INVESTIGACIÓN EPIDEMIOLÓGICA DE LA EPOC: A PROPOSITO DE UNA HISTORIA APASIONANTE

IV REUNIÓN DE EPOC

TORRE DEL MAR, MÁLAGA

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APLICANDO LA EPIDEMIOLOGIA AL ESTUDIO DE LA EPOC

- Contaminación atmosférica(J Sunyer 1985-)
- Calidad de Vida (J Alonso 1990-)
- Agudizaciones (J Garcia Aymerich 1996-)
- Heterogeneidad fenotípica (JGA 2003-)

Air pollution in COPD: BCN STUDIES.

- COPD ERAs 1985-89 older than 35y.
- 4 hospitals (80% respiratory admissions BCN).
- Research based ER monitoring system.
- Catalunya mortality register 1985-95.
- Flexible deterministic record linkage.
- 6745 people alive at Dec 1989.
- 2576 deaths 1990-1995.

COPD and air pollution: BCN first studies.

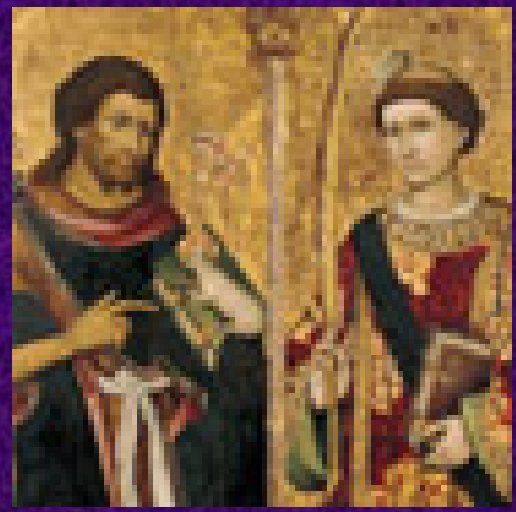
- Sunyer J. et al Am J Epidemiol 1991.
- Sunyer J. et al Am J Epidemiol 1993.
  - Use of time series
  - 25 ug/m3 SO2- 6-9% increase in ERAs.
  - Similar for BS in winter.

Sunyer J et al Am J Epidemiol 2000.

- Case-crossover design

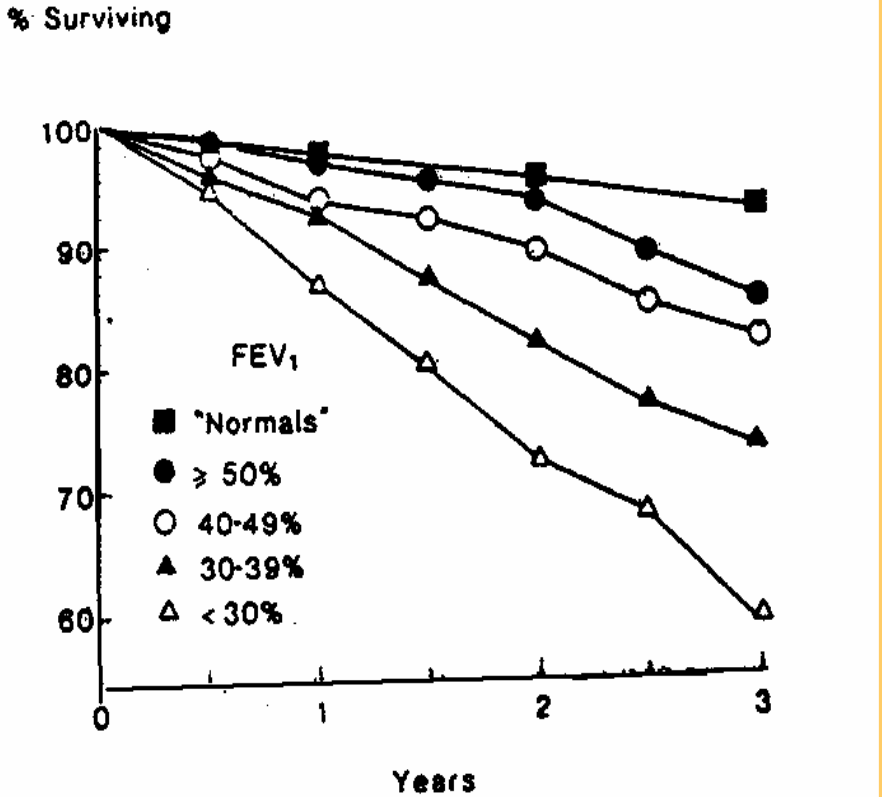
- Severity, age, increase the risk of mortality

Gothic paintings at MNAC, BCN



The functional paradigm in COPD

(Anthonisen NR, Am Rev Respir Dis 1986)

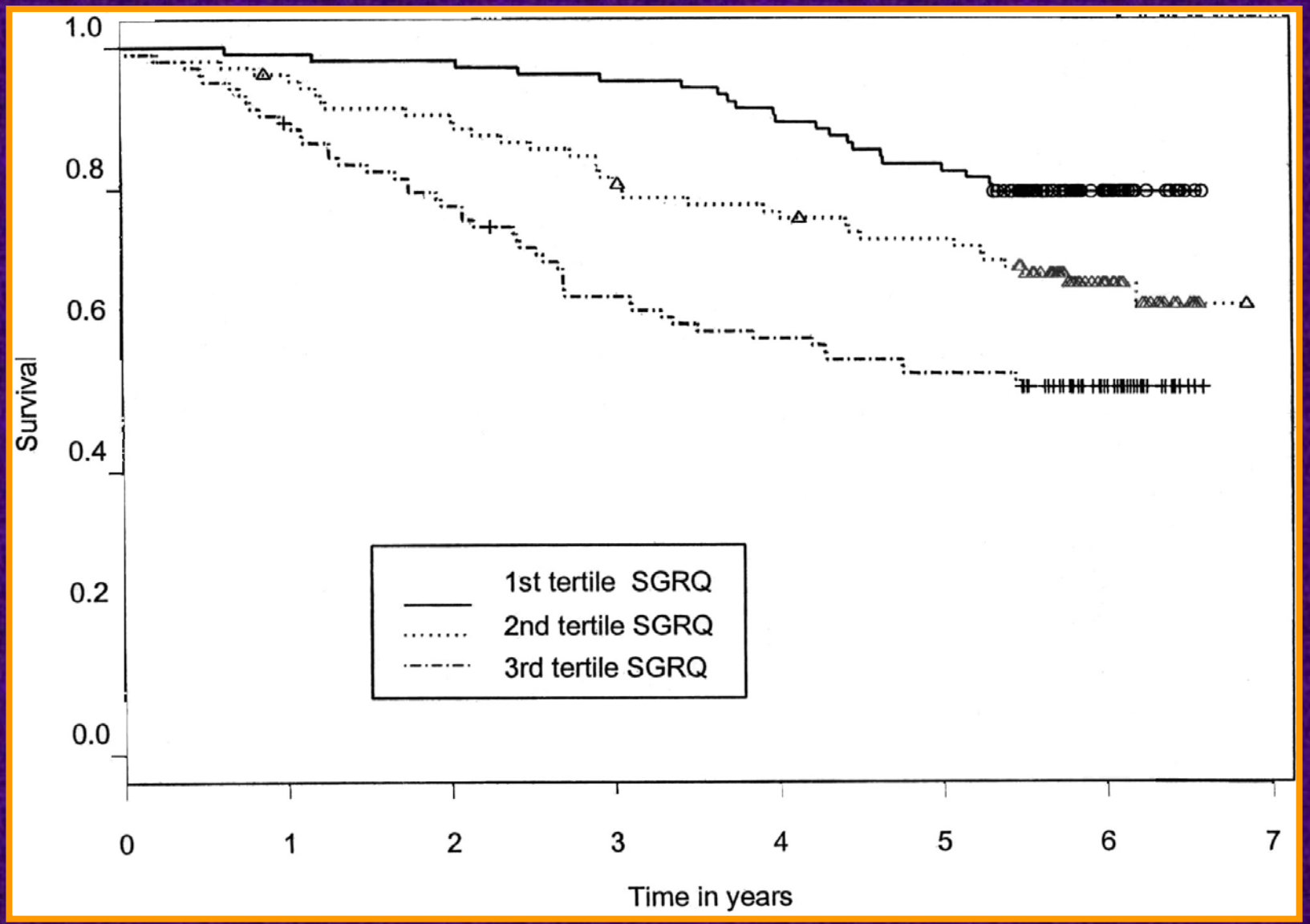


FEV1:

Main marker of prognosis

Main criteria for staging

Kaplan-Meier survival curves according to tertiles of SGRQ



SEPOC study (321 COPD patients)

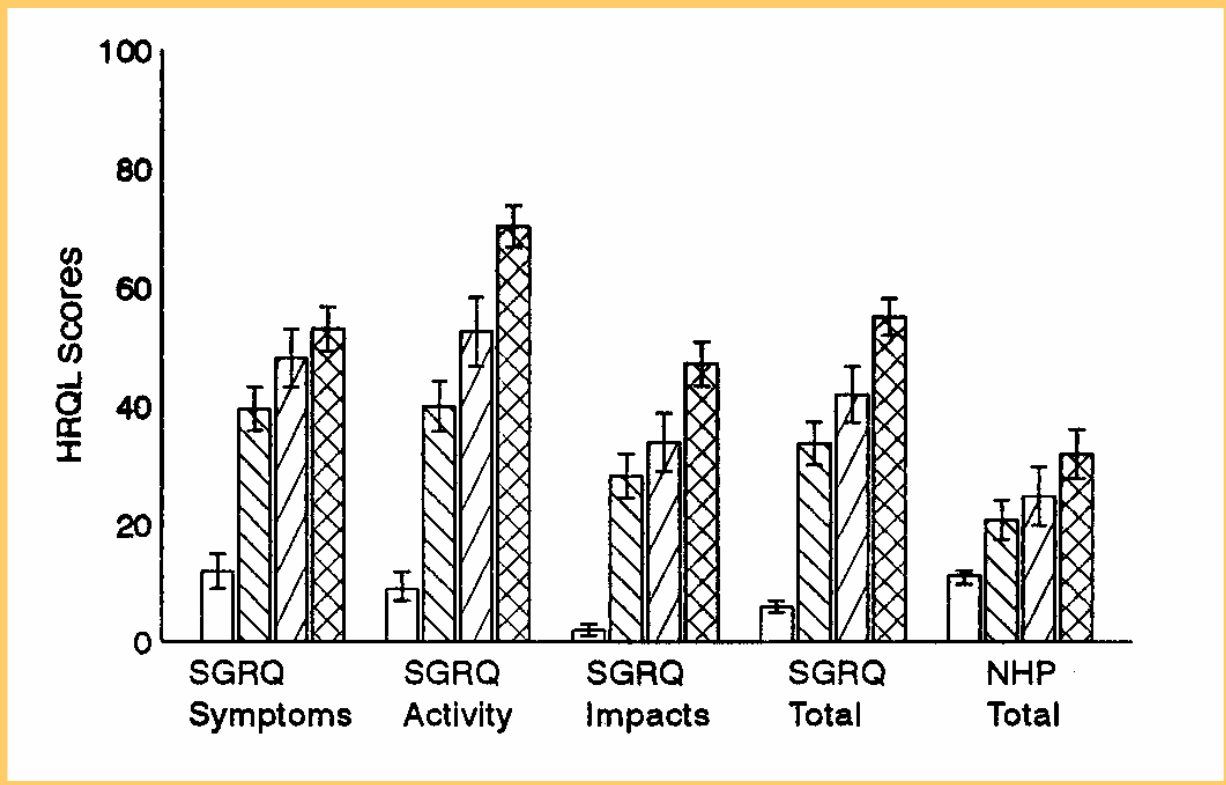
(Ferrer M et al. Ann Int Med 1997)

Reference values

FEV_1 > 49%

FEV_1 35 % - 49%

FEV_1< 35 %

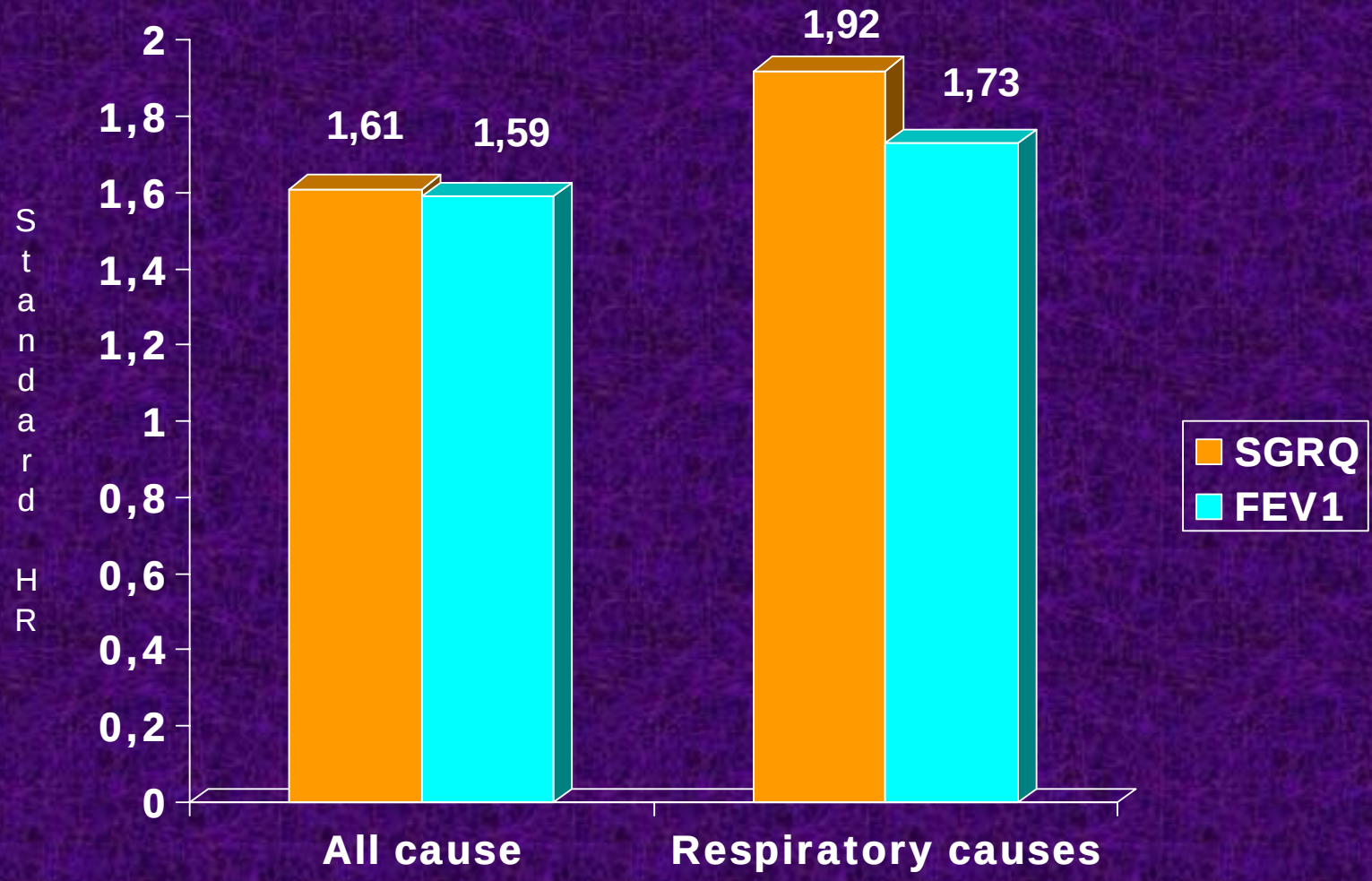


QL may be as important as FEV1 in the evolution of COPD !!!

Living and dying with COPD
(Lynn JL et al. JAMA 2000)

- “The study by Ferrer M (Ann Int Med 1997)... a surprising finding was that even patients with mild disease had a substantially compromised HRQL”
- “If future studies were able to determine whether HRQL was a strong predictor of death, in addition to FEV1, perhaps important regulatory functions related to end-of-life care could be adjusted properly”.

Role of QL in COPD mortality
Domingo A et al AJRCCM 2003



The BODE Index in COPD

(Celli B et al. NEJM 2004)

Table 5. Risk of Death from Any Cause and from Respiratory Failure, Pneumonia, or Pulmonary Embolism.*

Variable	Hazard Ratio (95% CI)	P Value
Risk of death from all causes		
Model I		
BODE score	1.34 (1.26–1.42)	<0.001
Model II		
BODE score	1.32 (1.23–1.40)	<0.001
Charlson index	1.05 (1.00–1.10)	0.06
Death from respiratory failure, pneumonia, or pulmonary embolism		
Model I		
BODE score	1.62 (1.48–1.77)	<0.001
Model II		
BODE score	1.63 (1.48–1.80)	<0.001
Charlson index	0.99 (0.93–1.07)	0.97

Risk Factors of Exacerbation of COPD: The EFRAM Study

Catalan Agency of Health Technology Assessment

Hospital Clínic, Germans Trias, Hospital del Mar, Hosptal de Bellvitge,

Respiratory and Environmental Health Research Unit, IMIM, Barcelona, Spain

Methods

- Design: cross-sectional
- Patients: systematic sample (1/2) of patients admitted for a COPD exacerbation, 1 year, 4 tertiary hospitals of the Barcelona area
- Measures:
  - Admission: questionnaire, anthropometric measurements
  - At least 3 months after admission (clinical stability): spirometric tests, arterial blood gas tensions

Prevalence of Risk Factors of Exacerbation
N=354 Indiv/405 Adm *

	Prev (95%CI)
No influenza vaccination	28 (24-33)
No pneumococcal vaccination	96 (93-97)
No rehabilitation	86 (82-89)
No LTOT when $PO_2 \leq 55mmHg$	28 (20-39)
LTOT<15 h/day	19 (13-26)
Fail essential MDI manoeuvres	43 (38-48)
Current smoking	26 (22-30)
Passive smoking in non-smokers	21 (17-27)
Current occupational exposure	5 (3-8)
High air pollution exposure	65 (60-70)

* GEE model

Garcia-Aymerich J et al AJRCCM 2001 and Thorax 2003

	HR (95% CI)
≥3 admissions in the year prior to recruitment	1.66 (1.16-2.39)
% of predicted FEV_1	0.97 (0.96-0.99)
PO_2 (mmHg)	0.98 (0.97-1.00)
Controlled by:	
General practitioner	1.00
Pneumologist	1.66 (0.98-2.80)
Anticholinergics	1.81 (1.11-2.94)
Usual physical activity:	
<550 METs (1st tertile)	1.00
550-1625 METs (2nd tertile)	0.87 (0.60-1.27)
>1625 METs (3rd tertile)	0.54 (0.34-0.86)

Other studies showing the effects of PA in COPD

- Reduced lung function decline and COPD risk among smokers. **Garcia-Aymerich J et al AJRCCM 2007**
- Lower risk of both COPD admissions and mortality. **Garcia-Aymerich J et al Thorax 2006**
- Not due to time-dependent confounding. **Garcia-Aymerich J et al Ann Epidemiol 2008]**

PAC-EPOC:

Phenotype and Course of COPD

Funding sources: FIS, AATM, SEPAR, FUCAP, Novartis, Marató TV3 Catalunya, Red Respira-ISCIII,CIBERESP, CIBERESP, Astra Zeneca

Hypothesis

- COPD at the time of a **first hospital admission** shows a wide variability on its phisiopathological and clinical characteristics.
- Such variability can be classified in clinical / epidemiologically relevant subgroups.
- These subtypes will differ on its clinical and functional course, use of services and survival.

PAC-COPD study: a multidimensional approach

- Symptoms and Health status (Quality of life)
- Exacerbations and infection
- Lung function and gas exchange
- Emphysema and airways disease
- Cellular mechanisms: inflammation, proteolysis, oxidative stress
- Other systemic targets
- Central hemodynamics

THE COPD PHENOTYPIC MATRIX: a comprehensive non systematic review. Arch Bonconeumol 2009

- 6 phenotypic dimensions
- 26 phenotypic traits
- 650 potentially relational cells

Complete examination

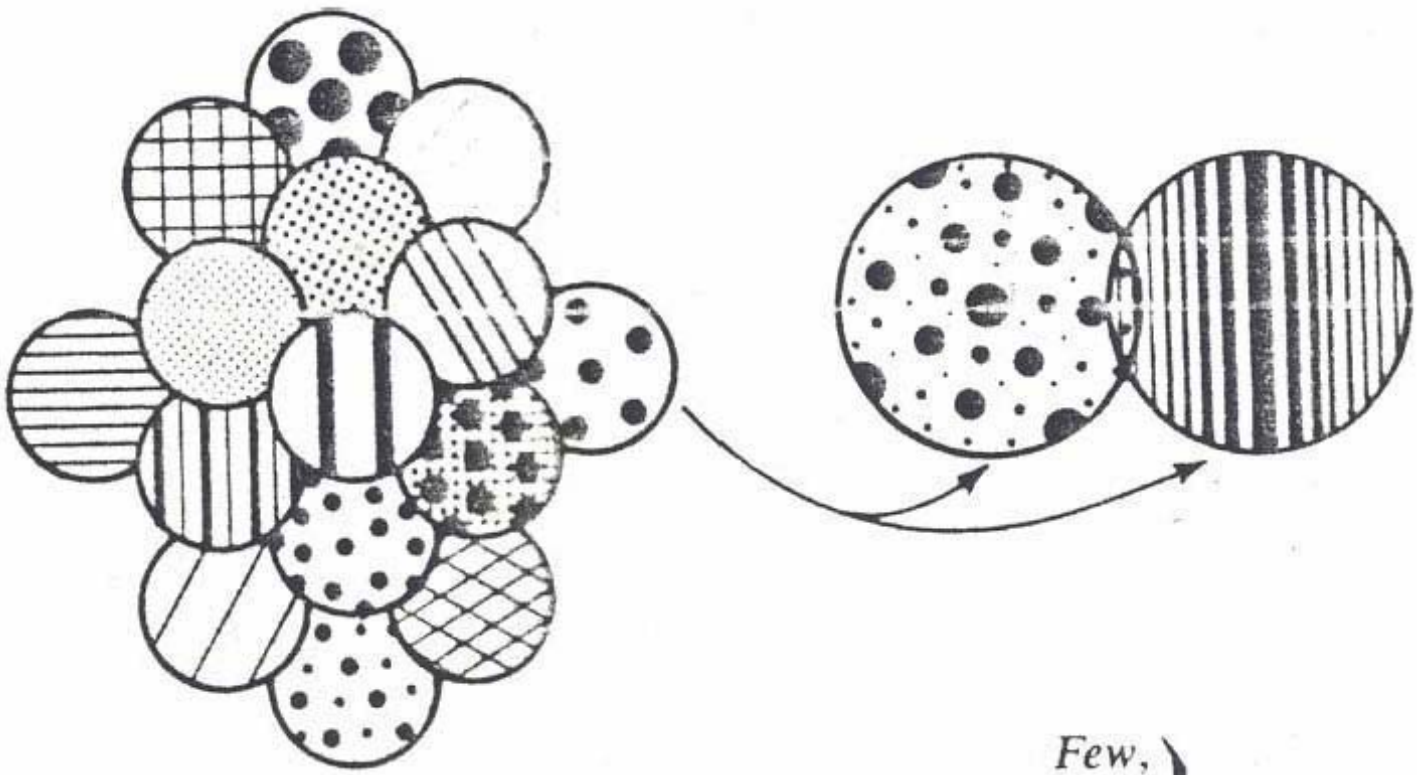
- Epidemioly questionnaires
- Quality of life
- Physical examination
- Bio-electric impendence
- Six minute walking test
- Blood (ADN/ARN, inflammation, oxidative stress)
- Electrocardiogram
- Echocardiogram
- Forced spirometry, corporal plethysmography, DLCO
- Basal gasometry
- Rx thorax (y TAC)
- Induced sputum
- Tests of muscular function (PIM, PEM, hand dynamometry)
- Visit 1 involves 4 visits.

Características (N: 342)	I n=19 (5.6%)	II n=164(48.0 %)	III n=132(38.6 %)	IV n=27 (7.9%)	p
Disnea (MMRC), m (DE)	1.73 (1.36)	2.29 (1.25)	2.88 (1.29)	3.74 (1.19)	<0.001
RV/TLC (%), m (DE)	44.5 (9.4)	51.5 (8.5)	60.3 (8.0)	67.7 (7.7)	<0.001
DLCO (% ref.), m (DE)	90.7 (18.4)	70.2 (17.9)	59.4 (18.4)	41.4 (21.1)	<0.001
PBD positiva, n (%)	9 (50.0)	36 (22.9)	23 (18.0)	1 (4.0)	0.003
PaO2 (mmHg), m (DE)	82.1 (10.9)	76.5 (10.8)	71.9 (9.5)	67.3 (7.6)	<0.001
PaCO2(mmHg), m (DE)	39.8 (4.3)	40.4 (4.8)	42.8 (5.4)	46.2 (5.2)	<0.001
6MWD (m), mediana (IQ)	460.0 (389.9-540.0)	442.6 (390.0-510.0)	441.0 (396.5-504.3)	417.5 (337.0-466.8)	0.119
IMC (Kg/m^2), m(DE)	29.1 (5.2)	29.2 (4.4)	27.7 (4.5)	23.9 (4.3)	<0.001
Índice de BODE, mediana (IQ)	0 (0-1)	1 (1-2)	3 (2-5)	5 (4-7)	<0.001

Analysis

1. List of dimensions and variables in each dimension
2. Factor analysis to reduce the number of variables in each dimension (still keeping most of the variance)
3. Cluster analysis to group subjects according to distance between factors selected

GENERAL PURPOSE OF FACTOR ANALYSIS



Lung function

Variable	1	2	3	4	5	6
fvcp postv~5	-0.00860	0.20311	**-0.84627**	0.04117	-0.16746	0.18251
fevp postv~5	0.41401	0.12214	**-0.75548**	0.16065	0.23694	0.02699
quo calcpo~5	0.58188	-0.02571	-0.22665	0.17410	0.46394	-0.15569
inc fvcv1F~5	-0.06586	**0.91629**	0.01971	-0.03586	-0.04380	0.06372
incp fvcv1~5	-0.11791	**0.92286**	0.09084	-0.04833	-0.01416	0.01317
inc fevv1F~5	0.03080	**0.87721**	-0.17269	0.02176	0.13396	-0.06804
incp fevv1~5	-0.11800	**0.90452**	0.03248	-0.02170	0.03111	-0.09469
vc prepv1F~5	0.07313	-0.09780	**-0.90956**	0.04714	-0.04991	0.15661
ic prepv1F~5	0.15382	-0.07724	**-0.79916**	-0.04816	0.20203	0.10124
tgv prepv1~5	**-0.96231**	0.08967	0.04178	-0.01044	-0.14548	-0.02842
rv prepv1F~5	**-0.94329**	0.09712	0.09486	-0.06462	-0.03218	-0.07574
tlc prepv1~5	**-0.89419**	0.03707	-0.36632	-0.04498	-0.06813	0.02944
rv tlcv1FFP5	**-0.71197**	0.11971	0.55187	-0.09426	0.05314	-0.09908
ic tlcv1FFP5	0.64803	-0.07294	-0.53081	0.00777	0.22768	0.06881
dlco vspFFP5	0.06050	0.07331	-0.31460	0.12055	**0.88489**	0.04393
va vspv1FFP5	-0.22915	-0.01279	-0.74378	0.11815	0.08704	-0.21158
kco vspv1F~5	0.20455	0.07115	0.10932	0.05598	**0.88948**	0.17870
po2 v1FFP5	0.07746	-0.04921	-0.14133	**0.92154**	0.10935	0.26185
pco2 v1FFP5	-0.02195	-0.00142	0.28370	-0.08725	-0.04973	**-0.80963**
ph v1FFP5	-0.02855	-0.02703	-0.01566	0.05506	0.01405	**0.80316**
satc v1FFP5	0.05155	0.02435	-0.14437	0.72610	0.08578	0.52223
ch v1FFP5	-0.10205	0.07100	-0.10132	-0.12521	-0.32091	-0.41412
gradalv1FFP5	-0.08711	0.04946	-0.01690	**-0.94872**	-0.08234	0.13685

hiperinsuflación

hiperreactividad

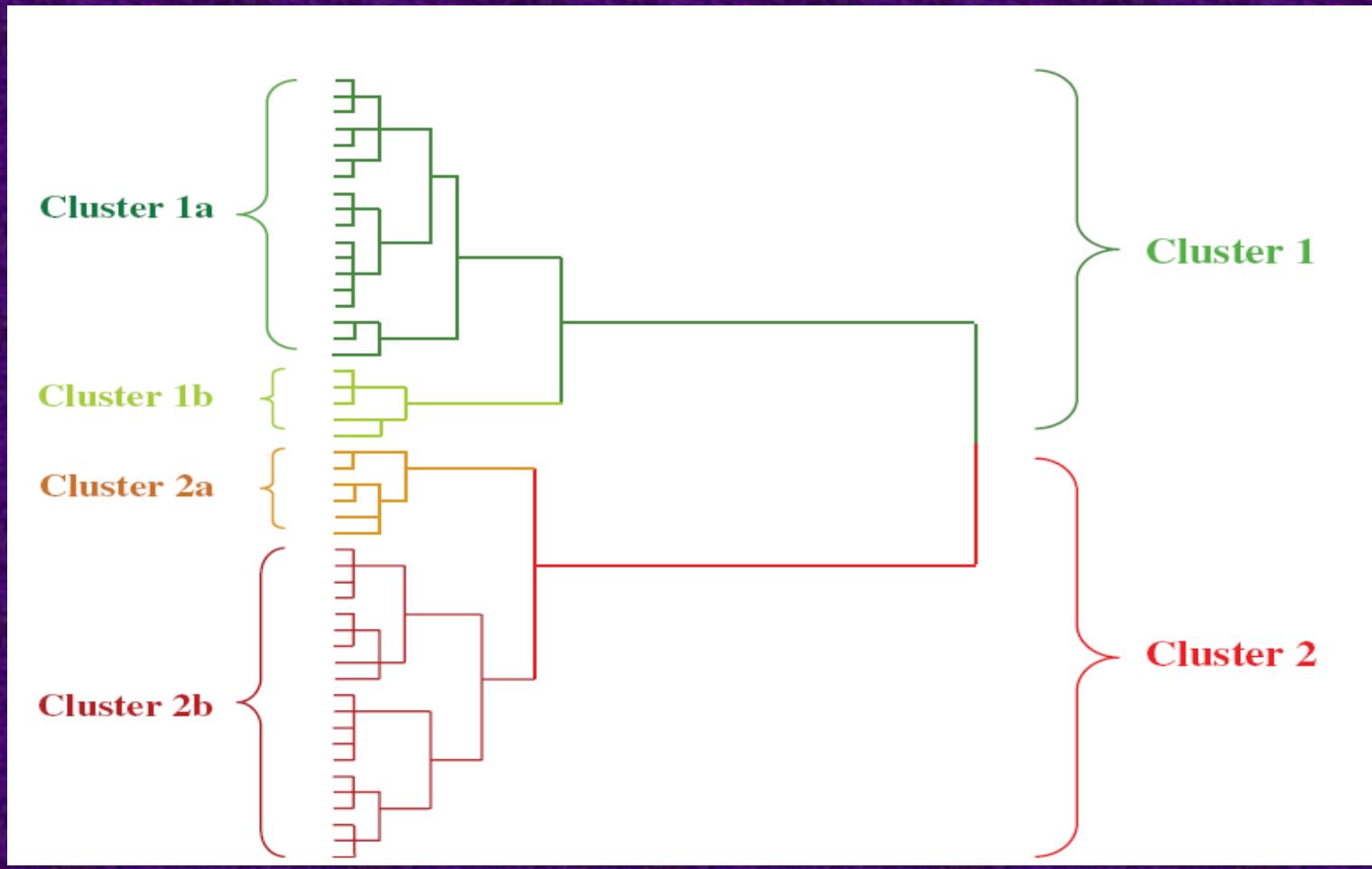
obstrucción

oxigenación

difusión de gases

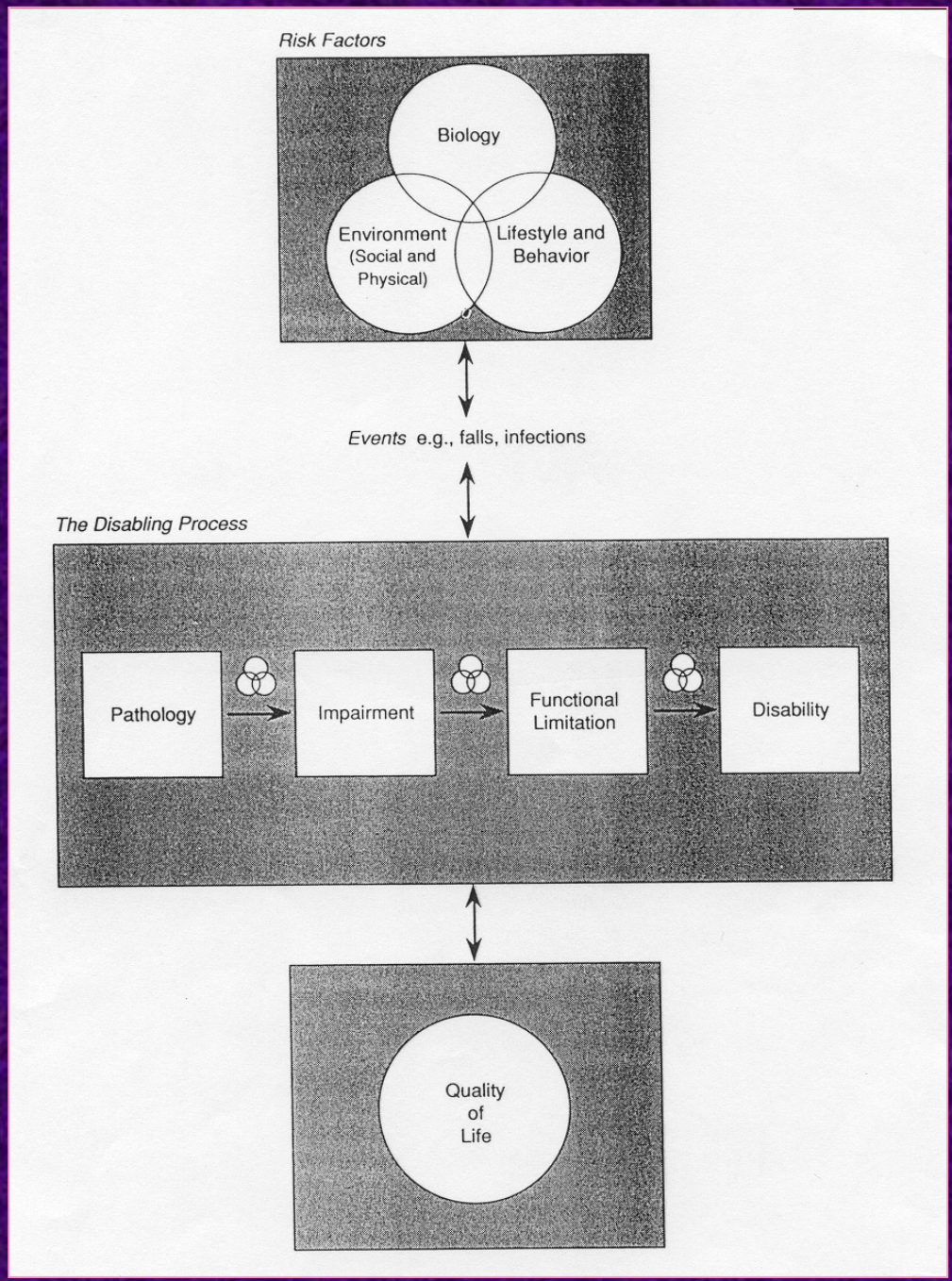
equilibrio AB

Cluster analysis

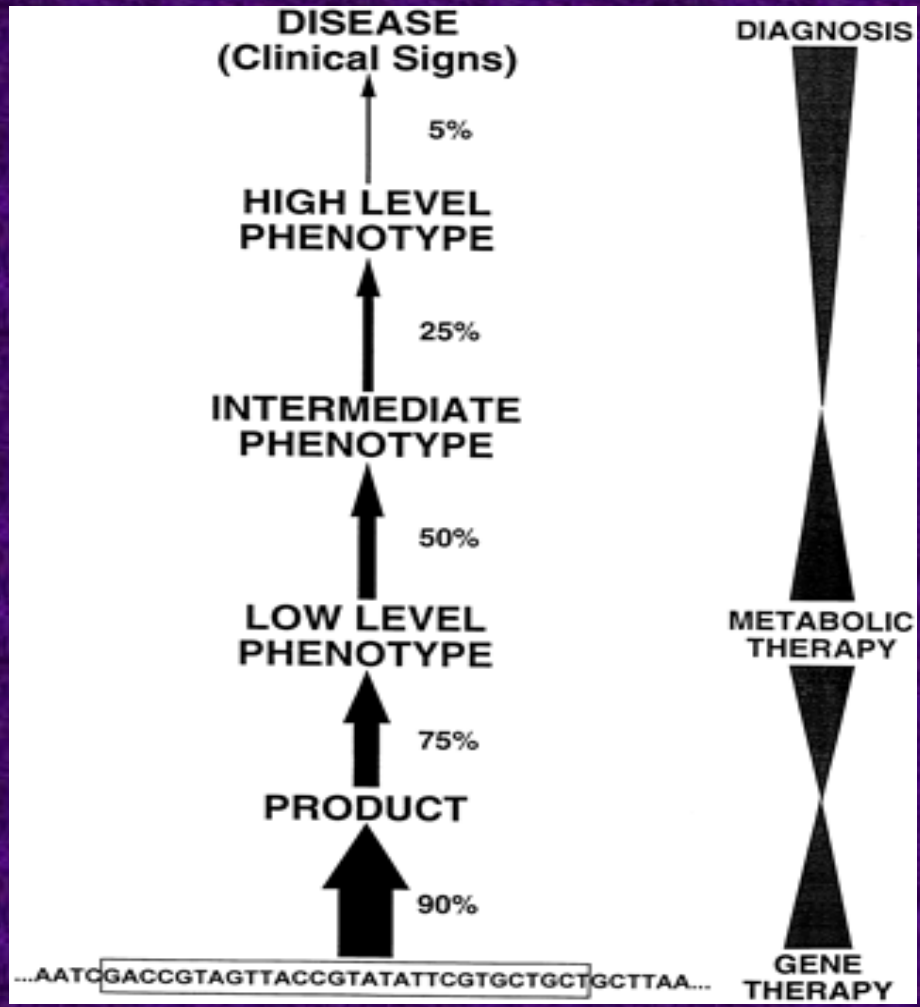


Análisis descriptivo de la heterogeneidad

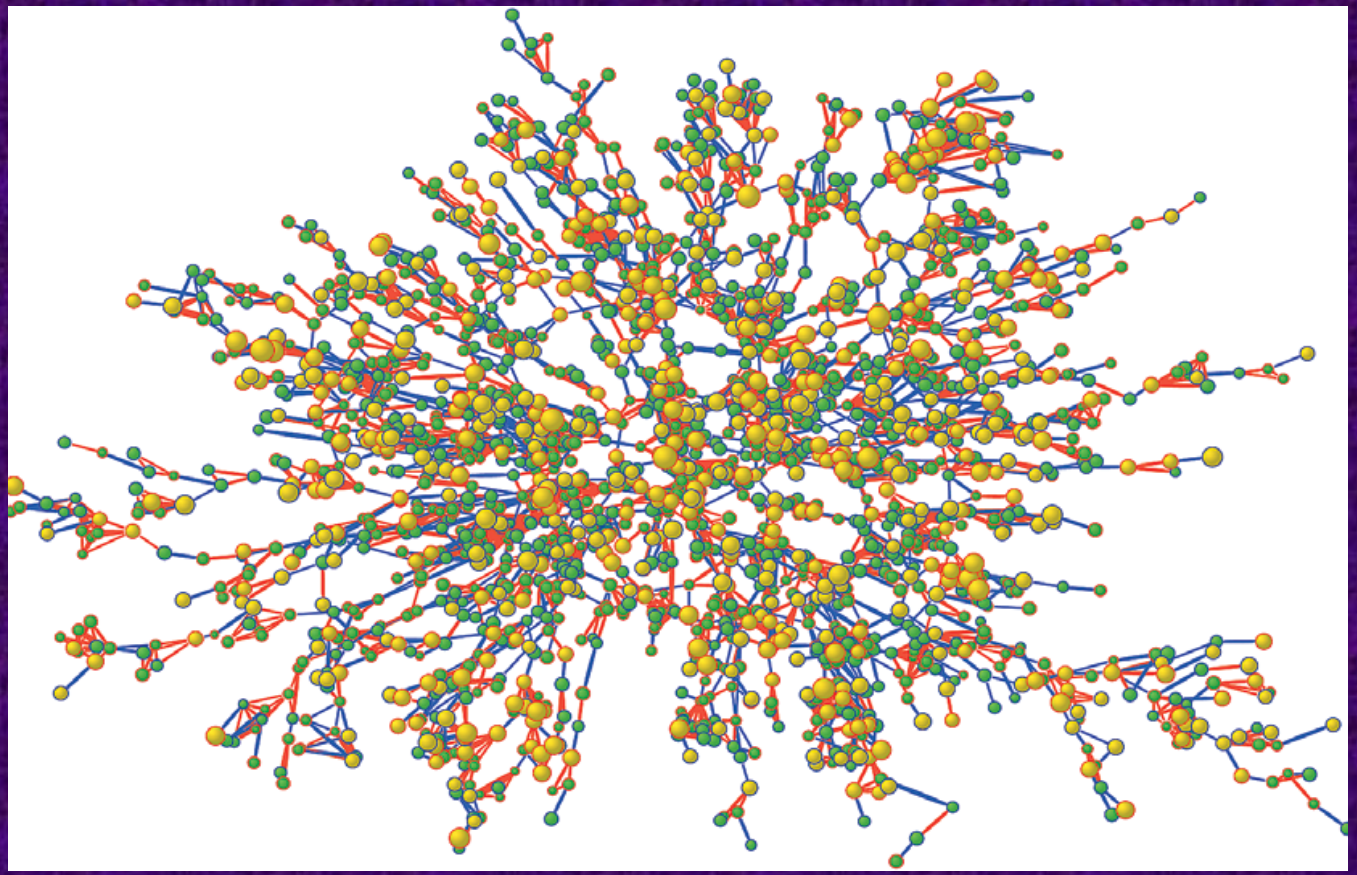
- Total variables 400
- Variables incluidas en el factorial 240
- Modelos factoriales 14
- Factores independientes 60
- Análisis de clusters 4 agrupaciones


Risk Factors
Biology
Environment (Social and Physical)
Lifestyle and Behavior
Events e.g., falls, infections
The Disabling Process
Pathology
Impairment
Functional Limitation
Disability
Quality of Life

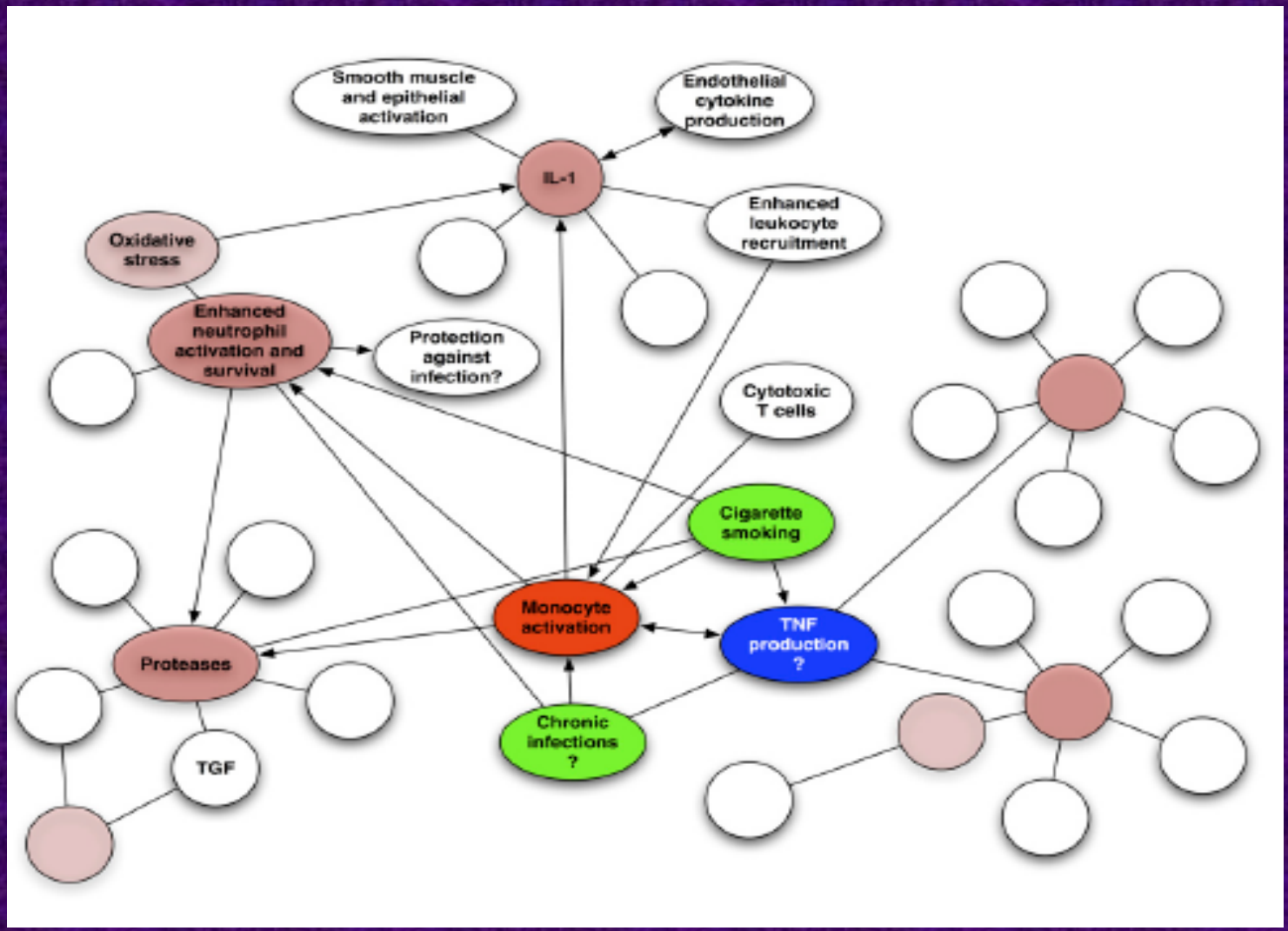
Phenomics: from systematic gene manipulation to complex phenotype dissection



The spread of obesitity in a large social network over 32 years. Christakis NA et al. NEJM 2007



Sabroe I et al. Models of COPD. Proc Am Thorac Soc. 2007



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