9a Jornada de Recerca de l'Institut Català de la Salut

Construint l'ecosistema en medicina respiratòria

16 de juny de 2017
Palau de Congressos de Lleida – La Llotja
Avinguda de Tortosa, 4 /// 25005 - LLEIDA

Medicina personalitzada en la malaltia pulmonar obstructiva crònica (MPOC)

Alvar Agustí

CLÍNIC BARCELONA Hospital Universitari

IDIBAPS Institut D'Investigacions Biomèdiques August Pi i Sunyer

UNIVERSITAT DE BARCELONA

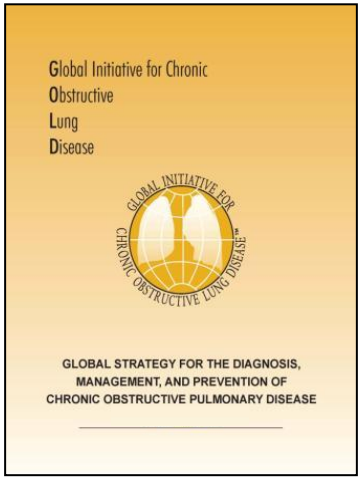
ciberes Centro de Investigación Biomédica en Red Enfermedades Respiratorias

BARCELONA RESPIRATORY NETWORK Collaborative research

GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE

Conflictes d’interès

Research grants/clinical trials:	AstraZeneca, GSK, Menarini, MSD
Lector for:	AstraZeneca, Boheringer-Ingelheim, Chiesi, Menarini, Teva, Novartis, GSK, Kyorin
Member of scientific (advisory) board:	AstraZeneca, Boheringer-Ingelheim,Chiesi, GSK, Novartis
Consultant:	None
Employer (including part-time):	None
Tobacco Industry relationship:	None



Tres idees per a la discussió

- Medicina personalitzada → Medicina de precisió

- Medicina *respiratòria* de precisió

- Aplicació a l'MPOC

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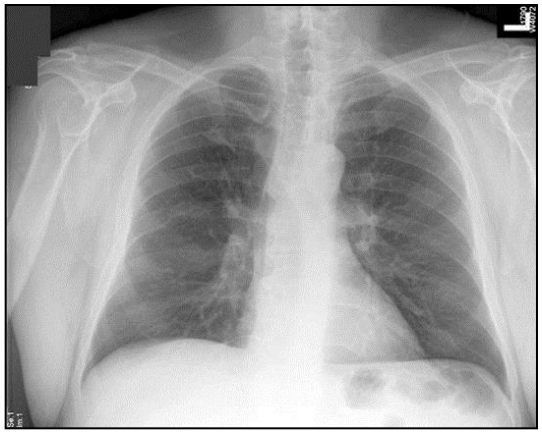
- Aplicació a la MPOC

La medicina SEMPRE ha estat personalitzada!



Risc POBLACIONAL

Risc INDIVIDUAL


TIME
THE
ANGELINA
EFFECT
Angelina Jolie's double mastectomy puts genetic testing in the spotlight. What her choice reveals about calculating risk, cost and peace of mind
BY JEFFREY KLUGER & ALICE PARK

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Precision Medicine — Personalized, Problematic, and Promising

J. Larry Jameson, M.D., Ph.D., and Dan L. Longo, M.D.

We define precision medicine as treatments targeted to the needs of individual patients on the basis of genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations.

doi: 10.1056/NEJMsb1503104

Principles of Precision Medicine

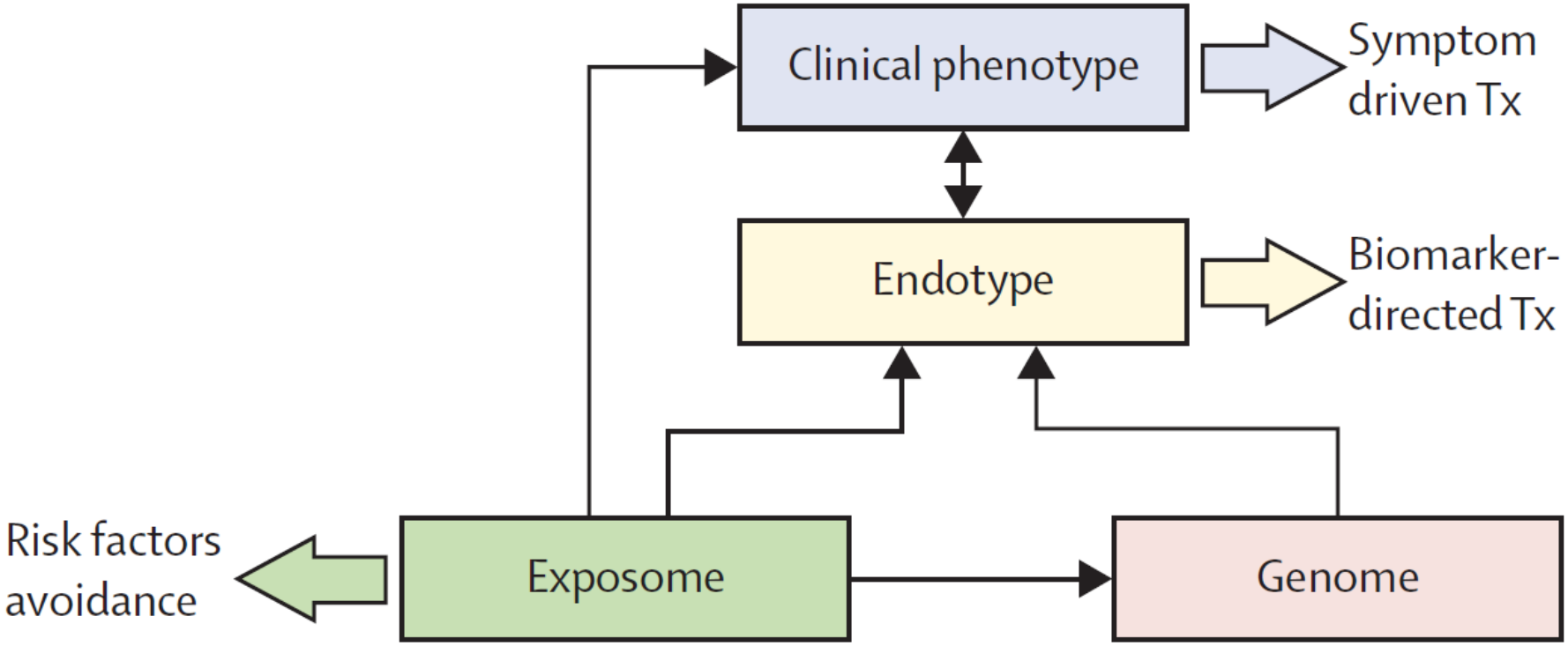
Same diagnosis

Same treatment

Courtesy of Prof. C. Vogelmeier

Current concepts in targeting chronic obstructive pulmonary disease pharmacotherapy: making progress towards personalised management

Prescott G Woodruff, Alvar Agusti, Nicolas Roche, Dave Singh, Fernando J Martinez



Lancet 2015; 385: 1789–98

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¿Cómo ves
la botella?
¿medio
vacia?
¿medio
llena?

Medicina respiratòria de precisió: mite o realitat?

Malaltia	"Abans"	"Ara"
Fibrosi quística	Res	Ivacaftor (potenciador CFTR)* Lumacaftor (corrector CFTR)*

* Homozigots mutació Phe508del CFTR

Medicina respiratoria de precisió: mite o realitat?

Malaltia	"Abans"	"Ara"
Fibrosi quística	Res	Ivacaftor (potenciador CFTR)* Lumacaftor (corrector CFTR)*
Càncer pulmó	Cirurgia, Quimio-Radio	Mutacions EGFR , kRAS, ALK Immunoteràpia

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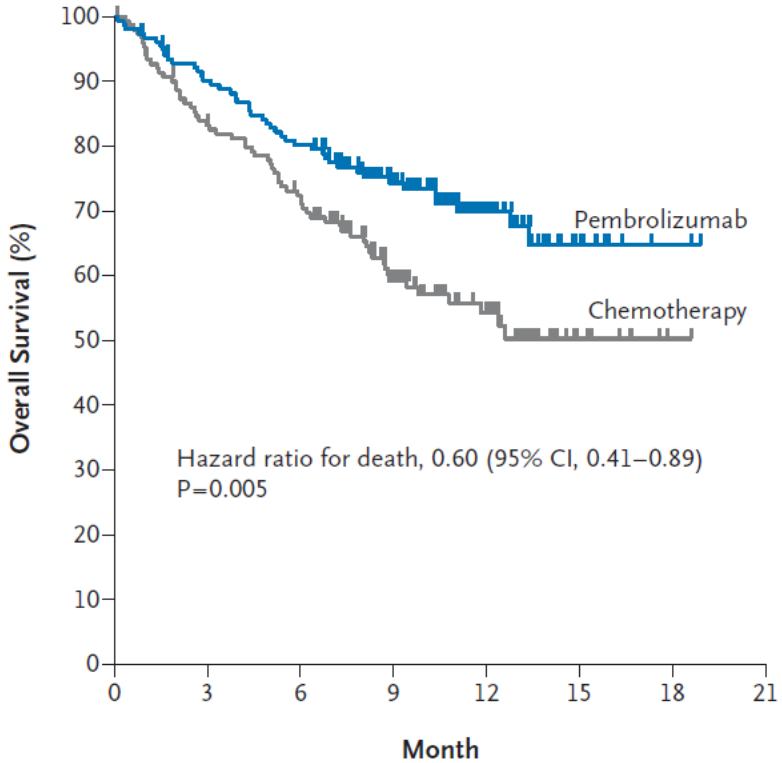
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pembrolizumab versus Chemotherapy for PD-L1–Positive Non–Small-Cell Lung Cancer

Martin Reck, M.D., Ph.D., Delvys Rodríguez-Abreu, M.D.,



No. at Risk

Pembrolizumab	154	136	121	82	39	11	2	0
Chemotherapy	151	123	106	64	34	7	1	0

This article was published on October 9, 2016, at NEJM.org.

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MPOC	Broncodilatadors	Roflumilast (PDE4 inhb.) Mepolizumab (IL5) Benralizumab (IL5Ra) …

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MPOC	Broncodilatadors	Roflumilast (PDE4 inhb.) Mepolizumab (IL5) Benralizumab (IL5Ra) …
Asma	Corticoides inhalats	Omalizumab (IgE) Mepolizumab (IL5) Benralizumab (IL5Ra) Lebrikizumab (IL13) Dupilumab (IL-4Rα/IL-13Rα1) …

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FPI	Res	Pirfenidone (FP "conservada") Nintedanib (FP "conservada")

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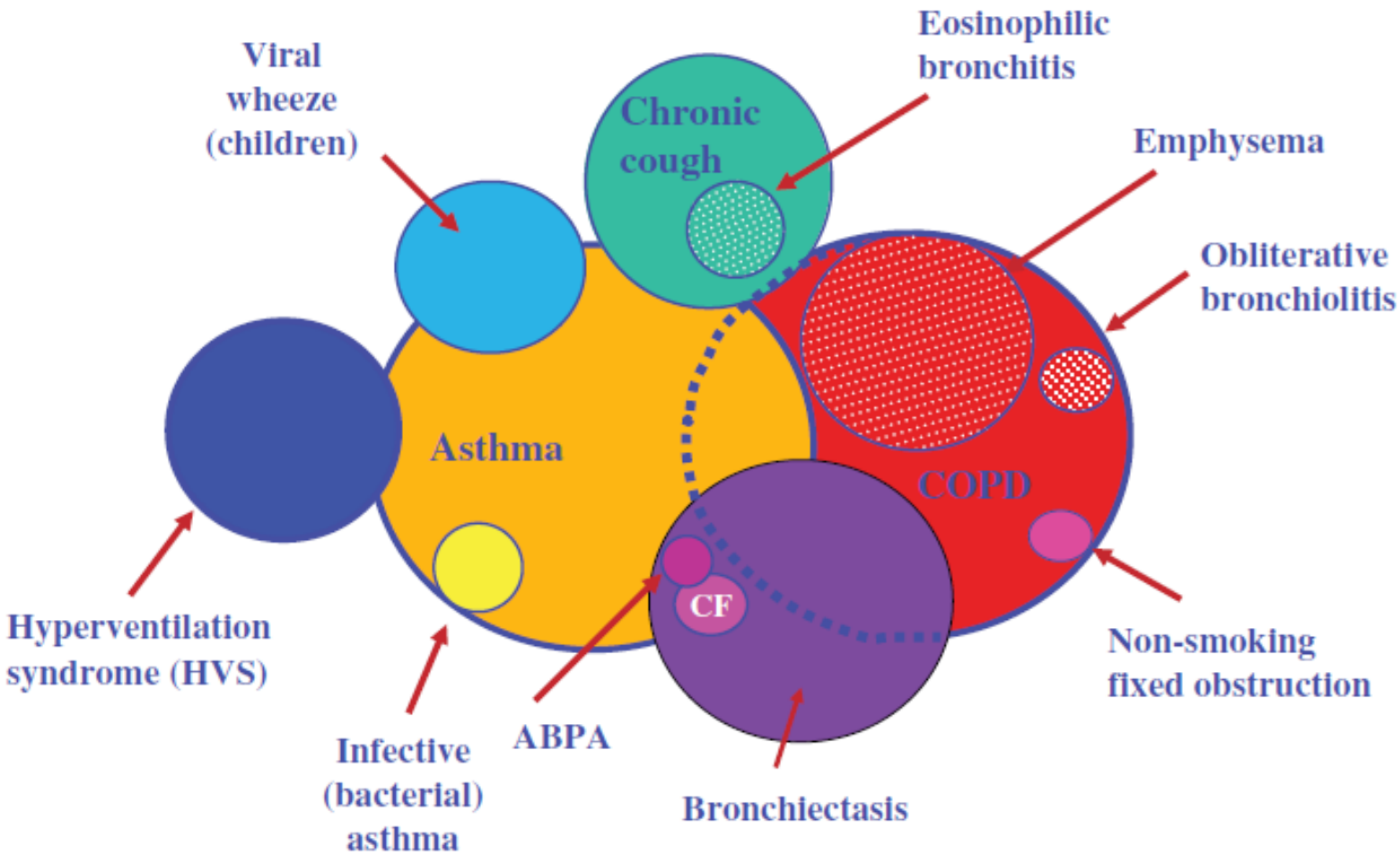
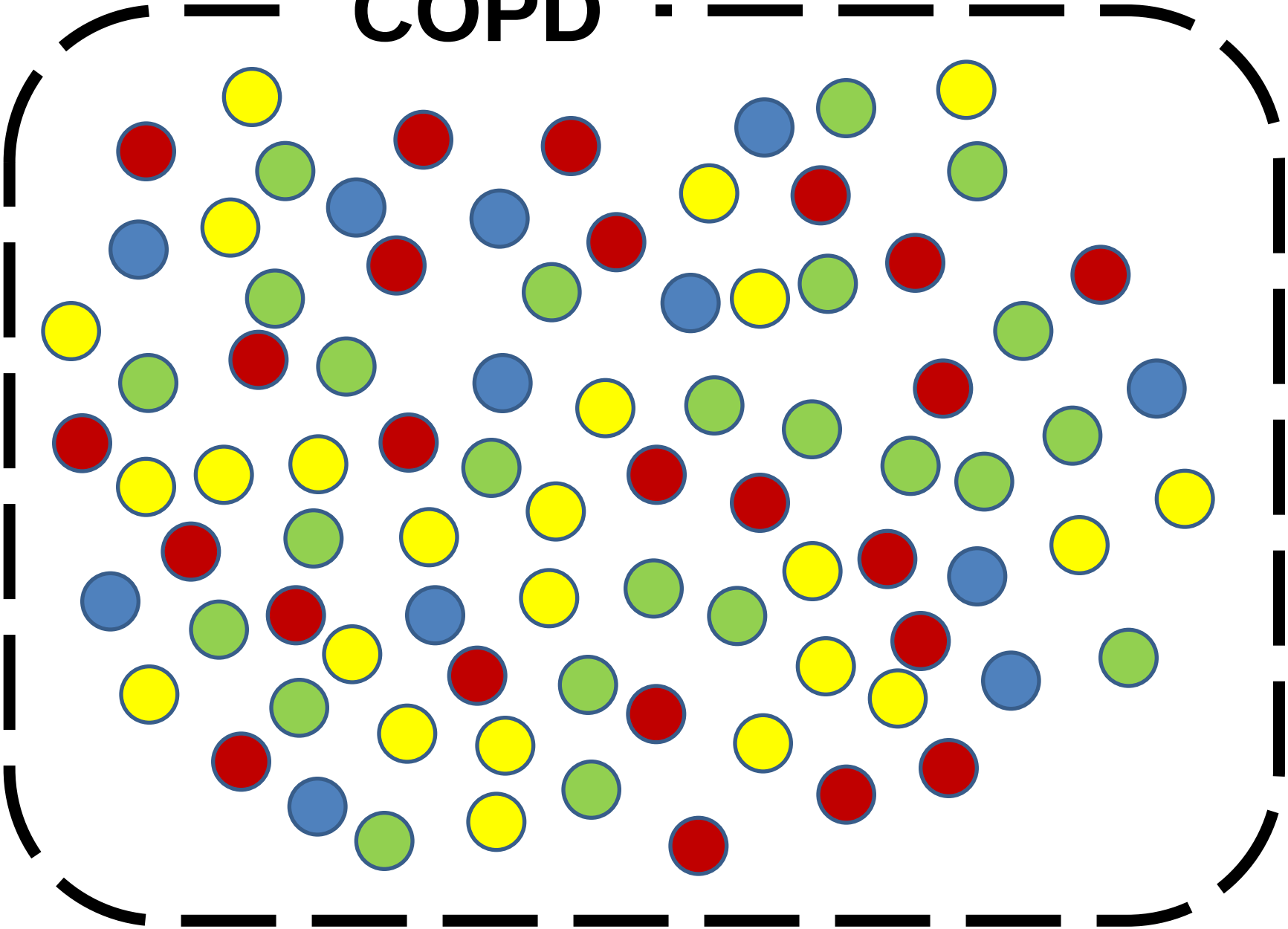


Wardlaw AJ et al. *Clin Exp Allergy 2005: 35(10): 1254-1262*

COPD



Agusti A. *Thorax* 69 (9):857-864, 2014

Clinical Commentary

Chronic Obstructive Pulmonary Disease Phenotypes

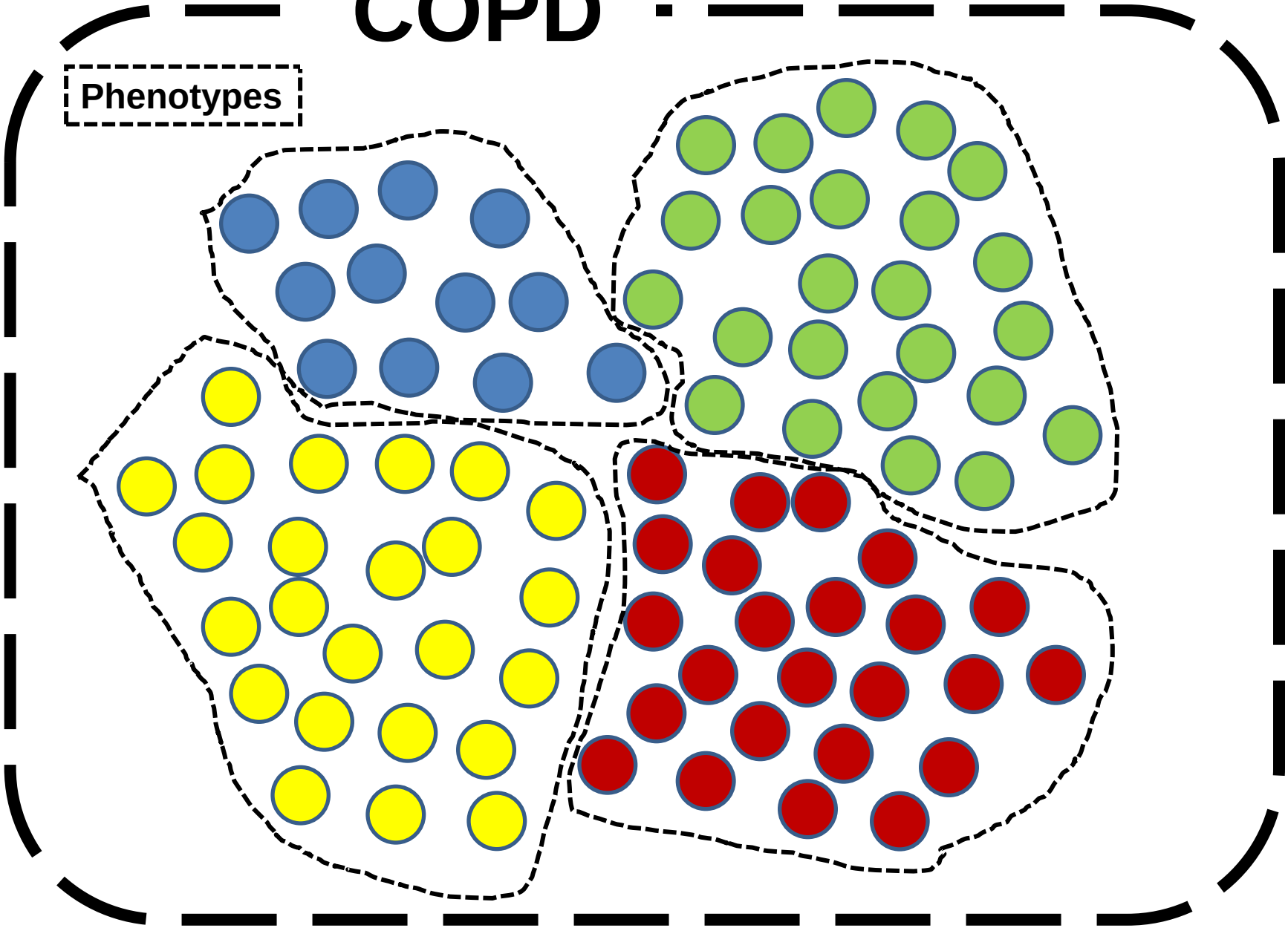
The Future of COPD

MeiLan K. Han[1], Alvar Agusti[3], Peter M. Calverley[4], Bartolome R. Celli[5], Gerard Criner[6], Jeffrey L. Curtis[1,7], Leonardo M. Fabbri[8], Jonathan G. Goldin[9], Paul W. Jones[10], William MacNee[11], Barry J. Make[12], Klaus F. Rabe[13], Stephen I. Rennard[14], Frank C. Sciurba[15], Edwin K. Silverman[5,16], Jørgen Vestbo[17], George R. Washko[5], Emiel F. M. Wouters[18], and Fernando J. Martinez[2]

Am J Respir Crit Care Med Vol 182. pp 598–604, 2010

‘‘a single or combination of disease attributes that describe differences between individuals with COPD as they relate to clinically meaningful outcomes (symptoms, exacerbations, response to therapy, rate of disease progression, or death).’

COPD



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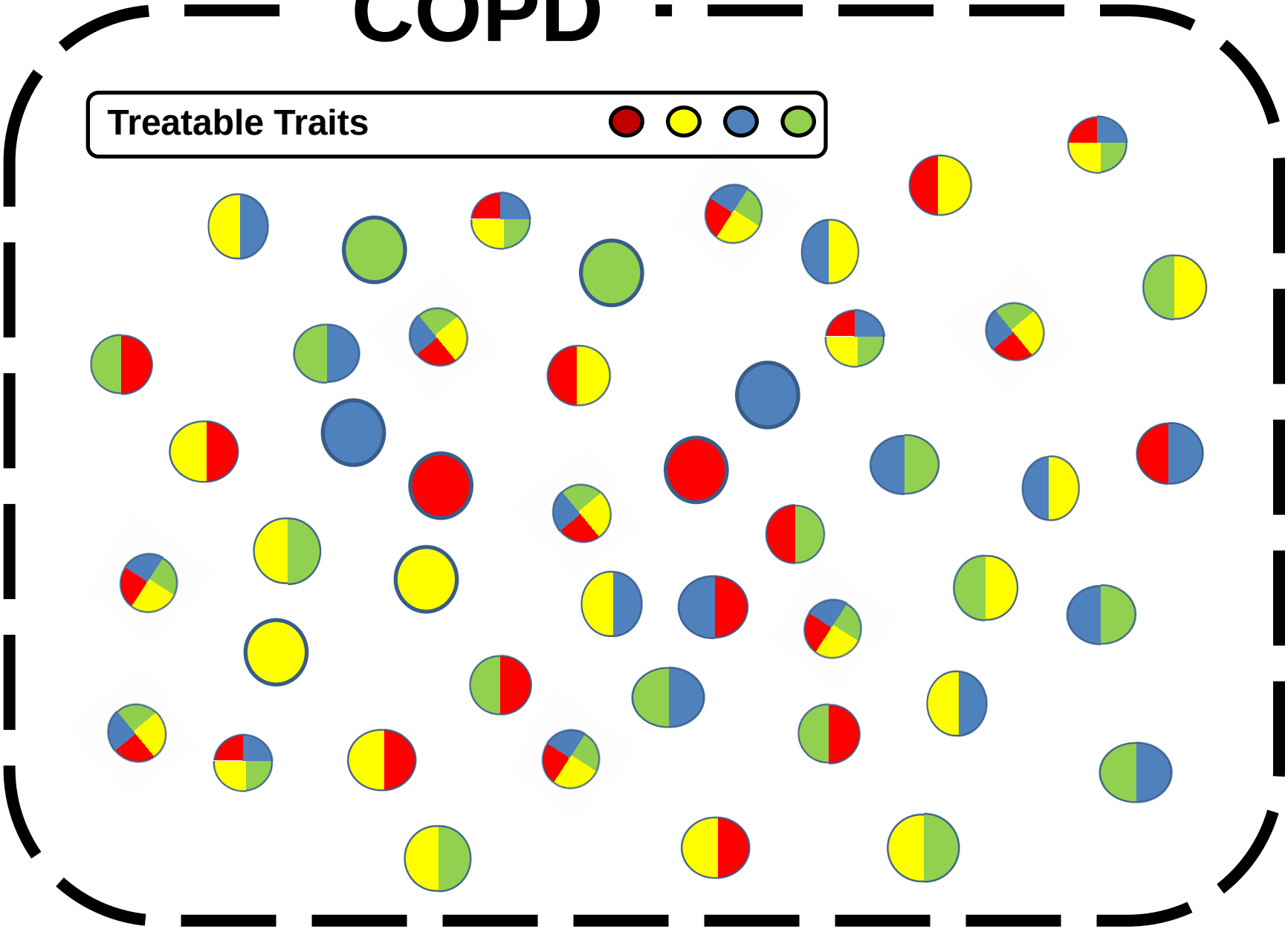

Agusti A. *Thorax* 69 (9):857-864, 2014

PERSPECTIVE
PRECISION MEDICINE FOR AIRWAY DISEASES

Treatable traits: toward precision medicine of chronic airway diseases

Alvar Agusti[1], Elisabeth Bel[2], Mike Thomas[3], Claus Vogelmeier[4], Guy Brusselle[5,6], Stephen Holgate[7], Marc Humbert[8], Paul Jones[9], Peter G. Gibson[10], Jørgen Vestbo[11], Richard Beasley[12] and Ian D. Pavord[13]

Eur. Resp. J. 2016; 47; 410

- We propose here a **precision medicine strategy** for the management of **patients with airway disease** that is "**label-free**" and based on the identification of "**treatable traits**" in each patient.

- These traits can be "treatable" based on "**phenotypic**" recognition or on deep understanding of the critical causal pathways ("**endotypes**").

- Treatable traits **can coexist** in the same patient and **change with time** (spontaneously or as a result of treatment)

- There are **pulmonary** and **extra-pulmonary** treatable traits as well as **behavioral/social risk factors** that merit individual attention and potential treatment

	TRAIT	TREATMENT
Pulmonary treatable traits		
	Airway smooth muscle contraction	Bronchodilators
	Eosinophilic airway inflammation	Corticosteroids / Type 2 biologics
	Chronic sputum production	Smoking cessation, macrolides
	Bacterial colonization	Macrolides
	Bronchiectasis	Macrolides
	Cough reflex hypersensitivity	Gabapentin
	Chronic respiratory failure	Oxygen / NIV / Lung Tx
	Pulmonary hypertension	Oxygen / NIV / Lung Tx
	Emphysema	Lung volume reduction surgery /LTx

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Extra-pulmonary treatable traits		
	Rhinosinusitis	Topical steroids / Surgery
	Deconditioning	Rehabilitation
	Cachexia	Diet / physical activity
	Obesity	Diet / physical activity / bariatric surgery
	Cardiovascular disease	ACE inhibitors / diuretics / β blockers
	Vocal cord dysfunction	Speech pathology therapy
	Depression	Cognitive & Behavioural therapy
	Anxiety	Anxiolytics
	Systemic inflammation	Statins ?

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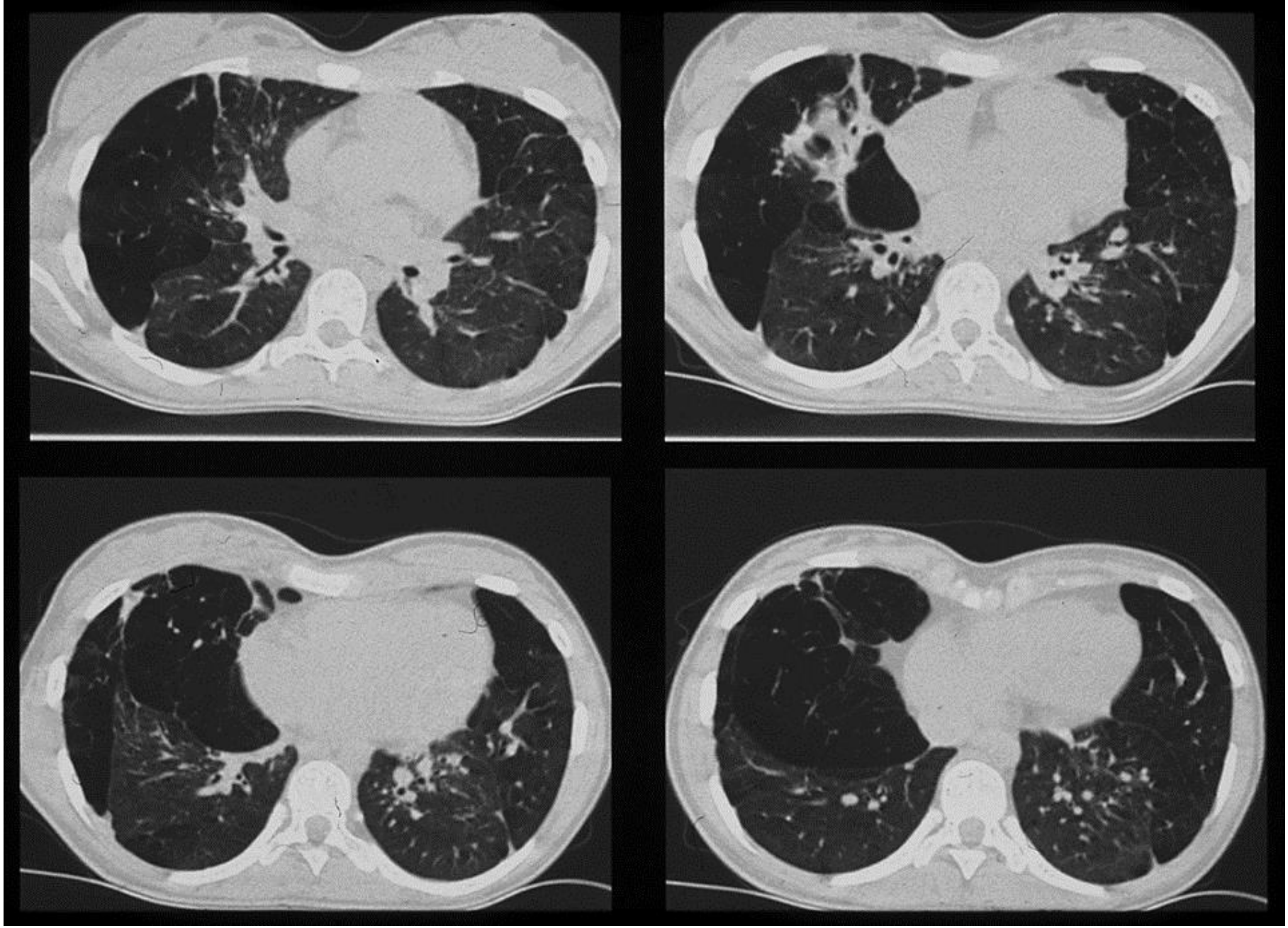
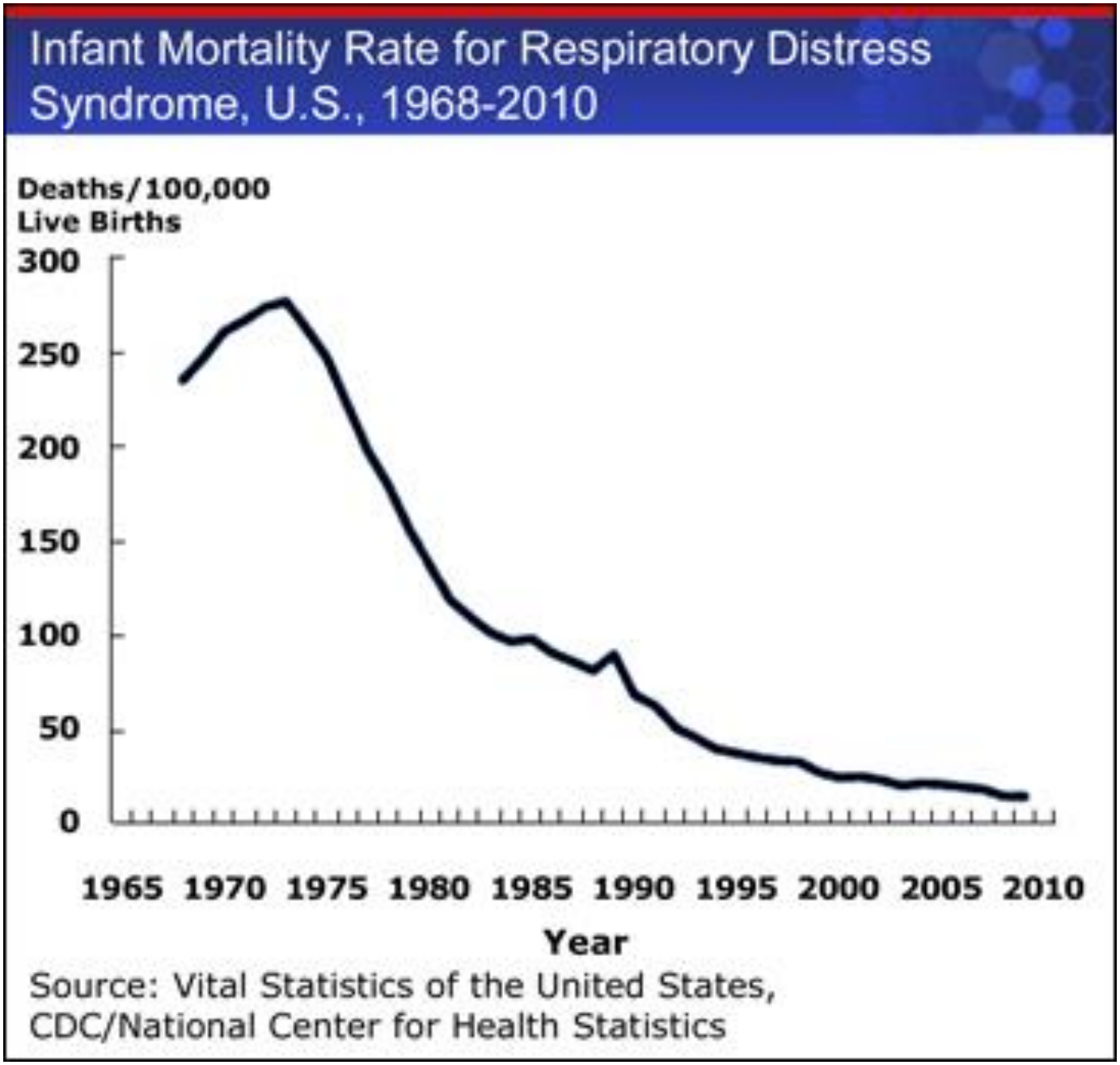
	Systemic inflammation	Statins ?
Treatable behaviour / life style factors		
	Poor inhalation technique	Education
	Non-adherence to treatment	Reassurance / Periodic check-up
	Smoking	Cessation support
	Exposure to sensitizing agents	Avoidance / desensitization
	Side effects of treatments	Treatment optimization
	Polypharmacy	Medication review
	Symptoms perception	Family therapy
	Poor family and social support	Education / self management support


Change is a process,
not an event.



HRCT in adolescent survivor of preterm birth (courtesy of Prof. A. Bush (London, UK) 2017)


Infant Mortality Rate for Respiratory Distress Syndrome, U.S., 1968-2010
Deaths/100,000 Live Births
300
250
200
150
100
50
0
1965 1970 1975 1980 1985 1990 1995 2000 2005 2010
Year
Source: Vital Statistics of the United States, CDC/National Center for Health Statistics

Rene Magritte (self-portrait)
21 November 1898 – 15 August 1967

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Moltes gràcies per la seva atenció

Alvar.Agusti@clinic.ub.es

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