

Genetic and environmental determinants of drug adherence and drug purchasing behaviour

Boston - Helsinki TC
November 25th, 2020

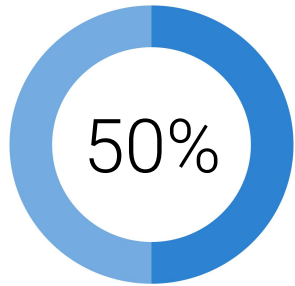
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Drug adherence: a critical barrier to treatment efficacy

Adherence

the extent to which a person's behaviour corresponds with agreed recommendations from a health care provider



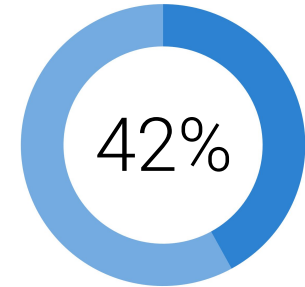
average adherence among patients suffering chronic diseases

WHO. *Adherence to long-term therapies: evidence for action*. 2003

OR: 1.78

association between poor adherence and mortality

Simpson et al. *A meta-analysis of the association between adherence to drug therapy and mortality*. BMJ. 2006



of the total drug acquisition costs is due to non-adherence

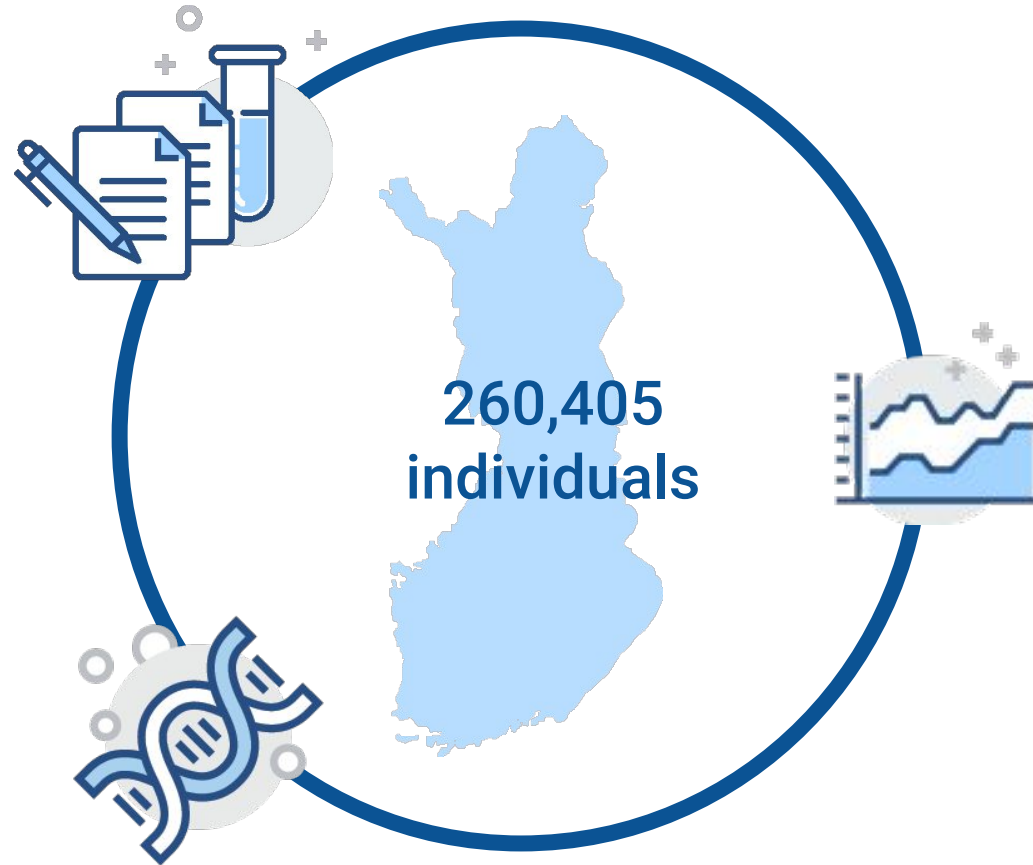
Hovstadius, B., Petersson, G. *Non-adherence to drug therapy and drug acquisition costs in a national population - a patient-based register study*. BMC Health Serv Res. 2011

Objective

Investigate the genetic contribution to drug adherence to identify correlated health and behavioural traits and causal risk factors

The FinnGen research project

National healthcare registries
(115,740,626 longitudinal data points)



Association analyses
and results

Genome data
(16,962,023 imputed markers)

The FinnGen drug purchase register

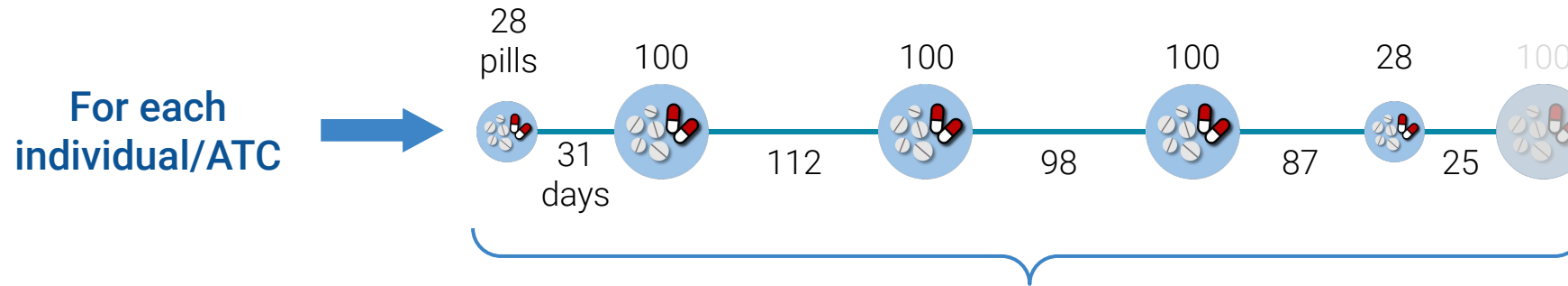


more than 20 years timespan

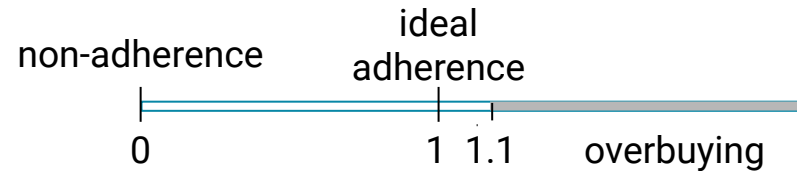


59,605,493 total purchases of
reimbursable prescription drugs:
date of purchase | ATC | dosage | quantity

Quantifying drug adherence



$$\text{adherence} = \frac{\text{total quantity}}{\text{total purchasing days}}$$

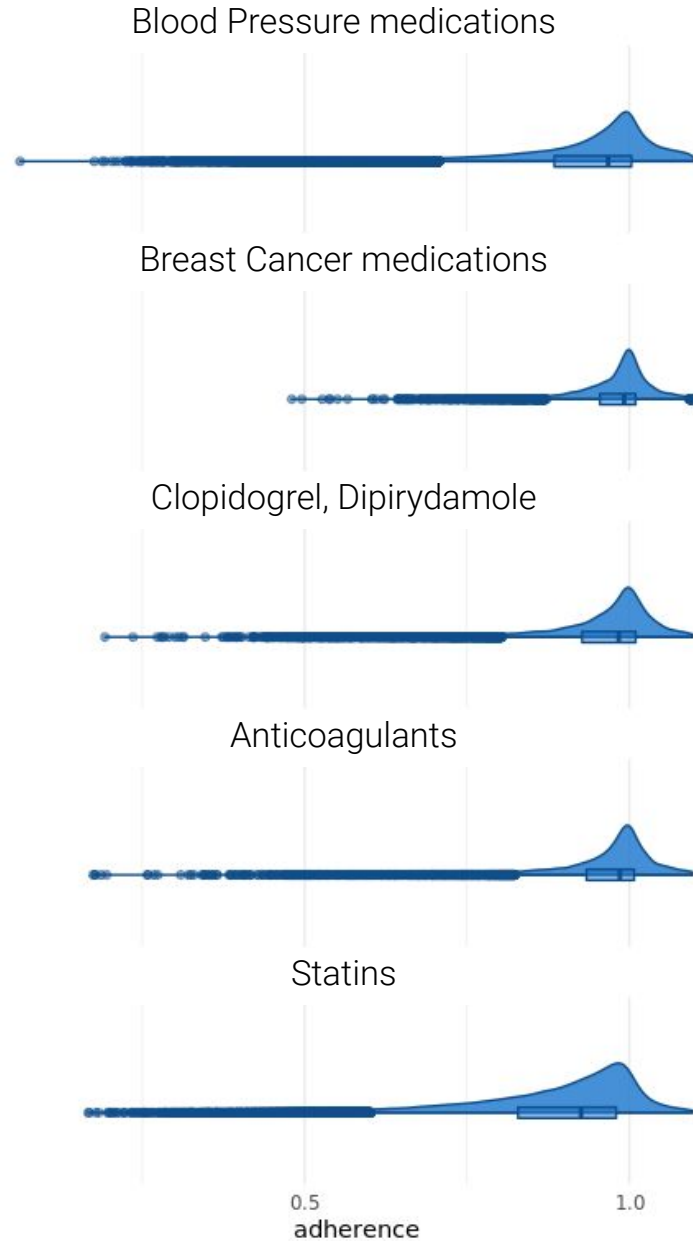


Medications included

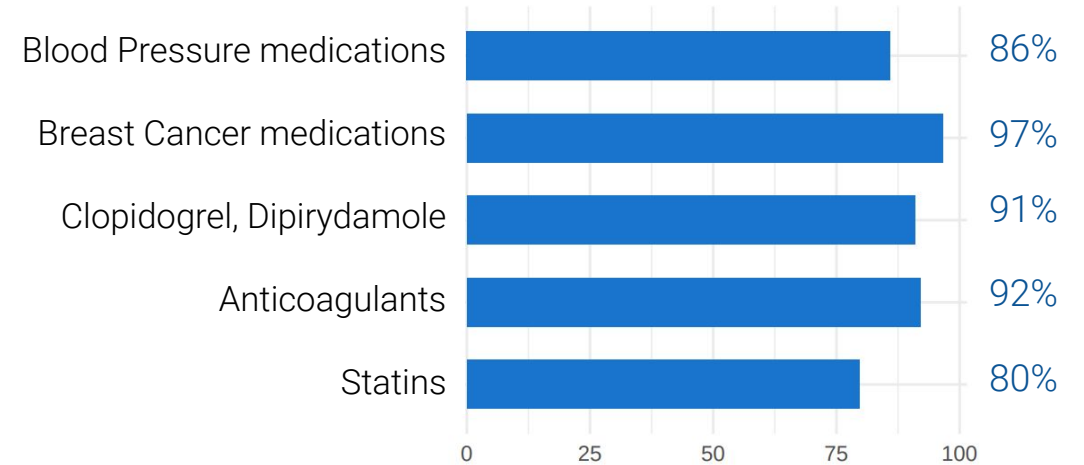
- Blood Pressure (BP) medications
 - antihypertensives
 - diuretics
 - calcium channel blockers
 - agents acting on the renin-angiotensin system
- Breast Cancer medications
- Clopidogrel, Dipyridamole
- Direct Oral Anticoagulants (DOAC)
- Statins

Medication	Users	Tot purchases
Blood Pressure medications	84,705	3,850,000
Breast Cancer medications	5,799	79,213
Clopidogrel, Dipyridamole	14,201	214,401
Anticoagulants	10,936	142,314
Statins	77,773	2,424,752

Adherence to each medication



Proportion of “good adherers” (adherence>0.8)



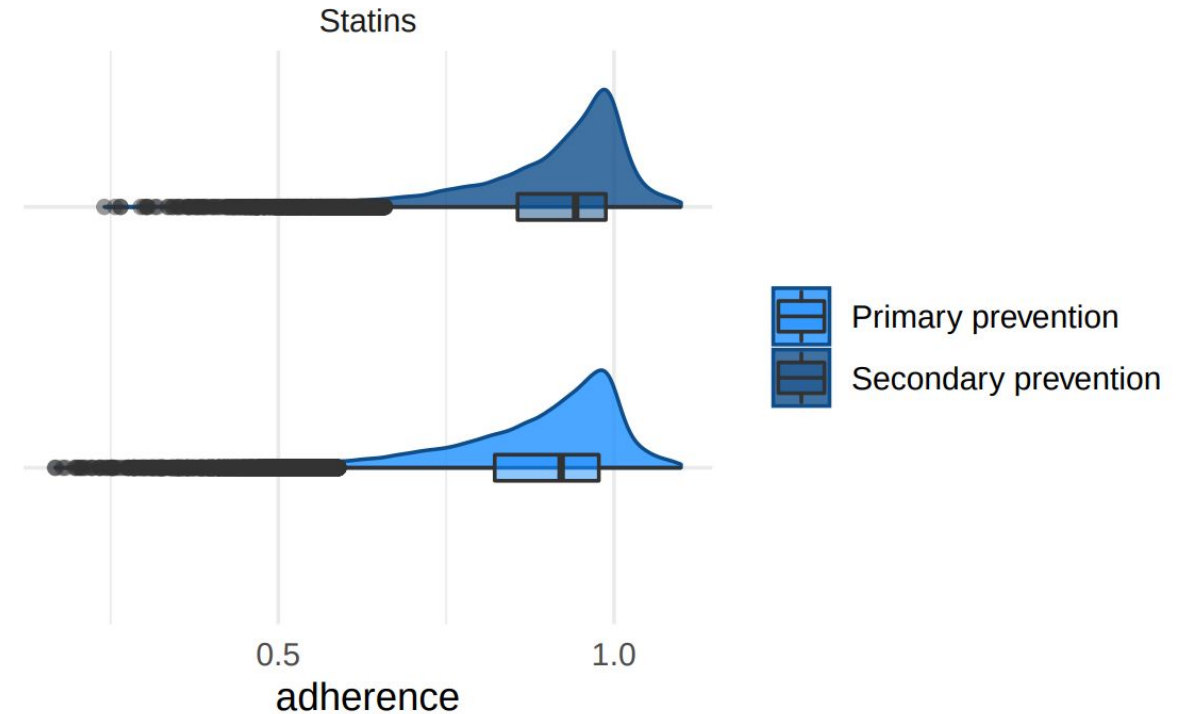
Adherence to statins by type of prevention

Secondary prevention

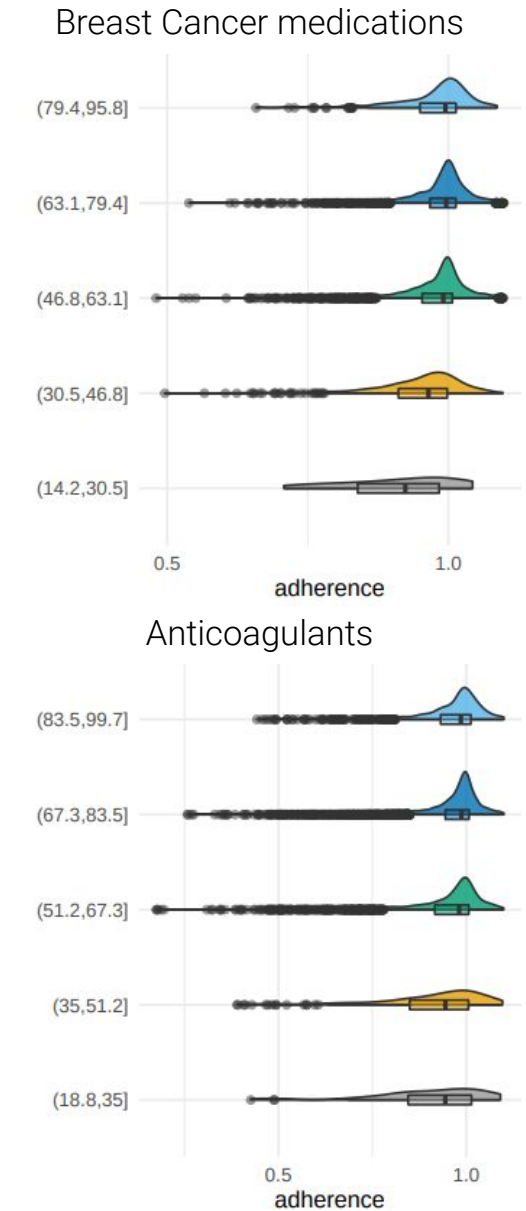
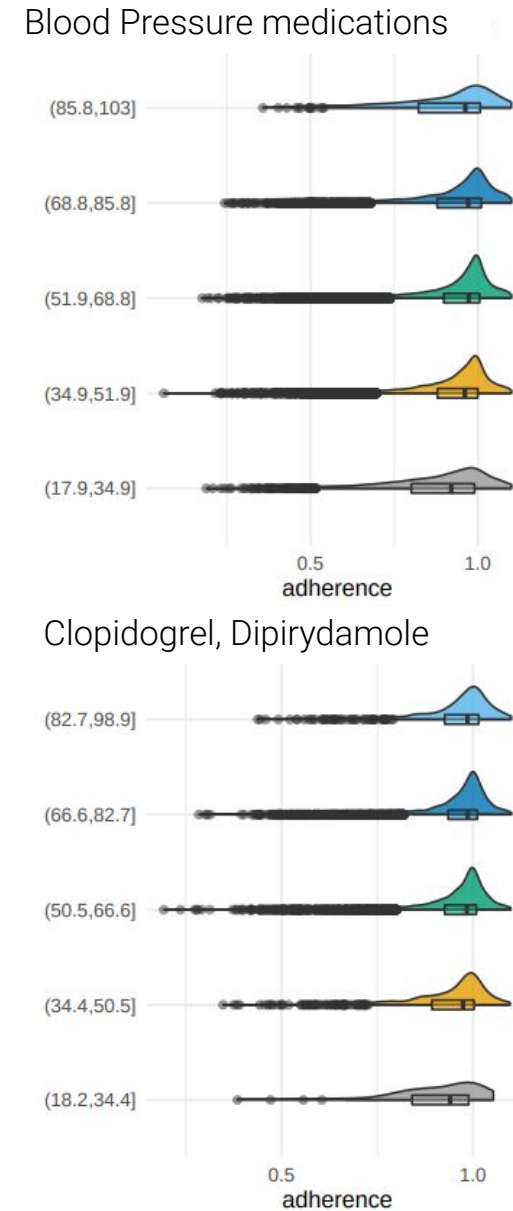
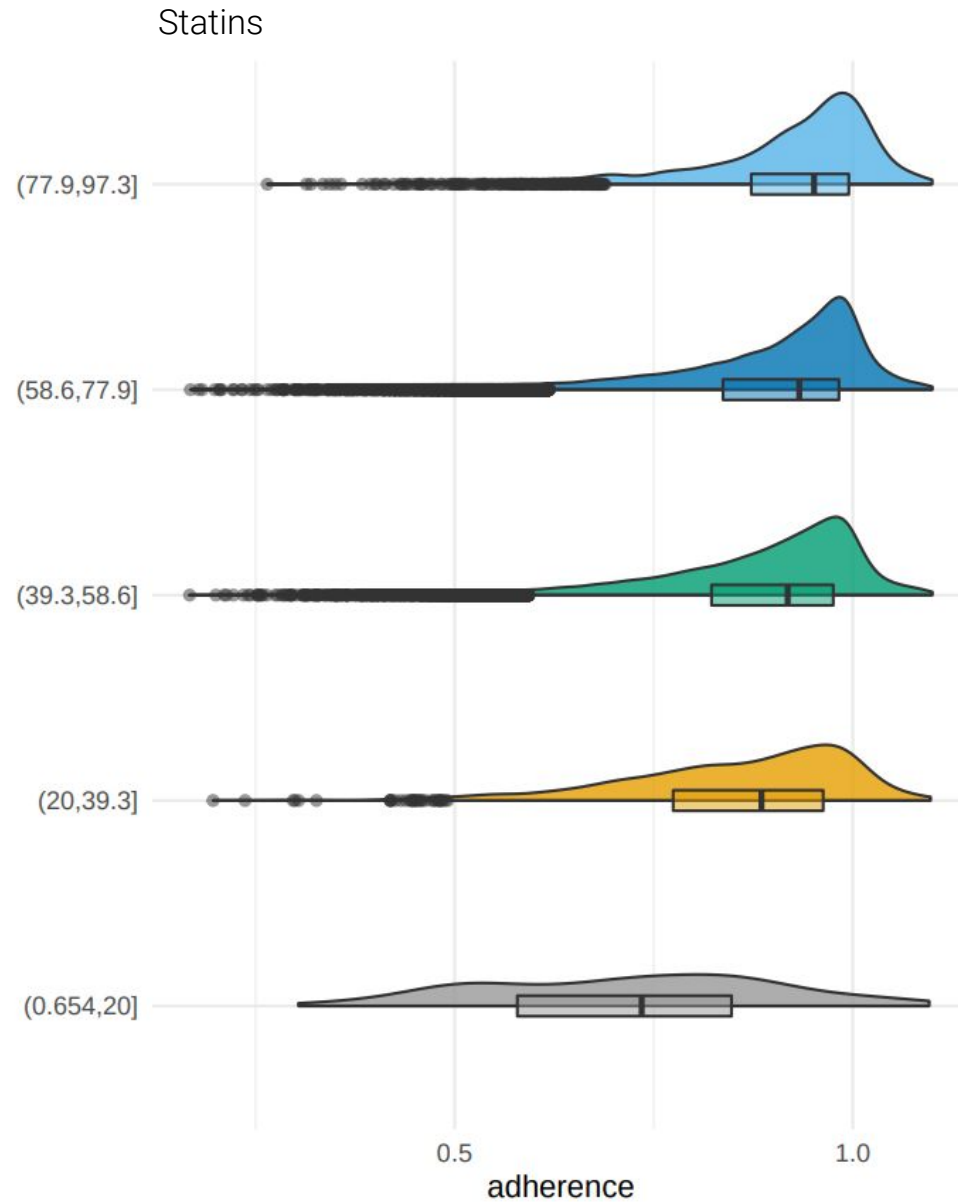
starting treatment after major cardiovascular event:

- myocardial infarction
- stroke
- coronary heart disease
- atherosclerosis

Adherence (mean±SD)	
Primary prevention	Secondary prevention
0.88±0.13	0.91±0.12
P = 2.5x10 ⁻⁷⁹	

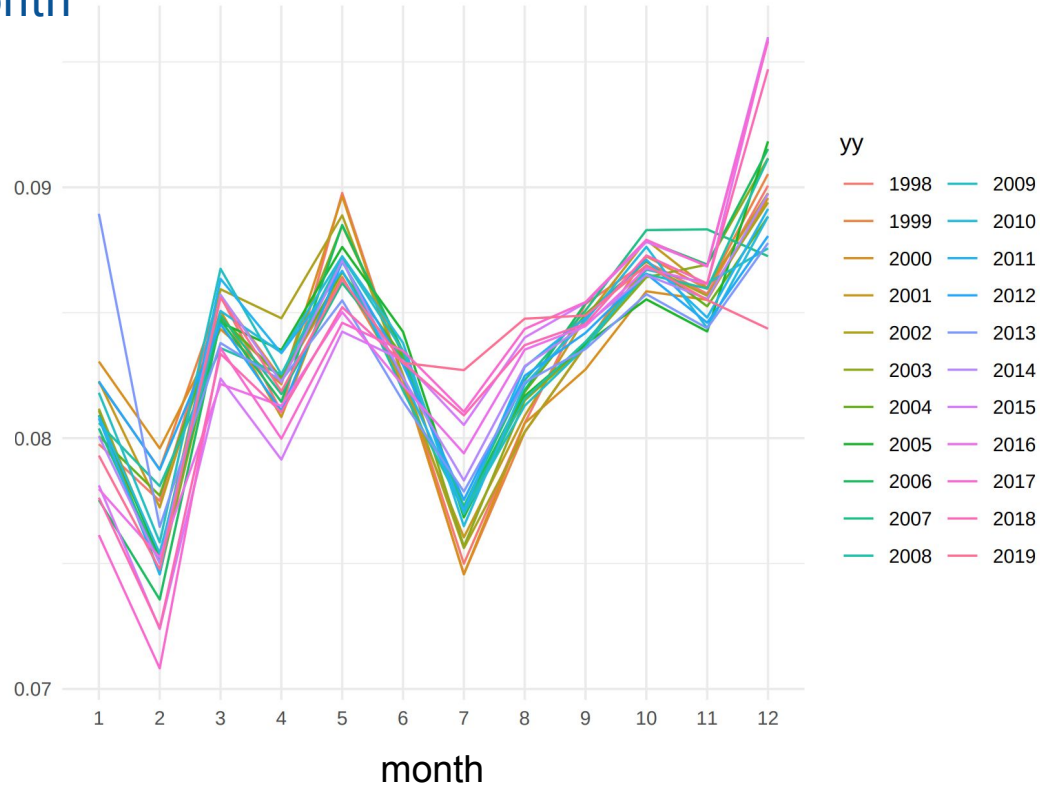


Adherence is higher when the treatment is started at an older age

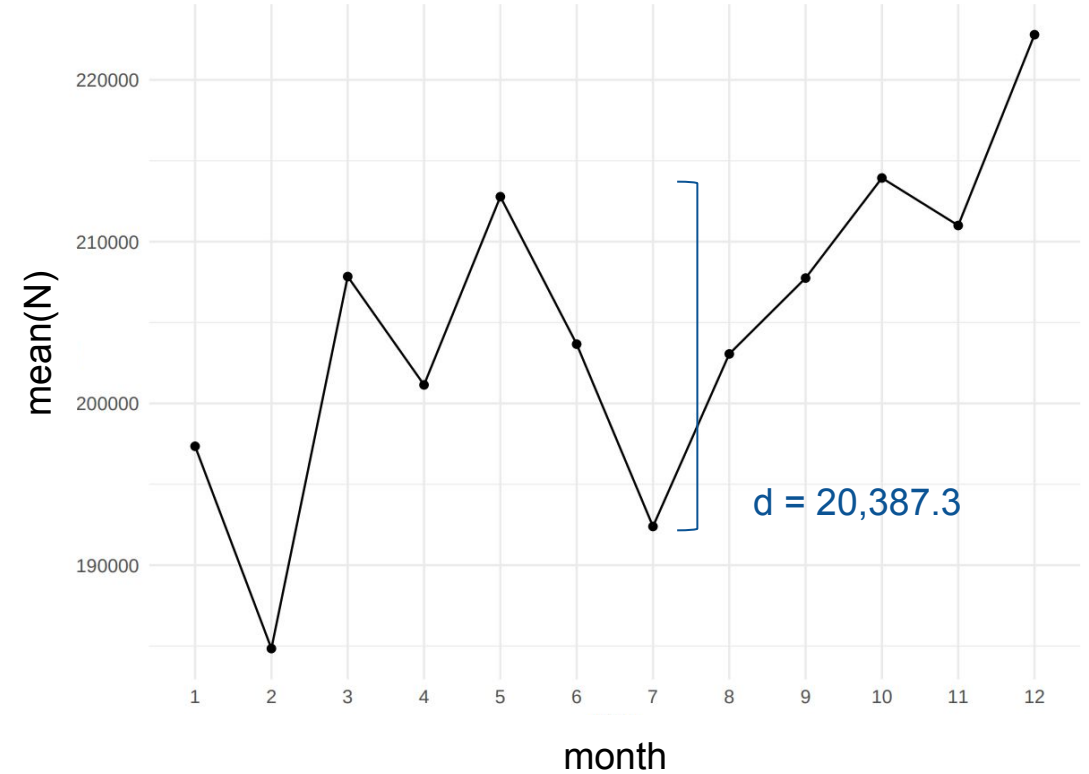


Seasonality trend in number of purchases

1998-2019 - proportion of purchases per each month

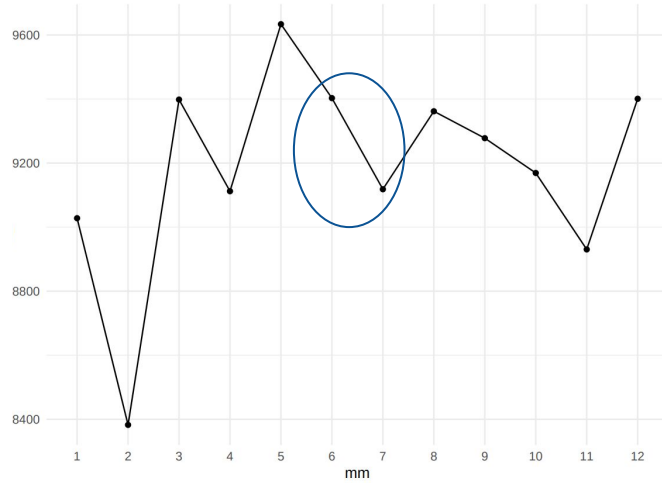


on average -20k purch. in June and July

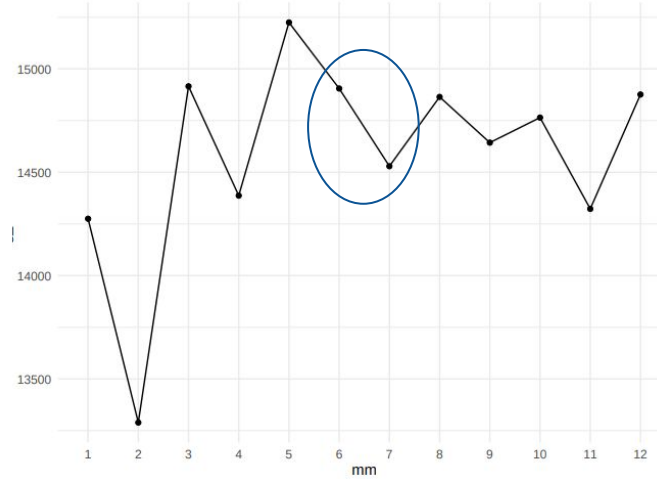


Seasonality trend in number of purchases per each medication

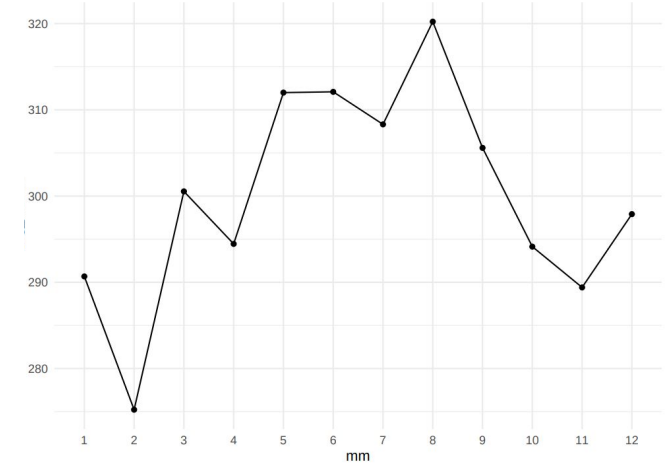
Statins



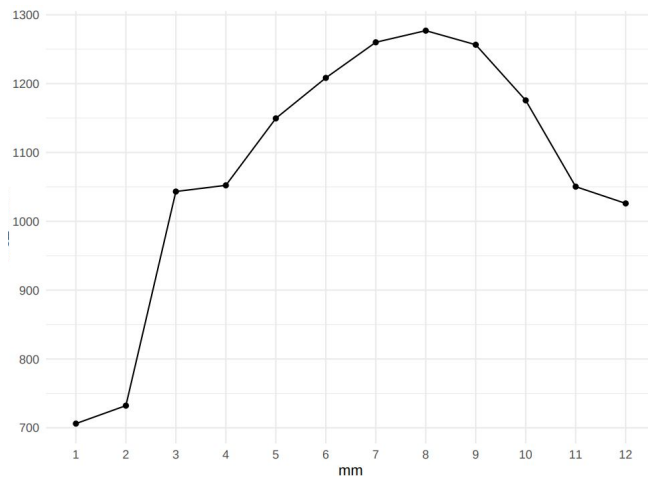
Blood Pressure medications



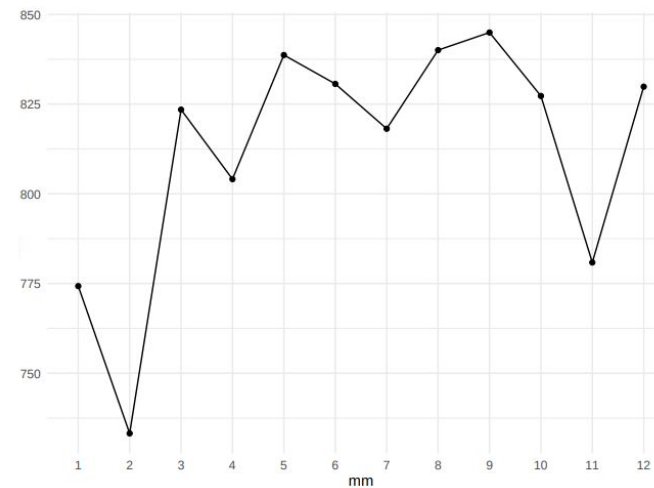
Breast Cancer medications



Anticoagulants



Clopidogrel, Dipirydamole



Purchasing regularity

Regular purchasing behaviour

low variance in intervals between purchases

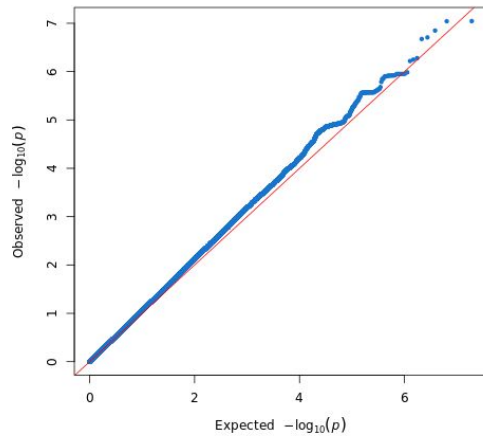


Correlation between adherence and purchasing regularity	
Blood Pressure medications	0.42
Breast Cancer medications	0.56
Clopidogrel, Dipyridamole	0.66
Anticoagulants	0.63
Statins	0.64

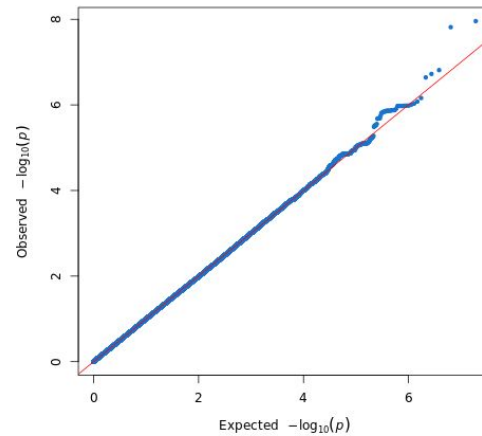
Association analysis results

adherence \sim SNP + AGE 1st PURCHASE + SEX + YEAR OF BIRTH + BATCH + PCs

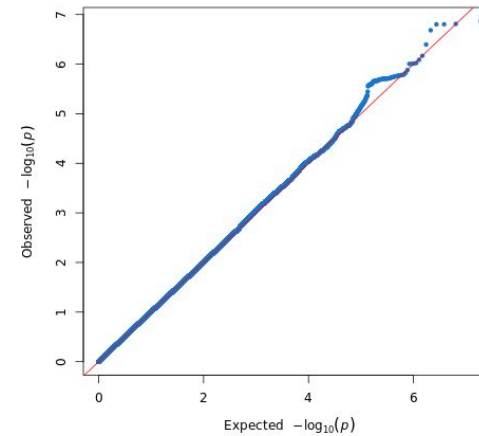
Blood Pressure medications
N 84,705



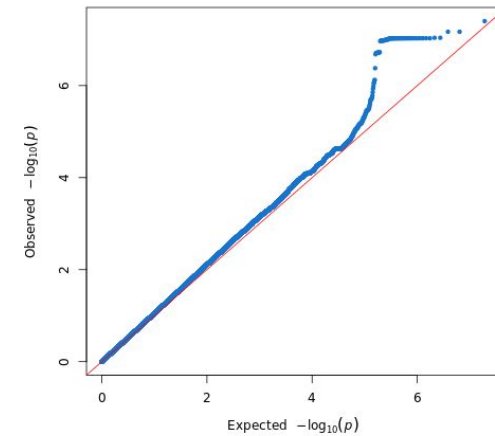
Breast Cancer medications
N 5799



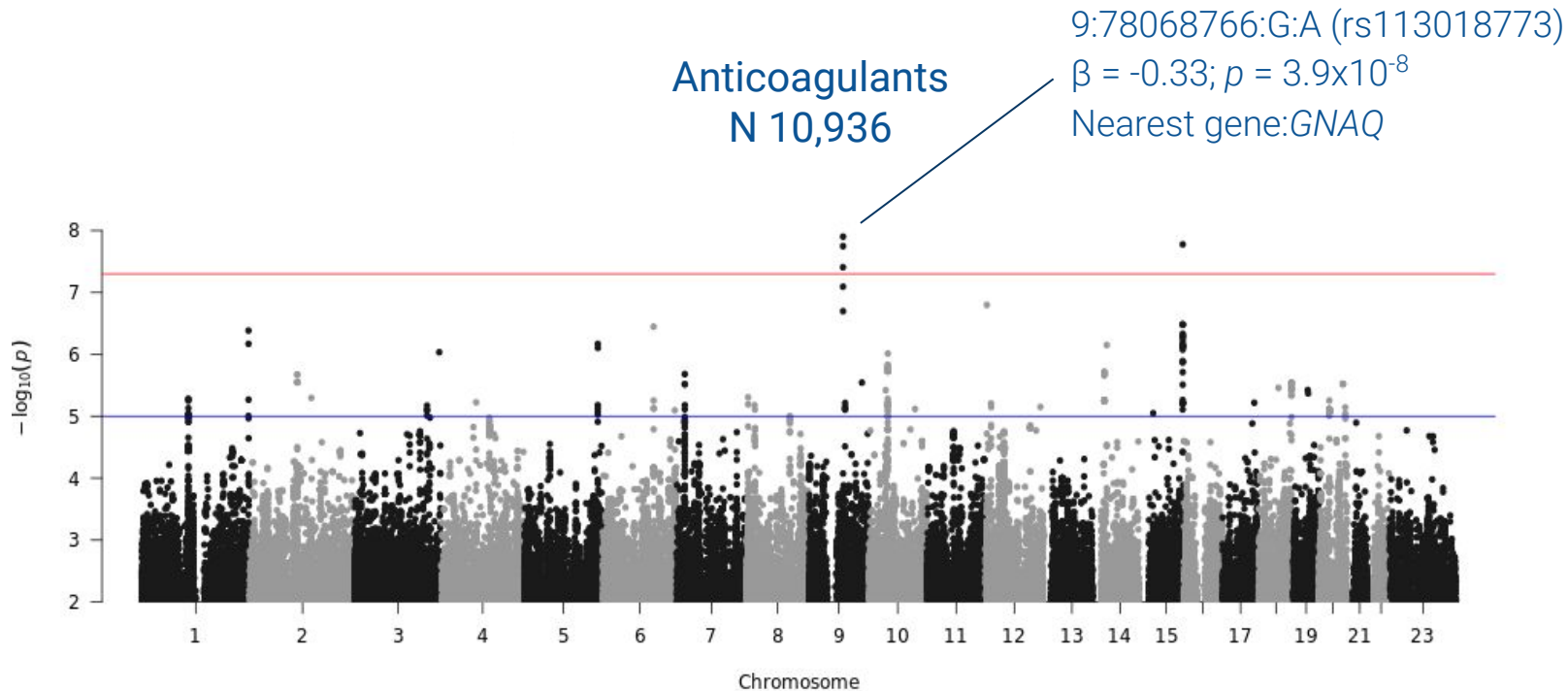
Dipyridamole, clopidogrel
N 14,201



Statins
N 77,773



Association analysis results - anticoagulants

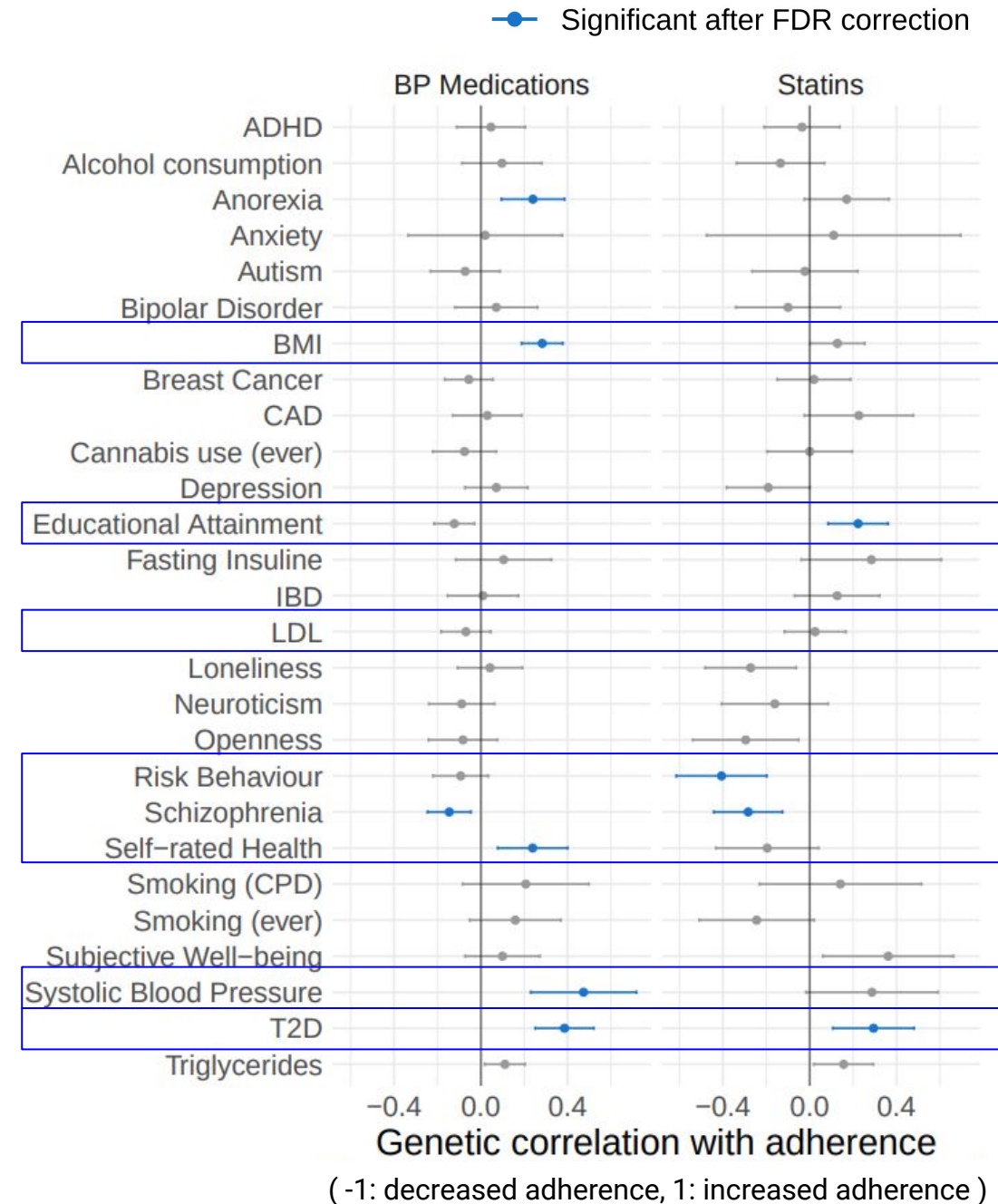


- *GNAQ* encodes for Guanine nucleotide-binding protein (G-protein)
- platelet activation mediated by G protein-coupled receptors

Genetic correlates of adherence

SNP-heritability:

- Blood Pressure medications:
 $h^2=0.027$, $p=1.9 \times 10^{-5}$
- Statins:
 $h^2=0.015$, $p=0.013$



Conclusions and future steps

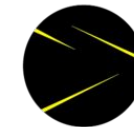
- no clear indication of genetic variants associated with adherence
- few studies include comprehensive information about drug purchases and behavioural traits
 - genetics allows to link these sources of information and identify traits driving adherence
- drug adherence is related to behavioural aspects
- future steps:
 - Mendelian Randomization to identify causal risk factors
 - test effect of known pharmacogenetic variants on adherence
 - comparison with UKBB (prescription data only)

Acknowledgments

- Andrea Ganna, PhD
- Sakari Jukarainen, MD-PhD
- Tuomo Kiiskinen, MD
- Matti Pirinen, PhD
- DSGE Lab

code:

<https://github.com/dsgelab/drugs-purchasing>



Data Science - Genetic Epidemiology Lab

