

Data analytics to enable ***X-wide Association Studies (XWASs)***

Chirag J Patel

(with Nam Pho, Jake Chung, and Arjun Manrai)

ISEE pre-conference tutorial, part 1

Ottawa, Canada

8/26/18



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DEPARTMENT OF
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XWAS tutorial in R markdown

(R code)

Freely available exposome data for your research
(NHANES: ~40,000 individuals and 1,000 variables)

Materials for teaching and demonstration

Resources Index (for today's session)

<http://bit.ly/xwas> with nhanes

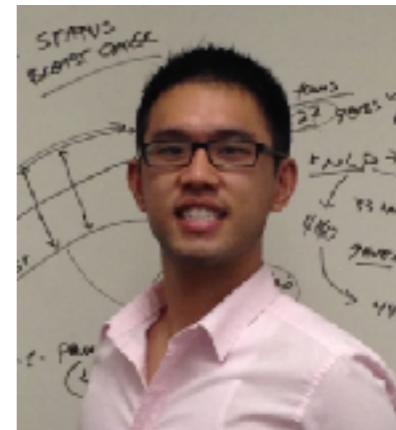
Please let us know if you are using the resources
(or provide feedback)!

Chirag



  @chiragjp

Nam



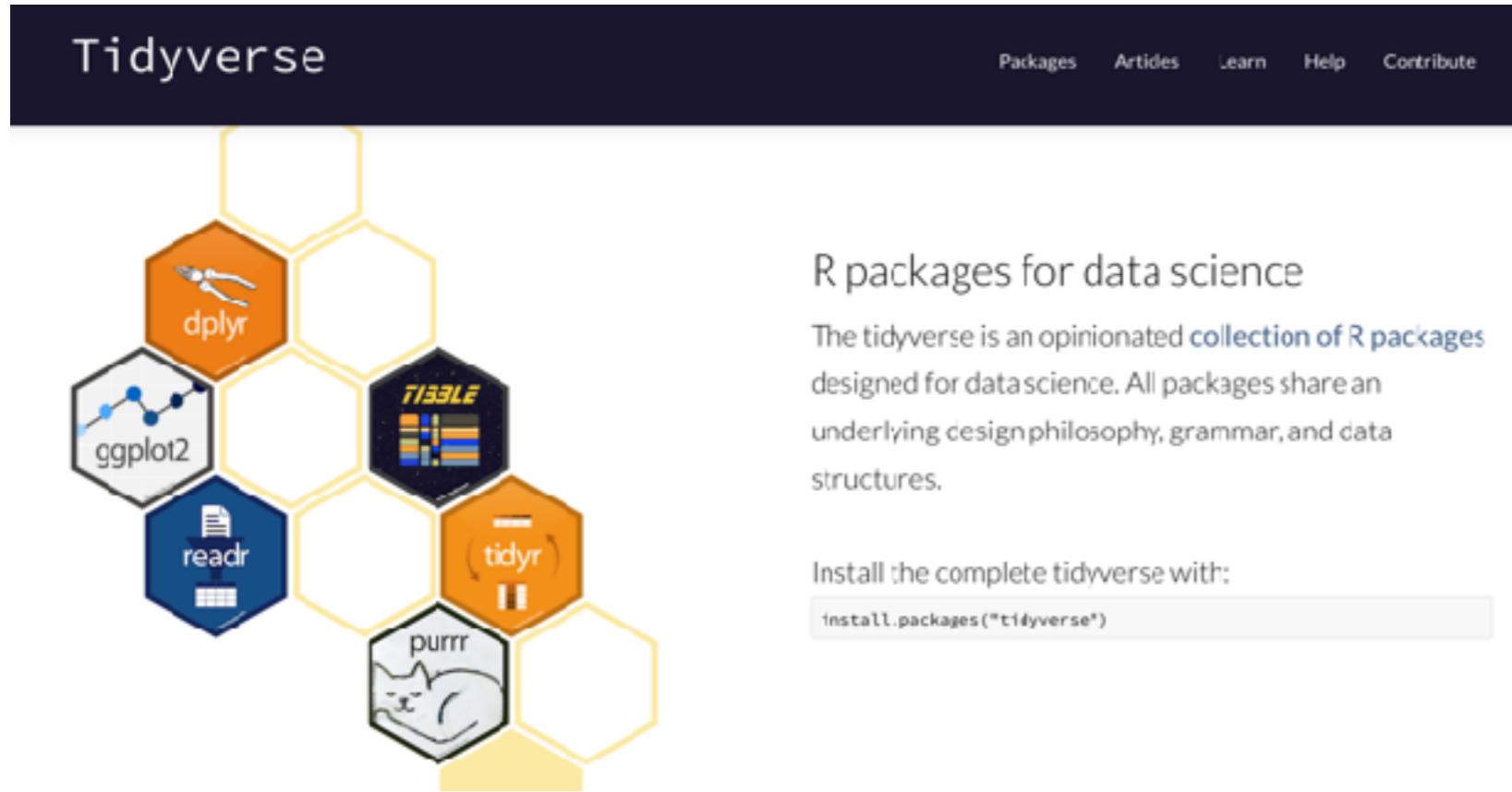
  @nampho2

first...

learn ***RStudio***, the ***tidyverse***, and ***github***
... practice ***regression methods!***

Intro to Data Science: *Integrating Genomes, Exposomes, and Phenomes*

Syllabus, references and readings



Tidyverse

Packages Articles Learn Help Contribute

R packages for data science

The tidyverse is an opinionated collection of R packages designed for data science. All packages share an underlying design philosophy, grammar, and data structures.

Install the complete tidyverse with:

```
install.packages("tidyverse")
```

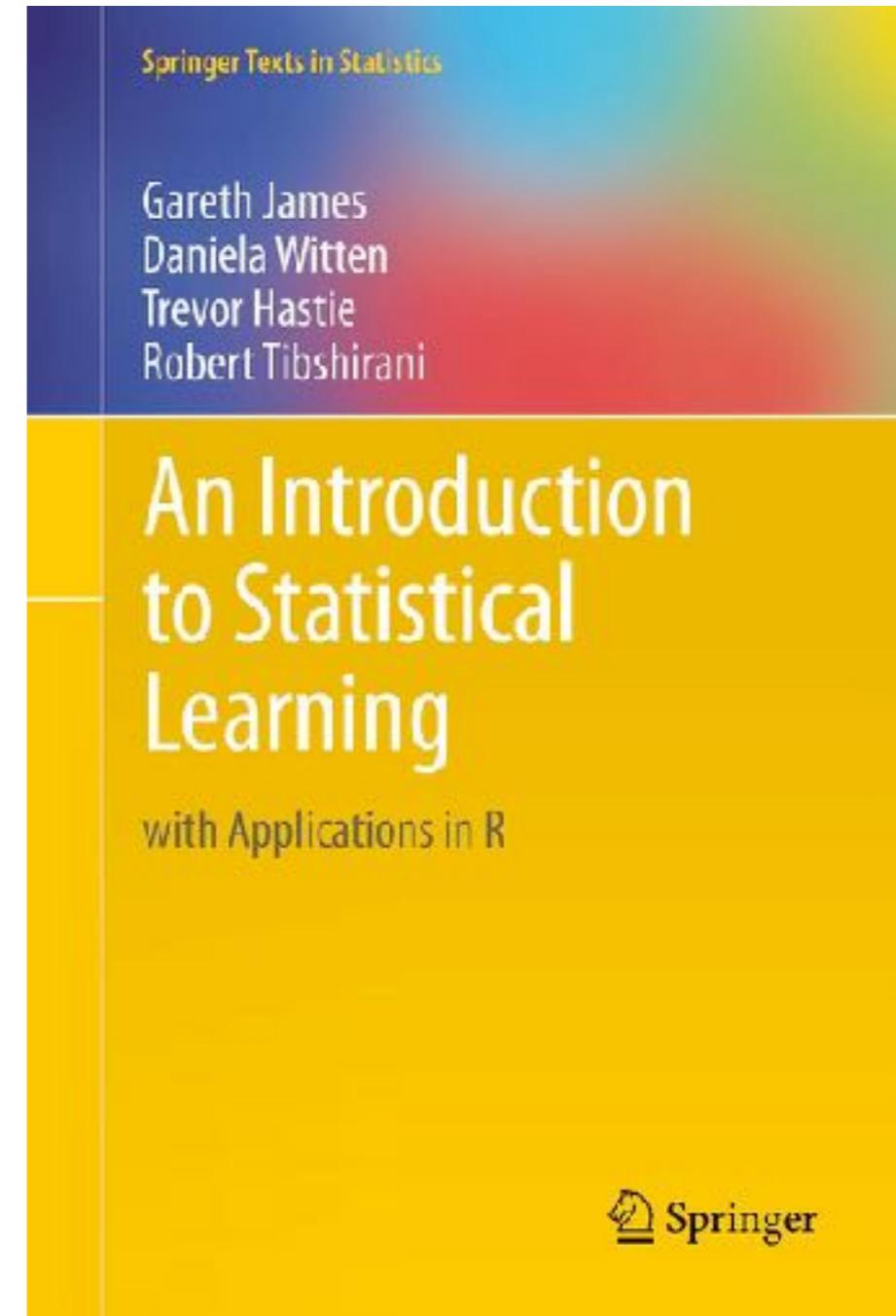
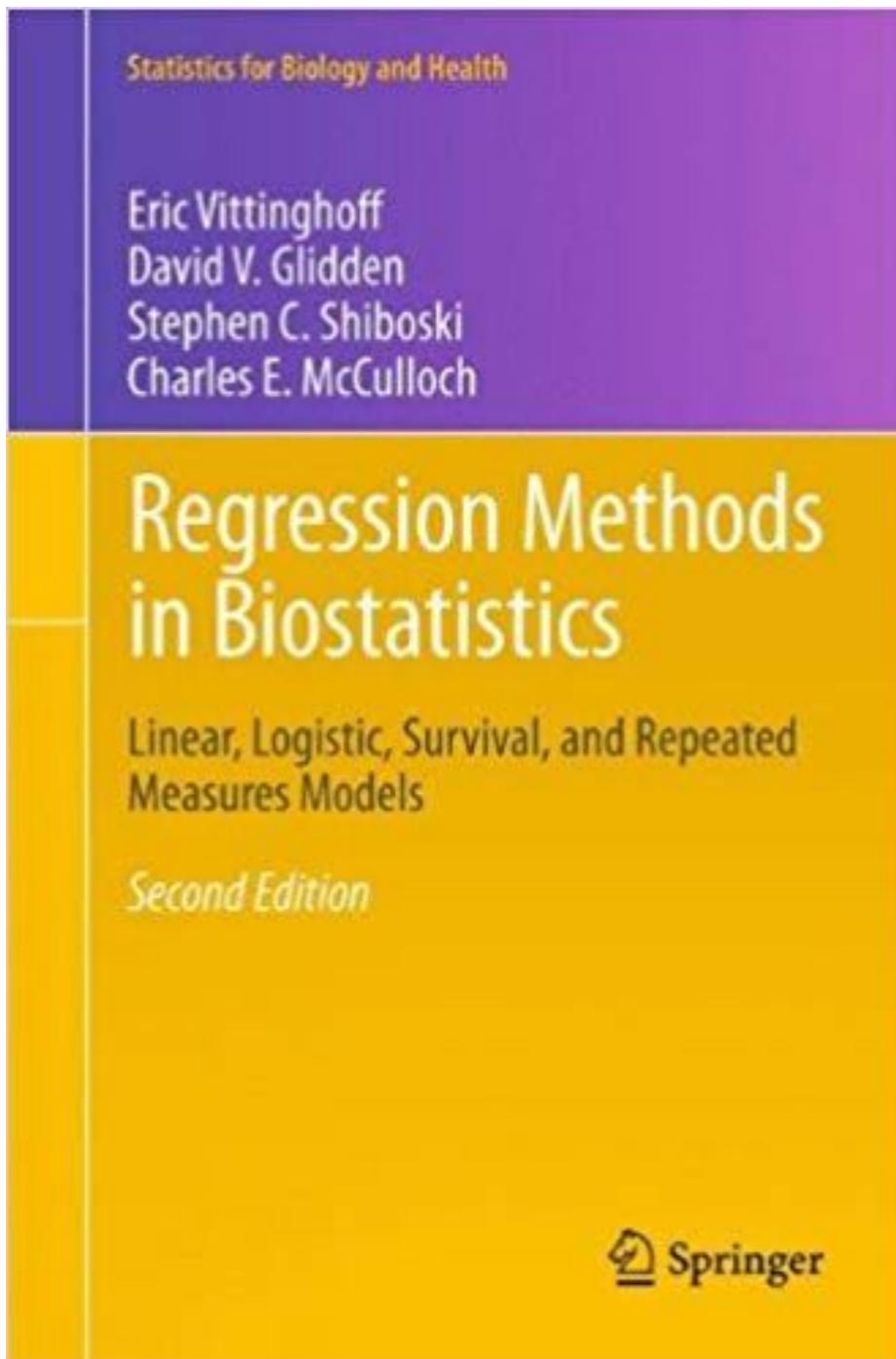


Hadley Wickham
Studio; tidyverse; ggplot; dplyr

~90% (or more) of data science effort in ***processing*** – learn to do it efficiently, reproducibly, and quickly!

Intro to Data Science: *Integrating Genomes, Exposomes, and Phenomes*

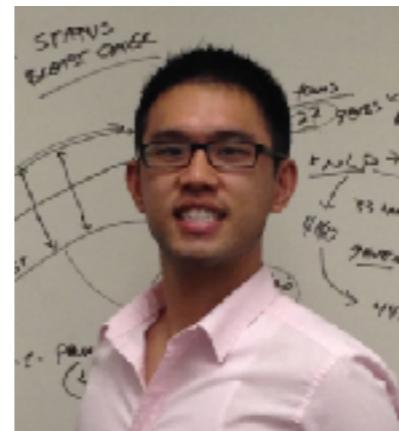
Syllabus, references and readings



<http://bit.ly/CORREXC>

Please let us know if you are using the resources
(or provide feedback)!

Nam Pho



@nampho2

Or me: @chiragjp

Arjun Manrai



@manrai

Jake Chung



@jakemk

Real quick:
What is the *exposome*? What is the *phenome*?

exposome

internal

lead (serum)

nutrients (serum)

infection (urine)

metabolome

external

geography

air pollution

income

phenome

function

expression

telomeres

metabolome

diseases

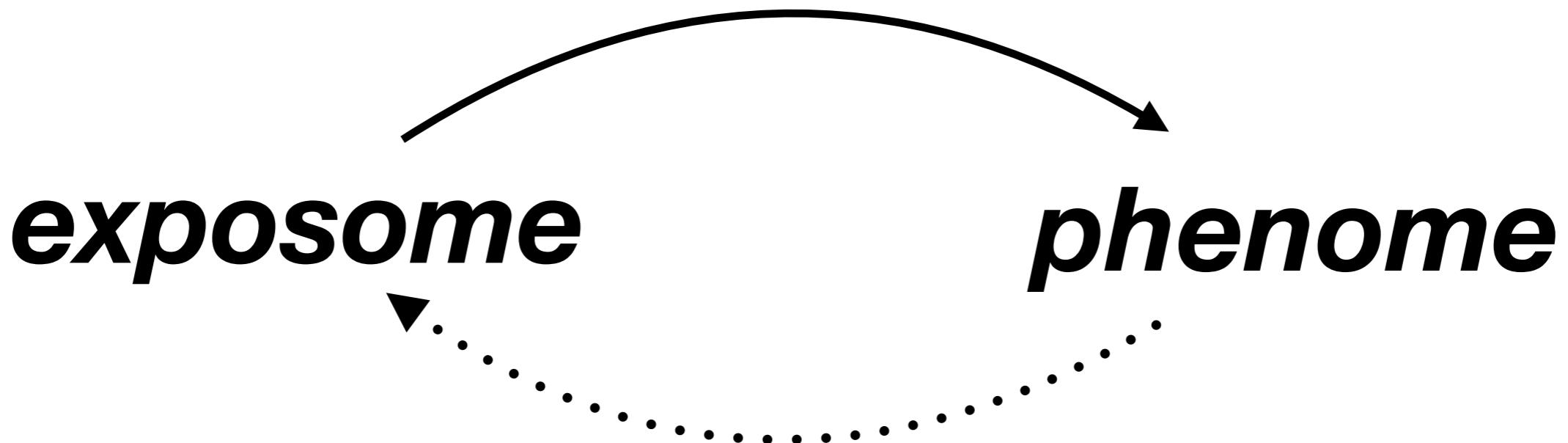
diabetes

cancer

heart disease

Exposome associated with the ***phenome***?

...and vice versa?

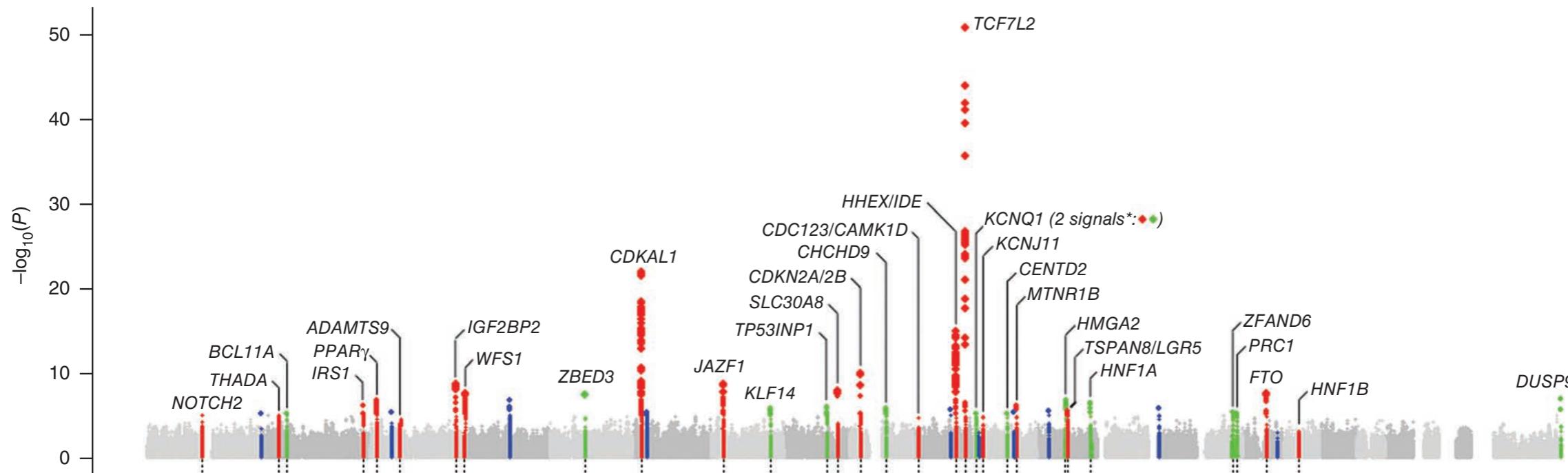


Analytic tools and big data infrastructure required to associate *exposome* with *phenome*!

We can learn a thing or two from ***genomics*** investigation...



Computational approaches fueled discovery of genetic variants in disease (example: genome-wide association [GWAS])



GWAS in Type 2 Diabetes
Voight et al, Nature Genetics 2012
N=8K T2D, 39K Controls

A search engine for robust, reproducible genotype-phenotype associations...

But genotypes are static and have little correlation –

There are *non-trivial* data analytic challenges in searching for exposome-phenome associations!

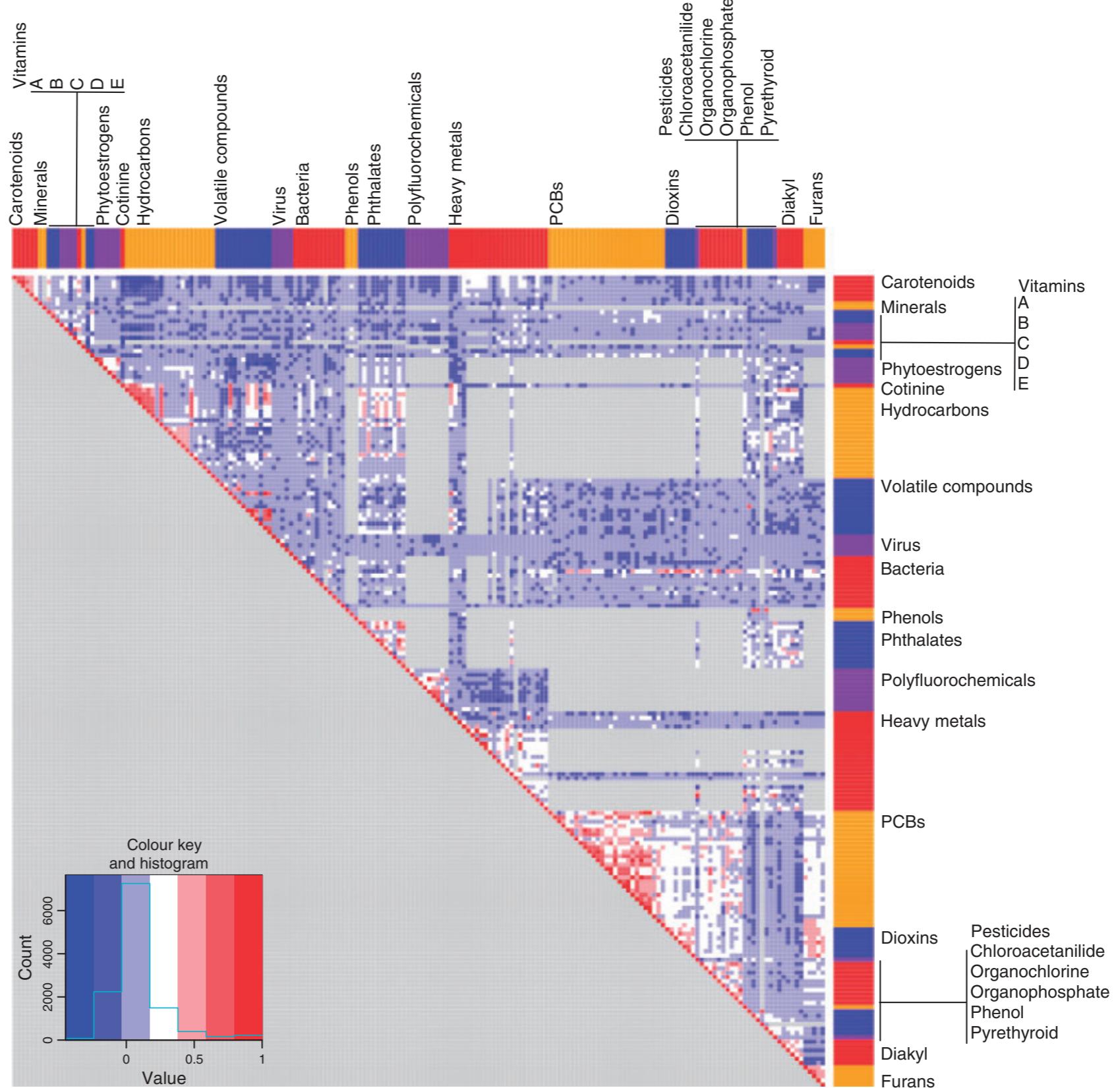
(but we will get started today!)

Dense correlational web of the exposome leads
to complications in determining:

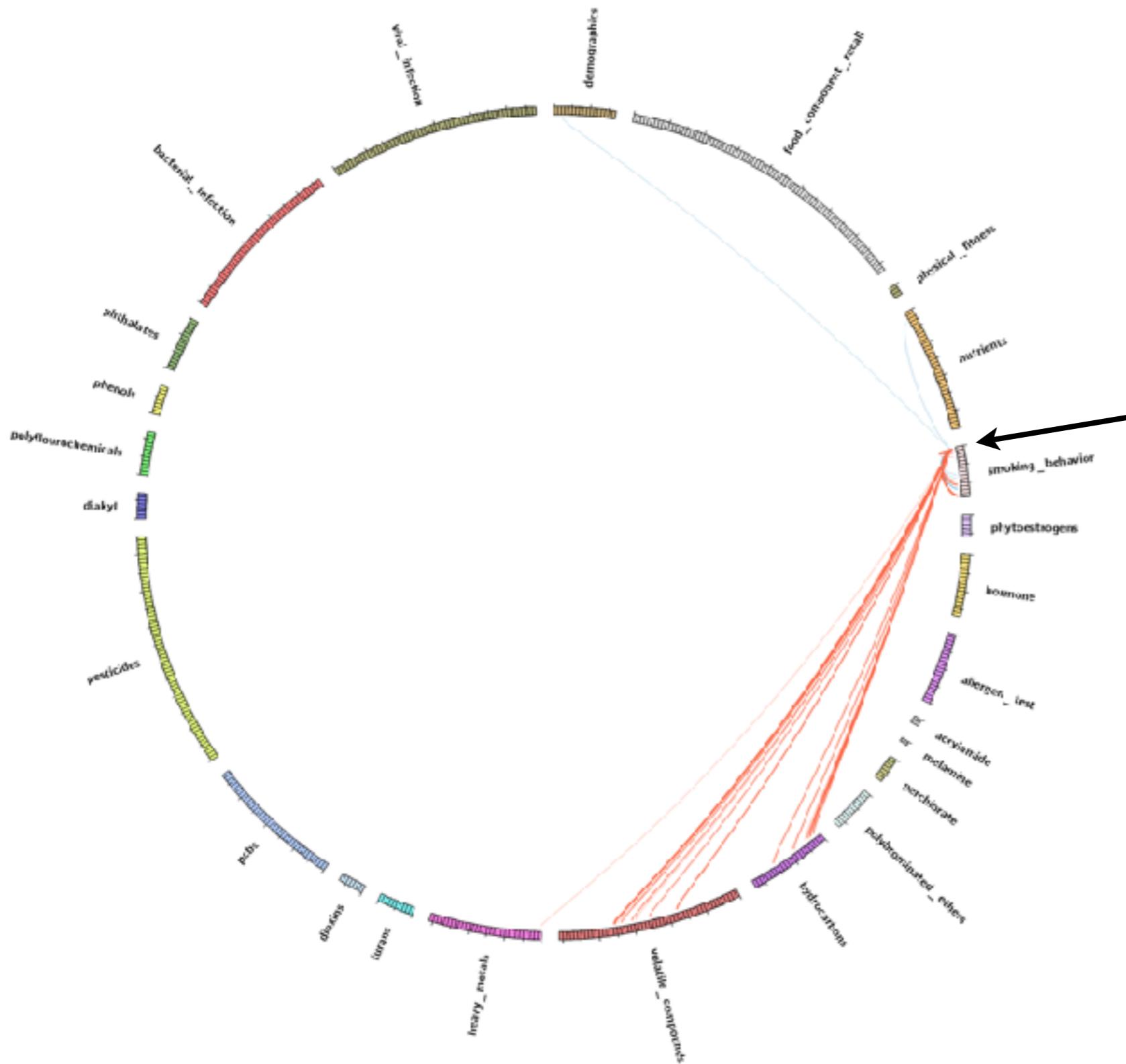
what causes what?

the influence of confounding bias?

how many environmental factors are part of the exposome??? (10? 1000? 10000? Infinite?)



Interdependencies of the **exposome**: Correlation globes paint a complex view of exposure

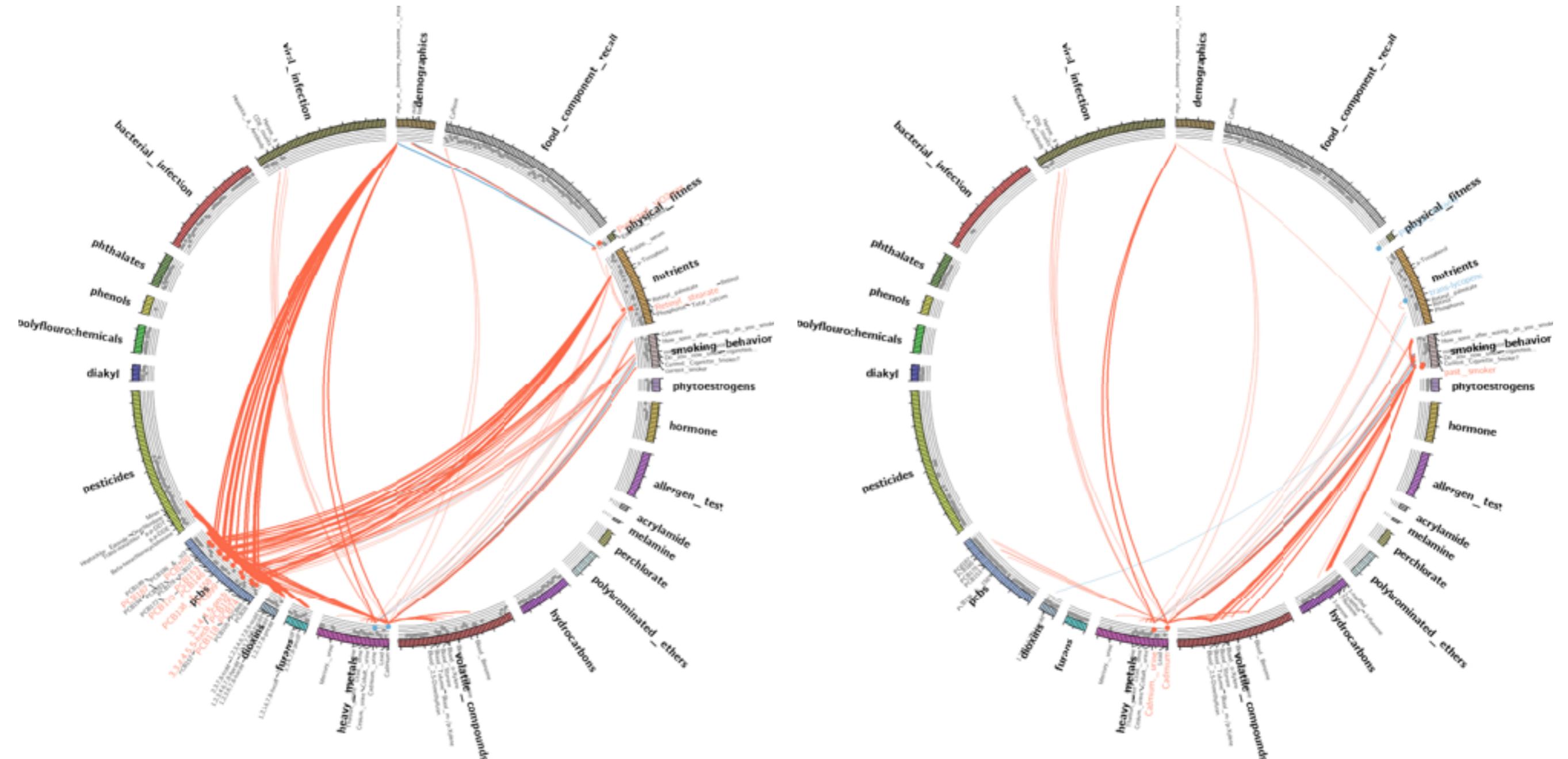


for each pair of E :
Spearman ρ
(575 factors: 81,937 correlations)

permuted data to produce
“null ρ ”
sought replication in > 1
cohort

Pac Symp Biocomput. 2015
JECH. 2015

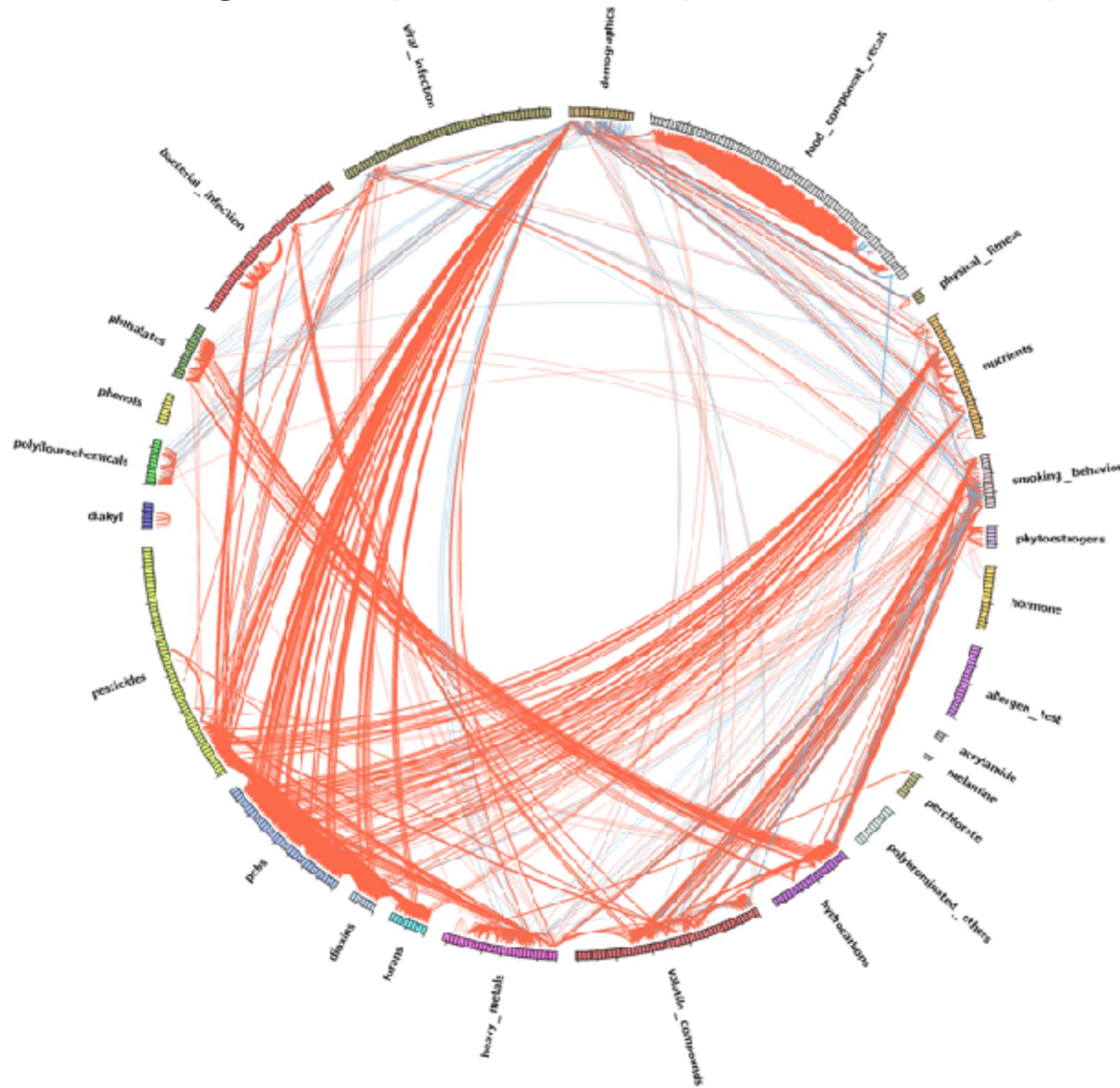
Interdependencies of the **exposome**: Telomeres vs. all-cause mortality



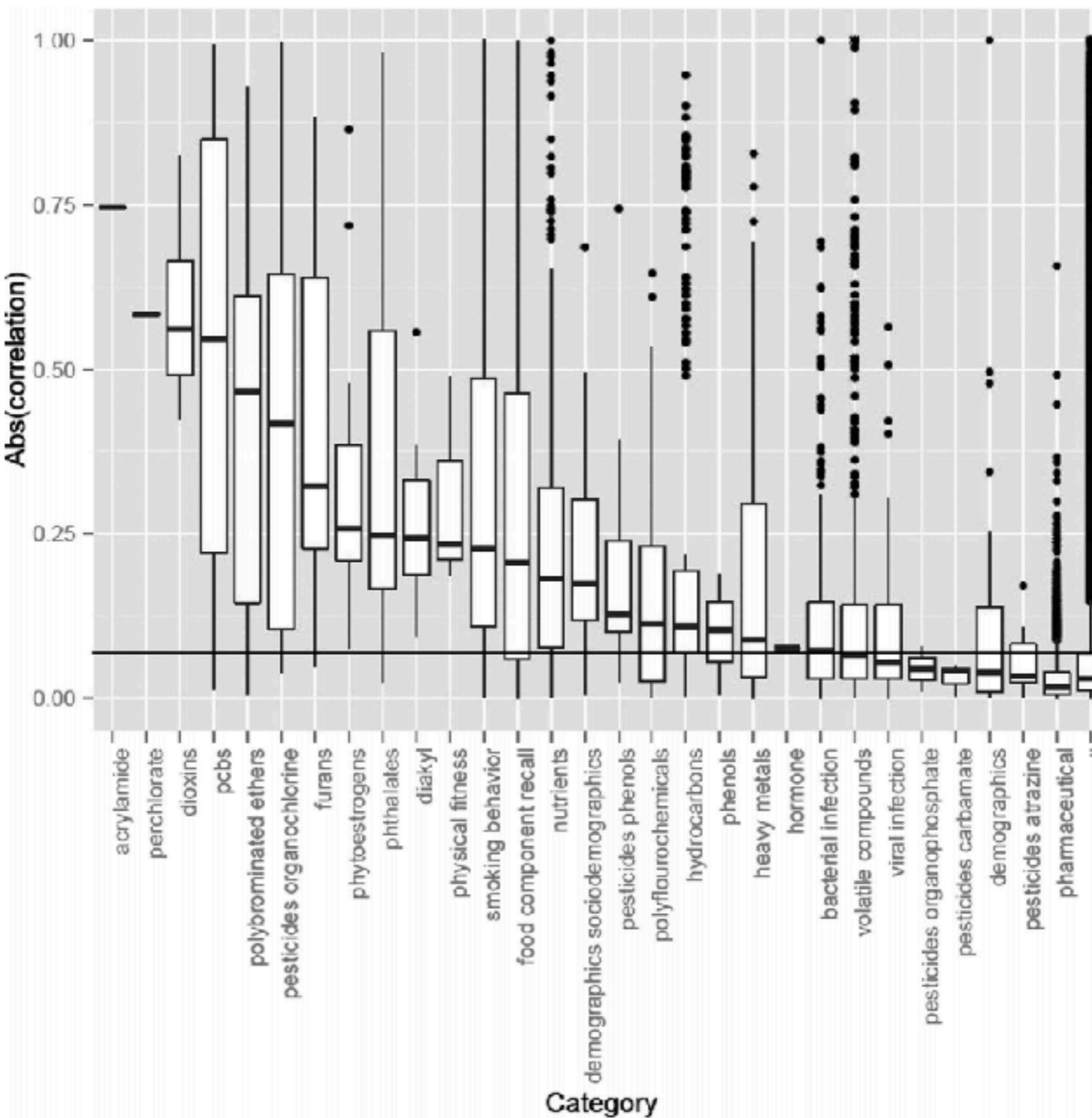
Telomere Length

All-cause mortality

Interdependencies of the ***exposome***: Correlation globes paint a complex view of exposure



Interdependencies of the **exposome**: Modest correlation size (Spearman/biserial $\rho < 0.5$)



Interdependencies of the **exposome**: Modest correlations ~ number of **effective variables (Meff)** ~= the **number of variables measured (M)**!

Table 2 Number of variables in each of the 32 exposure, demographics or behaviour categories

Category (measurement type)	M	Meff	Mdiff	p Value
Polychlorinated biphenyls (s)	38	23.79	14.21	0.002
Dioxins (s)	7	4.90	2.10	0.01
Acrylamide (s)	2	1.44	0.56	0.03
Organochlorine pesticides (s)	13	9.95	3.05	0.005
Polybrominated ethers (s)	11	8.47	2.53	0.006
Furans (s)	10	7.99	2.01	0.006
Perchlorate (u)	2	1.66	0.34	0.03
Smoking behaviour (s/sr)	14	11.65	2.35	0.004
Phthalates (u)	13	10.85	2.15	0.005
Food component recall (sr)	74	63.92	10.08	0.0008
Phytoestrogens (u)	6	5.22	0.78	0.01
Hydrocarbons (u)	21	18.47	2.53	0.003
Nutrients (s)	29	26.32	2.68	0.002
Volatile compounds (s)	38	34.60	3.40	0.001
Physical fitness (sr*)	3	2.78	0.22	0.02
Diakyl metabolites (u)	6	5.59	0.41	0.009
Socioeconomics (SES) (sr)	9	8.49	0.51	0.006
Demographics (sr)	8	7.55	0.45	0.007
Polyfluorochemicals (s)	12	11.39	0.61	0.004
Phenol pesticides (u)	7	6.65	0.35	0.008
Heavy metals (s/u)	29	27.68	1.32	0.002
Bacterial infection (s/u)	33	32.19	0.81	0.002
Viral infection (s)	16	15.72	0.28	0.003
Phenols (u)	3	2.97	0.03	0.02
Atrazine-like pesticides (u)	6	5.98	0.02	0.008
Hormone (s)	2	1.99	0.01	0.03
Pharmaceutical (sr)	107	106.78	0.22	0.0005
Organophosphate pesticides (u)	4	4.00	0.00	0.01
Carbamate pesticides (u)	4	4.00	0.00	0.01
Melamine (u)	1	1.00	0.00	0.05
Chloroacetanilide pesticides (u)	1	1.00	0.00	0.05
Pyrethroid pesticides (u)	1	1.00	0.00	0.05
Total	530	476.0	54.0	0.0001

M, number of variables in category; Meff, effective number of variables after taking into account correlation; Mdiff, difference between M and Meff; p value, indicative correlation-adjusted Bonferroni p value threshold (0.05/Meff).

*Denotes quantitative assessment of physical activity (VO₂Max) was also measured.
s, serum; sr, self-report; u, urine.

$$M_{\text{eff}} = 1 + (M - 1) \left(1 - \frac{\text{Var}(\lambda_{\text{obs}})}{M} \right).$$

If everything was correlated:

Meff = 1!

If everything was
not correlated (independent):

Meff = M!

How large of a role does ***shared environment*** play a significant role in co-exposure of the exposome?



Possible to capture ***household*** and ***gender*** influence on variation of ***E***?

Does living together mean higher correlation?
E of individuals in the same home ***predictive*** of others?

Longitudinal Investigation of Fertility and the Environment (LIFE): a prospective study of couples desiring to become pregnant

- Reproductive age (**18-40** for females; **>18** for males)
- **N=501 couples** (Michigan and Texas) in 2005-2007 living in the same home
- Data collected in couples' home
 - urine, blood, semen (at baseline and at month 1)



**Germaine Buck Louis
(NICHD)**



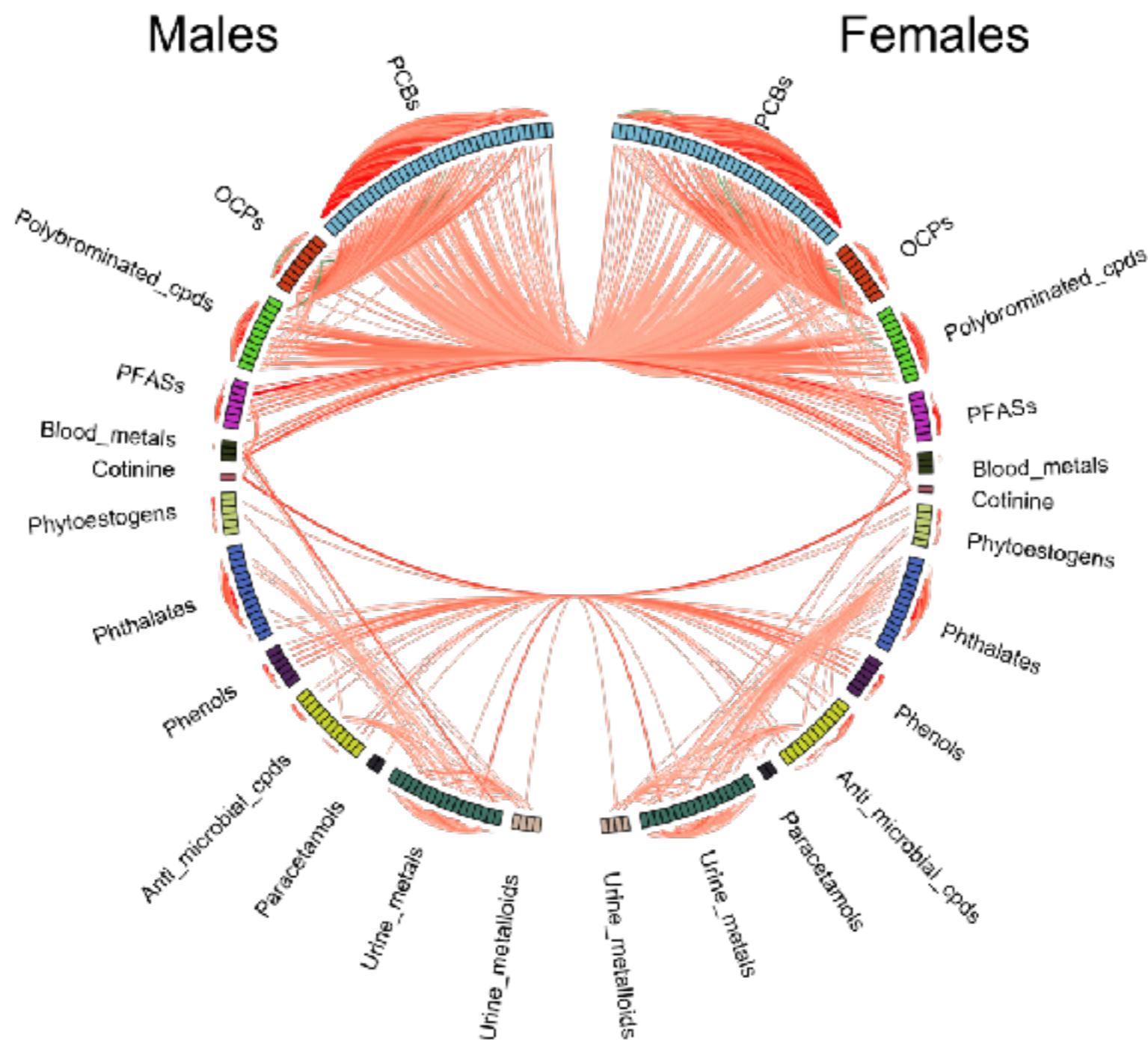
Jake Chung

Buck Louis et al, 2013
Buck Louis et al, 2014
Chung et al, ES&T 2018

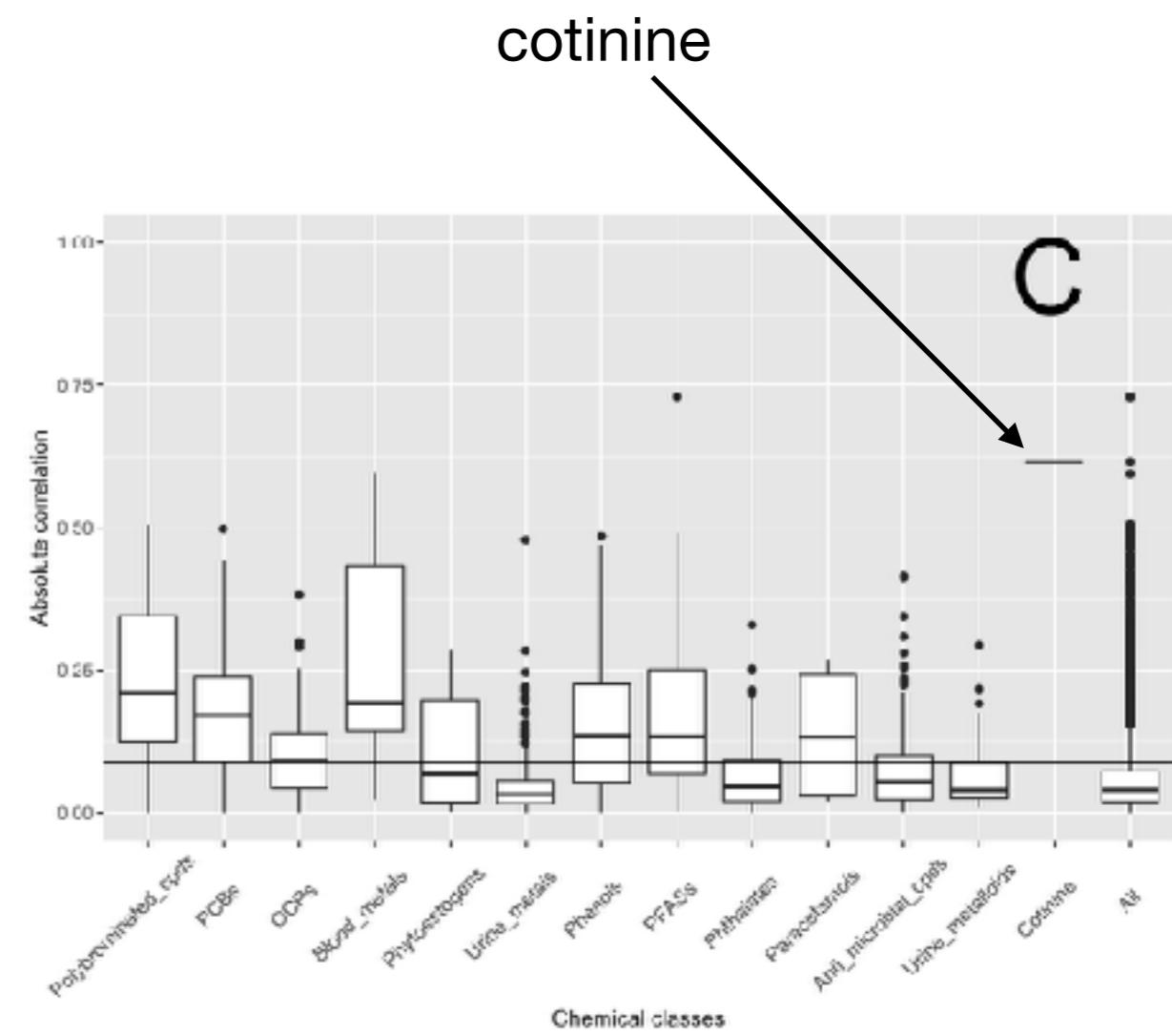
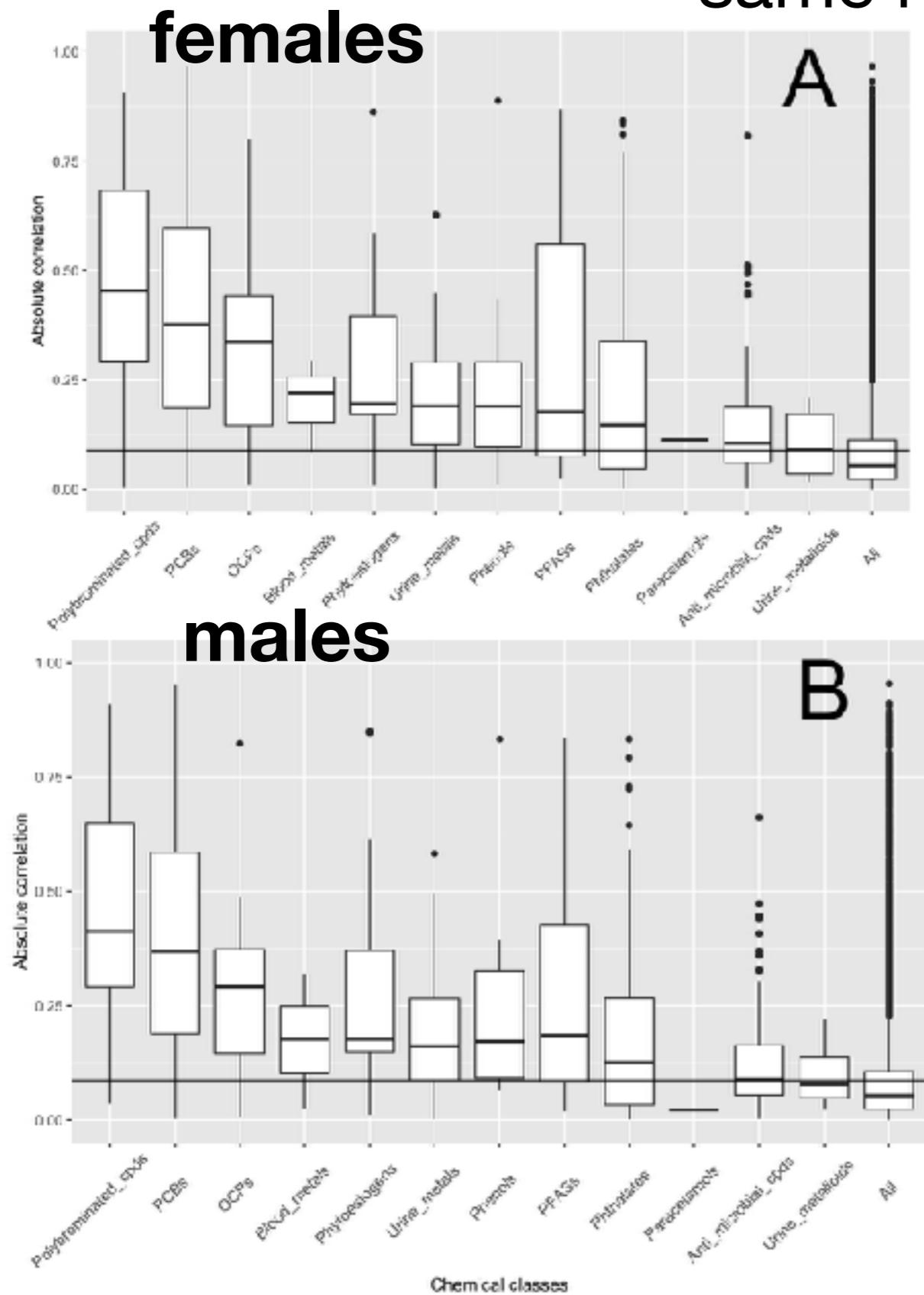
Longitudinal Investigation of Fertility and the Environment (LIFE): a prospective study of couples with many indicators of *E!*

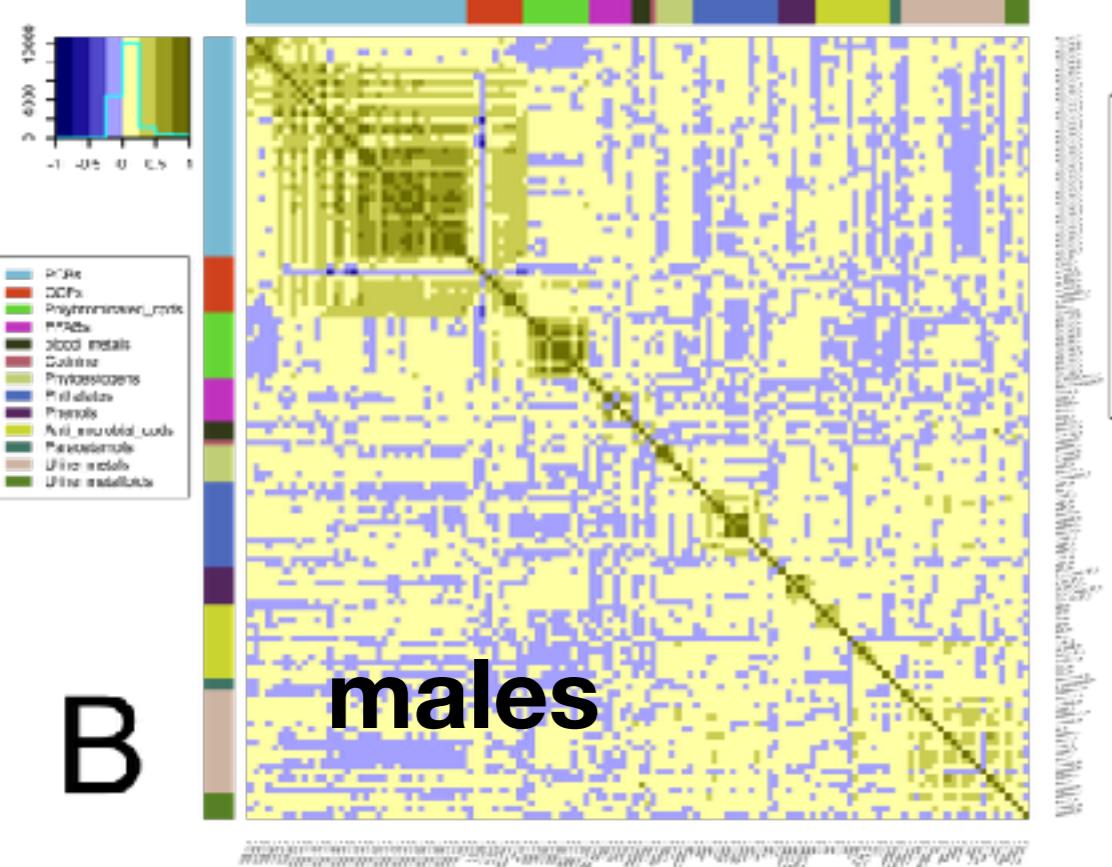
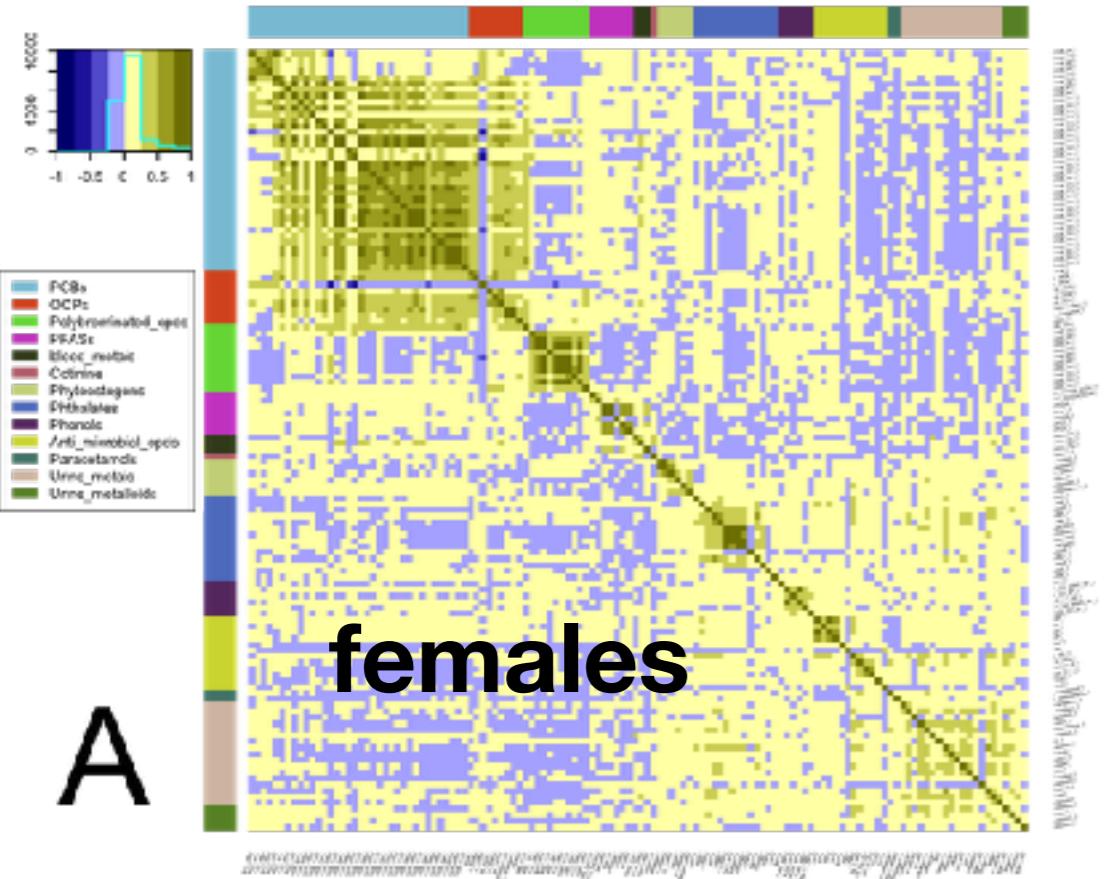
Chemical classes	No.	Chemicals
Serum persistent organic compounds		
Polychlorinated biphenyls (PCBs)	36	Congeners: 28, 44, 49, 52, 66, 74, 87, 99, 101, 105, 110, 114, 118, 128, 138, 146, 149, 151, 153, 156, 157, 167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 196, 201, 206, and 209
Organochlorine pesticides (OCPs)	9	Hexachlorobenzene (HCB), β -hexachlorocyclohexane (β -HCH), γ -hexachlorocyclohexane (γ -HCH), oxychlordane, <i>trans</i> -nonachlor, p,p' -DDT, o,p' -DDT, p,p' -DDE, and mirex
Polybrominated chemicals	11	Brominated biphenyl (BB 153); brominated diphenyl ethers (BDEs) congeners: 17, 28, 47, 66, 85, 99, 100, 153, 154, and 183
Polyfluoroalkyl substances (PFASs)	7	2-(<i>N</i> -ethyl-perfluorooctane sulfonamido) acetate (Et-PFOSA-AcOH), 2-(<i>N</i> -methyl-perfluorooctane sulfonamido) acetate (Me-PFOSA-AcOH), perfluorodecanoate (PFDeA), perfluorononanoate (PFNA), perfluorooctane sulfonamide (PFOSA), perfluorooctane sulfonate (PFOS), and perfluorooctanoate (PFOA)
Urinary non-persistent organic compounds		
Phytoestrogens	6	Genistein, daidzein, O-desmethylangolensin, equol, enterodiol, and enterolactone
		Mono (3-carboxypropyl) phthalate (mCPP), monomethyl phthalate (mMP), monoethyl phthalate (mEP), mono (2-isobutyl phthalate) (mIBP), mono-n-butyl phthalate (mBP), mono (2-ethyl-5-carboxyphenyl) phthalate (mECPP), mono-[(2-carboxymethyl) hexyl] phthalate (mCMHP), mono (2-ethyl-5-oxohexyl) phthalate (mEOHP), mono (2-ethyl-5-hydroxyhexyl) phthalate (mEHHP), monocyclohexyl phthalate (mCHP), monobenzyl phthalate (mBzP), mono (2-ethylhexyl) phthalate (mEHP), mono-isonyl phthalate (mNP), and monooctyl phthalate (mOP).
Phthalate metabolites	14	Total bisphenol A (BPA); benzophenones (BPs): 4-hydroxybenzophenone (4-OH-BP), 2,4-dihydroxybenzophenone (2,4-OH-BP), 2,2',4,4'-tetrahydroxybenzophenone (2,2',4,4'-OH-BP), 2-hydroxy-4-methoxybenzophenone (2-OH-4-MeO-BP), and 2,2'-dihydroxy-4-methoxybenzophenone (2,2'-OH-4-MeO-BP)
Phenols	6	Triclosan (TCS) and triclocarban (TCC); parabens: methyl paraben (MP), ethyl paraben (EP), propyl paraben (PP), butyl paraben (BP), benzyl paraben (BzP), heptyl paraben (HP), 4-hydroxy benzoic acid (4-HB), 3,4-dihydroxy benzoic (3,4-DHB), methyl-protocatechuic acid (OH-Me-P), and ethyl-protocatechuic acid (OH-Et-P)
Anti-microbial chemicals	12	
Paracetamol & derivatives	2	Paracetamol and 4-aminophenol
Others		
Blood metals	3	Cadmium (Cd), lead (Pb), and mercury (Hg)
Serum cotinine	1	Cotinine
Urine metals	17	Manganese (Mn), chromium (Cr), beryllium (Be), cobalt (Co), molybdenum (Mo), cadmium (Cd), tin (Sn), caesium (Cs), barium (Ba), nickel (Ni), copper (Cu), zinc (Zn), tungsten (W), platinum (Pt), thallium (Tl), lead (Pb), and uranium (U)
Urine metalloids	4	Selenium (Se), arsenic (As), antimony (Sb), and tellurium (Te)

Dense correlational web in **LIFE** comparable to **NHANES**:
90% spearman correlations ranging from -0.3 to 0.3



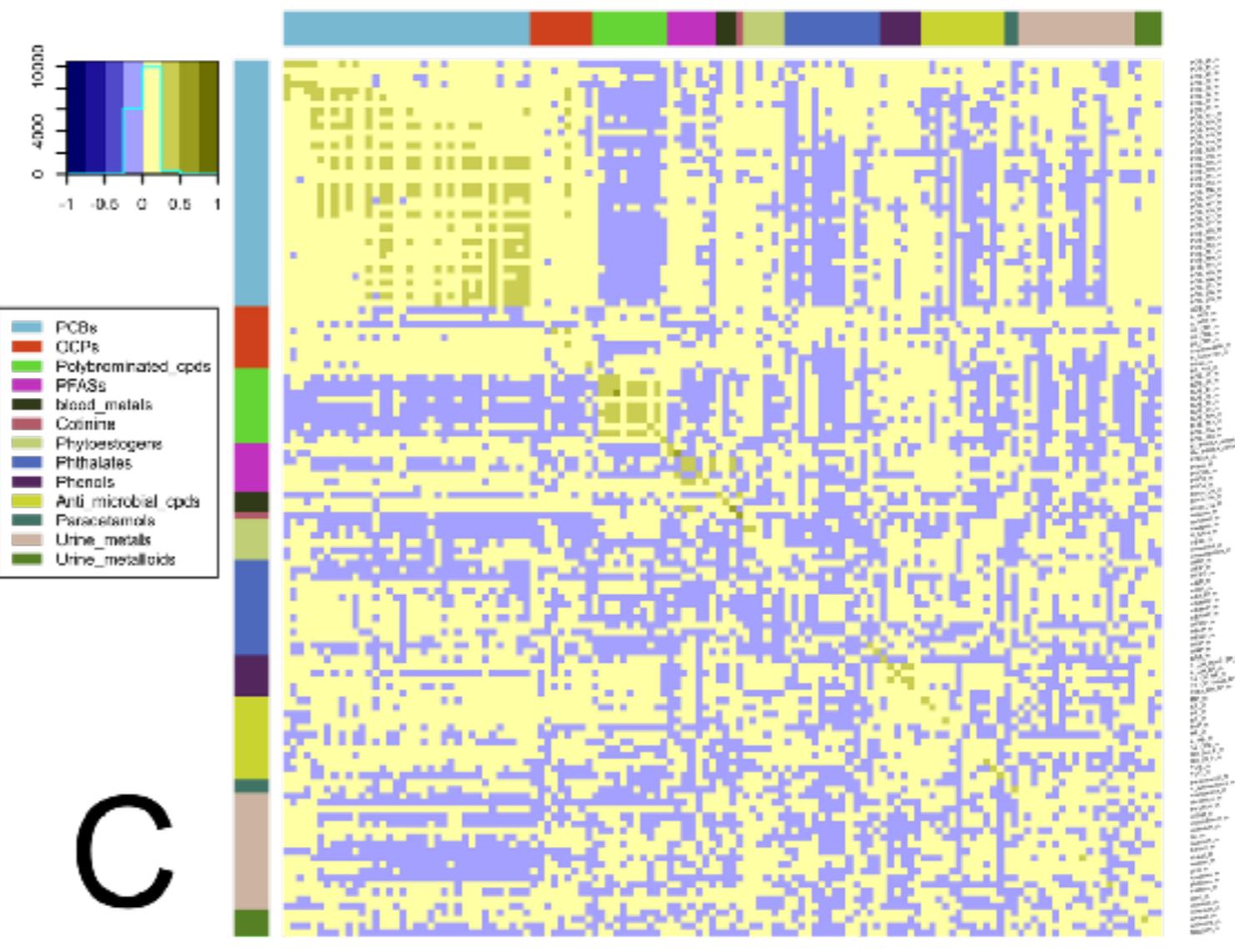
$\text{cor}(\text{persistent } E) > \text{cor}(\text{non-persistent } E)$
 (but this pattern **diminishes** between couples in the
 same household!)





Co-**E** patterns between
females and males are *similar*

... however:
males and females *within* household
weaker!

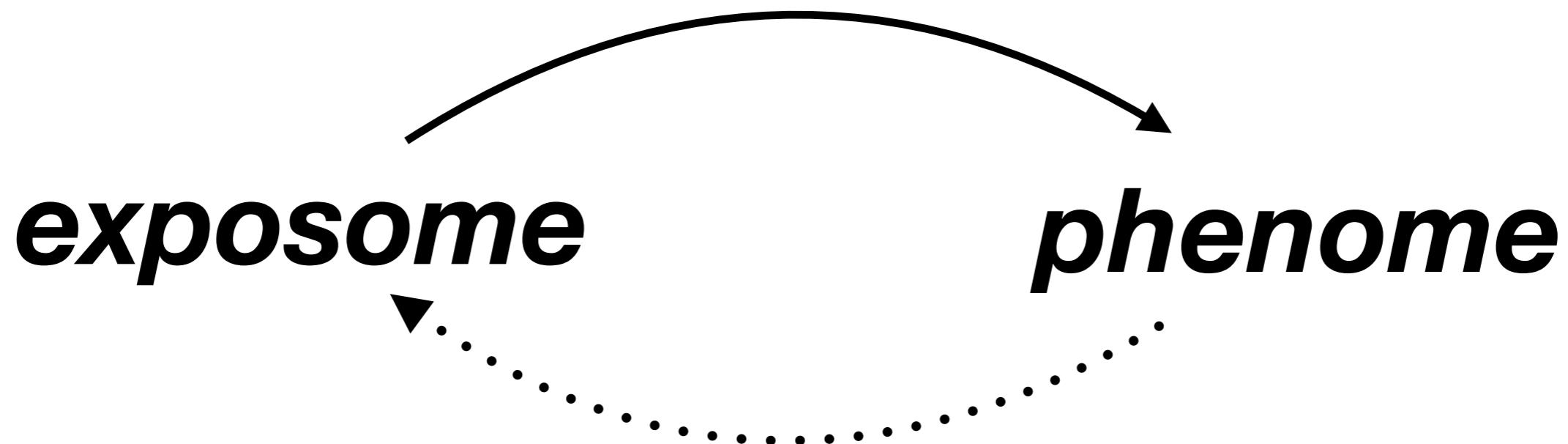


Household < specific environment in co-occurring exposures



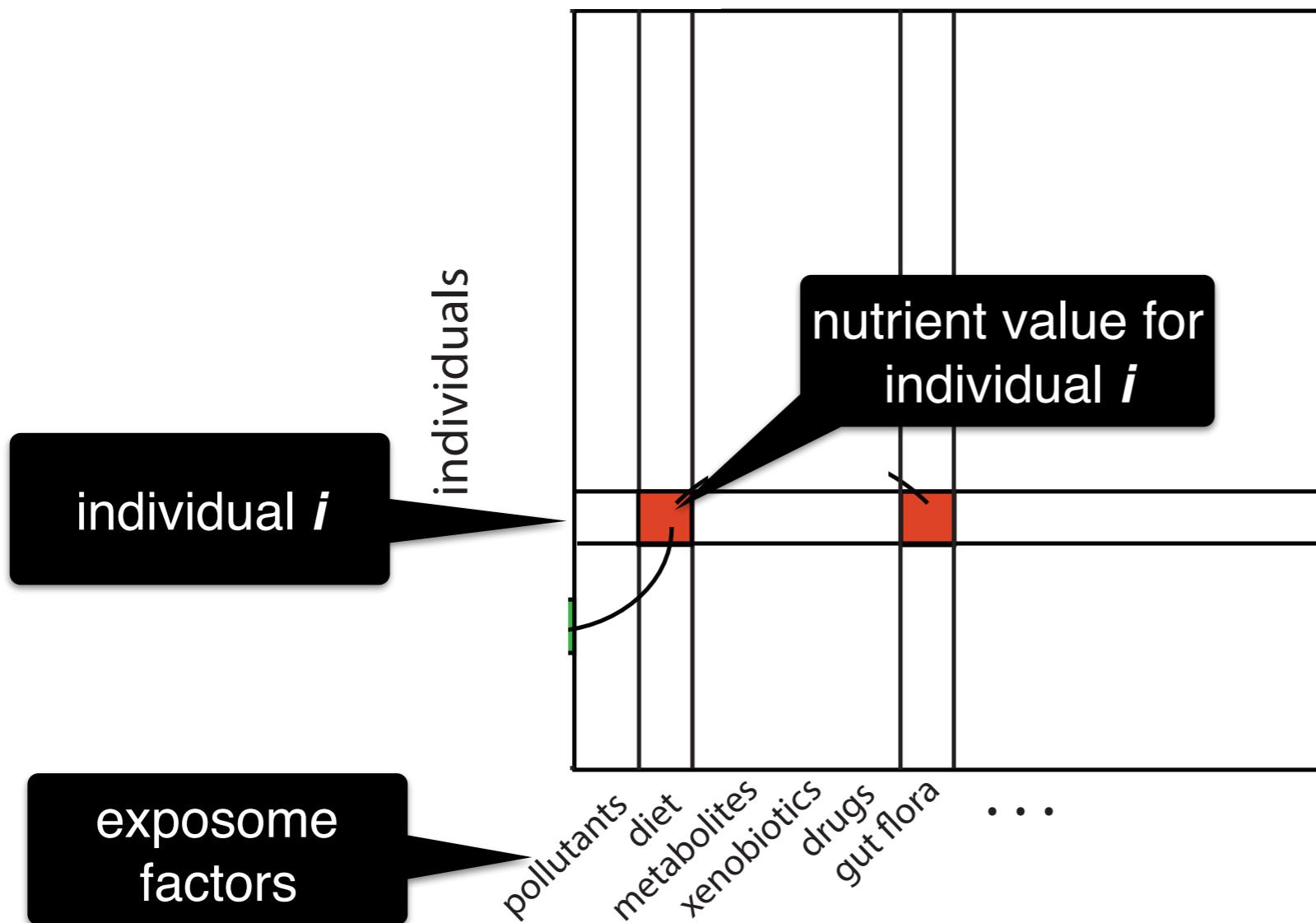
implications for **sampling, routes of exposure:**
where do we sample? - *individuals!*

X-wide Association Investigations: Correlating the exposome with the phenome



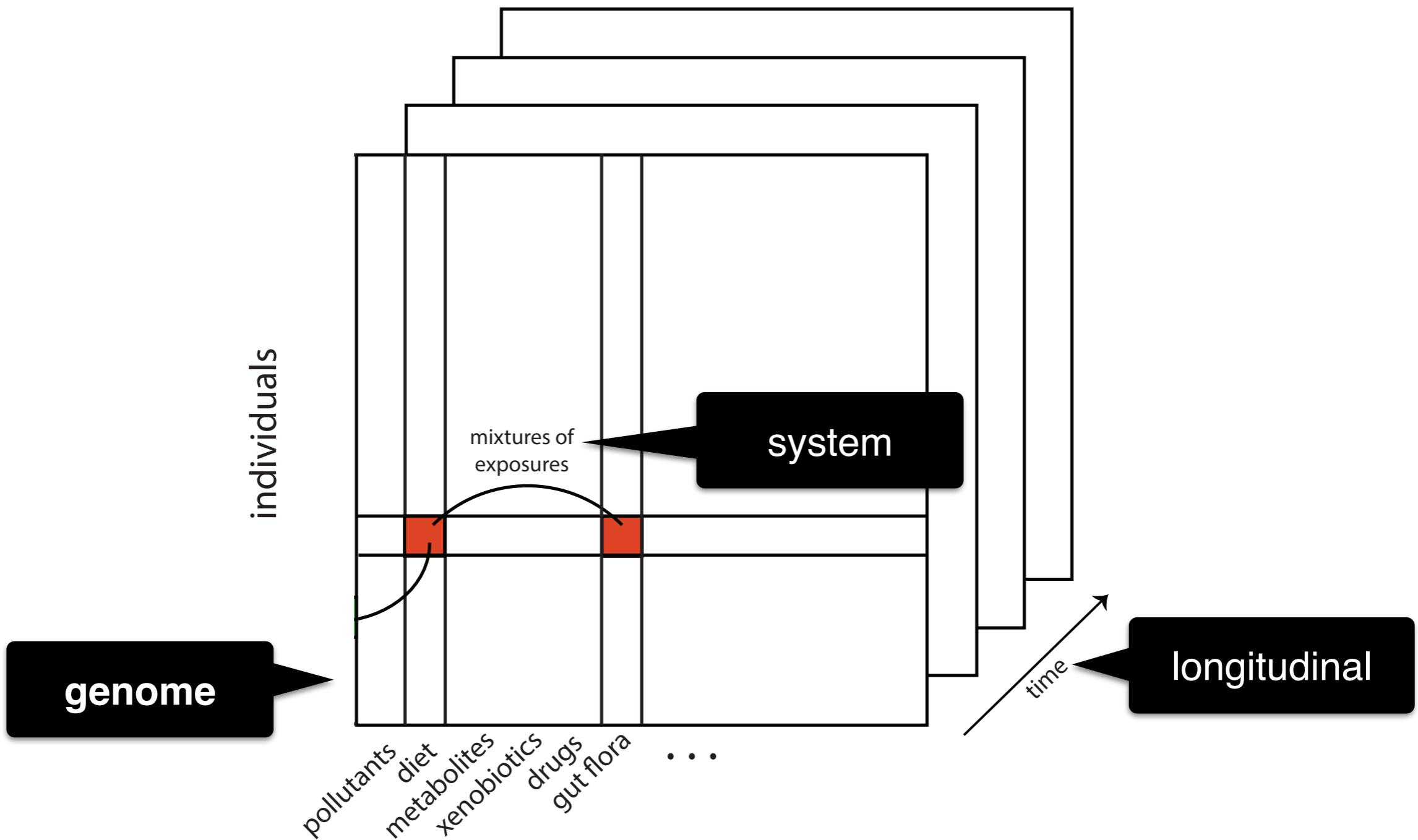
What will the ***exposome*** data structure look like?:

a ***high-dimensioned 3D*** matrix of
(1) ***exposure*** measurements
on (2) ***individuals*** as a function of (3) ***time***



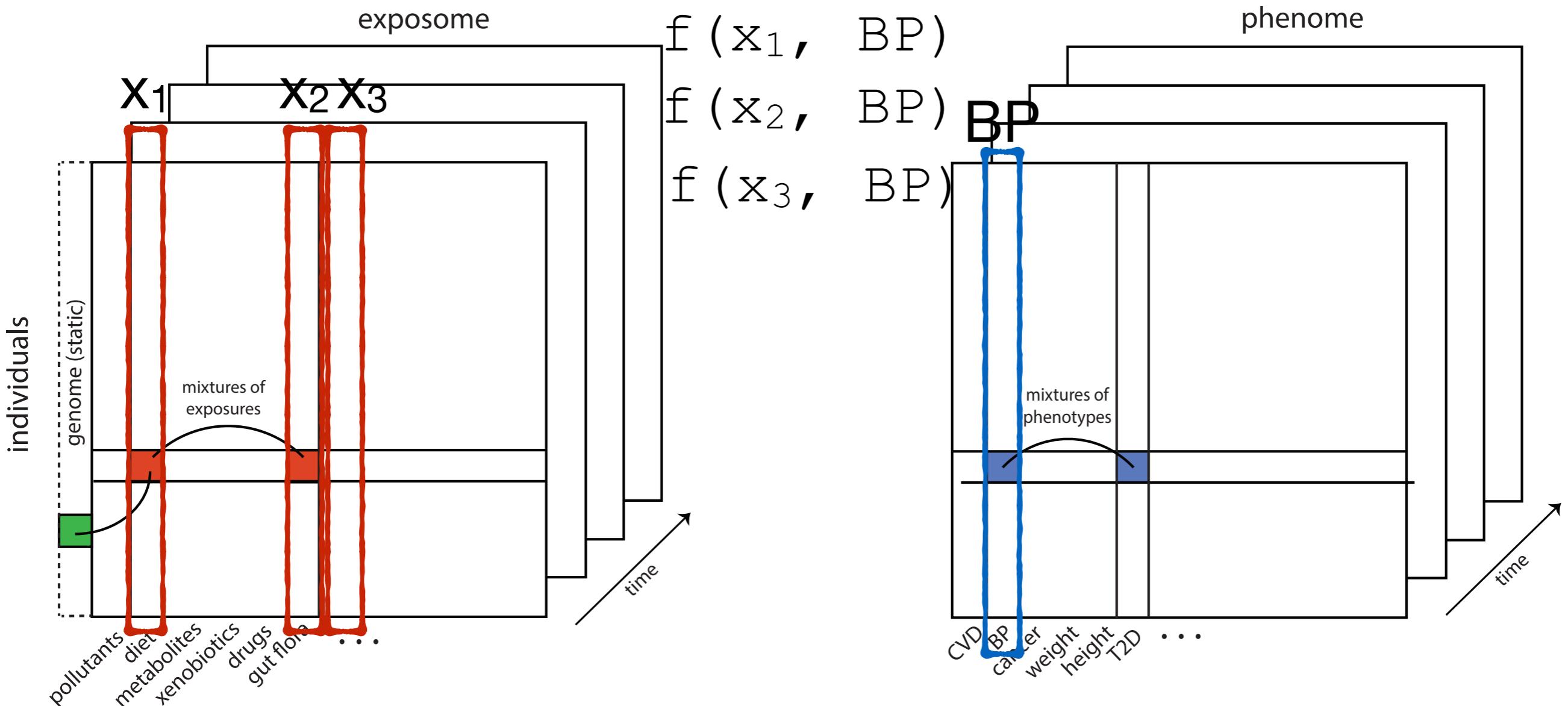
What will the ***exosome*** data structure look like?:

a ***high-dimensioned 3D*** matrix of
(1) ***exposure*** measurements
on (2) ***individuals*** as a function of (3) ***time***



A schematic of a data-driven search for ***exposome-phenome*** associations:

Associating all of the ‘red’ with the ‘blue’



Where f = association function
(regression, correlation, etc)

‘pseudo-code’ for implementation of an XWAS: *how would you do it?*

```
y = [blood pressure values for cohort]
association_list = empty_list()
for each x in list of exposures:
    association_test=f(x,y)
    append(association_list, association_test)

multiplicity_correct(association_list)

volcano_plot(y, x, association_list)
```

What is stored in y ?

What is stored in association_list ?

What can f be?

What does append do?

What is the reason for $\text{multiplicity_correct}$?

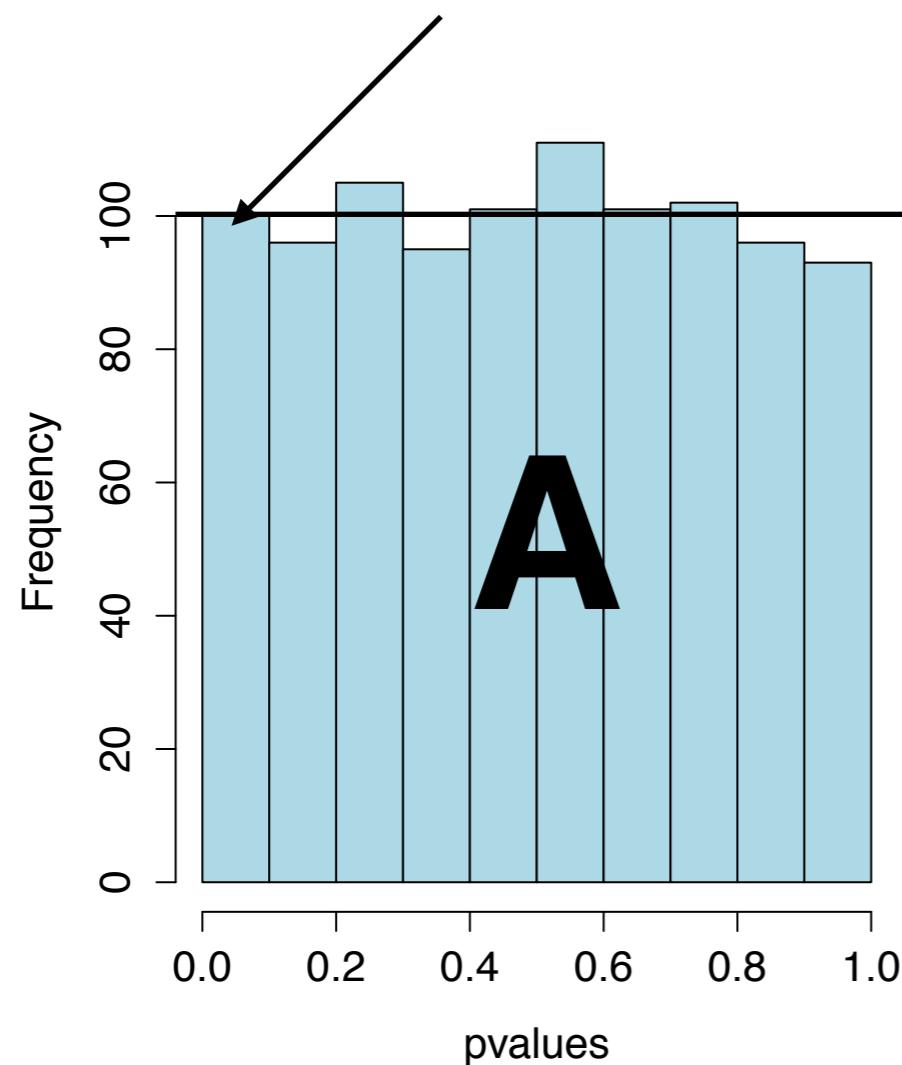
Multiplicity: how to determine signal from noise?
type 1 error (spurious findings)

*Suppose you are testing 1000 exposures in case-control study
(disease vs. healthy)...*

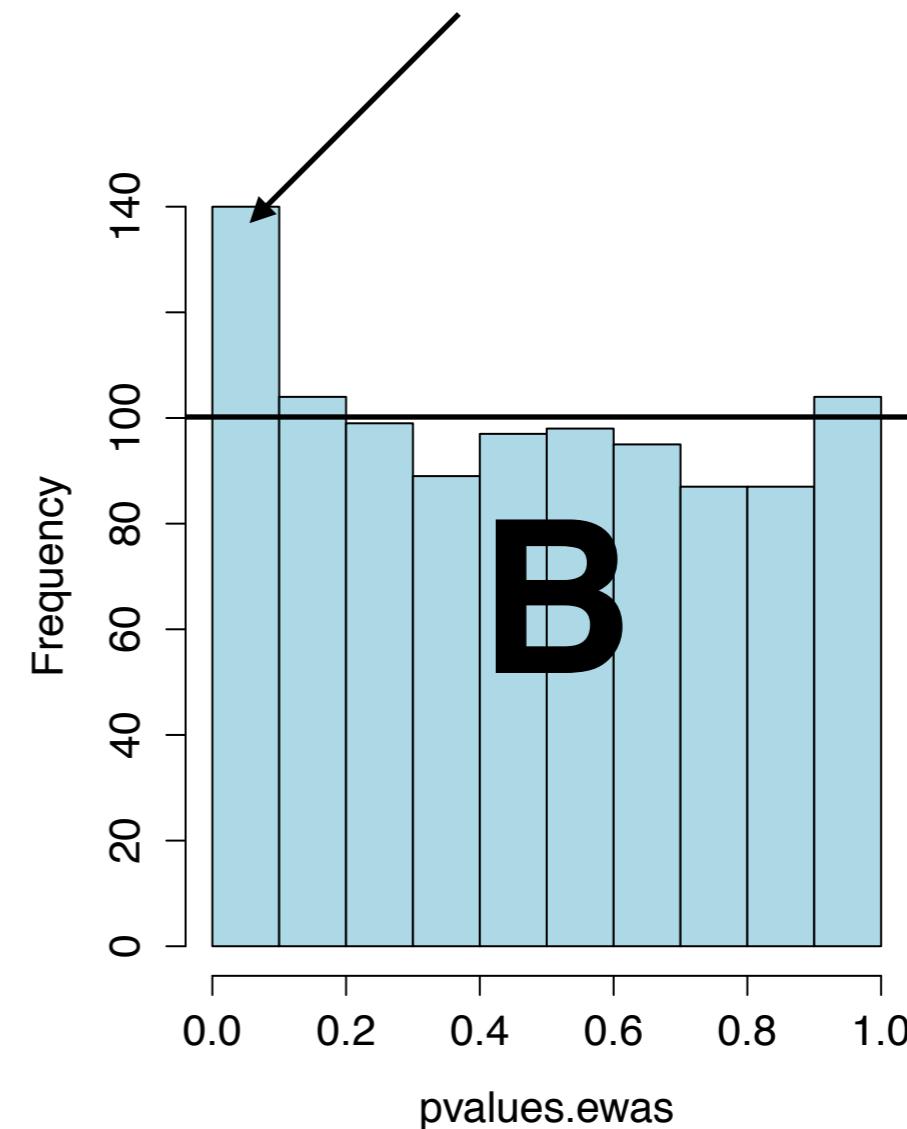
... and there were no difference between the cases and controls...

...how many findings would be “significant” at a p-value threshold of 0.05 (due to chance)?

Regime of multiple tests and “*signal to noise*”:
Histogram of p-values in 2 scenarios: no difference and 5% different

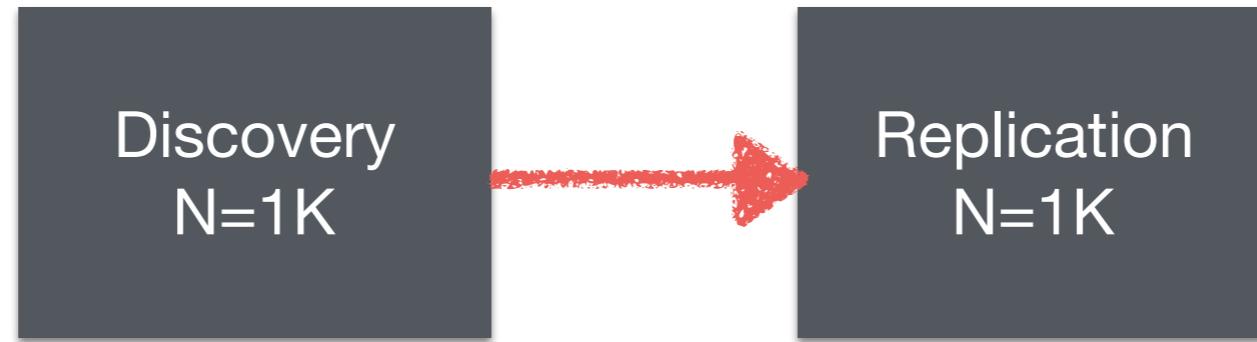


No difference
(no true associations)



5% exposures different
(5% true associations)

The tension between type 1 and type 2 errors: ***Power*** and ***replication*** for robust associations!



Discovery sample sizes must be large to overcome
multiple testing and mitigate ***winner's curse***

Replication sample size must be large to detect
association

The *false discovery rate*: A *powerful* approach for multiple hypothesis correction

J. R. Statist. Soc. B (1995)
57, No. 1, pp. 289–300

Controlling the False Discovery Rate: a Practical and Powerful Approach to Multiple Testing

By YOAV BENJAMINI† and YOSEF HOCHBERG

Tel Aviv University, Israel

[Received January 1993. Revised March 1994]

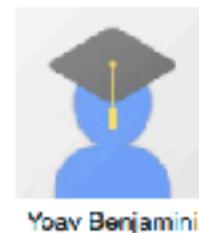
SUMMARY

The common approach to the multiplicity problem calls for controlling the familywise error rate (FWER). This approach, though, has faults, and we point out a few. A different approach to problems of multiple significance testing is presented. It calls for controlling the expected proportion of falsely rejected hypotheses – the false discovery rate. This error rate is equivalent to the FWER when all hypotheses are true but is smaller otherwise. Therefore, in problems where the control of the false discovery rate rather than that of the FWER is desired, there is potential for a gain in power. A simple sequential Bonferroni-type procedure is proved to control the false discovery rate for independent test statistics, and a simulation study shows that the gain in power is substantial. The use of the new procedure and the appropriateness of the criterion are illustrated with examples.

Keywords: BONFERRONI-TYPE PROCEDURES; FAMILYWISE ERROR RATE; MULTIPLE-COMPARISON PROCEDURES; *p*-VALUES

- “**powerful**”: *p*-value threshold less stringent than Bonferroni
- an estimate of frequency of **false discoveries** at a given threshold!

The *false discovery rate*: A *powerful* approach for multiple hypothesis correction



Controlling the false discovery rate: a practical and powerful approach to multiple testing

Authors	Yoav Benjamini, Yosef Hochberg
Publication date	1995/1/1
Journal	Journal of the royal statistical society. Series B (Methodological)
Pages	289-300
Publisher	Blackwell Publishers
Description	The common approach to the multiplicity problem calls for controlling the familywise error rate (FWER). This approach, though, has faults, and we point out a few. A different approach to problems of multiple significance testing is presented. It calls for controlling the expected proportion of falsely rejected hypotheses—the false discovery rate. This error rate is equivalent to the FWER when all hypotheses are true but is smaller otherwise. Therefore, In problems where the control of the false discovery rate rather than that of the FWER is ...
Total citations	Cited by 37060



Scholar articles [Controlling the false discovery rate: a practical and powerful approach to multiple testing](#)
Y Benjamini, Y Hochberg - Journal of the royal statistical society. Series B (..., 1995
[Cited by 37060](#) - Related articles - All 47 versions

- “**powerful**”: pvalue threshold less stringent than Bonferroni
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The *false discovery rate*: A *powerful* approach for multiple hypothesis correction

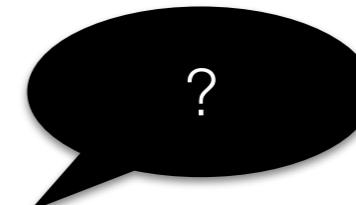
TABLE 1
Number of errors committed when testing m null hypotheses

	<i>Declared non-significant</i>	<i>Declared significant</i>	<i>Total</i>
True null hypotheses	U	V	m_0
Non-true null hypotheses	T	S	$m - m_0$
	$m - R$	R	m

$$\text{FDR} = V / R$$

- “**powerful**”: pvalue threshold less stringent than Bonferroni
- an estimate of frequency of **false discoveries** at a given threshold!

How can I compute the *False Discovery Rate*?



False Discovery Rate Estimation:
The *expected* rate of false positives

$$= \frac{\# \text{ false positives} \leq \alpha}{\# \text{ findings} \leq \alpha}$$

$$\frac{50 \text{ false positives} \leq 0.05}{100 \text{ findings} \leq 0.05} = 0.5$$

? # false positives (α)

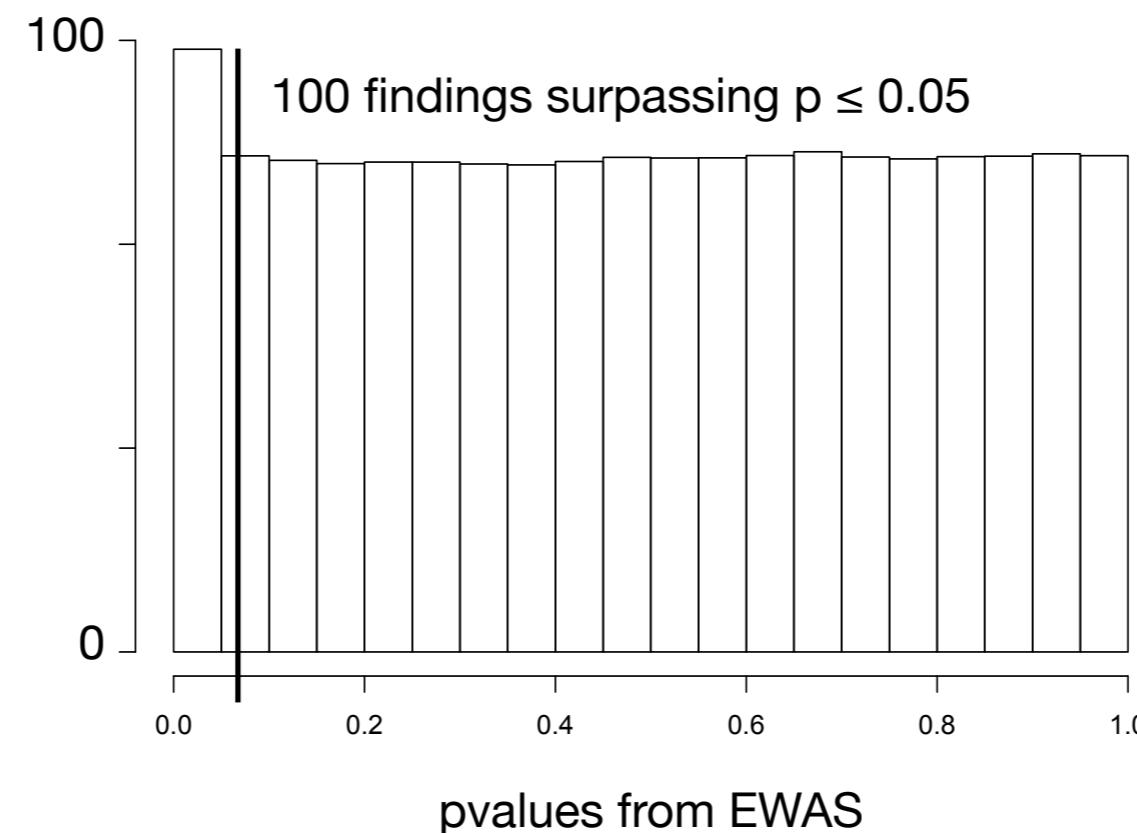


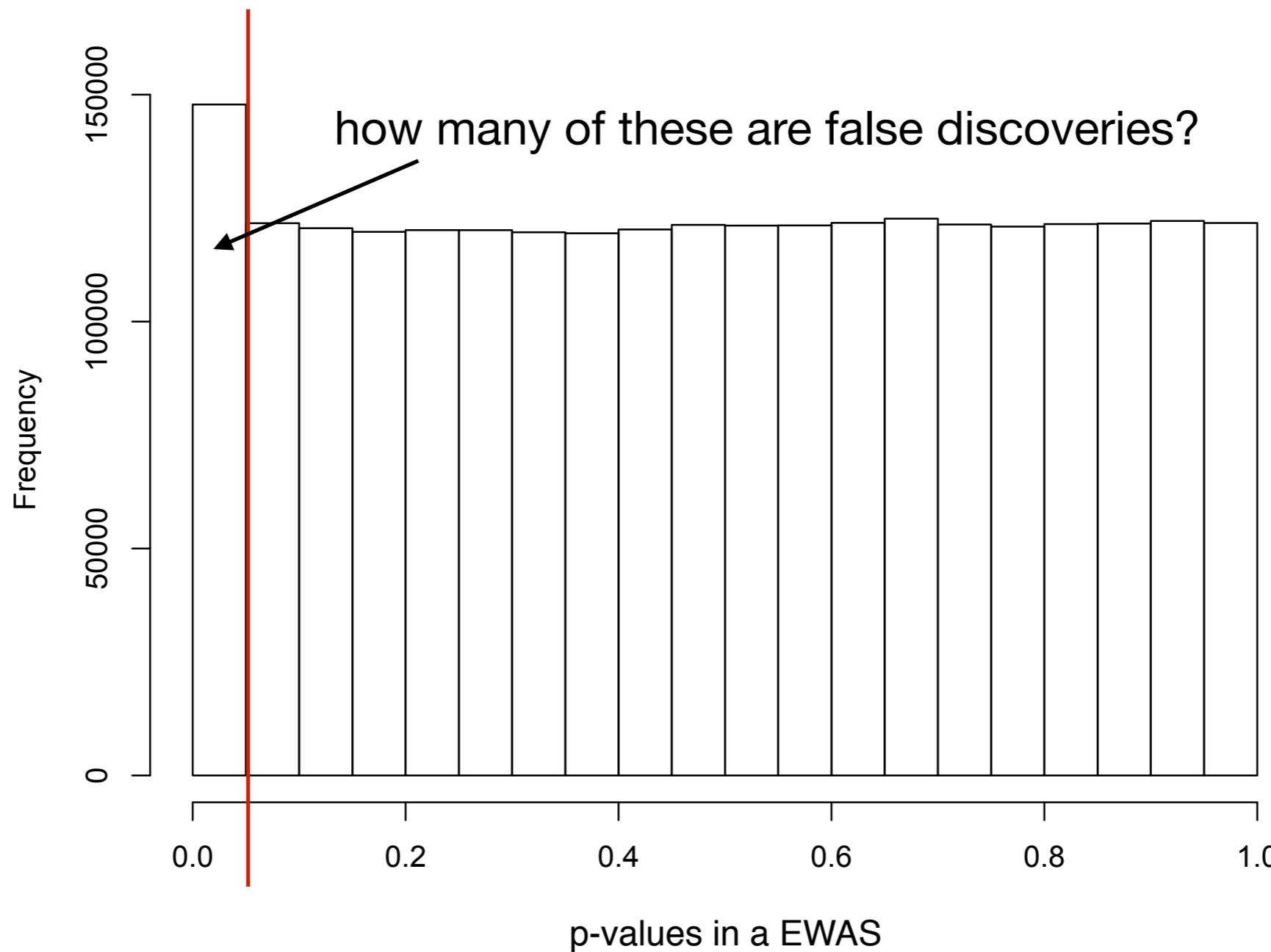
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	$m - R$	R	m

We don't know $V!$

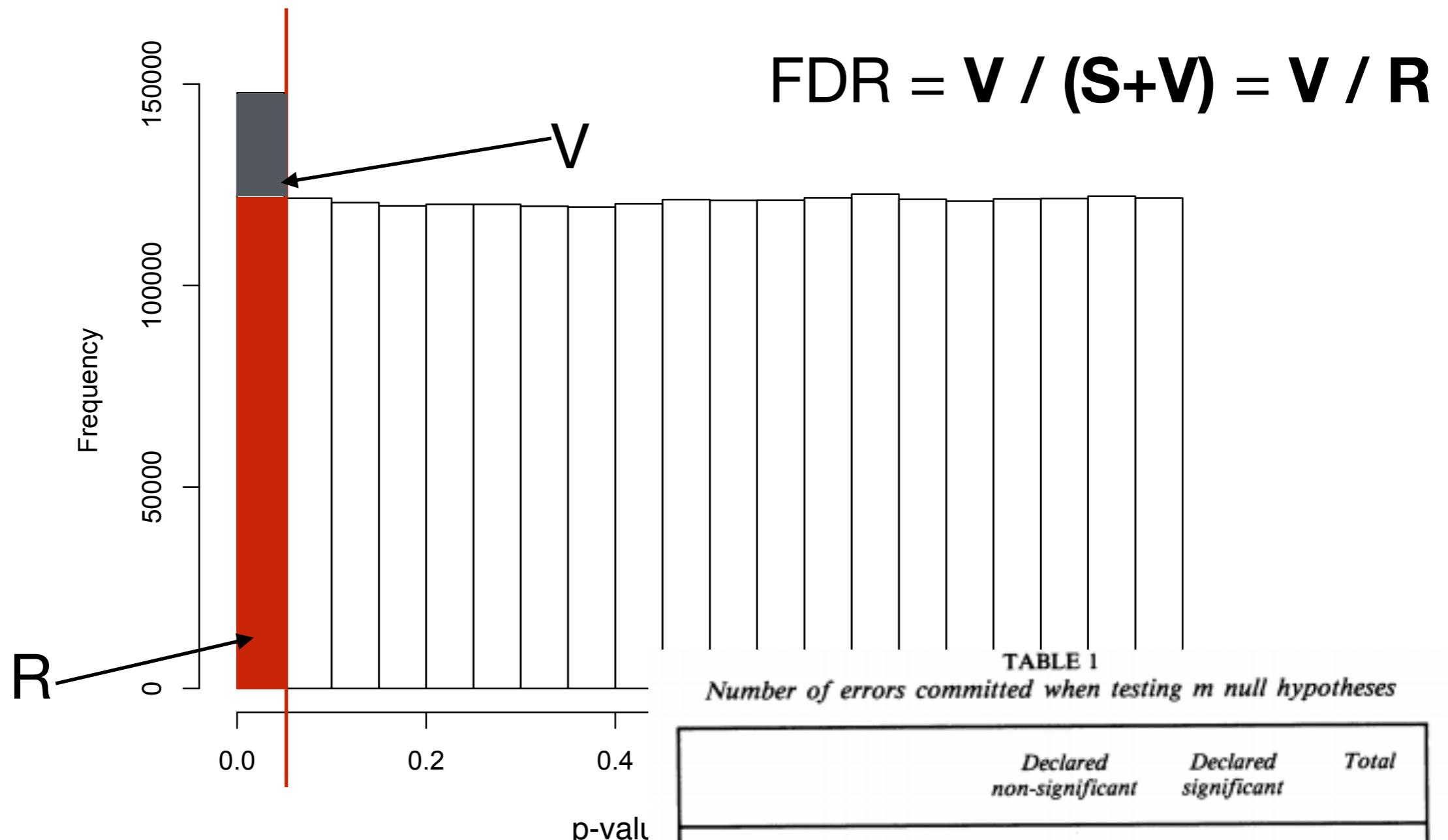
What is the ***False Discovery Rate***?

The expected number of false discoveries at a given significance threshold



What is the ***False Discovery Rate***?

The expected number of false discoveries at a given significance threshold



How can I compute the ***False Discovery Rate?*** *empirically deriving the null distribution through permutation tests*

False Discovery Rate Estimation:
The *expected* rate of false positives

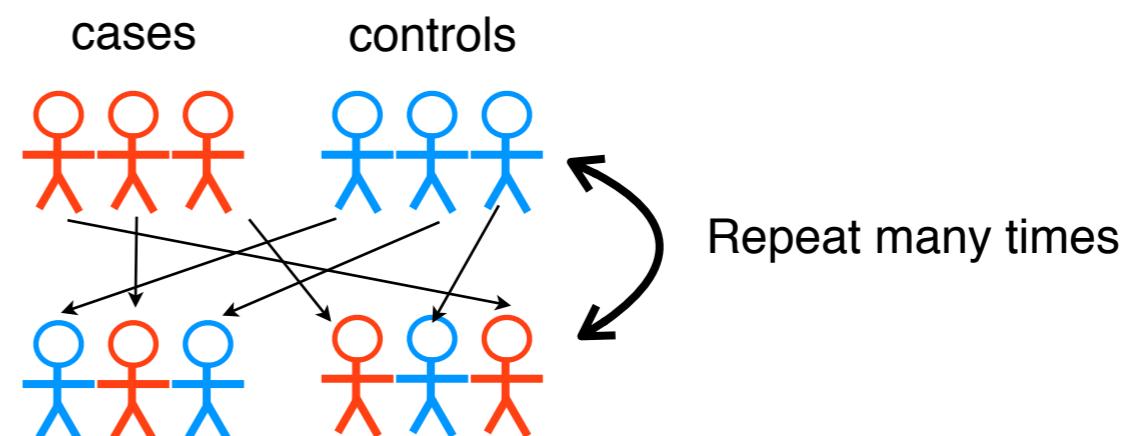
$$= \frac{\# \text{ false positives} \leq a}{\# \text{ findings} \leq a}$$

$$\frac{50 \text{ false positives} \leq 0.05}{100 \text{ findings} \leq 0.05} = 0.5$$

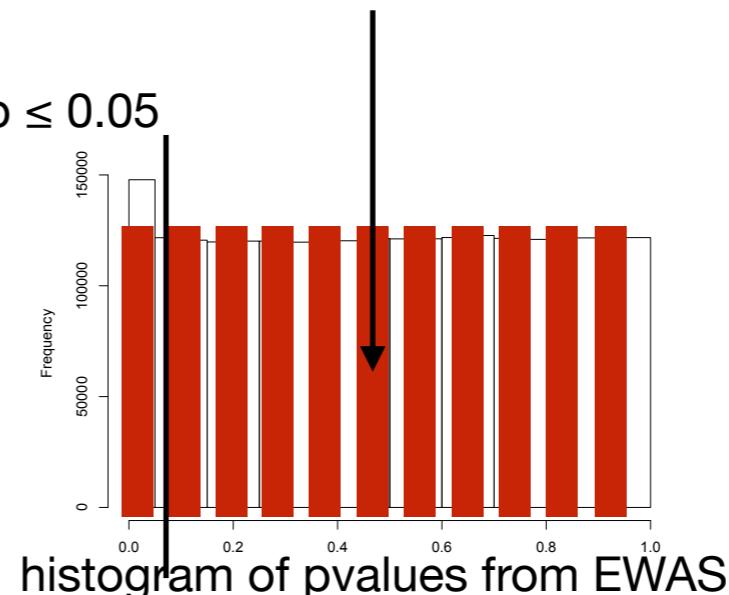
? # false positives (a)

“Shuffle” (permute) disease and non-diseased participants

Re-run EWAS



100 findings surpassing $p \leq 0.05$



How can I compute the *False Discovery Rate?*

Benjamini-Hochberg “step-up” method

first, choose a threshold, q

Benjamini and Hochberg (1995) showed that when the test statistics are independent the following procedure controls the FDR at level $q \cdot m_0/m \leq q$.

Next, sort p-values

THE BENJAMINI HOCHBERG PROCEDURE. Let $p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(m)}$ be the ordered observed p -values. Define

$$(1) \quad \text{find } k \quad k = \max \left\{ i : p_{(i)} \leq \frac{i}{m} q \right\},$$

and reject $H_{(1)}^0, \dots, H_{(k)}^0$. If no such i exists, reject no hypothesis.

$$p(i) * m/i \leq q$$

Benjamini and Hochberg (1995) showed that when the test statistics are independent the following procedure controls the FDR at level $q \cdot m_0/m \leq q$.

THE BENJAMINI HOCHBERG PROCEDURE. Let $p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(m)}$ be the ordered observed p -values. Define

$$(1) \quad k = \max \left\{ i : p_{(i)} \leq \frac{i}{m} q \right\},$$

and reject $H_{(1)}^0 \cdots H_{(k)}^0$. If no such i exists, reject no hypothesis.

$$p(i) * m/i \leq q$$

0.01, 0.2, 0.5, 0.45, 0.06, 0.04, 0.004, 0.02, 0.1, 0.07

0.5, 0.45, 0.2, 0.1, 0.07, 0.06, 0.04, 0.02, 0.01, 0.004

$$0.004 * 10 / 1 \leq 0.05?$$

$$0.01 * 10 / 2 \leq 0.05?$$

$$0.02 * 10 / 3 \leq 0.05?$$

Any reach significance at an FDR < 0.05?

How can I compute the *False Discovery Rate?*
Benjamini-Hochberg “step-up” method

0.04, 0.04, 0.04, 0.04, 0.04, 0.04, 0.04, 0.04, 0.04, 0.04, 0.04

Any here reach significance at an FDR < 0.05?

How can I compute the *False Discovery Rate*?
Benjamini-Hochberg “step-up” method

```
p.adjust(p, 'fdr')
```

What does this return?

Consideration of multiplicity of modeling scenarios.

Example: *Vibration of Effects*, the empirical distribution of effect sizes due to model choice

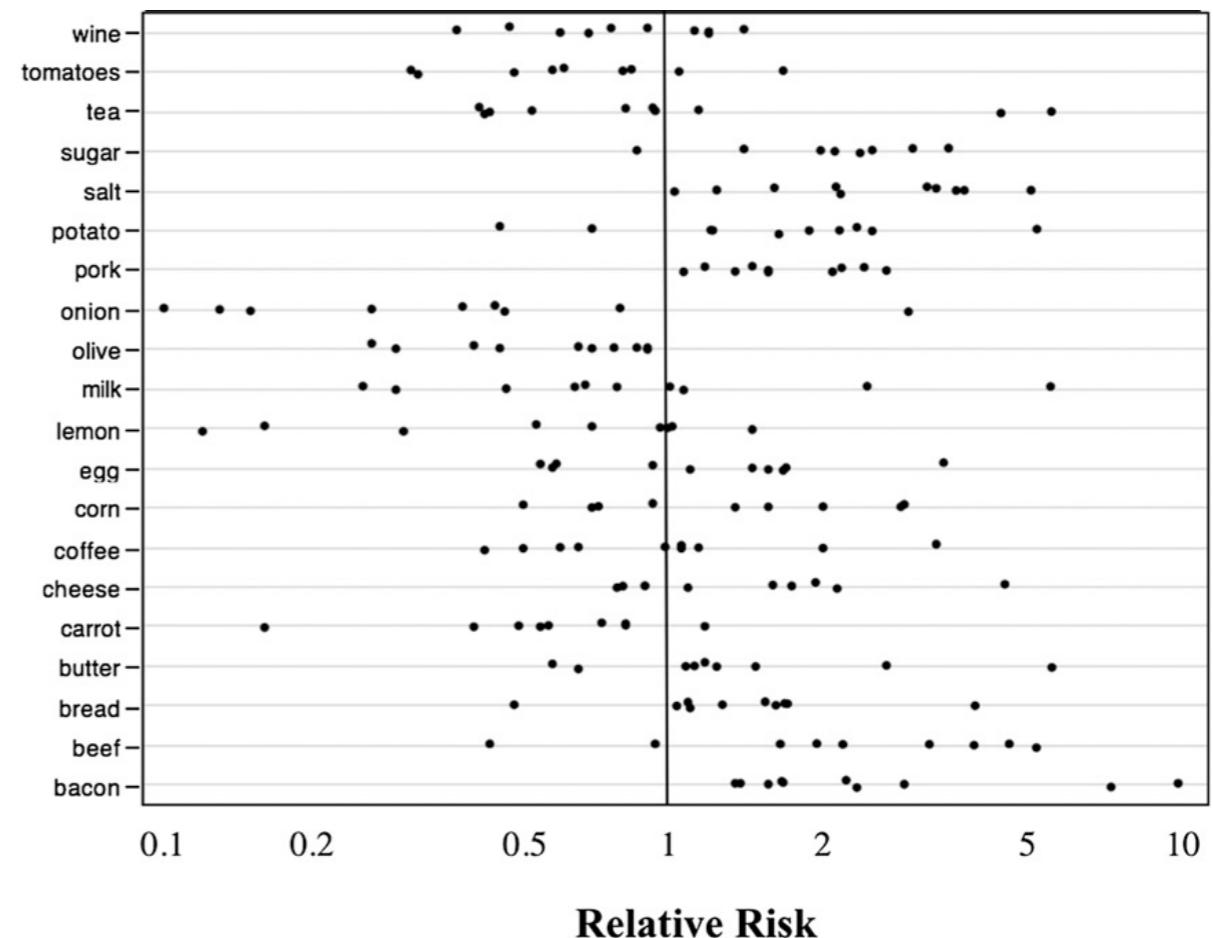
Example of *fragmentation*: Is everything we eat associated with cancer?

50 random ingredients from
*Boston Cooking School
Cookbook*

Any associated with cancer?

Of 50, 40 studied in cancer risk

Weak statistical evidence:
non-replicated
inconsistent effects
non-standardized



youtube.com

≡ YouTube john oliver science

Everything we eat both causes and cures cancer

● One medical study

Food	Protects against cancer	Causes cancer
Wine	0.5	1.0
Tomatoes	0.5	1.0
Tea	0.5	1.0
Milk	0.5	1.0
Eggs	0.5	1.0
Cane	0.5	1.0
Coffee	0.5	1.0
Butter	0.5	1.0
Beef	0.5	1.0

SOURCE: Schatzkin and colleagues, American Journal of Clinical Nutrition

13:38 / 19:27

Last Week Tonight with John Oliver: Scientific Studies (HBO)

LAST WEEK TONIGHT

LastWeekTonight

Subscribe 3,770,125

7,383,606 views

+ Add to Share *** More

86,632 2,652

Published on May 8, 2016

John Oliver discusses how and why media outlets so often report untrue or incomplete information as science.

SHOW MORE

<https://www.youtube.com/watch?v=0Rnq1NpHdmw>

A maze of associations is one way to a **fragmented** literature and **Vibration of Effects**

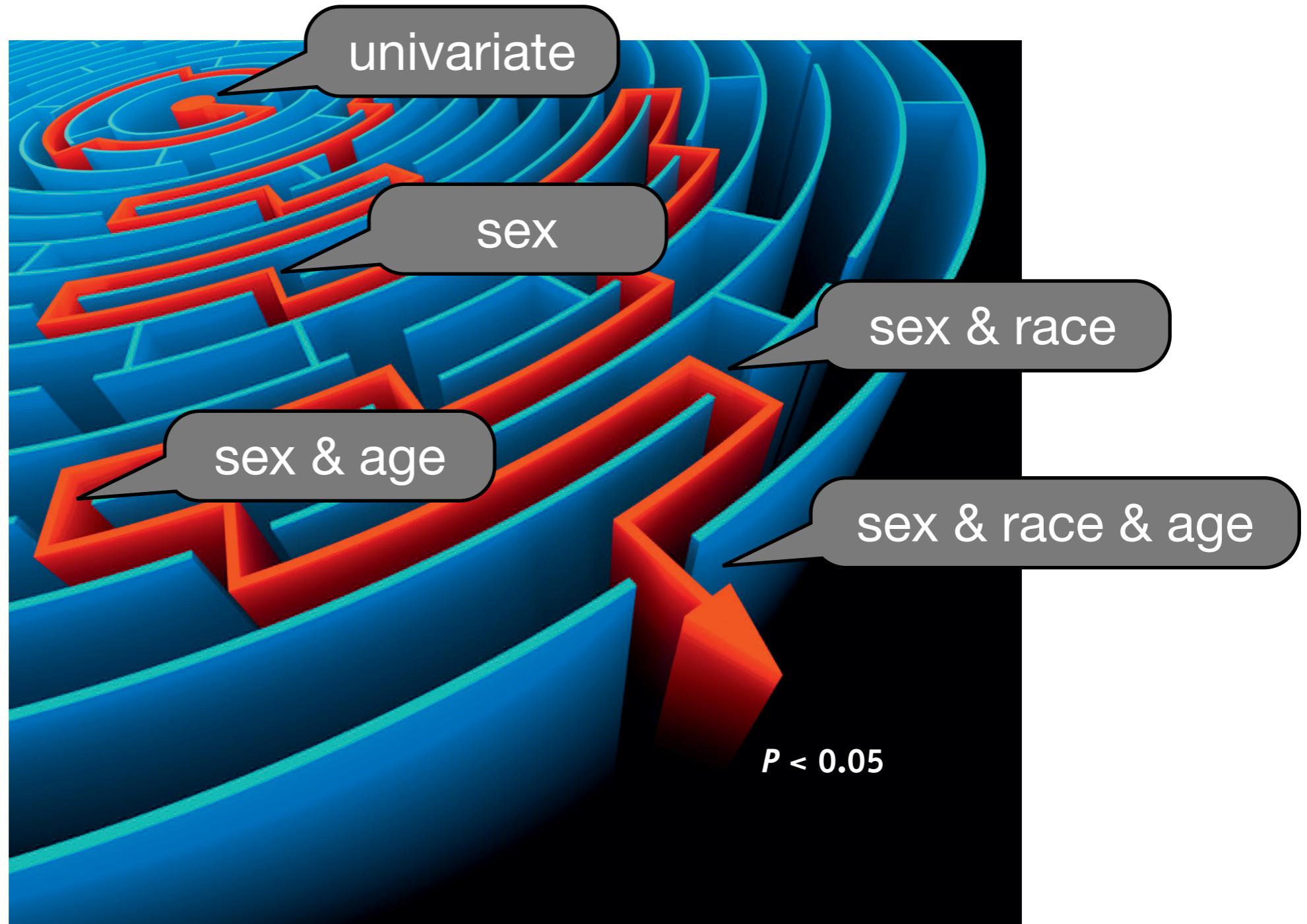
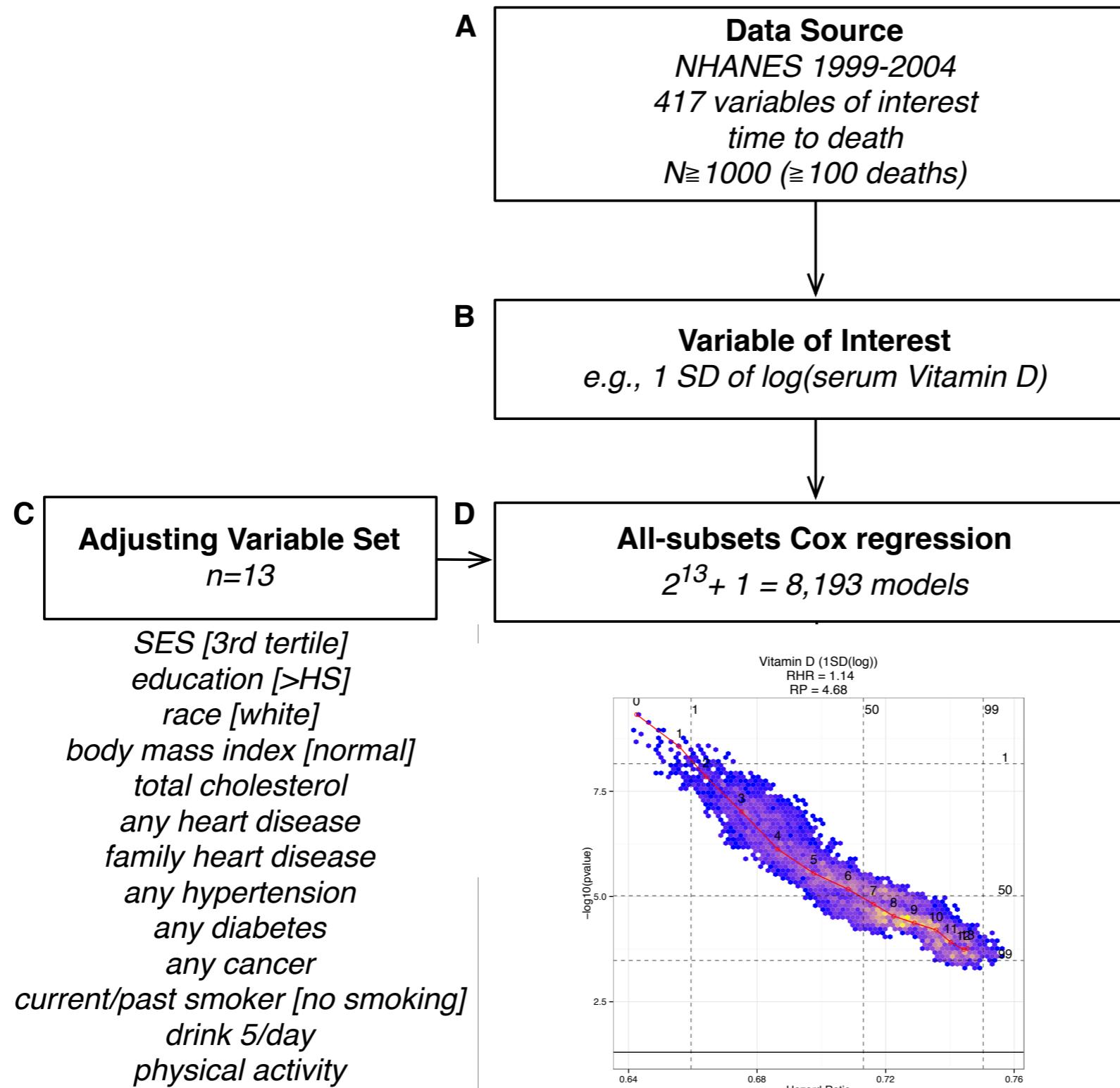
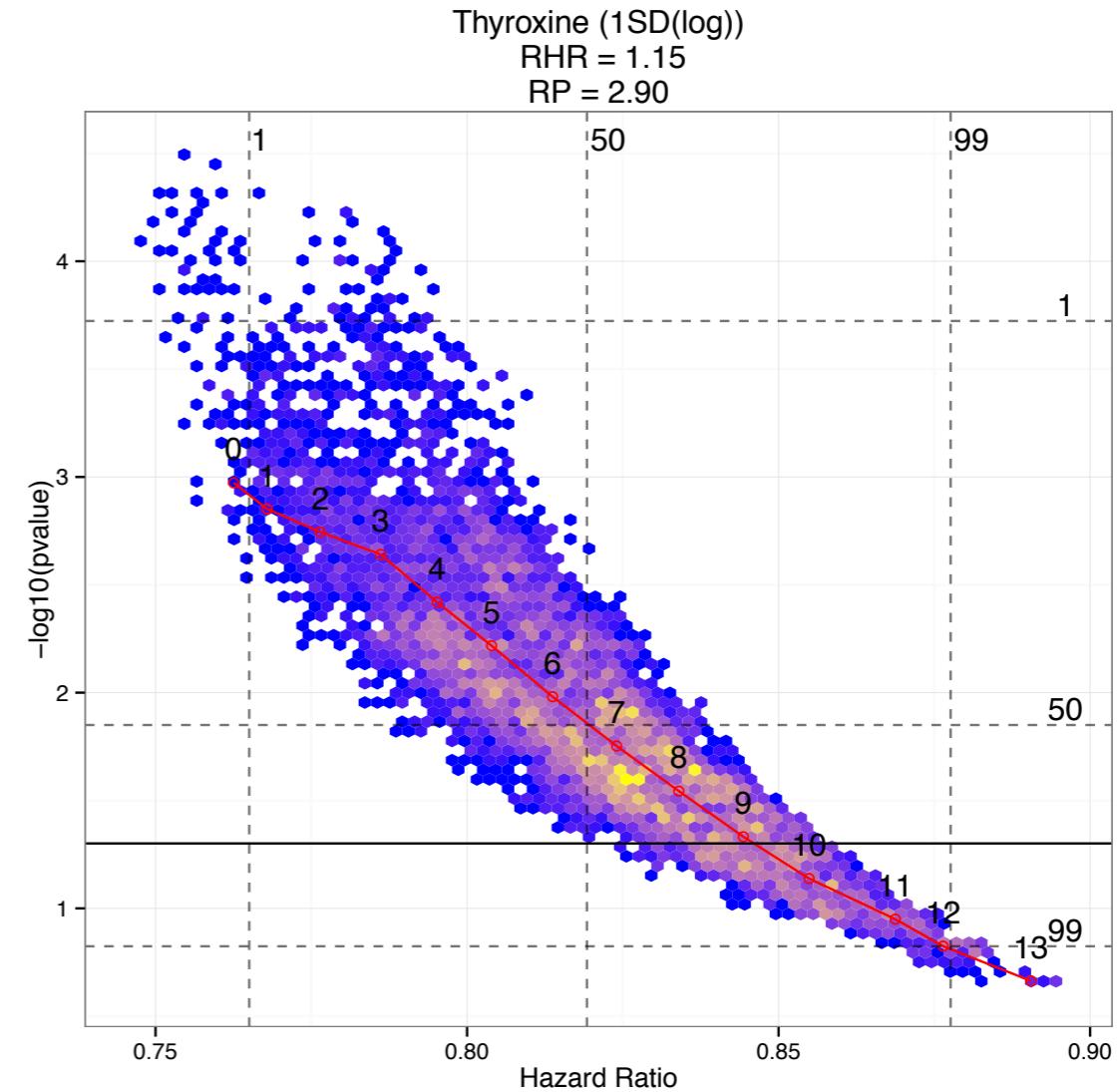
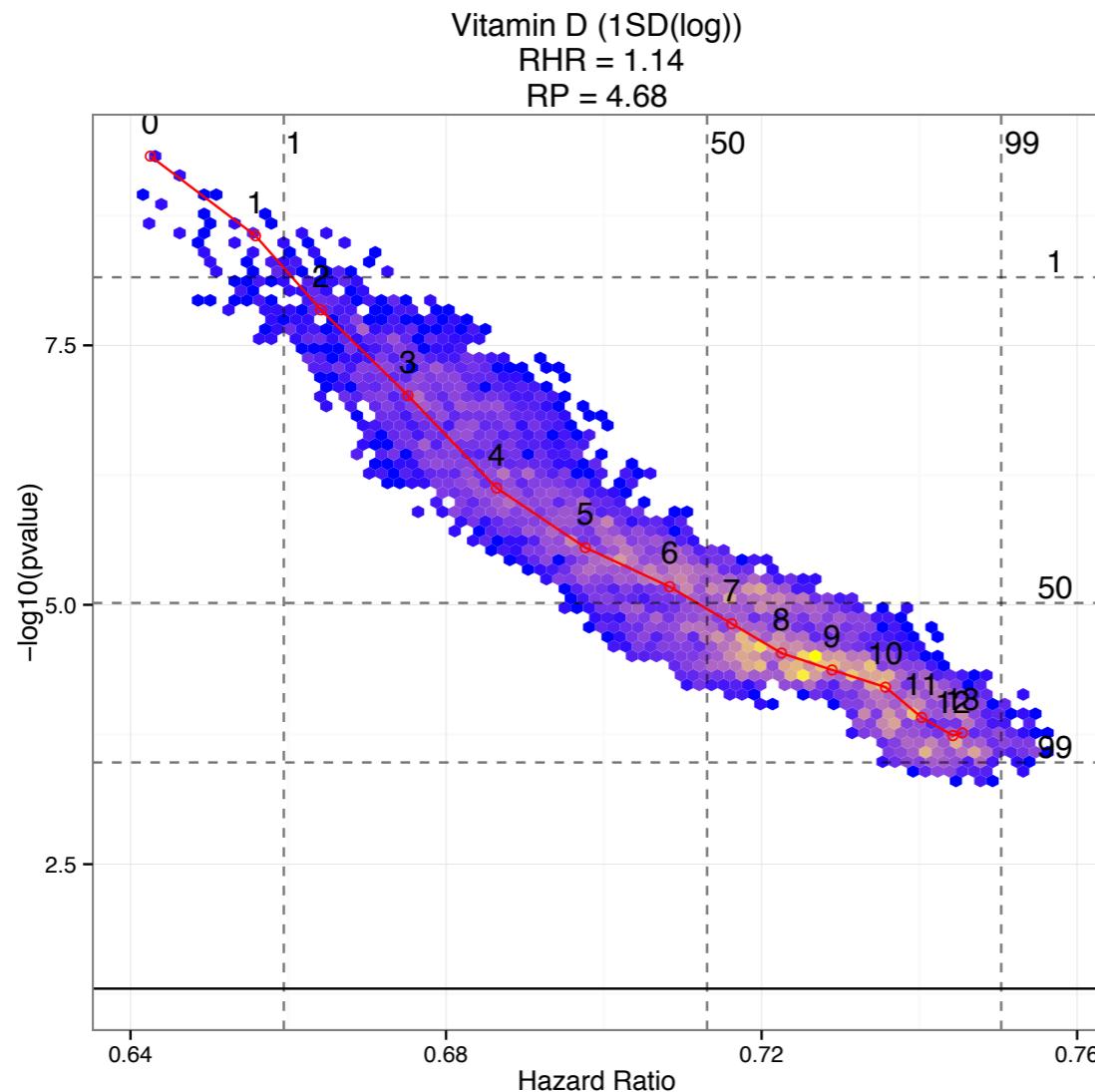


Figure 3. The path through a complex process can appear quite simple once the path is defined. Which terms are included in a multiple linear regression model? Each turn in a maze is analogous to including or not a specific term in the evolving linear model. By keeping an eye on the p-value on the term selected to be at issue, one can work towards a suitably small p-value. © ktsdesign – Fotolia

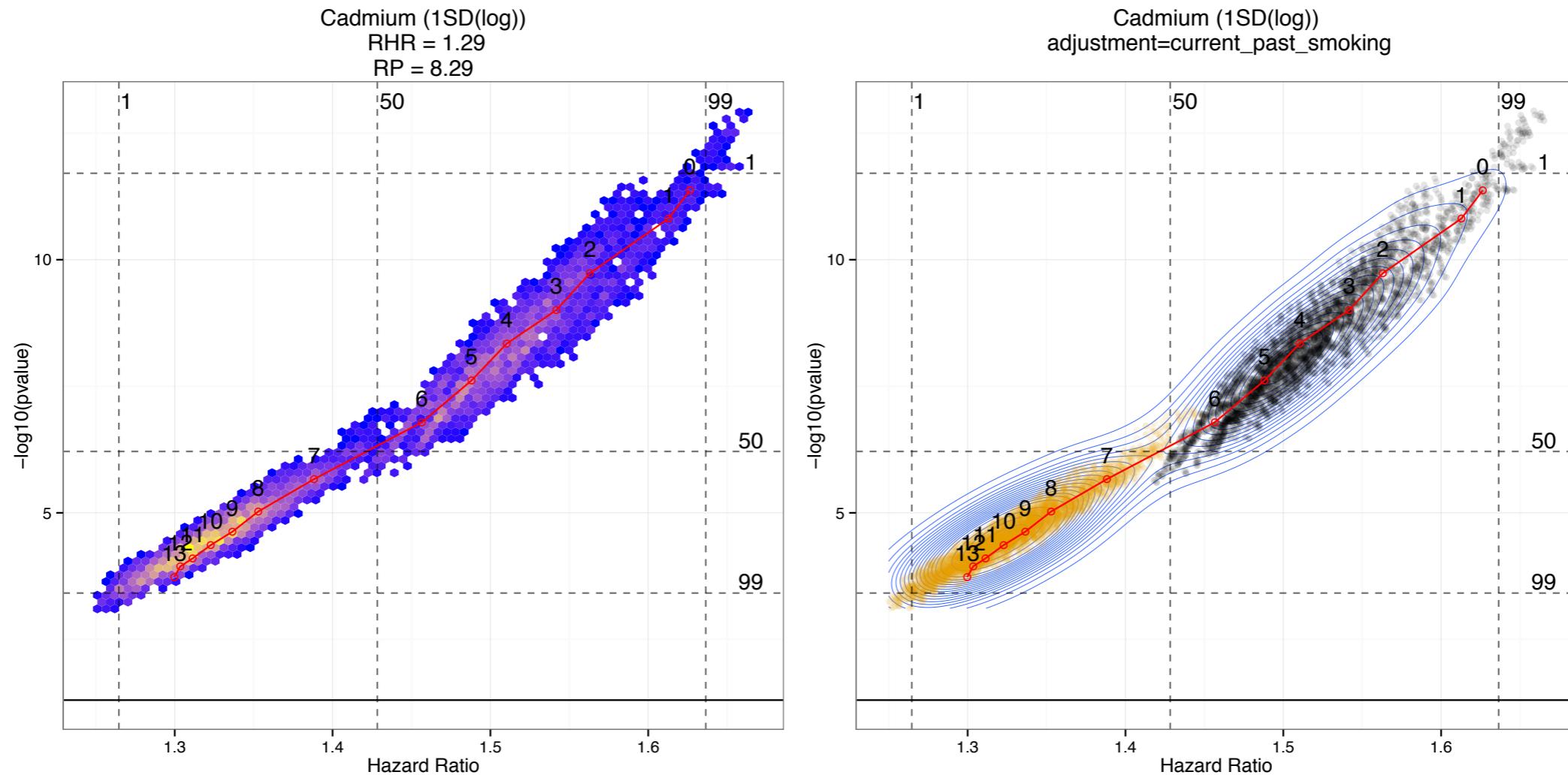
Distribution of associations and p-values due to model choice: Estimating the ***Vibration of Effects (or Risk)***



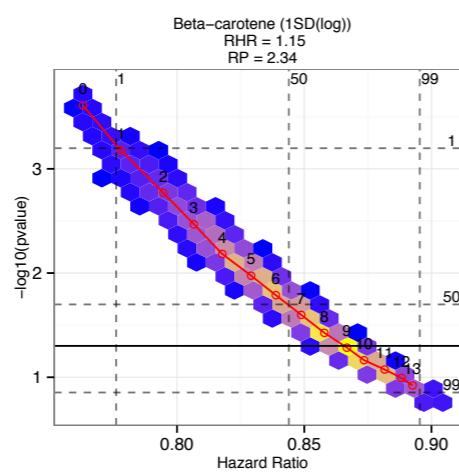
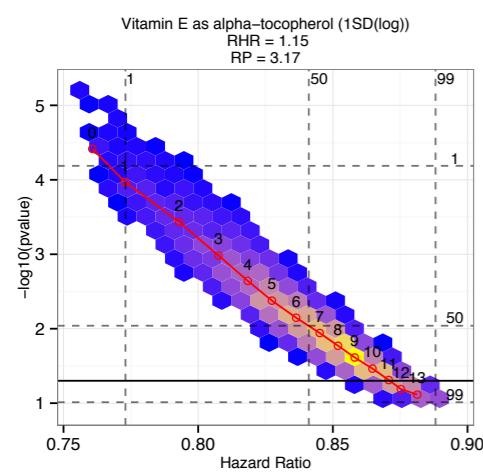
The *Vibration of Effects*: Vitamin D and Thyroxine and attenuated risk in mortality



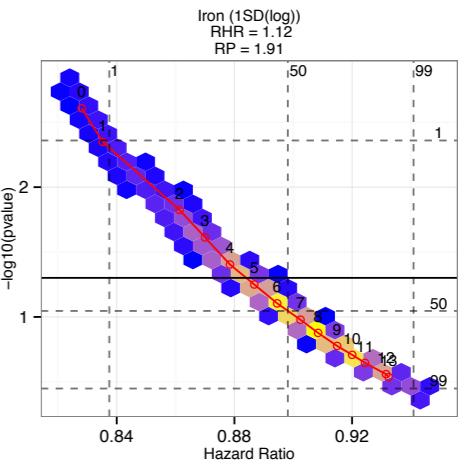
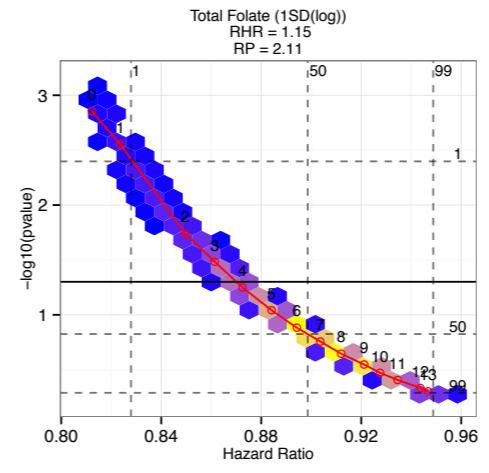
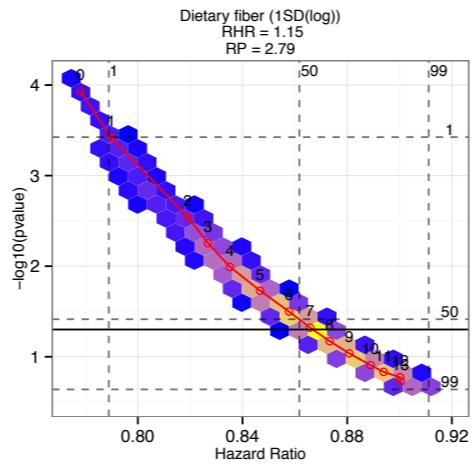
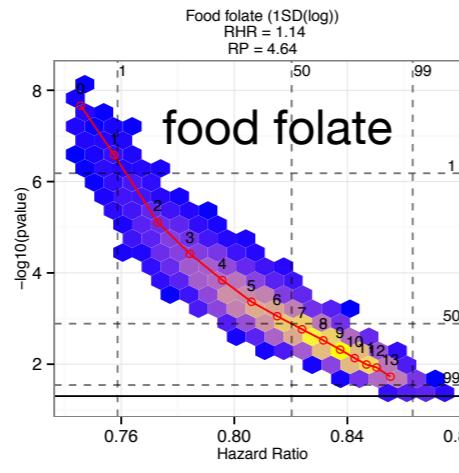
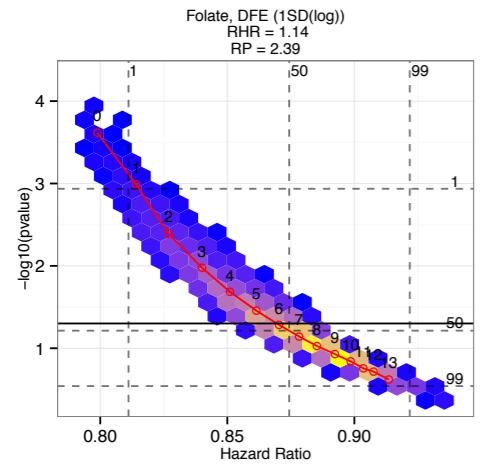
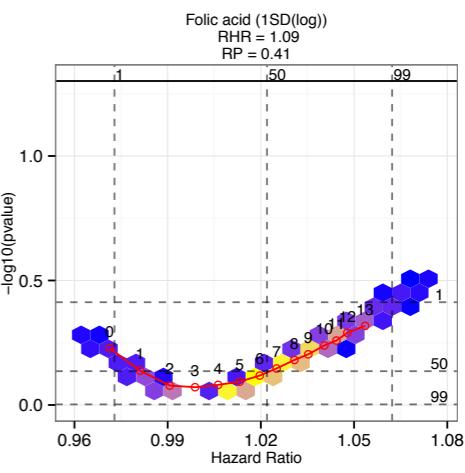
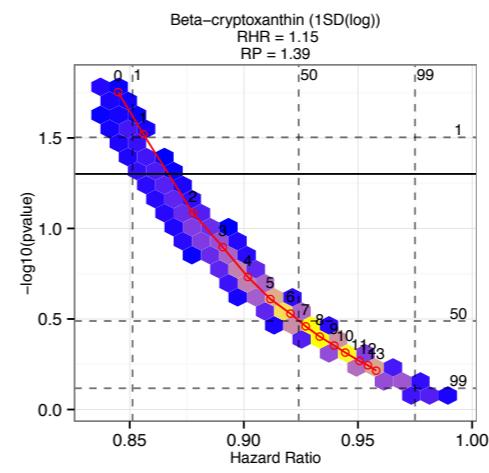
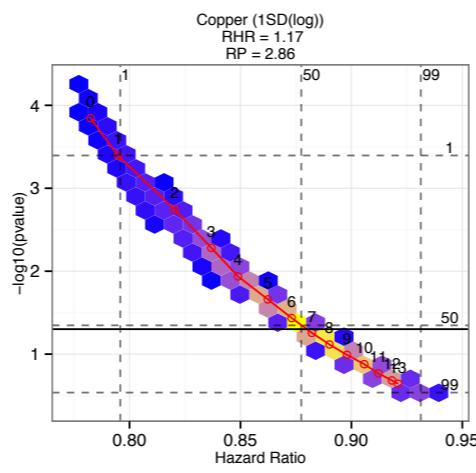
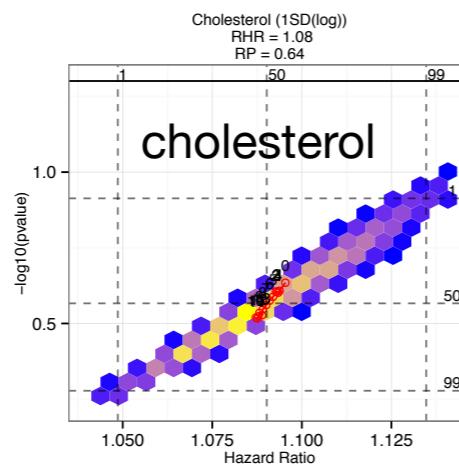
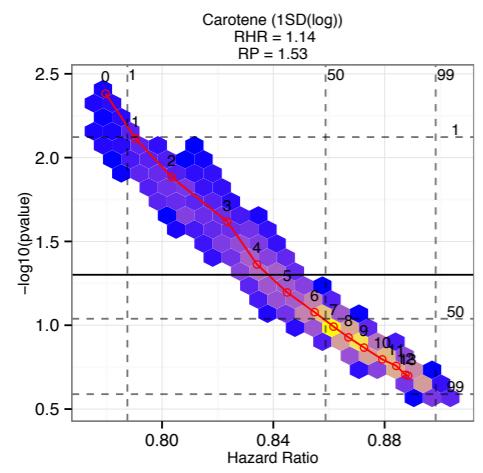
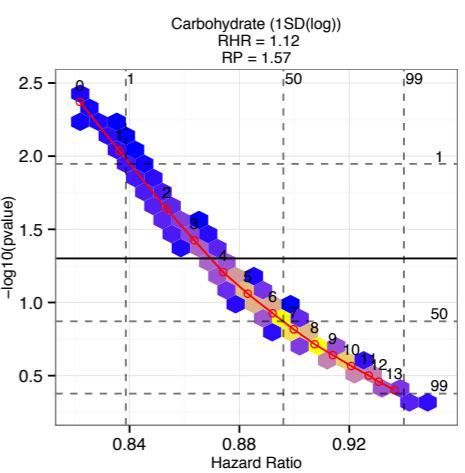
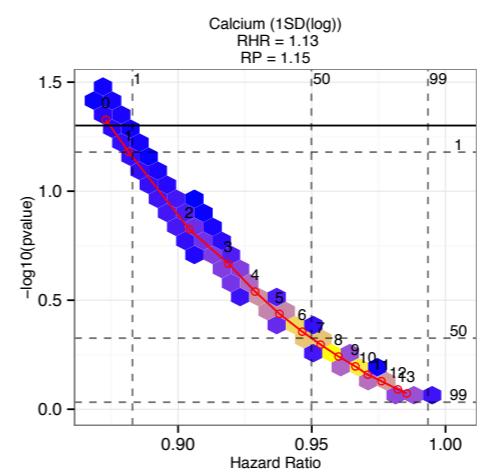
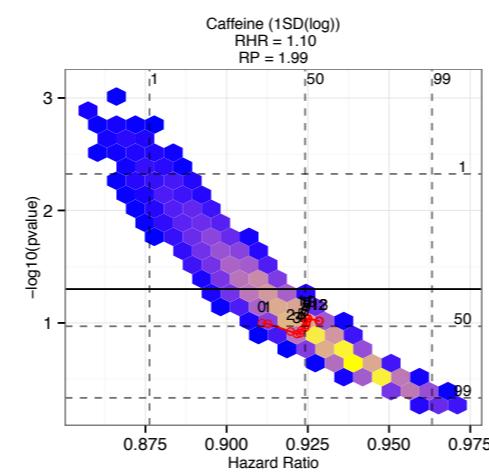
The *Vibration of Effects*: shifts in the effect size distribution due to select adjustments (e.g., adjusting **cadmium levels with smoking status**)

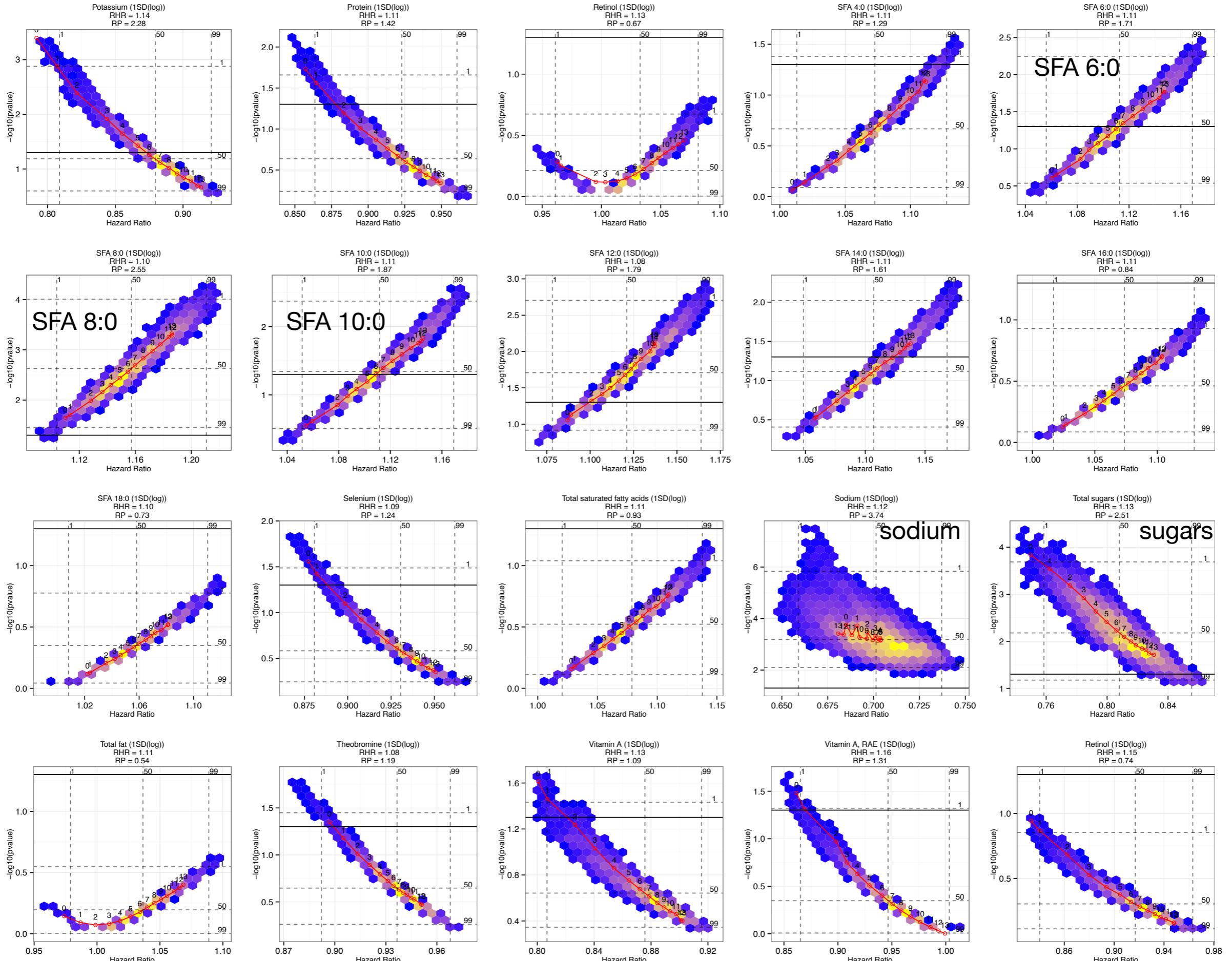


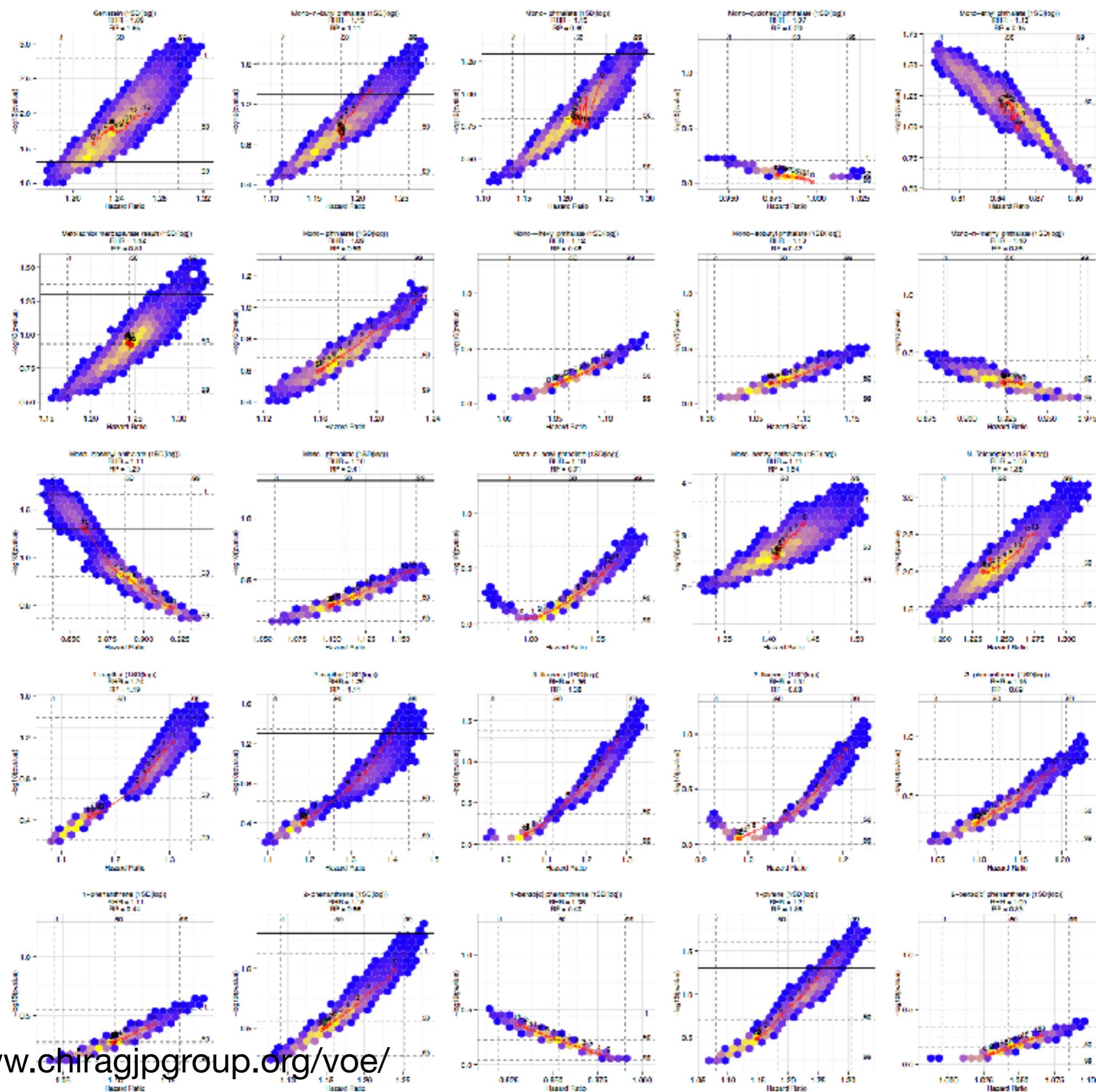
β -carotene

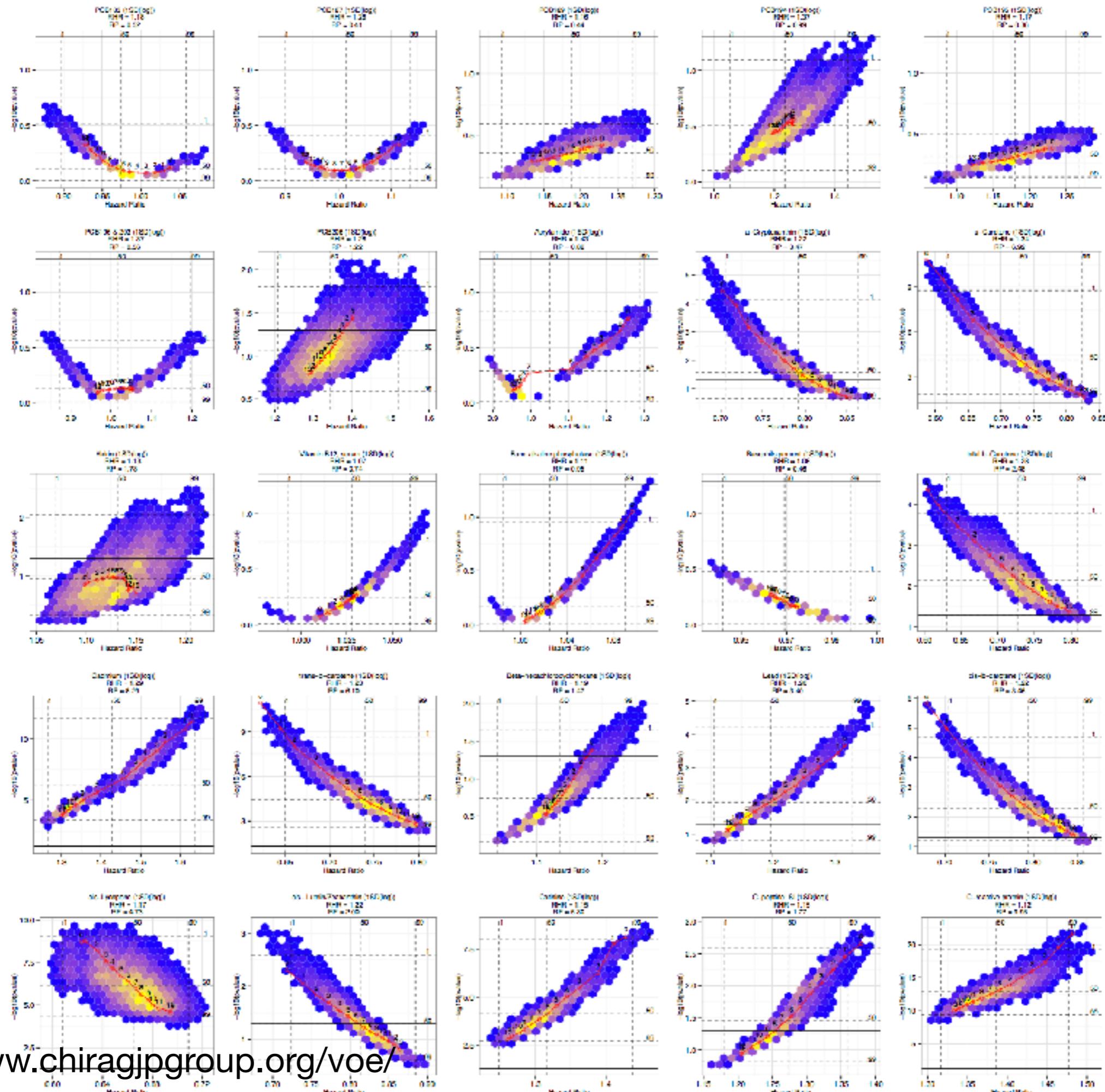


caffeine

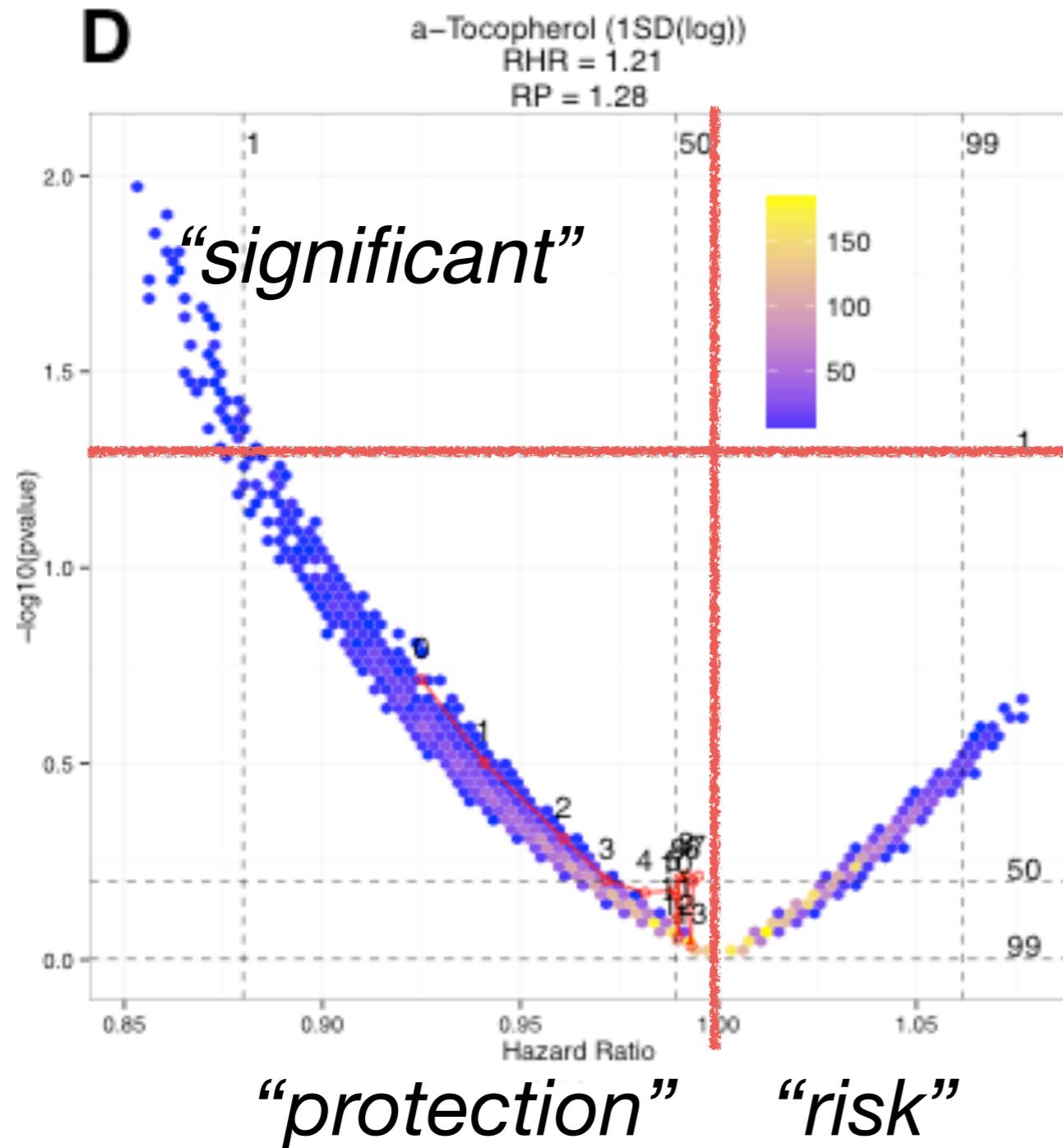








The **Vibration of Effects**: beware of the Janus effect (both **risk** and **protection**?!)



Brittanica.com

Janus (two-faced) risk profile

Risk and **significance** depends on modeling scenario!

For the second session today...

Extensible & open-source analytics software
(R code)

Freely available exposome data for your research
(NHANES: ~40,000 individuals and 1,000 variables)

Materials for teaching and demonstration



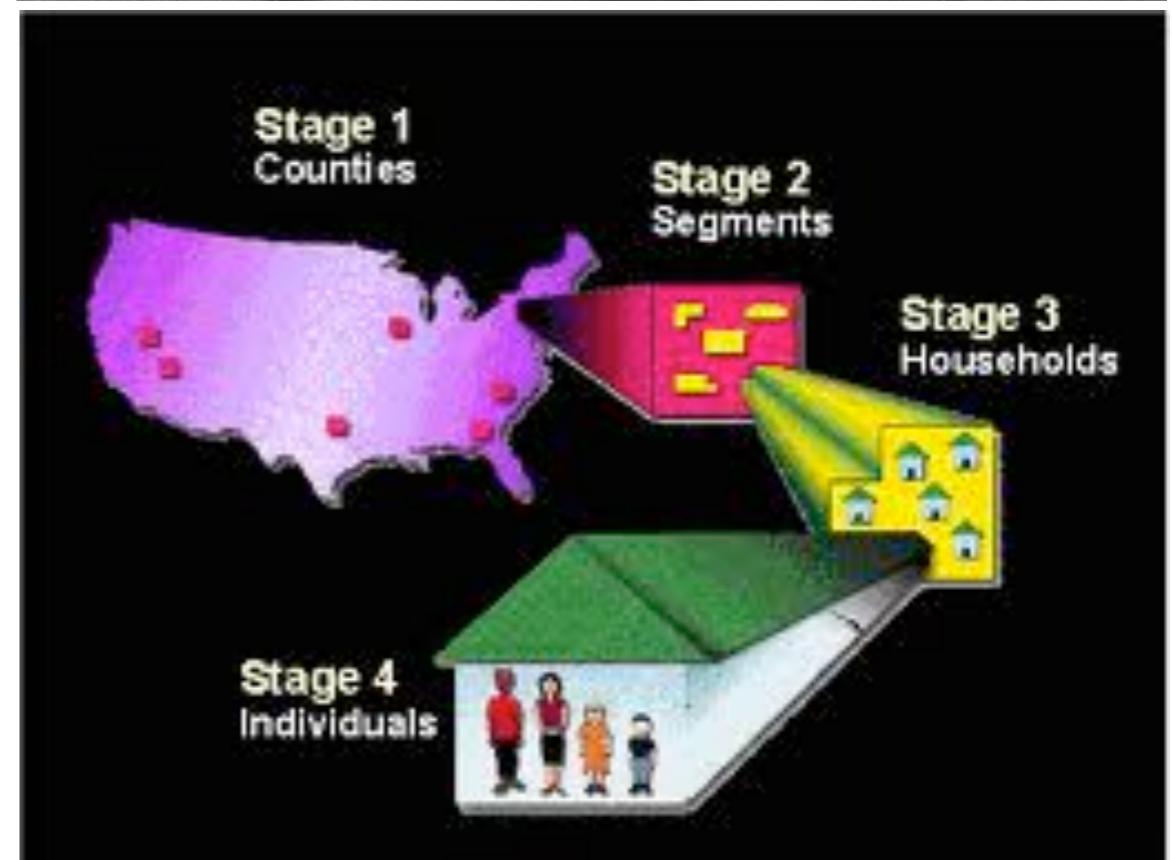
Fully merged dataset: National Health and Nutrition Examination Survey

since the 1960s
now biannual: 1999 onwards
10,000 participants per survey

>250 exposures (serum + urine)

>200 quantitative clinical traits
(e.g., serum glucose, lipids, body mass index, telomeres)

Death index linkage (cause of death)



Ready to analyze! N=41K with >1000 variables
(let us know; we can give you a DOI)

in review

13 XWAS-related manuscripts

preterm birth

type 2 diabetes

type 2 diabetes genetics

lipids

blood pressure

income

mortality

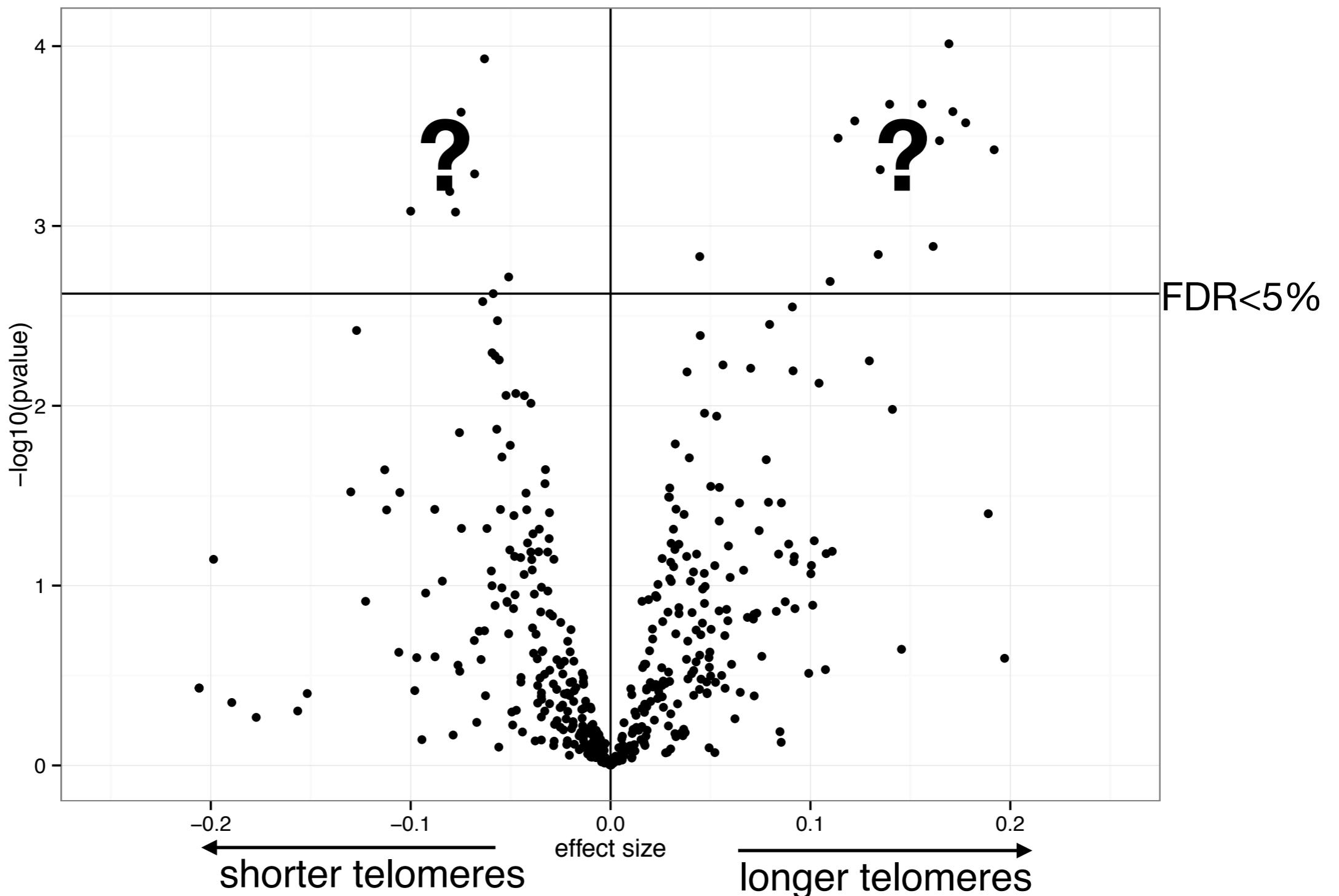
telomere length

methodology (5)

<http://correct>

Associations in *Telomere Length*:

Can you identify the associations in this graph?



median N=3000; N range: 300-7000

IJE, 2016

Resources Index (for today's session)

<http://bit.ly/xwas> with nhanes

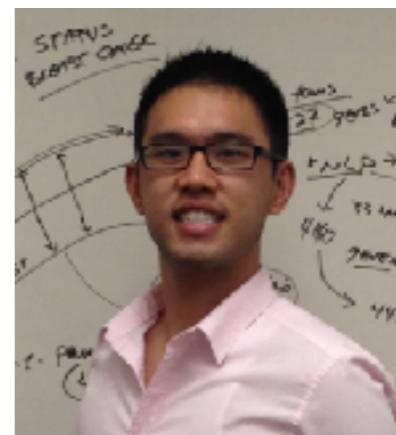
Please let us know if you are using the resources
(or provide feedback)!

Chirag



  @chiragjp

Nam



  @nampho2

Resources Index

Papers and repositories

Papers:

<https://paperpile.com/shared/PtvEae>

Sample size for EWAS:

https://github.com/jakemkc/ewas_sample_size

Correlation Globes (stratified):

https://github.com/jakemkc/exposome_variability

Correlation Globes:

https://github.com/chiragjp/exposome_correlation

Vibration of Effects

<https://github.com/chiragjp/voe>

Exposome cohort data (NHANES 1999-2006)

https://github.com/chiragjp/nhanes_scidata

Acknowledgements

RagGroup

Nam Pho

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Jenn Grandfield

Michal Preminger

Stanford

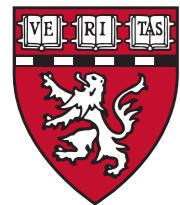
John PA Ioannidis



NIH Common Fund
Big Data to Knowledge



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Biomedical Informatics

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