

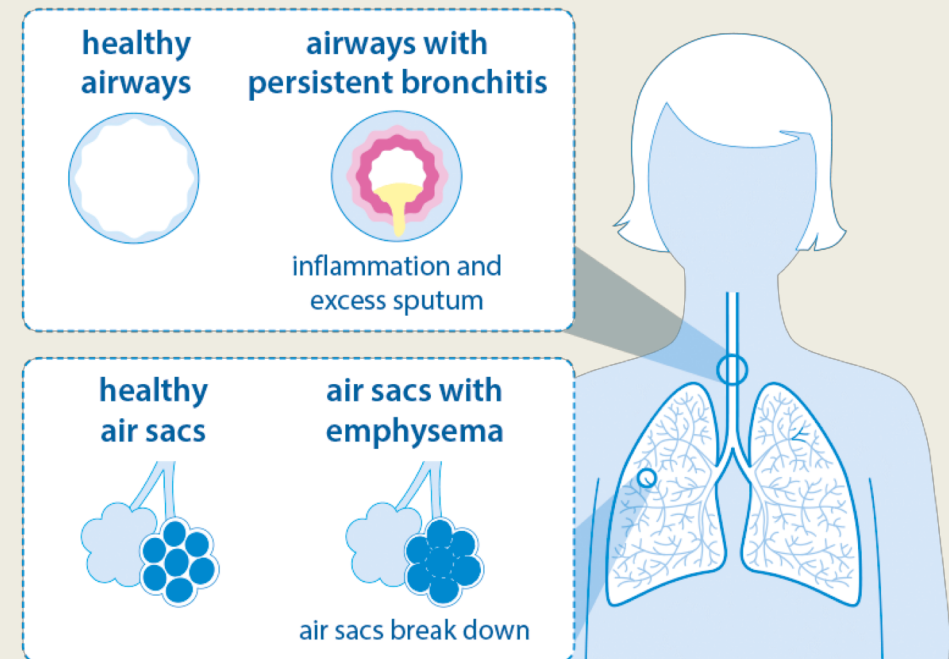
Discovering clinically relevant COPD patient subtypes in CALIBER

Maria Pikoula
m.pikoula@ucl.ac.uk

Chronic obstructive pulmonary disease (COPD)

COPD is a lung disease characterized by **chronic obstruction** of lung airflow that interferes with normal breathing and is **not fully reversible**.

- Bronchitis: **airways** are inflamed and narrowed.
- Emphysema affects the **air sacs** at the end of the airways in the lungs.



COPD burden

- Not simply a "smoker's cough" but an under-diagnosed, life-threatening lung disease.
- Prevalence: 251 million cases globally in 2016.*
- More than 90% of COPD deaths occur in low and middle-income countries.

Severity

GOLD grade (spirometry)

Severity	FEV1 % predicted
Mild (GOLD 1)	≥ 80
Moderate (GOLD 2)	50 - 79
Severe (GOLD 3)	30 - 49
Very severe (GOLD 4)	< 30

FEV₁ (Liters):

Volume that has been exhaled at the end of the first second of forced expiration

FEV₁ % predicted:

FEV₁ of the patient divided by the average FEV₁ in the population for any person of similar age, sex and body composition.

MRC shortness of breath scale

Grade	Activity affected
1	Only strenuous activity
2	Vigorous walking
3	With normal walking
4	After a few minutes of walking
5	With changing clothing

Acute Exacerbations of COPD

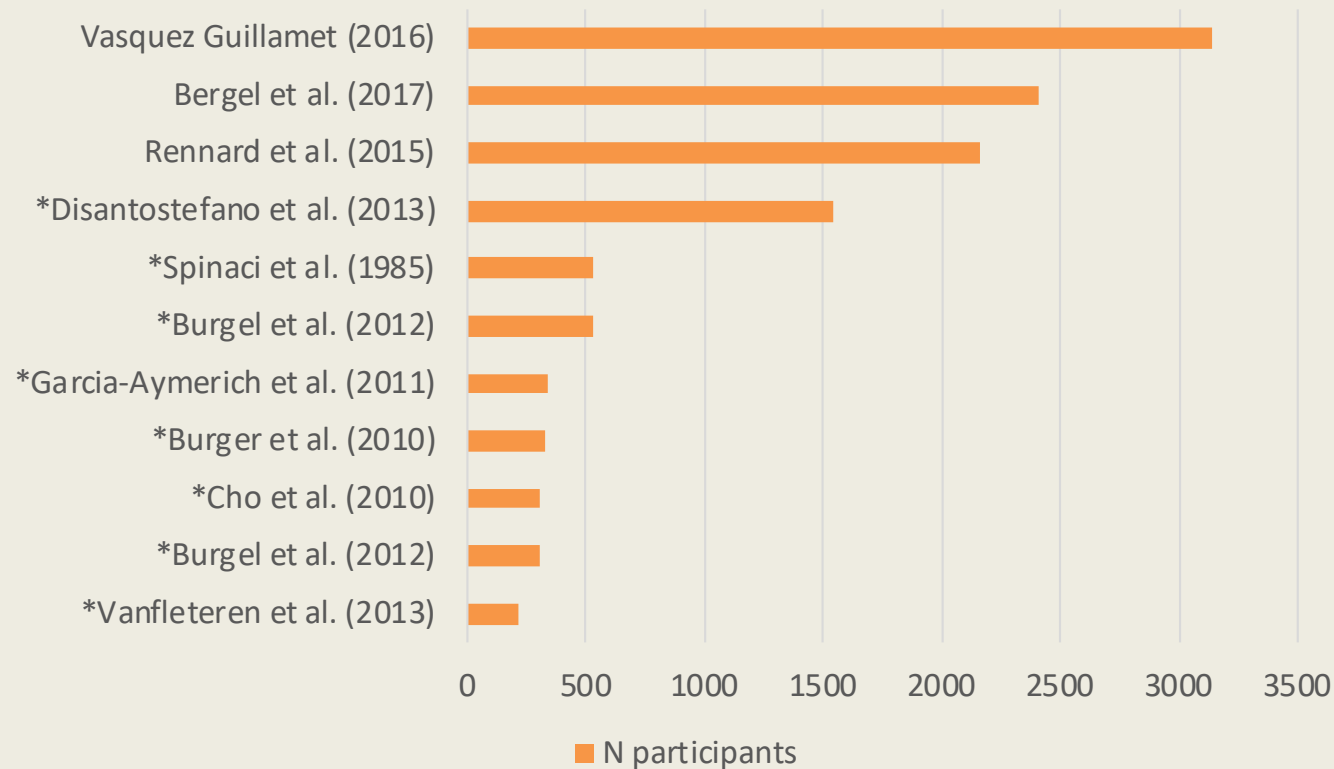
- Acute exacerbations are a major driver of the disease
- The factors that govern AECOPD and disease progression are not well-understood

Study aims

- I. Use electronic health records data to discover new subtypes of COPD with in a **hypothesis – free** analysis.
- II. Evaluate subtypes with regards to **clinically relevant** outcomes such as AECOPD

Cluster analysis in COPD

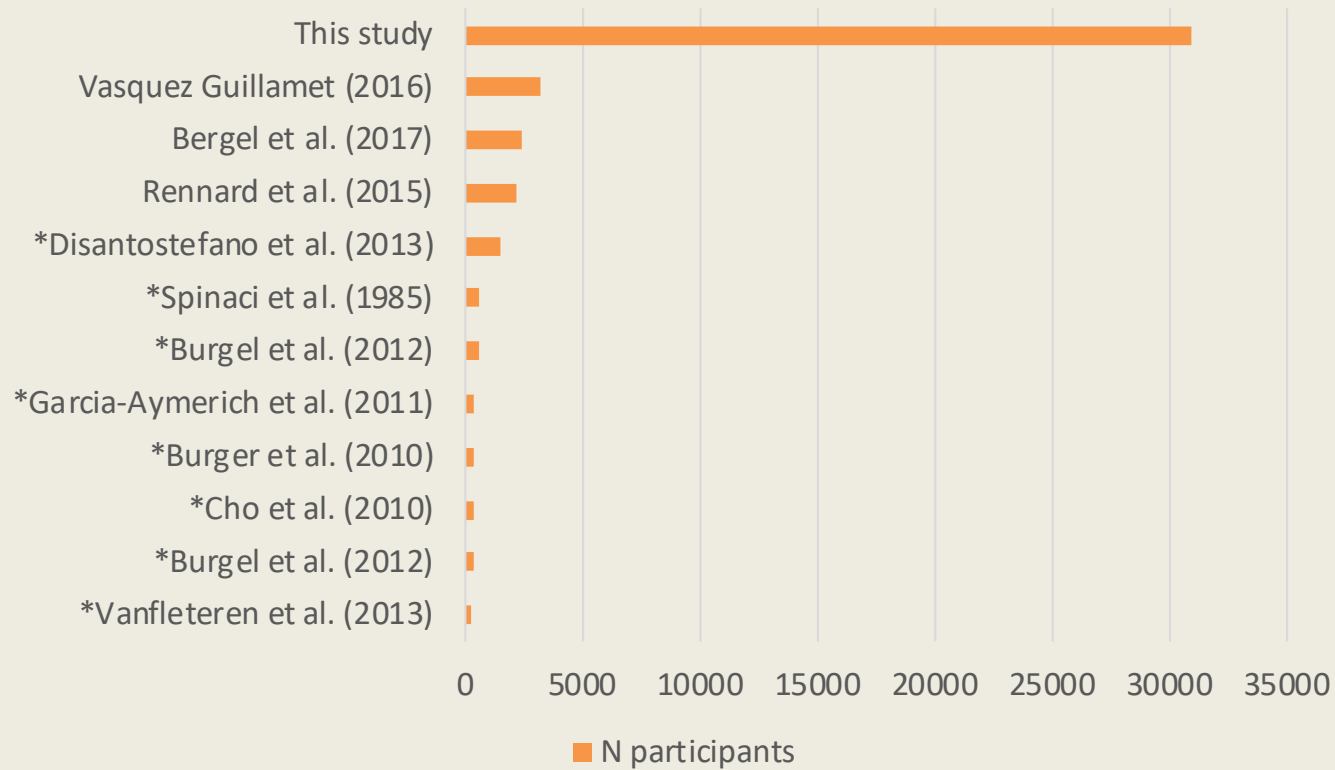
Literature review 1985 - 2017



* Pinto et al. *Respiratory Research* 2015

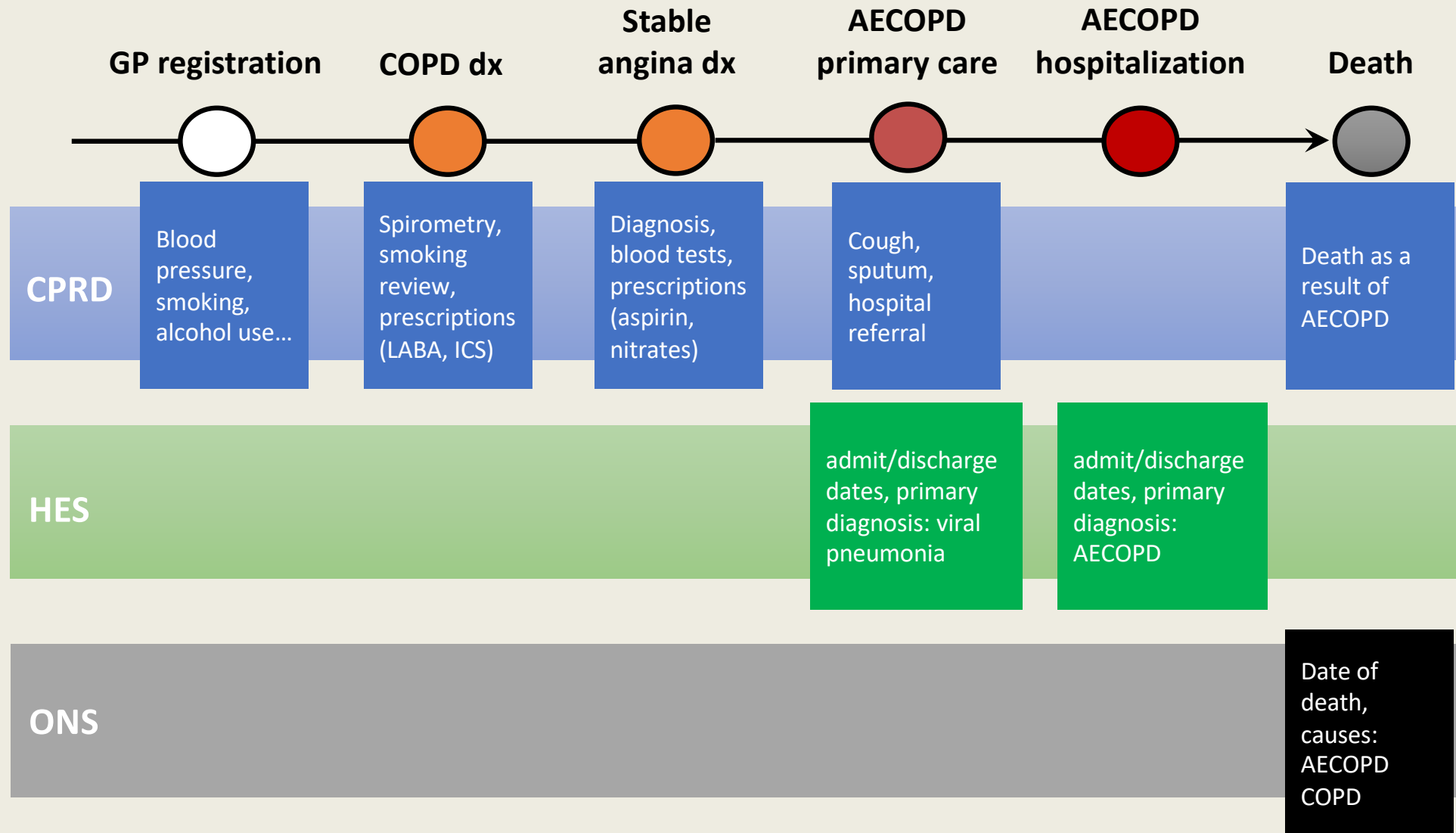
Cluster analysis in COPD

Literature review 1985 - 2017



* Pinto et al. *Respiratory Research* 2015

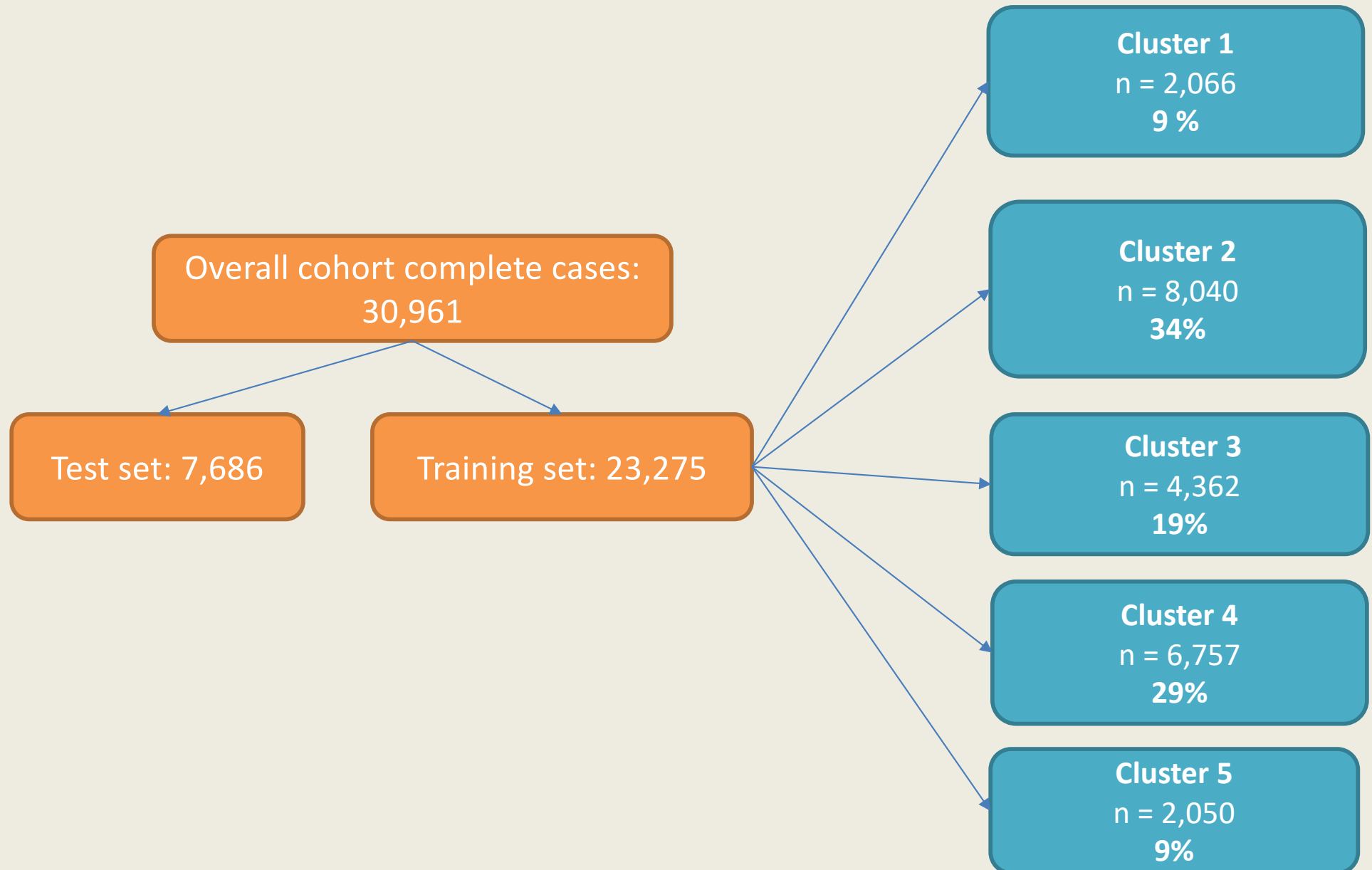
CALIBER data resource



Methods

- **COPD phenotype** using validated Read codes and smoking status
- **15 risk factors:** Sex, BMI, GOLD grade, smoking status, anxiety, depression, atopy, chronic rhinosinusitis, hypertension, heart failure, ischemic heart disease, diabetes, gastroesophageal reflux disease, therapy regimen
- **K-means** clustering algorithm on complete cases, find optimal solution
- **Label clusters** based on defining characteristics

Results

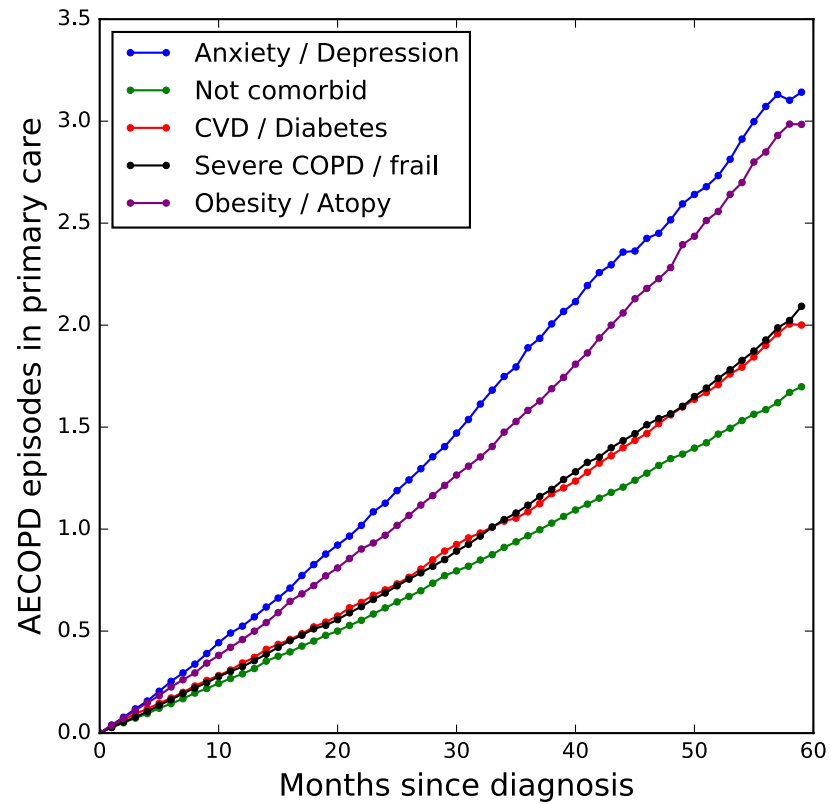


Results – Cluster characteristics

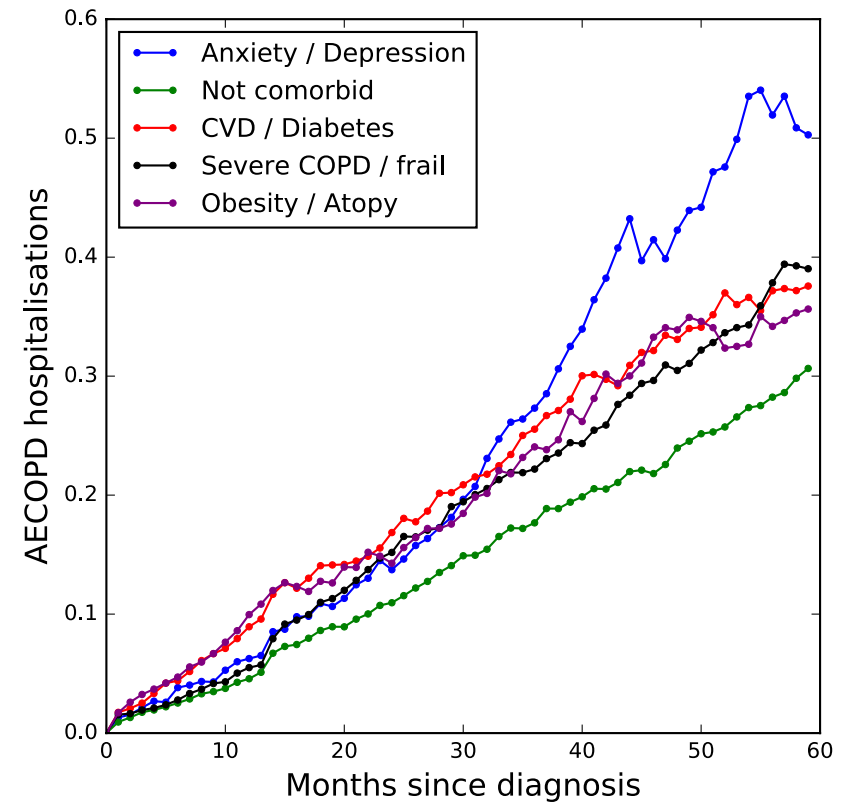
	Overall cohort	1: Anxiety/ Depression	2: Not comorbid	3: CVD / Diabetes	4: Severe COPD / frail	5: Obesity / Atopy
N	30,961	2,066	8,040	4,362	6,757	2,050
Male patients %	55	18	68	81	37	43
BMI % Underweight	4	9	0	0	10	0
BMI % Obese	30	18	32	54	11	53
Depression %	11	66	0	2	3	22
Atopy %	12	15	11	14	9	22
Heart failure %	15	5	10	46	2	24
GOLD						
% 1 (least severe)	26	35	24	22	27	29
% 4 (most severe)	3	3	2	2	6	1
High Eosinophils %	66	50	73	76	54	66

Clinical Evaluation: AECOPD

Primary care exacerbations



Hospitalizations



Clinical Evaluation: Respiratory /CVD mortality

Age-adjusted Cox regression

Characteristic	Hazard ratio
Age	1.08 [1.07 – 1.08]
Cluster	
Not comorbid	1
Anxiety / Depression	1.28 [1.13 – 1.46]
CVD / Diabetes	1.49 [1.38 – 1.60]
Severe COPD / Frailty	1.30 [1.20 – 1.40]
Atopy / Obesity	1.15 [1.03 – 1.30]

Conclusions & Impact

- COPD patient subtypes can be identified using routinely generated EHR from primary care.
- Previous findings on CVD and diabetes diabetes were reproduced, and the trend is similar for exacerbations
- Anxiety and depression are distinct comorbidities potentially driving disease progression in younger, female patients
- Atopic and potentially asthmatic patients form a distinct cluster with overall better prognosis

Future directions

- Longitudinal evolution of COPD subtypes
- Models that allow patient membership of more than one subtype
- Genetic associations (UK Biobank)
- The role of comorbid respiratory conditions: Asthma and bronchiectasis



**Spiros
Denaxas**



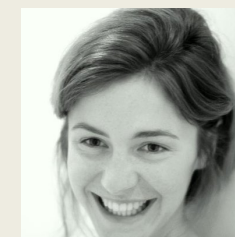
**Natalie
Fitzpatrick**



**Nonie
Alexander**



**Alicia
Uijl**



**Maxine
Mackintosh**



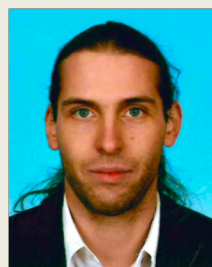
**Arturo
Gonzalez-Izquierdo**



**Kenan
Direk**



**Ghazaleh
Fatemifar**



**Vaclav
Papez**



**Michalis
Katsoulis**



**Colin
Josephson**



Jennifer K Quint



Marcos Barreto