

Harnessing Real-world Data: for Adaptive Healthcare Systems

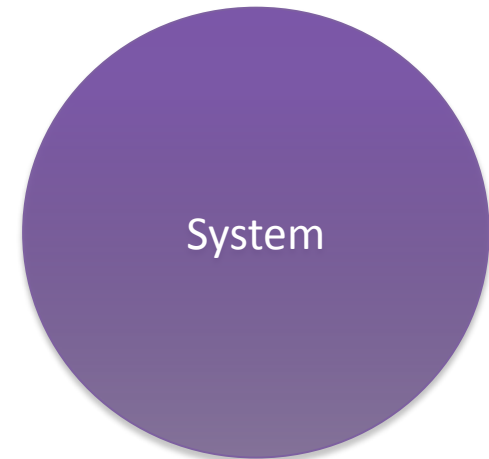
PRISME SIG: Patient Centred R&D,
Alderley Park, 21st May 2012

Iain Buchan

Patient at the Centre of What?



Evidence base about the average patient predicting < 30% of treatment response



Real-world evidence =

Evidence base (average patient)

∪

Me (and n-of-1 of my responses)

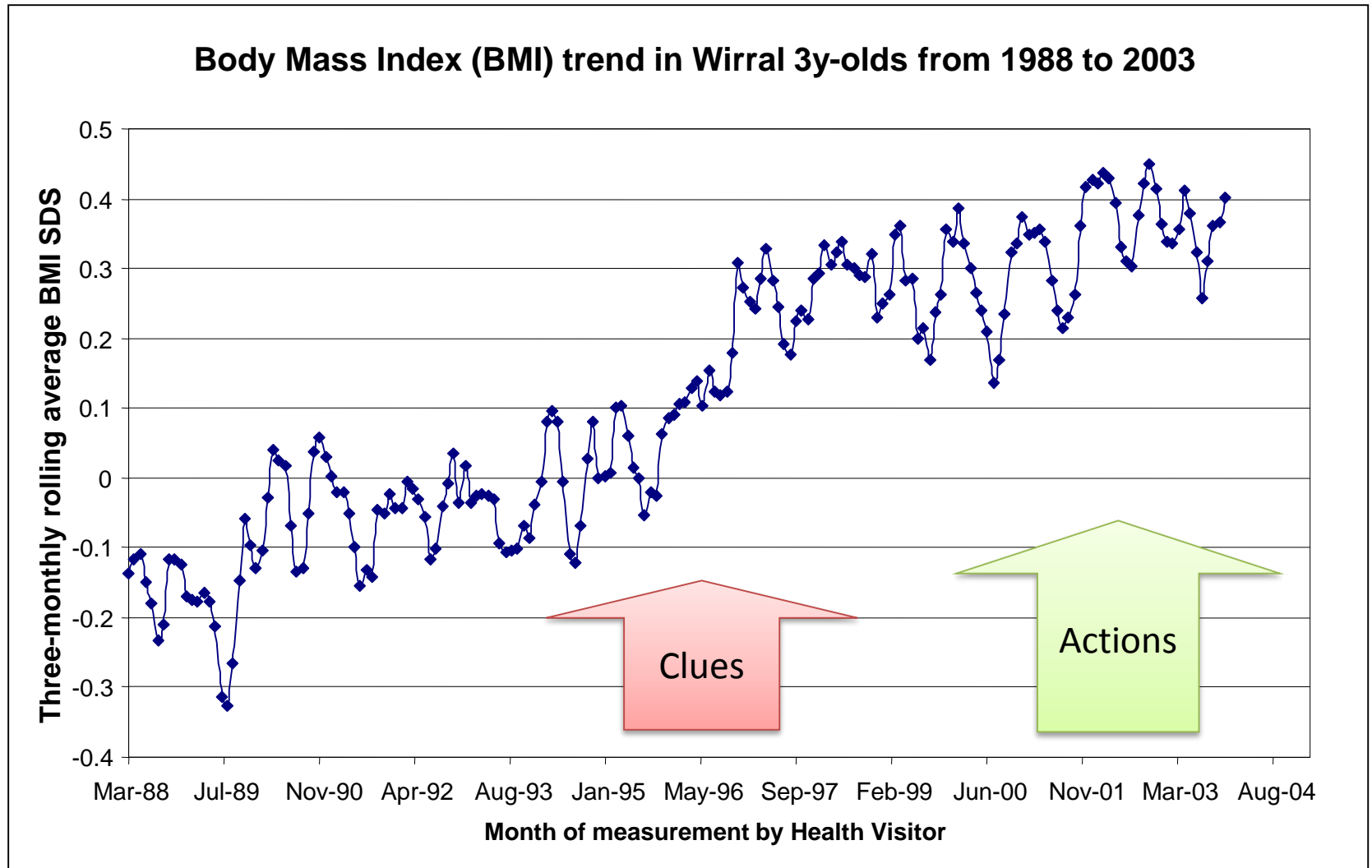
∪

My care setting

Troublesome Threes

- 3 Ingredients
 - Data; Models; Expertise
- 3 Myths
 - Big data warehouses are the solution
 - Science provides the models to utilise the data
 - Clinicians will continue to be the main source of data
- 3 Pipelines
 - R&D; Quality Improvement; Payor & Public Health

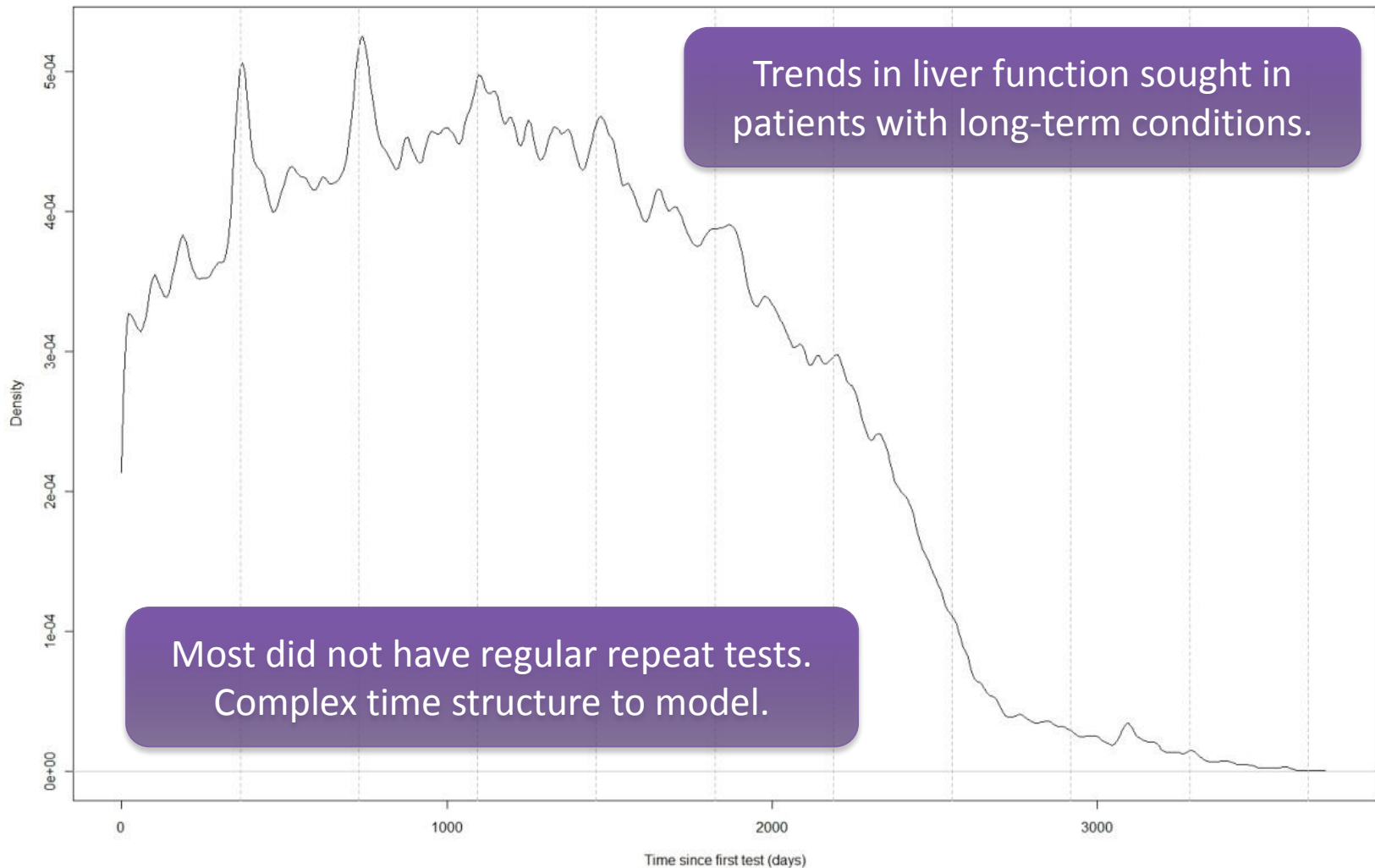
Dormant Data



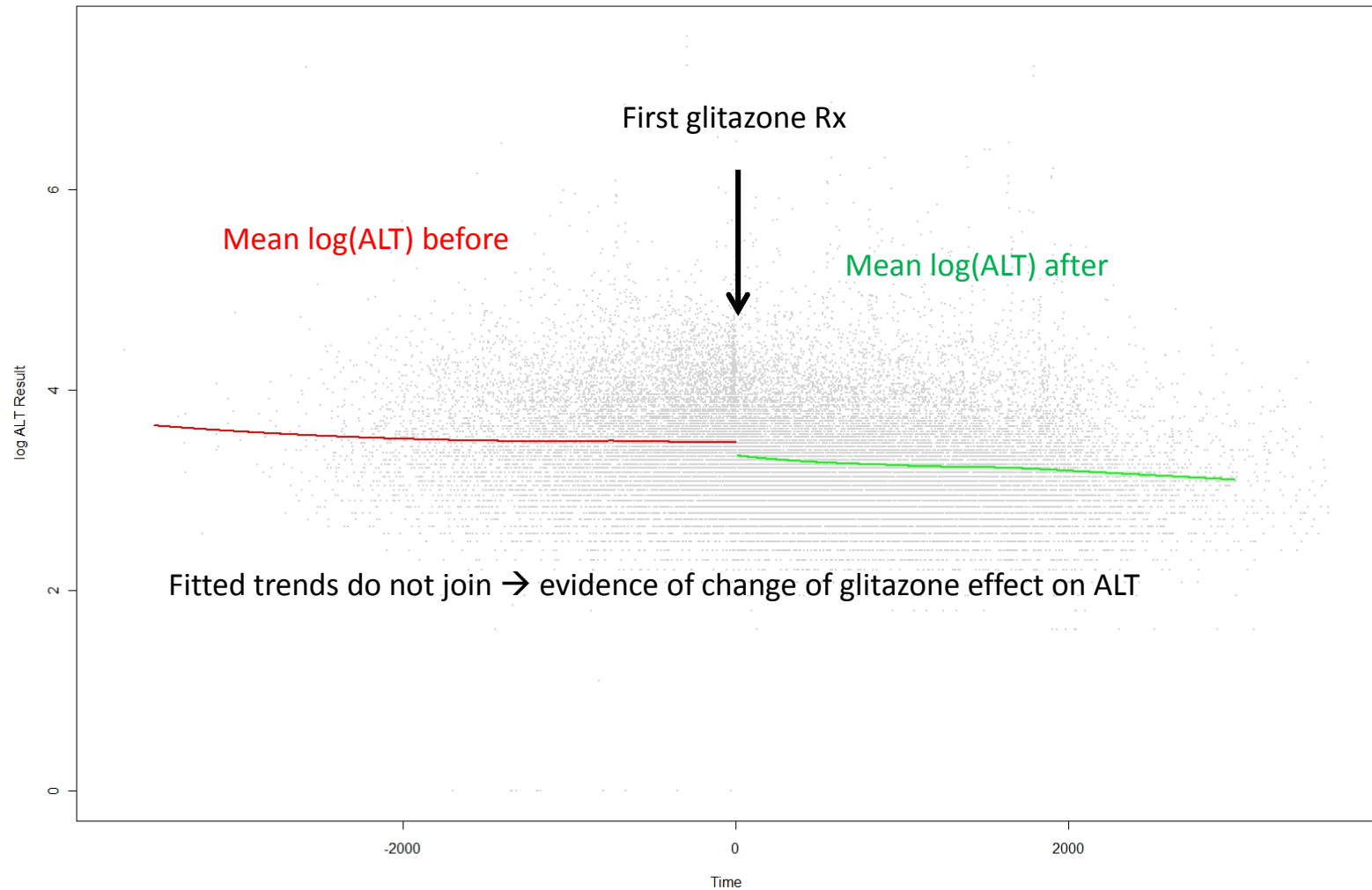
SDS = standard deviation score from 1990 British Growth Reference charts – adjusts for age and sex of the child

Easily Disregarded Data

ALT Test Times for Type 2 Diabetics



Improved Liver Function on Starting Glitazone

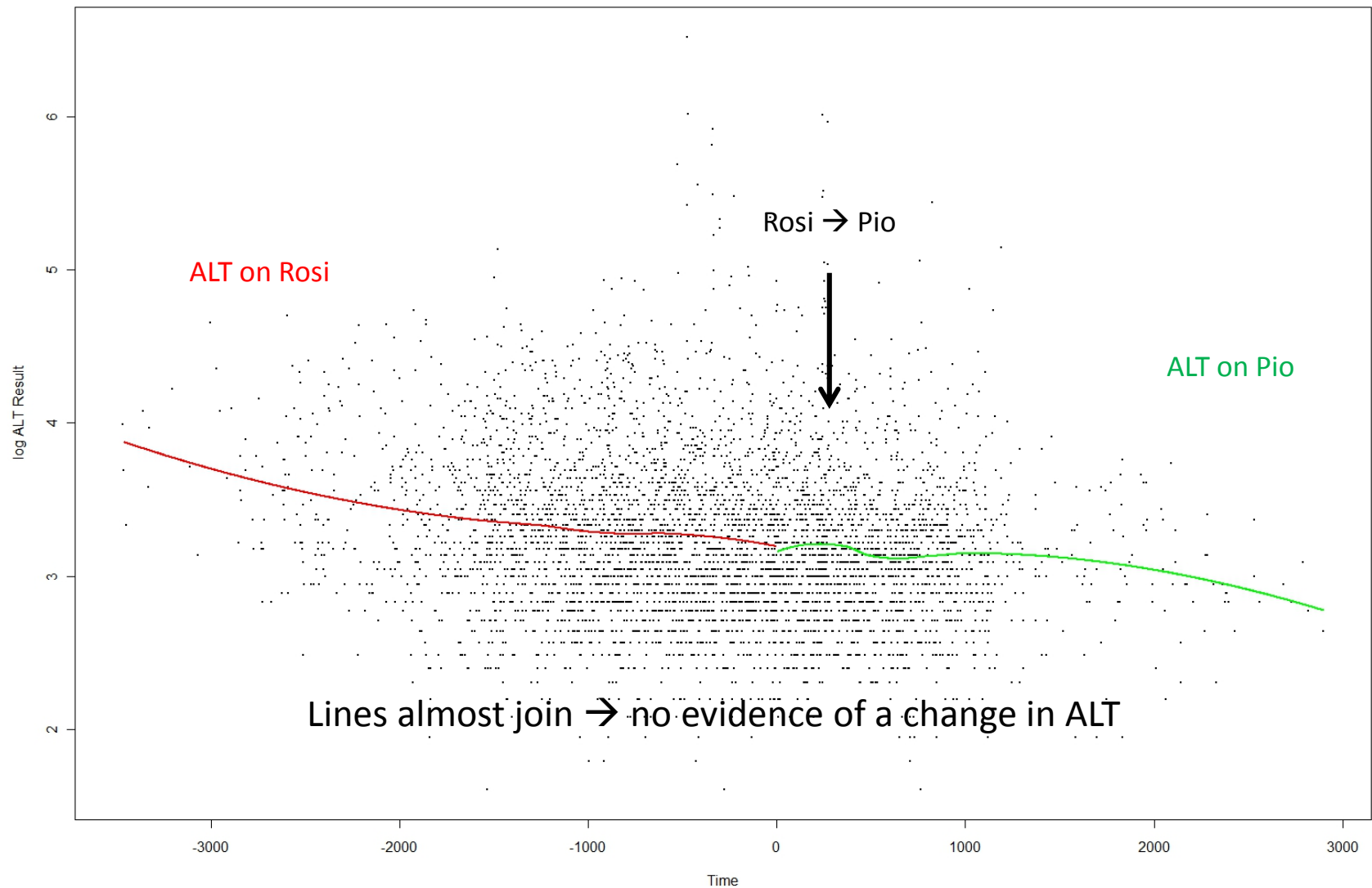


Decrease (pooled) = 0.15 (se=0.009), $p < 1 \times 10^{-59}$

Similar irrespective of co-prescriptions {G = 0.12; GM = 0.16; GS = 0.16; GSM = 0.15}

G = glitazone, M = metformin, S = sulphonylurea}

Rosiglitazone to Pioglitazone: No Liver Signal



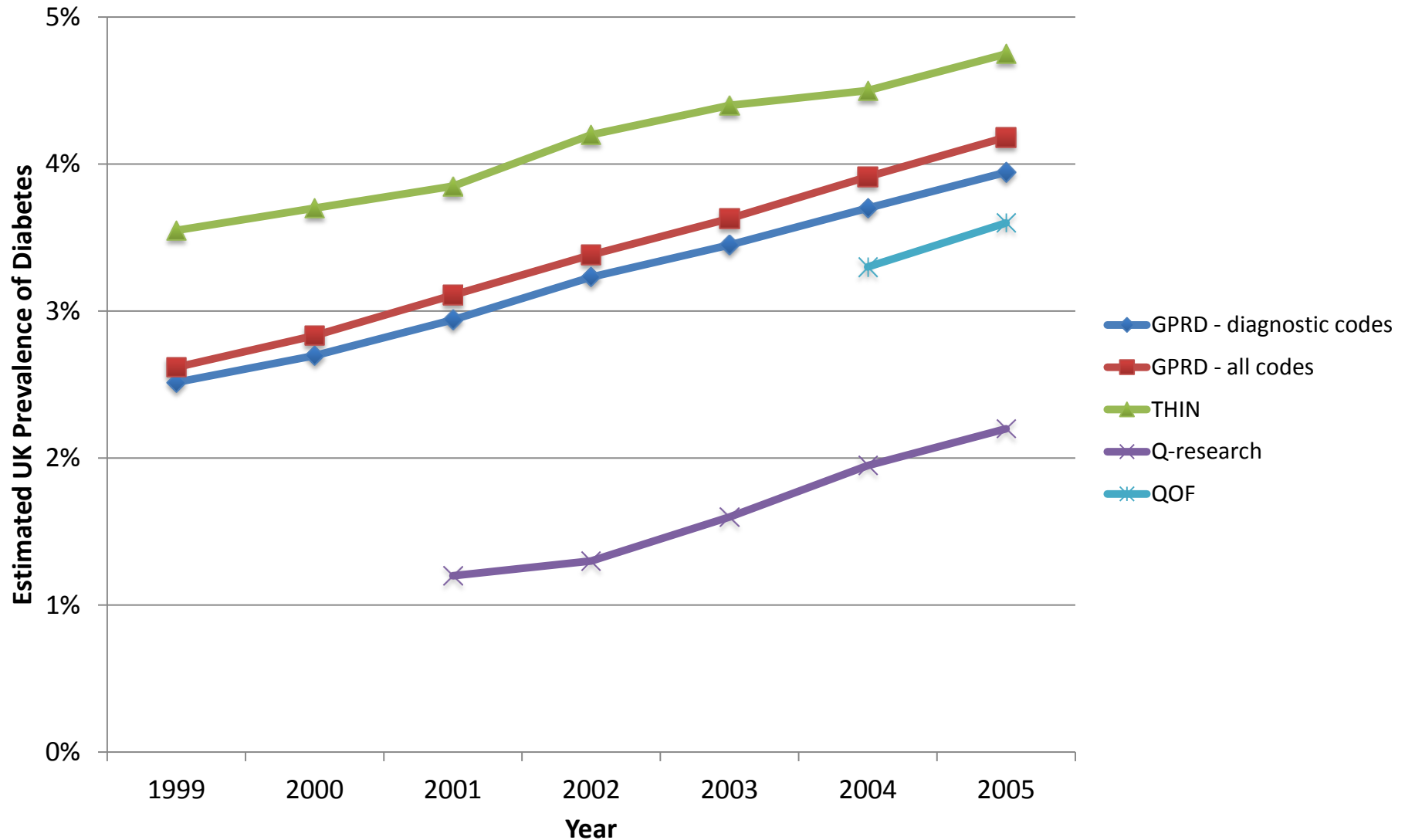
Trapped Data

- Narrative
 - Vioxx risk of MI detectable pre-2004
 - By text mining 154k RA patient notes
 - Not by ICD-9 codes from same notes
 - Repeated for 2 other risks

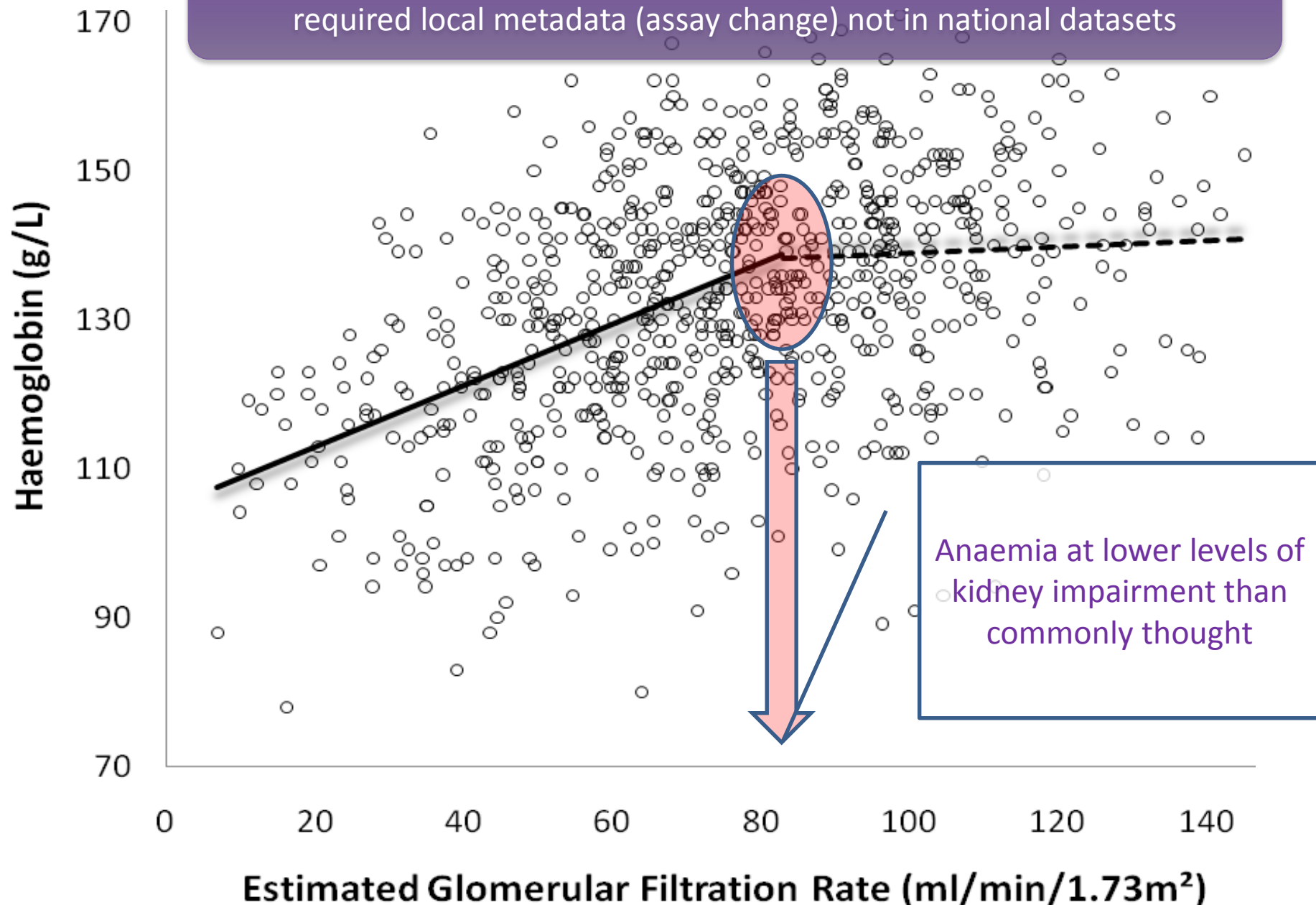
LePendou et al. 2012, J BioMed Sem 3(1):S5
- Rubrics
 - Code for type 2 diabetes annotated “DM r/o”
 - Access blocked by some ethics committees

Miscoded Data

UK Diabetes Prevalence from Different Databases



Clinical (audit) question leading to scientific finding:
required local metadata (assay change) not in national datasets

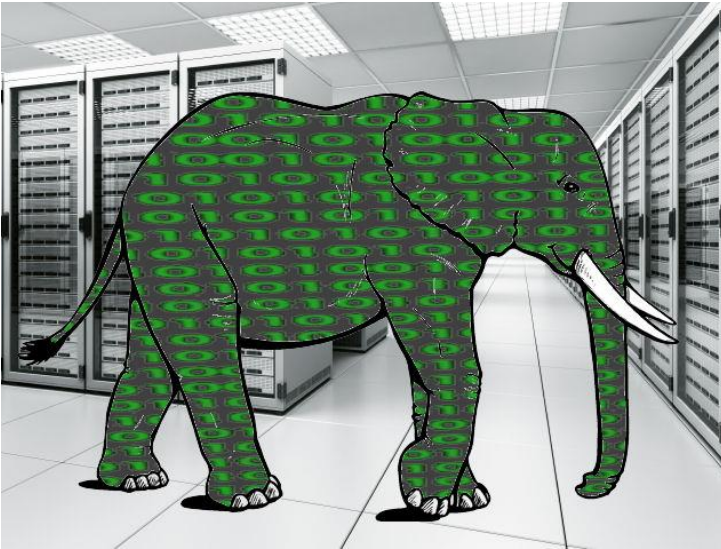


Data Warehouses are not the Solution

- Need contextual metadata continuously adding value to big data
- Need engaged communities adding the metadata
- OMOP lessons
 - Current big data only for crude effects
 - Different answers from different datasets & methods

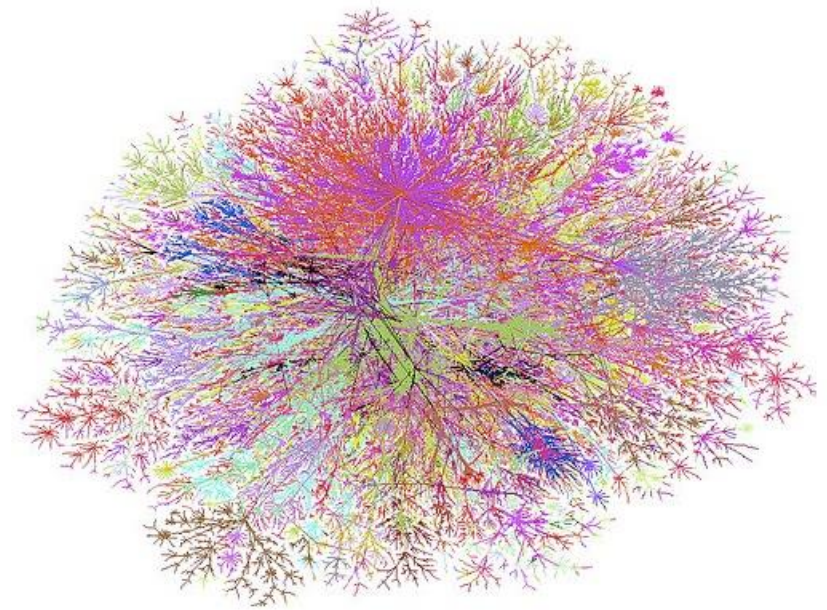


Big Data in Context



Datasets
(+ models)
(searched by experts)

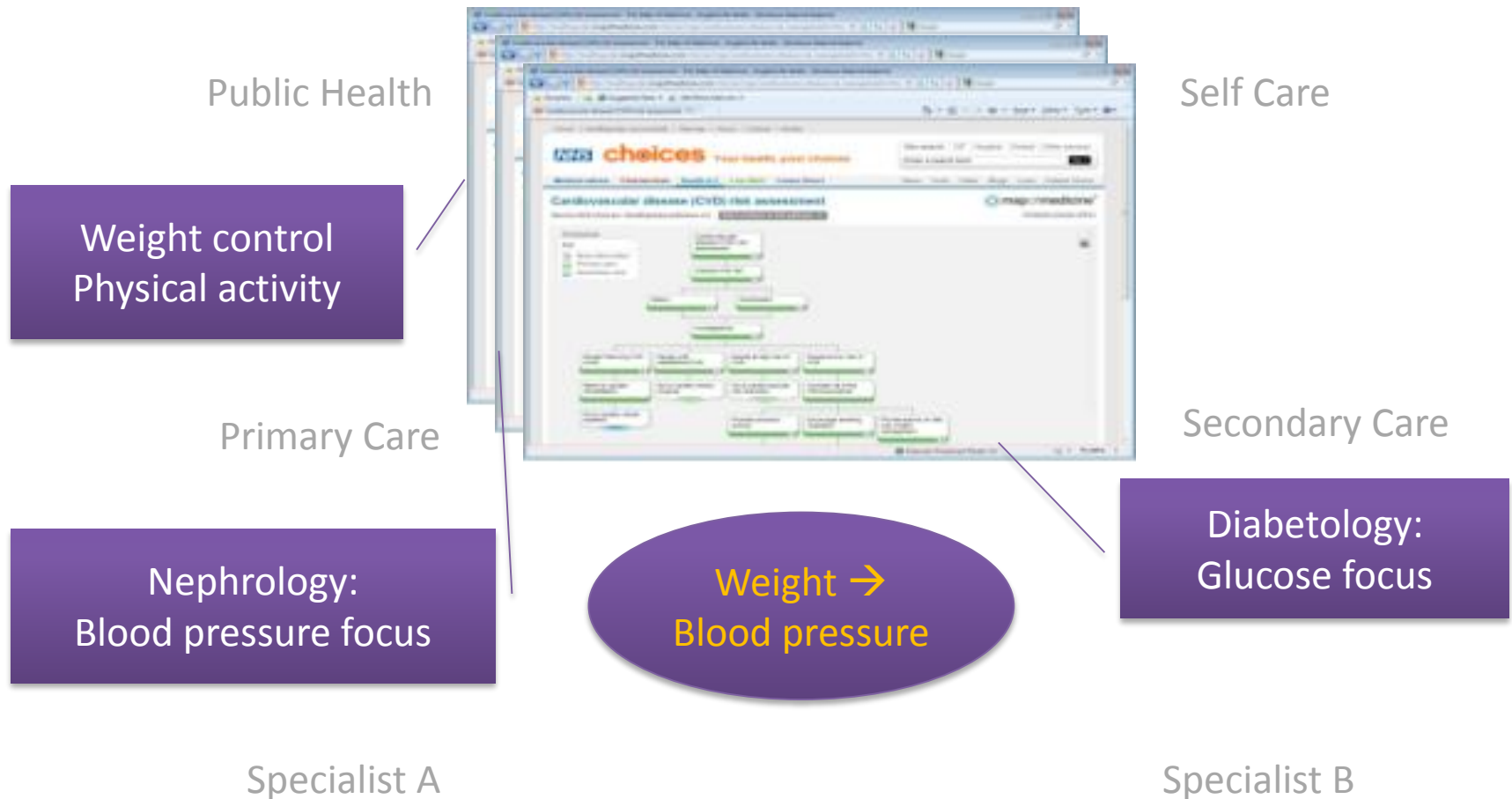
or



Data \cup Models \cup Expertise
“sense-making network”

Fragmented Evidence & Workflows

Patient is the **union**, not the sum of pathways
Need **usefully complex** models of health & care

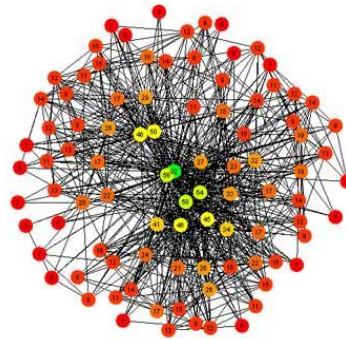


Health Records
& Knowledge Silos

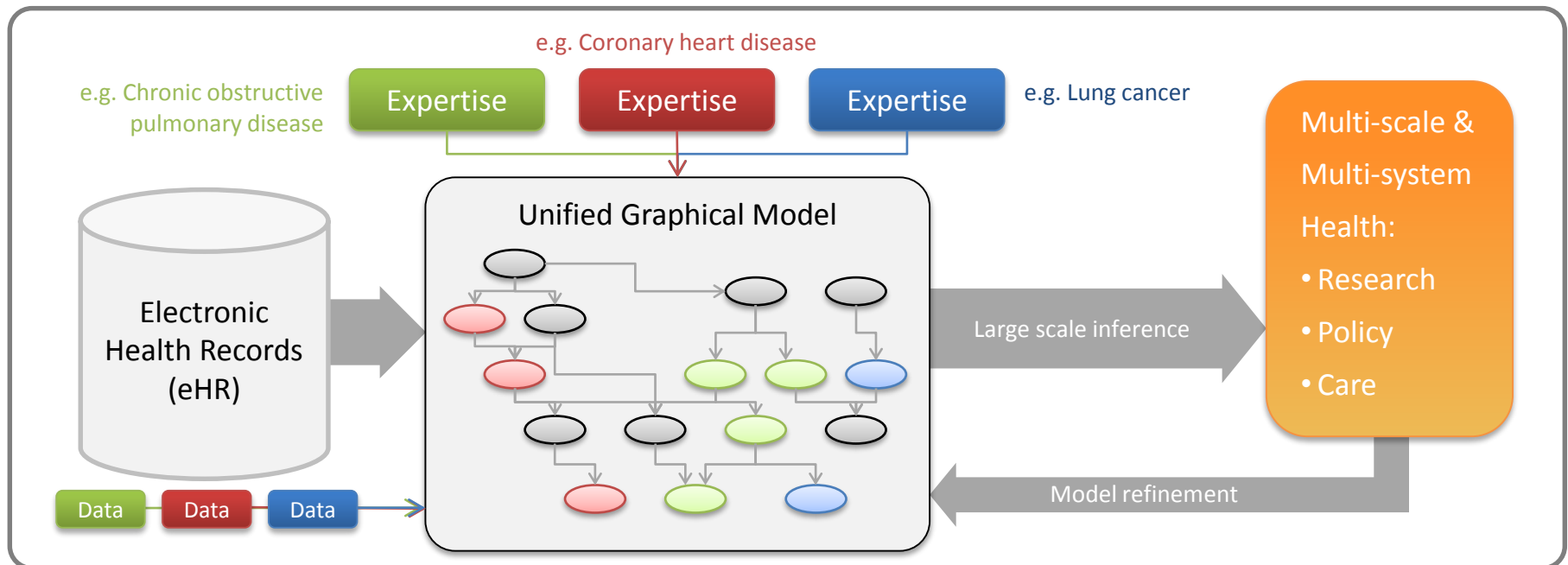
Data-intensive Paradigm -shift

Health Avatars
& Dynamic Models

Open Unifying Modelling:
Across mechanisms and contexts

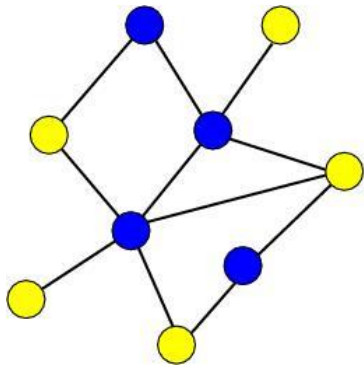


\cup models = Avatar

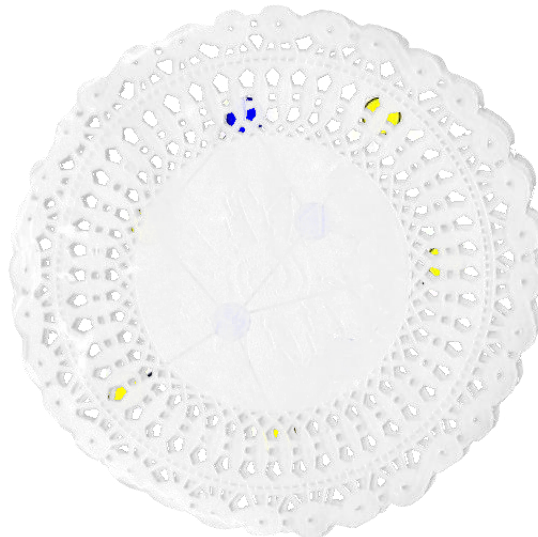


Not About Mining Big Data

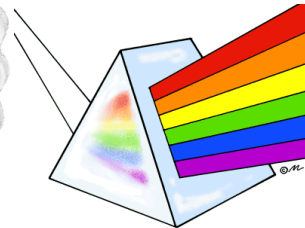
Problem Space



Observation Space



Data Space



Country	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	Total
Bangladesh	8,221	8,678	8,845	8,848	7,215	7,171	6,482	4,816	8,081	11,487	78,832
Canada	10,790	11,880	10,164	8,861	10,202	10,003	10,510	11,067	21,478	152,888	152,888
China	54,802	55,226	48,125	43,835	60,111	76,818	77,208	55,898	64,008	42,866	613,333
Colombia	14,150	12,845	11,781	9,898	14,438	16,798	18,845	14,720	18,878	28,571	157,887
Cuba	26,000	24,432	17,200	14,132	20,811	27,790	28,372	9,292	20,460	38,301	233,896
Dominican R.	31,887	22,882	17,881	17,884	17,886	21,315	22,884	28,198	30,482	27,884	255,282
Kenya	8,501	8,882	8,818	8,884	7,881	8,788	10,812	7,881	8,811	11,888	87,888
Si Lemany	17,888	17,888	14,888	14,888	22,812	19,272	19,188	28,211	28,788	31,188	228,888
Germany	6,788	6,818	6,812	6,811	7,818	6,888	6,881	6,884	7,888	9,884	79,832
Ghana	8,781	7,778	7,782	7,788	9,781	11,881	10,278	14,888	17,888	18,878	138,881
Greece	8,881	7,881	8,881	8,881	9,788	8,881	8,881	8,881	8,881	9,118	71,818
Haiti	18,788	18,881	14,884	18,832	22,884	27,128	28,788	12,281	13,888	14,838	174,837
Honduras	5,871	7,811	8,841	8,888	8,888	8,881	8,881	8,881	8,881	7,712	69,818
India	44,811	38,848	38,438	38,221	42,846	70,290	71,128	38,228	31,188	84,881	588,888
Iran	11,881	8,881	7,888	7,881	8,818	10,487	11,878	7,788	10,434	13,887	89,774
Israel	1,781	888	884	812	1,215	1,822	1,428	981	1,331	2,888	13,338
Japan	18,878	17,884	18,882	18,728	18,882	18,881	18,888	18,884	18,884	18,888	188,878
Japan	8,811	8,884	8,888	8,817	7,884	8,818	8,811	8,811	7,884	8,788	69,782
Korea	17,881	14,188	13,888	13,888	18,782	21,881	22,881	13,788	28,881	28,881	174,881
Mexico	188,888	188,888	113,888	147,871	173,878	208,438	278,888	118,888	178,884	181,441	1,841,381
Nicaragua	8,811	8,872	8,817	13,888	24,818	18,888	18,888	18,888	4,888	3,338	98,888
Nigeria	10,788	1,888	7,788	7,788	7,881	8,811	8,128	7,872	10,788	8,138	83,888
Poland	12,812	12,888	13,888	13,888	14,858	16,448	13,742	8,478	12,888	14,838	133,713
Peru	12,817	10,888	10,137	8,438	8,812	11,131	11,888	8,438	11,781	15,832	111,887
Philippines	18,438	17,221	12,888	11,888	14,438	18,124	19,188	42,281	17,837	69,148	475,288
Poland	15,788	12,888	8,438	8,788	13,114	11,818	12,748	15,718	14,282	15,432	118,888
Soviet Union	42,721	22,888	18,131	18,881	24,442	38,288	38,838	34,882	42,702	68,881	453,884
Tanzania	7,784	8,882	4,881	4,881	6,881	6,881	6,771	6,788	1,384	6,888	37,888
U.S.	13,384	10,888	8,884	7,888	13,385	18,438	18,181	8,837	18,818	18,888	133,188
Vietnam	42,811	28,434	17,218	28,381	28,781	35,811	35,837	22,881	39,114	32,784	303,882
Yugoslavia	11,888	14,438	8,881	8,881	17,881	18,438	14,438	8,881	17,884	23,188	181,888
Other	984,888	188,781	118,832	128,332	187,881	178,818	178,438	188,281	178,272	242,381	1,888,438
Total U.S.	988,881	788,888	688,191	688,881	888,887	1,888,818	1,888,732	788,882	888,142	1,182,372	8,737,812

$$y = b_1x_1 + b_2x_2 + b_3x_3 + c$$

...like squinting at an image through a doyley and prism

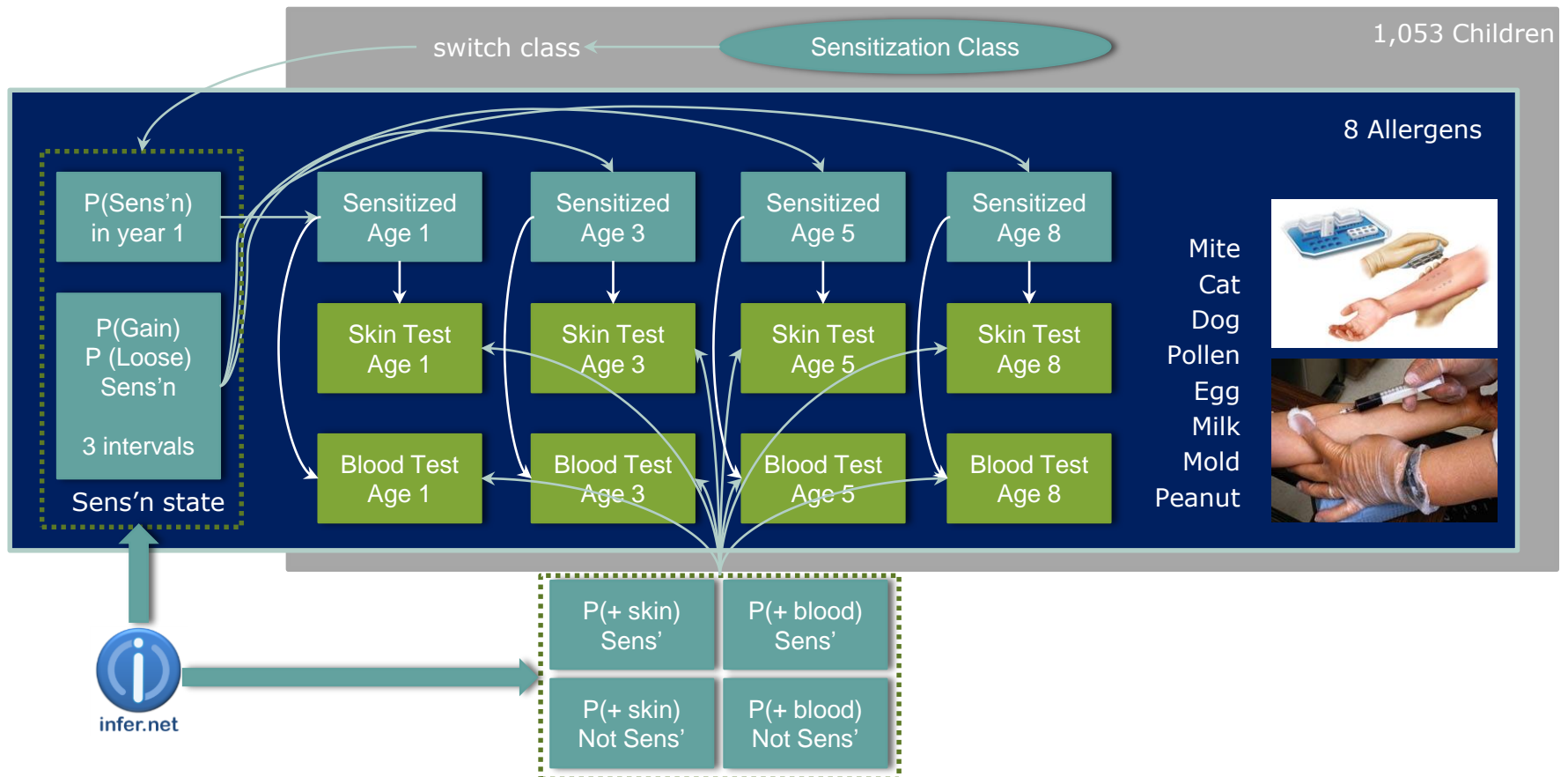
Need to harness networks of reasoning about models
Not just structure in big data

Model-based Machine Learning

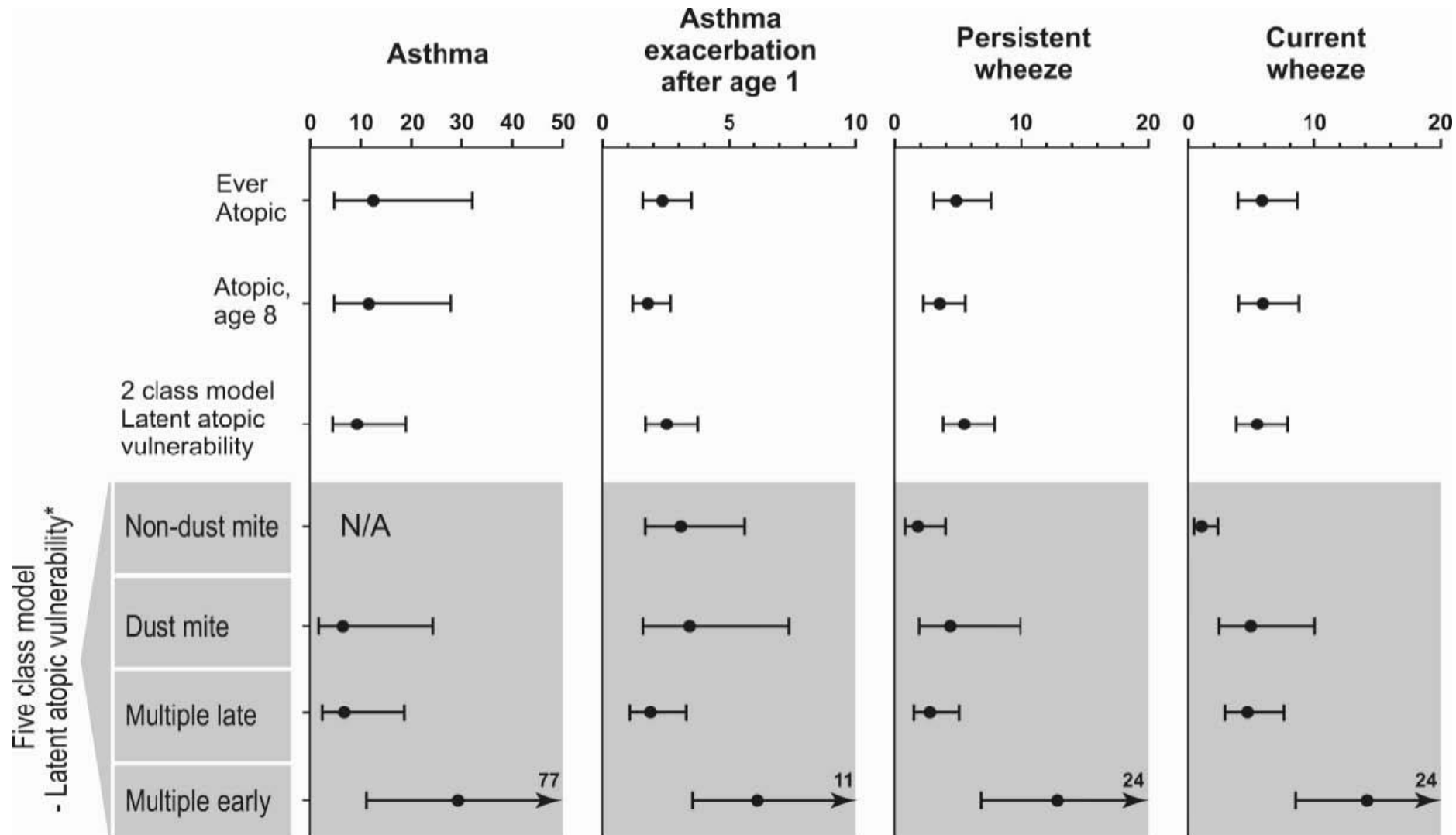
- Suspected myth: false division of children into allergic tendency (atopy) or not
- Life-course data: birth cohort of 1,000 children from Manchester with careful measurements
- Approach: unsupervised search for patterns of sensitisation → shape hypotheses



Unsupervised Clustering of Allergic Sensitisation Development

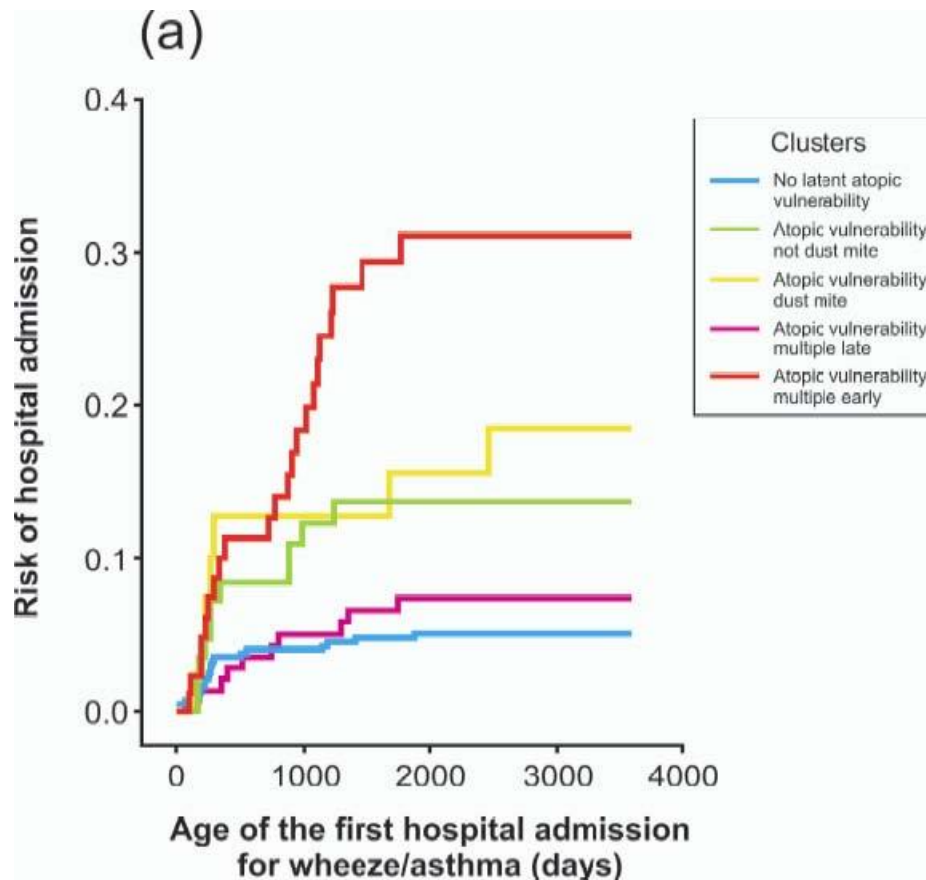


From 2 to 5 Useful Classes of Atopy

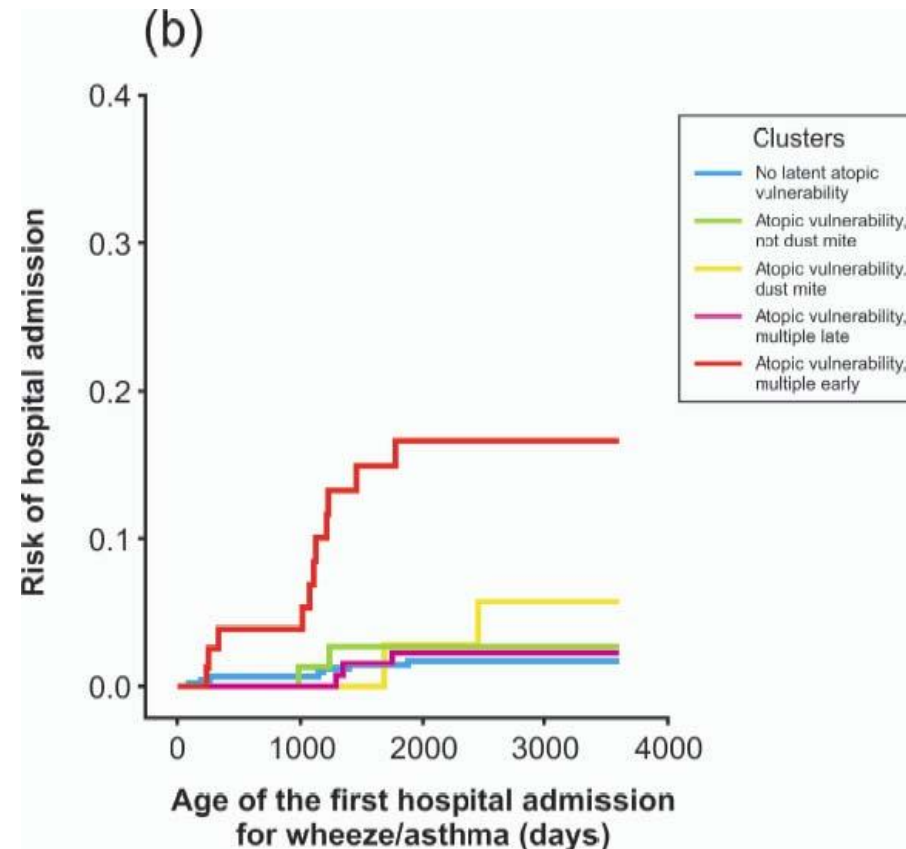


Predicted Real-world Outcomes

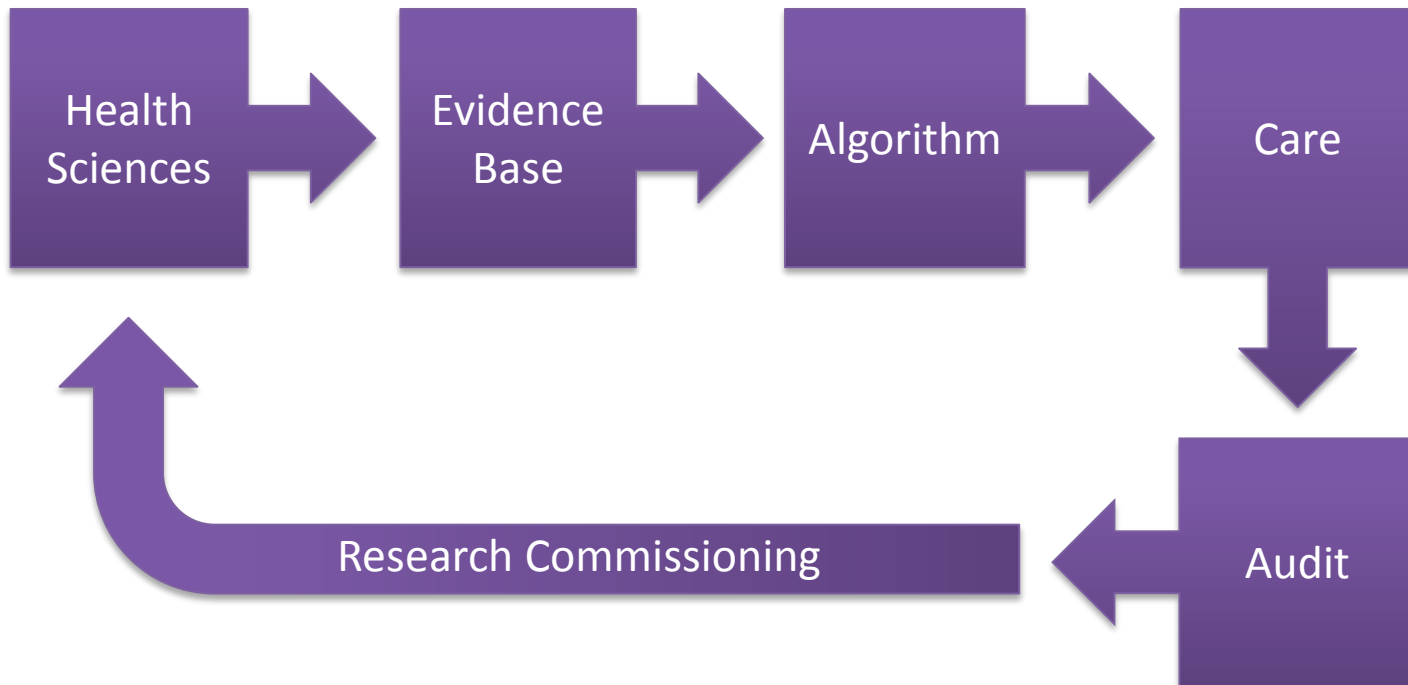
Admitted at Any Age



First Admitted > 3 Years Old
(remove early virus wheeze)



Mirage of Evidence

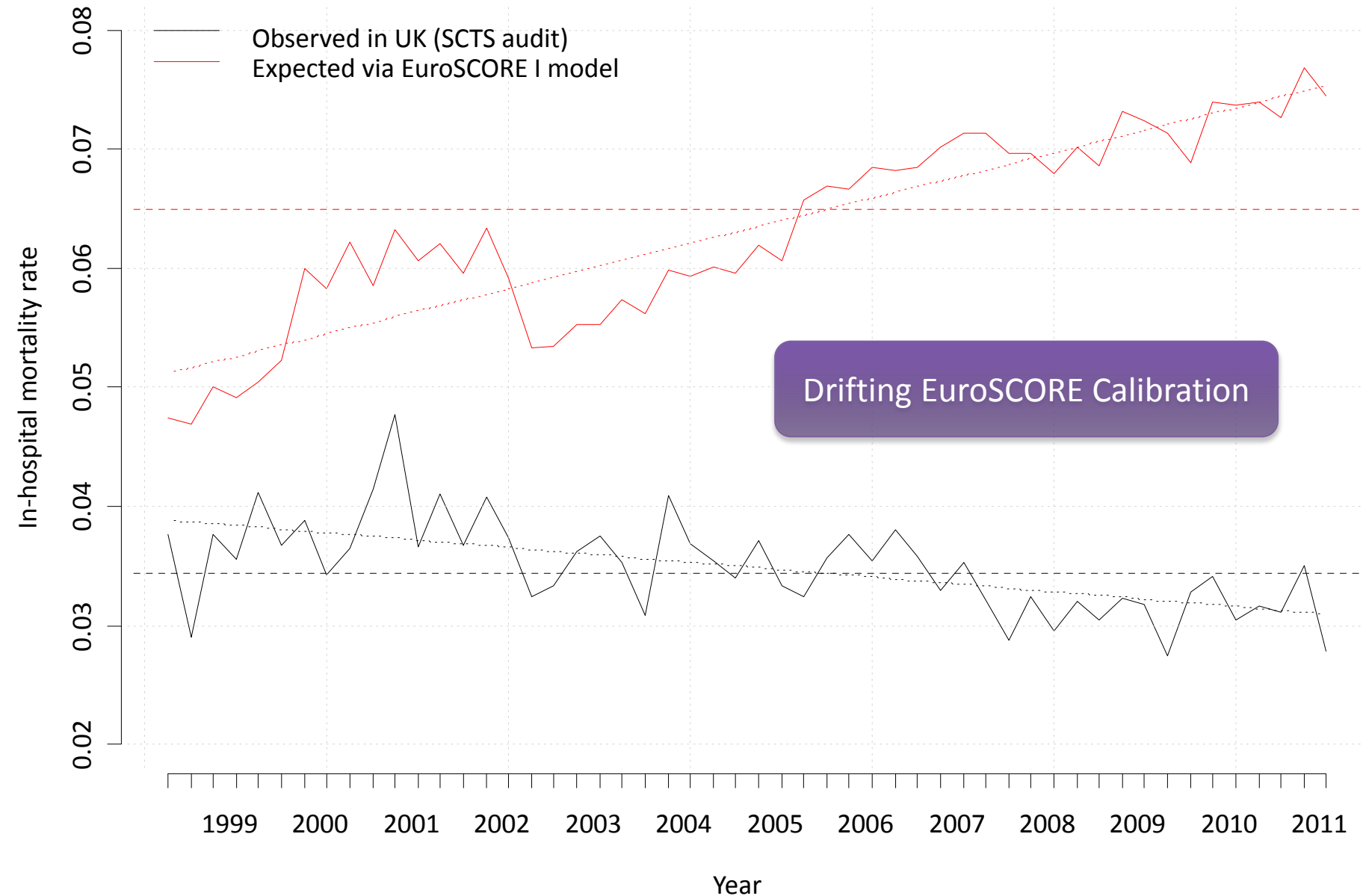


Reality: feedback is too little too late

Algorithms may be out of date by the time they are “validated”

Note EU Directive 2007/47

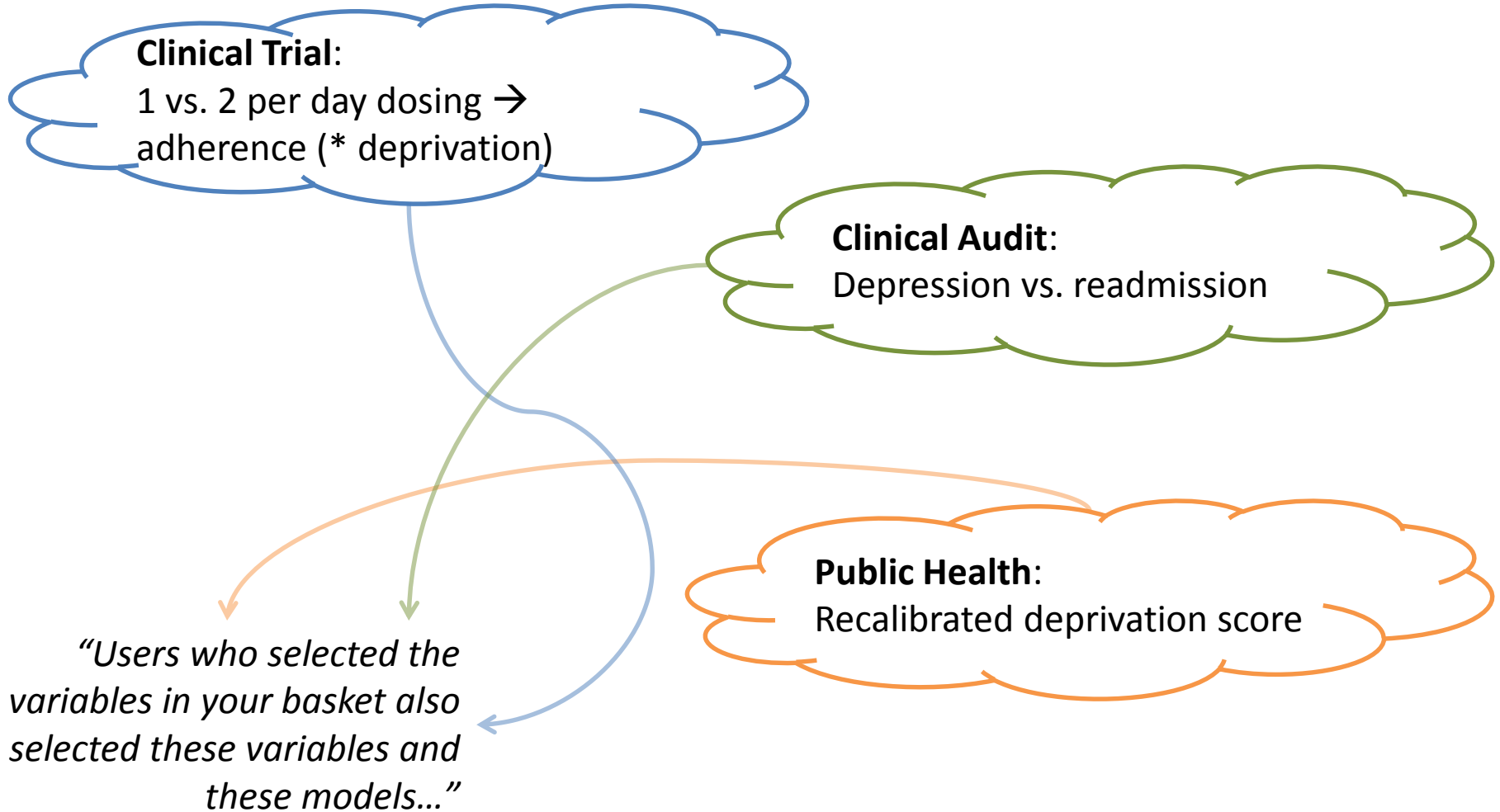
Predicting Mortality from Cardiac Surgery



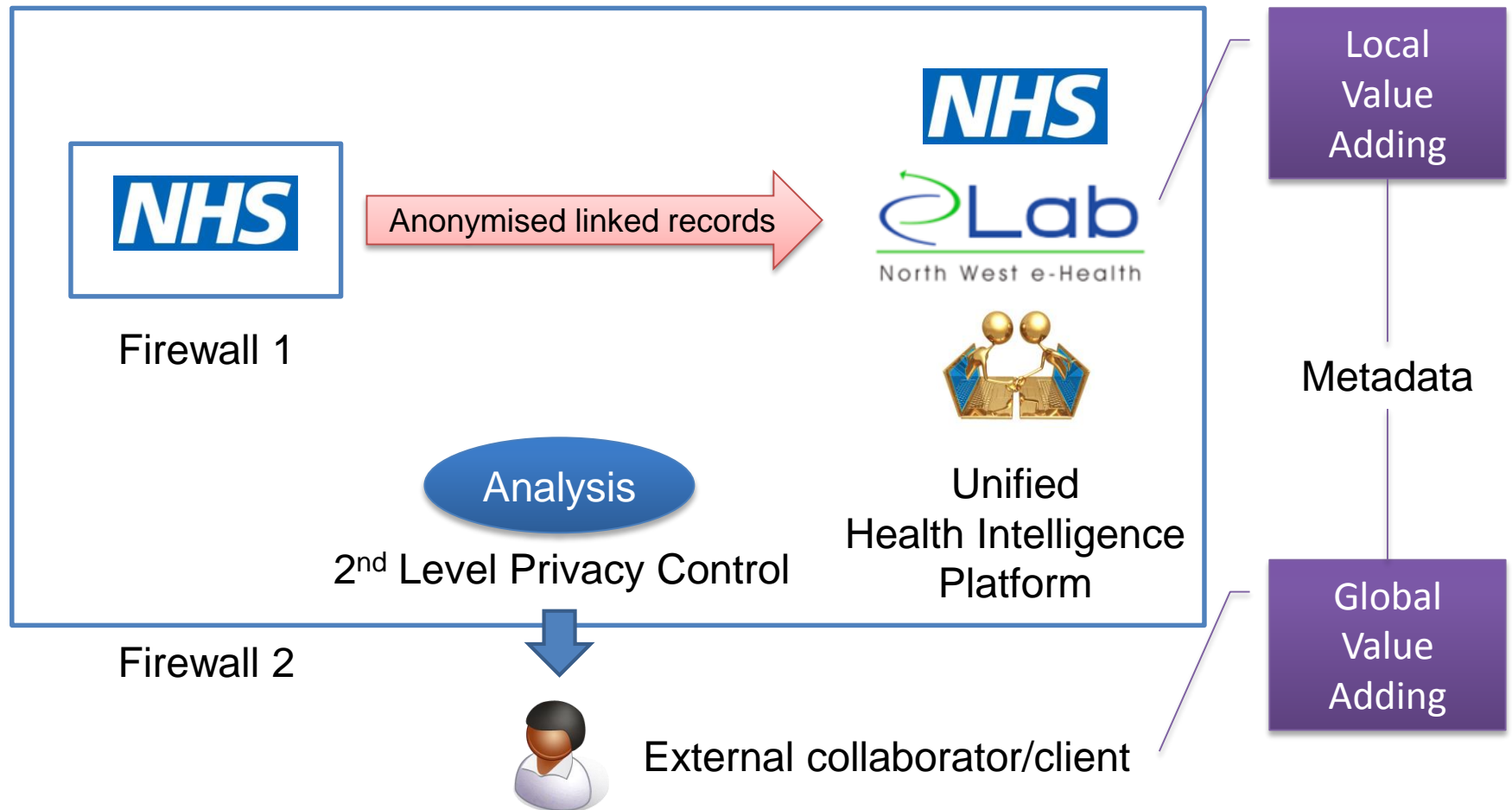
Re-inventing Reuse

- 3 Pipelines
 - Research and Development
 - Provider Quality Improvement
 - Payor & Public Health Evidence
- 1 Bottle-neck
 - Human resource to make sense of data

Potential to Borrow Strength



Health Intelligence 'e-Lab' from/for a Population



Data queries: From this...

```
select distinct PatientID, GPPracticeCode from Patients where DeathDate is null and PatientID in (select distinct PatientID from Patients where
Dob<=1991 and PatientID in (select distinct PatientID from Patients where Dob>=1931 ) ) and PatientID in (select distinct PatientID from Patients
where PatientID in (select distinct j.PatientID from Journal j where j.ReadCode in
('C21.', 'C2A.', 'C2D.', 'C2G2', 'C1021', 'C109.', 'C1094', 'C1095', 'C1097', 'C1099', 'C109D', 'C109F', 'C109G', 'C109H', 'C109J', 'C10F.', 'C10F4', 'C10F5', 'C10F7',
'C10F9', 'C10FD', 'C10FF', 'C10FG', 'C10FH', 'C10FJ', 'L1806', 'X40J5', 'X40J6', 'X40JK', 'XaELQ', 'XaFn7', 'XaFn8', 'XaFn9', 'XaFWI', 'XSETp', 'XU70f', 'XU71F', 'XUK
OO', 'XULXc', 'XUPHn', 'XUSbx') and j.EntryDate<@p4DateLimit1 ) ) and PatientID not in (select distinct PatientID from Patients where PatientID in
(select distinct j.PatientID from Journal j where j.ReadCode in
('1226', '12C2', '12C3', '12C5', '12C8', '12CA', '12CB', '12CC', '12CD', '12CE', '12CF', '12CG', '12CH', '12CJ', '12CL', '12CM', '12CN', '12CP', '12CR', '12C
S', '12CT', '12J3', '14A.', '14A3', '14A4', '14A5', '14A6', '14AD', '14AH', '14AJ', '14AL', '14AM', '14AN', '14AP', '14AQ', '14AR', '14H1', '187.', '1110', '113
.', '115.', '116.', '1J60', '1O1.', '2241', '679X', '68B2', '68B6', '6C0.', '7721', '7722', '865.', '8651', '8652', '8653', '8654', '865Z', 'B1NZ', 'G12.', 'G121', 'G
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G235', 'G236', 'G23Z', 'G2Z.', 'G32.', 'G34.', 'G4.', 'G41.', 'G42.', 'G420', 'G43.', 'G44.', 'G440', 'G441', 'G442', 'G443', 'G444', 'G445', 'G446', 'G45.', '
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```

...to this

Study Overview

State

Feasibility

Study Members

- lucy (Creator)
- bruce (Viewer)
- gary (Editor)
- markdelderfield (Editor)
- normanstein (Editor)
- pat (Editor)
- sarahthew (Editor)
- steph (Viewer)

Gender

Ethnicity

Smoker ☒ 'N/A' (Not Applicable)
☐ Select:
☐ Current Smoker ☐ Ex-Smoker ☐ Never Smoked

Additional Criteria

☒ Include: Has Asthma

AND Asthma

AND Asthma attack diagnosis made less than 12 Months ago

Search for

☐ Search within term description

Diagnosis made More

Add with

☒ Include: Asthma Medications

☒ Exclude: BMI - Overweight

- Asthma
- Asthma attack
- Asthma NOS
- Cardiac asthma
- Asthma screening
- Intrinsic asthma
- Asthma confirmed
- Asthma attack NOS
- Asthma unspecified

Clinical Study Feasibility Assessment

[Farsite Home](#)[Protocol Templates](#)[Shared Criteria](#)[Research Networks](#)[Clinical Codes](#)[Help](#)

Options

- Create new study
- Create copy of this study
- Cancel Study
- Return to list of studies

Protocol Templates

- Create Template

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- normanstein (Editor)

MASCOT

[Description](#)[Protocol](#)[Estimates](#)

Study saved 31/08/2010 08:45:31

[Run](#)

Baseline

885 people

☒ Demographics

885 people

☒ Additional Criteria

☒ Include: Has Asthma

Asthma

<5 people

AND Asthma attack diagnosis made less than 12 Months ago

<5 people

☒ Include: Asthma Medications

☒ Exclude: BMI - Overweight

Recruitment Estimate

<5 people

[Edit](#)

Clinical Study Recruitment

Options

- Create new study
- Create copy of this study
- Cancel Study
- Return to list of studies

Protocol Templates

- Create Template

Study Overview

State

Approved

Study Members

- lucy (Creator)
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- markdelderfield (Editor)
- normanstein (Editor)
- pat (Editor)
- sarahthew (Editor)
- steph (Viewer)

MASCOT

Description

Protocol

Estimates

Attachments

GP Recruitment

Send To GPs

Study saved 31/08/2010 08:47:20

Add patient consent form

Choose File

No file chosen

and patient information sheet (if separate)

Choose File

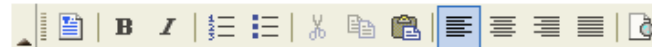
No file chosen

Add ethics approval letter

Choose File

No file chosen

Patient invitation letter template



[[GPSurgeryName]]

[[GPAddressLine1]]

[[GPTown]]

Dear [[PatientFirstName]] [[PatientLastName]]

We would like to invite you

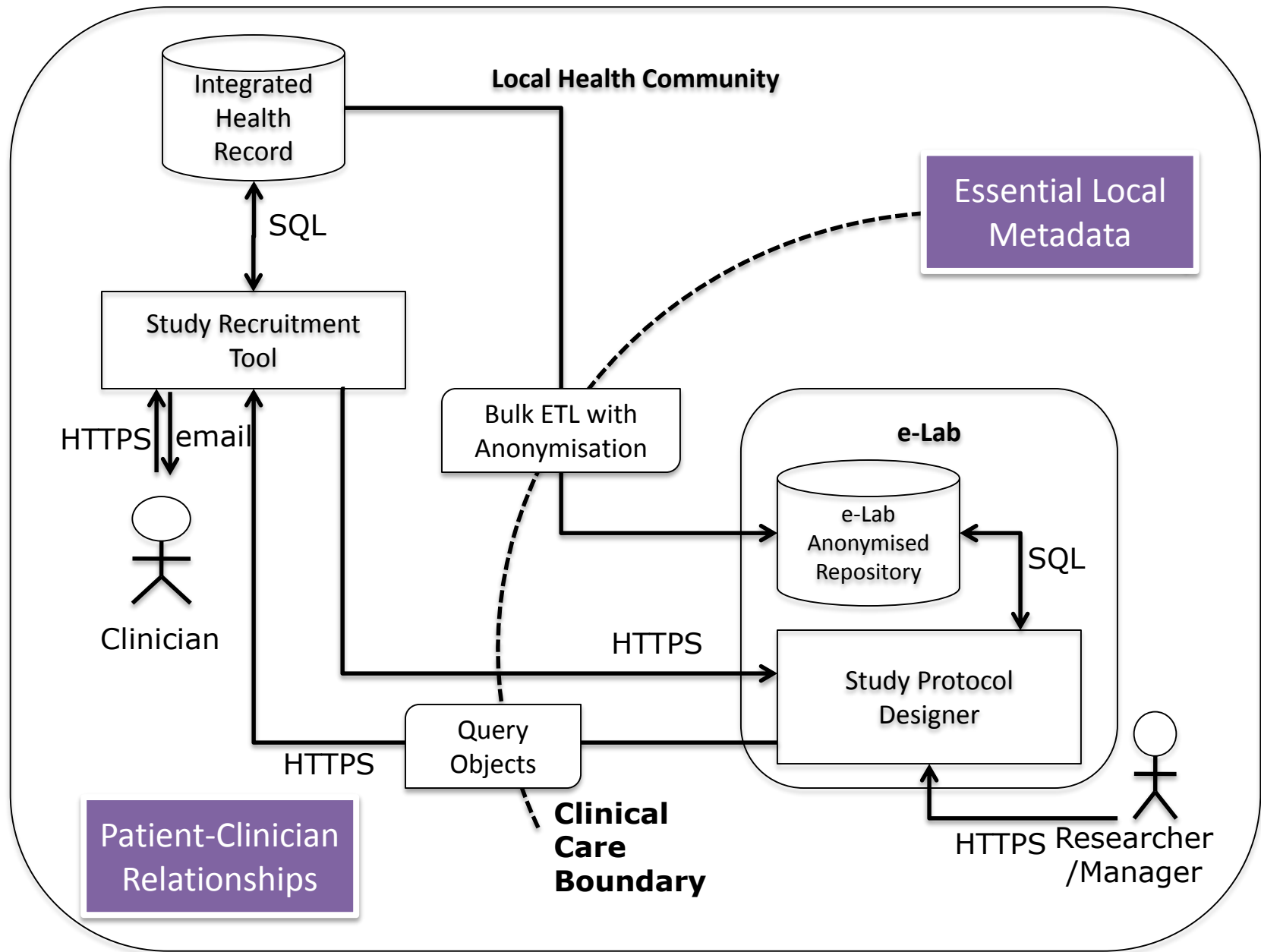
Patient

Address Line 1 Address Line 2 Address Line 3 Town County Postcode Title Firstname Lastname

GP

Surgery Name Address Line 1 Address Line 2 Address Line 3 Town County Postcode Firstname Lastname
Qualifications

Preserving Consent for Consent



Project Menu

► Project Details

- Data
- Documents
- Data Exploration
- Notes
- Snapshots
- People
- Hide/Delete Items

► Project Views

- Project Explorer
- My Projects
- Public Projects
- Help

Data

HBA1C by ward

Show Details

Show Permissions

Add a Note...

Add a File...

View data as grid

View data as chart

View data as map

View statistics

Statistics Workbench

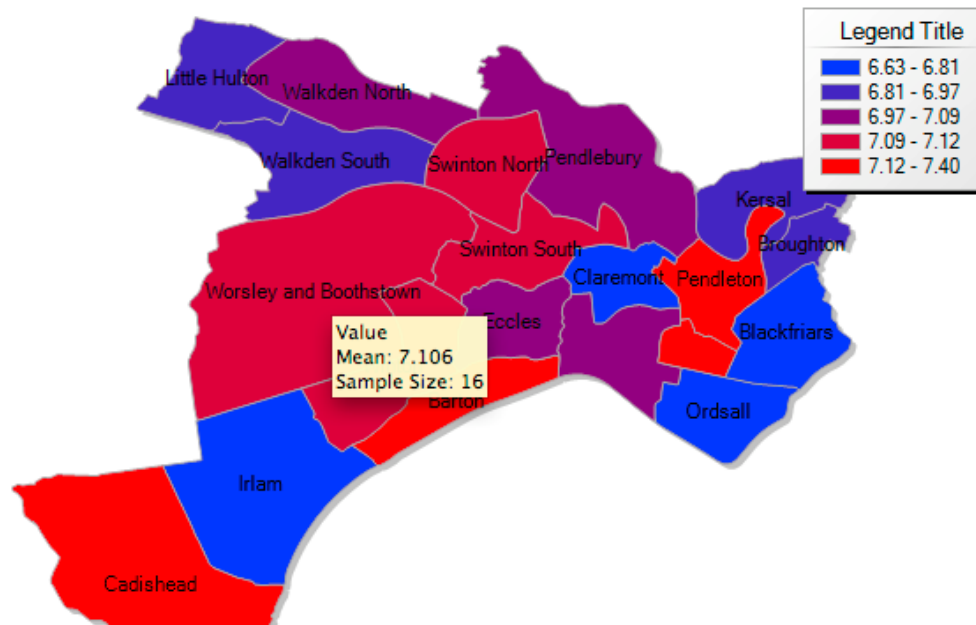
map

settings

Take snapshot

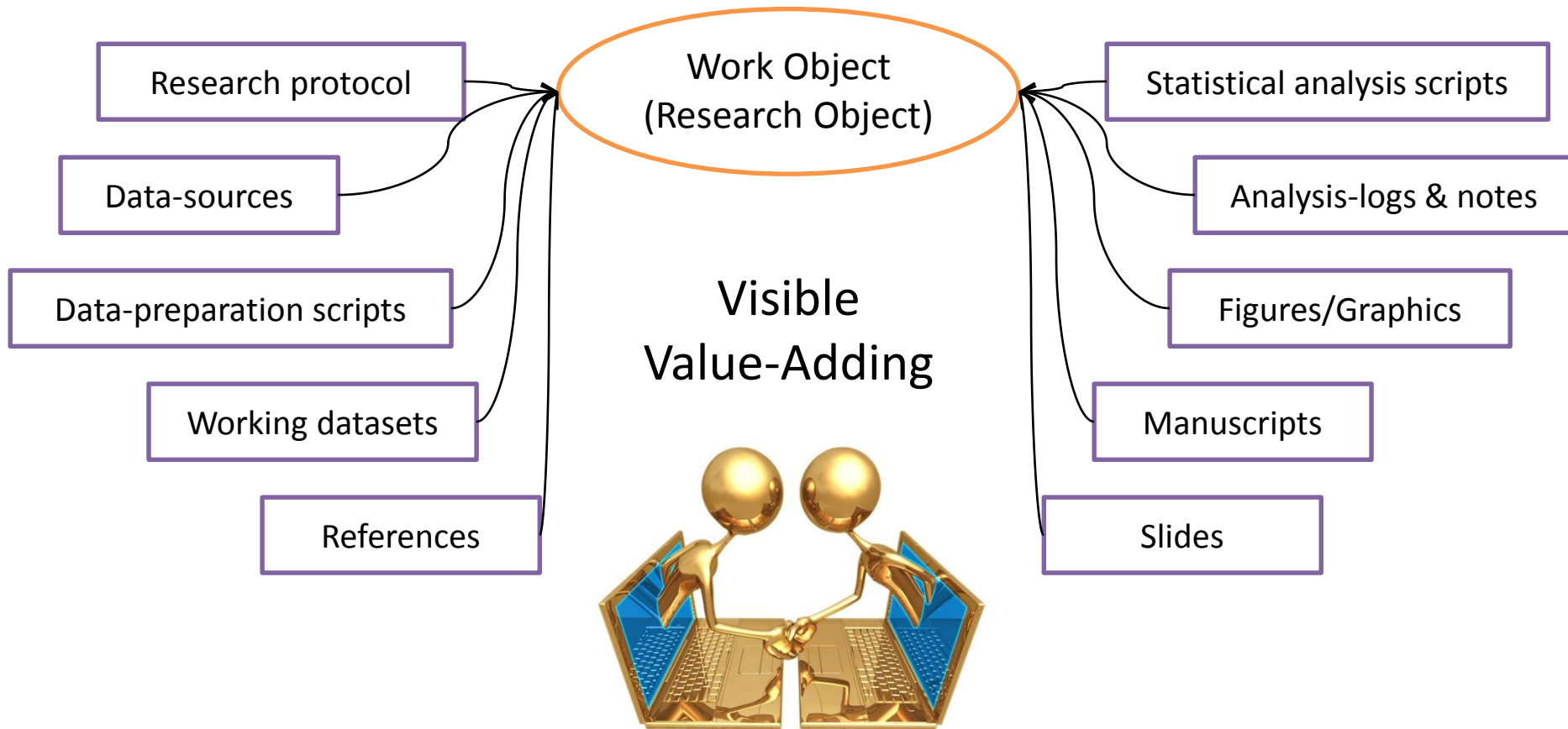
Save image to my computer

Mean HBA1C values by ward



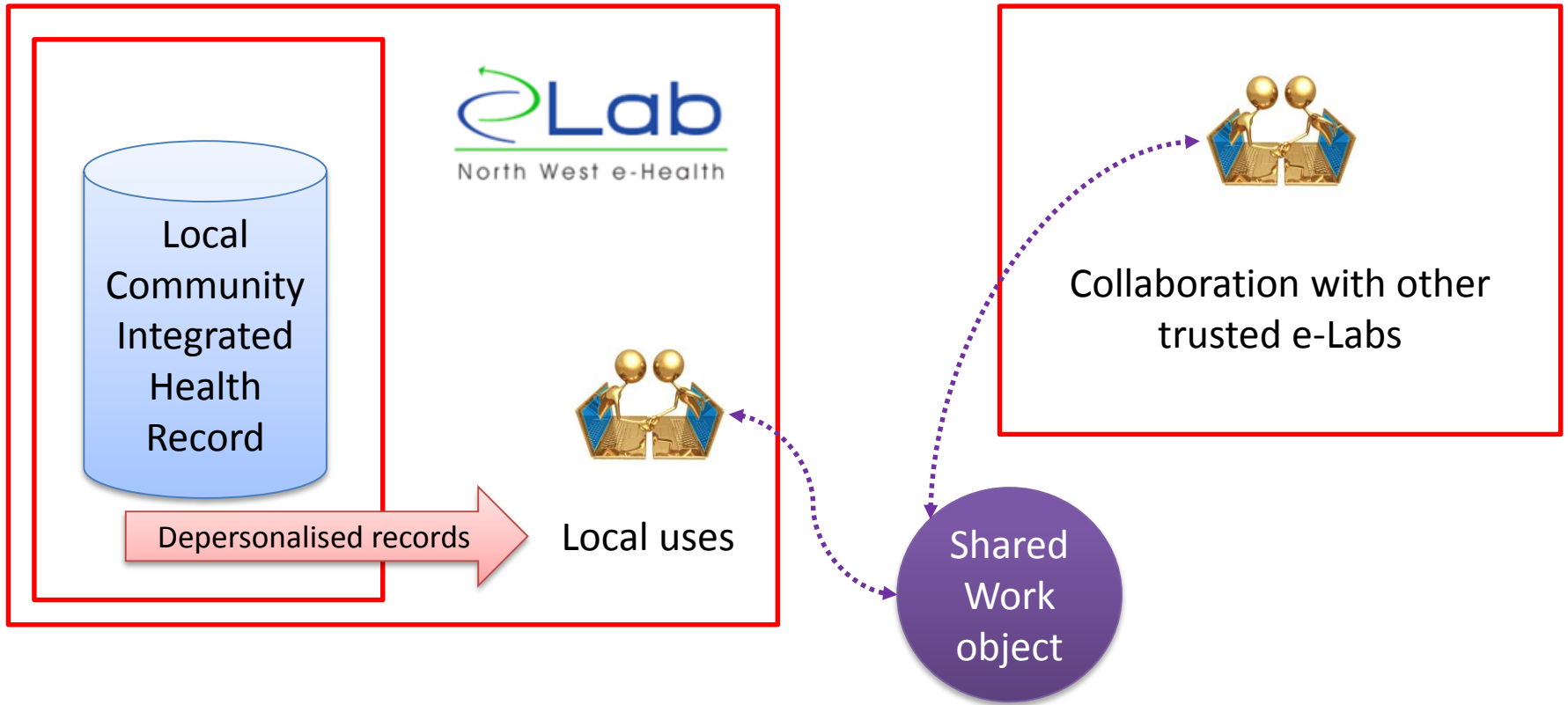
1 Website
Many uses
Many users
Common data
Population focus

e-Lab Currency: Work Object



Socially Stimulating Science & Service Intelligence, In-silico

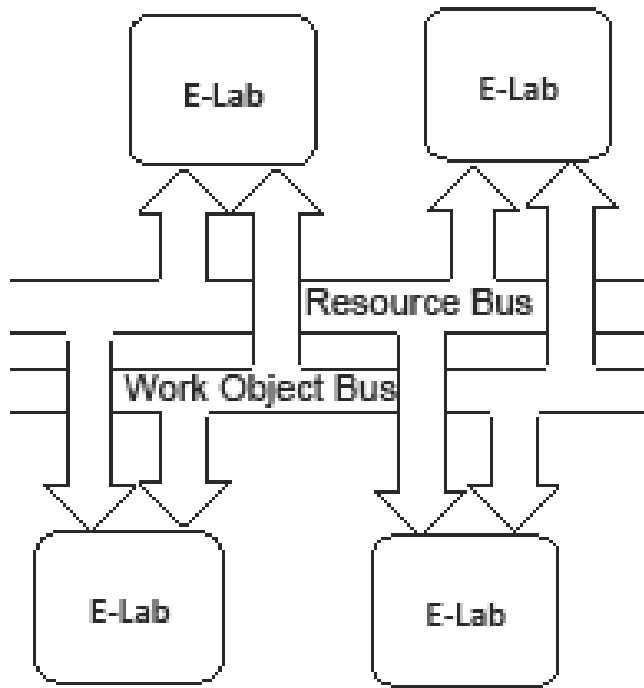
Data Sharing: Contextualised



Each locality can police the passage of objects at its boundary.

Changes to objects are fully auditable.

SOA for Borrowing Strength

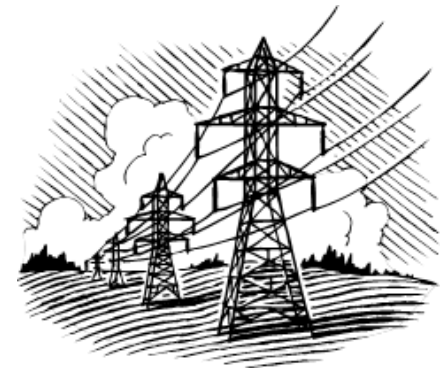


Federation of e-Lab communities
shares work objects without
remote data warehousing

Strength is borrowed
and costs reduced
by pooling expertise

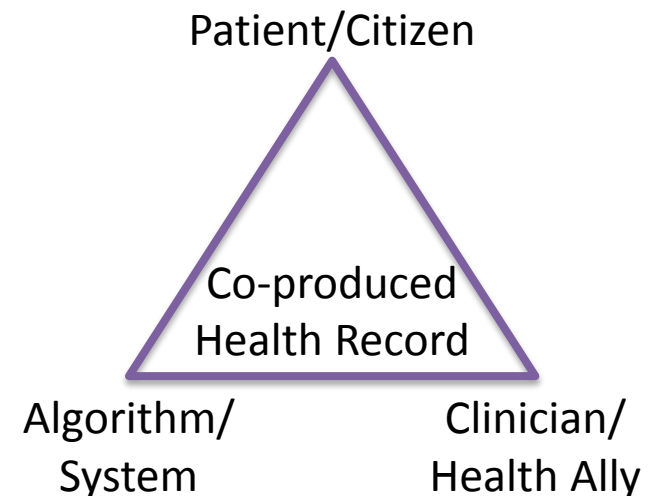
Harness Heterogeneity

Diversity of settings (disease-risk & treatment)
across regions
could be harnessed
to tease out evidence
with smaller samples
faster than at present

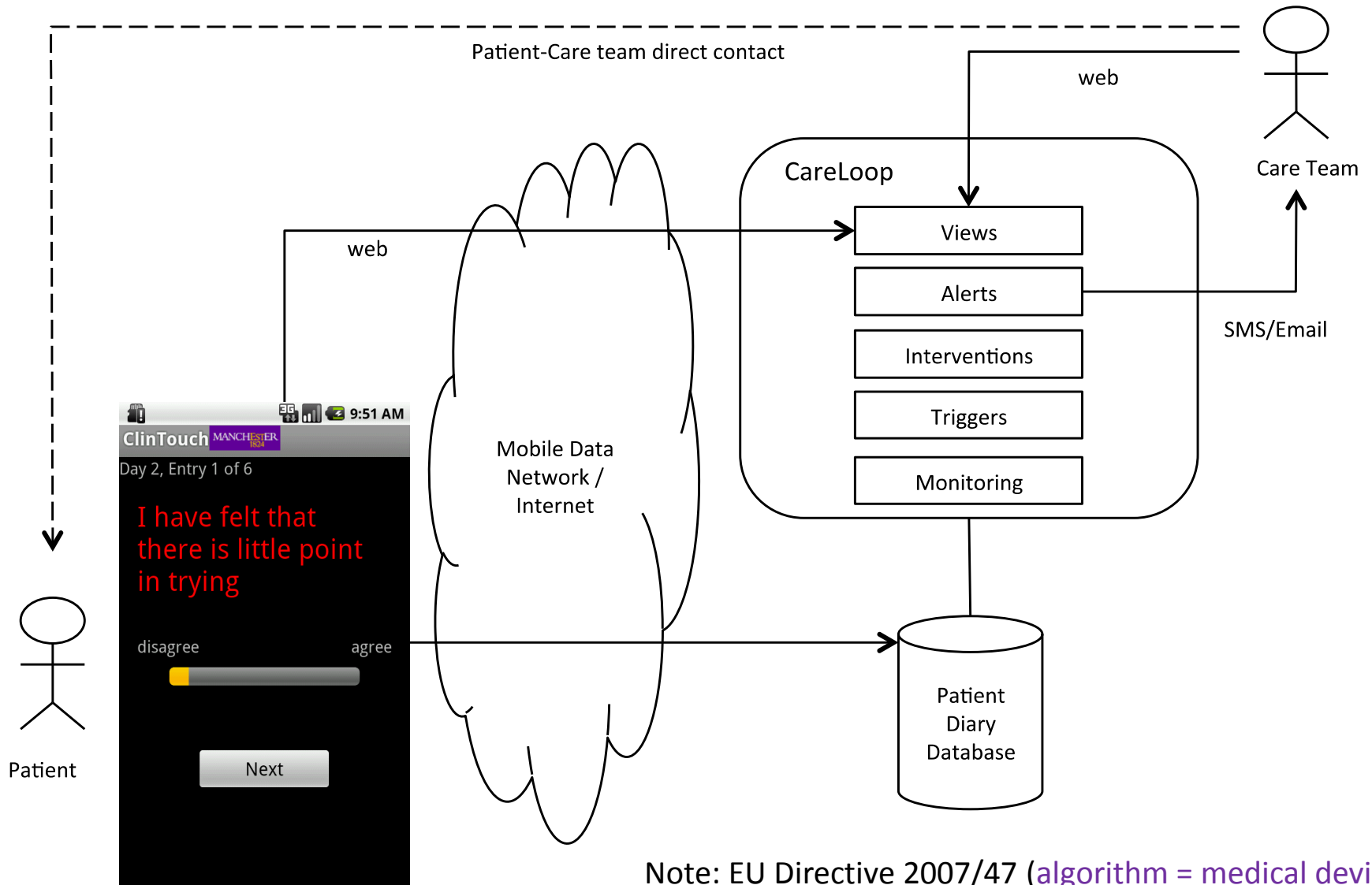


Toward m-Health: n-of-1 Gateway

- Dark areas
e.g. adherence vs. antibiotic resistance
- Current signal
“how did you get on with your medicine?...”
- m-Health
 - Smartphone app. with drug
 - Quality of life scores
 - Position and acceleration
 - Watch/plaster
 - Temperature
 - Pulse

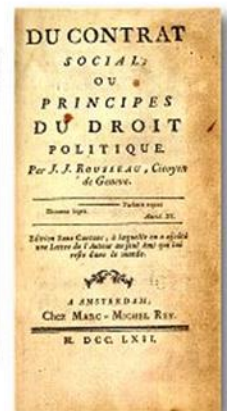
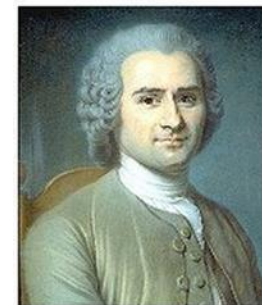


Med-App Ecosystem: Reducing Schizophrenia Relapse



Conclusion

- Current healthcare evidence predicts less than 30% of true outcomes
- Smart networking of data, models and expertise across environments is key to health system adaptation
- Payer, provider, industry and academia need to co-adapt in a social machine of R&D



Rousseau: "Social Contract"
Pre-competitive alliance framework