Building a ***search engine*** to find ***environmental*** and ***phenotypic factors*** associated with ***disease and health***

Chirag J Patel

Northeast Big Data Innovation Hub Workshop

02/24/17

HARVARD MEDICAL SCHOOL
DEPARTMENT OF Biomedical Informatics

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@chiragjp
www.chiragjpgroup.org

$$P \equiv G + E$$

Phenotype

P = G + E

Type 2 Diabetes
Cancer
Alzheimer's
Gene expression

Phenotype *Genome*

P = G + E

Type 2 Diabetes
Cancer
Alzheimer's
Gene expression

Variants

Phenotype *Genome* *Environment*

P = G + E

Type 2 Diabetes
Cancer
Alzheimer's
Gene expression

Variants

Infectious agents
Nutrients
Pollutants
Drugs

G

We are great at ***G*** investigation!

over **2400**
Genome-wide Association Studies (GWAS)
https://www.ebi.ac.uk/gwas/

E: ???

Nothing comparable to elucidate ***E*** influence!

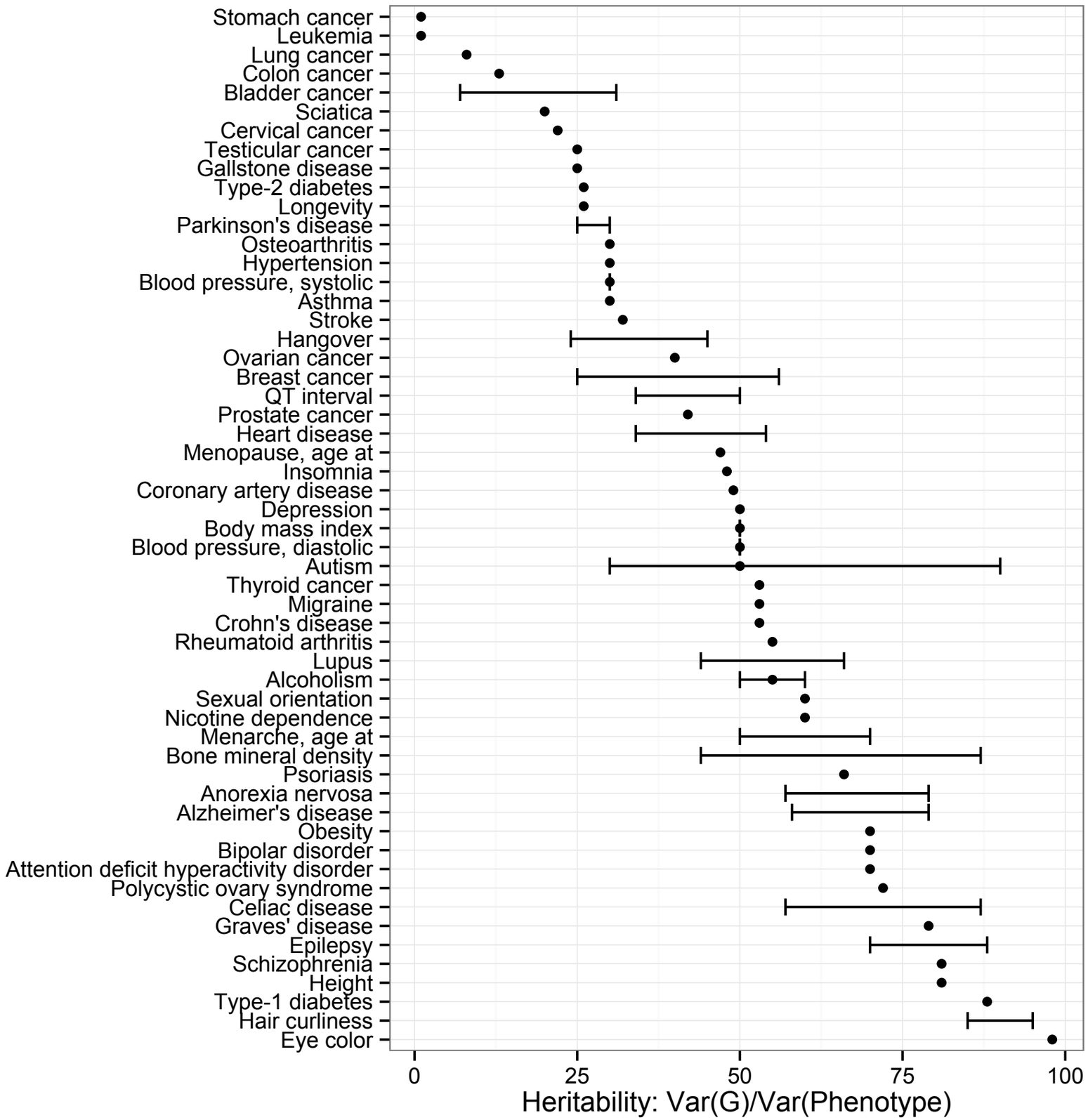
We lack high-throughput methods
and data to discover new ***E*** in ***P…***
until now!

Heritability (H^2) is the range of phenotypic variability attributed to genetic variability in a population

$$H^2 = \frac{\sigma^2_G}{\sigma^2_P}$$

Indicator of the proportion of phenotypic differences attributed to **G**.

G estimates for burdensome diseases are **low and variable:** massive opportunity for ***E*** *discovery*



Source: SNPedia.com

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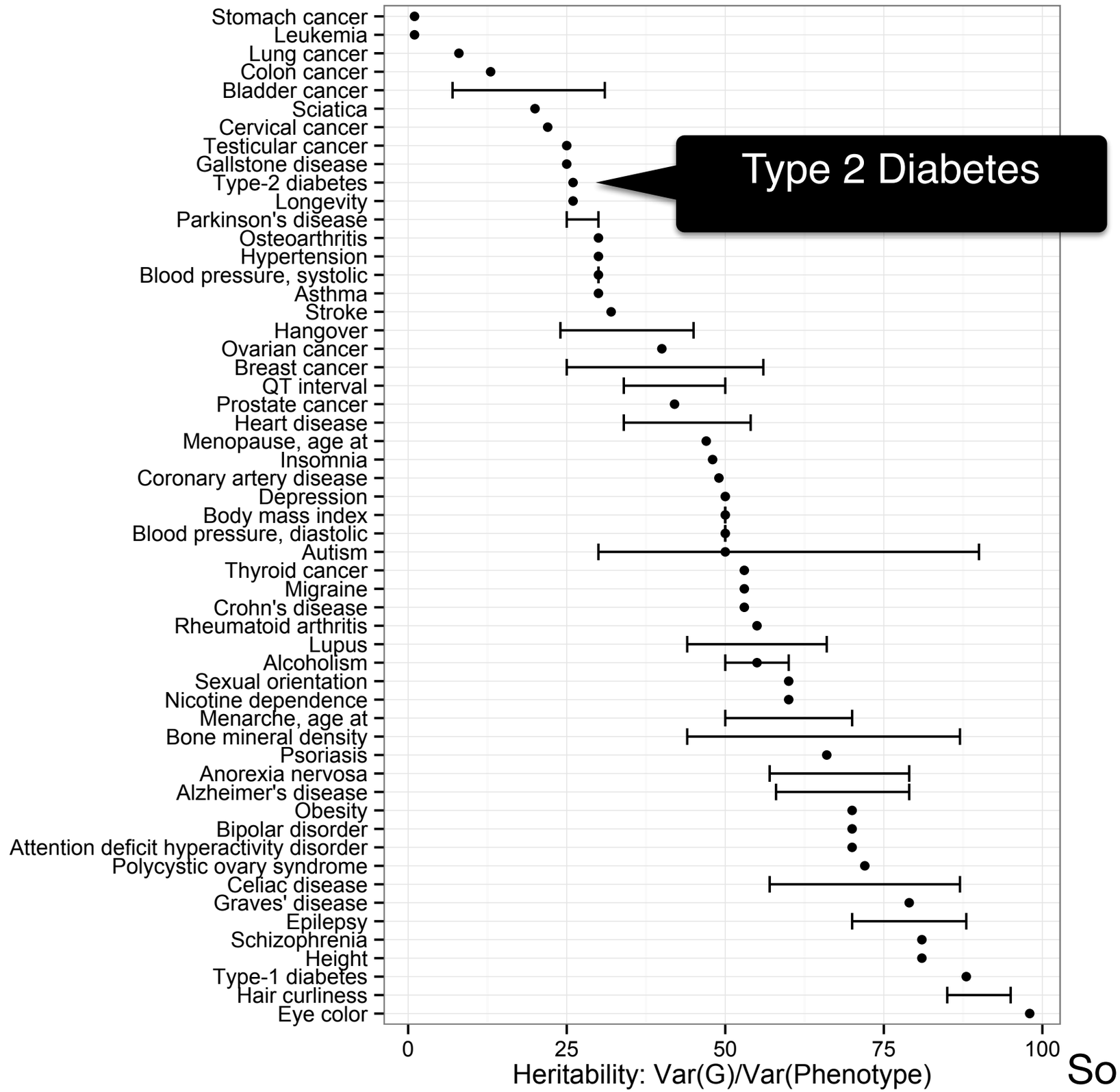

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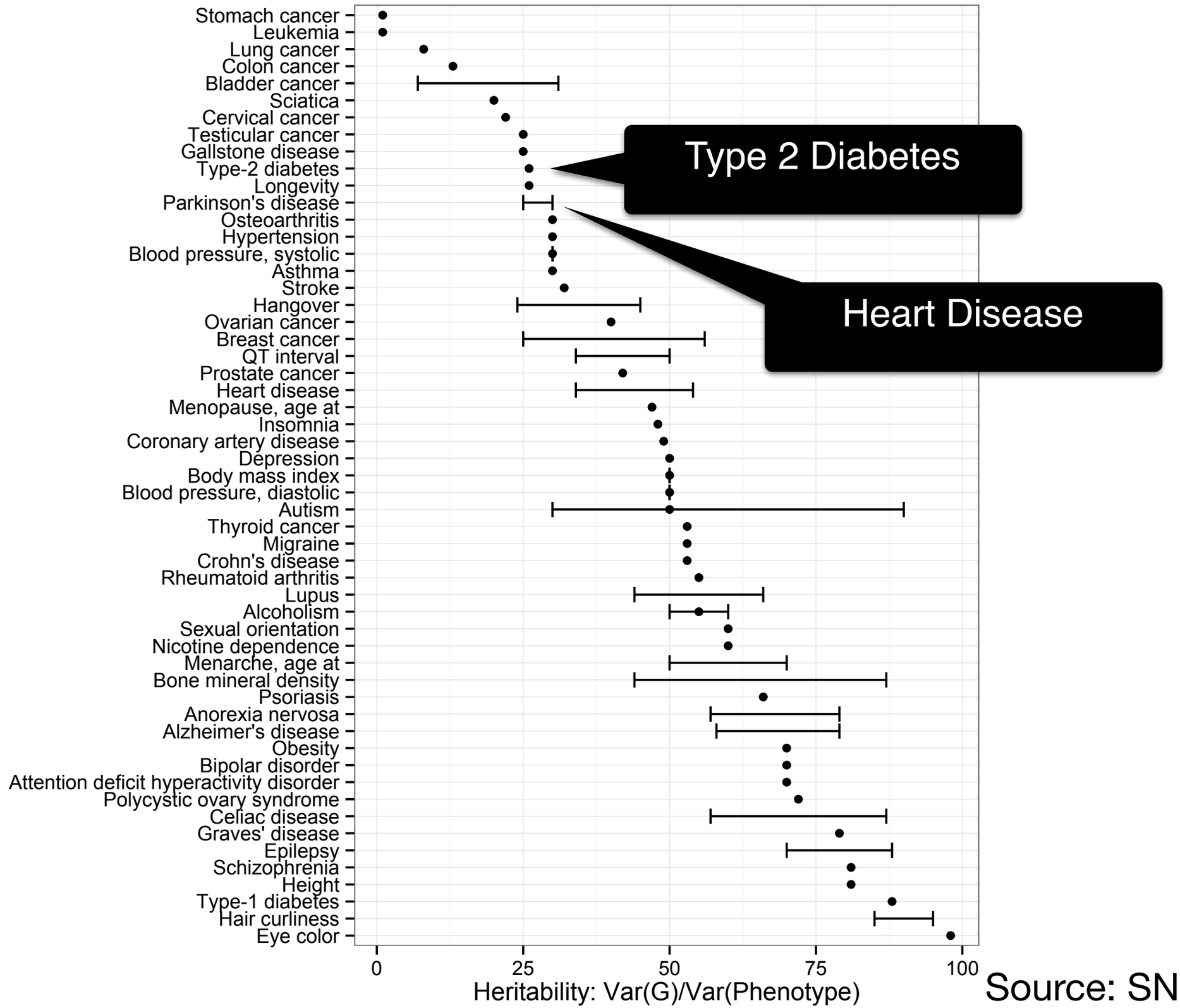

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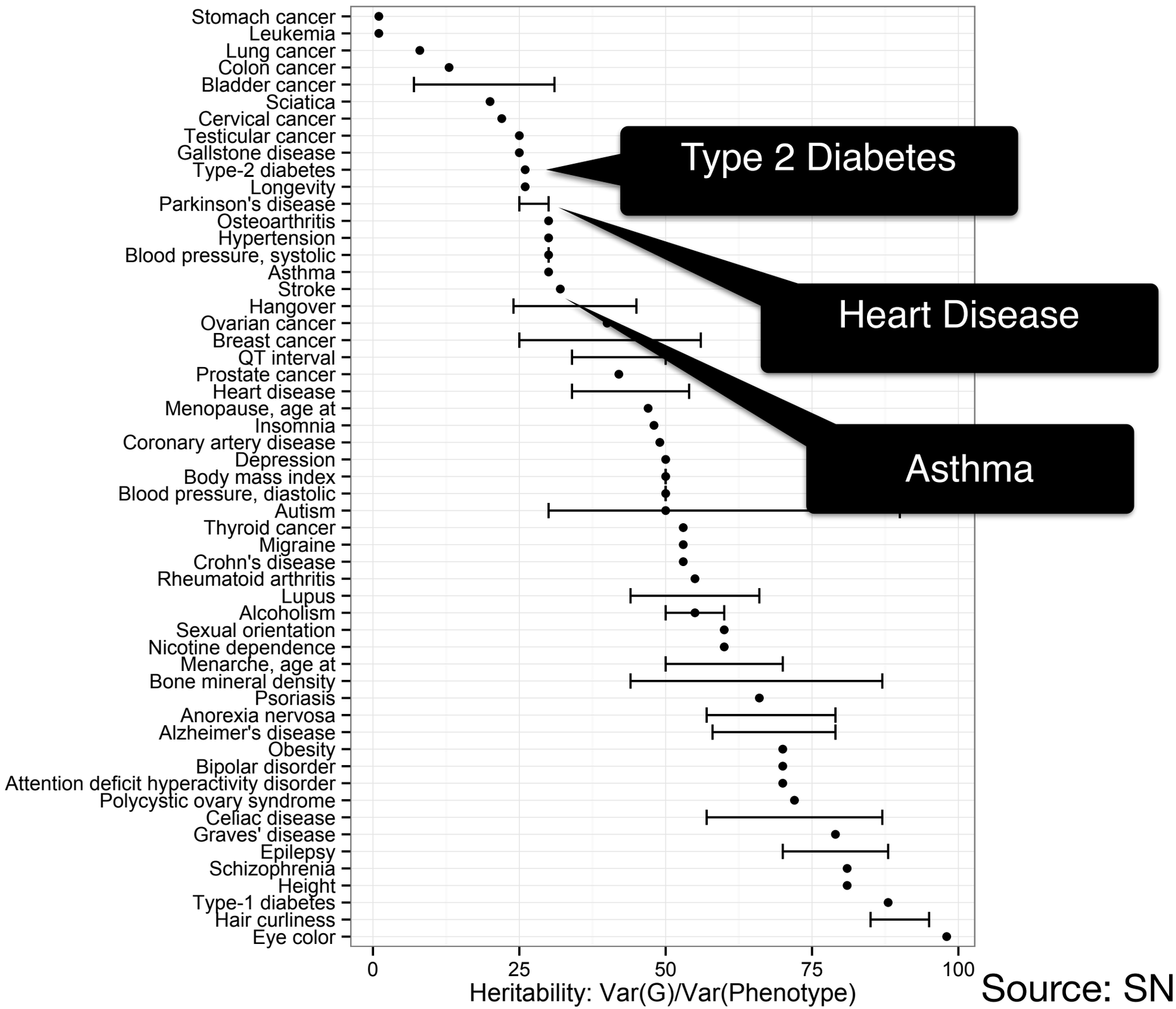

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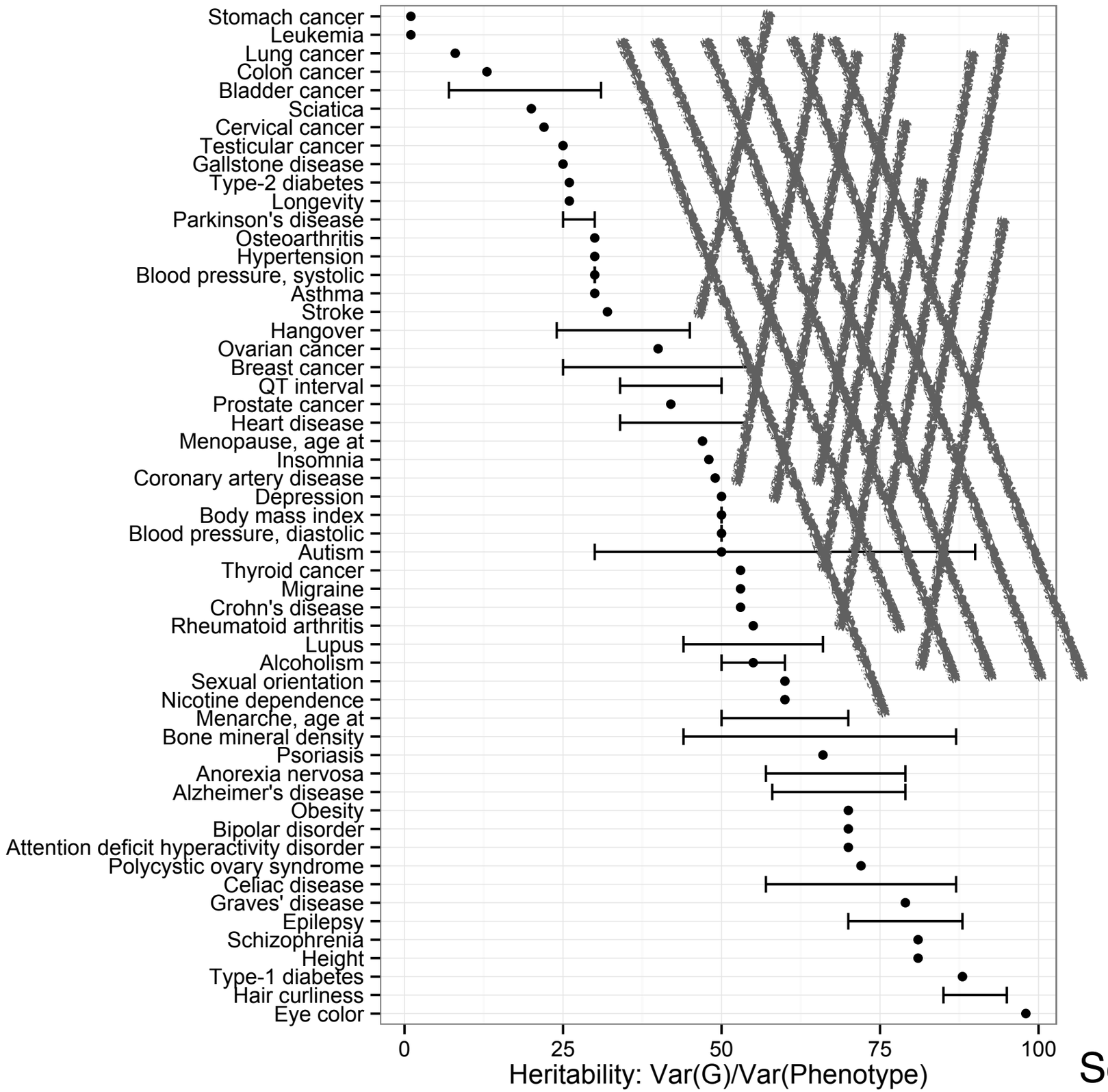

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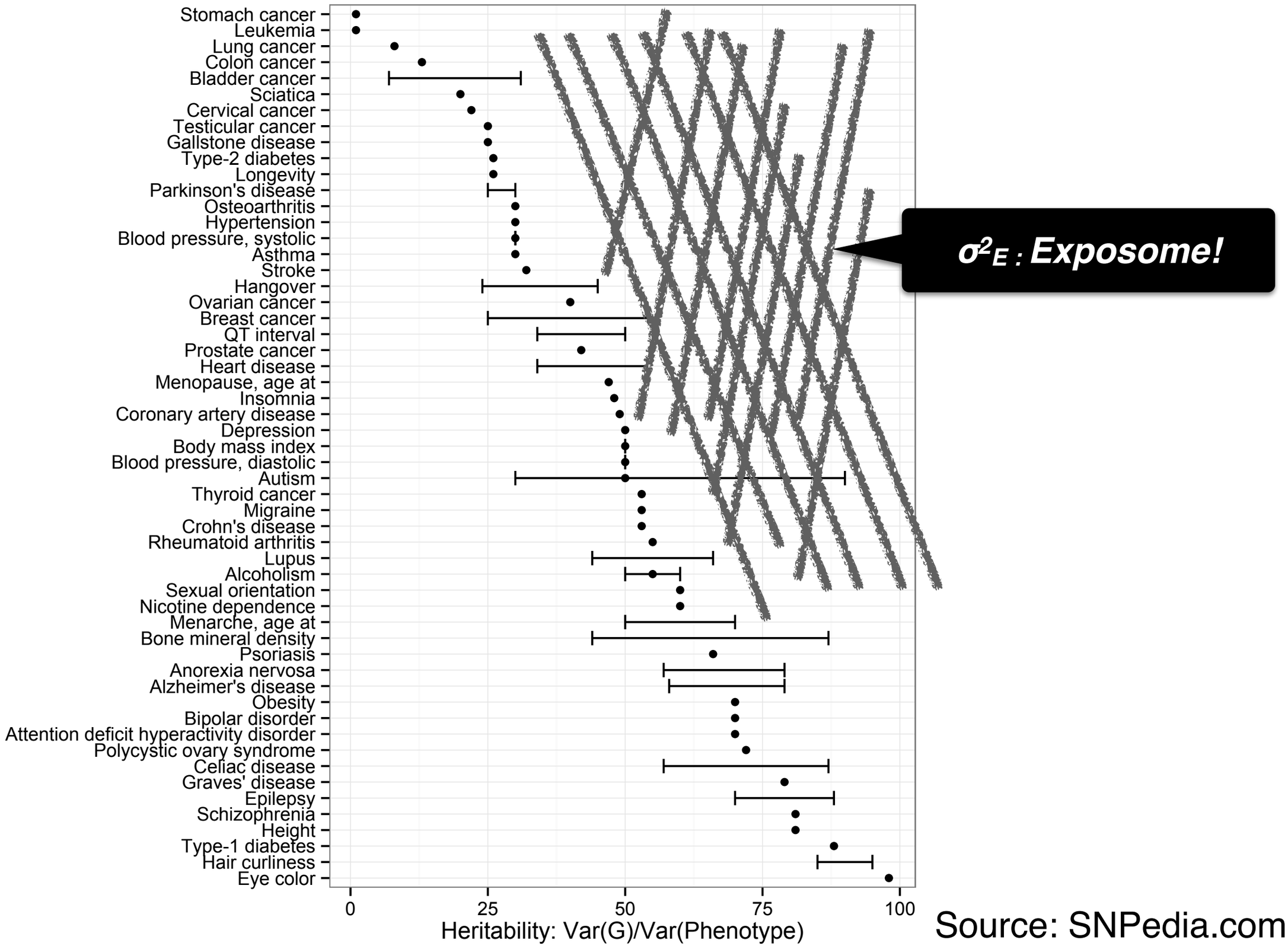

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How can we drive **discovery** of
environmental factors (**E**) in disease phenotypes (**P**)?

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Enhance **accessibility** of **clinical and environmental data,**
and **analytic artificial intelligence tools!**

Enhance **accessibility** of **large open data** and **tools** to drive **discovery** of environmental factors (**E**) in disease phenotypes (**P**)

Noémie Elhadad, PhD
Columbia

Greg Cooper, MD, PhD
Pittsburgh

Chirag Patel, PhD
Harvard

Vasant Honavar, PhD
Penn State

Where do we get disease (***P***) data?

wearable.com

Where do we get disease ***P*** data?

Health record data from your doctor!

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- Longitudinal data on ***millions*** of patients

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- Longitudinal data on ***millions*** of patients
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- Sitting there in institutional IT infrastructure
- ***OHDSI*** provides a ***unified model*** to **access** data ***across institutions***, *enhancing the scientific process*!

OHDSI

OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Noémie Elhadad, PhD
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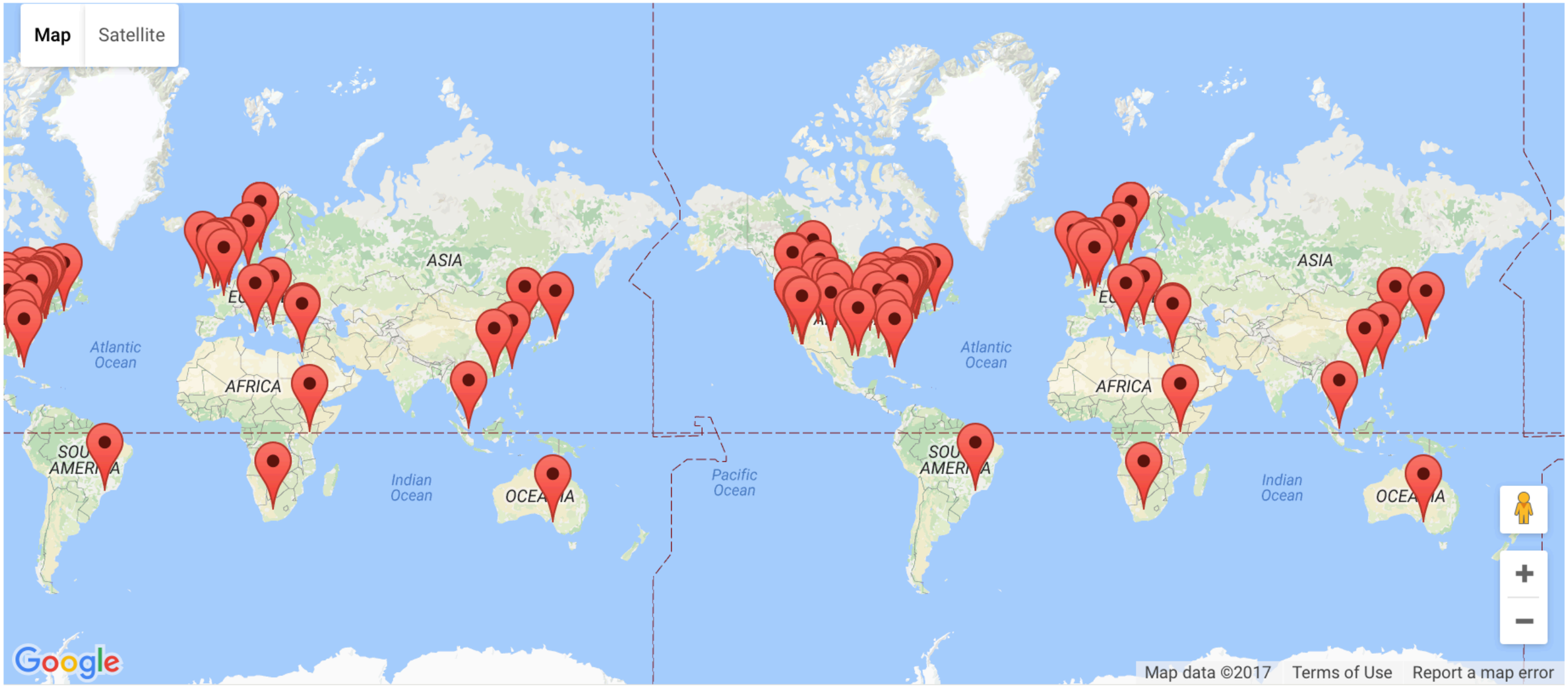
Capitalize on ***digitalized health record data***
(from around the world)!
High-powered dataset(s) for discovery.



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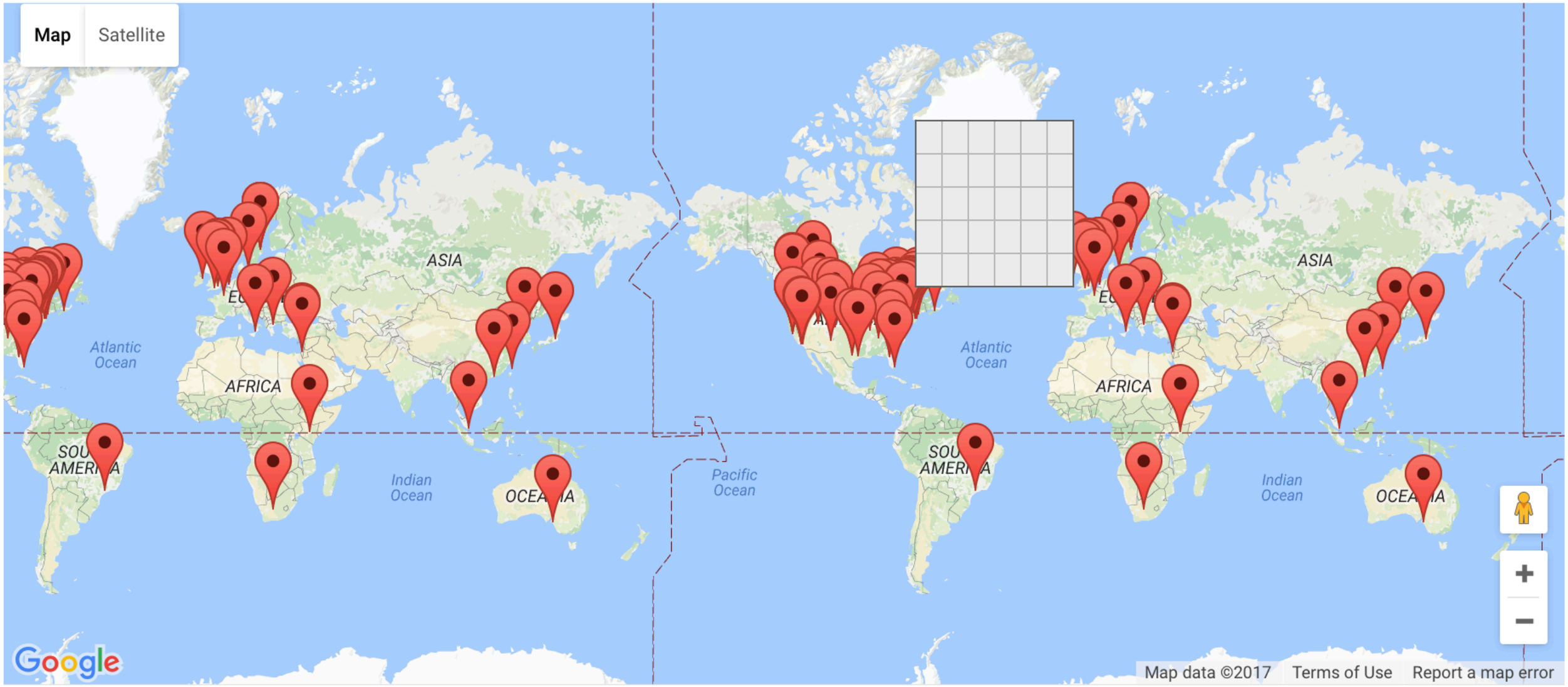

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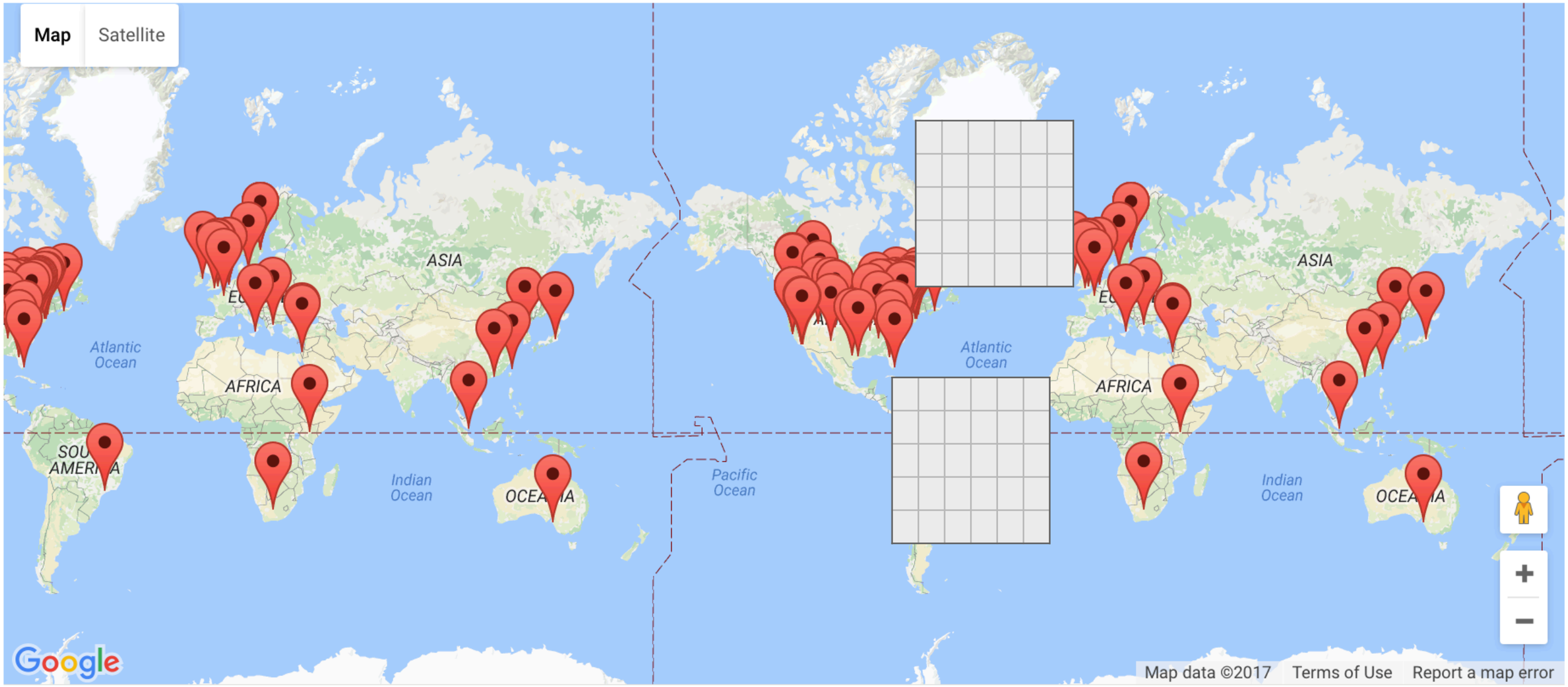

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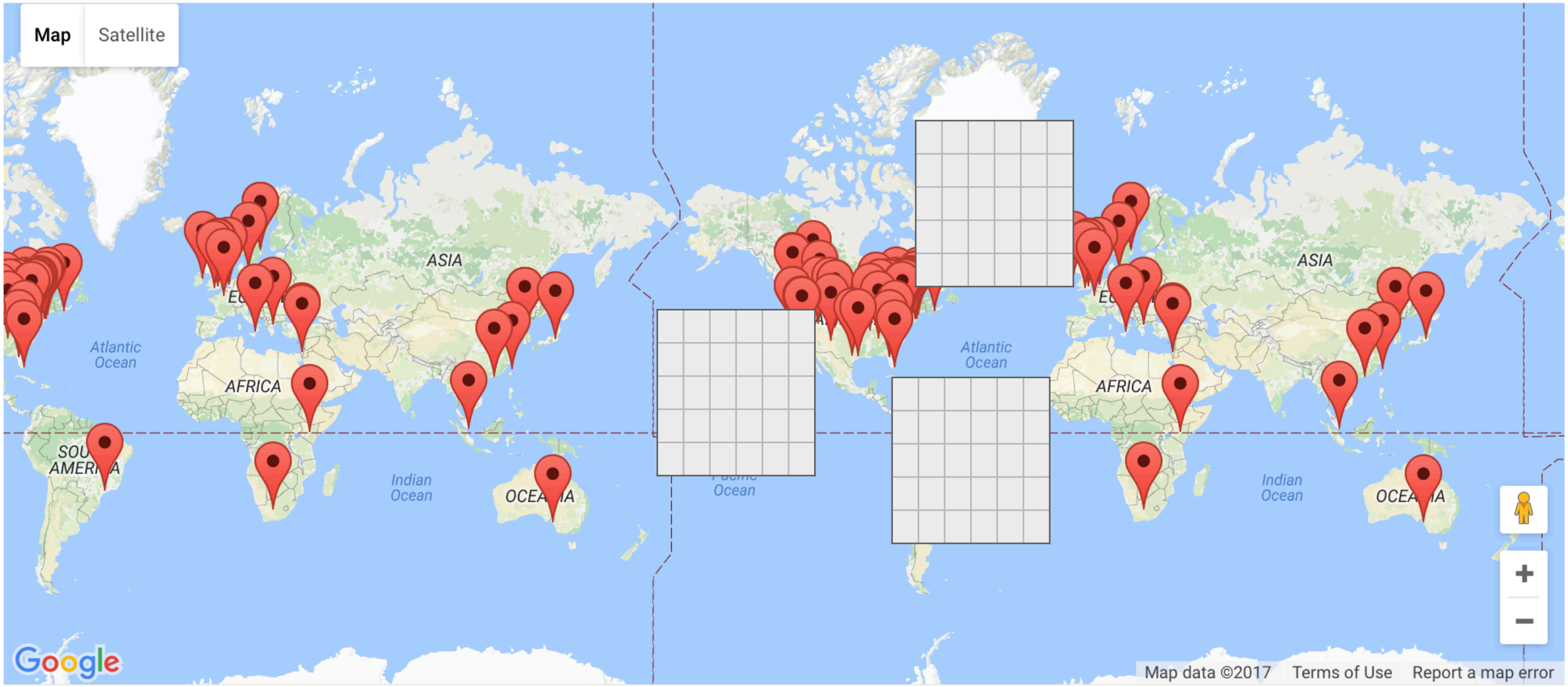

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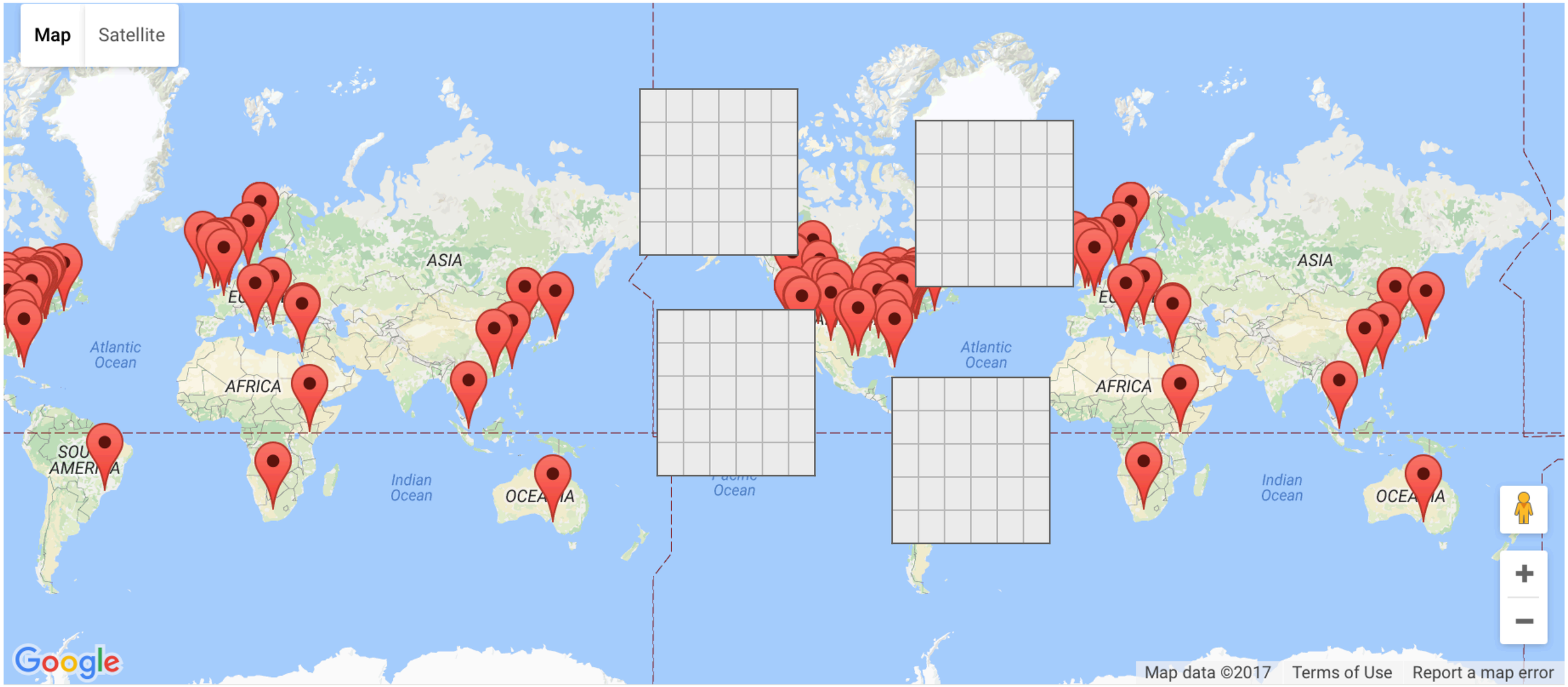

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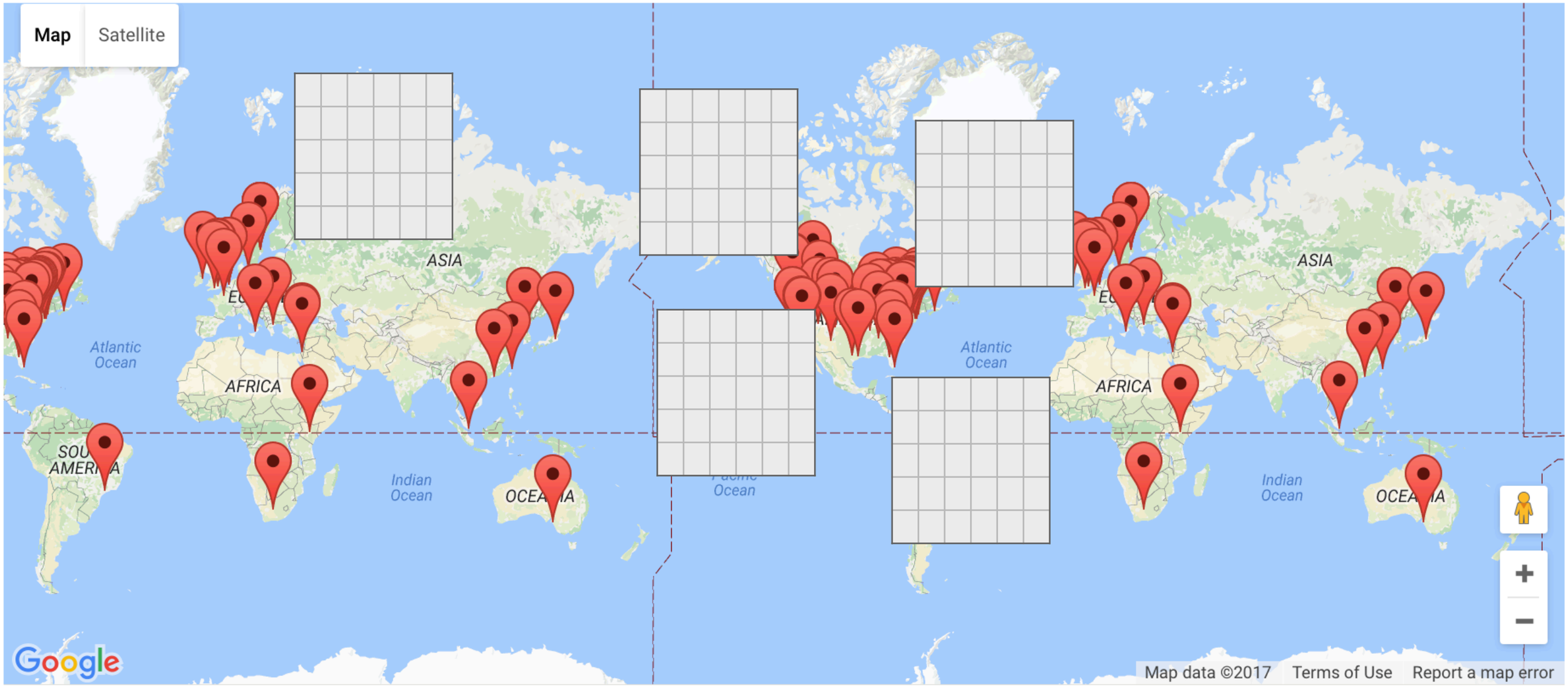

Where do we get ***environmental (E)*** data?

Examples of sources of disparate ***external*** exposome datasets available in the ***Exposome Data Warehouse***

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  - *CDC* Wonder, *USDA* Food Atlas

A key challenge:
mashing up ***Exposome Data Warehouse*** with patient data from ***OHDSI***

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OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

```
home zipcode
encounter time
```

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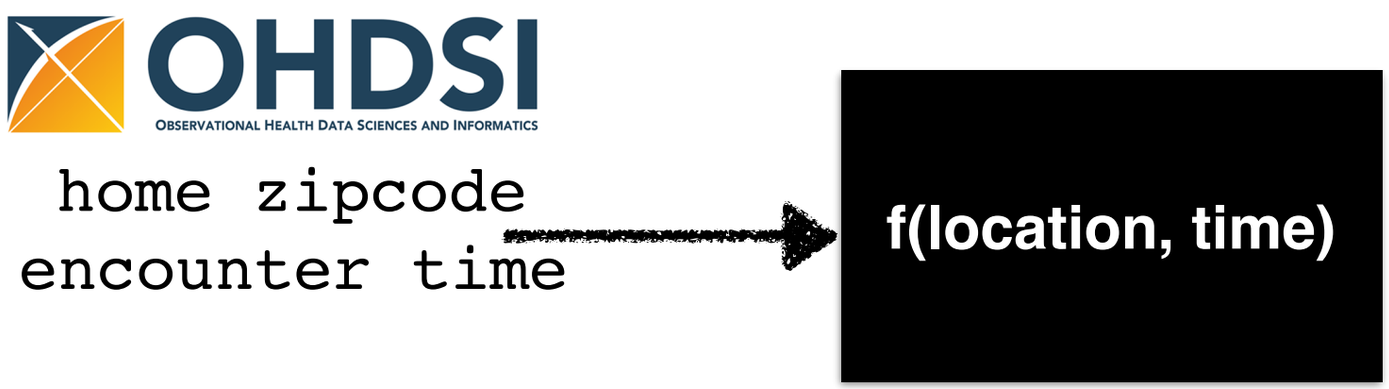

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OHDSI
Observational Health Data Sciences and Informatics

home zipcode
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→ **f(location, time)**

EPA *AirData*

American Community Survey

NOAA Climate

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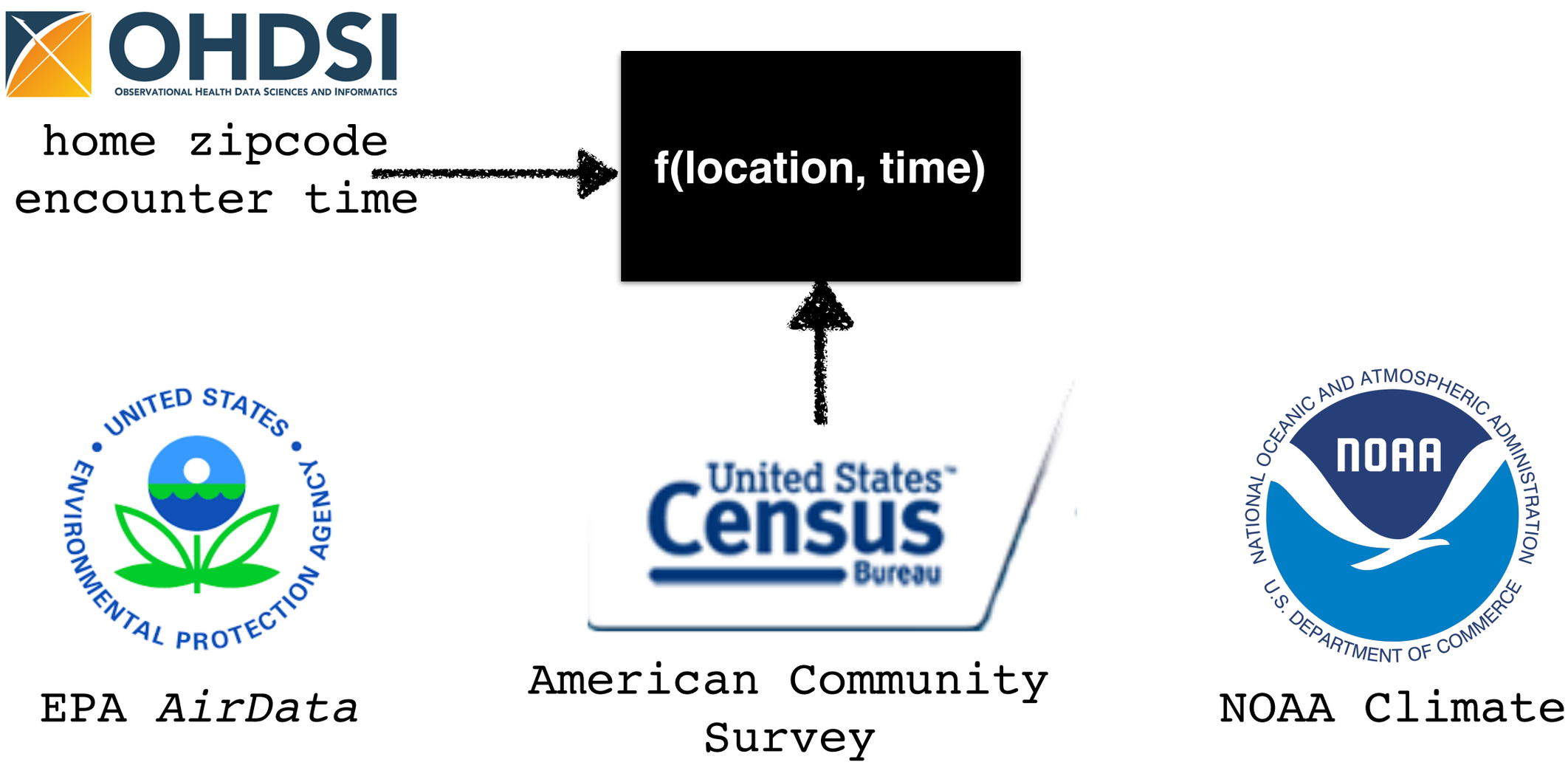

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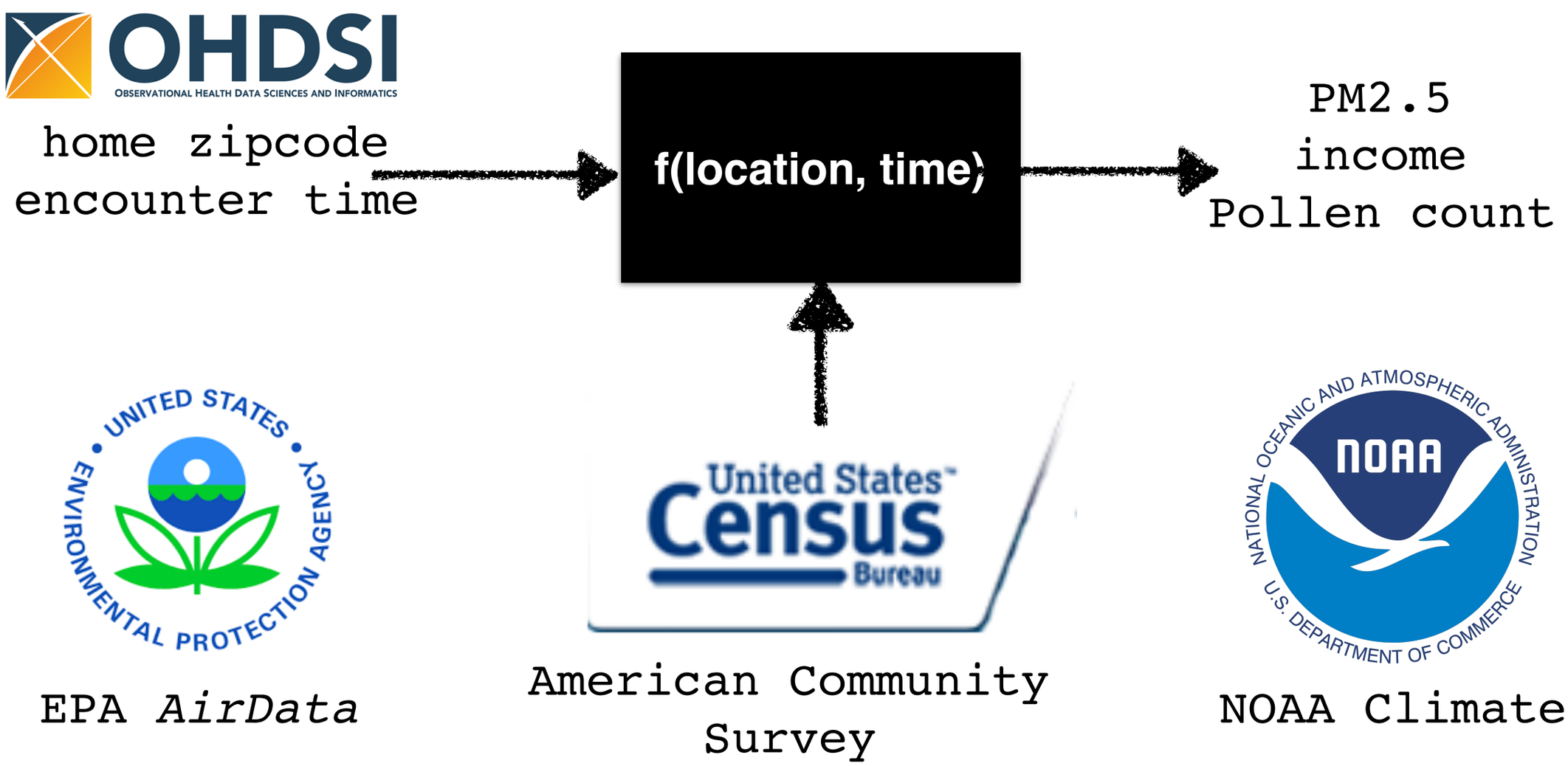


OHDSI

millions of patients

	age	**sex**	**E?**	***Time(E)***	***zip***
individual$_1$	21	F	no	12/11/2015	02215
individual$_2$	35	M	yes	1/1/2016	95376
individual$_3$	75	M	yes	3/5/1998	02124
..					
..					
..					
..					
...					
individual$_n$					

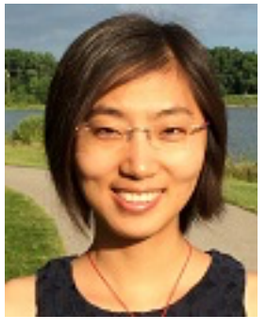
millions of patients

	OHDSI					EPA		NOAA		Census	
	age	**sex**	**E?**	***Time(E)***	***zip***	**Pb**	**PM2.5**	**Temp**	**Wind**	**hh income (K)**	**gini index**
$individual_1$	21	F	no	12/11/2015	02215	23	50	20	0	50	0.20
$individual_2$	35	M	yes	1/1/2016	95376	10	23	70	15	100	0.1
$individual_3$	75	M	yes	3/5/1998	02124	0	3	55	30	30	0.50
..											
..											
..											
..											
...											
$individual_n$											

Will it work? yep!

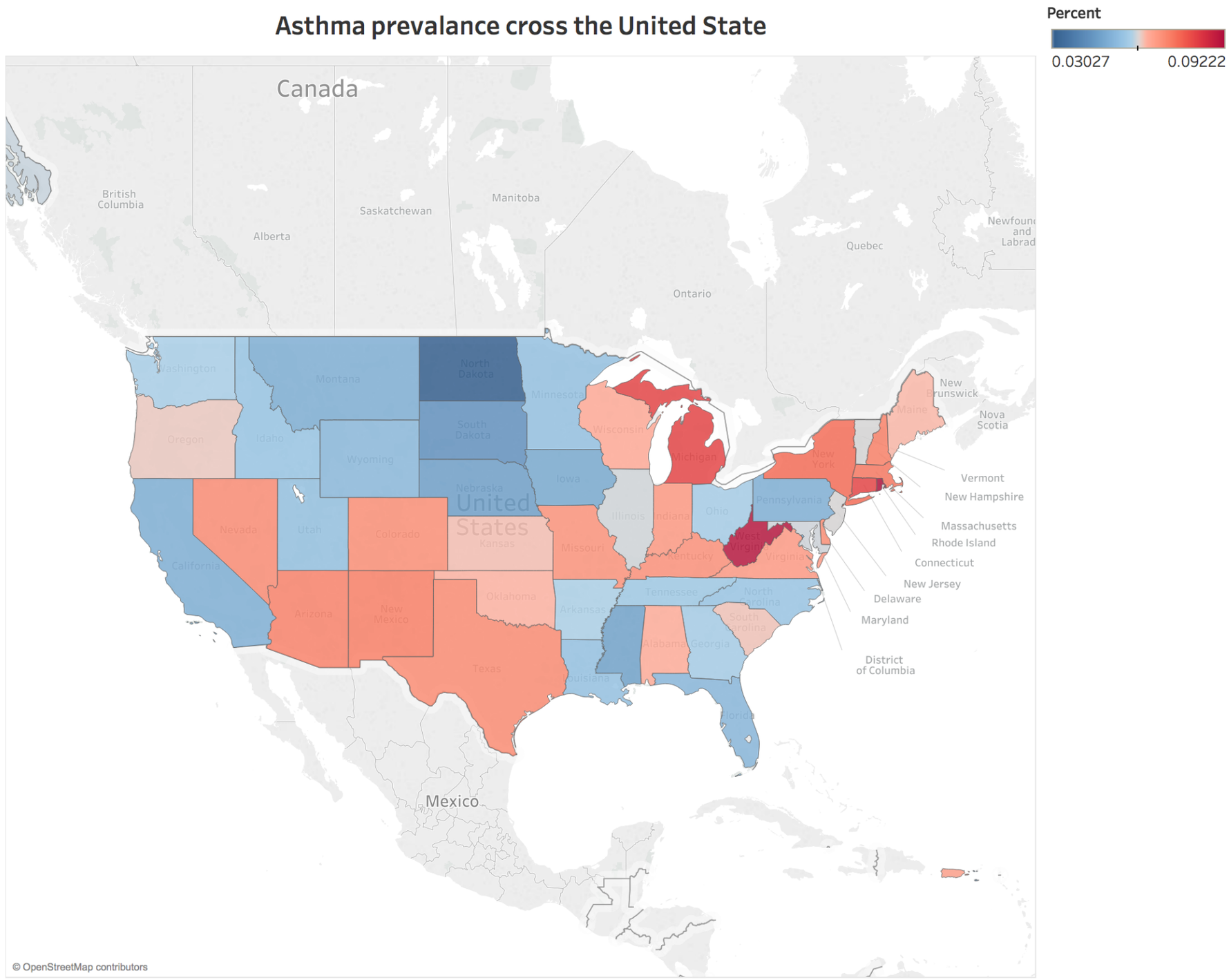
Does temperature (and weather) influence asthma-related pediatric ER visits?

- **Children <= 17 y/o** with >=1 ICD9 code corresponding to 493.*
- **N=56K, >84K ER visits**
- Weather station data
  - (daily **temperature**, **wind**, **humidity**)
- **Case-crossover design** (only investigated cases)



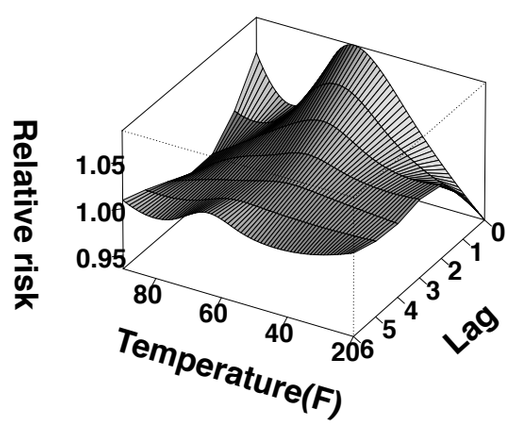
Yeran Li, PhD (MS, HSPH)
Chirag Lakhani, PhD (HMS)
Yun Wang, PhD (Post-doc, HSPH)

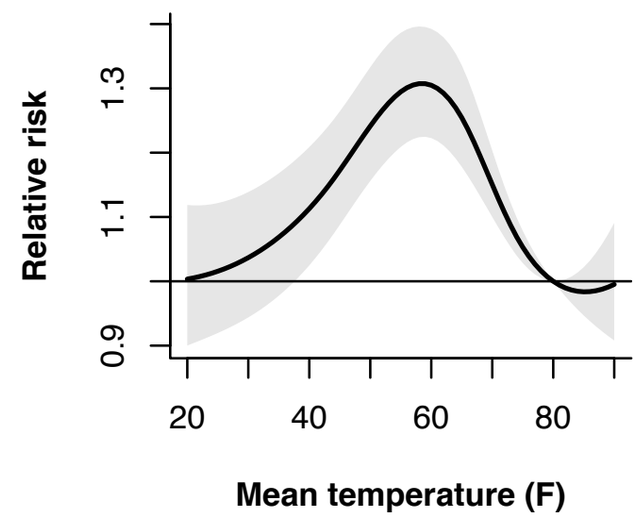
Prevalence of asthma attack varies across the US

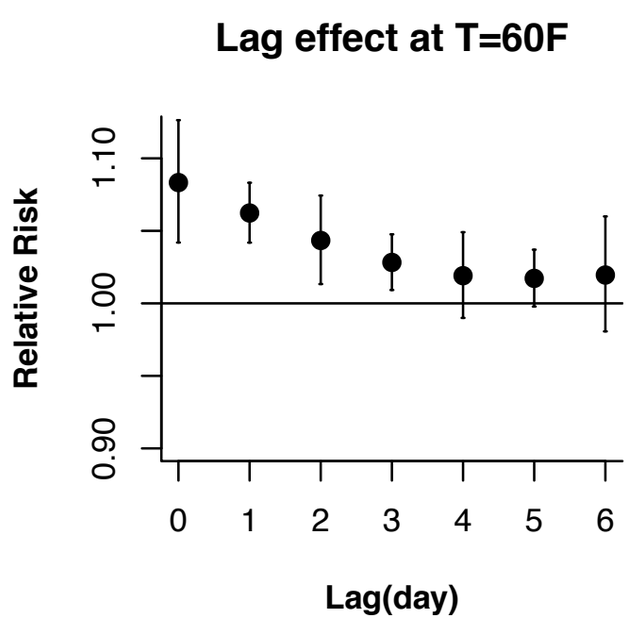


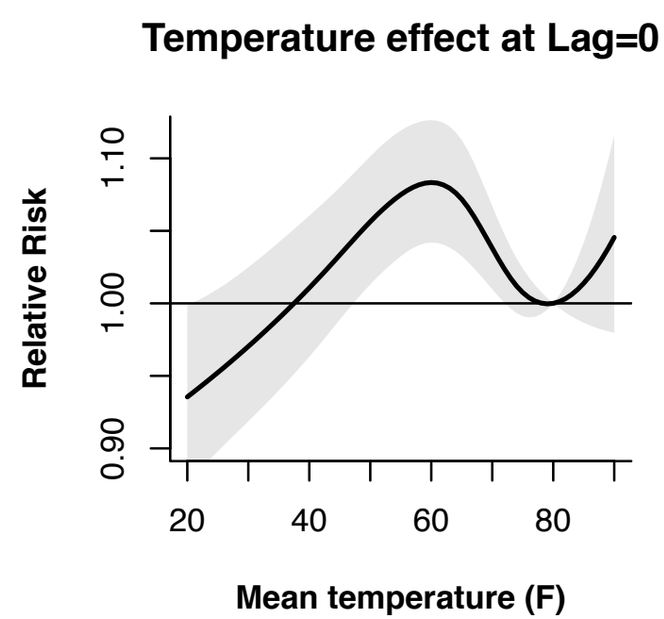
Does temperature influence asthma ER visits?: *yes*!

Relative risk of asthma attack by mean temperature

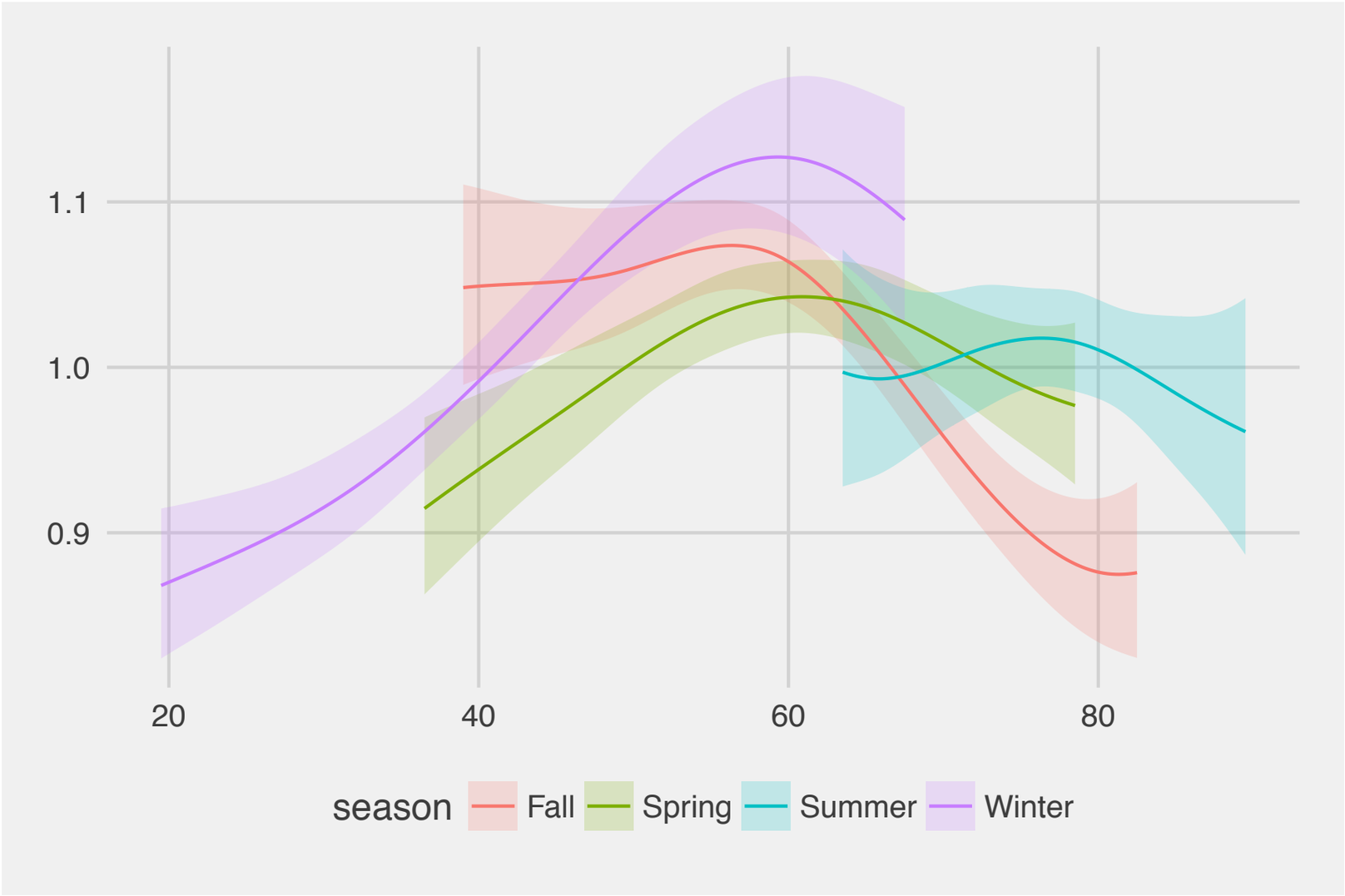




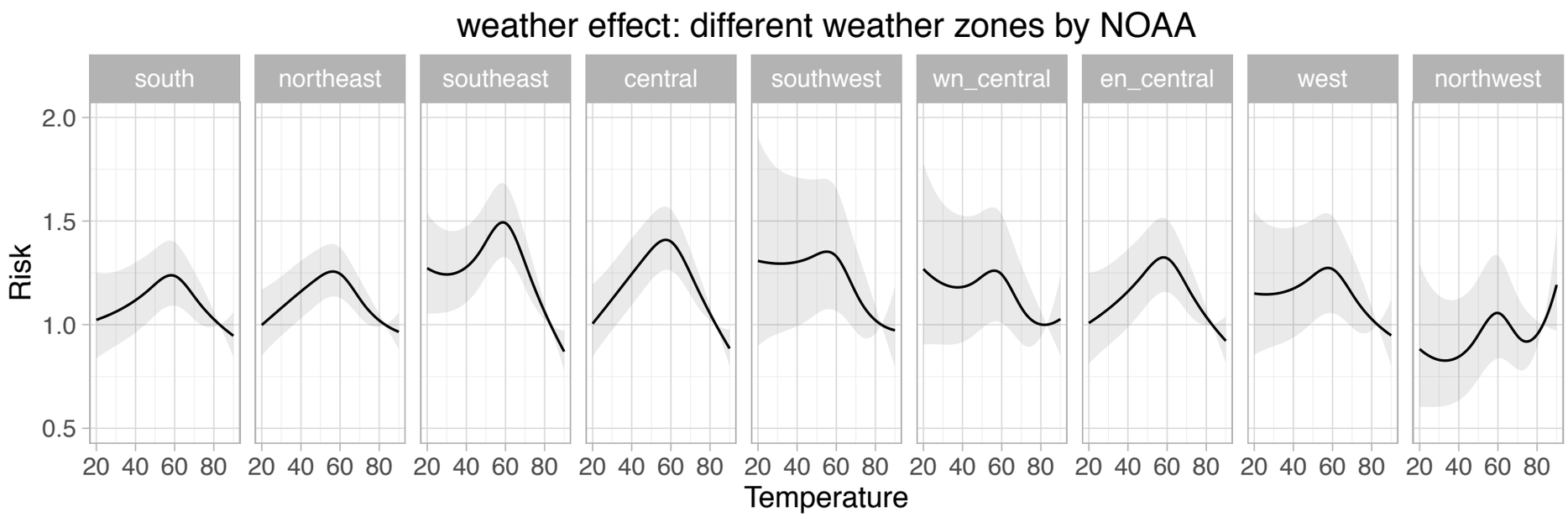


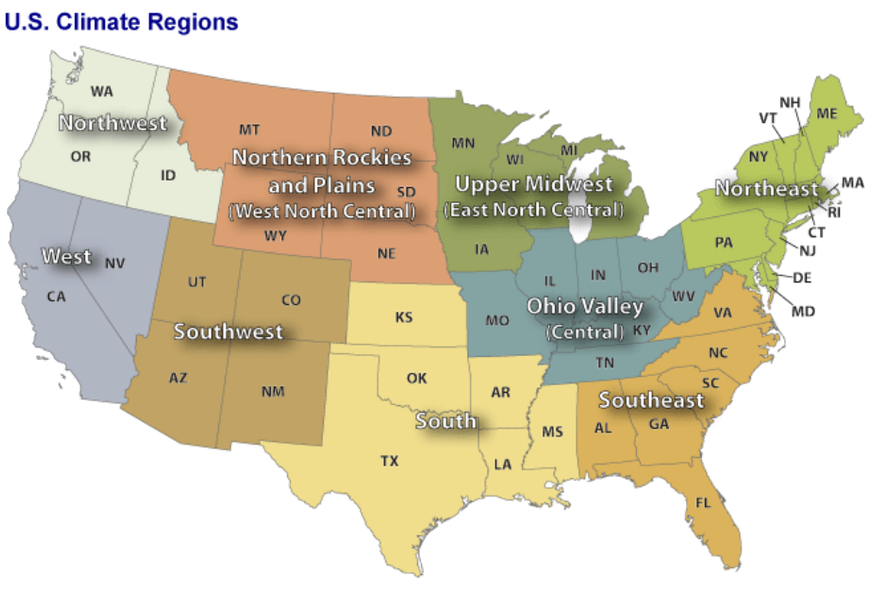


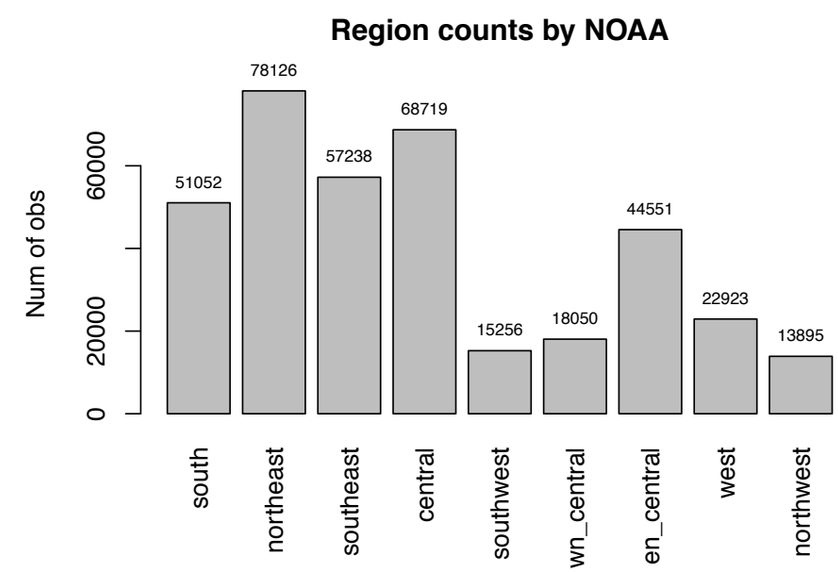
Rates of asthma attacks depend on season?: ***yes!***



Rates of asthma attacks dependent on region?: ***yes!***







https://www.ncdc.noaa.gov/monitoring-references/maps/us-climate-regions.php

weather.com

The Weather Channel | 47 ° New York, NY | 53 ° Brookline Village,... | US | °F | Search city, zip or place

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Today | Hourly | 5 Day | 10 Day | Weekend | Maps | Monthly | More Forecasts

SPECIAL WEATHER STATEMENT Until 10:00am , Thu Feb 23 — 2

NEW YORK, NY
as of 9:28 am EST

47°
CLOUDY
feels like **46°**
H **65°** / L **53°**
UV Index **1 of 10**

Snowstorm Underway: Blizzard Conditions Expected

RIGHT NOW

Wind	SW 4 mph
Humidity	90%
Dew Point	45°
Pressure	29.90 in ↓
Visibility	4.0 mi

RADAR | CLOUDS | RADAR & CLOUDS | WEATHER IN MOTION →

NEXT 36 HOURS

HOURLY → | 10 DAYS →

TODAY	TONIGHT	FRI	FRI NIGHT	SAT
AM CLOUDS/PM SUN				
HIGH 65°	LOW 53°	HIGH 64°	LOW 53°	HIGH 59°
20%	40%	10%	10%	90%

Cloudy skies early, then partly cloudy this afternoon. High around 65F. Winds light and variable.

WIND	HUMIDITY	UV INDEX	SUN
SSW 5 mph	72%	3 of 10	↑ 6:38 am ↓ 5:40 pm

PLAN YOUR DAY

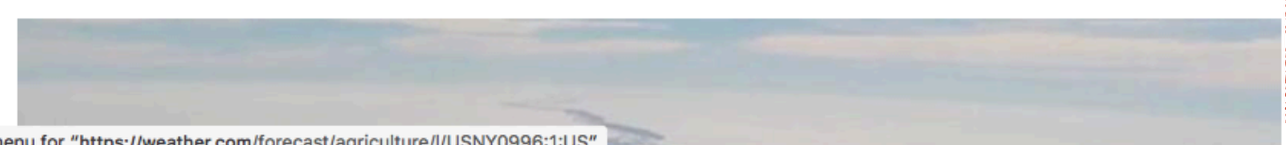
VERY GOOD — **Pollen/Breathing/Mold**
VIEW ALL ALLERGENS →
Presented by Flonase

Out of Growing Season
FARMING FORECAST →
Powered by Ram Trucks

Good Road Conditions

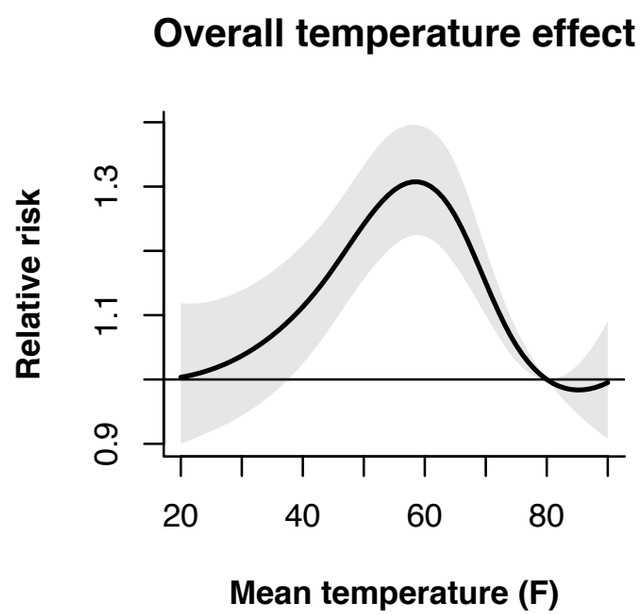
WEATHER HEADLINES

VIEW ALL →



Display a menu for "https://weather.com/forecast/agriculture/l/USNY0996:1:US"

Does temperature (and weather) influence asthma-related ER visits in kids?: the tip of the iceberg!



What other scientific questions?

- what is influence of **pollen**?
- what is the influence of **air pollution**?
- what about **adults**?

Can we replicate the analysis?

- different **populations**
- using different **data**
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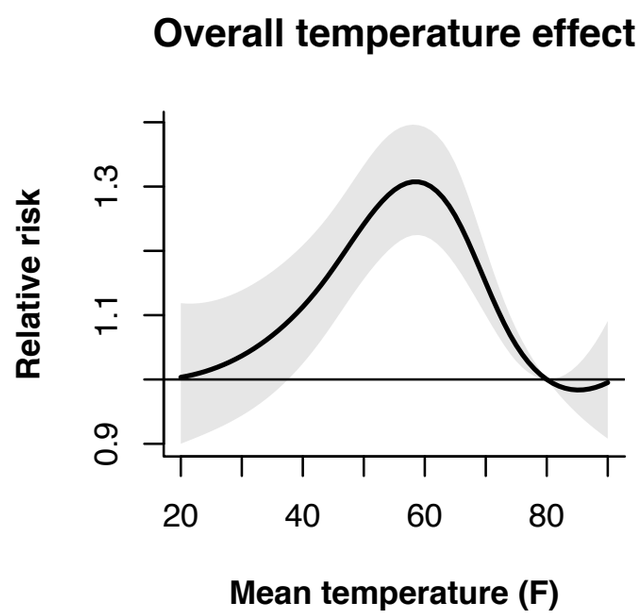

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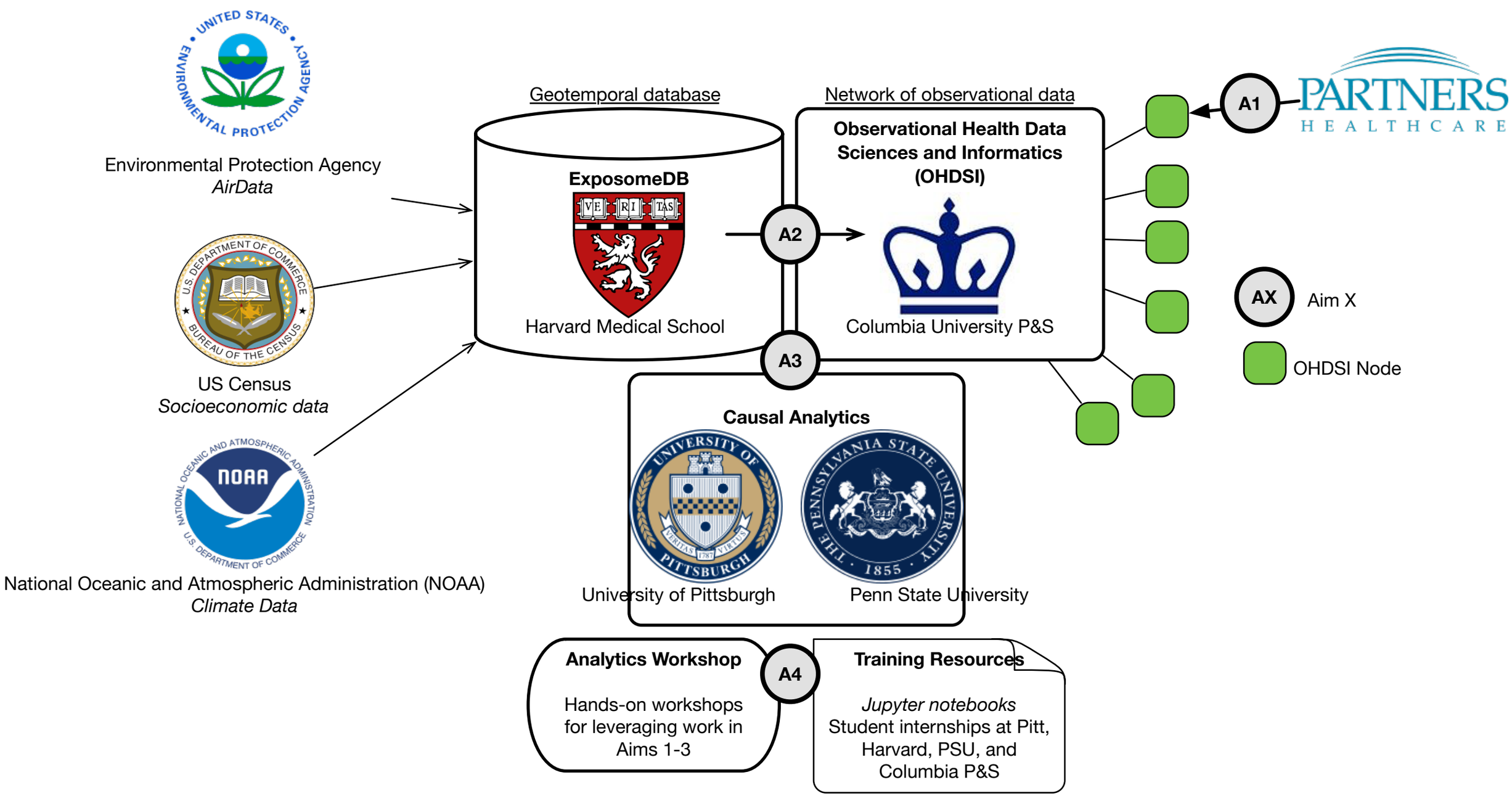
OHDSI
OBSERVATIONAL HEALTH DATA SCIENCES AND INFORMATICS

Integrating the ***ExposomeDB*** with ***OHDSI*** and causal modeling tools to drive and demonstrate discovery.



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What is the effect of ***air pollution*** levels in ***disease*****?**

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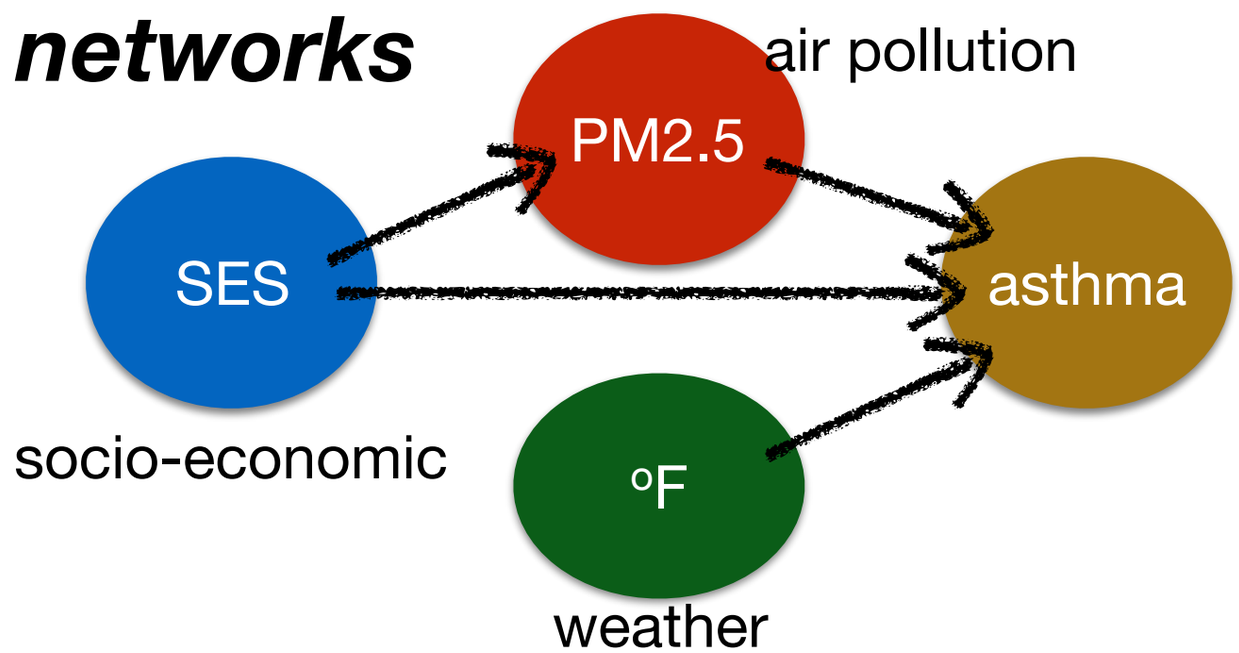
What pharmaceutical **drugs** lead to **adverse health outcomes**?

We will harness tools in machine learning extract ***signal from noise***!

bayesian networks



Greg Cooper, MD, PhD
Pittsburgh

case-crossover

Systematic assessment of pharmaceutical prescriptions in association with cancer risk: a method to conduct a population-wide medication-wide longitudinal study

Chirag J. Patel[1], Jianguang Ji[2], Jan Sundquist[2], John P. A. Ioannidis[3] & Kristina Sundquist[2]

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Penn State

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Causal Web

our user-friendly web application for performing causal discovery analysis on big data using large memory servers at the Pittsburgh Supercomputing Center. Use this software if you want to quickly try out a causal discovery algorithm or if you have big data that cannot be analyzed on your local hardware.

The software currently includes:

- Fast Greedy Equivalence Search (FGES) for continuous variables
- Fast Greedy Equivalence Search (FGES) for discrete variables
- Greedy Fast Causal Inference (GFCI) algorithm for continuous variables

User guide Web app

Causal Command

a Java library and command line implementation of algorithms for performing causal discovery on big data. Use this software if you are interested incorporating analysis via a shell script or in a Java-based program. The 'Software' button below leads to a comprehensive repository. Choose the 'causal-cmd-x.x.x -jar-with-dependencies.jar' from the downloads list when using this as an executable via the command line or as an API in a Java program.

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User guide Software

Display a menu

http://www.ccd.pitt.edu/tools/

Integrating the ***ExposomeDB*** with ***OHDSI*** and **analytics** to drive and demonstrate discovery **<u>by the community</u>!**

(trainees especially welcome)

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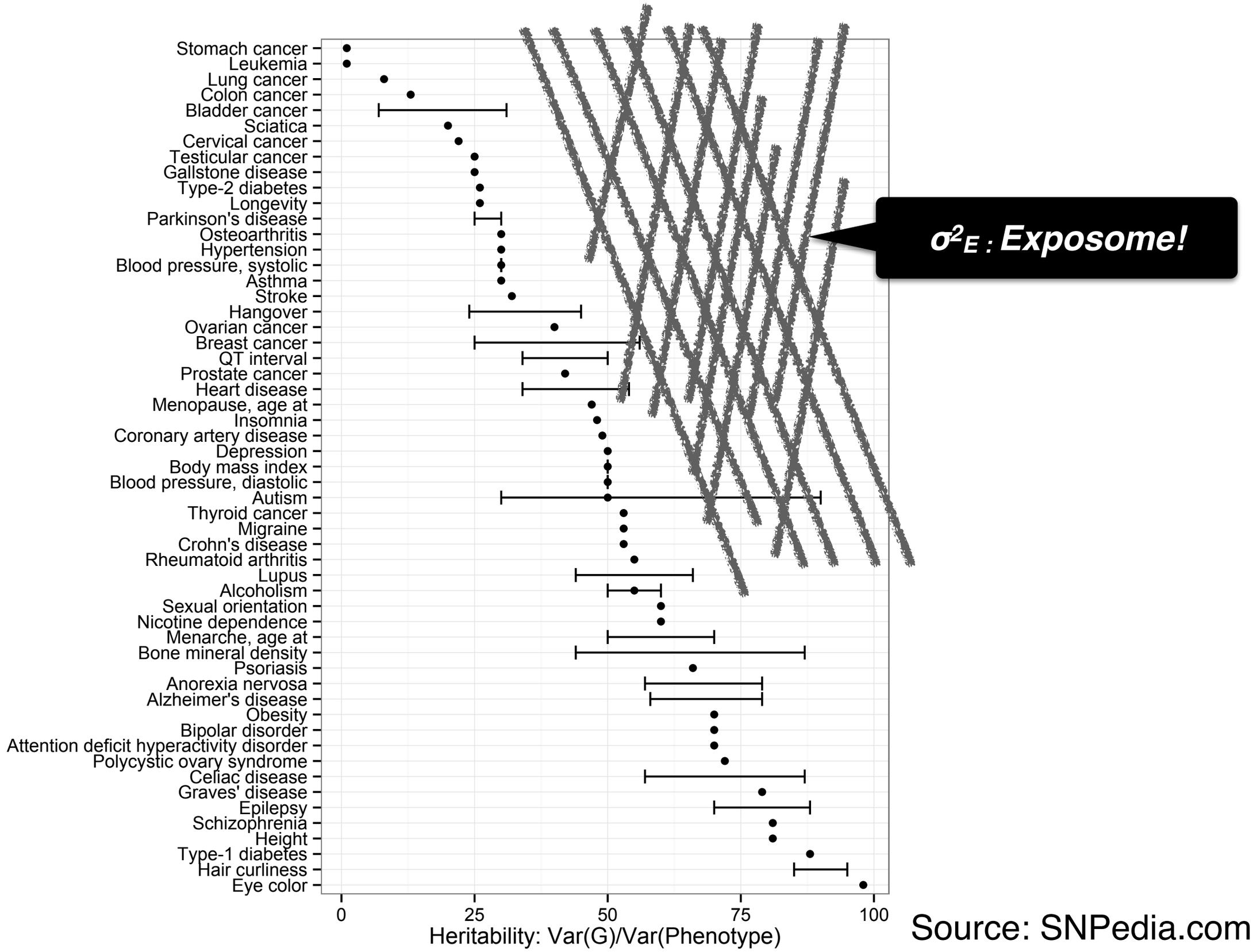
- dissemination of electronic training resources

Many hypotheses are possible to address: useful for **can we build a machine learning predictor to estimate *E*?**



Source: SNPedia.com

Thanks

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NIEHS National Institute of Environmental Health Sciences

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