Analysis of longitudinal data:

* Mixed effect model, interaction on time

Methods on effectiveness of classifying/screening disease:

* Survival analysis on the classifying groups: according to the classification.
  + Spirometry screening for COPD?: only able to identify at late stage where damages were already taken place.
  + GOLD classifications?: too simple, not representative enough.
  + CT scans(imaging factors of COPD)?:

Defining early COPD:

* Trajectories to COPD:
  + Histograms
  + FEV1>=80% vs FEV1<80%
  + Line plots on changing of FEV1
* Childhood asthma🡪 COPD in adulthood
* Childhood factors: maternal, paternal, childhood asthma, resp infection.
* Maternal perinatal supplementation (Vit. A supplied resulted in better lung function)
* Early screening?
  + Asymptomatic doesn’t mean healthy
  + Activity level
* Intervention, and reevaluate after 14.5 years🡪 ones with succeeded intervention have reduction on mortality.
* Uterus, childhood, early adulthood.
* Smokers with preserved lung function (those with normal FEV1/FVC >=0.7, FEV1> LLN)
  + Have exacerbation (antibiotic or steroid)
  + Exercise limitation
* Inflammatory makers considered:
  + Significant: systematic: CRP, Fibrinnate
  + Insignificant: type 2: eosinophil, ige…
* Subjects in middle age have higher odds ratio in having respiratory disease.
* Prevention of lung disease in young adulthood: (study of fitness)
* Method: Testing difference among the variable among the quartiles: sex stratified
  + Ex: for the lowest quartile, the average BMI is the highest.
* Greater fitness is associated with less decline in lung function
* Lung function decline is associated with mortality, so important to study the risk factors.
* Environmental factor( indoor- outdoor air pollution, cooking methods)
* Longitudinal
* Linear mixed effect models adjusting for age, sex, ….
* Result plot: x- axis: FEV1, y – axis: related variables, horizontal boxplots on 95% CI of testing on the stratification (w/ accelerated decline on lung function vs. w/o declined lung function)

Eosinophil counts and Asthma (marker for Asthma)

* Eos count of 3% or more
* Eos + reversibility + bmi at 30 🡪 good predictor
* Hypothesis generation – pre-clinical validation – Assay development – Molecular Epidemiology – Clinical implementation

Longitudinal study and biomarker (LAM: Lymphangioleiomyomatosis)

* Behaves like cancer
* LONGITUDINAL: US, Canada, Europe, and Southeast Asian
* Biomarkers:
  + CT scan: cyst size, percent lung involvement with cyst, lung texture in vicinity of cysts, pneumothorax, Pleural effusions, interstitial markings, multifocal micronodule.
  + Pathology
  + Physiology: DLco, FEV1, bronchodilator response
  + Exercise testing
  + EPO, PRL, ANG, IGF,
    - EPOR, PRLR, ATR1, ATR2, IGF1R
  + Circulating LAM cells: phenotypic & genetic heterogeneity

Biomarker driven therapy:

* Lung cancer heterogeneity
  + EGFR, ALK, ROS1
* Survival plot to compare among cancers
* EGFR chemotherapy improves progression-free survival rate to patient who have EGFR mutation-positive

Surrogate gone Wrong/ Mepolizumab/CAST trials

* Blood eosinophils
* Encainide and flecanide
* Torcetrapid

ACOS:

* 57053 participants from Denmark (1993-1997)
* 662 with ACOS
* Higher incidents for women
* Mortality: ACOS 25.9 > COPD 23.1 > Asthma 7.9
  + Age 55-60
* Have at least one contact of COPD or Asthma

Long term Ozone exposure—percent emphysema

* Mortality
* Ozone induced emphysema (CT)—COPD(partially overlaps with emphysema)
* Longitudinal – spatial ratio
  + Outcomes= cross sectional + longitudinal \* time + transient
  + Cross-sectional exposure, long-term average
* Mesa lung cohort
* Sensitivity analysis: shorter term windows- 1 year
* Average O3 vs study regions
* Effect modification: dichotomization by conditions: BMI <30, education level, gender, age groups.

Baseline lung functions, emphysema

* Population having African ancestry have lower baseline lung function than those with European white ancestry. (FEV1/FVC)
* White have more emphysema

COPD:

* more lung cancer incidence( per 1000 person year)
* no copd has higher % mortality reduction (both all-cause and lung cancer- specific)

Eosinophils in COPD:

* eos in COPD blood and sputum have been associated with exacerbation
* blood eos < vs >= 200/ml
* sputum eos < vs >= 1.25%