More air for later - determinants of the lung function plateau, piama 23-25 years investigation

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Primary Objective: We will investigate the following primary research questions:1. What are exposomic factors that predict the maximum attained level of lung function? 2. What are genetic predictors of the maximum attained level of lung function? 3...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON54030

Source
ToetsingOnline

Brief title
PIAMA 23-25 year investigation

Condition

- Respiratory disorders NEC
- Environmental issues

Synonym
maximum lung function, spirometry

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Utrecht
Source(s) of monetary or material Support: Longfonds

Intervention

Keyword: COPD, Epigenetics, Exposomics, Lung function plateau

Outcome measures

Primary outcome

postbronchodilator FEV1 (testing of reversibility).

Secondary outcome

FEV1, FVC and FEF25-75 before bronchodilator, and LCI (Lung Clearance Index)

Study description

Background summary

COPD is one of the leading causes of morbidity and mortality worldwide. Although COPD generally manifests at older age, events early in life may significantly contribute to impaired lung function. It has been estimated that half of COPD cases can be attributed to low lung growth leading to a low maximum level of lung function attained in early adulthood (*the plateau*). This underlines the importance of investigating the determinants of the plateau.

Study objective

Primary Objective:
We will investigate the following primary research questions:
1. What are exposomic factors that predict the maximum attained level of lung function?
2. What are genetic predictors of the maximum attained level of lung function?
3. Which airway epithelial DNA methylation signatures are linked to the maximum attained level of lung function?

Secondary Objective(s):
Which multi-omics prediction signatures that can be derived from genomics, epigenomics, transcriptomics, and internal (i.e. chemical exposome measures and respiratory microbiome) and external exposome can classify subjects with a low maximum attained level of lung function?

Study design

We will invite all participants of the PIAMA (Prevention and Incidence of Asthma and Mite Allergy) birth cohort around age 25 years, and measure pre- and post-bronchodilator FEV1, FVC, and FEF25-75, perform multiple breath washout tests (MBW) to determine the lung clearance index (LCI), draw blood for exposomic analyses and measurements of total and allergen specific IgE as well as some cardio metabolic markers, perform nasal brushing for epigenetic and transcriptomic analyses and naso- and oropharyngeal swabs for respiratory microbiota analyses.
We will relate the plateau to external (e.g. air pollution, green space, physical activity) and internal (e.g. chemical) exposome measures of PIAMA participants collected throughout the life-course from before birth up to 23-25 years. Combined with our (epi)-genetics and microbiota data, we aim to determine a multi-omics signature of low lung function in early adulthood, which can be used to detect subjects at risk of subsequent COPD.

Study burden and risks

We will address the current Covid19 epidemic in our program: Complaints like fever, cough, sore throat, difficulty breathing, runny nose and sneezing in 24 hours before the appointment has to result in cancelation of the visit. Also a positive self-test results in postponing of the appointment for at least 6 weeks. During the COVID-19 epidemic, we will take extra safety measures for participants and research assistants to avoid cross-infections during the clinical examinations, e.g. no overlap in visits, 1.5 m distance between people when possible, extra surface and materials cleaning in research area, hand disinfection, airing of the research room, gloves, glasses and mask for the research assistant. The research assistant performs a selftest on the day of examinations, and will cancel all visits in case of a positive test.
The reversibility test involves administration of a short-acting ß2-sympathicomimetic bronchodilator (e.g. salbutamol) during the lung function tests. To reduce risks to minimal, we will consider as contra-indications any presence of thyreotoxicosis, heart failure, heart attacks or surgery in the past 3 months, hypertension, or use of heart glycosides. Salbutamol is a standard asthma drug, used by some PIAMA participants as part of their asthma treatment. As lung function measurements are affected by pregnancy, we will postpone the investigations when the participant is in the second half of pregnancy.
In the past, nasal brushing caused slight inconvenience, and therefore we used topical lidocaine spray for analgesia. We have now developed a soft brush that can be applied with minimal discomfort to the participant. No lidocaine spray is necessary anymore. This soft brush was applied in over 200 6-year-old children participating in the MAKI trial (https://www.umcutrecht.nl/en/Research/Strategic-themes/Child-Health-science-for-life/Respiratory-infections/Respiratory-syncytial-virus/Clinical-trials-and-studies/Maki-trial), without noticeable problems, such as tearing, and nose bleeding.
All tests will be performed by trained and experienced personnel, and if any

discomfort can be expected, it will most likely be from venipuncture. The inconvenience expected, however, is very likely to be minimal and transient. In past PIAMA clinical evaluations, participants voluntarily performed practically all tests without any complaints or discomfort. Risk and burden in participating are therefore minimal. However, if previous experiences in some of the tests were uncomfortable for a participant, the tests involved can be skipped upon the participant*s request.
Obviously, performing this clinical evaluation in PIAMA participants is essential considering the great amount of data we already have on these subjects. However, the PIAMA population is a group of young adults from the general population and findings in this group will be translatable to the current Dutch population in this age range.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

These are the participant of the ongoing PIAMA birth cohort study

Exclusion criteria

not applicable, if exclusion for certain test is necessary, other tests can still be performed.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-10-2021
Enrollment:	1750
Type:	Actual

Ethics review

Approved WMO Date:	29-09-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	10-03-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	27-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-04-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL74439.041.20