Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Epidemiology and Public Health
Chronic Disease and Epidemiology Unit
Genetic Epidemiology of Non-Communicable Diseases

THE VALUE OF POPULATION-BASED STUDIES AND THEIR ASSOCIATED BIOBANKS IN STUDYING LONG TERM EXPOSURE EFFECTS

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on Behalf of

Prof. Dr. Nicole Probst-Hensch's Group

Challenges when studying associations between exposure and outcomes with long latencies

Study Designs

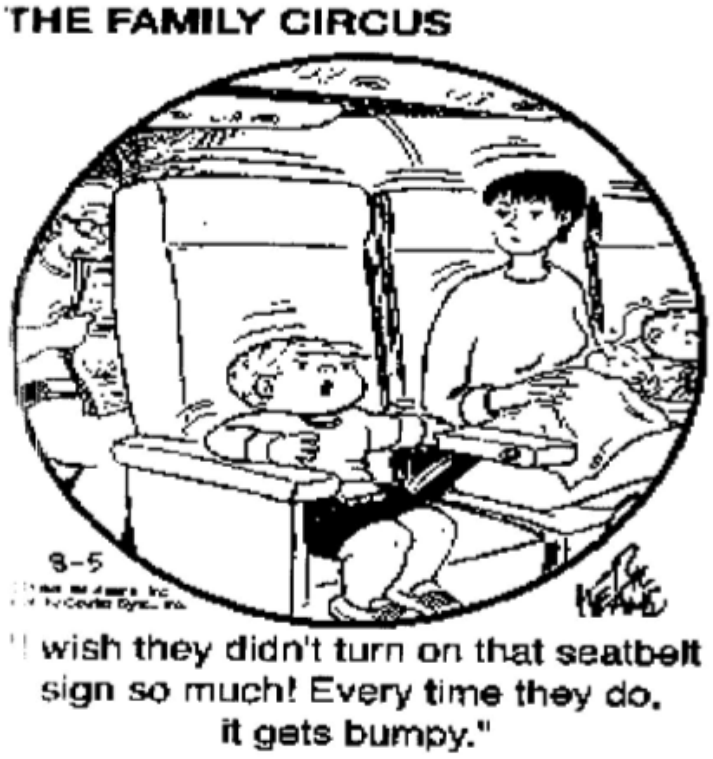
Observational Studies

Increasing Strength of Scientific Evidence

- ❑ < Confounding Factors
- ❑ Decreasing Biases
- ❑ Temporality

Strengths of Prospective Population-Based Cohort Studies

- Results can be generalizable to the entire population
- Incidence of the disease
  - ❑ Relative Risks
- Temporal relationship
- Possibility to study multiple exposures and outcomes
  - ❑ Multifactorial diseases



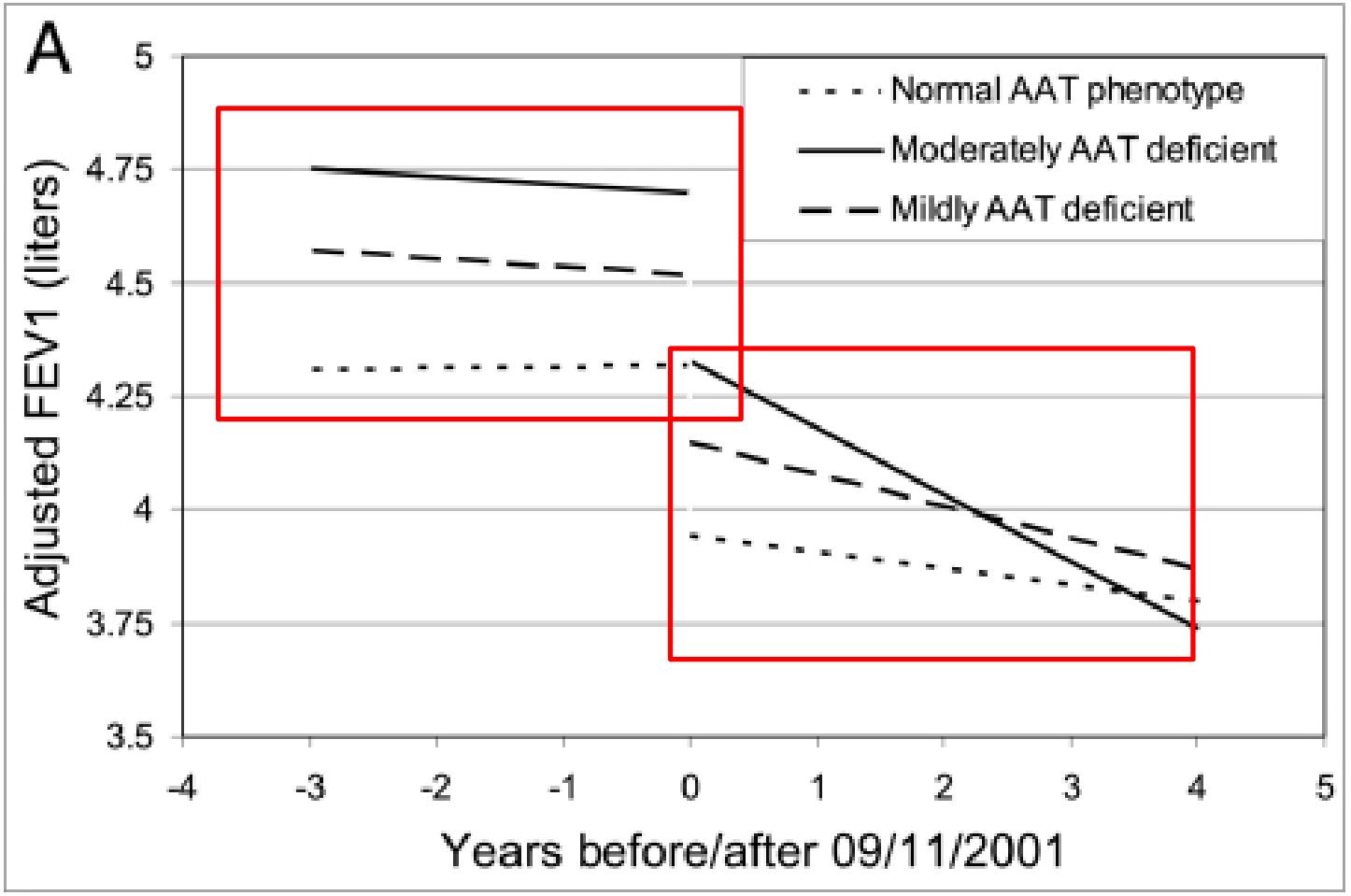
Biobanks

- Repository for biologic materials
  - Whole blood
  - Saliva
  - Urine
  - DNA

- Biologic markers
  - Of exposure
  - For susceptibility
  - Of early disease

- Help quantify the occurrence of the disease including gene-environment interactions

Gene – Environment Interaction



Banauch et al., 2010

Challenges

In Measuring Exposures Associated With Long Latency Diseases

1. Cumulative exposures
2. Recall bias, incomplete measurements, inaccurate data
3. Critical window
   - Easier to identify for acute or moderately short exposures
4. Multiple exposures

Strengths

of Cohort Studies and Biobanks in Measuring Exposure Associated with Long Latency Diseases

1. Cumulative exposures
2. Recall bias, incomplete measurements, inaccurate data
3. Critical window
   - Easier to identify for acute or moderately short exposures
4. Multiple exposures

1. Prospective AND Longitudinal measurements, active follow-ups
2. Triangulation of data
   - Questionnaires, biomarkers, national exposure data

Longitudinal measurements of same participants

SAPALDIA

26 Year Old Prospective, Longitudinal and Population-Based Cohort Study of the Swiss TPH

SAPALDIA

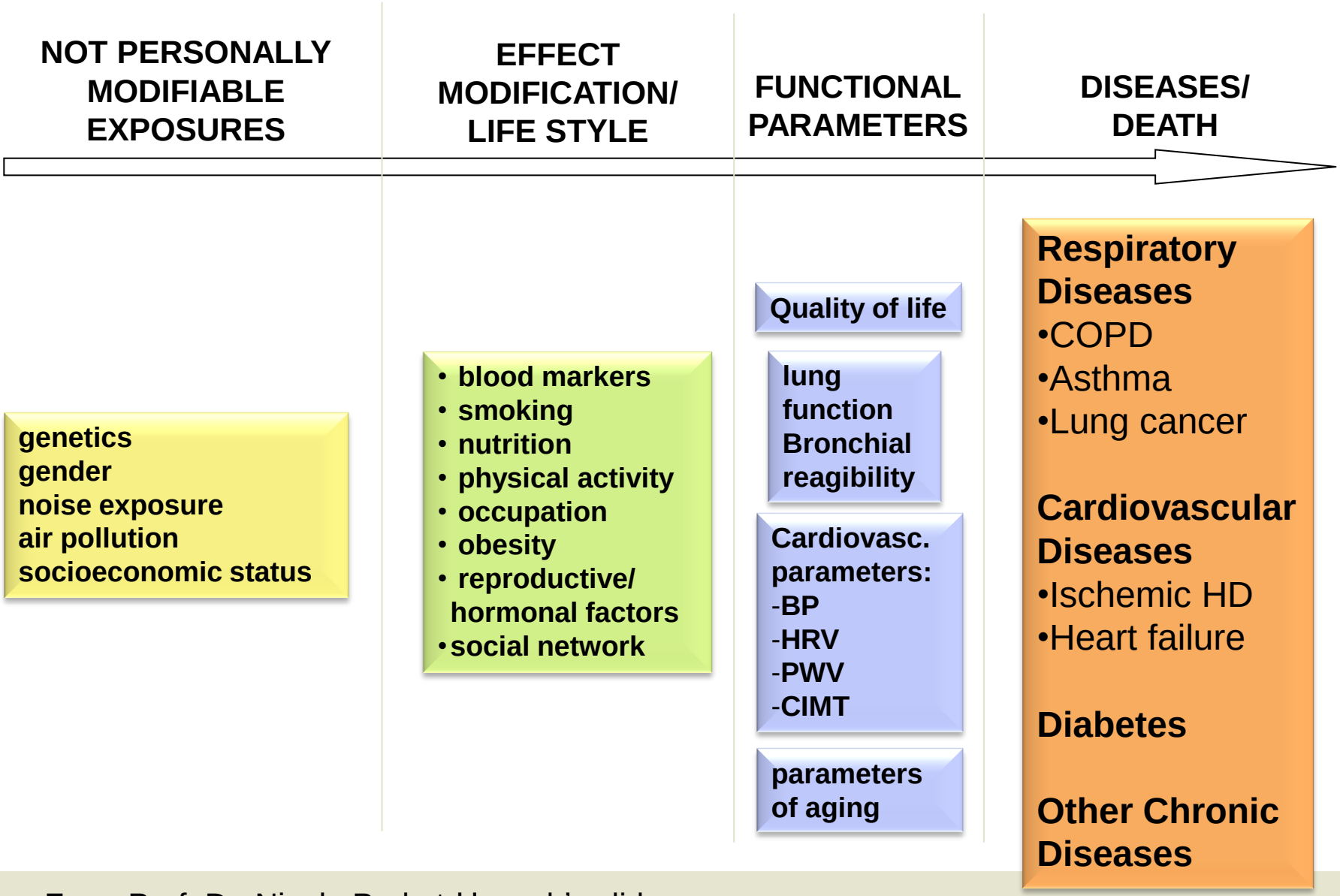
Swiss Study on Air Pollution and Lung Disease in Adults

1. SAPALDIA 1: 1991, n = 9651
2. SAPALDIA 2: 2002, n = 8047
3. SAPALDIA 3: 2010, n = 6139
4. SAPALDIA 4: 2017, n = ?

SAPALDIA

- Prospective population based-cohort study
  - Longitudinal study with 4 time-points
  - Same participants
  - 26 years of follow-up
  - High attrition
- Data obtained through
  - Questionnaires
  - Phone interviews
  - In person assessment
- Biobank
  - Saliva, urine, stool
  - Serum, plasma, whole blood
  - DNA

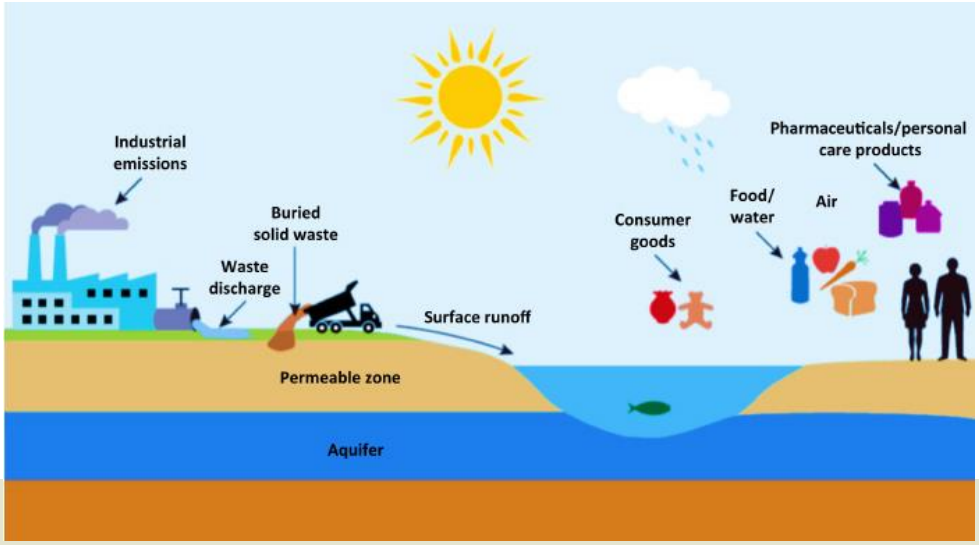
SAPALDIA Data



From Prof. Dr. Nicole Probst-Hensch's slides

Strengths of SAPALDIA: Exposure Assessment

1. Prospective assessment of exposures in various geographic areas
2. Cumulative exposures
3. Broad and rich data on risk factors, effect modifiers
4. Broad adult age range
5. Incidence of chronic diseases and presence of comorbidities
6. Biologic markers of exposure

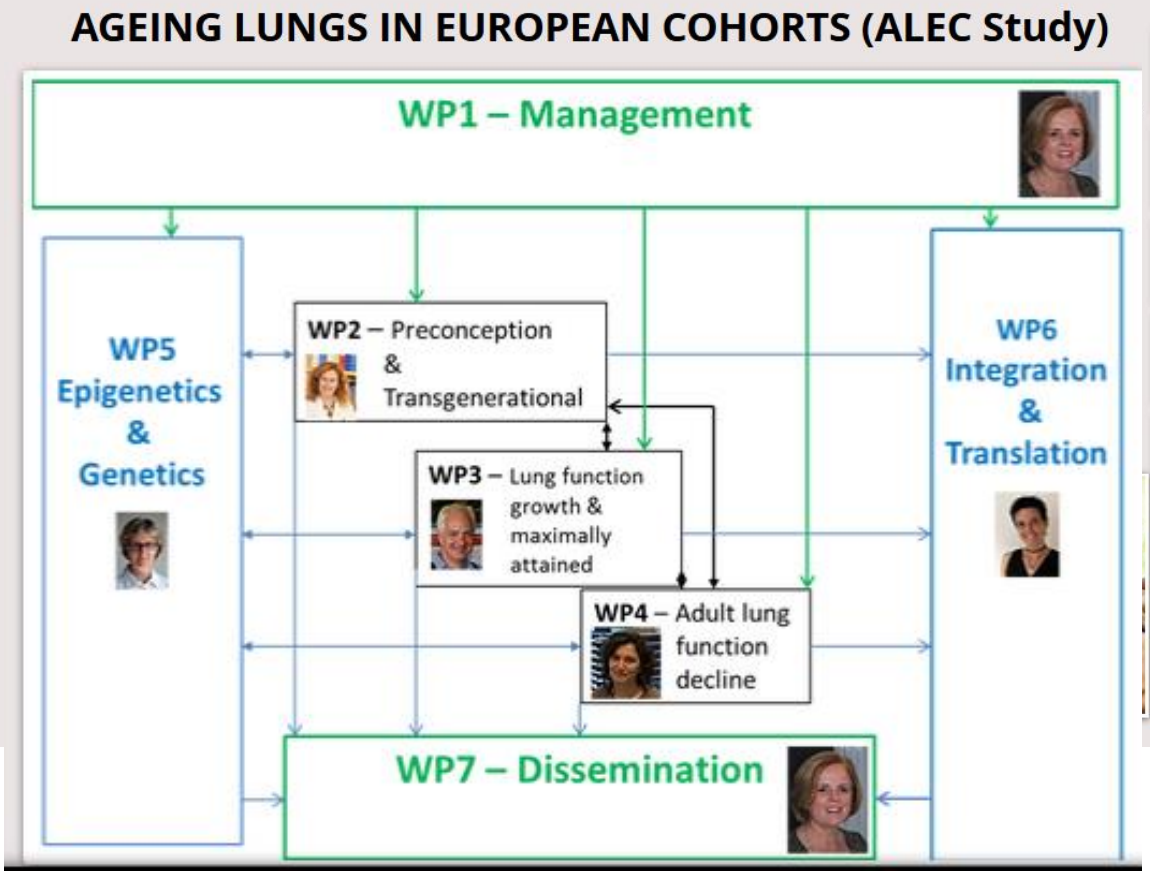


Strengths of SAPALDIA: Analytical Possibilities

1. Cross-sectional analyses for each time-point
2. Longitudinal Analyses
3. Prediction Analyses

Epigenome - Wide Association Study on Lung Function

The ALEC project

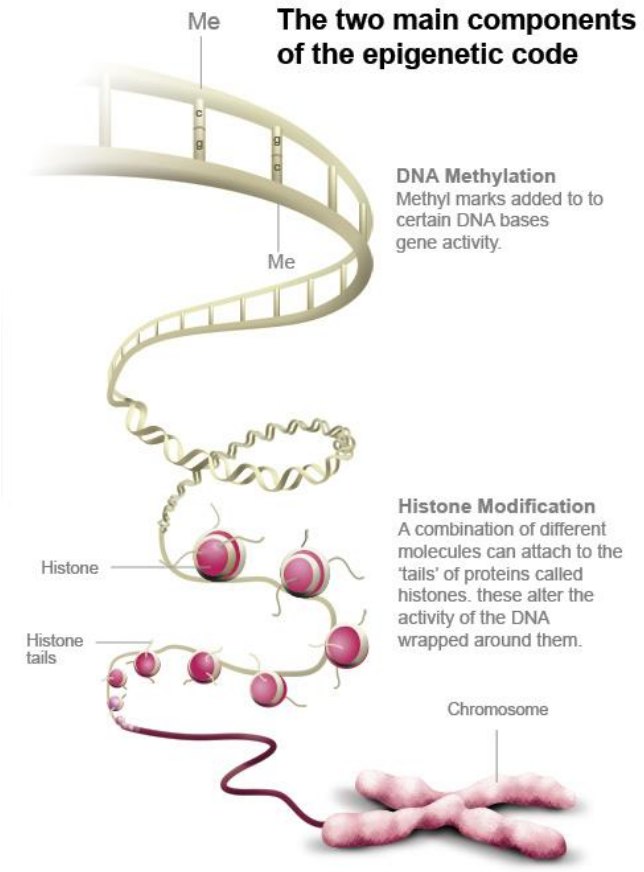


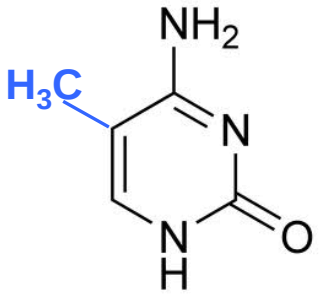
Goal: To generate a predictive risk score for COPD

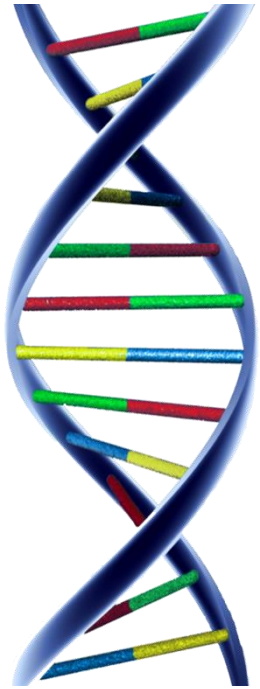
Prof. Dr. Nicole Probst-Hensch has the lead on the work package 5

- How genetic and epigenetic changes impact lung function

DNAm – an Epigenetic Mechanism







Smoking and Lung Function

- **Aim:** To identify lung function methylation signals related to smoking in the three ALEC population-based cohorts, ECRHS, NFBC, SAPALDIA.

- Smoking is the **STRONGEST** & **MODIFIABLE** predictor of poor lung health

- **Goal:** To understand Smoking Mechanisms in Lung Disease

DNAm and Lung Function

Smoking-related DNAm patterns have the potential for understanding of biological mechanisms of long-term exposure to tobacco smoke

1. DNAm sites shown to be associated with smoking exposure AND also with lung disease (Zhu et al., Gao et al. 2015)
2. Different patterns of DNAm reported for active smokers, passive smoking exposure (in utero), never smokers (Joehanes et al. 2016)

DNAm and Lung Function con't

Smoking-related DNAm patterns have the potential for improved assessment of long-term exposure to tobacco smoke

4. Methylation levels of CpGs can but do not always return toward that of never smokers after years of smoking cessation (Joehanes et al. 2016, Ambatipudi et al (2016))
   - The CpGs whose methylation did not return to baseline levels may serve as markers for follow-up of former smokers for secondary cancer prevention
5. Enrichment for CPGs in genes related to respiratory lung phenotype was found (Joehanes et al. 2016)

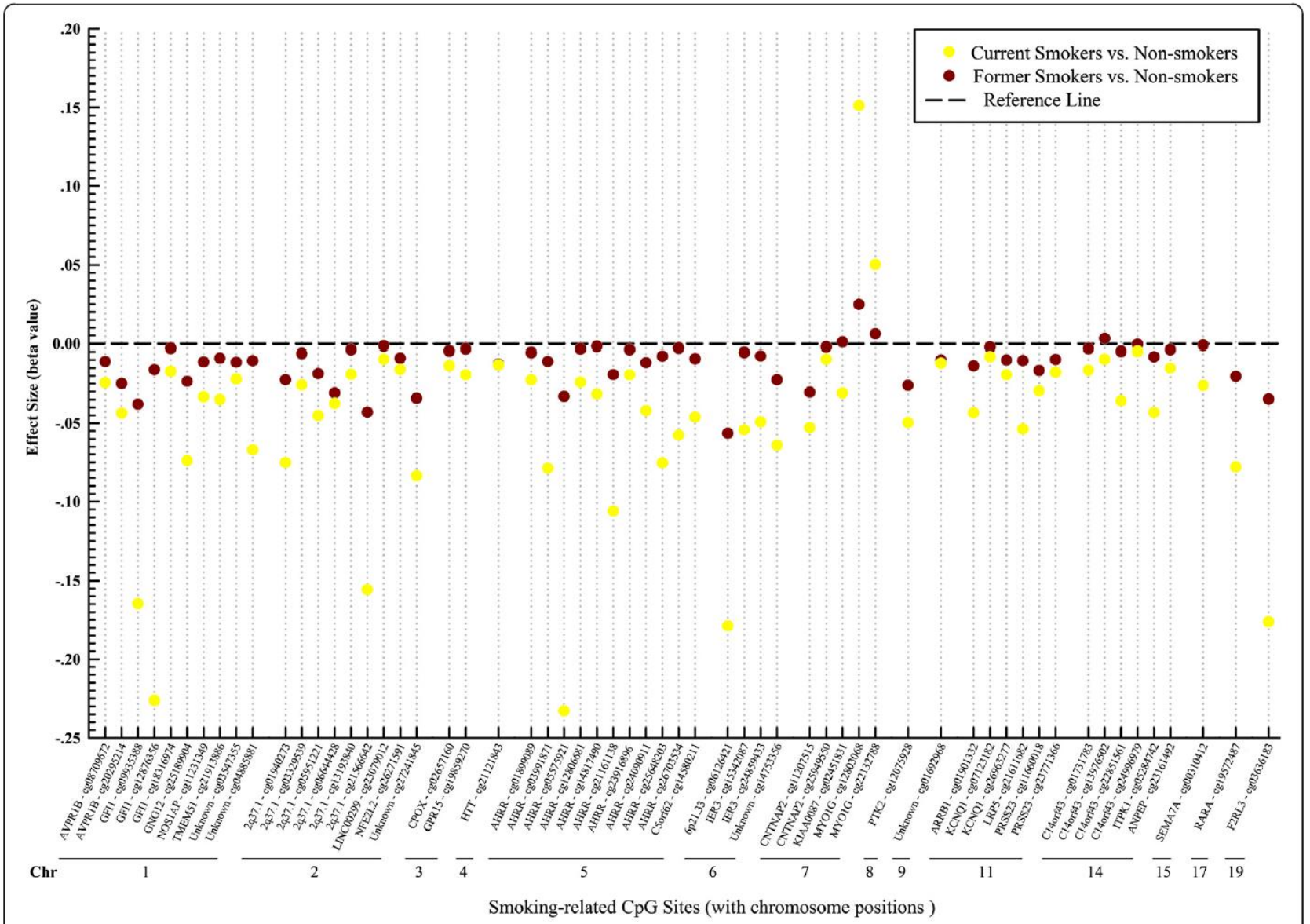
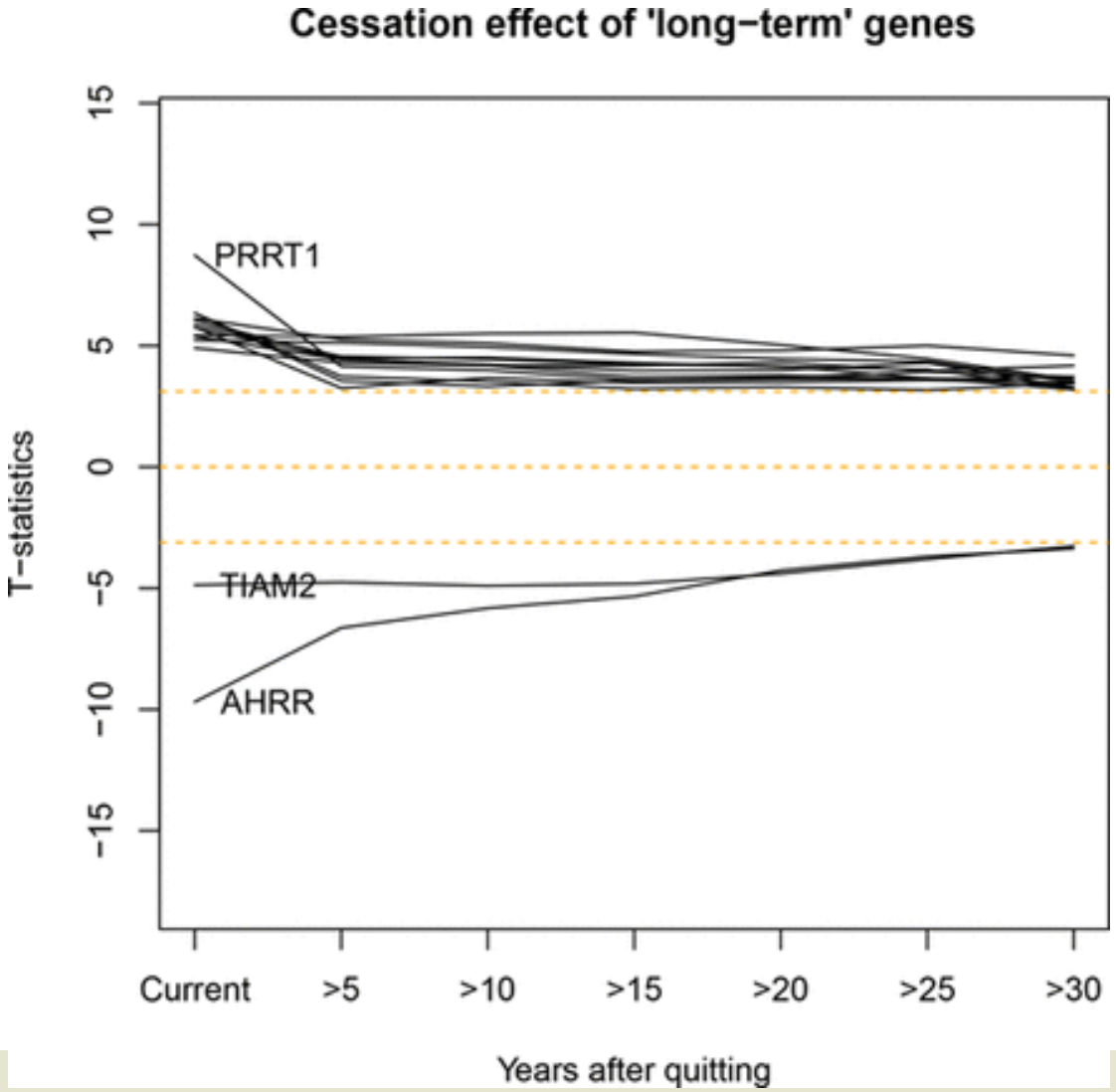


Fig. 3 Effect sizes of smoking-induced methylation for current smokers and former smokers compared with non-smokers. *Chr* chromosome position, used the publically available data of Zeilinger et al. (median beta values) [6]

Gao et al. 2015

Trajectories of cytosine–phosphate–guanine (CpG) sites that did not return to never-smoker levels within 30 years after cessation.



Joehanes et al. 2016

Conclusion

Biomarkers (genetic and DNAm) improve the assessment of exposures related to outcomes with long latencies

1. Appropriate assessment of exposures
2. Not ready in most cases for individual risk prediction
3. Important research instruments to improve causal understanding of modifiable risk factors
4. Point to mechanism of action mediating the smoke effect
5. Could be used in the future in personalized medicine

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SAPALDIA participants

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