

Public Health in the Era of Personalized Health

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Personalized Health – the Promise

Improved understanding of causal disease risks and mechanisms to prevent disease from occurring...

Screening for disease before symptoms occur, allowing timely interventions...

Diagnosing the disease more precisely, leading to more effective treatment...

Selecting the specific medication that will best treat the disease...

➡ the focus is on the individual

Public Health – the Mission

Kass NE Am J Public Health 2001

the community rather than the **individual** is the patient

governmental and other institutional bodies rather than
treating physicians are the providers

 the focus is **community** well-being

The Ethical Dilemma in Public Health

Lee LM Am J Public Health 2012

Principles of clinical ethics:

- health care provider's responsibility to protect patient
- 4 essential principles used by hospital ethics committees: ***autonomy; beneficence; non-maleficence; justice***

Principles of public health ethics:

- Public Health authority's responsibility to use the information to maintain or improve population health
- the community is the patient

SEE ETHICAL DILEMMAS RELATED TO COVID-19

Citizen Cohorts - for Personalized & Public Health

130 of 215 Mio. USD invested into the U.S. Precision Medicine Initiative are allocated to build the 1 Mio citizen “All of Us” cohort with an associated biobank <https://allofus.nih.gov>

Cohort benefit for personalized and public health:

- Primary prevention - improve understanding of causal disease risks and of preventive behaviour
- Risk and disease screening – identify and test utility of biomarkers
- Diagnosis and treatment – evaluate health care and health systems

Cohort & Biomarker Data

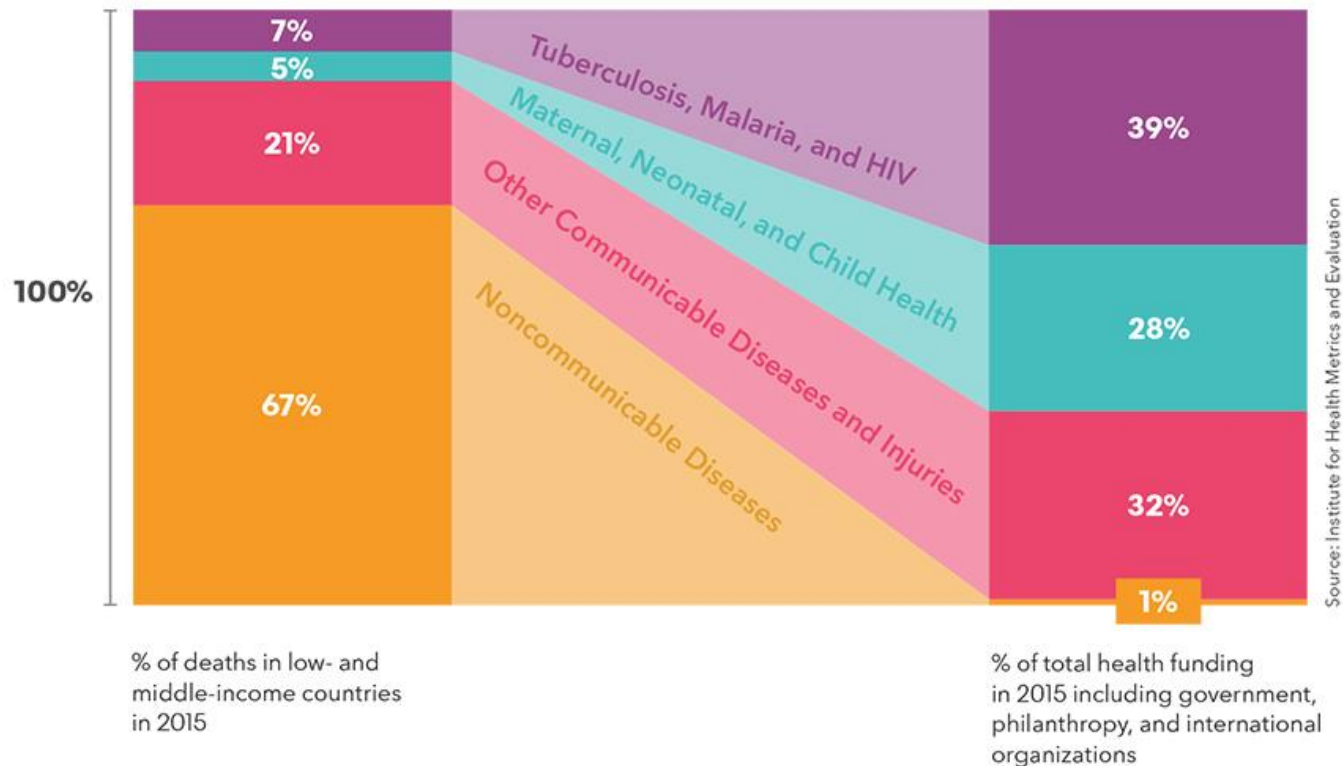
Primary prevention

-

improve understanding
of causal disease risks
and
of preventive behaviour

Non-Communicable Diseases

Noncommunicable diseases account for **67% of deaths** in low- and middle-income countries but only **1% of health funding** addresses them



<http://www.healthdata.org/acting-data/michael-bloomberg-uses-burden-disease-data-focus-attention-ncds>

The relevance of preventing NCDs

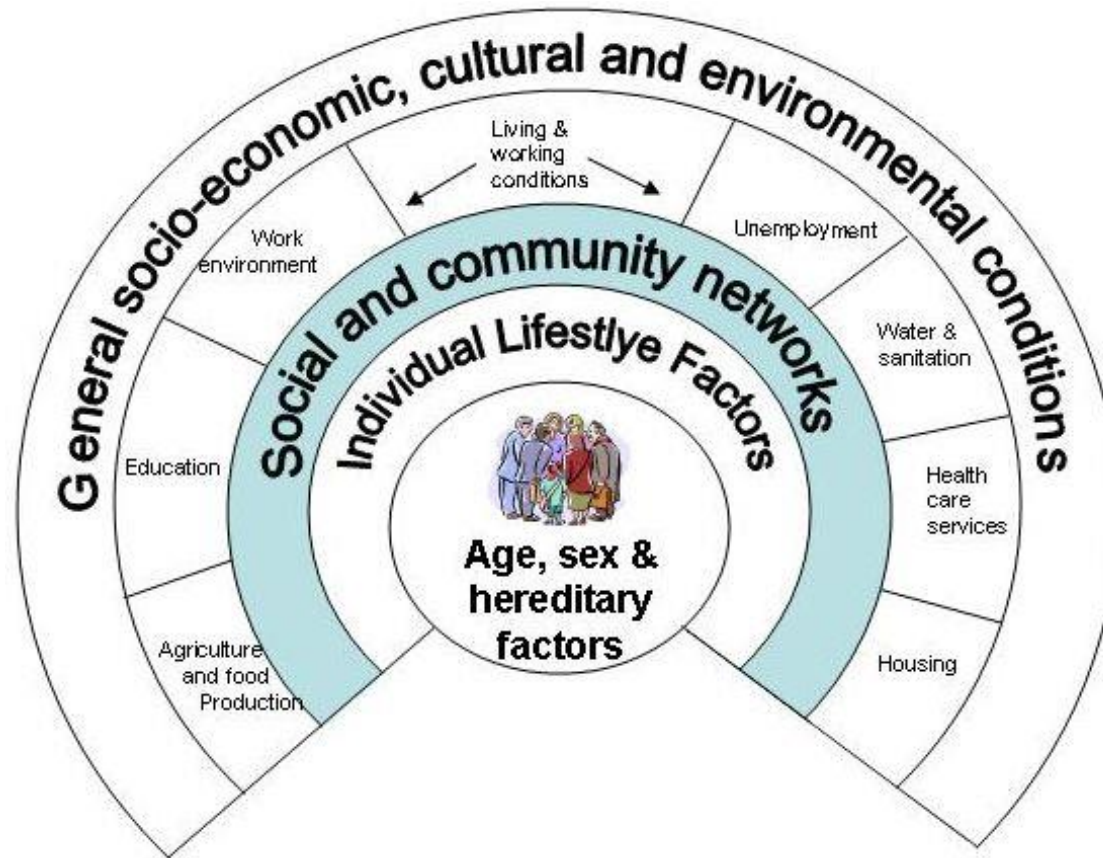
treatment of NCDs is costly - increasingly so due to personalized and high-technology interventions

treatment of NCDs is often lifelong and disabilities remain - years lived with disability are increasing

treatment of NCDs contributes to poverty and social stratification

treatment of NCDs overwhelms health systems in low and middle income countries and increasingly in high income countries

The complexity of NCDs which risks are causal—where to intervene



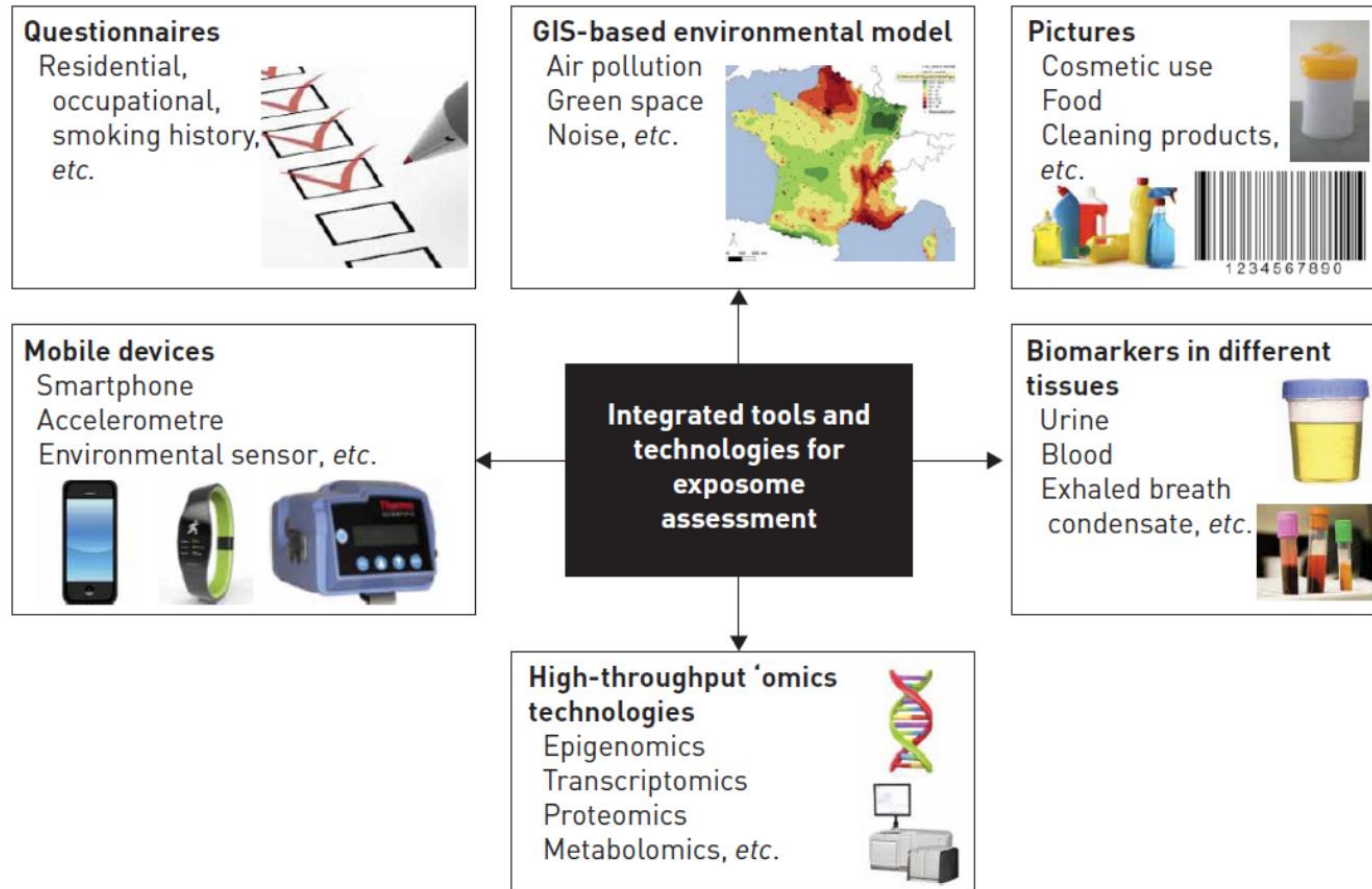
Dahlgren and Whitehead Model

Understanding causal disease risks

Challenges:

- correlation of hazards
- mixtures and diversity of hazards – with additive, competing, synergistic effects – measured or unmeasured
- measurement error in exposure and susceptibility
 - technical
 - considerable spatial, temporal, intraindividual variation
 - long latency period
- measurement error in phenotype
- small effects
- confounding
- unknown modes of action & causalities

Exposome Research



The Opportunities of Biomarkers

Wild et al. Environ Mol Mutagen 2013

improvement of exposure assessment - biomarkers of exposure

identification of susceptibilities - biomarkers of susceptibility

improvement of phenotype classification – biomarkers of disease

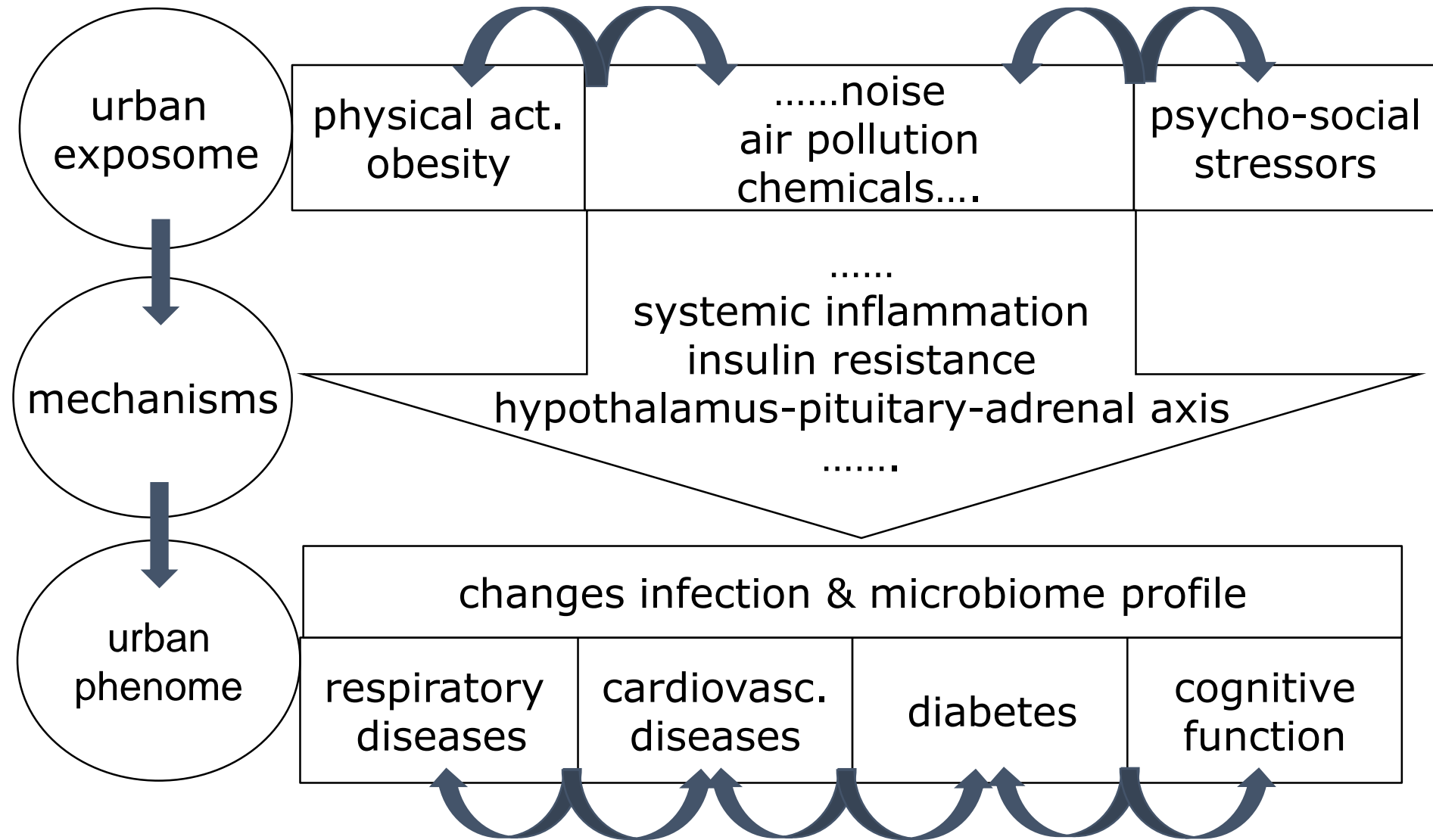
interrogation of biological mechanisms – mediating biomarkers

provision of short-term outcomes in intervention studies – biomarkers of early disease

Patel C Pac Sym Biocomput 2015; Sun YV Advances in Genetics 2016

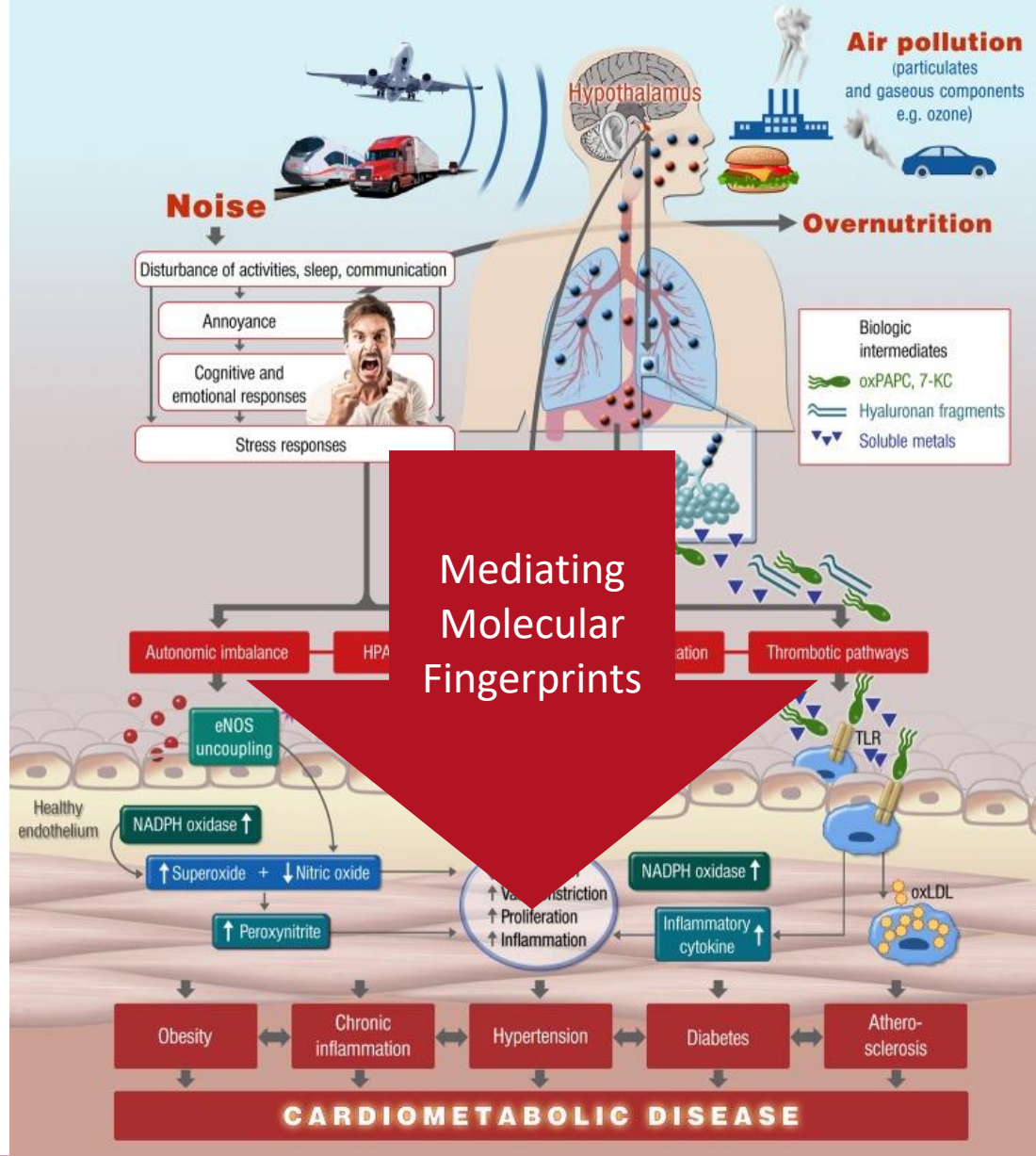


Public Health relevant causal pathways



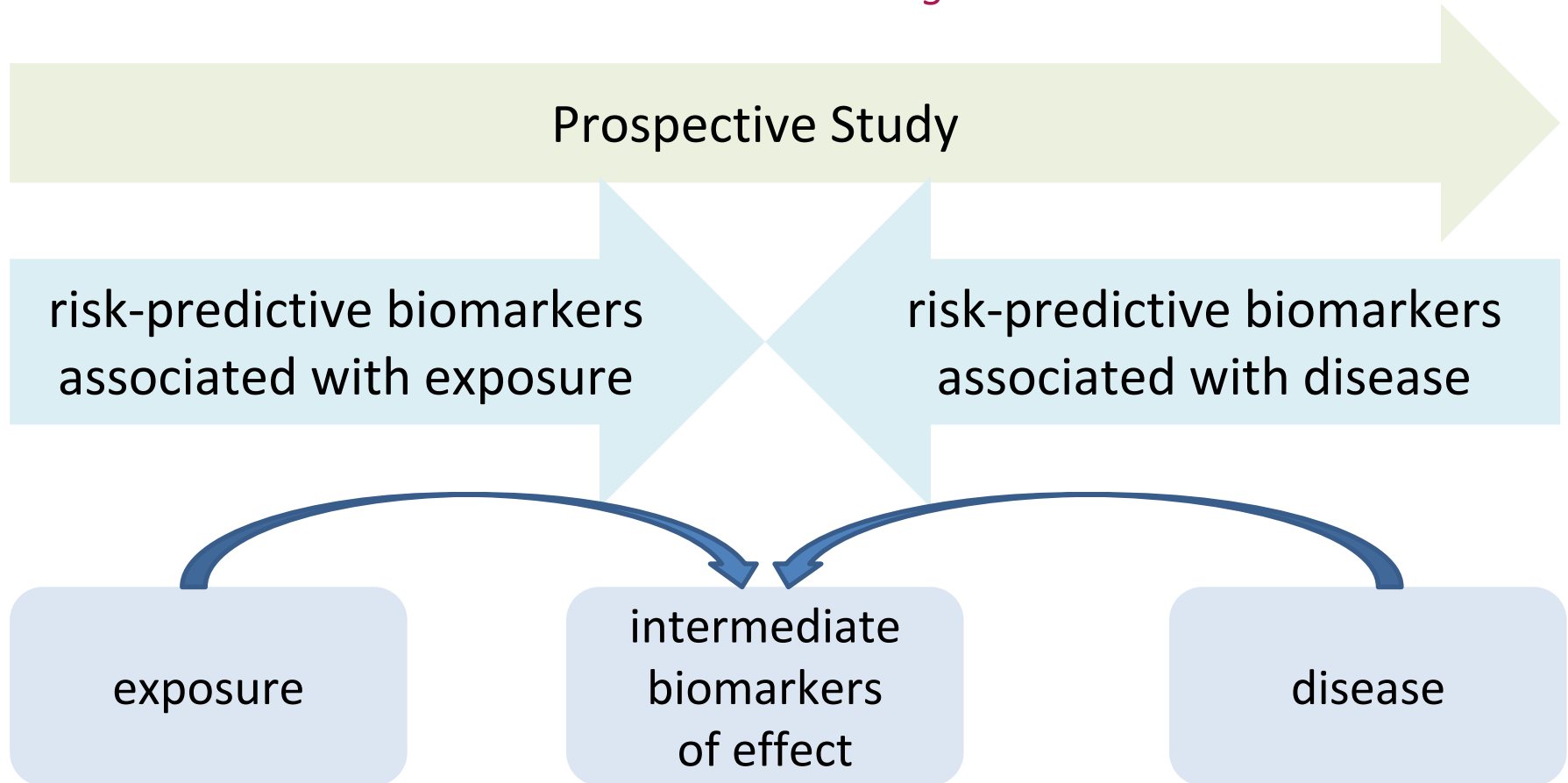
Proposed mediating pathophysiological mechanisms of cardiometabolic disease induced by environmental air pollution and noise

Münzel T et al.
European Heart Journal
2017;38, 557–564



Meet-in-the-Middle Concept

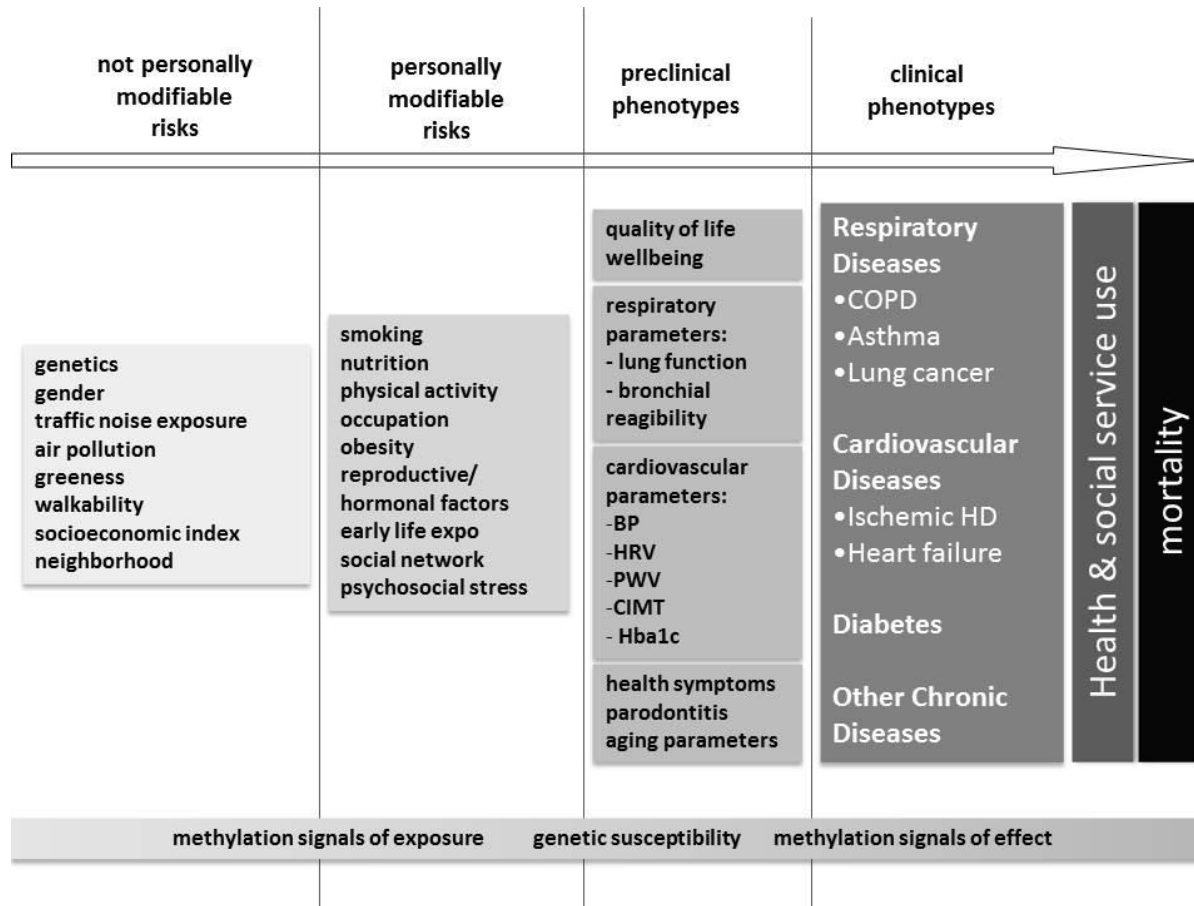
Vineis P et al. Environmental Molecular Mutagenesis 2013



SAPALDIA – Swiss-wide chronic disease biobank

complex data towards understanding of complex diseases

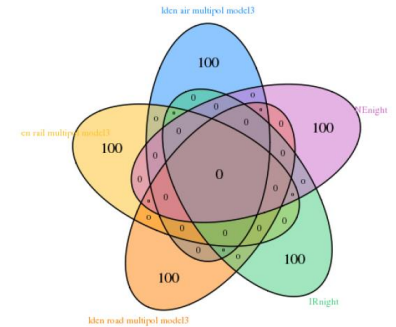
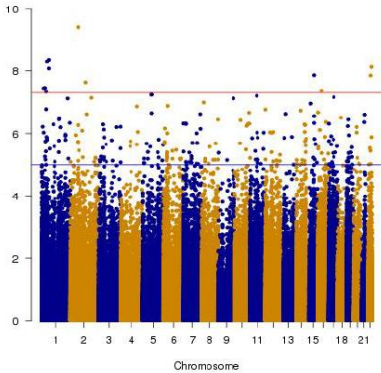
9651 participants, 8 communities, 30 years of follow-up and address history, 5 surveys



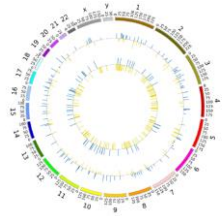
Meet-in-the-Middle Concept

Vineis P et al. Environmental Molecular Mutagenesis 2013

Epigenome-Wide Association with Transportation Noise



Enrichment for published DNA-methylation signals associated with insulin resistance?



Arner et al. Diabetologica 2016;59

Noise-related DNA-methylation signals predicting the incidence of diabetes?

The Urban Exposome: H2020 Expanse

PI: Vermeulen R; Vermeulen R et al. Science 2020;367:392

Ecosystems

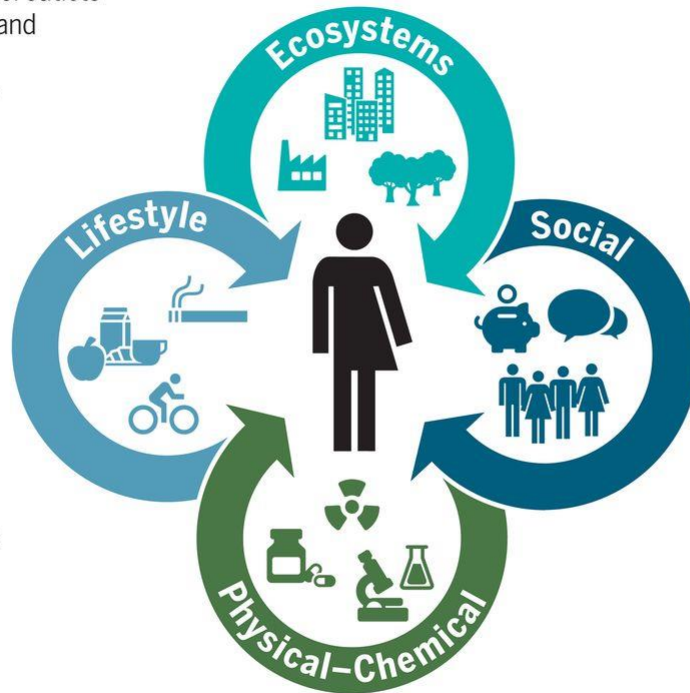
Food outlets, alcohol outlets
Built environment and urban land uses
Population density
Walkability
Green/blue space

Lifestyle

Physical activity
Sleep behavior
Diet
Drug use
Smoking
Alcohol use

Social

Household income
Inequality
Social capital
Social networks
Cultural norms
Cultural capital
Psychological and mental stress

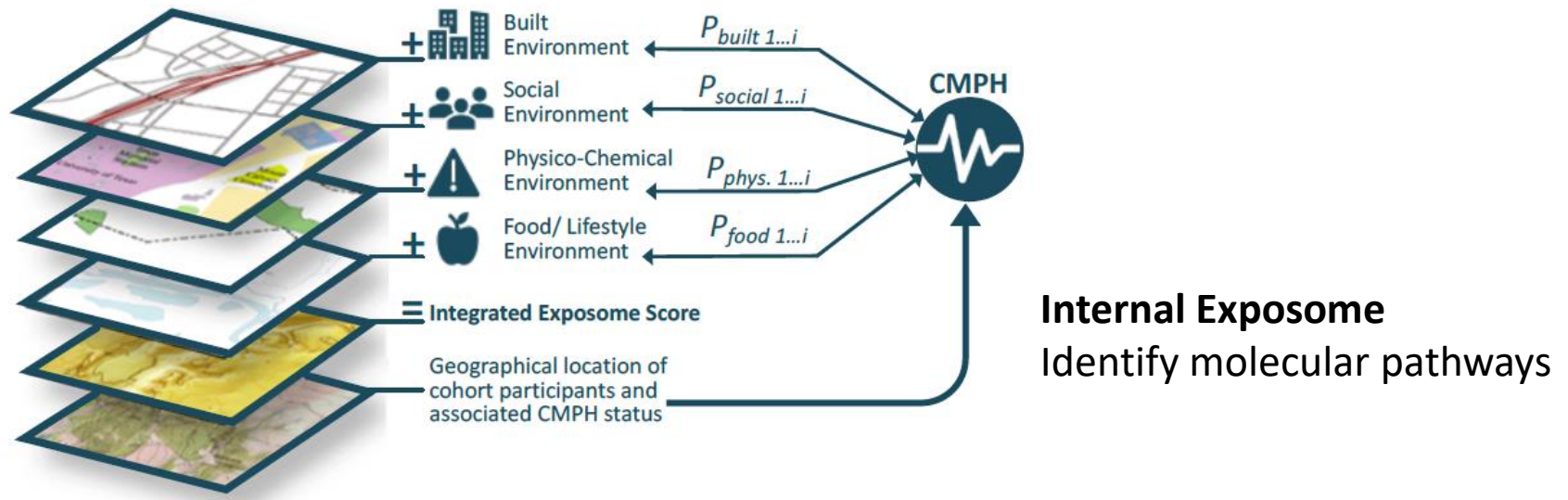


Physical-Chemical

Temperature/humidity
Electromagnetic fields
Ambient light
Odor and noise
Point, line sources, e.g. factories, ports
Outdoor and indoor air pollution
Agricultural activities, livestock
Pollen/mold/fungus
Pesticides
Fragrance products
Flame retardants (PBDEs)
Persistent organic pollutants
Plastic and plasticizers
Food contaminants
Soil contaminants
Drinking water contamination
Groundwater contamination
Surface water contamination
Occupational exposures

Expanse Project

PI: Vermeulen R; Vermeulen R et al. Science 2020;367:392



Exposome Map:

Assign exposome scores to geographical locations

Identify hotspots of elevated health risk

Wearables—evaluate long-term utility

Wearables promise to promote healthy lifestyles

Test this hypothesis in the context of cohorts:

What are characteristics of cohort participants who do or do not use wearables?

Does wearing a fitness tracker lead to **sustained** increases in physical activity?

Cohort & Biomarker Data

Risk and disease screening

—

identify and test utility of biomarkers

Precision – Prevention: Genetic Risk Prediction?

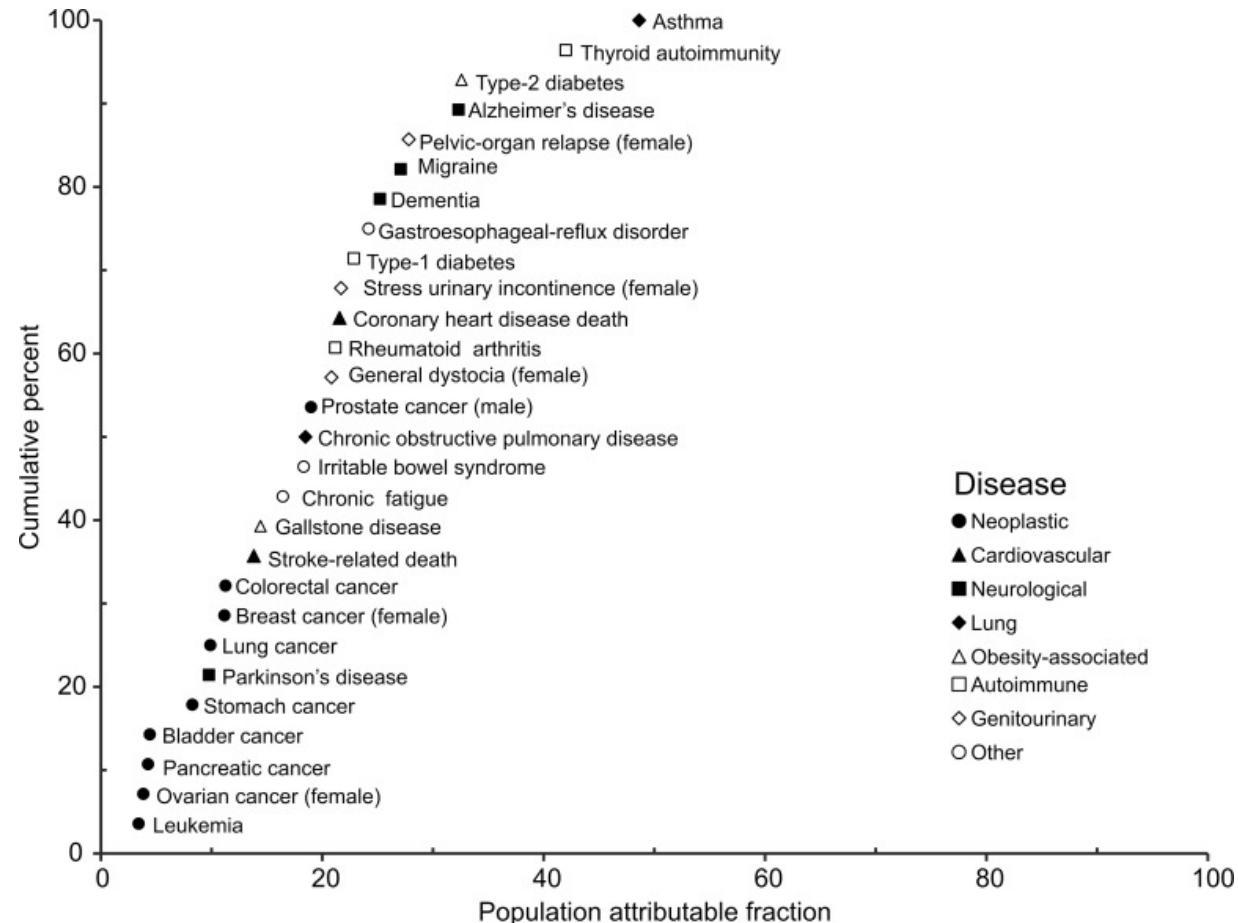
Rappaport SM. PloS One 2016; 016; 11(4): e0154387

Population-attributable
fraction
for genetics
in various disease
groups



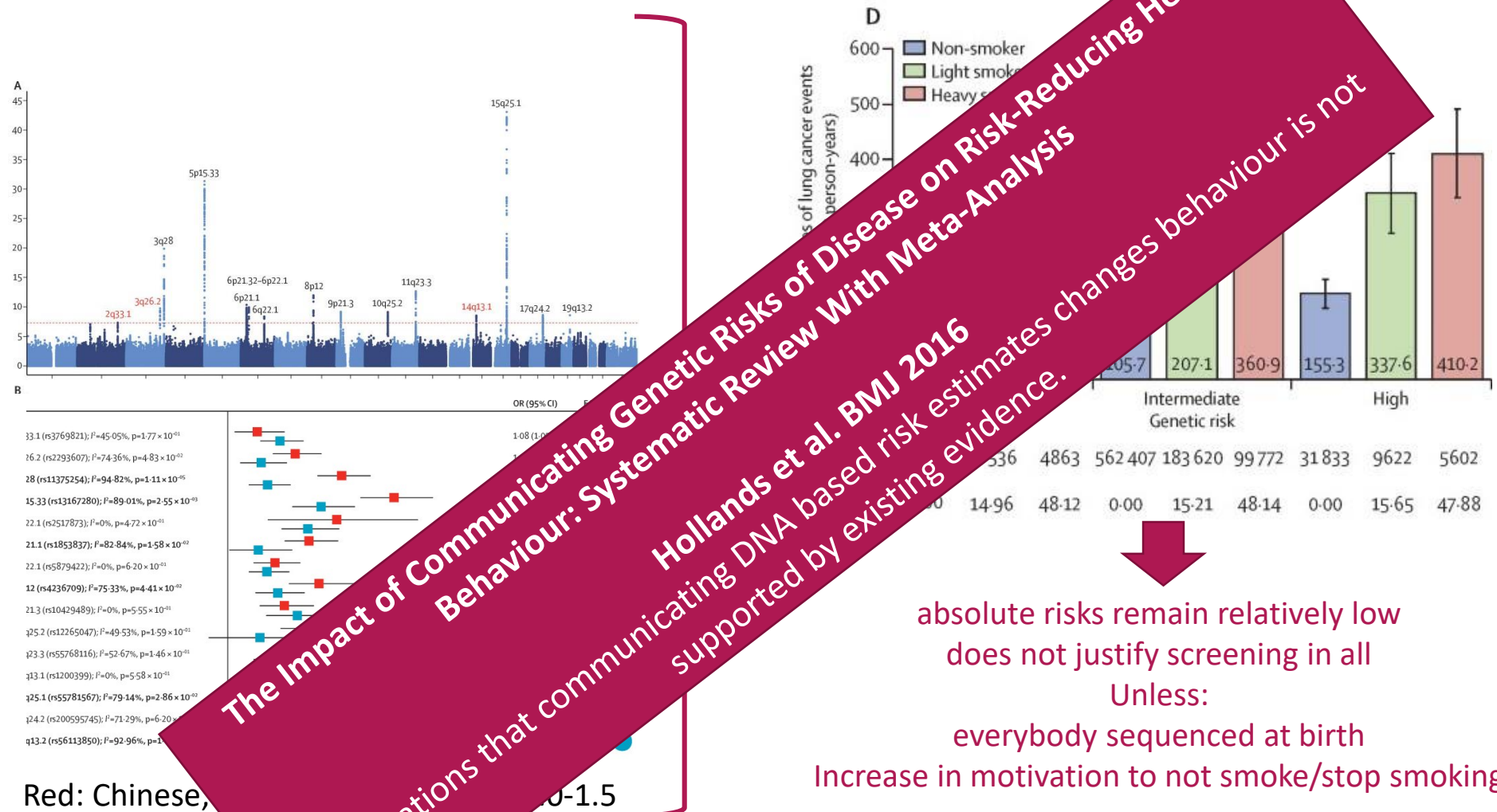
**Genetic Factors Are
Not the Major Causes
of Chronic Diseases**

except for
monogenetic/familial
disorders



Utility of polygenic genetic risk test – non-small cell lung cancer

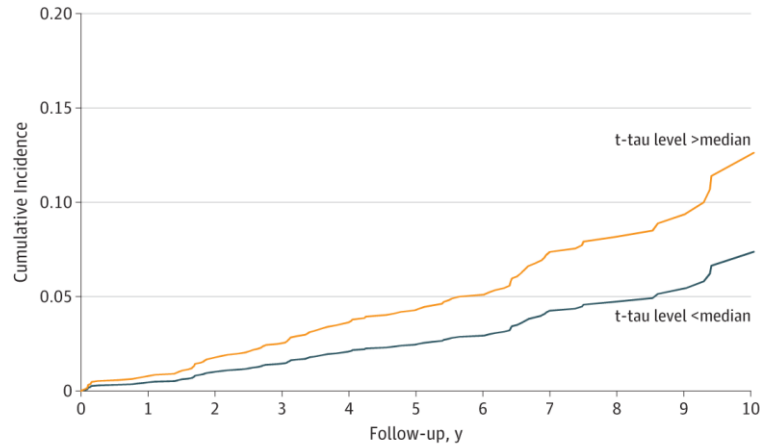
Dai J et al. Lancet Resp Med 2019;7:881



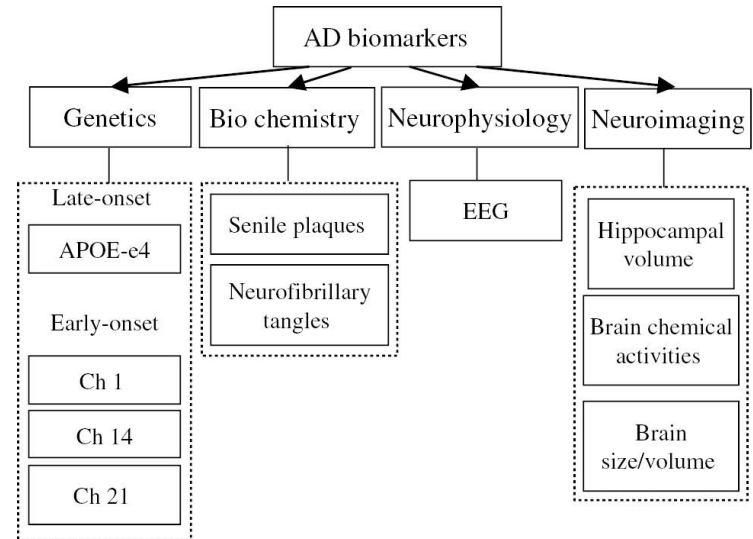
Risk/Disease screening: time variant biomarkers

Pase M et al. JAMA Neurol 2019;76:598; Mirzaei et al. Rev Neurosci 2019;27:857

B Alzheimer disease dementia



o. at risk											
All participants	1453	1362	1292	1220	1148	1077	846	543	324	150	58
t-tau level >median	727	672	624	579	528	490	389	254	153	72	28
t-tau level <median	726	690	668	641	620	587	457	289	171	78	30



Plasma total Tau level measured in prospectively sampled blood predicting dementia



Broad biomarker information obtained prospectively in cohorts

Relevance of the «Healthy Reference»

Cohort & Biomarker Data

Diagnosis and treatment
—
evaluate health care
and
health systems

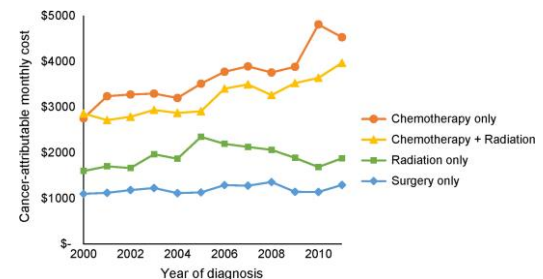
Personalized Lung Cancer Treatment

Sheehan DF et al. Cancer Med 2019;8:94; Cherny et al. Ann Oncol 2016; 27:1423

- lung cancer comprises a multitude of genetically distinct diseases.
- EGFR tyrosine kinase inhibitors are used as first and second-line treatments in lung cancer
- EGFR testing is required before treatment decision

Improvements in cancer treatments (survival; quality of life) have come at a very substantial cost, and in the past decade, the average price of new anticancer agents has more than doubled, from \$4500 to >\$10 000 per month

Temporal change in average monthly lung cancer-attributable costs in the U.S.



Global Access to EGFR Tests & Treatments

Carbonnaux et al. ERJ 2016;47:1331

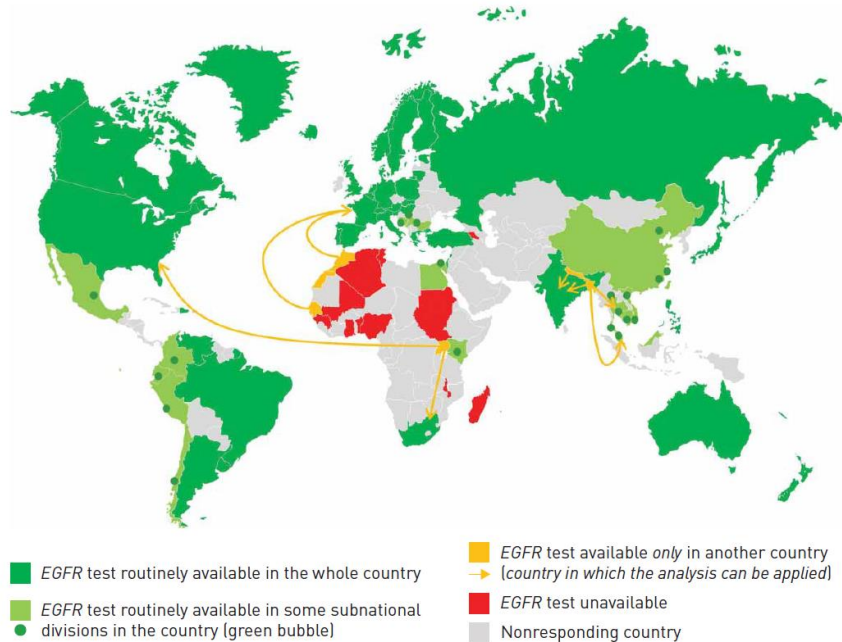


FIGURE 1 Worldwide map of the availability of epidermal growth factor receptor gene (EGFR) mutation testing. Study conducted between April 2014 and November 2014.

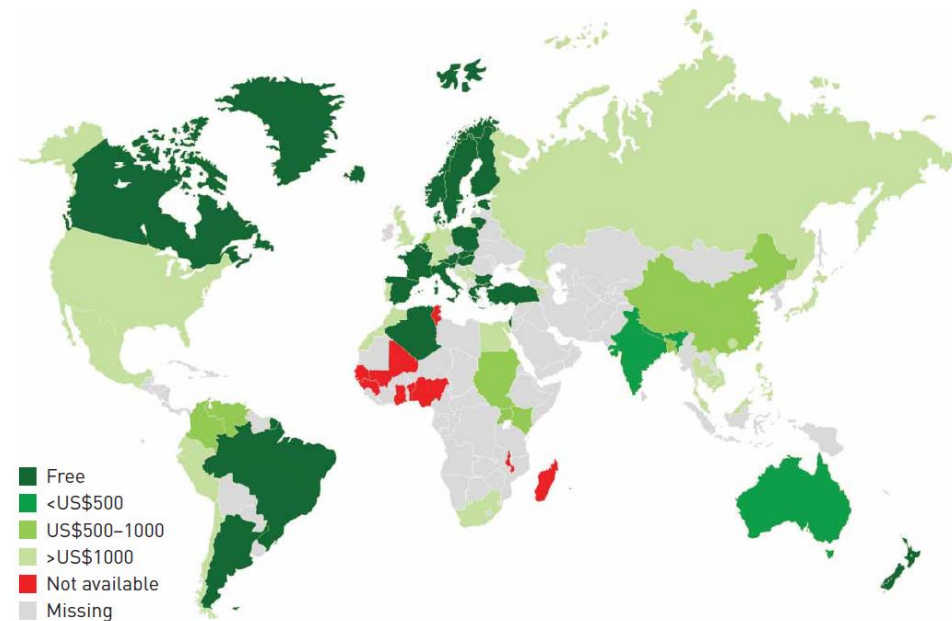
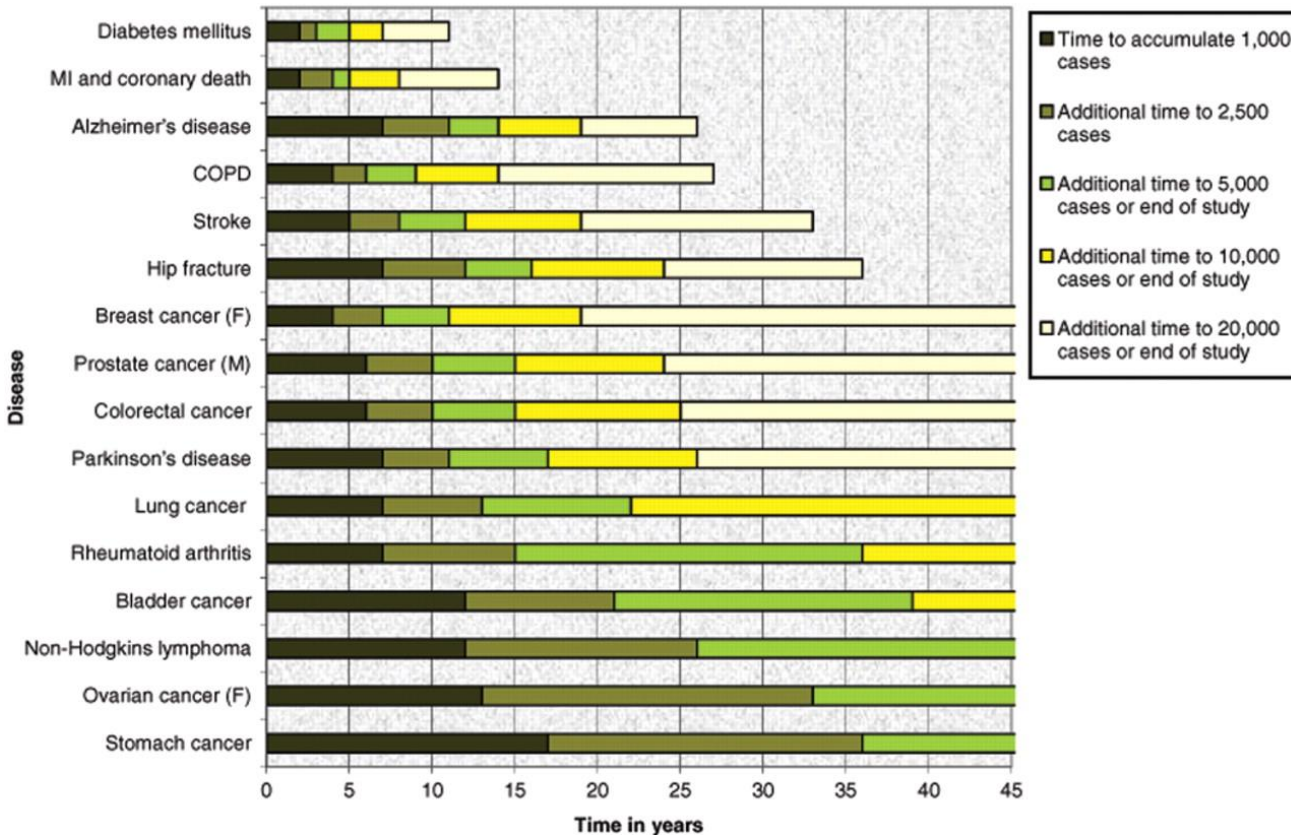


FIGURE 3 Erlotinib availability and cost. Study conducted between April 2014 and November 2014.

The need for large sample size: sufficient endpoints

UK cohort 500 000 men & women 40–69 years

Burton P R et al. *Int. J. Epidemiol.* 2009;38:263-273



Example Lung cancer:

social equity
in access to

- lung cancer screening
- timely diagnosis
- personalized treatments

A Swiss Cohort Platform

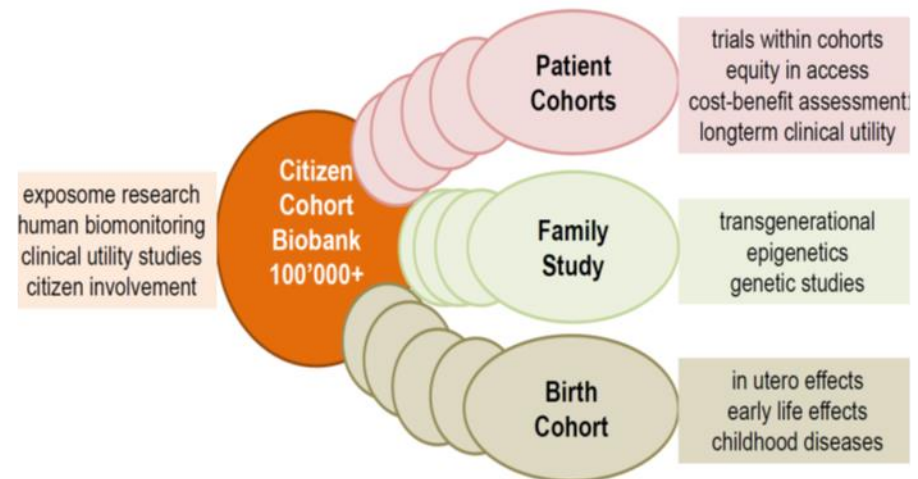


Schweizer Gesundheitsstudie Für mich – Für uns



pilot study with 1000 citizens

- Swiss-wide
- 100'000+ citizens 20-69
- interview-examination-sensing-biosampling-imaging
- interdisciplinary collaboration
- duration > 10 years





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