

Genomic Biomarkers - Role in Predictive Medicine and in Deciphering Causation for Other Biomarkers

2nd Conference Validation of Biomarkers

March 28th, 2019 - Basel

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Present : Head Clinical Chemistry Lab, CHUV Lausanne, Switzerland

From August 2019 : Chair in Genomic Medicine @ McGill

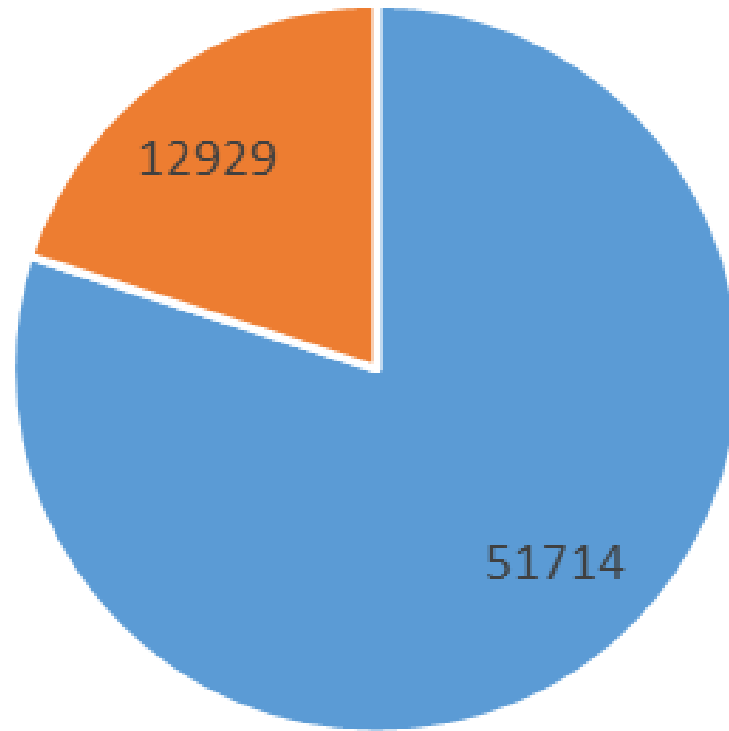
Unil
UNIL | Université de Lausanne



Part 1 :

Genomic Biomarkers in Predictive / Preventive Medicine

Costs of non-communicable diseases in CH



■ NTD ■ Others

Data from 2011, expressed in MCHF.

<https://www.bag.admin.ch/bag/fr/home/themen/strategien-politik/nationale-gesundheitsstrategien/strategie-nicht-uebertragbare-krankheiten.html>

Needs

Health

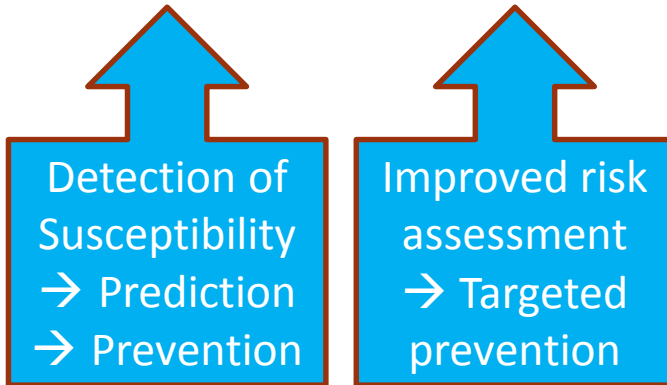
NCD



Needs

Health

NCD



Needs

Health

NCD



Needs

Health

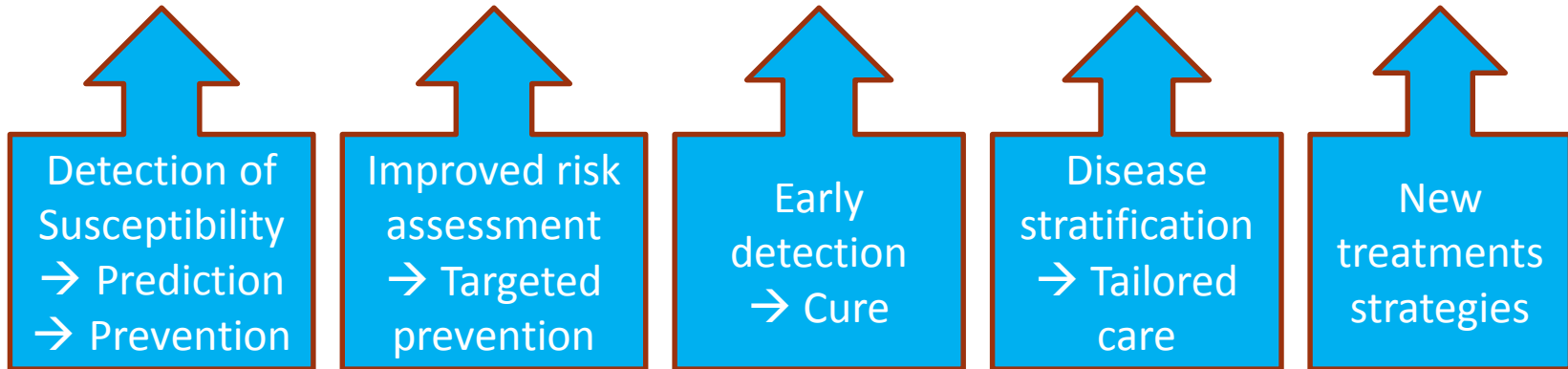
NCD



Needs

Health

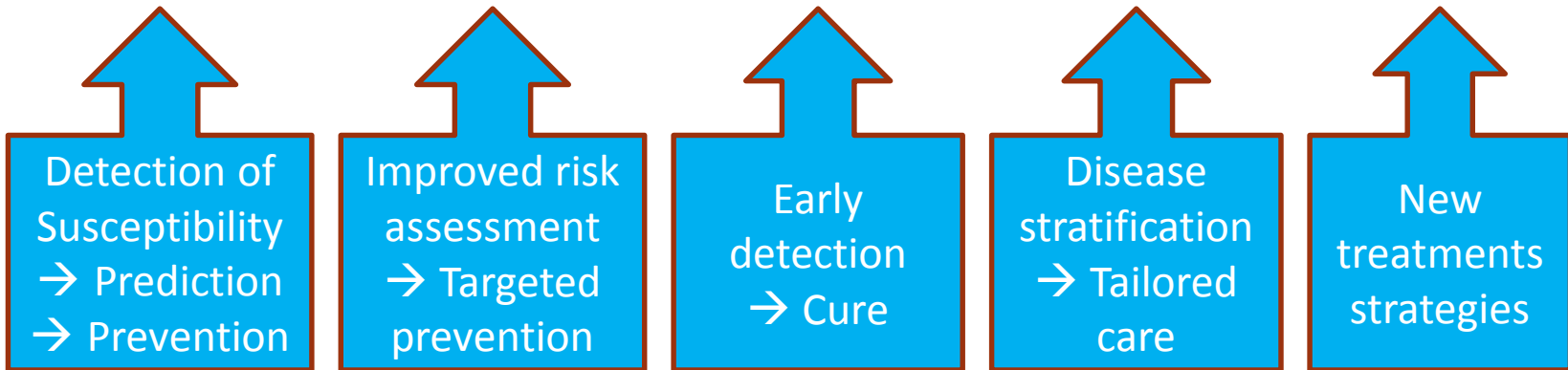
NCD



Needs

Health

NCD

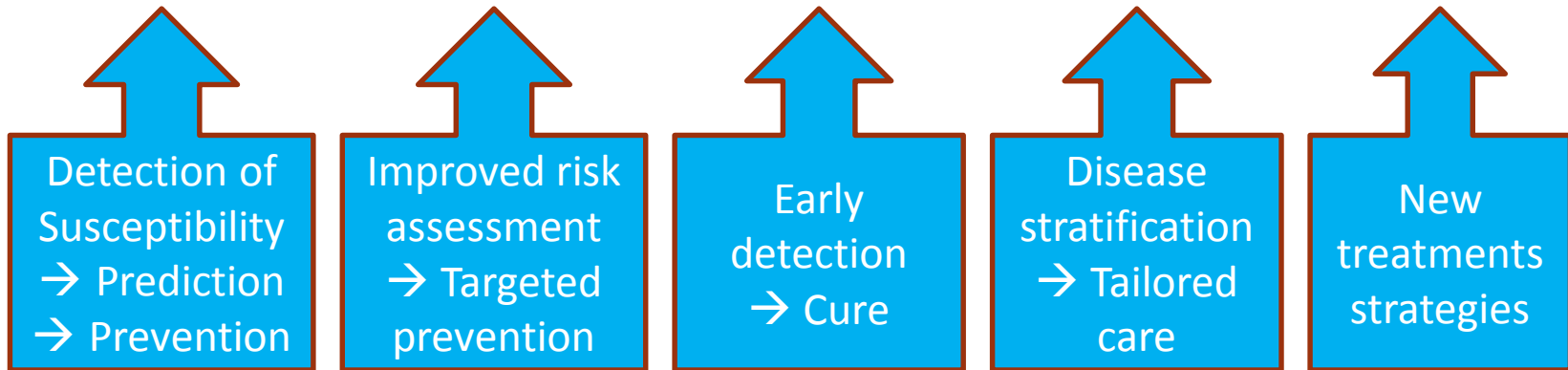


New biomarkers

Needs

Health

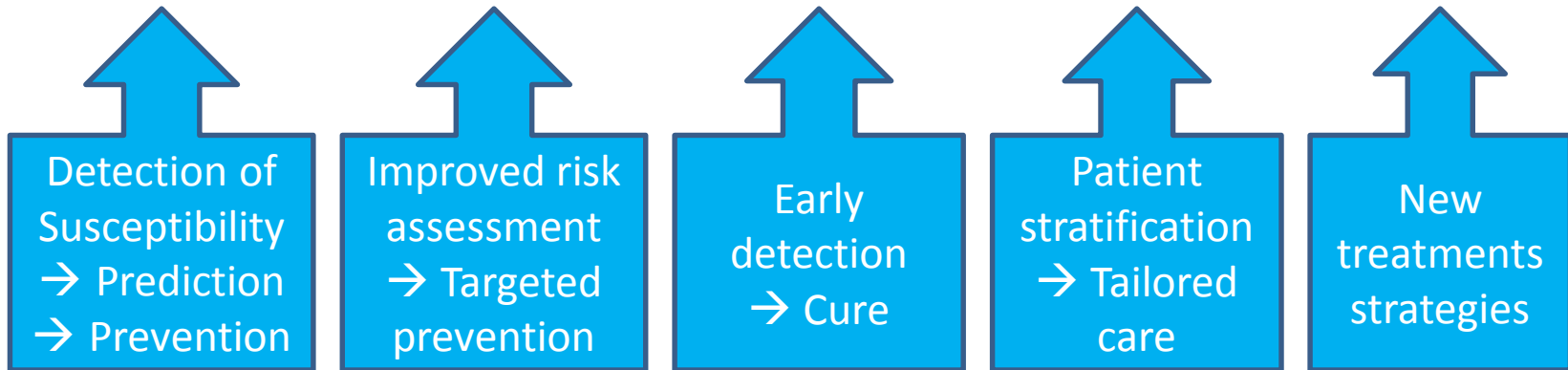
NCD



Genomic medicine 2019

Health

NCD

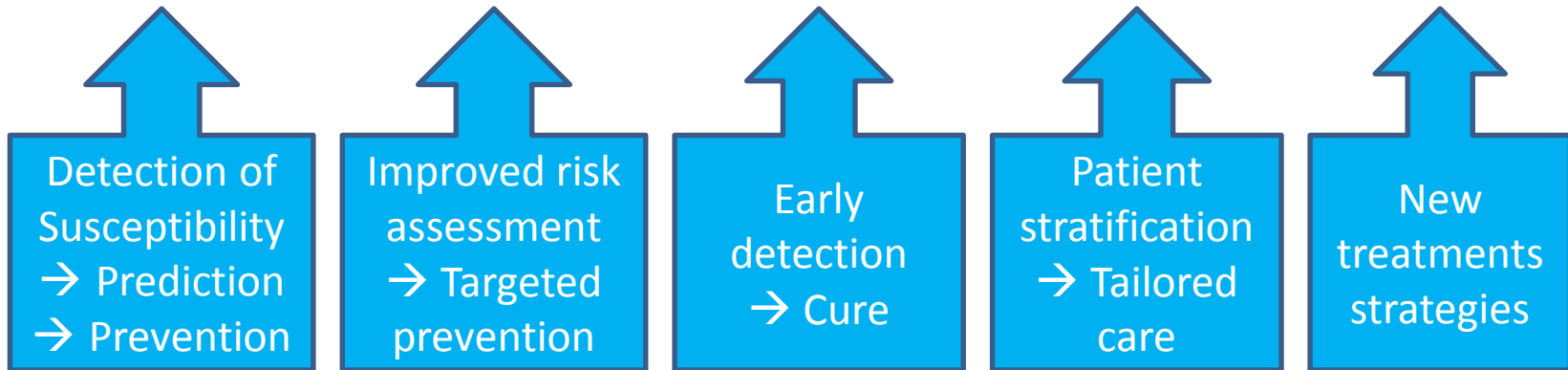


Reimbursed

Genomic medicine 2019

Health

NCD

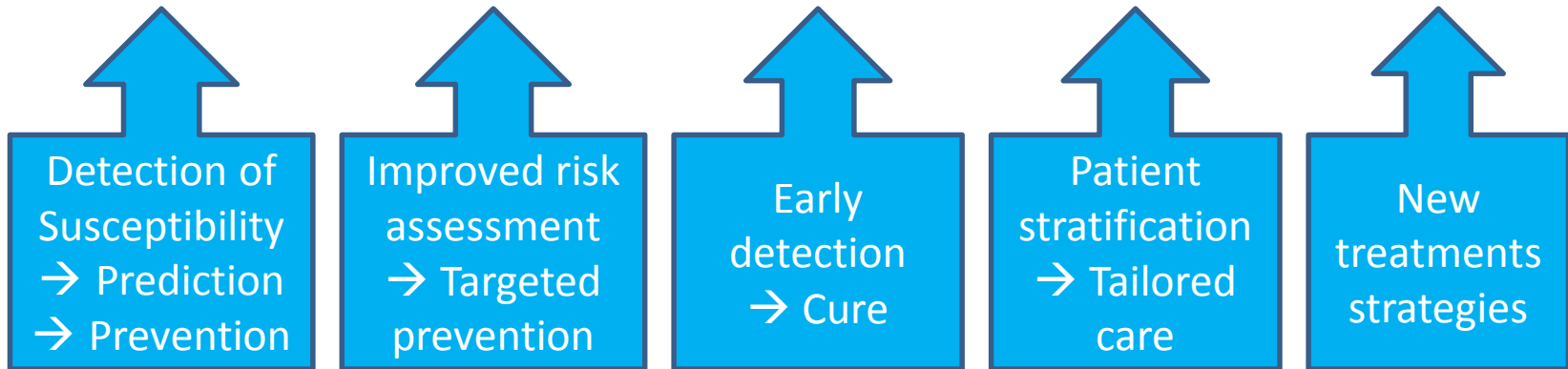


Reimbursed

Genomic medicine 2019

Health

NCD

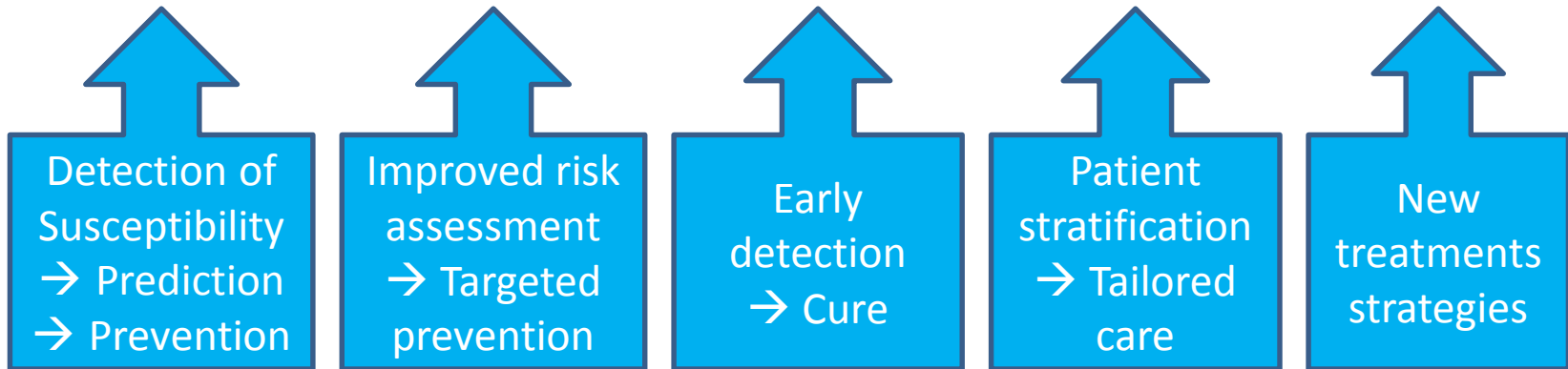


Reimbursed

Genomic medicine 2019

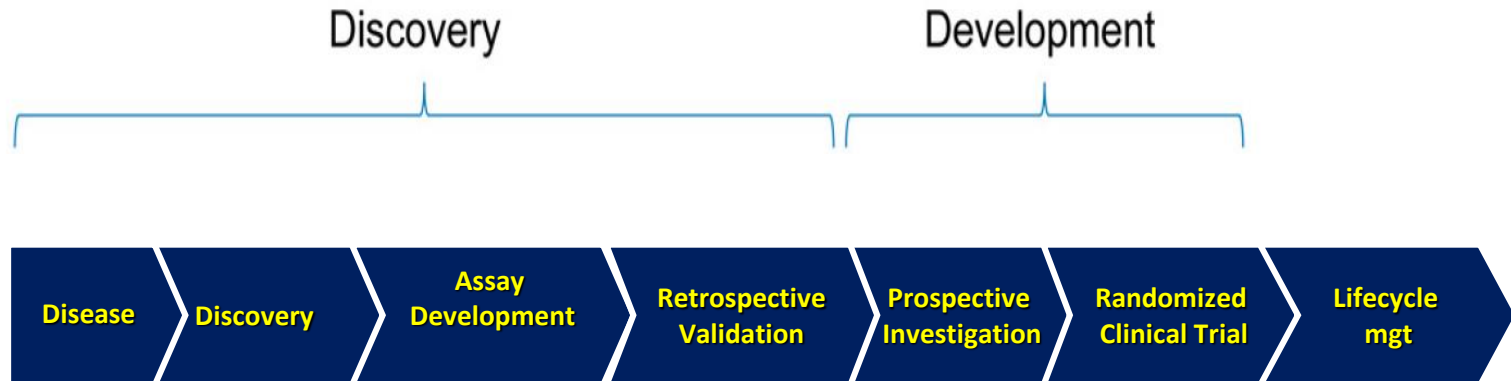
Health

NCD

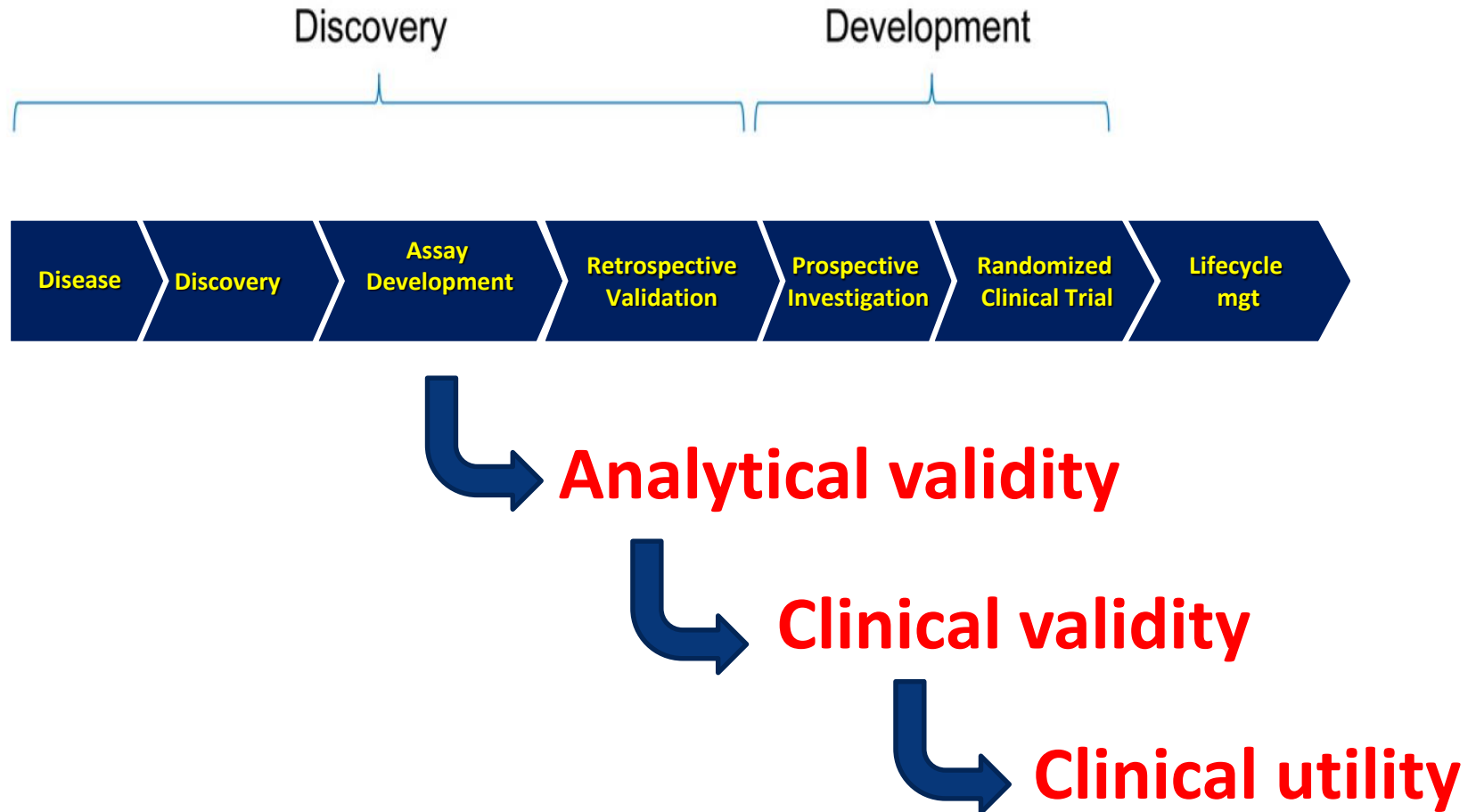


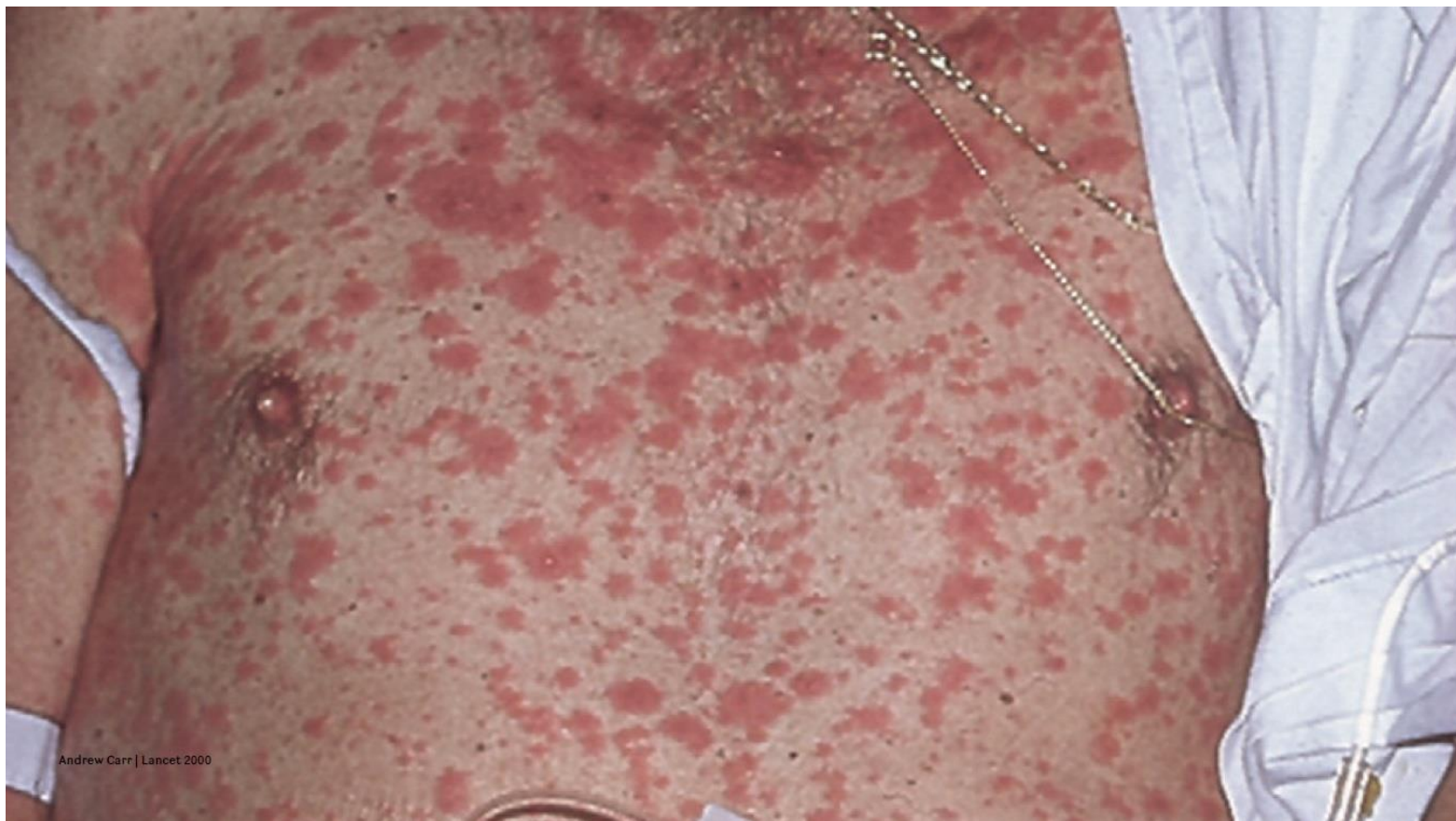
Reimbursed

The road to a new biomarker



The road to a new biomarker





Andrew Carr | Lancet 2000

Abacavir and HLA B*5701 : A 20-Year Story

1998 2000 2002 2004 2006 2008 2010 2012 2014 2016



FDA approval

Detailed description of HSR

Genetic association with HLA B*5701

Predict-1

FDA label

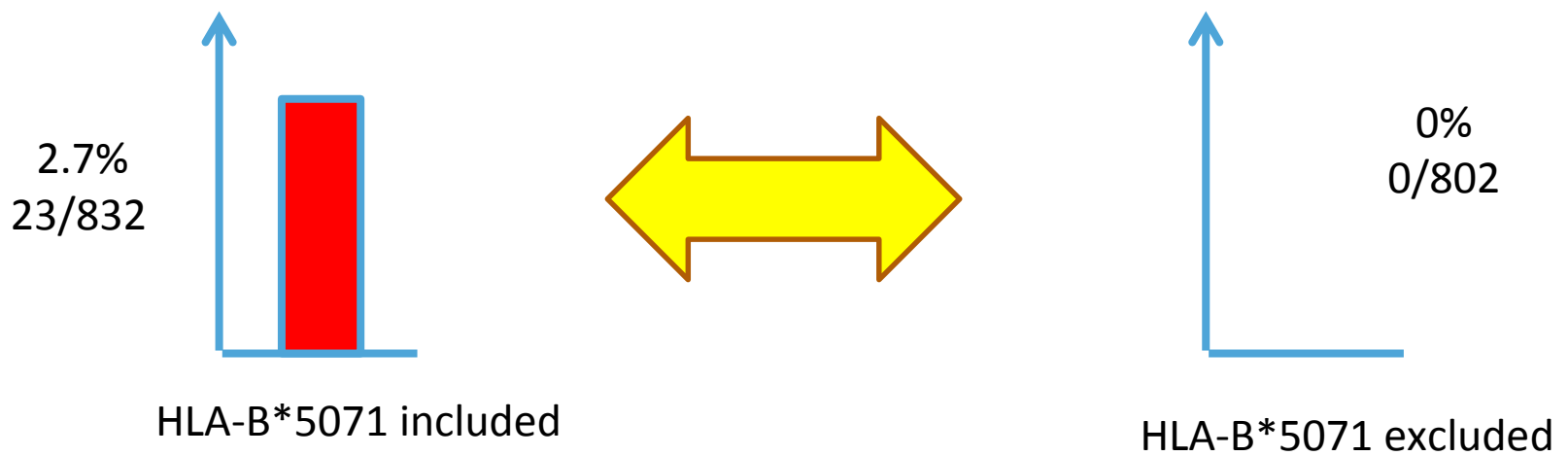
FOPH approval

Abacavir and HLA B*5701 : The Predict Trial

The NEW ENGLAND JOURNAL of MEDICINE

N ENGL J MED 358;6 WWW.NEJM.ORG FEBRUARY 7, 2008

HLA-B*5701 Screening for Hypersensitivity to Abacavir





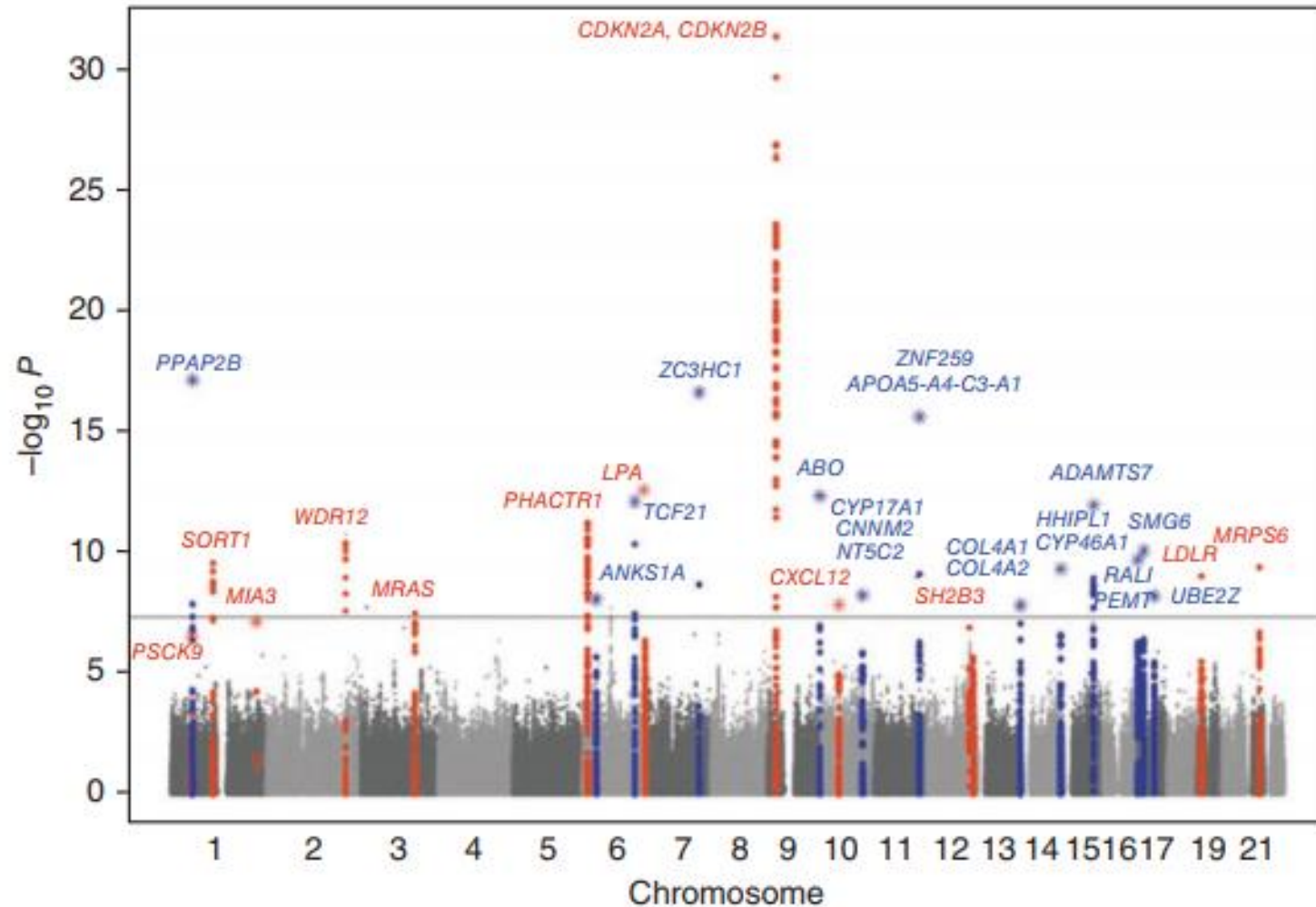
**CoLaus :
Population
Cohort**



**Observation
cohort**

- Population-based
- Age: 35-75 ans
- 6734 participants
- Extensive phenotype
- Biological + genomic data
- 15 year follow-up
- 400+ publications

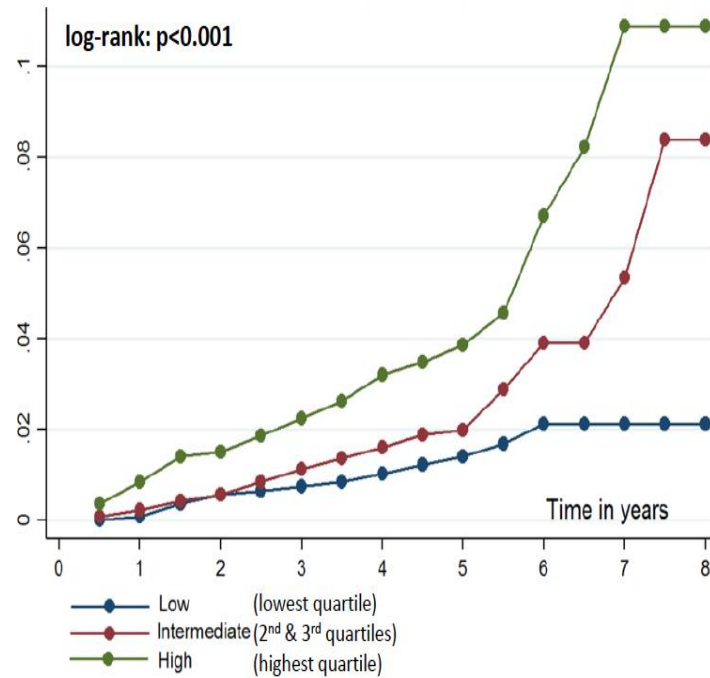
GWAS Coronary Artery Disease



Nature Genetics 2011; 43 : 333-7

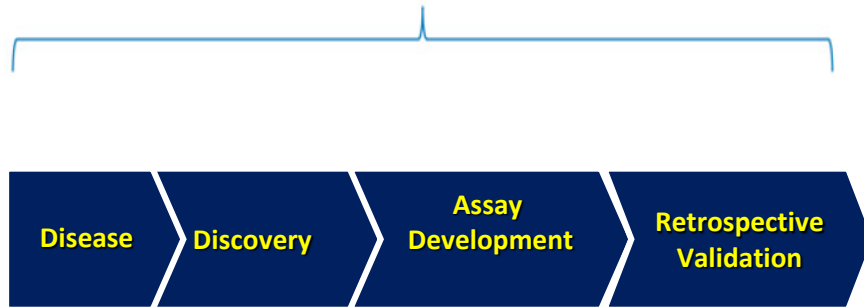
ATVB 2010; 30 : 2267-74

CoLaus : Genetic score to predict CAD



The road to a new biomarker

Discovery

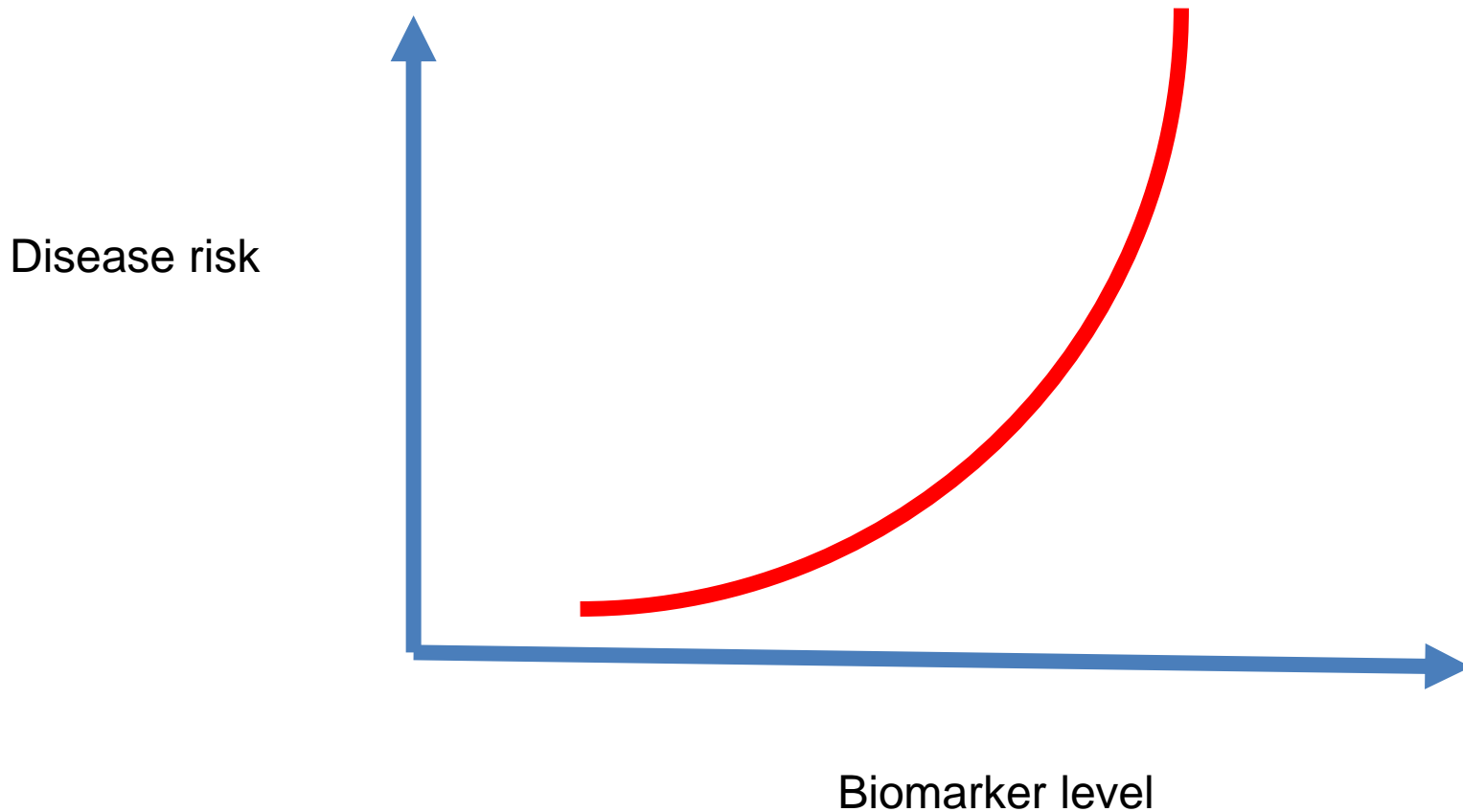


 **Analytical validity**

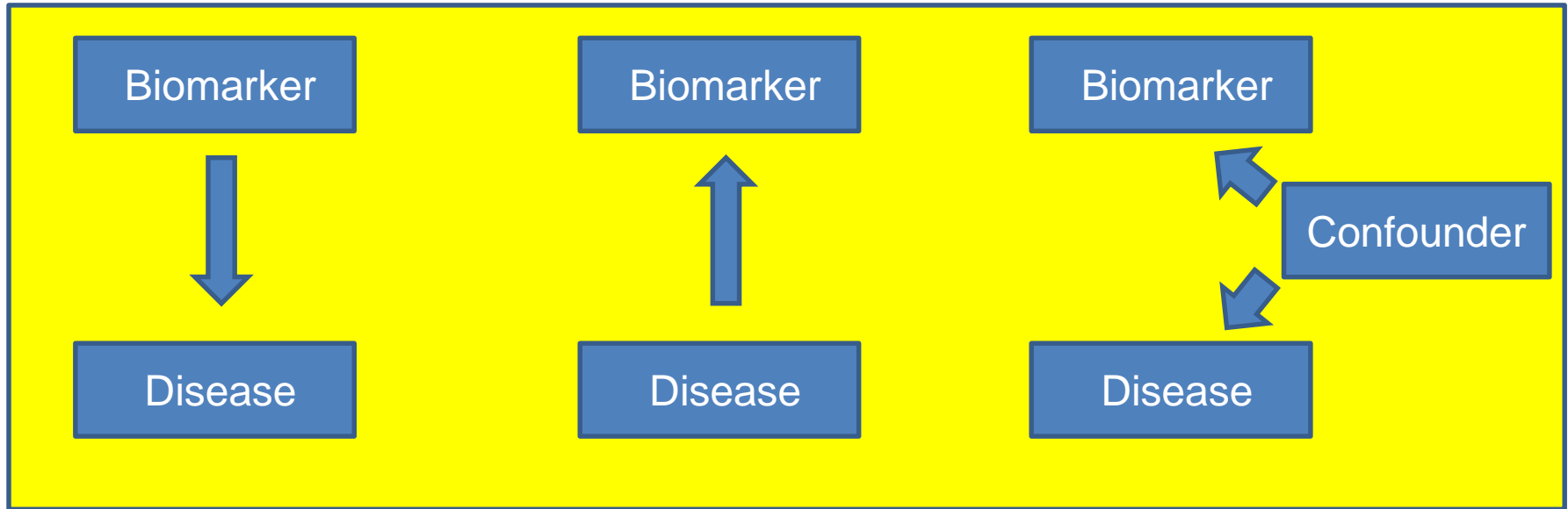
Part 2 :

Genomic Biomarkers in Deciphering Causation – Mendelian Randomization

Relationship between Biomarker and Disease Risk



Biomarkers and Diseases



Causation



Target for Intervention + Surrogate
(e.g. LDL-C and CAD)

Reverse causation



Surrogate
(e.g. creatinine and CKD)

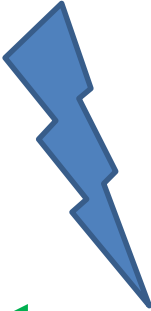
Confounder



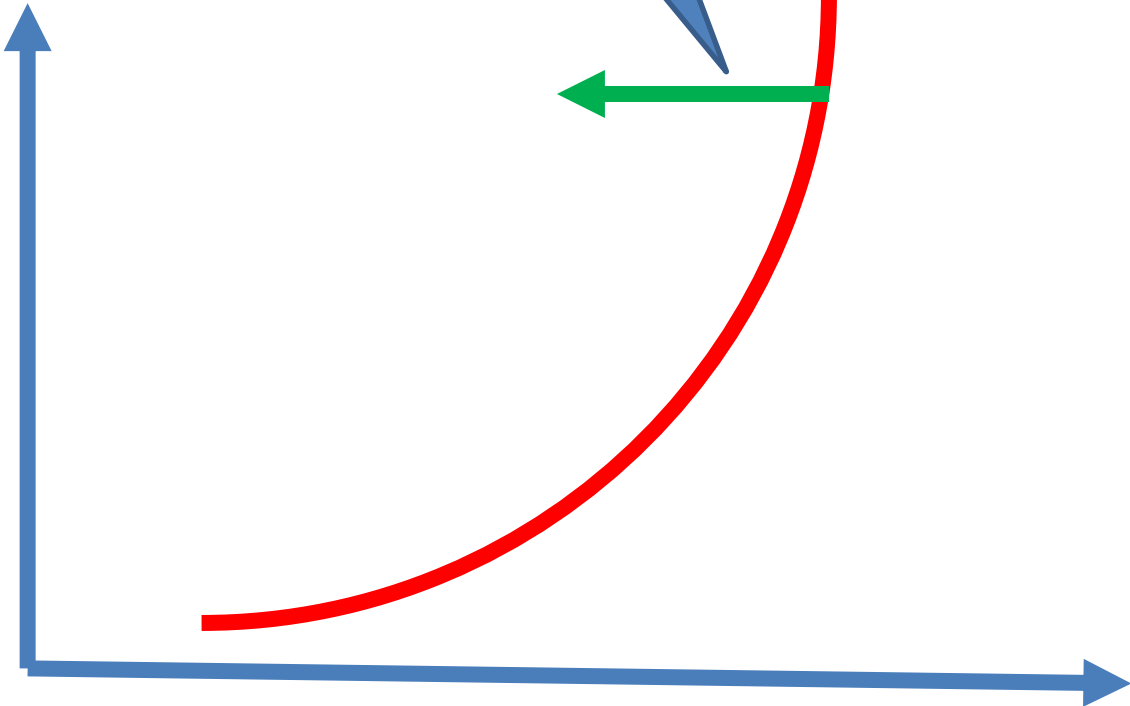
?
(e.g. inflammation, CRP and CAD)

Deciphering Causality

Specific intervention

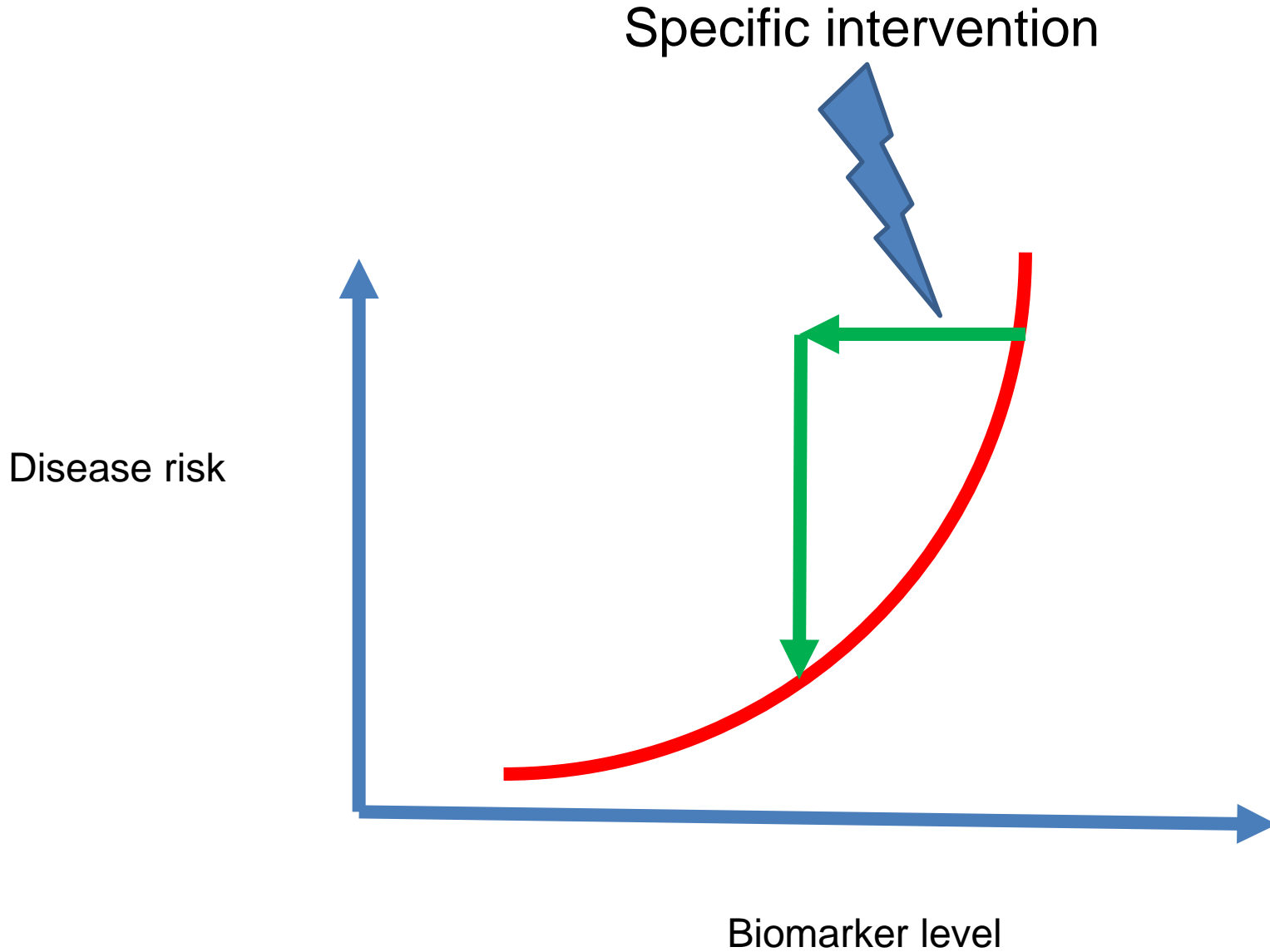


Disease risk

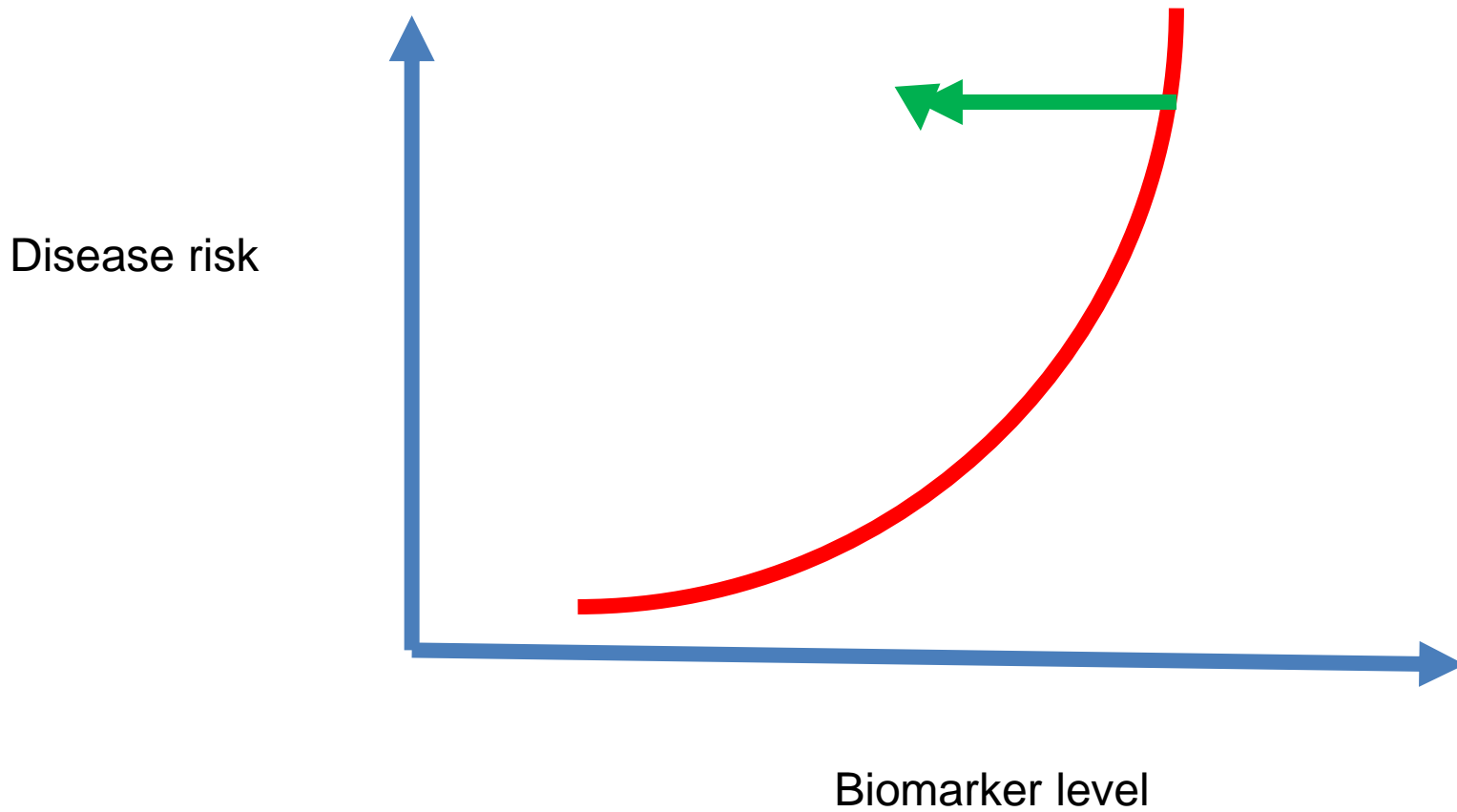


Biomarker level

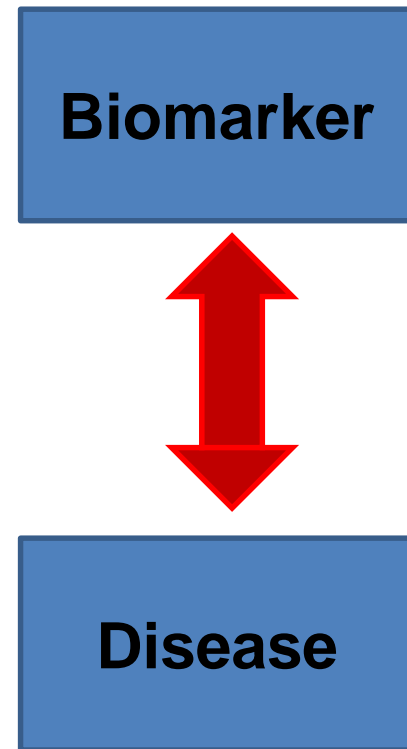
Causality



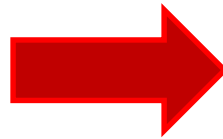
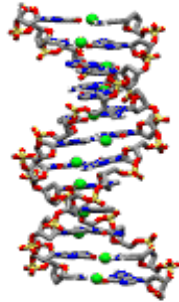
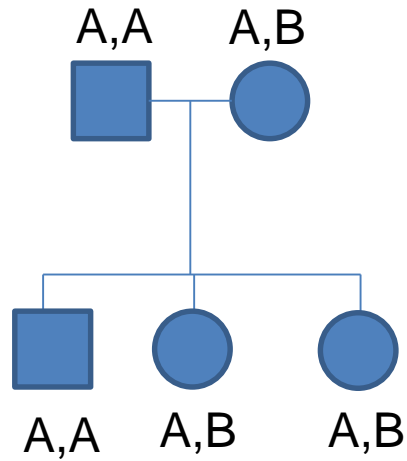
Lack of Causality



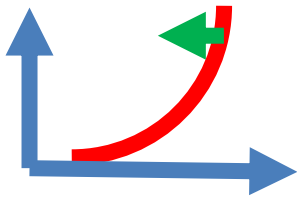
Mendelian Randomization : Concept



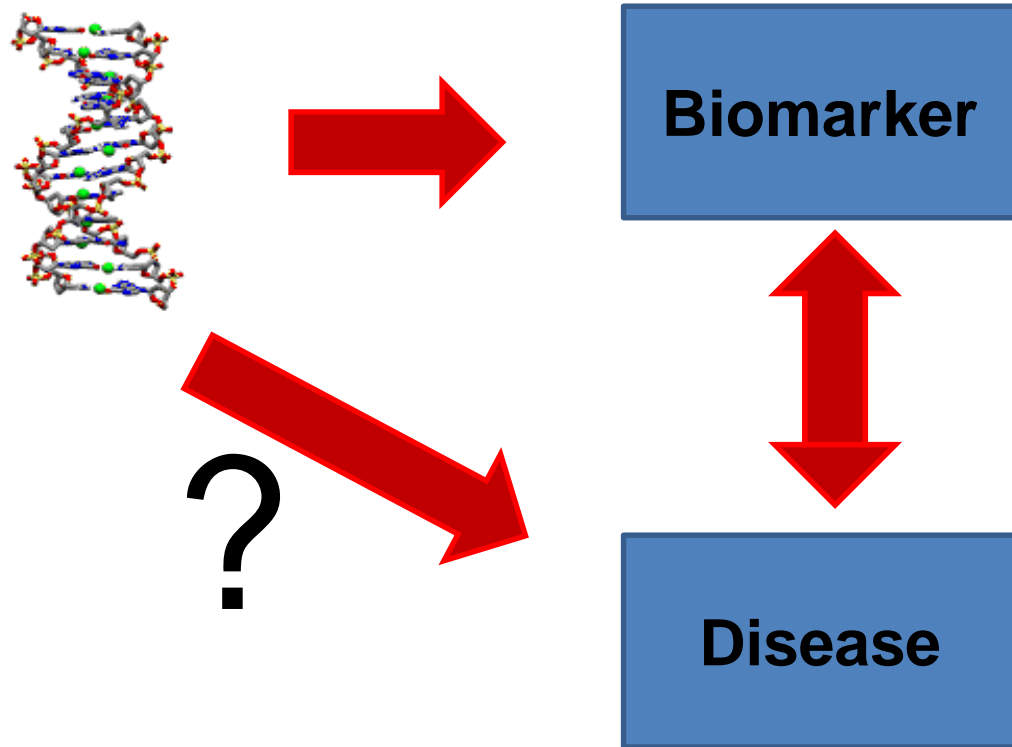
Mendelian Randomization : Concept



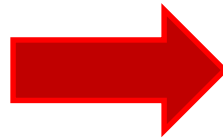
Biomarker



Mendelian Randomization : Concept



Mendelian Randomization : LDL-C and CAD

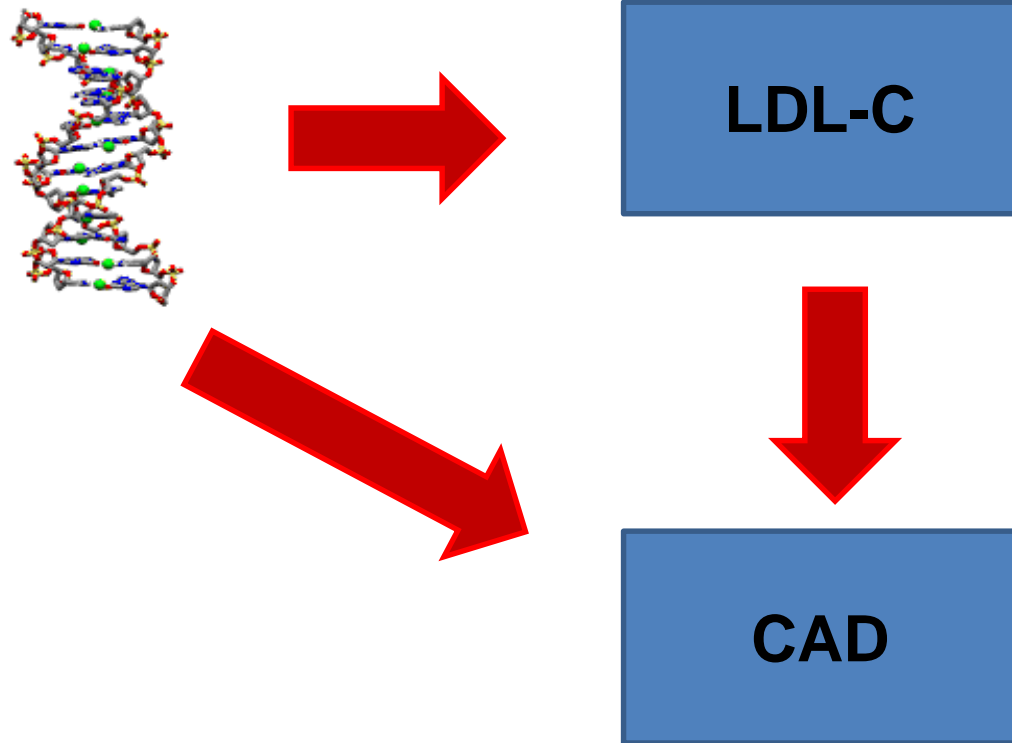


LDL-C

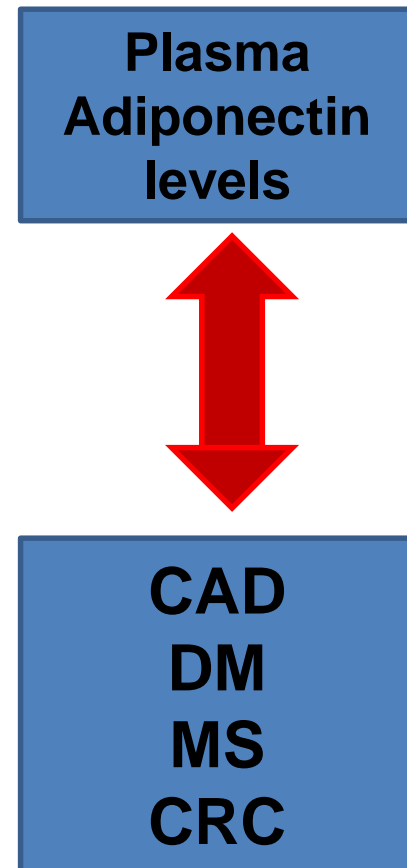


CAD

Mendelian Randomization : LDL-C and CAD

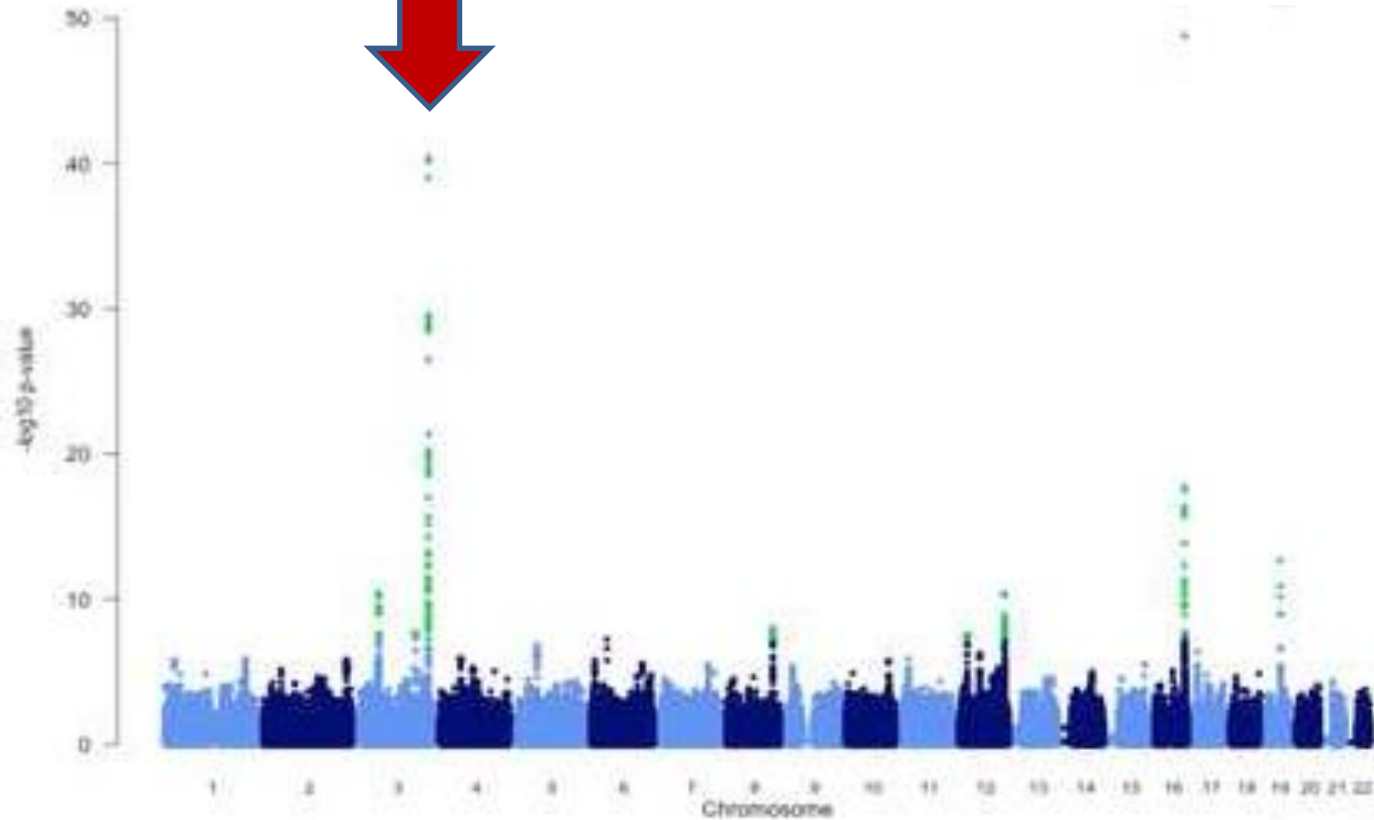


Mendelian Randomization : Adiponectin



GWAS Analysis of Adiponectin Levels

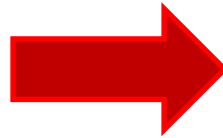
AdipoQ



N = 29342 Europeans

Brent Ritchards, PLOS Genetics, 2014

Mendelian Randomization : Adiponectin

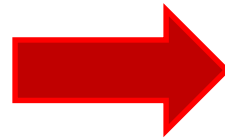
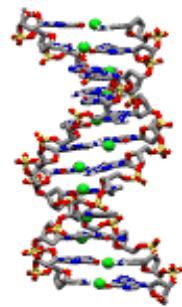


**Plasma
Adiponectin
levels**



**CAD
DM
MS
CRC**

Mendelian Randomization : Adiponectin



**Plasma
Adiponectin
levels**



**CAD
DM
MS
CRC**

Conclusions

- Genomic biomarkers used for prediction and prevention of single-gene and chromosomal (NIPT) diseases : reimbursed
- Genomic biomarkers for complex conditions :
Need for demonstration of clinical utility
- Mendelian randomization as a unique opportunity to demonstrate causality for association between non-genomic molecular biomarkers and disease and use for drug target validation.

Acknowledgments

- CoLaus investigators, Lausanne
- Lausanne Institutional Biobank
- Former GSK colleagues
- Brent Richards (McGill)