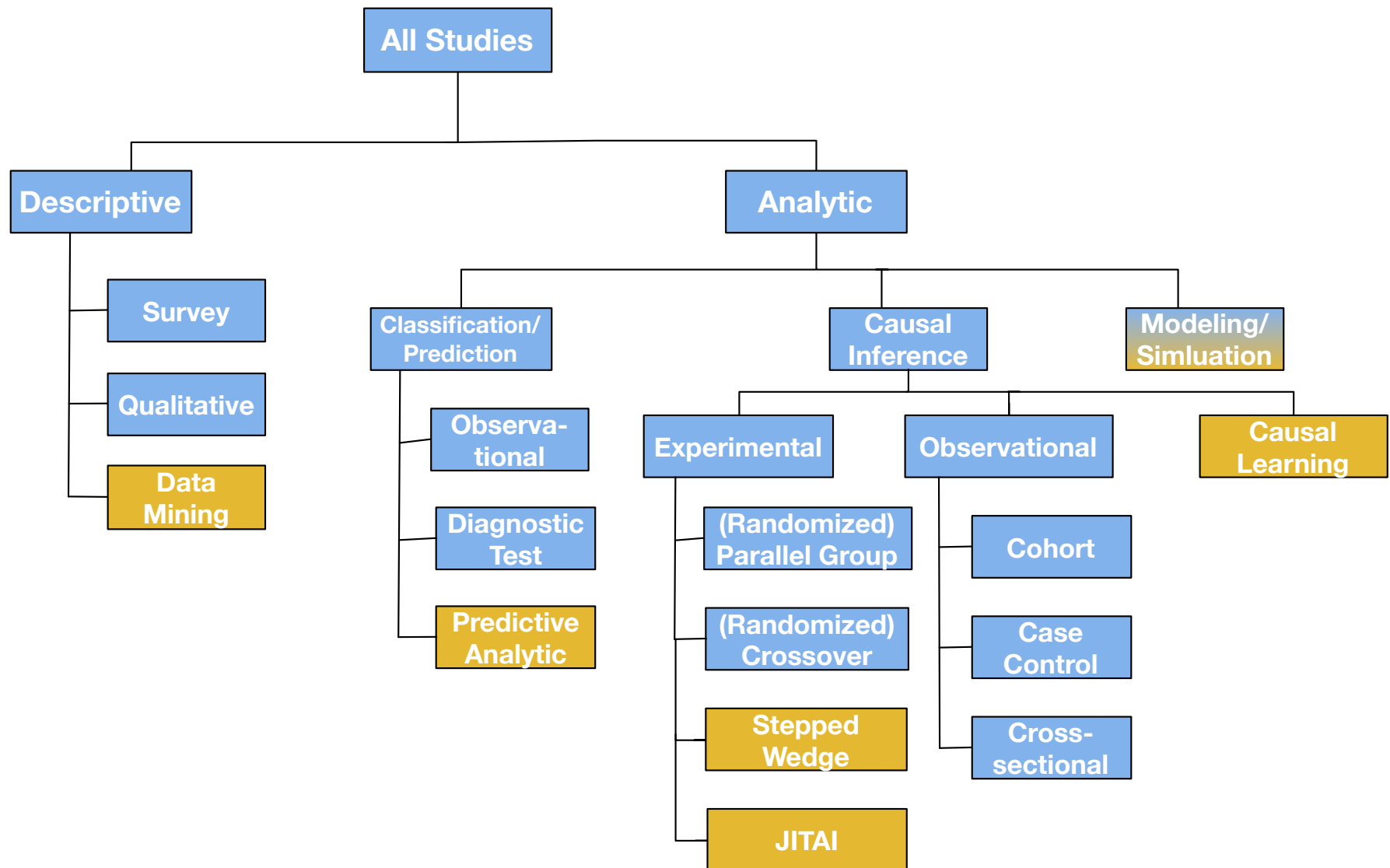
MRCT Framework for Data Sharing



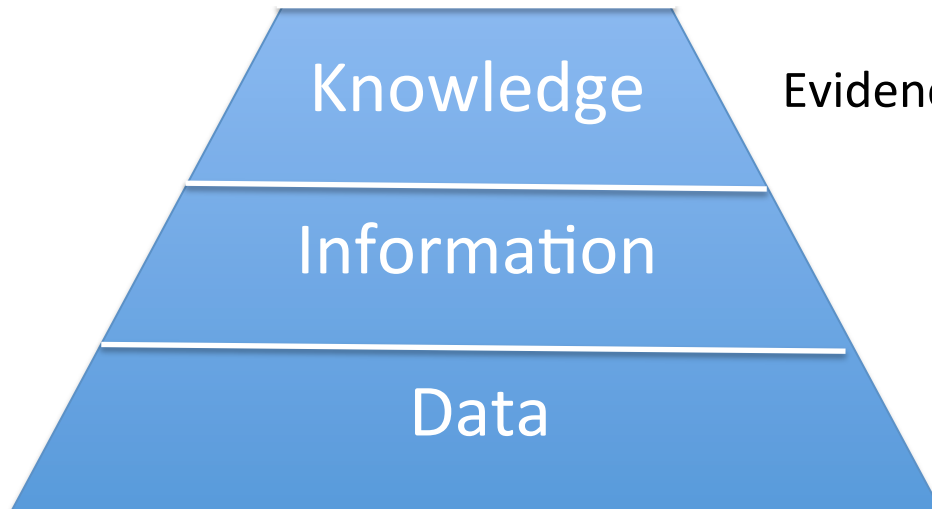
Linked Data, Living Evidence Syntheses



EBM "Owns" the Blue Boxes

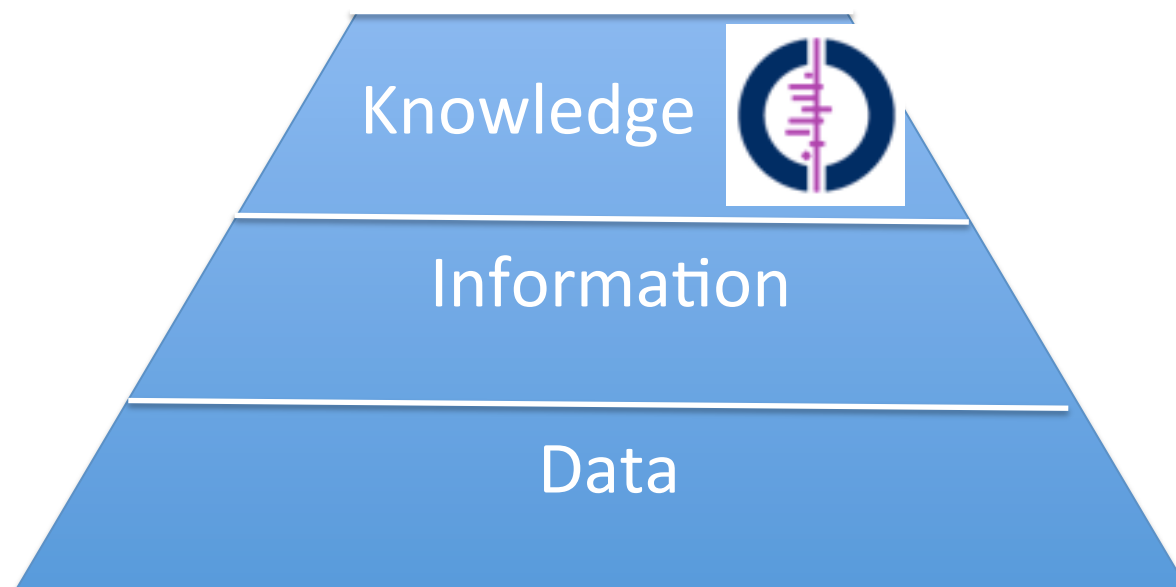


D-I-K Pyramid for Clinical Decision-Making



Evidence : data + "study" design + analysis

Cochrane's Enduring Vital Contributions



Additional References

- Laney, Douglas.
["The Importance of 'Big Data': A Definition". Gartner. Retrieved 21 June 2012.](#)
- <http://groups.ischool.berkeley.edu/archive/how-much-info/datapowers.html> (shakespeare)
- <http://bitesizebio.com/8378/how-much-information-is-stored-in-the-human-genome/>
- <http://spectrum.ieee.org/biomedical/devices/a-temporary-tattoo-that-senses-through-your-skin>
- <http://www.businessinsider.com/75-billion-devices-will-be-connected-to-the-internet-by-2020-2013-10>
- <https://ci.uchicago.edu/press-releases/national-science-foundation-awards-31-million-array-things-project>
- <http://scopeblog.stanford.edu/2015/08/06/myheart-counts-app-reaches-overseas-to-hong-kong-and-the-uk/>
- <http://www.pcori.org/sites/default/files/PCORI-Aspirin-Trial-Fact-Sheet.pdf>
- <http://www.cebm.net/study-designs/>
- <https://methodology.psu.edu/media/techreports/14-126.pdf>
- <http://www.infoworld.com/article/2613526/big-data/ibm-s-watson-becomes-a-cancer-treatment-adviser.html>
- <http://venturebeat.com/2014/07/18/inside-ibms-billion-dollar-bet-on-watson/2/>
- <http://mrctcenter.org/framework-data-sharing>