



**Seminari del Venerdì del Gruppo di Ricerca Geriatrica**

Brescia, 8 giugno 2018

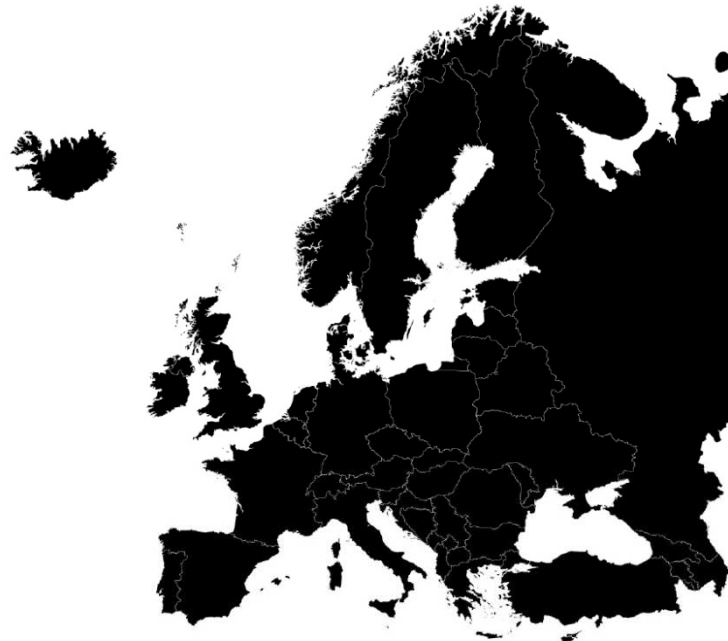


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# **La medicina respiratoria e le cause di morte nell'anziano**

**Piera Ranieri**

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600,000 people die every year in the EU  
from respiratory disease



1 in 8 deaths in the EU are from respiratory  
diseases



Morti attribuite a	Nel mondo	Sezione europea di OMS
Cardiopatia ischemica	7.3 milioni (12.8%)	2.4 milioni (24.7%)
Malattia cerebrovascolare	6.2 milioni (10.8%)	1.40 milioni (14.0%)
<b>Infezioni del tratto respiratorio inferiore</b>	<b>3.5 milioni (6.1%)</b>	<b>0.23 milioni (2.3%)</b>
<b>BPCO</b>	<b>3.3 milioni (5.8%)</b>	<b>0.25 milioni (2.5%)</b>
Sindromi enteritiche	2.5 milioni (4.3%)	0.03 milioni (0.3%)
HIV/AIDS	1.8 milioni (3.1%)	0.08 milioni (0.8%)
<b>Cancro di trachea/bronchi/polmoni</b>	<b>1.4 milioni (2.4%)</b>	<b>0.38 milioni (3.9%)</b>
<b>Tubercolosi</b>	<b>1.3 milioni (2.4%)</b>	<b>0.08 milioni (0.8%)</b>
Diabete mellito	1.3 milioni (2.2%)	0.17 milioni (1.7%)
Incidenti stradali	1.2 milioni (2.1%)	0.12 milioni (1.2%)

**Tabella 1** – Le 10 cause più comuni di morte nel 2008. Fonte: Organizzazione Mondiale della Sanità (OMS) Statistiche della Salute nel Mondo 2011.



THE EUROPEAN LUNG

*white book*

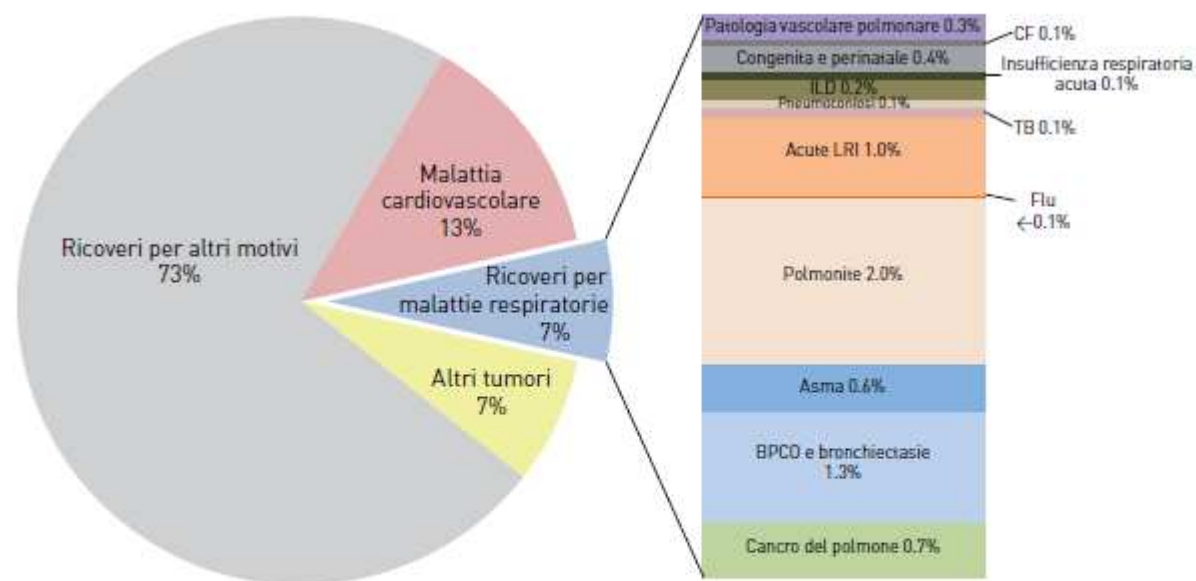
RESPIRATORY HEALTH AND DISEASE IN EUROPE



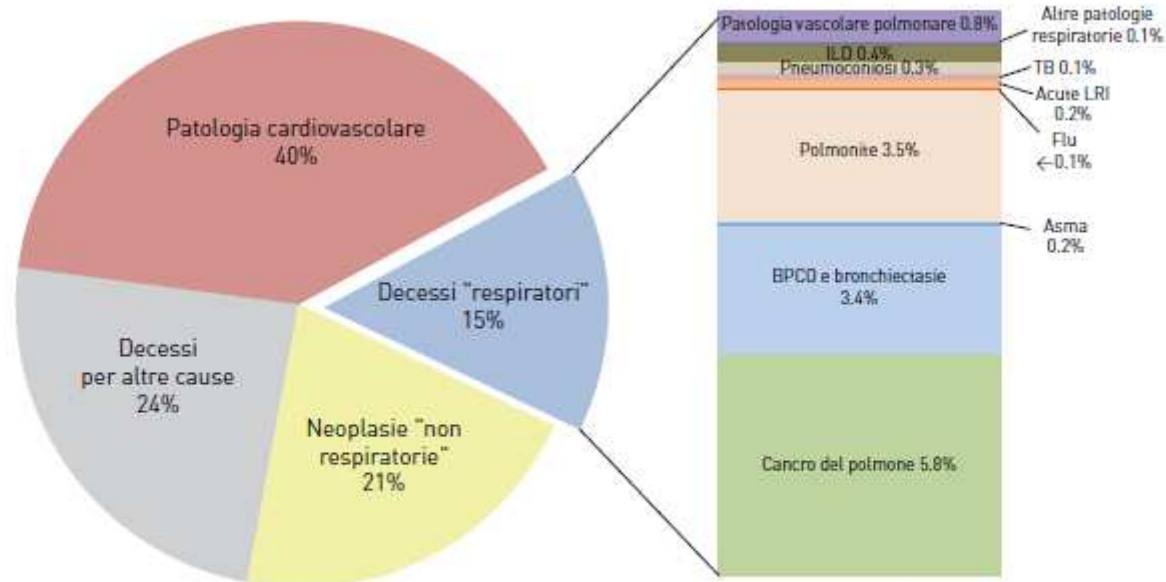
European respiratory society every breath counts

<b>DALY persa a causa di</b>	<b>Nel mondo</b>	<b>Sezione europea di OMS</b>
<b>Infezioni del tratto respiratorio inferiore</b>	<b>79 milioni (5.4%)</b>	<b>2.2 milioni (1.5%)</b>
HIV/AIDS	65 milioni (4.4%)	2.6 milioni (1.8%)
Cardiopatía ischemica	64 milioni (4.4%)	1.6 milioni (1.3%)
Sindromi enteritiche	56 milioni (3.8%)	1.1 milioni (0.7%)
Malattia cerebrovascolare	48 milioni (3.3%)	9.3 milioni (6.4%)
Incidenti stradali	45 milioni (3.1%)	3.4 milioni (2.4%)
<b>BPCO</b>	<b>33 milioni (2.3%)</b>	<b>2.9 milioni (2.0%)</b>
<b>Tubercolosi</b>	<b>29 milioni (2.0%)</b>	<b>1.7 milioni (1.2%)</b>
Diabete mellito	22 milioni (1.5%)	2.6 milioni (1.8%)
<b>Cancro di trachea/bronchi/polmoni</b>	<b>13 milioni (0.9%)</b>	<b>3.2 milioni (2.2%)</b>

**Tabella 2** – Le 10 cause più frequenti di attesa di vita perduta a causa della disabilità (DALY) nel 2008 nel Mondo.  
Fonte: OMS, Statistiche della Salute nel Mondo 2011.



**Figura 4** – Percentuali dei ricoveri ospedalieri da patologie respiratorie in nazioni selezionate di UE. CF: fibrosi cistica; ILD: malattie interstiziali polmonari; TB: tubercolosi; LRI: infezioni delle vie aeree inferiori; flu: influenza; BPCO: broncopneumopatia cronica ostruttiva. Le nazioni rappresentate sono quelle che hanno fornito la disponibilità di una codifica completa ICD-10 sia per i ricoveri ospedalieri che per i decessi (Austria, Croazia, Cipro, Repubblica Ceca, Danimarca, Finlandia, Lettonia, Lituania, Lussemburgo, Malta, Polonia, Slovenia, Slovacchia, Regno Unito). Fonte: World Health Organization World and Europe Detailed Mortality Databases.



**Figura 3** – Percentuali dei decessi causati da patologie respiratorie in nazioni selezionate di UE. ILD: malattie interstiziali polmonari; TB: tubercolosi; LRI: infezioni delle vie aeree inferiori; Flu: influenza; BPCO: broncopneumopatia cronica ostruttiva. Le nazioni rappresentate sono quelle che hanno fornito la disponibilità di una codifica completa ICD-10 sia per i ricoveri ospedalieri che per i decessi (Austria, Croazia, Cipro, Repubblica Ceca, Danimarca, Finlandia, Lettonia, Lituania, Lussemburgo, Malta, Polonia, Slovenia, Slovacchia, Regno Unito). Fonte: World Health Organization World and Europe Detailed Mortality Databases.



<b>Percentuali di decessi nel mondo</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>
Infezioni delle vie aeree inferiori	6.1	5.5	4.2
BPCO	5.8	6.6	8.6
Cancro di trachea/bronchi/polmone	2.4	2.8	3.4
Tubercolosi	2.4	1.6	3.4
<b>Percentuale di morti nella Sezione Europea di OMS</b>	<b>2008</b>	<b>2015</b>	<b>2030</b>
Infezioni delle vie aeree inferiori	2.3	2.2	1.9
BPCO	2.5	2.7	3.2
Cancro di trachea/bronchi/polmone	3.9	3.9	4.1
Tubercolosi	0.8	0.7	0.4

**Tabella 3** – Proiezione della proporzione dei decessi dovuti alle principali malattie respiratorie.  
Fonte: WHO, World Health Statistics 2011.

Per il 2030 l'Organizzazione Mondiale della Sanità (OMS) stima che le quattro maggiori patologie respiratorie, potenzialmente fatali (**polmonite, tubercolosi, cancro del polmone e BPCO**) saranno responsabili di circa **un quinto dei decessi totali**, contro il dato di un sesto, registrato nel 2008. Nell'ambito della Sezione Europea dell'OMS, ci si aspetta una percentuale stabilizzata a circa un decimo della mortalità totale, con un incremento relativo a BPCO e cancro del polmone, bilanciato dalla diminuzione della quota dovuta alle infezioni del tratto respiratorio inferiore e alla tubercolosi

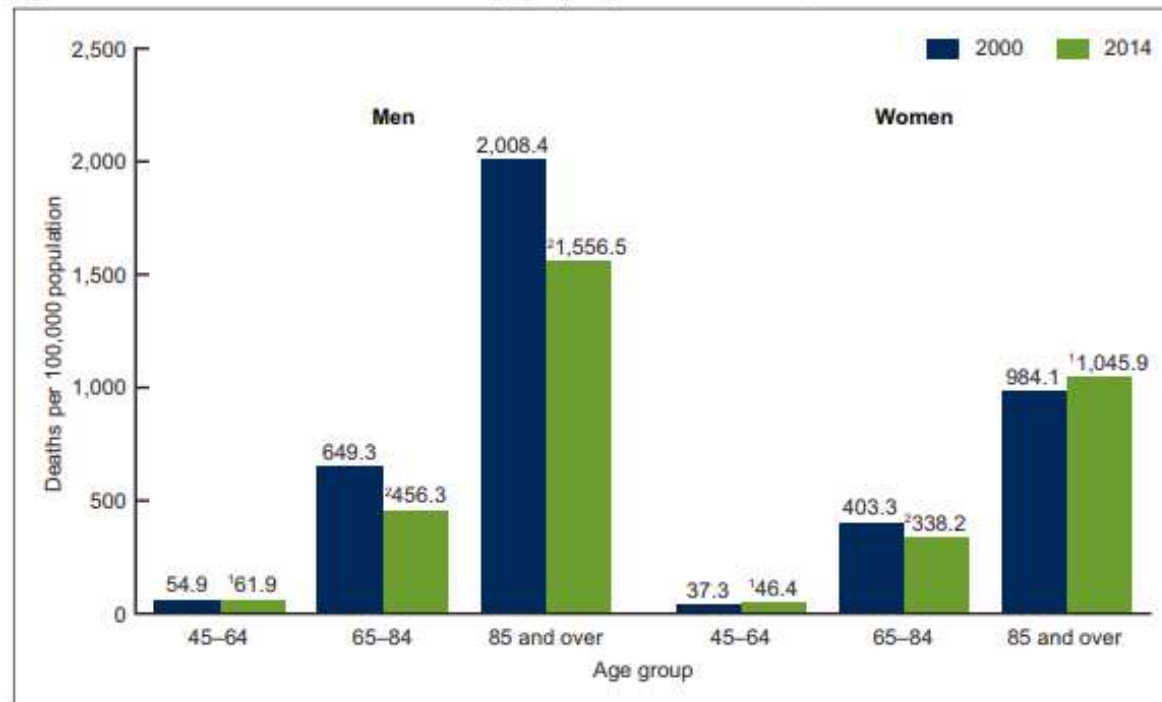
## COPD-related Mortality by Sex and Race Among Adults Aged 25 and Over: United States, 2000–2014

Hanyu Ni, Ph.D., and Jiaquan Xu, M.D.

### The COPD-related death rate increased for men and women aged 45–64 and for women aged 85 and over between 2000 and 2014.

- Between 2000 and 2014, the COPD-related death rate decreased 29.7% for men aged 65–84 and 22.5% for men aged 85 and over but increased 12.8% for men aged 45–64 (Figure 2).

Figure 2. COPD-related death rates for selected age groups, by sex: United States, 2000 and 2014



<sup>1</sup>Statistically significant increase in COPD-related death rate between 2000 and 2014 ( $p < 0.05$ ).

<sup>2</sup>Statistically significant decrease in COPD-related death rate between 2000 and 2014 ( $p < 0.05$ ).

NOTES: COPD is chronic obstructive pulmonary disease. COPD-related deaths were identified as those with COPD (ICD-10 code J40–J44) reported anywhere on the death certificate (i.e., as an underlying or a contributing cause of death). Access data table for Figure 2 at: [http://www.cdc.gov/nchs/data/databriefs/db256\\_table.pdf#2](http://www.cdc.gov/nchs/data/databriefs/db256_table.pdf#2).

SOURCE: NCHS, National Vital Statistics System mortality data, 2000 and 2014.

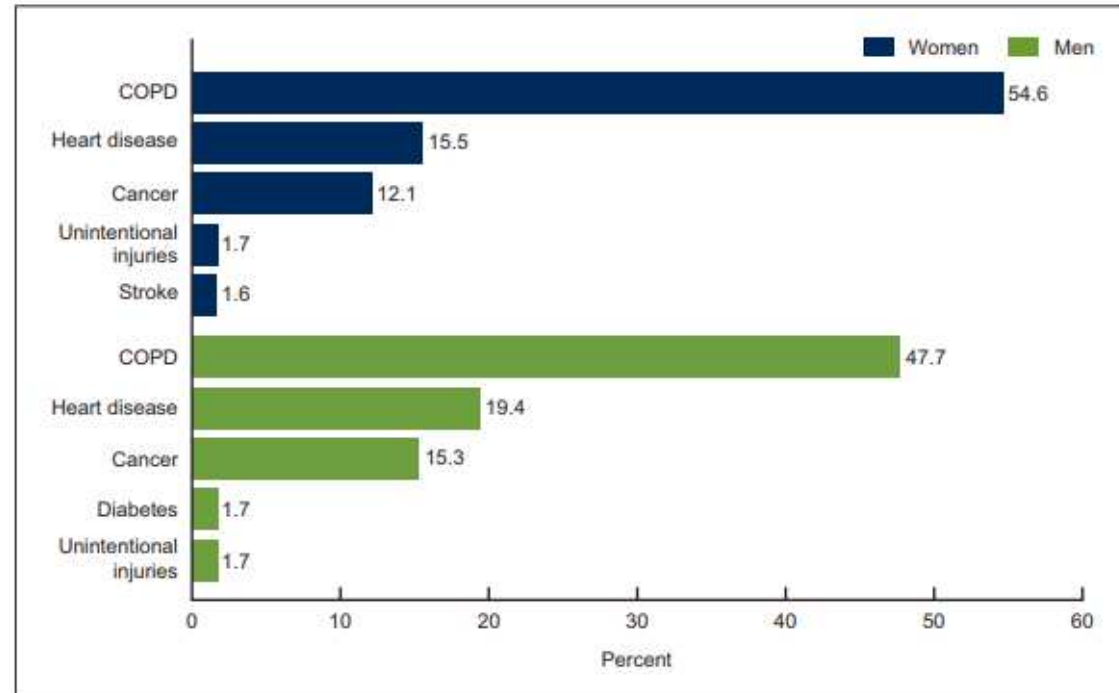
**COPD-related Mortality by Sex and Race Among Adults Aged 25 and Over: United States, 2000–2014**

Hanyu Ni, Ph.D., and Jiaquan Xu, M.D.

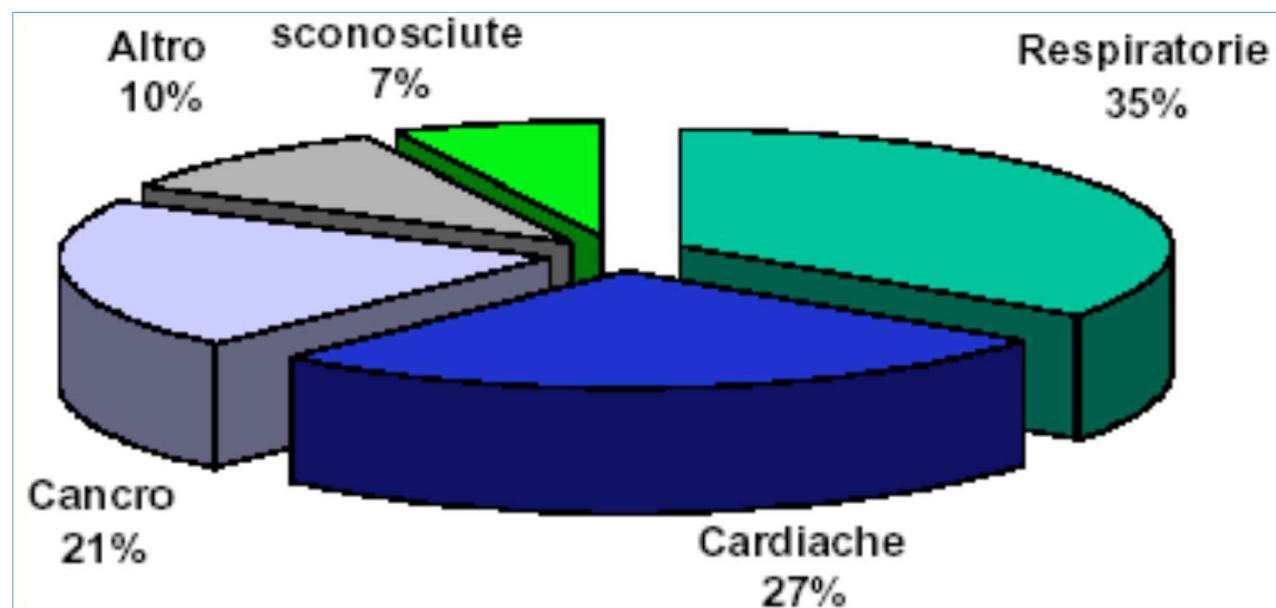
**Approximately one-half of all COPD-related deaths had COPD as the underlying cause of death for both men and women in 2014.**

- In 2014, COPD was the underlying cause of death for 47.7% of COPD-related deaths for men aged 25 and over (Figure 5). Other major underlying causes of death included heart disease (19.4%), cancer (15.3%), diabetes (1.7%), and unintentional injuries (1.7%).
- For women in the same age group, COPD was the underlying cause of death for 54.6% of COPD-related deaths occurred in 2014. Other major underlying causes of death included heart disease (15.5%), cancer (12.1%), unintentional injuries (1.7%), and stroke (1.6%).

Figure 5. Top five underlying causes of death for COPD-related deaths for adults aged 25 and over, by sex: United States, 2014



## Studio TORCH: cause di morte a tre anni in 6112 pz con BPCO (FEV1<60%)



**Table 1** Classification of cause-specific mortality (n = 911)

System	%	Subcategory	%
Cardiovascular	26	Congestive heart failure	3
		Myocardial infarction	3
		Stroke	4
		Sudden death	16
Respiratory	35	COPD	27
		Pneumonia	8
		Other	<1
Cancer	21	Lung	14
		Other	7
Other cause	10		
Unknown cause	8		

Only 40% of deaths were judged to be related to COPD.  
Thus, rigorous investigation for comorbidities and management thereof could have been potentially lifesaving for the 60% of deaths that were related to other factors

# AGING and COMORBILITY

Aging is an important known risk factors for most chronic diseases, however there is variability in the burden of chronic diseases affecting the old.

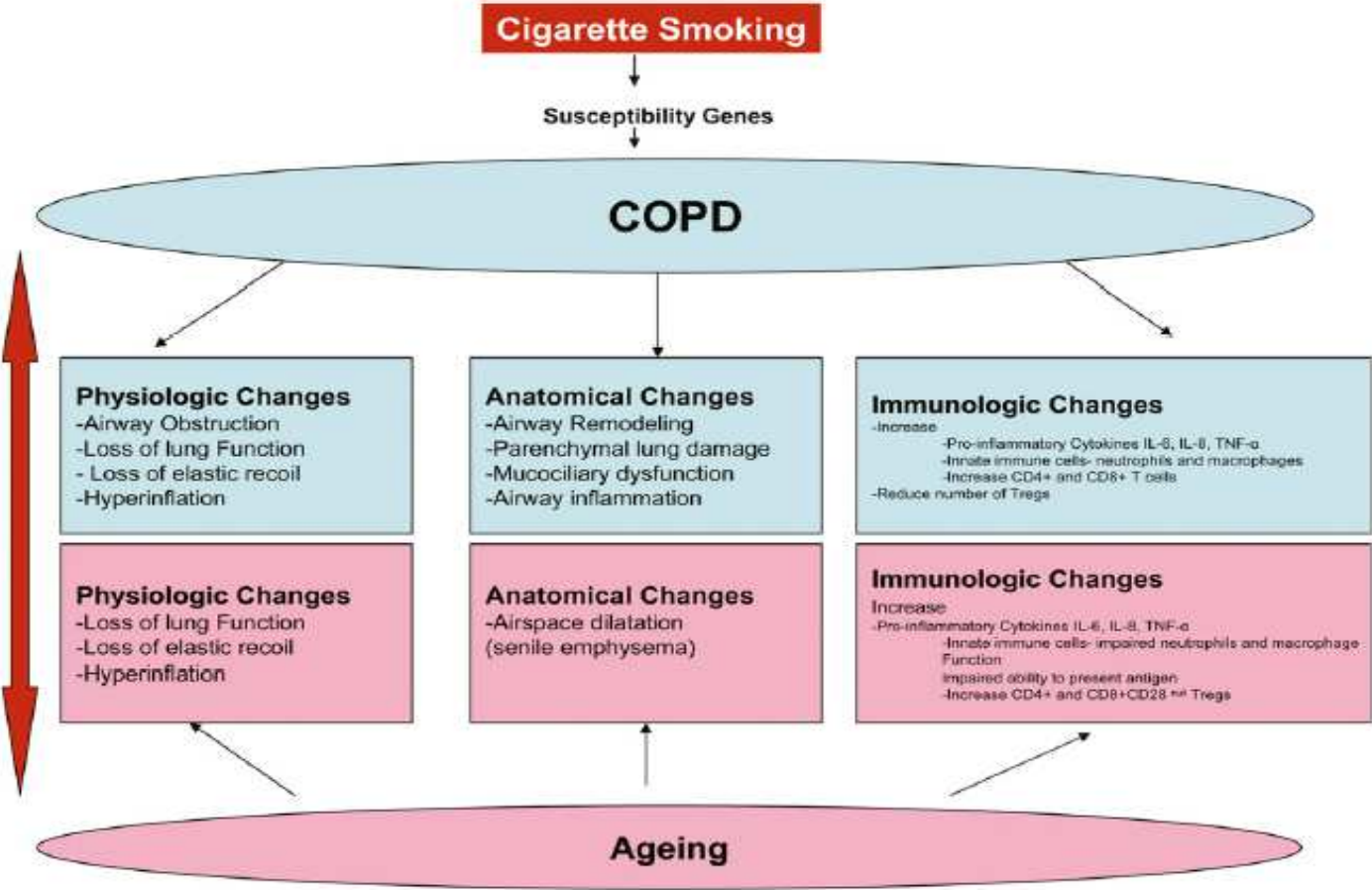
**Understanding this variability is key to differentiating pathologic from successful or normal aging.**

The co-occurrence of chronic diseases is not a phenomenon of simple chance, but rather the expression of complex biological interactions between a susceptible individual and the cumulative effect of environmental exposures, differentially affecting body systems

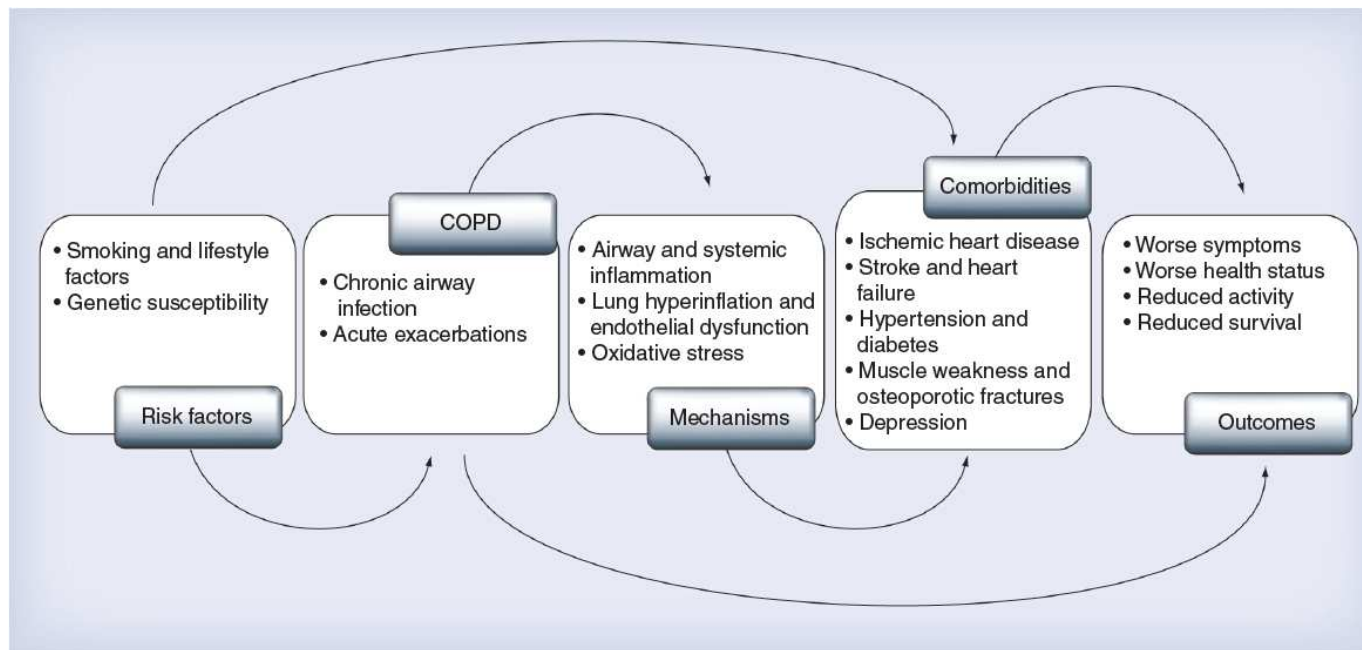
# **COPD and COMORBILITY**

Chronic Obstructive Pulmonary Disease (COPD) is a representative model of a disease to help discern pathologic from normal aging: COPD is a disease which affects millions of people, is the third leading cause of death worldwide, has a natural history that is relatively well understood and frequently occurs with comorbidities

# Le convergenze parallele di invecchiamento e BPCO



## Il complesso percorso che collega la BPCO e le sue principali comorbidità



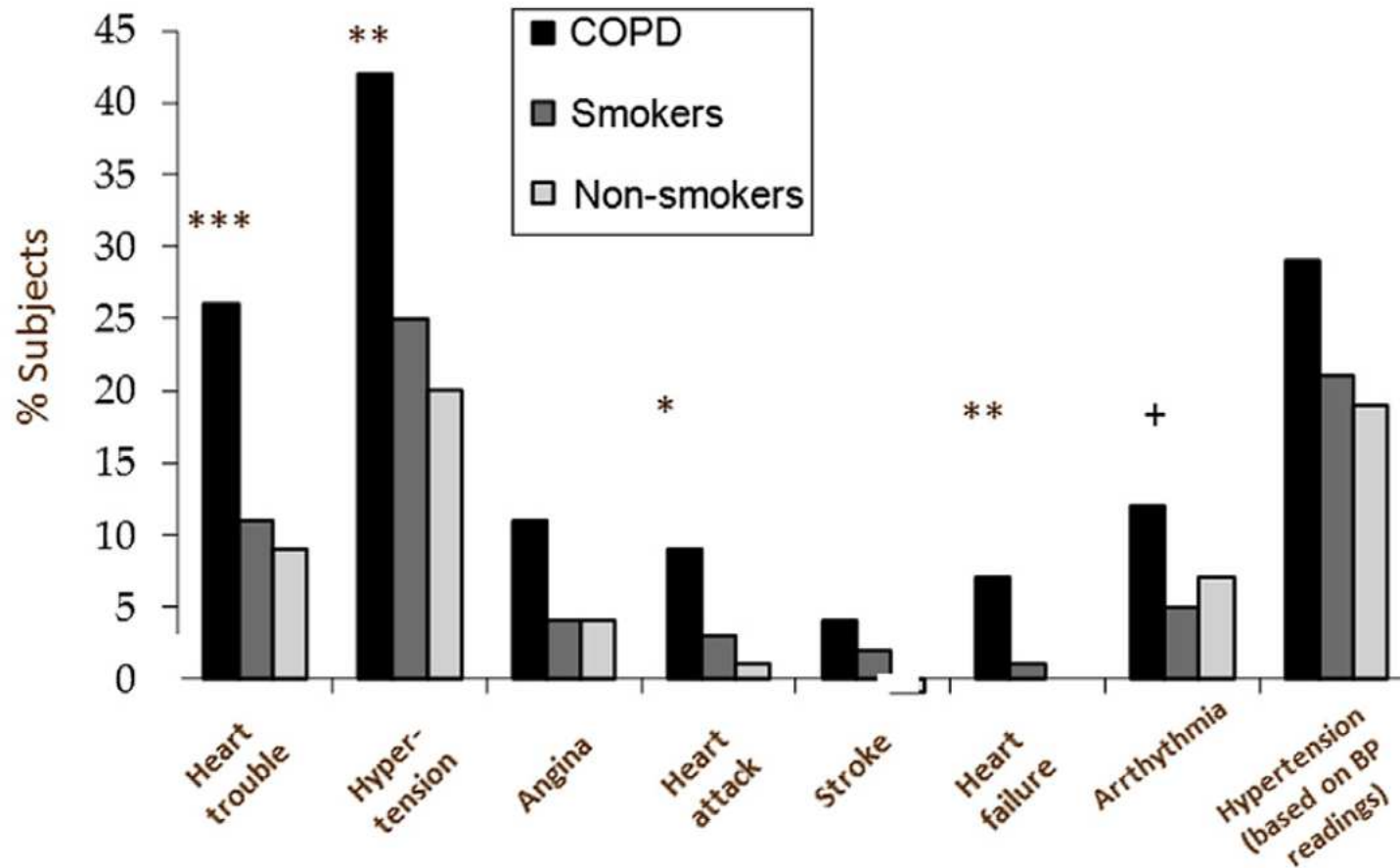
Patel e Hurst, *Expert Rev Respir Med* 2011

# Impatto clinico della comorbidità nei pazienti affetti da BPCO

- Diminuzione della qualità della vita
- Incremento nella frequenza di riacutizzazioni
- Incremento della mortalità

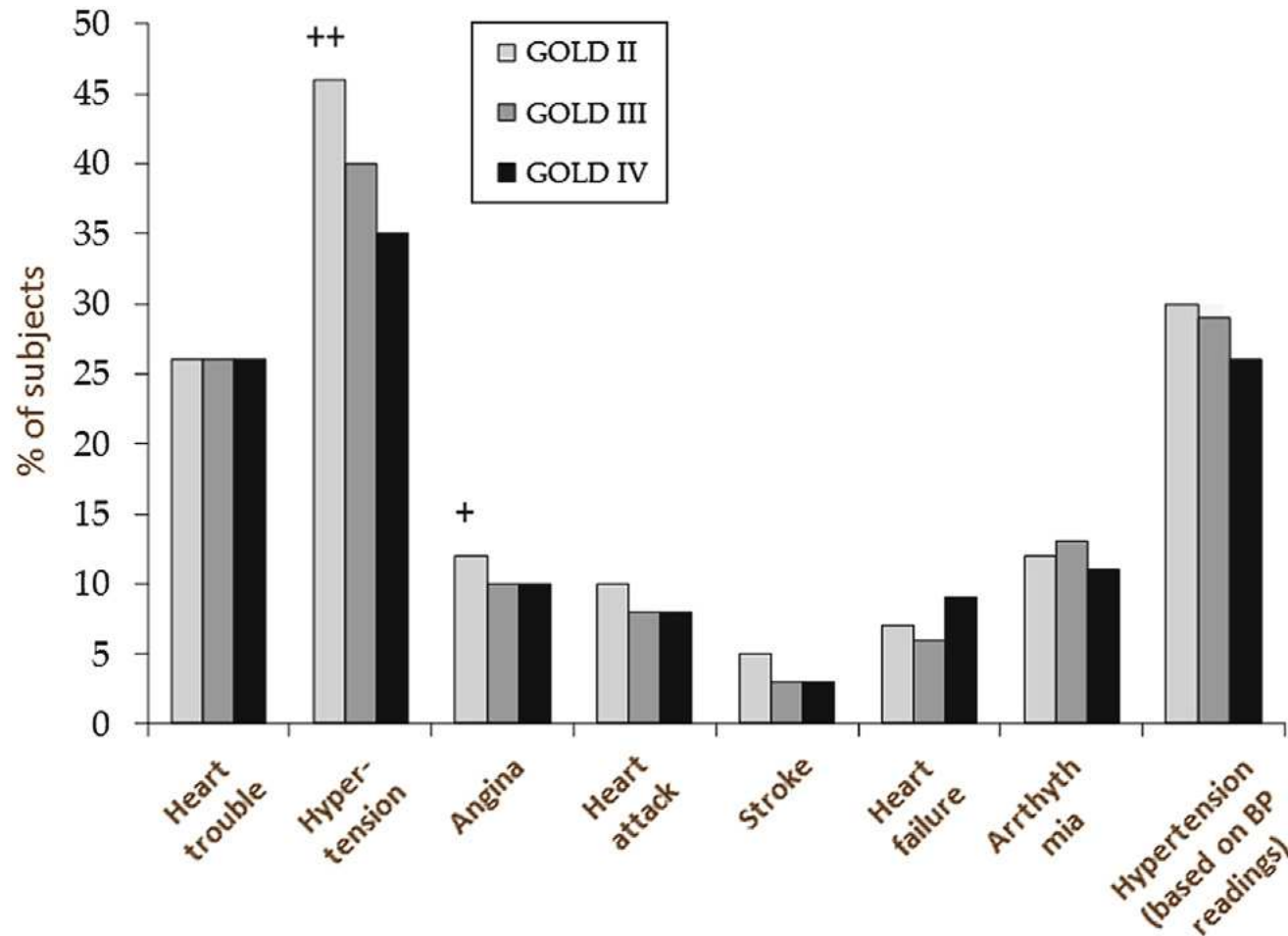
Smith MC and Wrobel JP. *Intern J COPD*; 2014. 871-888

## Percentage of COPD subjects, smokers and nonsmokers with **cardiovascular** comorbidities



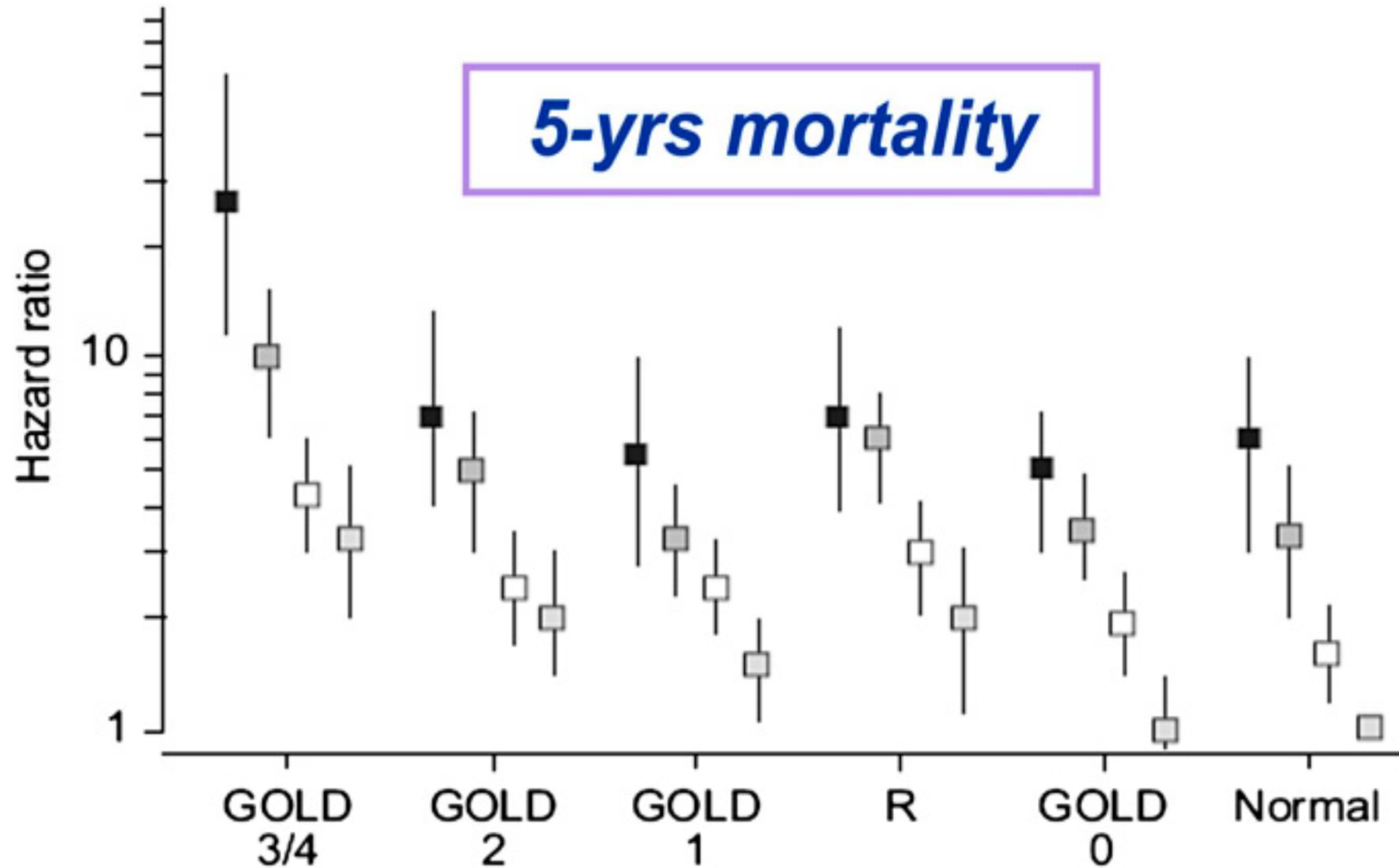
Miller et al. - Respiratory Medicine (2013) 107, 1376-1384

## Percentage of COPD subjects with **cardiovascular** comorbidities by GOLD stage of disease



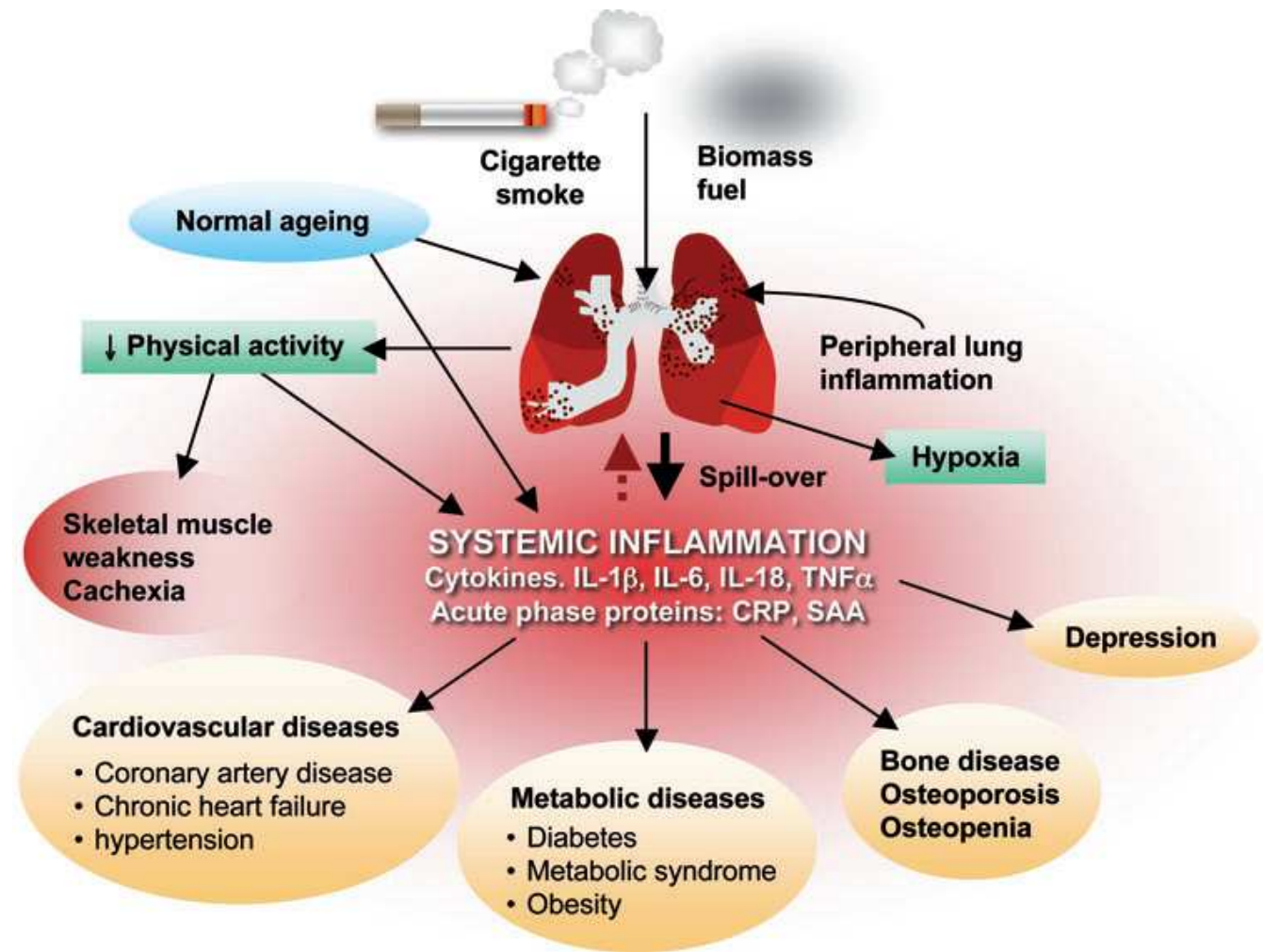
Miller et al. - Respiratory Medicine (2013) 107, 1376-1384

## Relationship between the risk of death and the number of comorbid diseases



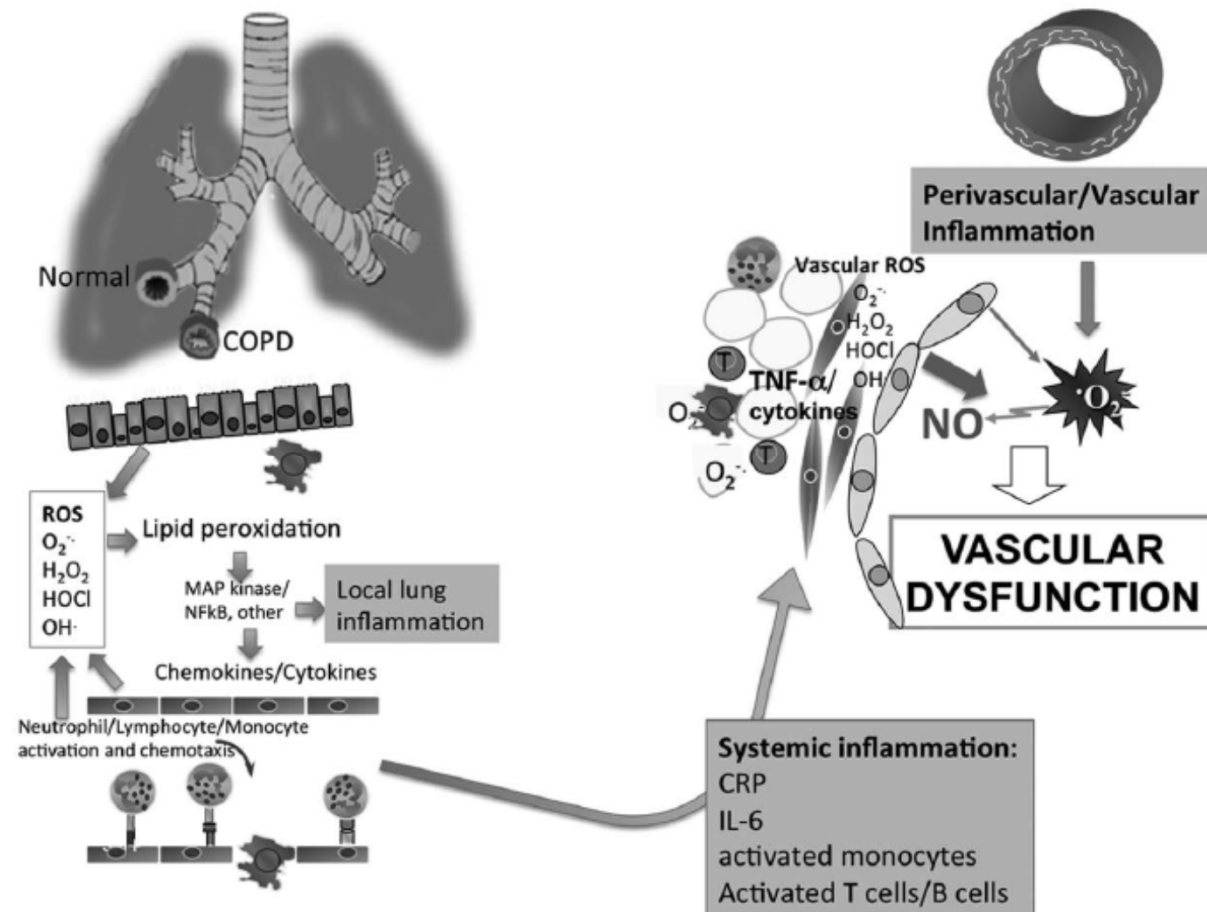
Models adjusted for age, sex, race, smoking status, education level, and body mass index

Mannino DM et al.. ERJ 2008, 2:962–969



Barnes PJ Chronic Obstructive Pulmonary Disease: Effects beyond the Lungs. 2010

# Possible mechanisms of COPD-induced vascular dysfunction

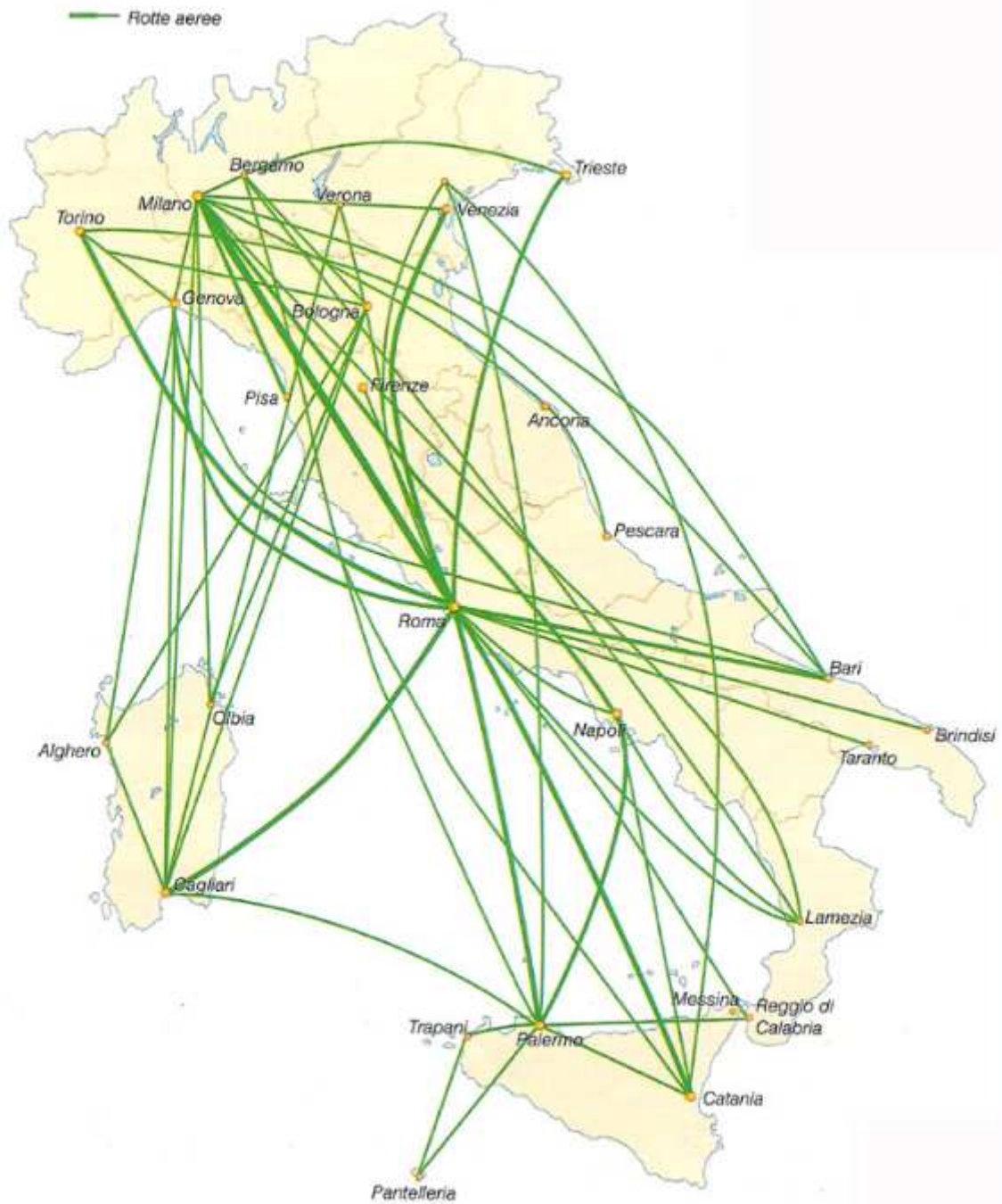


Tomasz J. Guzik, Tomasz Grodzicki- Hypertension. 2014;63:444-446.

# COPD comorbidities network

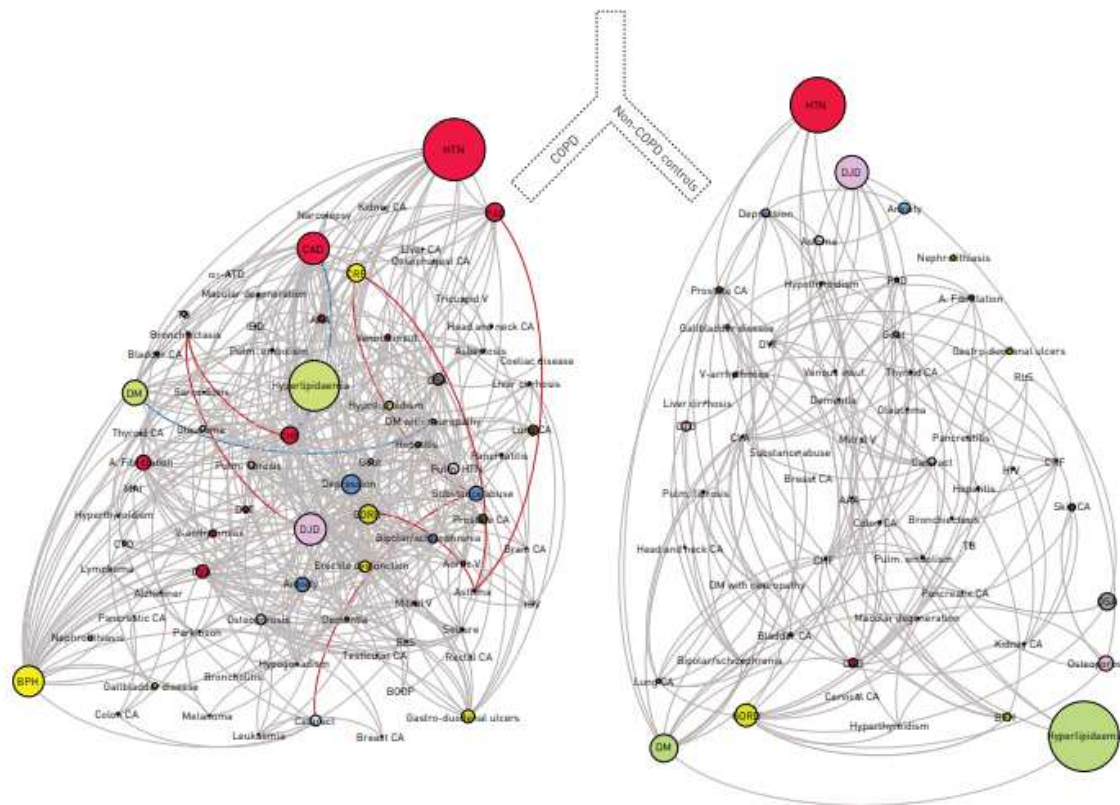
Miguel J. Divo<sup>1</sup>, Ciro Casanova<sup>2</sup>, Jose M. Marin<sup>3</sup>, Victor M. Pinto-Plata<sup>1</sup>,  
Juan P. de-Torres<sup>4</sup>, Javier J. Zulueta<sup>4</sup>, Carlos Cabrera<sup>5</sup>, Jorge Zagaceta<sup>4</sup>,  
Pablo Sanchez-Salcedo<sup>4</sup>, Juan Berto<sup>4</sup>, Rebeca Baz Davila<sup>2</sup>, Ana B. Alcaide<sup>4</sup>,  
Claudia Cote<sup>6</sup> and Bartolome R. Celli<sup>1</sup>, The BODE Collaborative Group

**In a cohort of 1969 chronic obstructive pulmonary disease (COPD) patients and 316 non-COPD controls, we applied a network-based analysis to explore the associations between multiple comorbidities**



# COPD comorbidities network

Miguel J. Divo<sup>1</sup>, Ciro Casanova<sup>2</sup>, Jose M. Marin<sup>3</sup>, Victor M. Pinto-Plata<sup>1</sup>, Juan P. de-Torres<sup>4</sup>, Javier J. Zulueta<sup>4</sup>, Carlos Cabrera<sup>5</sup>, Jorge Zagaceta<sup>4</sup>, Pablo Sanchez-Salcedo<sup>4</sup>, Juan Berto<sup>4</sup>, Rebeca Baz Davila<sup>2</sup>, Ana B. Alcaide<sup>4</sup>, Claudia Cote<sup>6</sup> and Bartolome R. Celli<sup>1</sup>, The BODE Collaborative Group



The resulting COPD comorbidity network had 428, 357 or 265 linkages depending on the statistical threshold used ( $p \leq 0.01$ ,  $p \leq 0.001$  or  $p \leq 0.0001$ ). There were more nodes and links in COPD compared with controls after adjusting for age, sex and number of subjects.

COPD patients are affected by larger number of multiple interlinked morbidities which clustering pattern may suggest common pathological processes or be utilised for screening and/or therapeutic interventions

## COPD comorbidities network

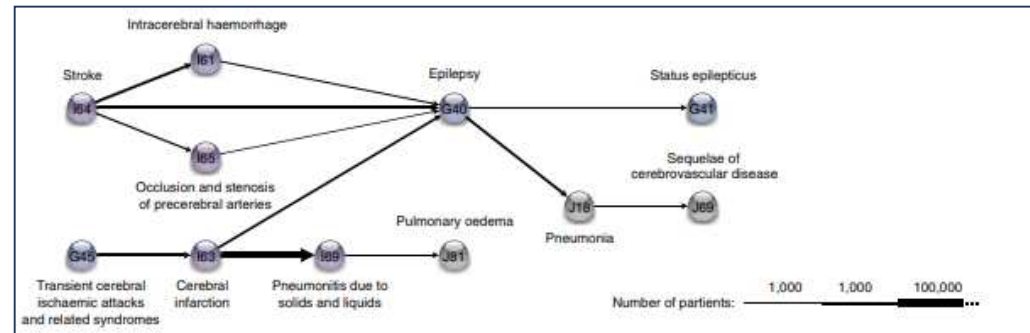
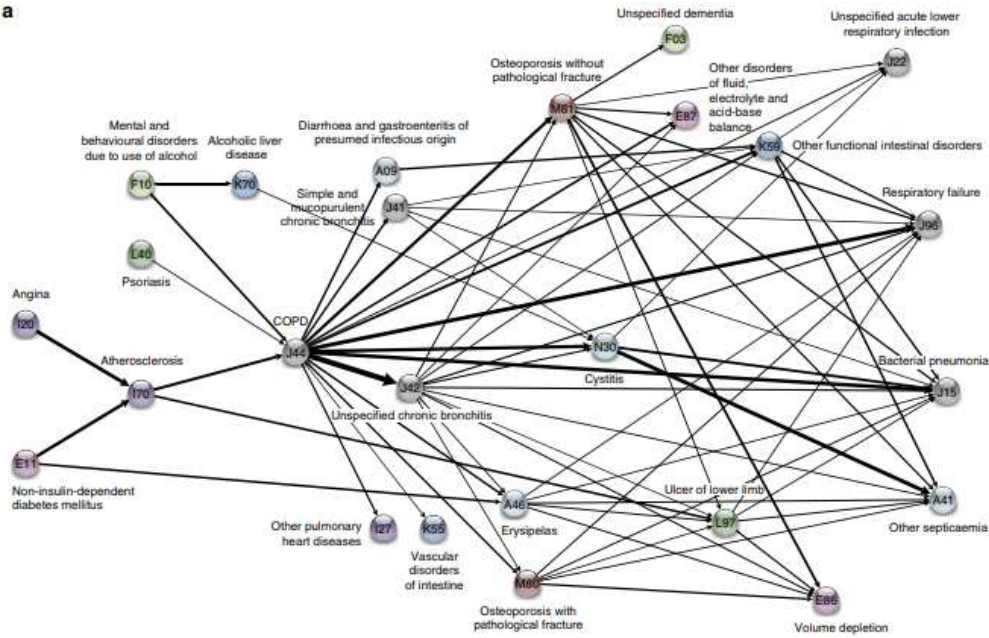
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	COPD	Non-COPD	
<b>Comorbidities per patient<sup>#</sup></b>			
Comorbidities (whole)	4 [2-7; 0-20]	2 [0-3; 0-14]	<0.0001
Comorbidities by age			
≤55 years	4 [1-6; 0-14]	1 [0-2; 0-7]	<0.0001
>55-<65 years	4 [2-6; 0-19]	2 [1-4; 0-8]	<0.0001
≥65 years	5 [3-7; 0-20]	2 [3-4; 0-14]	<0.0001
Comorbidities by sex			
Male	4 [2-7; 0-20]	2 [1-3; 0-14]	<0.0001
Female	3 [1-5; 0-14]	1 [0-3; 0-8]	<0.0001

A key prerequisite for precision medicine is the estimation of disease progression from the current patient state.

In a big data longitudinal study of the entire Danish population (6.2 million subjects), **COPD was identified as a disease central to the progression of other chronic diseases**

a



Follow-up di 15 anni  
6.2 milioni di pazienti

Jensen AB. Et al, Nature Communications, 2014

# Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort

Popolazione di studio: 27.617 >40 anni

Miguel J. Divo<sup>1†\*</sup>, Bartolome R. Celli<sup>1‡</sup>, Beatriz Poblador-Plou<sup>2‡</sup>, Amaia Calderón-Larrañaga<sup>2</sup>, Juan Pablo de-Torres<sup>3</sup>, Luis A. Gimeno-Feliu<sup>2</sup>, Juan Bertó<sup>3</sup>, Javier J. Zulueta<sup>3</sup>, Ciro Casanova<sup>4</sup>, Víctor M. Pinto-Plata<sup>5</sup>, Carlos Cabrera-Lopez<sup>6</sup>, Francesca Polverino<sup>1</sup>, Jonás Carmona Piréz<sup>2</sup>, Alexandra Prados-Torres<sup>2‡</sup>, Jose M. Marin<sup>7‡</sup>, on behalf of the EpiChron—BODE Collaborative Group<sup>†</sup>

**Table 1. Subjects' characteristics.**

Demographics	COPD	Controls	p-value
Number	27,617	2,7617	
<b>Age brackets distribution (n, % of total for the group)</b>			
Age 40–55	3,267 (12%)	3,267 (12%)	
Age 56 to 65	5,169 (19%)	5,605 (20%)	
Age 66 to 75	7,768 (28%)	8,989 (33%)	
Age 76 to 85	8,764 (32%)	7,522 (27%)	
Age > 85	2,649 (10%)	2,234 (8%)	
<b>Gender (n, % of total for the group)</b>			
Male n (%)	19378 (70%)	19378 (70%)	
Female n (%)	8239 (30%)	8239 (30%)	
<b>Number of comorbidities per patient (Mean, SD, 95% CI)</b>			
Comorbidities (whole)	4.9 ± 3.4 (4.8–4.9)	3.1 ± 2.6 (3.1–3.2)	<0.001
Male	4.7 ± 3.3 (4.7–4.8)	3.0 ± 2.5 (2.9–3.0)	<0.001
Female	5.4 ± 3.6 (5.3–5.4)	3.5 ± 2.7 (3.5–3.6)	<0.001

## Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort

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Table 3. Prevalence comparison of those diseases mostly occurring in elders.

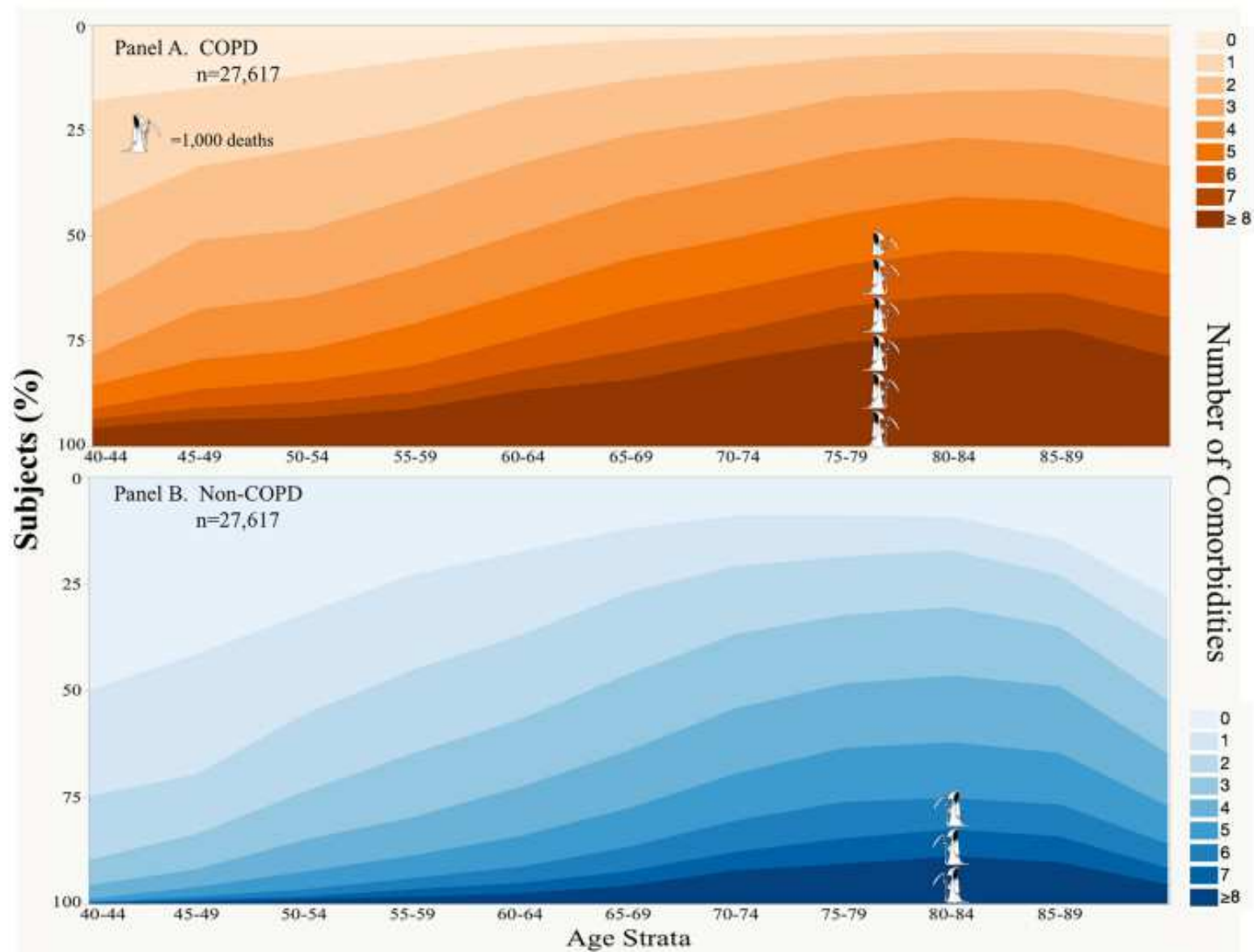
		≤55 years	56–65 years	66–75 years	76–85 years	>85 years
Degenerative Joint Disease	Non-COPD	4.81%	13.38%	22.02%	27.05%	23.41%
	COPD	8.69%	18.48%	25.24%	30.53%	28.95%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	< .0001
Atherosclerosis	Non-COPD	0.00%	0.23%	0.33%	0.73%	1.12%
	COPD	0.43%	1.22%	2.09%	3.05%	3.55%
	<i>Fisher's exact test</i>	0.0001	< .0001	< .0001	< .0001	< .0001
Hearing Loss	Non-COPD	2.82%	5.42%	7.03%	8.26%	7.34%
	COPD	4.81%	7.54%	8.55%	10.98%	11.55%
	<i>Fisher's exact test</i>	< .0001	< .0001	0.0003	< .0001	< .0001
Osteoporosis	Non-COPD	1.93%	5.85%	7.87%	9.45%	6.58%
	COPD	3.95%	9.67%	11.10%	12.44%	12.31%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	< .0001
Cataract	Non-COPD	0.70%	3.76%	11.49%	20.58%	16.83%
	COPD	1.93%	6.73%	16.90%	25.22%	21.22%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	0.0001
Benign Prostatic Hypertrophy	Non-COPD	0.61%	6.05%	13.84%	16.46%	13.47%
	COPD	1.29%	8.03%	17.83%	22.39%	19.18%
	<i>Fisher's exact test</i>	0.0069	< .0001	< .0001	< .0001	< .0001

## Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort

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**Table 3. Prevalence comparison of those diseases mostly occurring in elders.**

		≤55 years	56–65 years	66–75 years	76–85 years	>85 years
Skin CA	Non-COPD	0.34%	0.93%	1.45%	2.52%	3.36%
	COPD	0.43%	1.08%	1.96%	3.19%	4.15%
	<i>Fisher's exact test</i>	0.6895	0.4396	<b>0.0113</b>	<b>0.0111</b>	0.1534
Lung CA	Non-COPD	0.03%	0.27%	0.30%	0.27%	0.09%
	COPD	1.19%	2.09%	2.27%	1.32%	0.45%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	<b>0.0279</b>
Dementia	Non-COPD	0.18%	0.25%	1.78%	6.60%	11.32%
	COPD	0.43%	0.81%	2.95%	8.28%	14.76%
	<i>Fisher's exact test</i>	0.1148	< .0001	< .0001	< .0001	<b>0.0004</b>
Depression	Non-COPD	7.35%	8.05%	9.04%	10.08%	10.03%
	COPD	16.19%	14.95%	12.40%	14.98%	15.89%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	< .0001
Chronic Renal Failure	Non-COPD	0.06%	0.20%	0.71%	1.25%	1.92%
	COPD	0.52%	1.06%	2.33%	5.33%	7.97%
	<i>Fisher's exact test</i>	<b>0.0007</b>	< .0001	< .0001	< .0001	< .0001
Coronary Artery Disease	Non-COPD	0.80%	3.41%	5.51%	7.20%	6.76%
	COPD	3.46%	6.81%	10.16%	11.95%	13.82%
	<i>Fisher's exact test</i>	< .0001	< .0001	< .0001	< .0001	< .0001



## Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort

Miguel J. Divo<sup>1†\*</sup>, Bartolome R. Celli<sup>1‡</sup>, Beatriz Poblador-Plou<sup>2‡</sup>, Amaia Calderón-Larrañaga<sup>2</sup>, Juan Pablo de-Torres<sup>3</sup>, Luis A. Gimeno-Feliu<sup>2</sup>, Juan Bertó<sup>3</sup>, Javier J. Zulueta<sup>3</sup>, Ciro Casanova<sup>4</sup>, Victor M. Pinto-Plata<sup>5</sup>, Carlos Cabrera-Lopez<sup>6</sup>, Francesca Polverino<sup>1</sup>, Jonás Carmona Piréz<sup>2</sup>, Alexandra Prados-Torres<sup>2‡</sup>, Jose M. Marin<sup>7‡</sup>, on behalf of the EpiChron—BODE Collaborative Group<sup>†</sup>

- There were 1,294 patients (4.6%) with the diagnosis of COPD admitted to a hospital during the year preceding study enrolment and 107 (0.3%) in the non-COPD cohort
- There were 5,247 deaths documented in the COPD cohort (19%) compared to 2,911 in the non-COPD (11%) group, and the difference is statistically significant ( $p < 0.001$ ).
- In a logistic regression model age, number of comorbidities and carrying the diagnosis of COPD were significantly correlated with an increased risk for death ( $p < 0.001$ ).
- The odds ratio for 3-year mortality was:
  - 2.75 (95% CI 2.66–2.84) for every 10 years of age increase,
  - 1.09 (95% CI 1.08–1.10) for every increment in the number of comorbidities
  - 1.65 (95% CI 1.56–1.74) for carrying the diagnosis of COPD.

## Chronic Obstructive Pulmonary Disease (COPD) as a disease of early aging: Evidence from the EpiChron Cohort

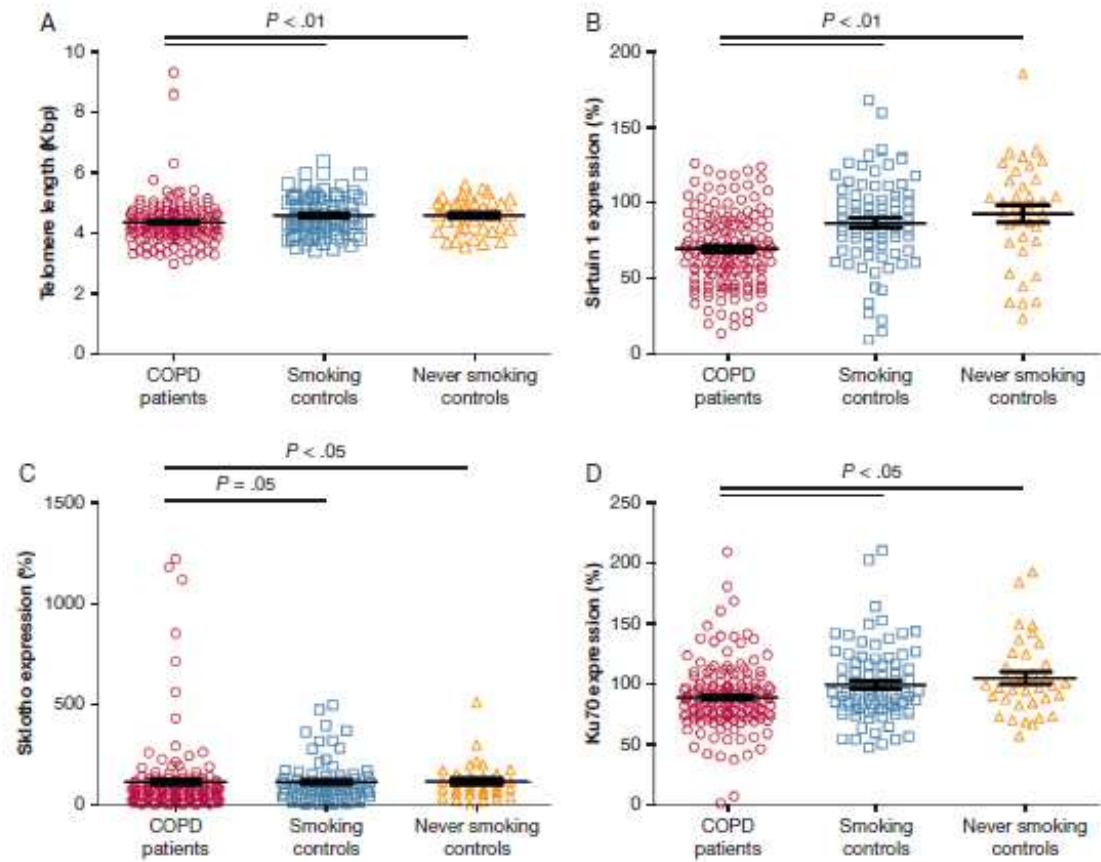
Miguel J. Divo<sup>1†\*</sup>, Bartolome R. Celli<sup>1‡</sup>, Beatriz Poblador-Plou<sup>2‡</sup>, Amaia Calderón-Larrañaga<sup>2</sup>, Juan Pablo de-Torres<sup>3</sup>, Luis A. Gimeno-Feliu<sup>2</sup>, Juan Bertó<sup>3</sup>, Javier J. Zulueta<sup>3</sup>, Ciro Casanova<sup>4</sup>, Victor M. Pinto-Plata<sup>5</sup>, Carlos Cabrera-Lopez<sup>6</sup>, Francesca Polverino<sup>1</sup>, Jonás Carmona Piréz<sup>2</sup>, Alexandra Prados-Torres<sup>2‡</sup>, Jose M. Marin<sup>7‡</sup>, on behalf of the EpiChron—BODE Collaborative Group<sup>†</sup>

- The process of aging is defined as the progressive decline in body function and homeostasis leading to an increasing vulnerability to disability, multimorbidity and death
- This study confirms the known increased vulnerability for comorbidities that comes with age, but emphasizes that carrying the diagnosis of COPD enhances this risk.
- This study suggest the presence of early aging in patients with COPD; the diseases characteristically occurring in the elderly, the prevalence was higher in subjects with COPD compared with those without the disease

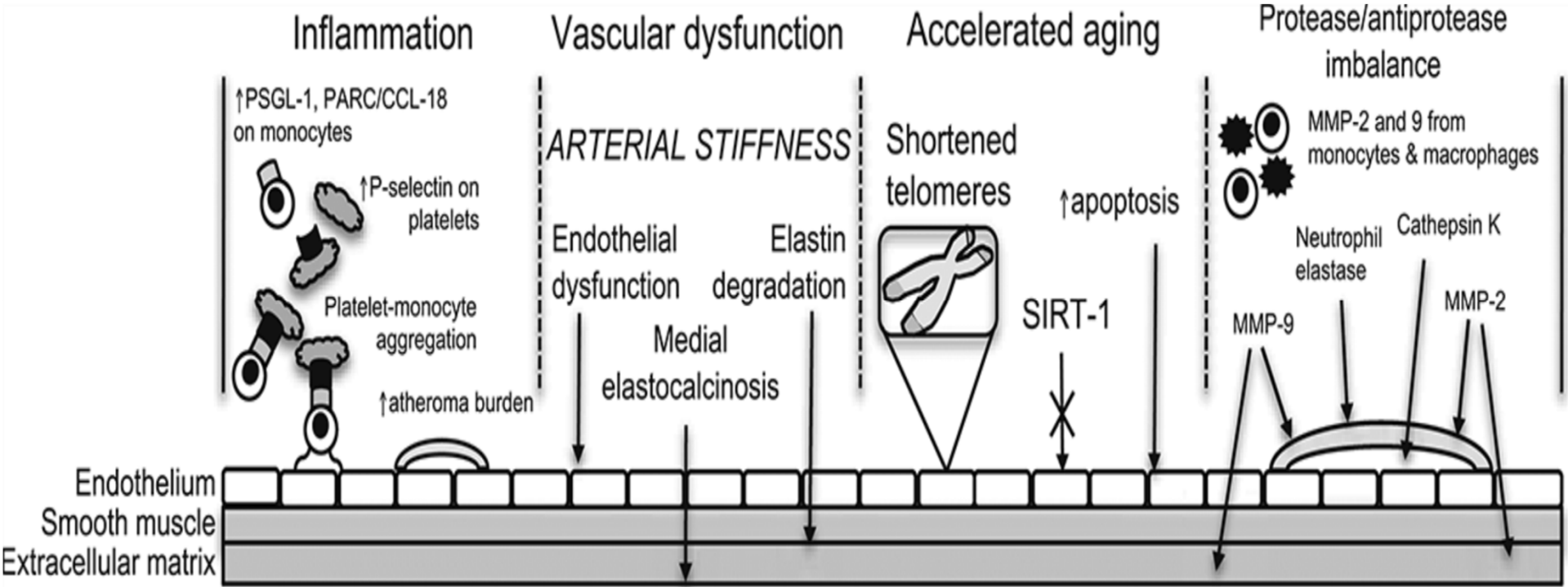
# Various Mechanistic Pathways Representing the Aging Process Are Altered in COPD



Erica P. A. Rutten, PhD; Poomima Gopal, MSc; Emiel F. M. Wouters, MD, PhD; Frits M. E. Franssen, MD, PhD; Geja J. Hageman, PhD; Lowie E. Vanfleteren, MD, PhD; Martijn A. Spruit, PhD; and Niki L. Reynaert, PhD



# Cardiovascular Disease in COPD- Mechanisms



RESEARCH

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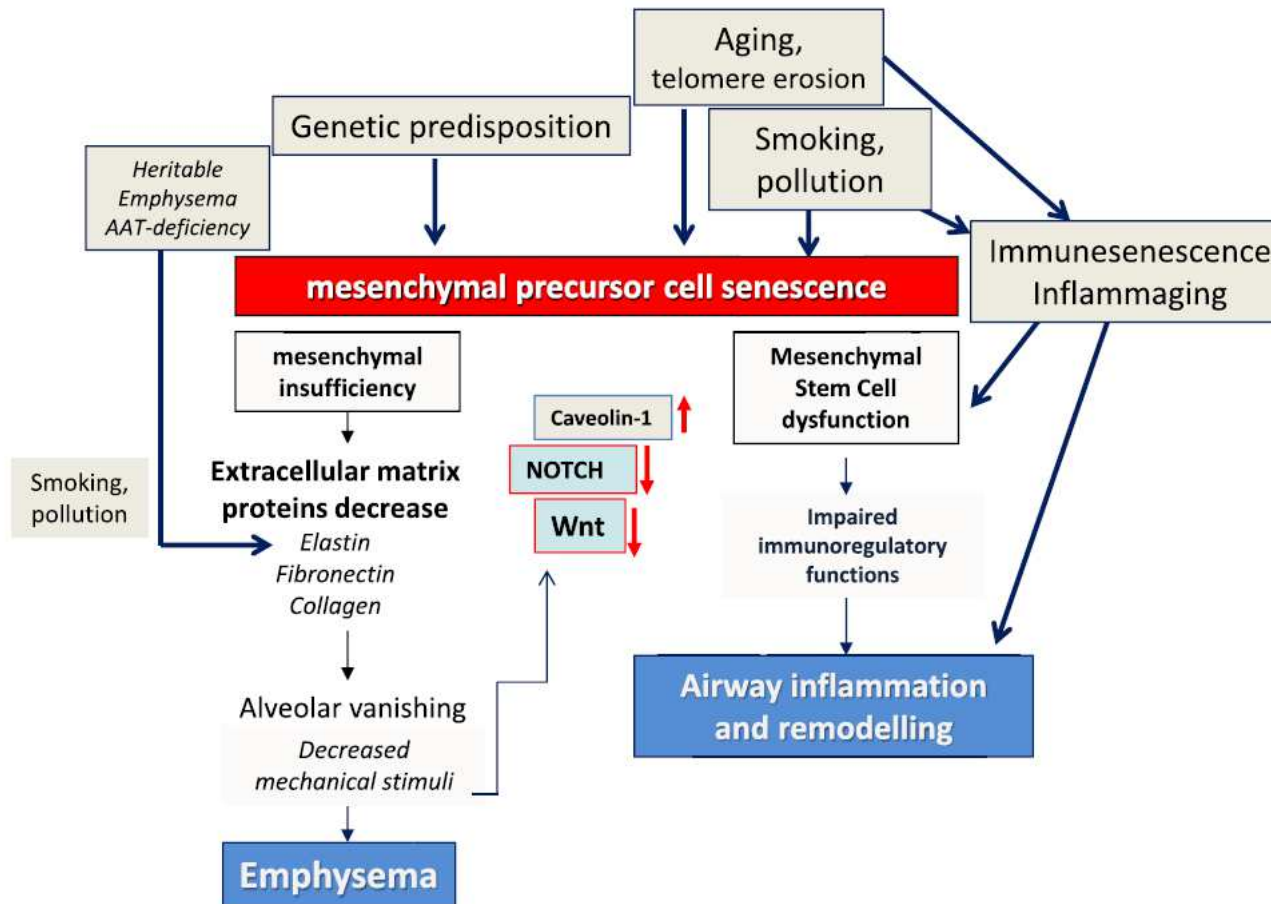
## Telomere shortening and accelerated aging in COPD: findings from the BODE cohort



Córdoba-Lanus Elizabeth<sup>1\*</sup>, Cazorla-Rivero Sara<sup>1</sup>, Espinoza-Jiménez Adriana<sup>1</sup>, Juan P. de-Torres<sup>3</sup>, Pajares María-José<sup>4</sup>, Aguirre-Jaime Armando<sup>1</sup>, Celli Bartolomé<sup>5</sup> and Casanova Ciro<sup>1,2</sup>

This longitudinal observational study we found that compared with smoker controls, an accelerated telomere shortening occurs in patients with COPD, even if they had shorter telomeres at baseline. Interestingly, the speed of shortening relates inversely to baseline telomere length. However, the telomere length and its rate of shortening did not relate to clinical and lung function parameters and their change over time, making telomere length change an unlikely useful

## General scheme describing the different steps of COPD/emphysema pathogenesis

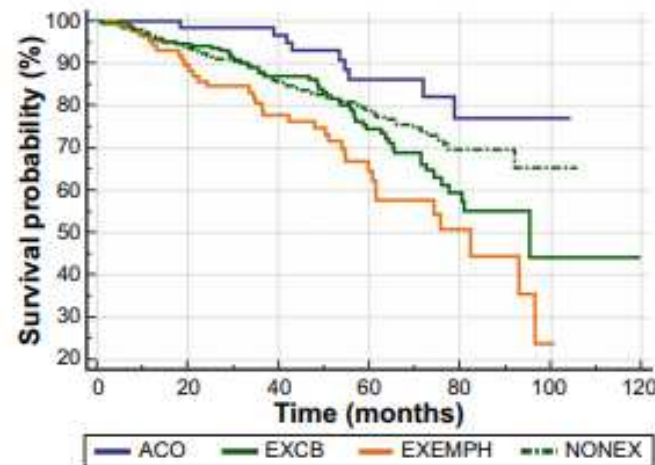


Chilosi et al. - Translational Research 2013;162:156–173)

# Strategia vincente

- Controllo dei fattori di rischio (FUMO e ATTIVITA' FISICA)
- DIAGNOSI PRECOCE di BPCO
- FENOTIPIZZAZIONE del paziente

# Mortality in COPD patients according to clinical phenotypes



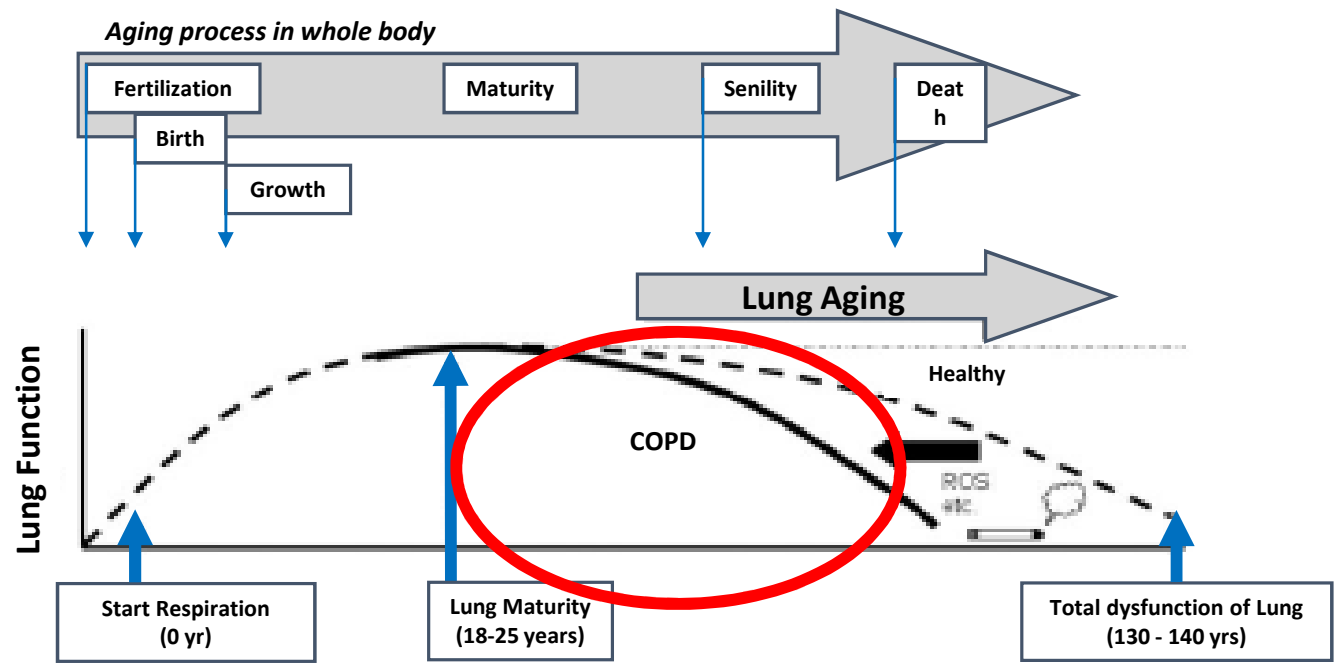
Number at risk							
	0	20	40	60	80	100	120
ACO	75	63	53	36	14	1	0
EXCB	194	174	130	73	28	3	0
EXEMPH	91	73	54	30	12	1	0
NONEX	531	429	306	174	51	4	0

Figure 1 Kaplan–Meier survival curves for the different phenotypes.

**Abbreviations:** ACO, asthma–COPD overlap; EXCB, exacerbator with chronic bronchitis; EXEMPH, exacerbator with emphysema; NONEX, nonexacerbator.

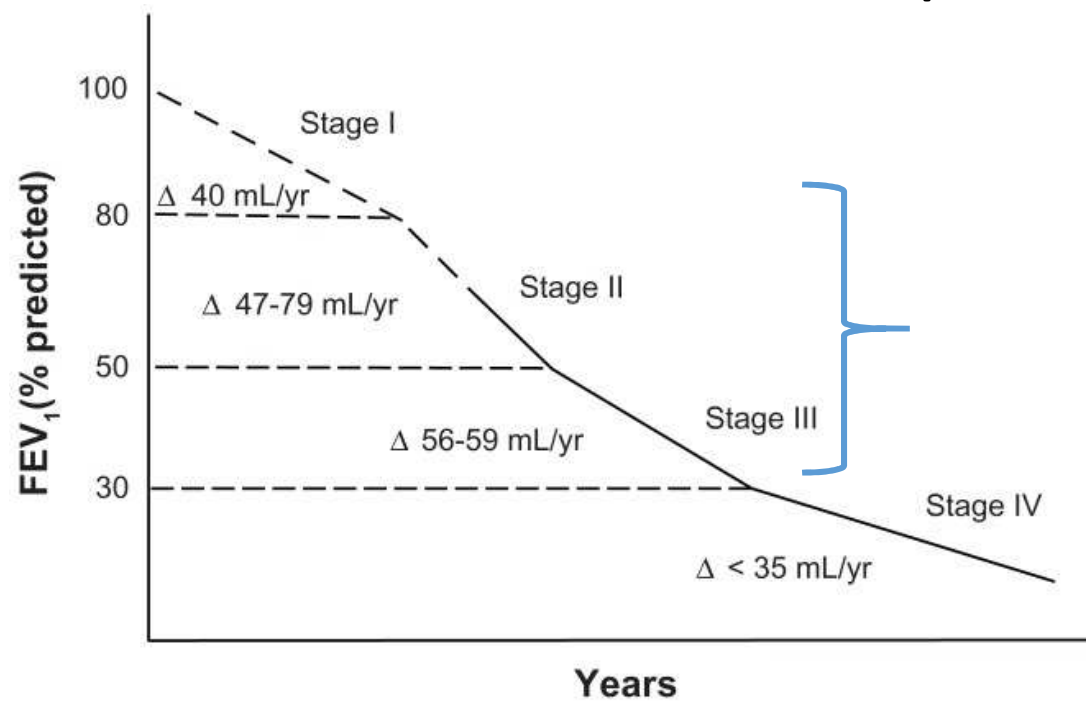
# Strategia vincente

- Controllo dei fattori di rischio (FUMO e ATTIVITA' FISICA)
- DIAGNOSI PRECOCE
- FENOTIPIZZAZIONE del paziente
- Trattamento adeguato ed appropriato rispetto al fenotipo, fin dalle fasi precoci della malattia
- L'obiettivo è di ridurre il DECLINO FUNZIONALE (maggiore efficacia nel controllare il declino funzionale da parte dei farmaci, nelle fasi più precoci della BPCO) e prevenire le RIACUTIZZAZIONI



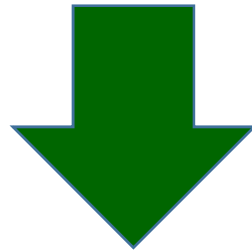
Ito, 2009

## Il declino funzionale è accelerato nei pazienti lievi-moderati: la necessità di un trattamento precoce



# Take Home Messages

- Controllo dei fattori di rischio (FUMO e ATTIVITA' FISICA)
- DIAGNOSI PRECOCE
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**RIDURRE LA MORTALITA'**

Vi ringrazio per l'attenzione