ALEC project: Ageing Lungs in European Cohorts

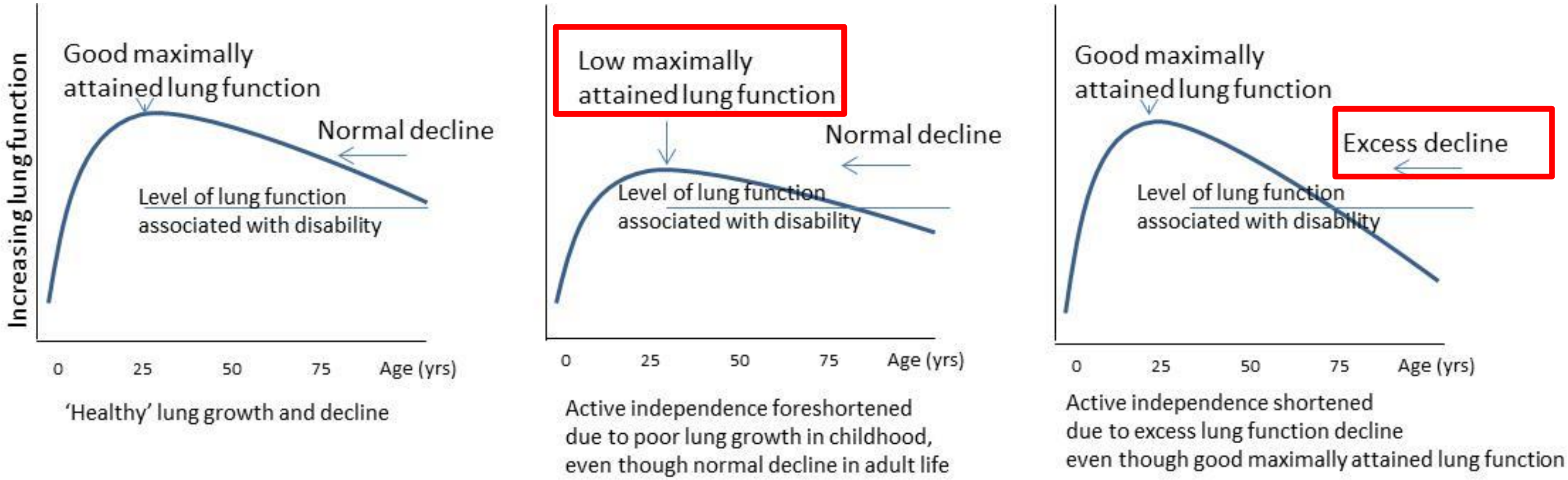
Judith Garcia Aymerich, BRN seminar
Barcelona 2018

ISGlobal Barcelona Institute for Global Health
Institució CERCA Centres de Recerca de Catalunya

Abnormalities of lung growth and lung ageing

- Low maximally attained lung function
    - Lung function at birth
    - Lung function growth
- Rapid decline
- Low maximally attained lung function AND rapid decline

- Risk factors may operate across the lifecourse …and even across generations



Ageing Lungs in European Cohorts (ALEC)

- identify determinants of lung function
- collate new data on pre-conception and transgenerational determinants
- identify change in DNA methylation patterns occurring as adults age and their association with disease development and environmental exposures
- generate a predictive risk score for low lung function and COPD that accounts for combined effects of factors across the lifecourse
- implement an online interactive tool for personalised risk prediction
- identify knowledge gaps

H2020 ref 633.212
Cost total: 7.271.433 €
Contribució de la UE: 5.534.094 €
Durada: maig 2015 - maig 2019

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ALEC cohorts

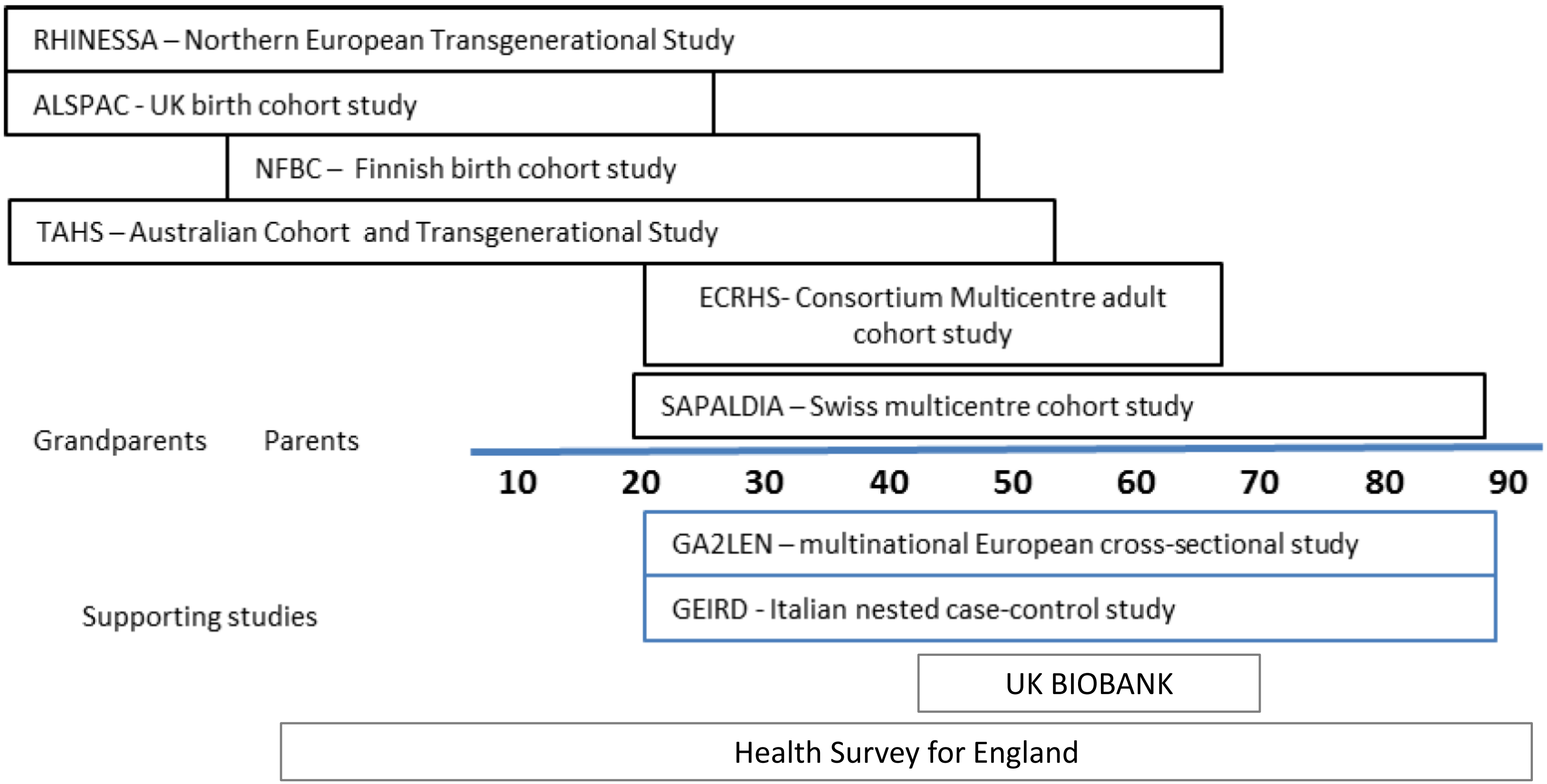
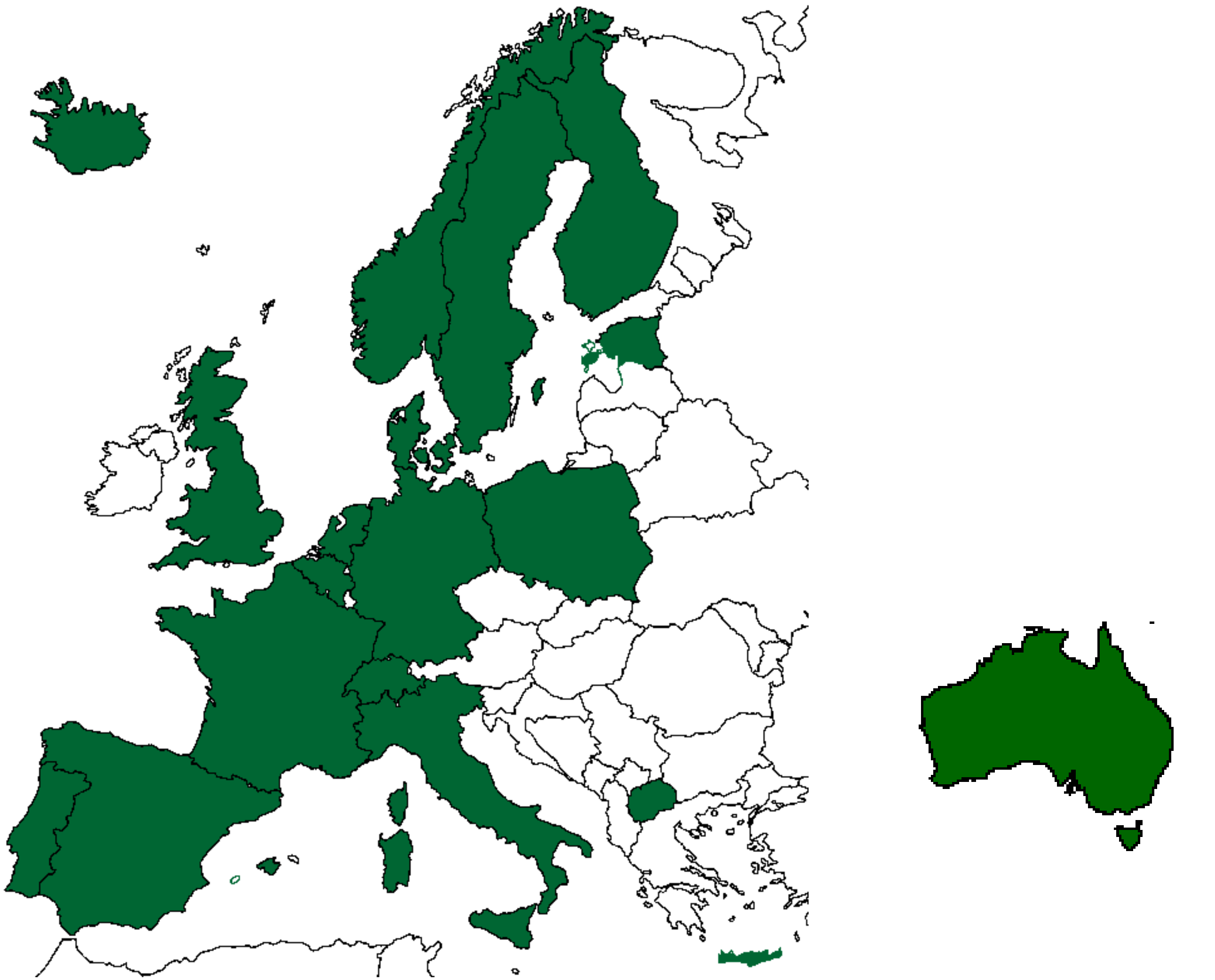
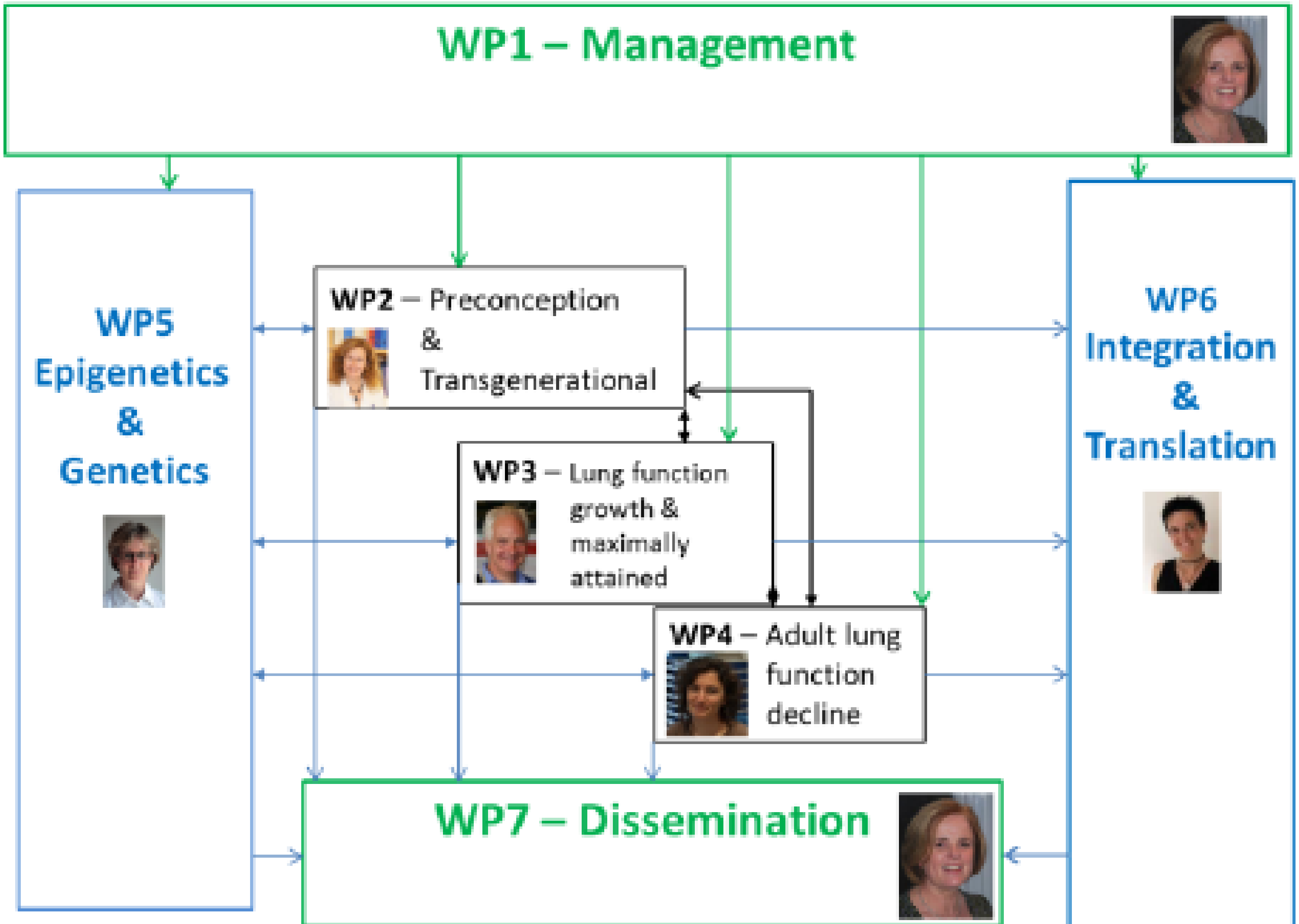


Figure 3 Maps showing geographical distribution of studies within ALEC



ALEC Workstreams



Transgenerational determinants

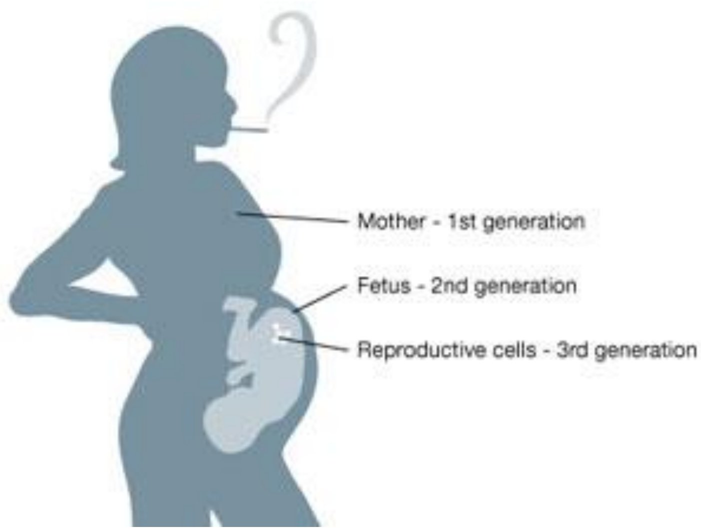


Image from www.urmc.rochester.edu

Environmental exposure

ORIGINAL ARTICLE

Grandmother's smoking when pregnant with the mother and asthma in the grandchild: the Norwegian Mother and Child Cohort Study

Editor's choice
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Maria C Magnus,[1] Siri E Håberg,[2] Øystein Karlstad,[3] Per Nafstad,[1,4] Stephanie J London,[5] Wenche Nystad[1]

…grandmother's smoking when pregnant with the mother increased the risk of asthma in the grandchild independent of the mother's smoking status…unmeasured confounding may be present...

But what about **FATHERS?**

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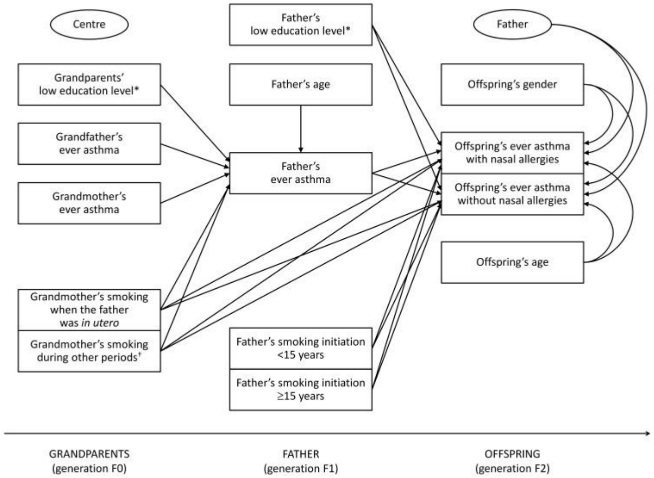

IEA

International Journal of Epidemiology, 2018, 1–12
doi: 10.1093/ije/dyy031
Original article

Original article

A three-generation study on the association of tobacco smoking with asthma

Simone Accordini,[1*] Lucia Calciano,[1] Ane Johannessen,[2] Laura Portas,[1] Bryndis Benediktsdóttir,[3] Randi Jacobsen Bertelsen,[4,5] Lennart Bråbäck,[6] Anne-Elie Carsin,[7,8,9] Shyamali C Dharmage,[10] Julia Dratva,[11,12] Bertil Forsberg,[6] Francisco Gomez Real,[4] Joachim Heinrich,[13] John W Holloway,[14] Mathias Holm,[15] Christer Janson,[16] Rain Jõgi,[17] Bénédicte Leynaert,[18] Andrei Malinovschi,[19] Alessandro Marcon,[1] Jesús Martínez-Moratalla Rovira,[20,21] Chantal Raherison,[22] José Luis Sánchez-Ramos,[23] Vivi Schlünssen,[24,25] Roberto Bono,[26] Angelo G Corsico,[27] Pascal Demoly,[28,29] Sandra Dorado Arenas,[30] Dennis Nowak,[13,31] Isabelle Pin,[32,33,34] Joost Weyler,[35] Deborah Jarvis[36,37†] and Cecilie Svanes[2,5†]; on behalf of the Ageing Lungs in European Cohorts (ALEC) Study

Associations of tobacco smoking with asthma across three generations – paternal line

Generation		F1: Father's ever asthma OR (95% CI)	F2: Offspring's ever asthma with nasal allergies RRR (95% CI)	F2: Offspring's ever asthma without nasal allergies RRR (95% CI)
F0	Grandmother's ever asthma (present vs absent)	3.08 (1.96–4.85)	–	–
	Grandfather's ever asthma (present vs absent)	2.38 (1.51–3.75)	–	–
	Grandparents' education level[a] (low vs high)	0.96 (0.71–1.30)	–	–
	Grandmother's smoking (vs not smoking)			
	when the father was *in utero*	0.82 (0.47–1.44)	1.60 (0.95–2.68)	1.08 (0.55–2.13)
	during other periods (or unknown smoking period)	1.02 (0.62–1.67)	1.24 (0.81–1.91)	1.35 (0.87–2.09)
F1	Father's age (1-year increase)	0.99 (0.96–1.02)	–	–
	Father's ever asthma (present vs absent)	–	2.37 (1.63–3.43)	1.70 (1.14–2.53)
	Father's education level[a] (low vs high)	–	0.47 (0.27–0.83)	0.87 (0.49–1.53)
	Father's smoking initiation (vs not smoking)			
	<15 years of age	–	1.19 (0.74–1.90)	1.43 (1.01–2.01)
	≥15 years of age	–	0.98 (0.71–1.36)	0.88 (0.70–1.11)
F2	Offspring's gender (female vs male)	–	0.71 (0.59–0.84)	0.83 (0.70–0.98)
	Offspring's age (1-year increase)	–	1.00 (0.98–1.02)	0.96 (0.94–0.99)

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Childhood determinants

- Trajectories
- Hormones
    - MR using genes as a natural experiment
- Physical activity
- Body mass and composition
- Greenness

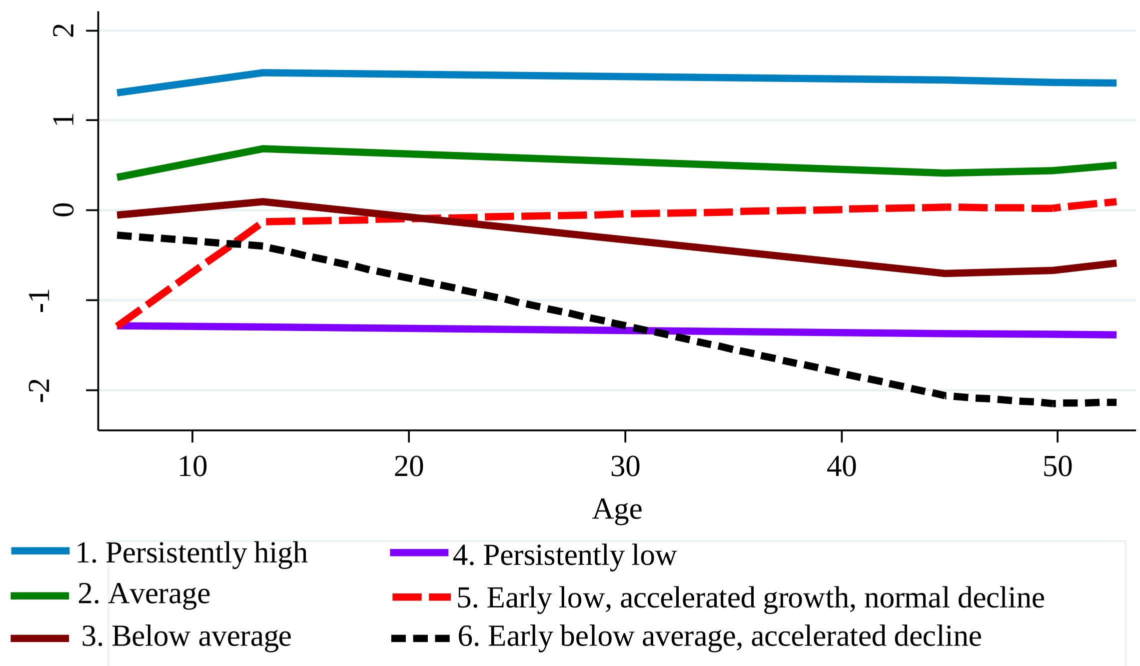
Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life

Dinh S Bui, Caroline J Lodge, John A Burgess, Adrian J Lowe, Jennifer Perret, Minh Q Bui, Gayan Bowatte, Lyle Gurrin, David P Johns, Bruce R Thompson, Garun S Hamilton, Peter A Frith, Alan L James, Paul S Thomas, Deborah Jarvis, Cecilie Svanes, Melissa Russell, Stephen C Morrison, Iain Feather, Katrina J Allen, Richard Wood-Baker, John Hopper, Graham G Giles, Michael J Abramson, Eugene H Walters, Melanie C Matheson*, Shyamali C Dharmage*

Summary
Background Lifetime lung function is related to quality of life and longevity. Over the lifespan, individuals follow

Lancet Respir Med 2018

Lung function trajectories age 7 to mid-50's



COPD at age 53 =
post-BD FEV_1/FVC <LLN

6%	27% of all cases
13%	13% of all cases
46 %	35% of all cases

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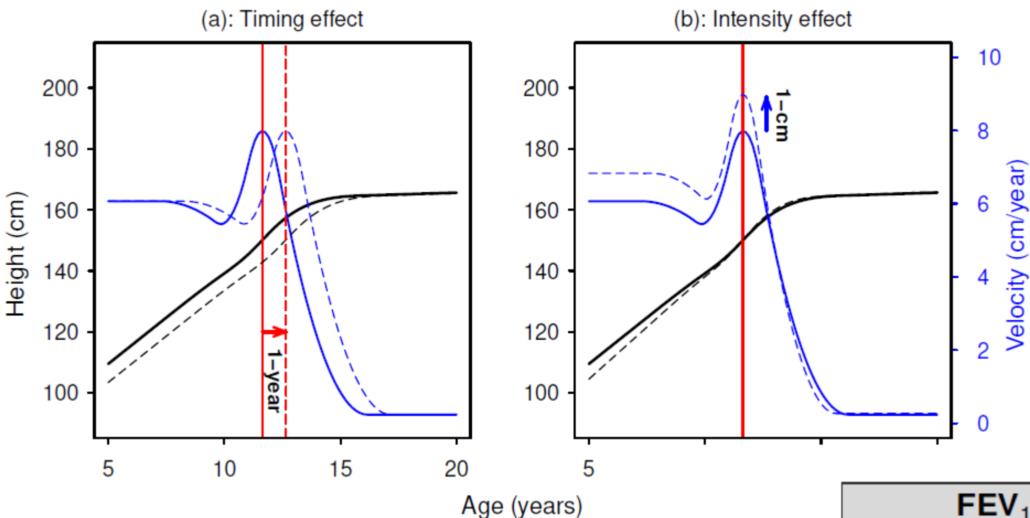
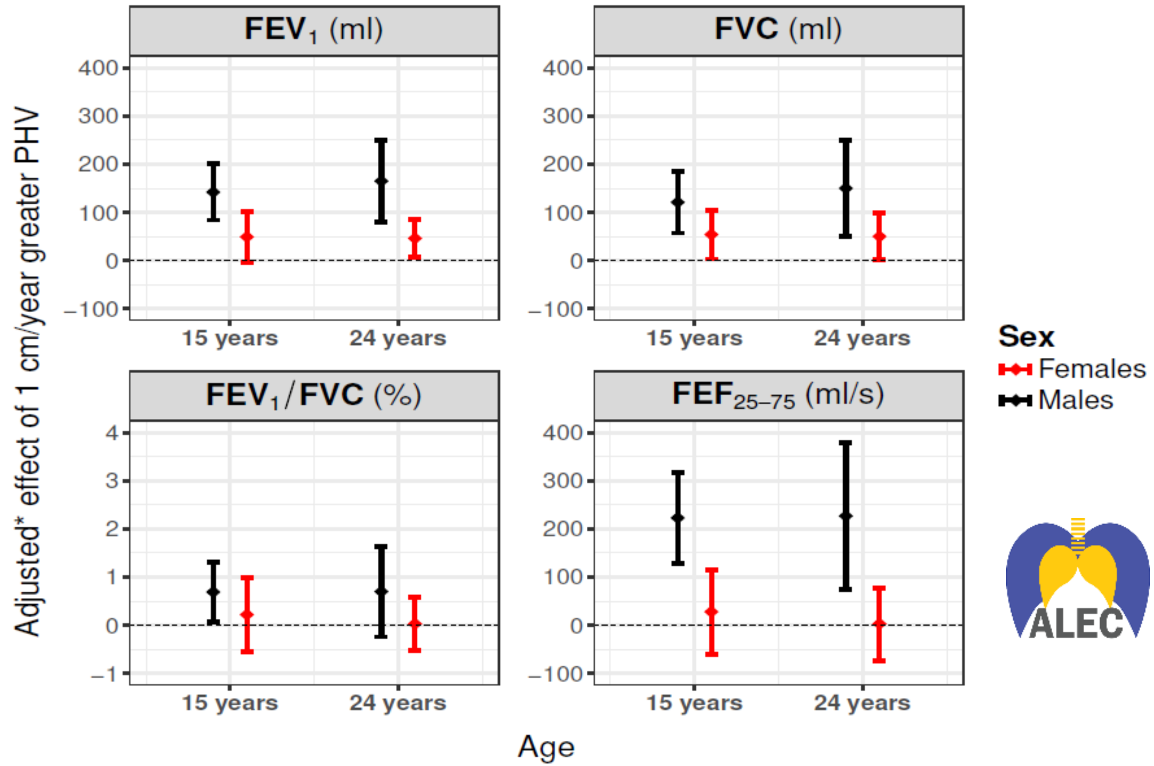
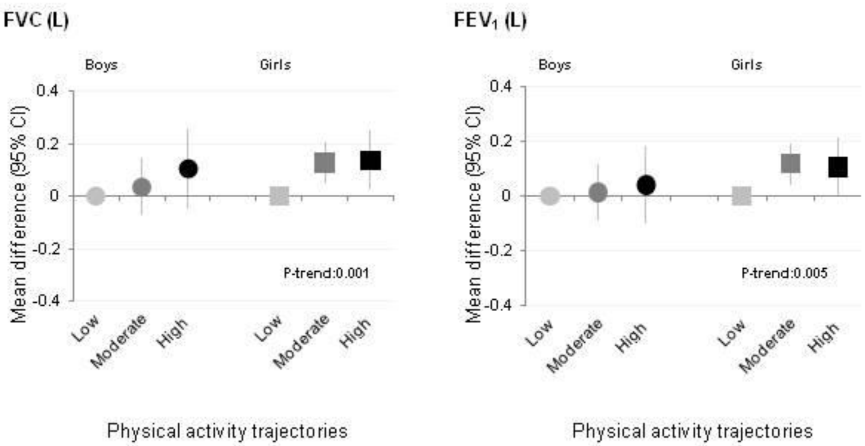
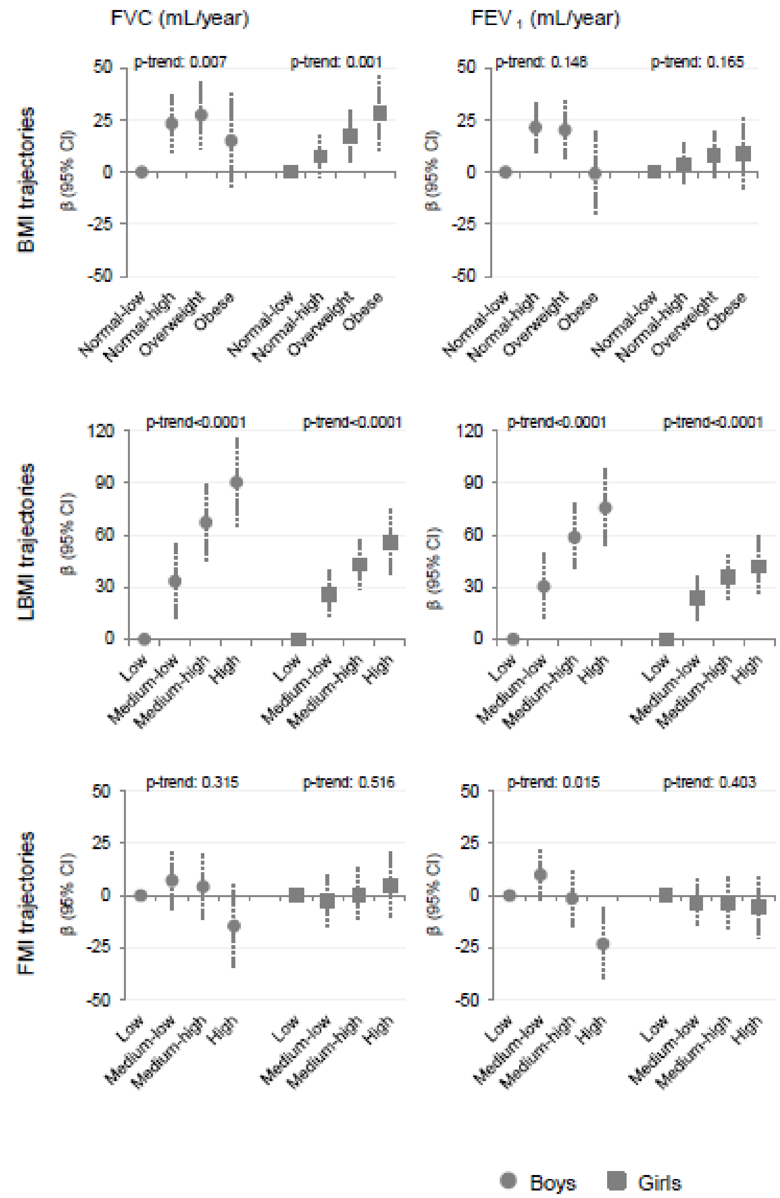
Puberty and lung function at peak (Mahmoud 2018, Am J Respir Crit Care Med)





Physical activity, body composition and lung function growth





Roda submitted; Peralta submitted

Adult determinants

- Early life factors
- Asthma and asthma treatment
- Sleep
- Physical activity
- Obesity
- Diet
- Occupation
- Hormones
- UV exposure
- Greenness

Thorax Online First, published on March 24, 2018 as 10.1136/thoraxjnl-2017-211158
Chronic obstructive pulmonary disease

ORIGINAL ARTICLE

Occupational exposures and 20-year incidence of COPD: the European Community Respiratory Health Survey

Theodore Lytras,[1,2] Manolis Kogevinas,[1,2,3,4] Hans Kromhout,[5] Anne-Elie Carsin,[1,2] Josep M Antó,[1,2,3,4] Hayat Bentouhami,[6] Joost Weyler,[6,7] Joachim Heinrich,[8] Dennis Nowak,[8] Isabel Urrutia,[9] Jesús Martinez-Moratalla,[10,11] José Antonio Gullón,[12] Antonio Pereira-Vega,[13] Chantal Raherison-Semjen,[14] Isabelle Pin,[15,16,17] Pascal Demoly,[18,19] Bénédicte Leynaert,[20] Simona Villani,[21] Thorarinn Gislason,[22,23] Cecilie Svanes,[24,25] Mathias Holm,[26] Bertil Forsberg,[27] Dan Norbäck,[28] Amar J Mehta,[29] Nicole Probst-Hensch,[30,31] Geza Benke,[32] Rain Jogi,[33] Kjell Torén,[34] Torben Sigsgaard,[35] Vivi Schlünssen,[35,36] Mario Olivieri,[37] Paul D Blanc,[38] Roel Vermeulen,[5] Judith Garcia-Aymerich,[1,2,3,4] Deborah Jarvis,[39,40] Jan-Paul Zock[1,2,3]

COPD incidence and occupational exposures

Ever exposed to	Relative risk (LLN)–ECRHS)	Population attributable fraction
Biological dusts	1.6 (1.1 to 2.3)	16.0
Mineral dusts	1.1 (0.7 to 1.7)	3.9
Gases and fumes	1.5 (1.0 to 2.2)	19.4
Vapours gas dusts & fumes	1.3 (0.9 to 2.0)	14.1
Herbicides	2.0 (0.7 to 4.1)	2.6
Insecticides	2.3 (1.1 to 4.2)	4.7
Fungicides	1.9 (0.9 to 3.6)	3.9
All pesticides	2.2 (1.1 to 3.8)	5.6

21%

No associations seen for aromatic, chlorinated or other solvents, or metals

Thorax Online First, published on January 6, 2018 as 10.1136/thoraxjnl-2017-210947
Respiratory epidemiology

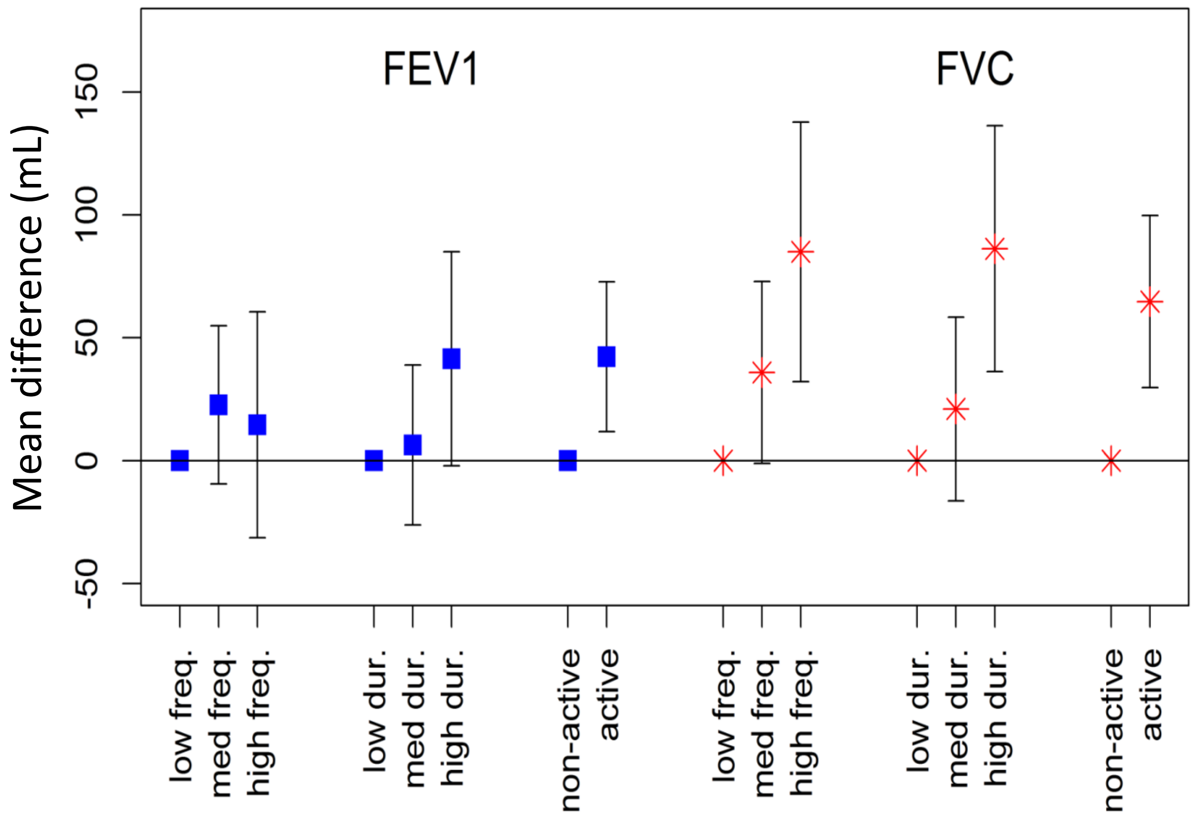
OPEN ACCESS

ORIGINAL ARTICLE

Leisure-time vigorous physical activity is associated with better lung function: the prospective ECRHS study

Elaine Fuertes,[1,2,3] Anne-Elie Carsin,[1,2,3] Josep M Antó,[1,2,3] Roberto Bono,[4] Angelo Guido Corsico,[5,6] Pascal Demoly,[7,8] Thorarinn Gislason,[9] José-Antonio Gullón,[10] Christer Janson,[11] Deborah Jarvis,[12,13] Joachim Heinrich,[14,15] Mathias Holm,[16] Bénédicte Leynaert,[17,18] Alessandro Marcon,[19] Jesús Martinez-Moratalla,[20,21] Dennis Nowak,[22,23] Silvia Pascual Erquicia,[24] Nicole M Probst-Hensch,[25,26] Chantal Raherison,[27] Wasif Raza,[28] Francisco Gómez Real,[29,30] Melissa Russell,[31] José Luis Sánchez-Ramos,[32] Joost Weyler,[33] Judith Garcia Aymerich[1,2,3]

Physical activity on lung function levels

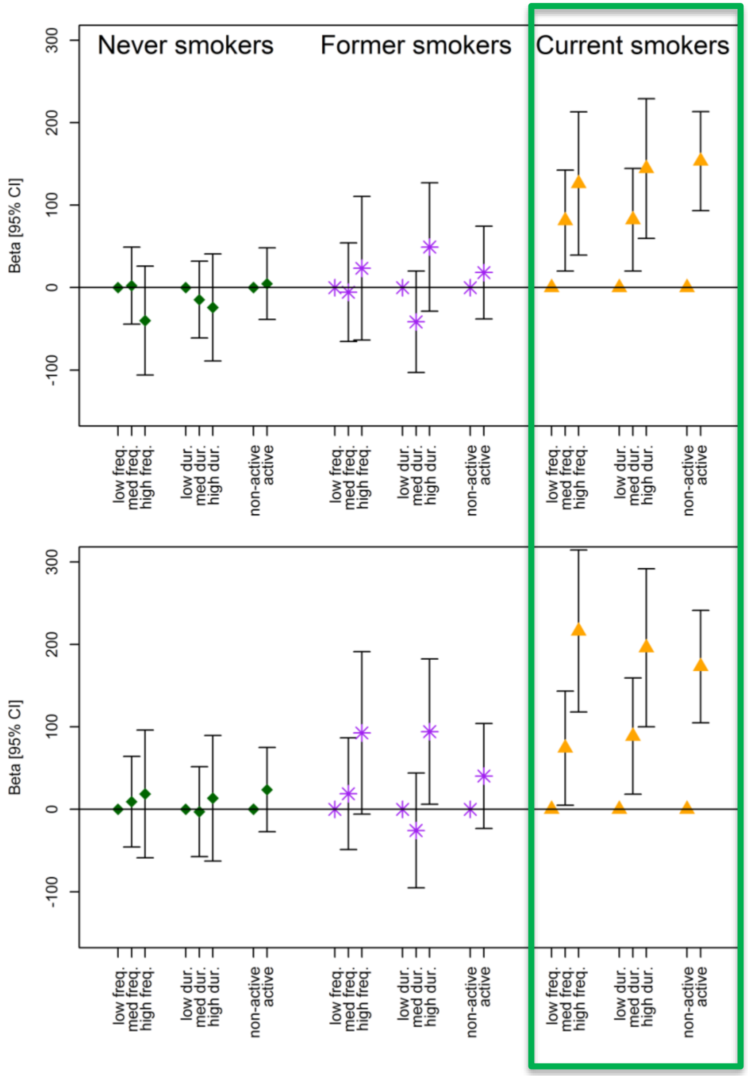


Higher physical activity levels associated with higher lung function

Adjusted for sex, age, age^2, height, weight, smoking status, secondhand smoke exposure, education and occupation

FEV1

FVC



- **Effects driven by current smokers**
- Stratification by sex, asthma, chronic disease, BMI did not alter conclusions
- No consistent effects for lung function *decline*

ORIGINAL ARTICLE
LUNG FUNCTION

Dietary antioxidants and 10-year lung function decline in adults from the ECRHS survey

Vanessa Garcia-Larsen[1], James F. Potts[2], Ernst Omenaas[3], Joachim Heinrich[4], Cecilie Svanes[5], Judith Garcia-Aymerich[6], Peter G. Burney[2,7] and Deborah L. Jarvis[2,7]

Dietary intake and lung function decline

Dietary intake (per-tertile increase)	Average decline in lung function mL·year^{-1} (continuous) regression coefficient (95% CI)						
	Never-smoker	p-value	Quit before ECRHS III	p-value	Smoker	p-value	p-value for interaction
Subjects n	270		255		109		
				FEV1			
Total fruit g	0.51 (−3.62, 4.65)	0.81	**6.41 (2.29, 10.5)**	**0.002**	3.83 (−2.93, 10.60)	0.26	**0.03**
Apple g	0.16 (−3.51, 3.82)	0.93	**4.79 (0.87, 8.72)**	**0.017**	0.62 (−6.22, 7.46)	0.86	0.09
Banana g	2.63 (−1.11, 6.37)	0.17	2.92 (−1.52, 7.35)	0.20	−0.82 (−7.70, 6.06)	0.81	0.25
Tomato g	0.52 (−3.36, 4.40)	0.79	**5.15 (0.87, 9.44)**	**0.019**	5.71 (−1.21, 12.63)	0.11	0.06
Herbal tea mL	−3.89 (−11.5, 3.71)	0.32	**12.8 (5.13, 20.54)**	**0.001**	1.97 (−13.36, 17.3)	0.80	0.21
Vitamin C mg	1.66 (−3.36, 6.69)	0.52	3.99 (−1.45, 9.44)	0.15	3.19 (−5.59, 11.97)	0.47	0.05
				FVC			
Total fruit g	0.13 (−4.79, 5.06)	0.96	**8.13 (2.22, 14.01)**	**0.007**	4.15 (−5.41, 13.7)	0.39	**0.04**
Apple g	1.45 (−2.91, 5.80)	0.51	**6.75 (1.14, 12.34)**	**0.018**	0.78 (−9.13, 10.69)	0.88	0.29
Banana g	4.07 (−0.54, 8.67)	0.08	6.23 (0.01, 12.5)	0.05	−3.79 (−13.6, 5.99)	0.44	**0.04**
Tomato g	1.02 (−3.66, 5.70)	0.67	**9.09 (3.04, 15.14)**	**0.003**	7.16 (−3.05, 17.37)	0.17	0.11
Herbal tea mL	−2.52 (−11.7, 6.67)	0.59	**14.4 (3.16, 25.69)**	**0.01**	12.34 (−9.47, 34.15)	0.26	0.11
Vitamin C mg	3.17 (−2.83, 9.16)	0.30	4.65 (−3.08, 12.37)	0.24	10.58 (−1.96, 23.11)	0.10	0.30

Bold font indicates a statistically significant p-value (<0.05). FEV1: forced expiratory volume in 1 s; FVC: forced vital capacity; ECRHS: European Community Respiratory Health Survey. #: Adjusted for height, age, country, sex, socio-economic status, body mass index, total energy intake, years of education and physical activity.

Epigenetics

- DNAm and lung function
- DNAm –focus in SERPINA1
- Biological clock
- Two step MR analyses looking at BMI and LF

Summary

- Novel data, novel results
- More to come…