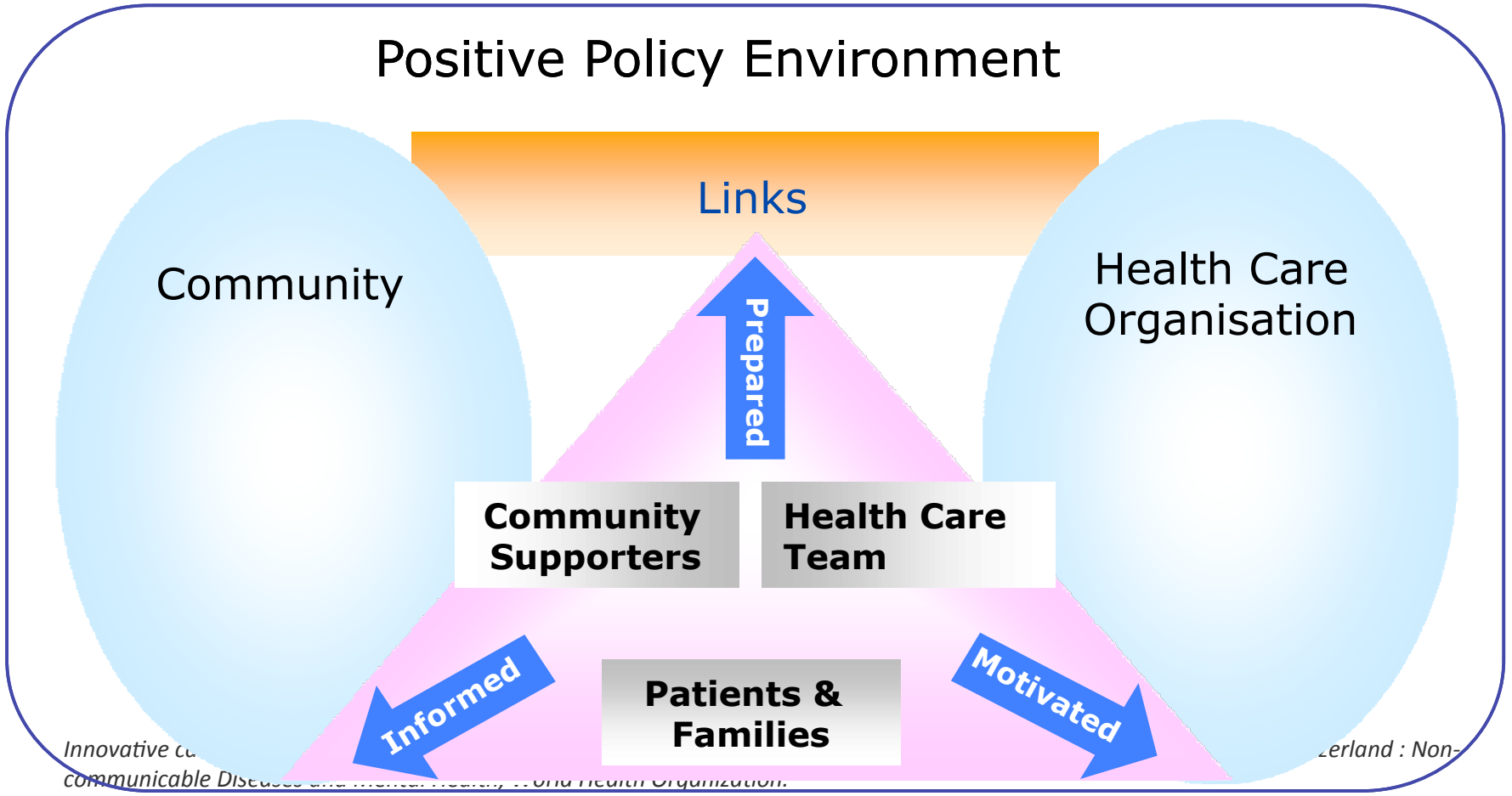
Integrating Care for Chronic Conditions: Toward a Systems Medicine Approach

Hospital Clinic.IDIBAPS.LINKCARE. University of Barcelona

Need for Health System Redesign deploying the Chronic Care Model



Innovative c… …erland : Non-communicable Diseases and Mental Health. World Health Organization.

Better Outcomes for Chronic Conditions

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4C medicine

Continuous processes

Communication

Collaboration

Confidentiality

4P medicine

Predictive

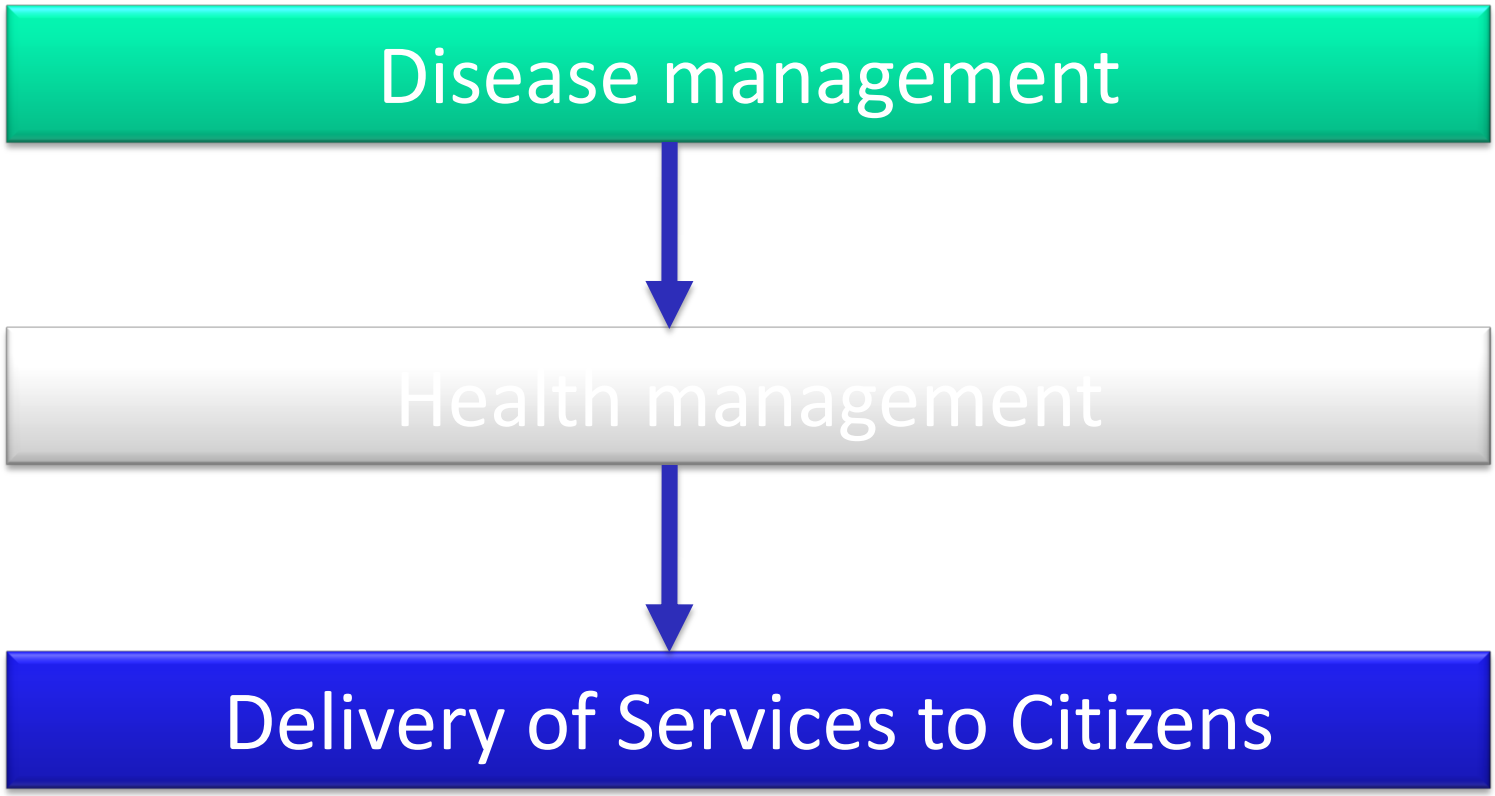
Personalized

Preventive

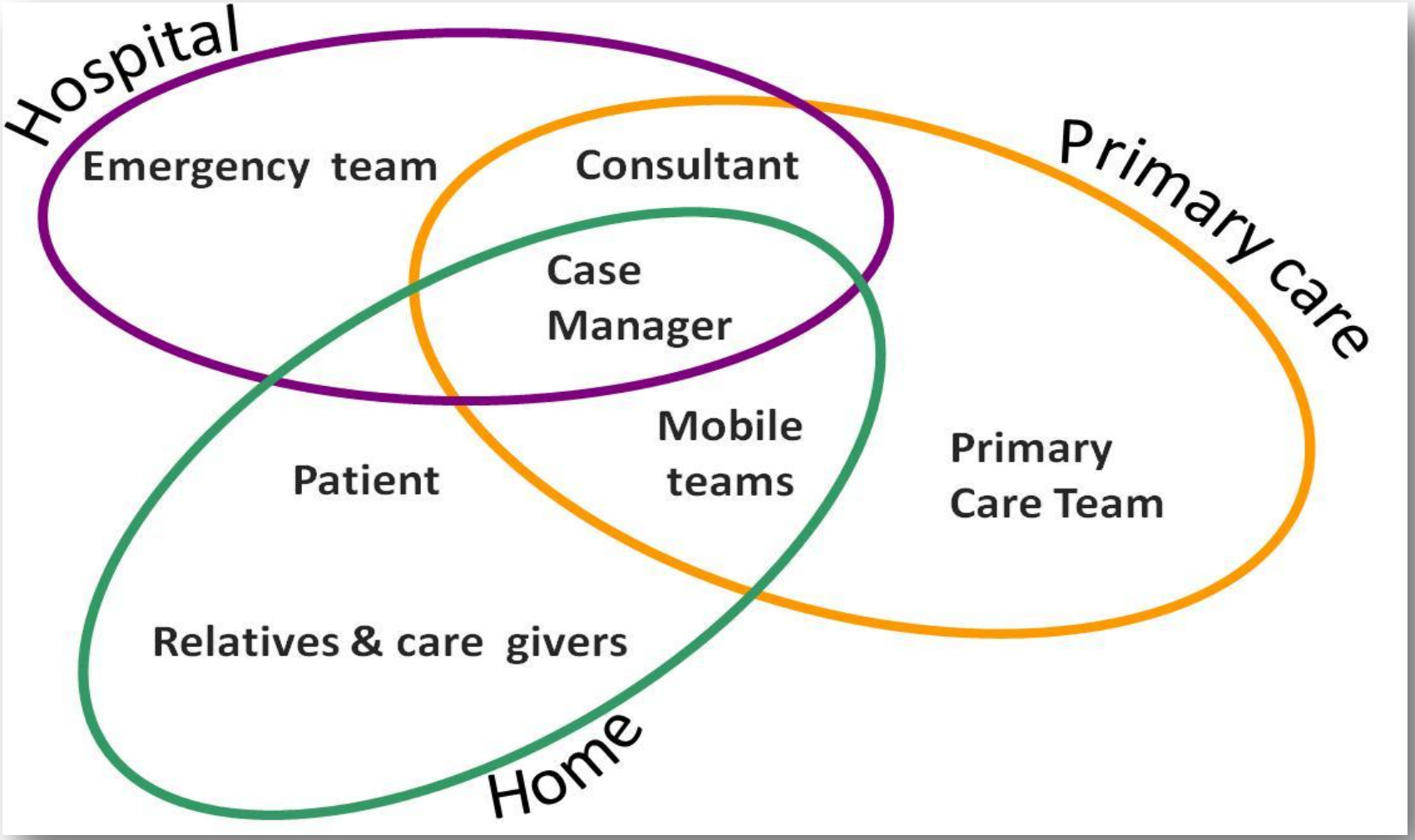
Participatory

Efficient patient management
Modulation of disease progress

Paradigm Change

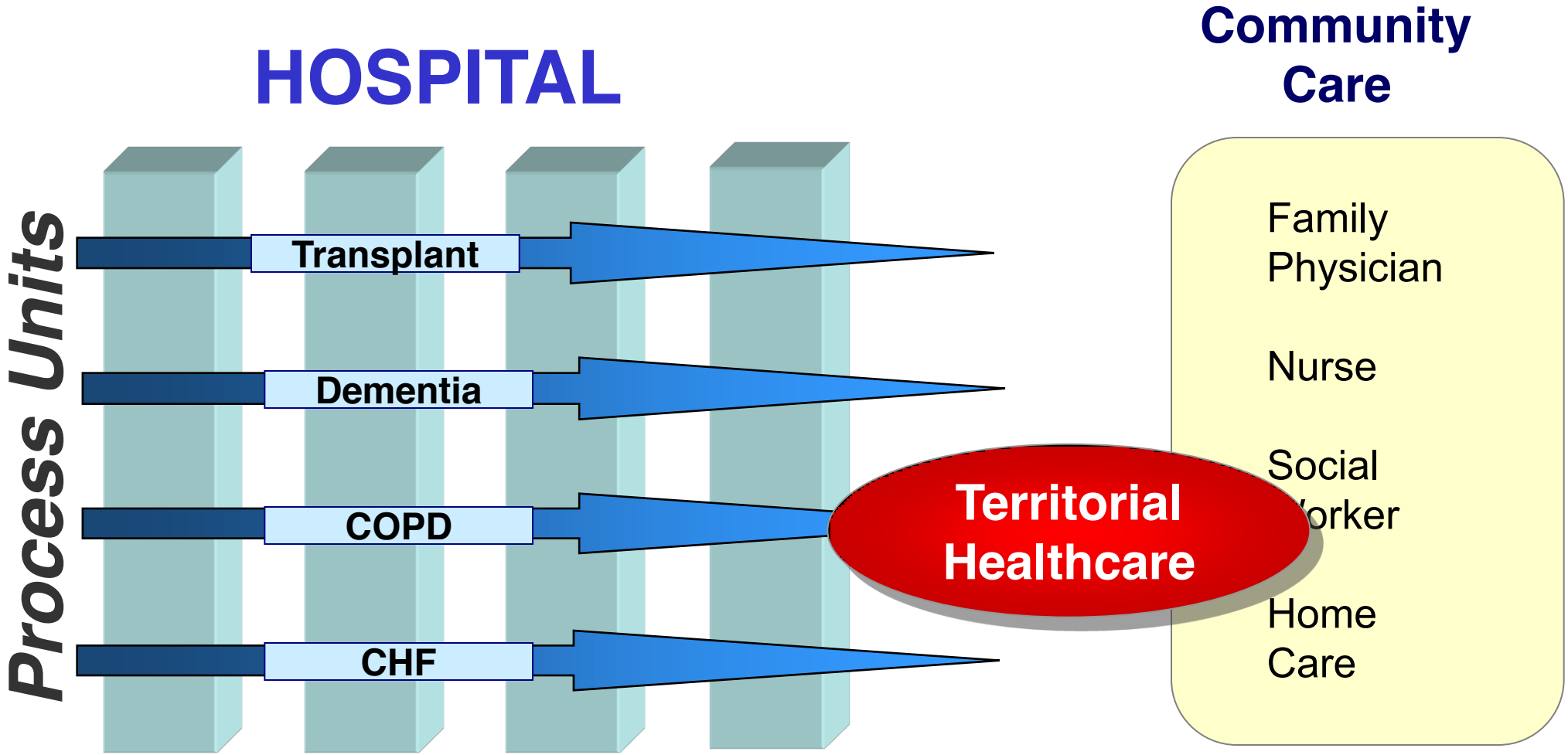


Redefinition of roles



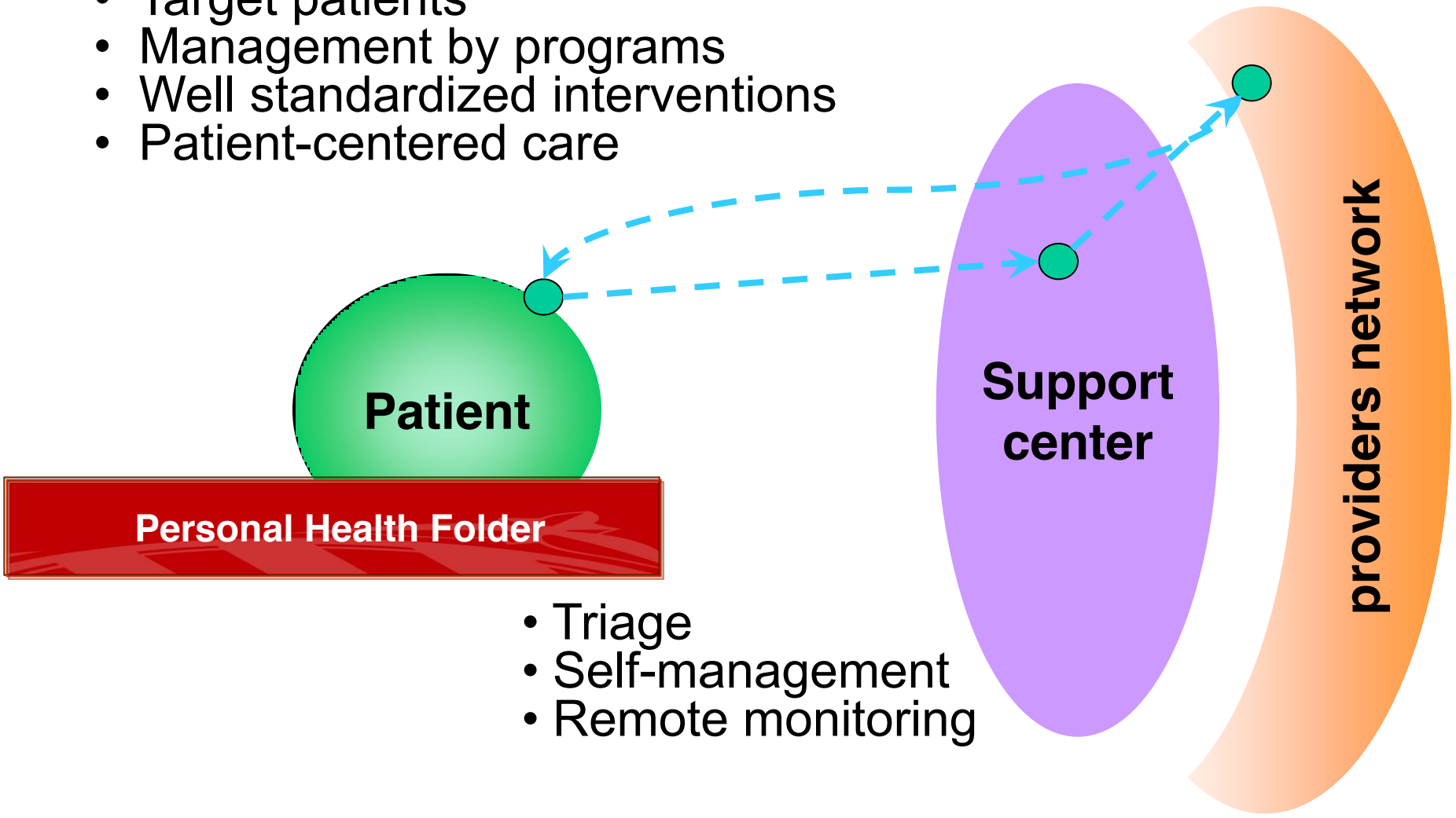
Deployment at Barcelona-Esquerra

Transferring Complexity to Primary Care and Home



Service model

- Target patients
- Management by programs
- Well standardized interventions
- Patient-centered care

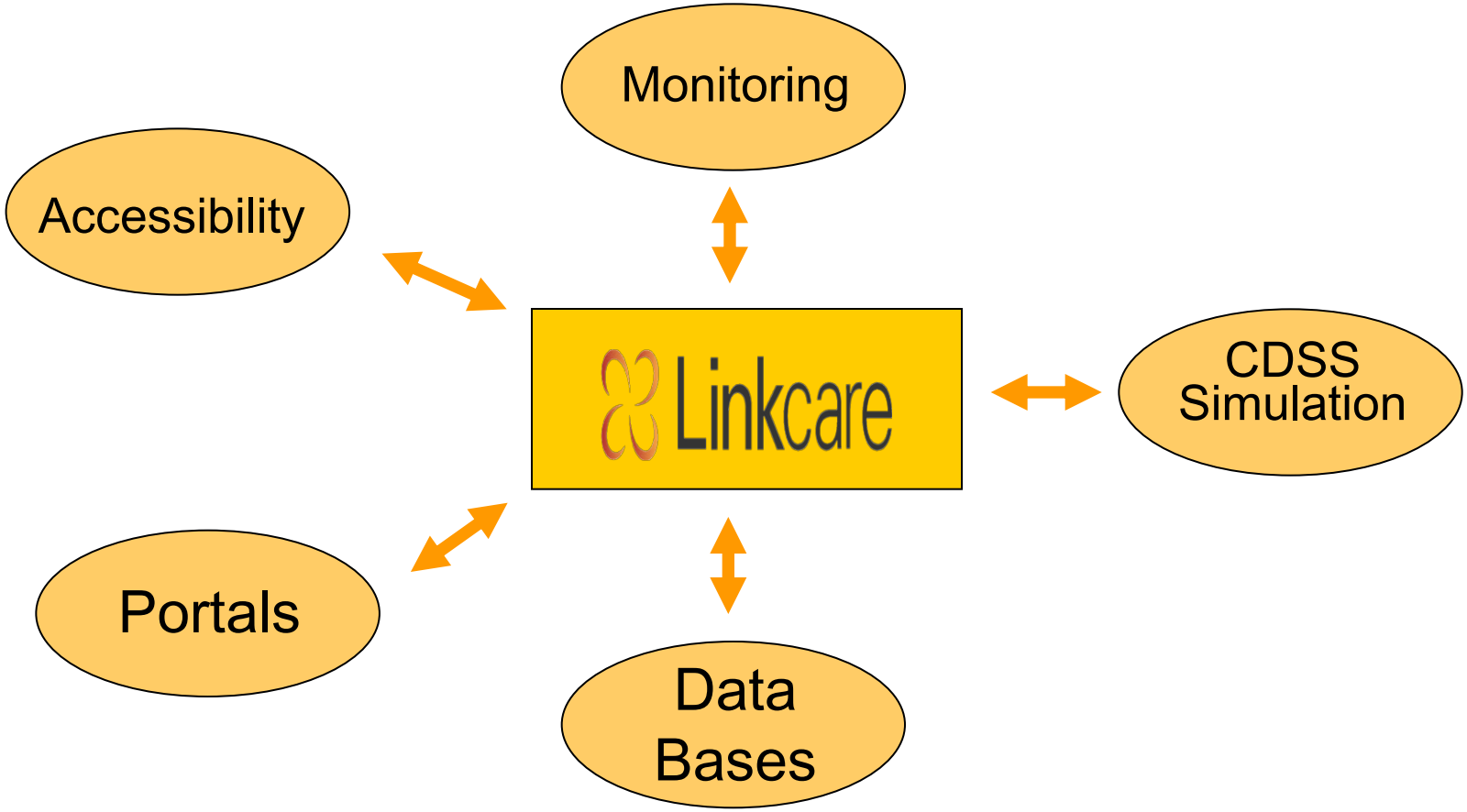


- Triage
- Self-management
- Remote monitoring

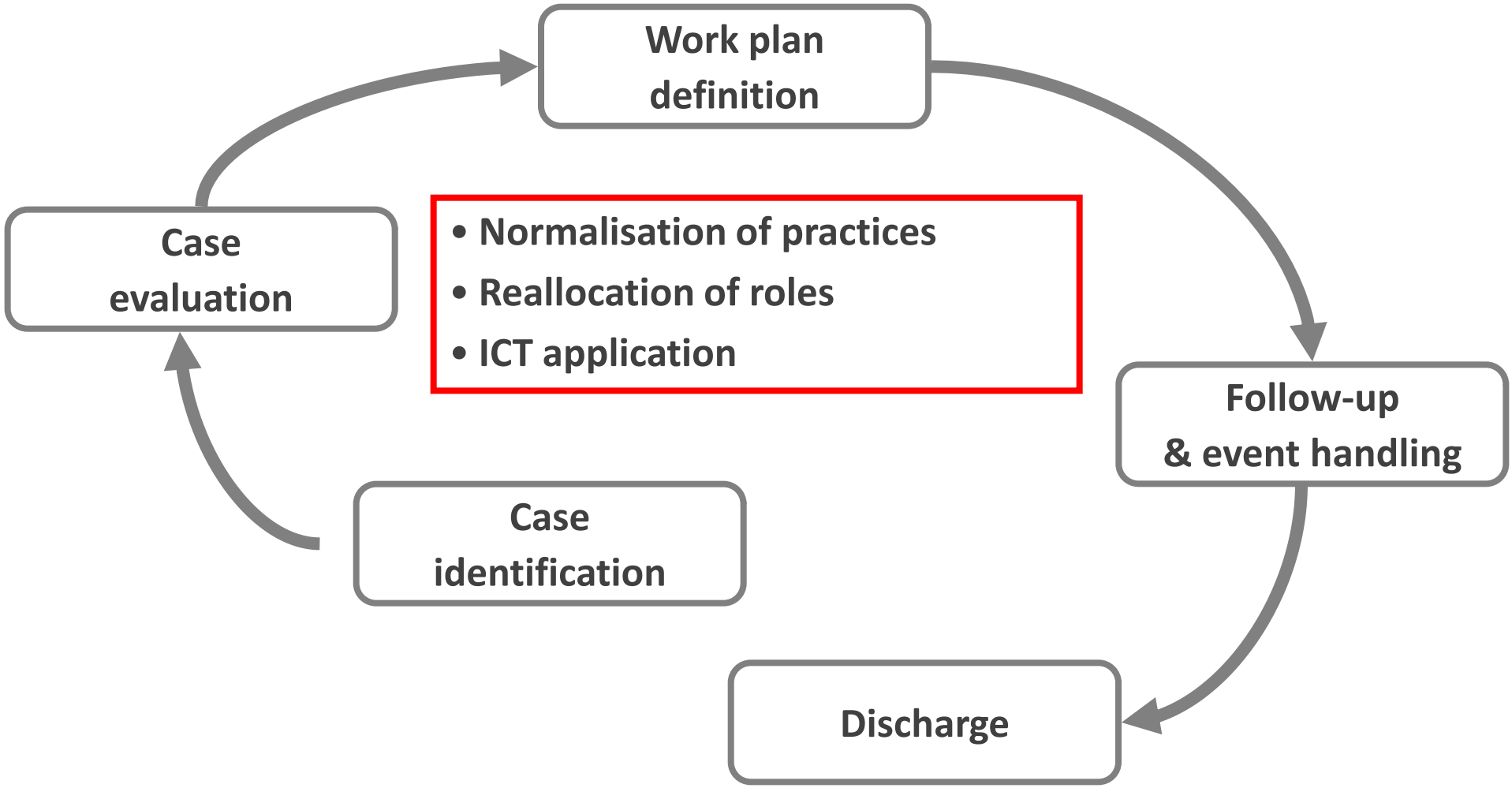
Linkcare vision

- **Web-based application addressed to management of chronic patients**
- **Platform supporting extensive use of services: modular, scalable and robust**
- **Potential for integration with a diversity of HIS and mobile systems**
- **Facilitating organizational interoperabiliy**
- **Prepared to support knowledge management applications**

Scheme


Monitoring
Accessibility
Linkcare
CDSS Simulation
Portals
Data Bases

Integrated Care Programs



Current Deployment at Barcelona Esquerra (AISBE)

Wellness & Rehabilitation

Frailty - Transitional care - Palliative care

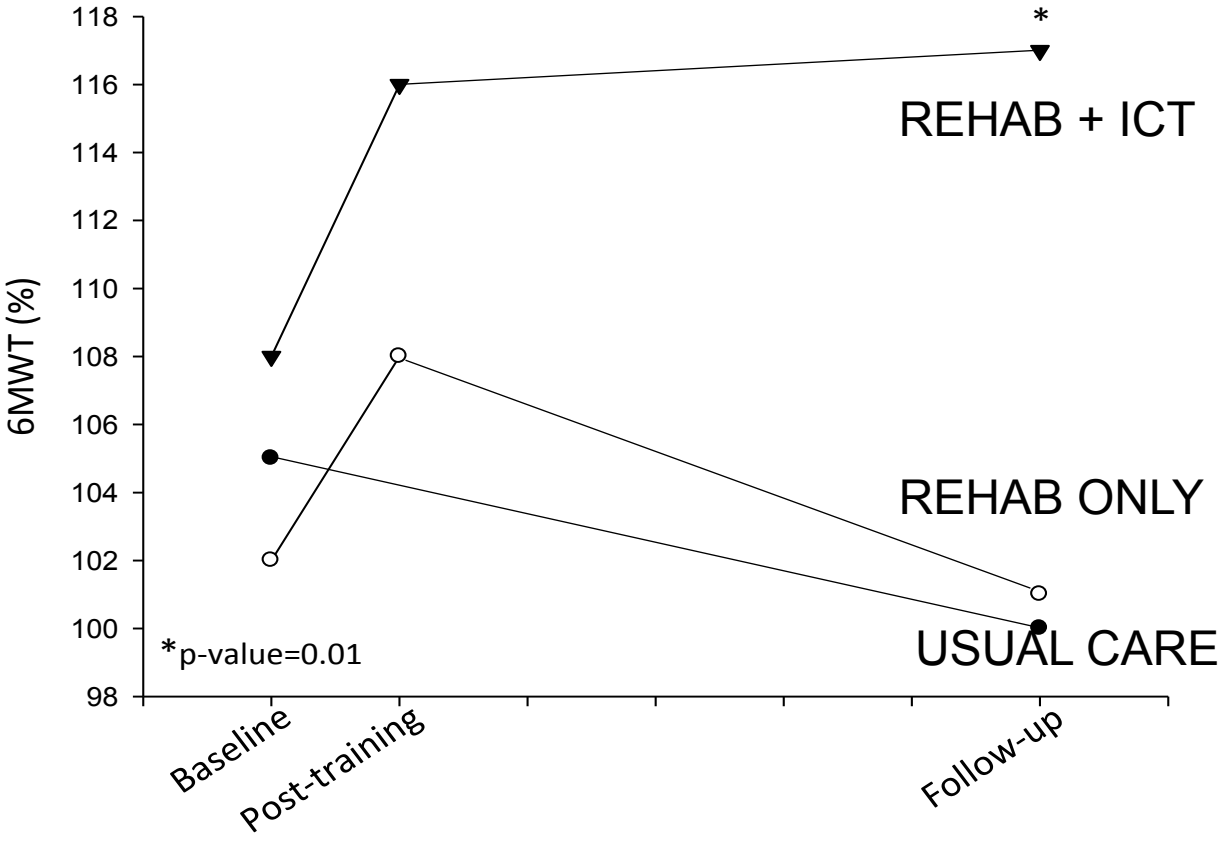
Home hospitalisation

Support

Wellness & Rehabilitation

BCN data

- Results: Sustainability of aerobic capacity, increased daily life activities and enhanced health-related quality of life



Baecke Total Score

p= 0.03

SGRQ Total Score

p= 0.02

Need for stratification by patient's risk profile

current practice

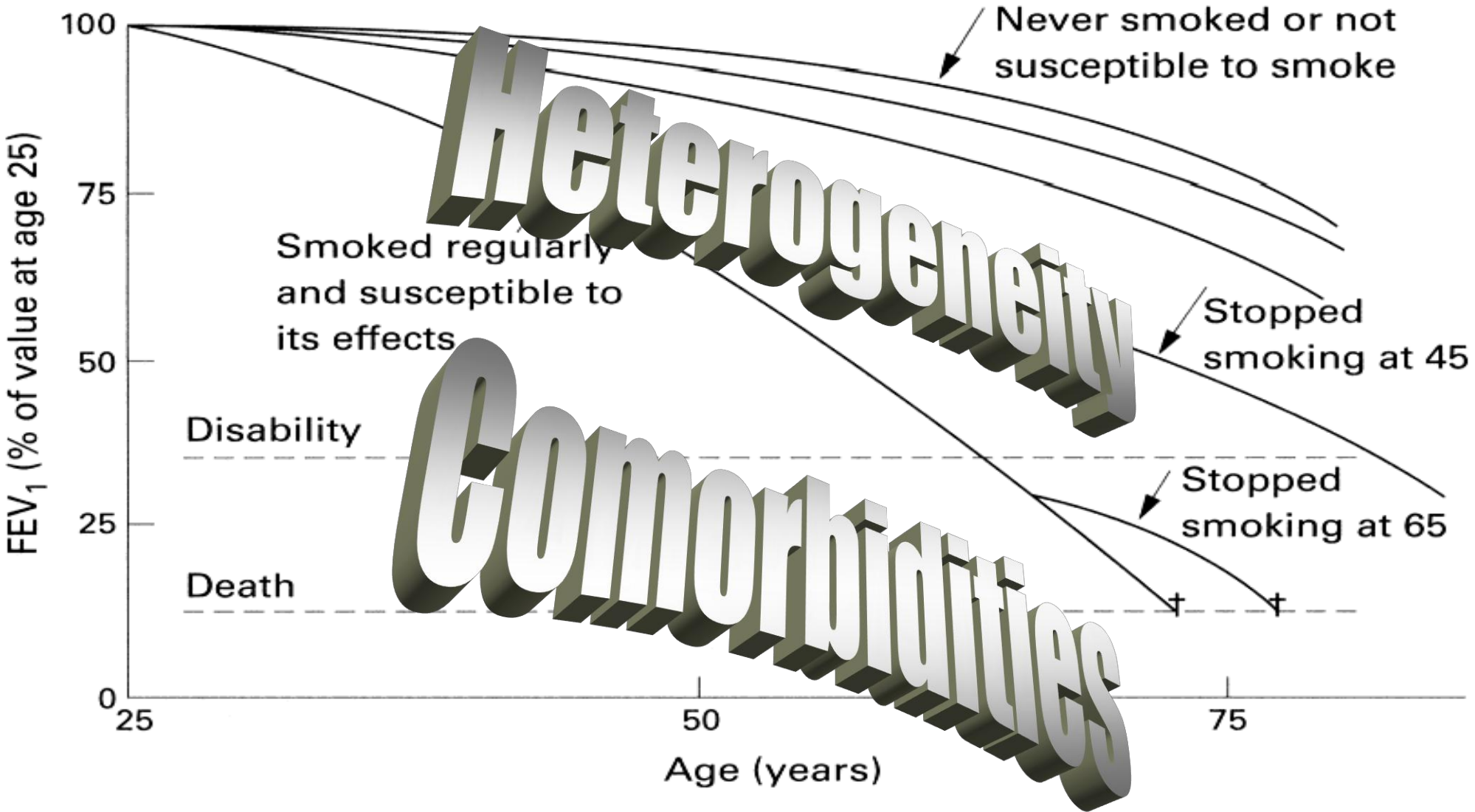
Based on patient's use of healthcare resources

future

Early identification of determinants of disease phenotypes

~ 20% Smokers show susceptibility for COPD

~ 20% COPD patients show low muscle mass (poor prognosis)

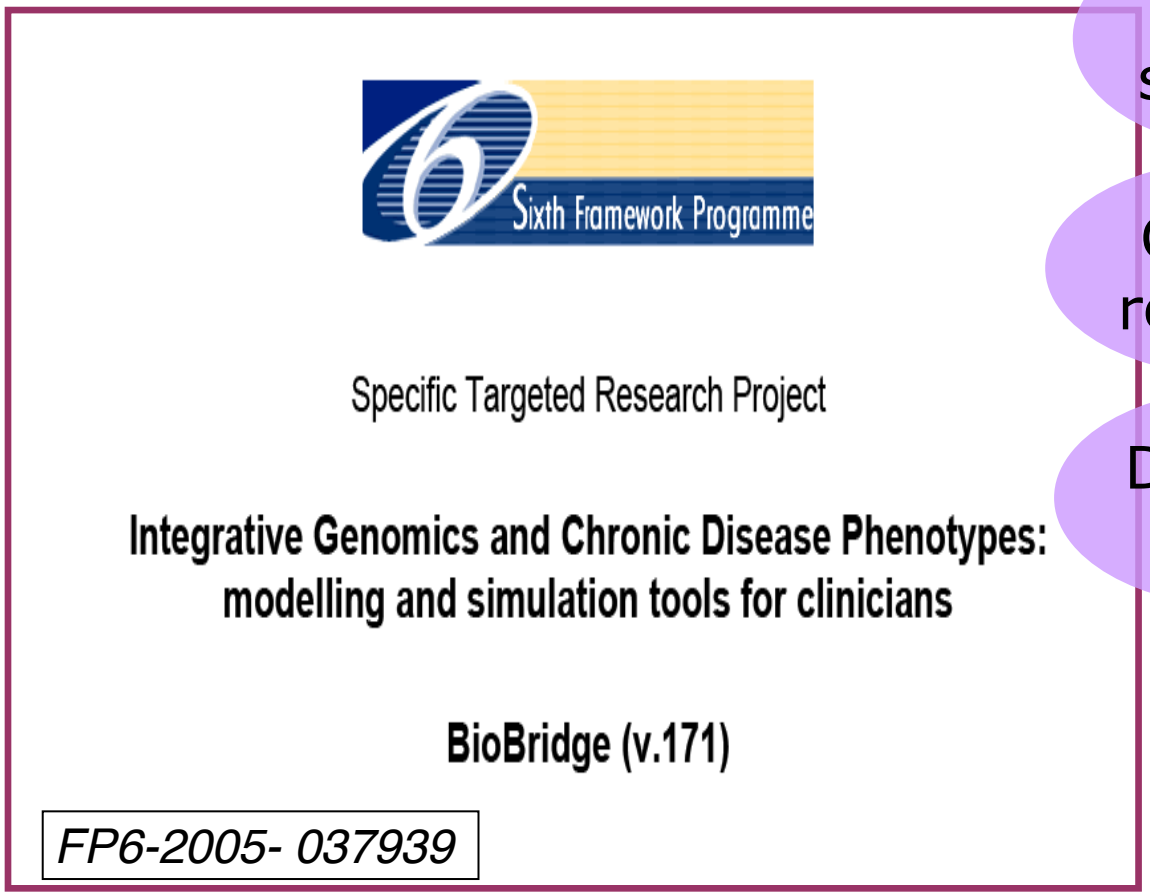


Biobridge project

(FP6-2005-LIFESCIHEALTH-7, Contract nº 037939)

www.biobridge.eu

December 2006 to June 2009



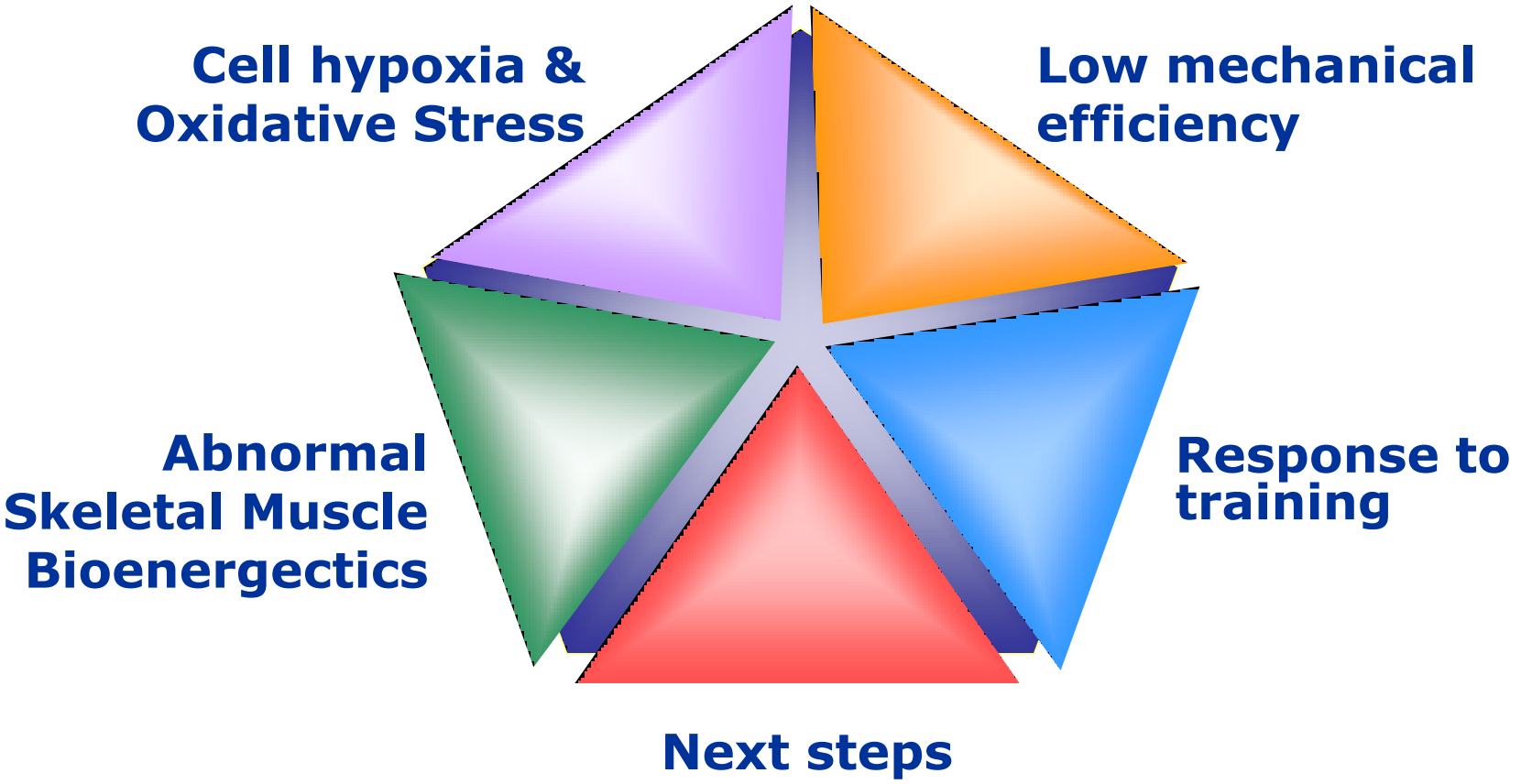
Basic science

Clinical research

Delivery of care

Skeletal Muscle Bioenergetics

Health & COPD


Cell hypoxia &
Oxidative Stress
Low mechanical
efficiency
Abnormal
Skeletal Muscle
Bioenergectics
Response to
training
Next steps

COPD patients

evidence of abnormal muscle redox

Naimi et al Clin Physiol Func Imaging 2011;31:124-31
Rabinovich et al Eur Respir J 2007;29(4):643-50.
Wagner PD Eur Respir J 2008; 31(3):492-501.
Semenza GL N England J Med 2011;365:537-47.
Rabinovich RA et al. Am J Respir Crit Care Med 2001; 164(7):1114-1118.
Rabinovich RA et al Respiration 2006; 73(6):757-761.
Barreiro E et al Thorax 2009; 64(1):13-19.
Koechlin C et al Am J Respir Crit Care Med 2004; 169(9):1022-1027.
Heunks LM et al Am J Physiol 1999; 277(6 Pt 2):R1697-R1704.
Rodriguez DA et al Free Radic Biol Med. 2011 Oct 4. [Epub ahead of print]

Is Oxidative Stress a Causal Event ?

Are the effects dependent upon patient susceptibility ?

There is evidence that nitroso-redox unbalance in COPD patients may generate muscle dysfunction

(mechanical-energetic uncoupling)

through post-translational mechanisms

(inhibition of s-nitrosylation)

likely involved in key underlying mechanisms of the systemic effects of the disease

OPEN ACCESS Freely available online PLoS COMPUTATIONAL BIOLOGY

A Systems Biology Approach Identifies Molecular Networks Defining Skeletal Muscle Abnormalities in Chronic Obstructive Pulmonary Disease

Nil Turan[1], Susana Kalko[2], Anna Stincone[1], Kim Clarke[1], Ayesha Sabah[1], Katherine Howlett[3], S. John Curnow[3], Diego A. Rodriguez[2], Marta Cascante[4], Laura O'Neill[3], Stuart Egginton[3], Josep Roca[2], Francesco Falciani[1]*

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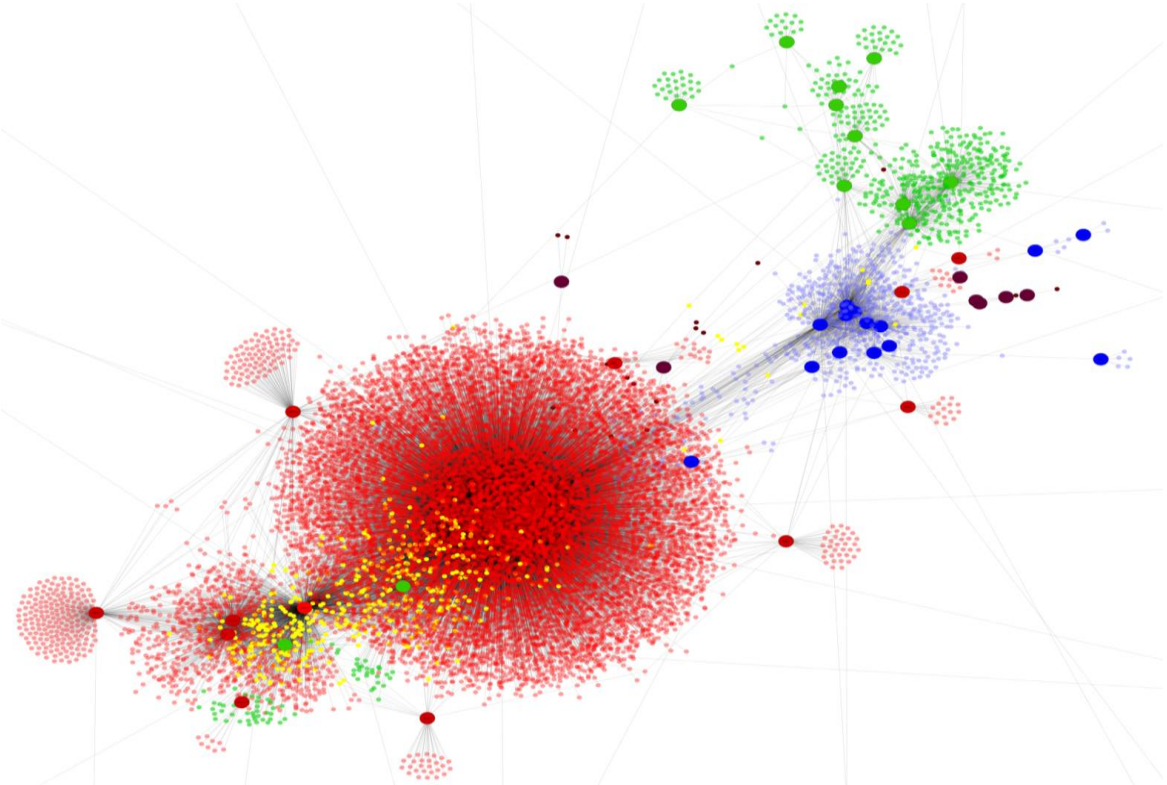


Turan N et al PLoS Comput Biol. 2011;7(9):e1002129.

✓ Abnormal interactions among bioenergetics, inflammation and tissue remodelling

✓ Lower and abnormal expression of genes in skeletal muscle

✓ Epigenetic changes associated to cell oxygenation

Abstract

Chronic Obstructive Pulmonary Disease (COPD) is an inflammatory process of the lung inducing persistent airflow limitation. Extensive systemic effects, such as skeletal muscle dysfunction, often characterize these patients and severely limit life expectancy. Despite considerable research efforts, the molecular basis of muscle degeneration in COPD is still a matter of intense debate. In this study, we have applied a network biology approach to model the relationship between muscle molecular and physiological response to training and systemic inflammatory mediators. Our model shows that failure to co-ordinately activate expression of several tissue remodelling and bioenergetics pathways is a specific landmark of COPD diseased muscles. Our findings also suggest that this phenomenon may be linked to an abnormal expression of a number of histone modifiers, which we discovered correlate with oxygen utilization. These observations raised the interesting possibility that cell hypoxia may be a key factor driving skeletal muscle degeneration in COPD patients.

Turan N et al PLoS Comput Biol. 2011;7(9):e1002129.

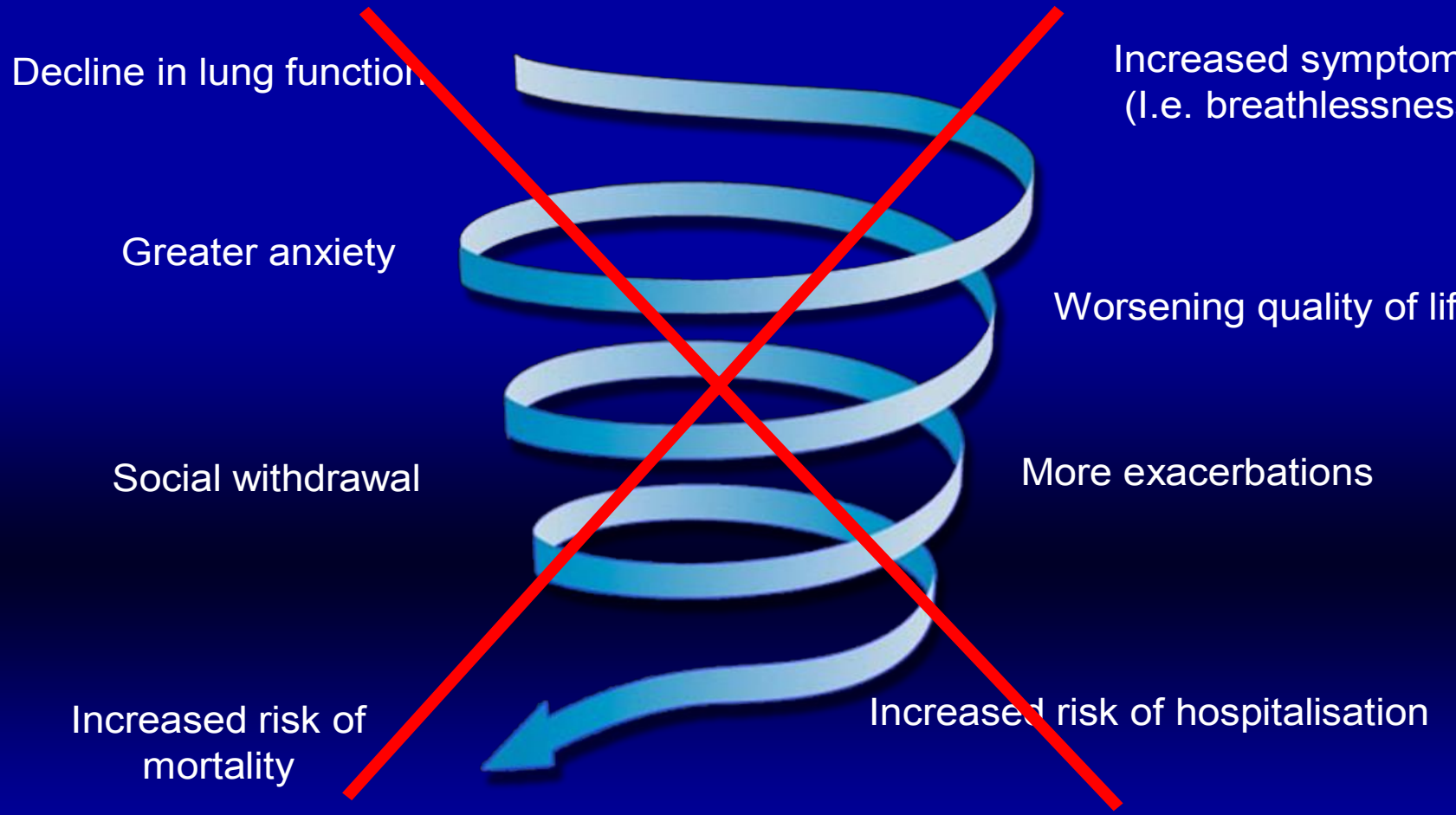
✓ Mitochondrial function is altered in advanced COPD with systemic effects

✓ Physical activity and muscle training should be early interventions in COPD patients

✓ Early identification of patients with increased susceptibility to develop systemic effects should trigger personalized interventions

✓ An integrative approach to disease understanting is needed

Disease Modification to Modulate Disease Progression



Well established clinical recommendations

ACTIVE LIFE STYLE

MUSCLE TRAINING AT EARLY DISEASE STAGES

PAC_COPD

Study aims

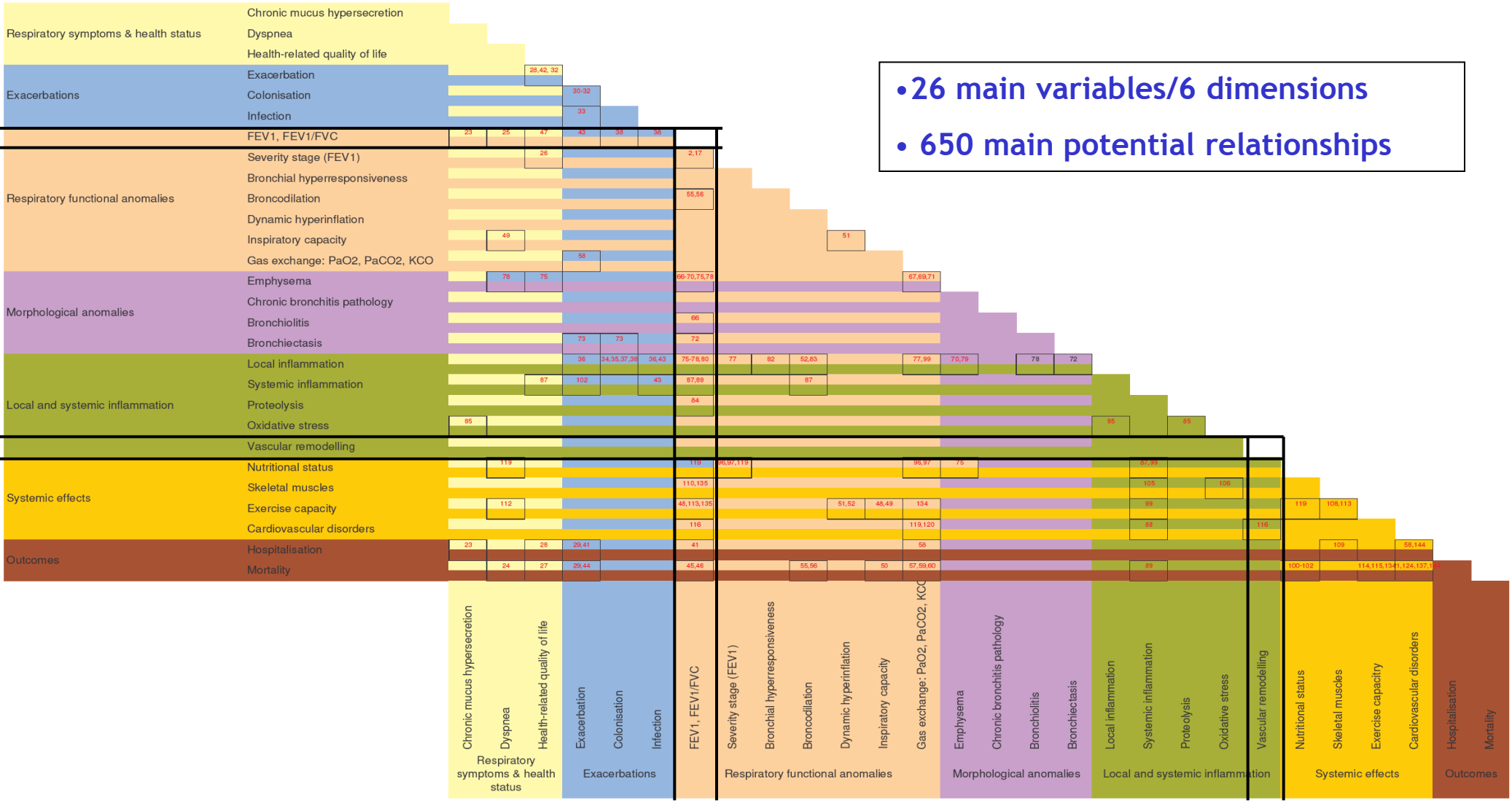
Identification and prospective validation of clinically relevant chronic obstructive pulmonary disease (COPD) subtypes

Garcia-Aymerich J et al ***Thorax*** *2011 May;66(5):430-7*

Hypothesis

- ✓ COPD at the time of a first hospital admission shows a wide variability on its physio-pathological and clinical characteristics
- ✓ Phenotypical heterogeneity in COPD can be classified in clinical / epidemiologically relevant subtypes
- ✓ These subtypes will differ on its clinical and functional course, use of services and survival

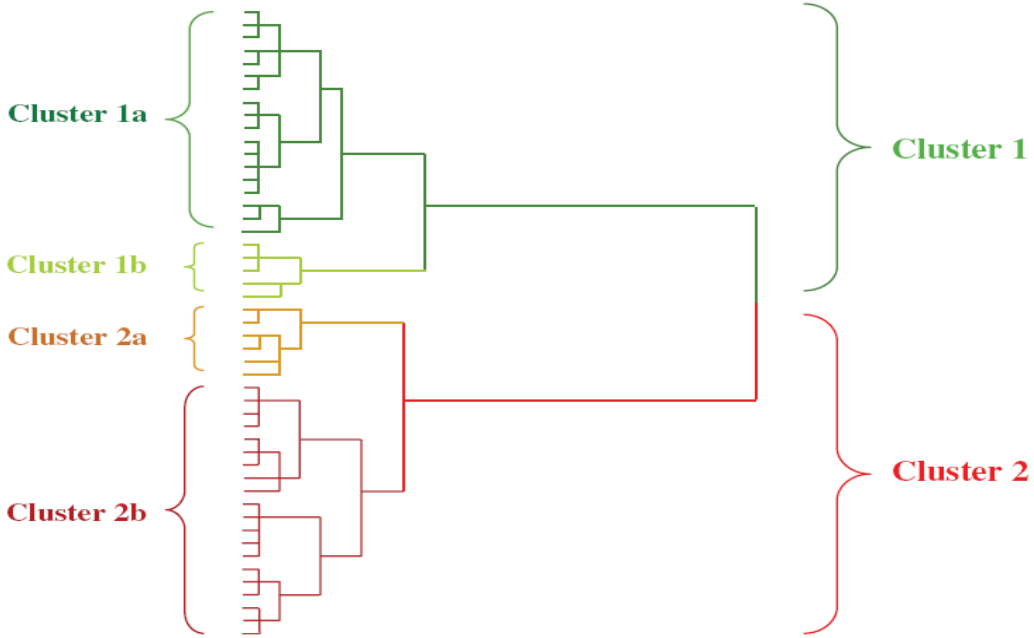
6 main dimensions

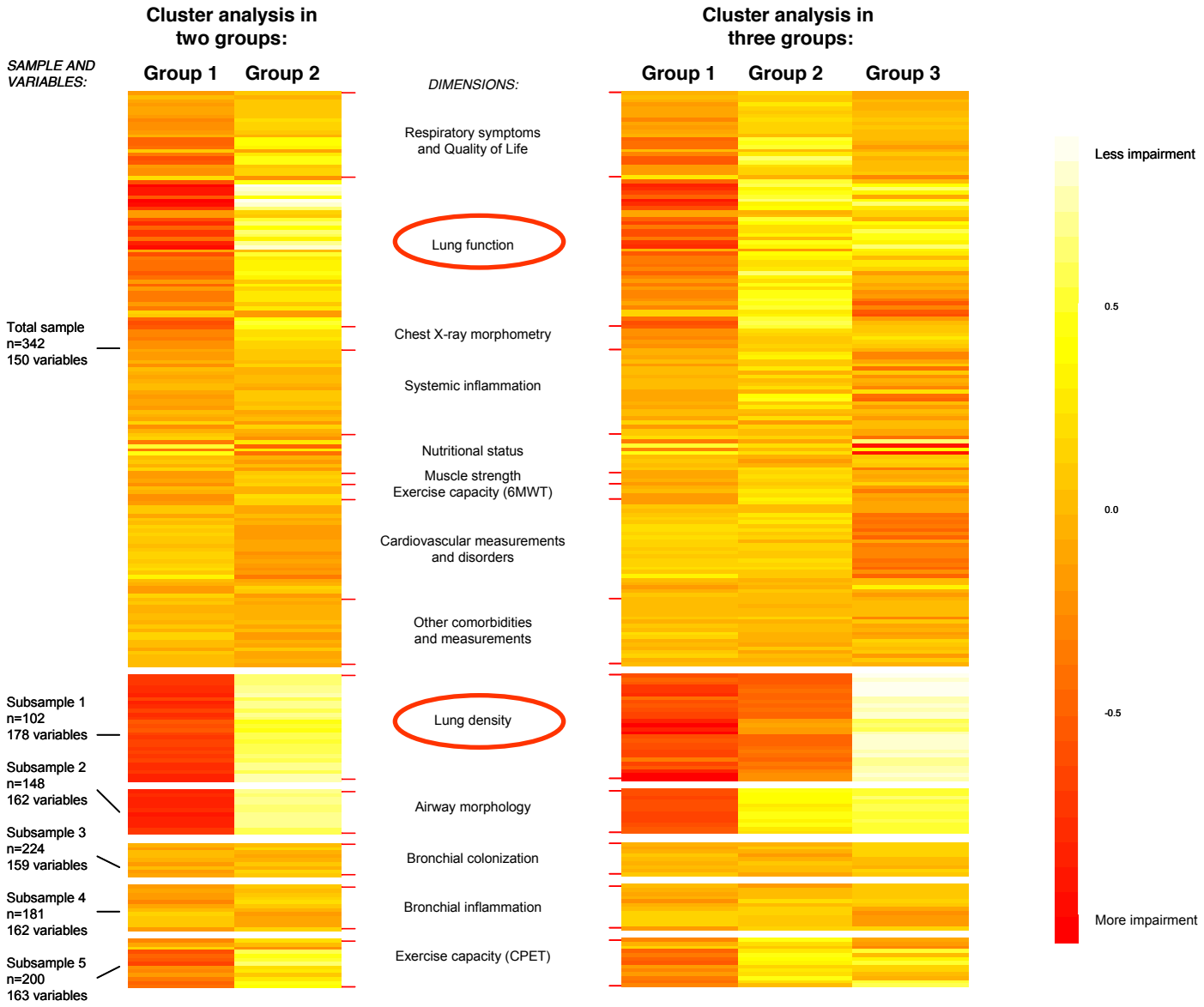


- 26 main variables/6 dimensions
- 650 main potential relationships

Analysis

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




Cluster analysis in two groups:
Cluster analysis in three groups:
SAMPLE AND VARIABLES:
Group 1
Group 2
Group 3
DIMENSIONS:
Respiratory symptoms and Quality of Life
Lung function
Chest X-ray morphometry
Systemic inflammation
Nutritional status
Muscle strength
Exercise capacity (6MWT)
Cardiovascular measurements and disorders
Other comorbidities and measurements
Lung density
Airway morphology
Bronchial colonization
Bronchial inflammation
Exercise capacity (CPET)
Total sample n=342 150 variables
Subsample 1 n=102 178 variables
Subsample 2 n=148 162 variables
Subsample 3 n=224 159 variables
Subsample 4 n=181 162 variables
Subsample 5 n=200 163 variables
Less impairment
0.5
0.0
-0.5
More impairment

Summary results

Group 1 - Severe Respiratory COPD

(n=126, 67 yrs, FEV1 38% pred)
all respiratory domains severely altered

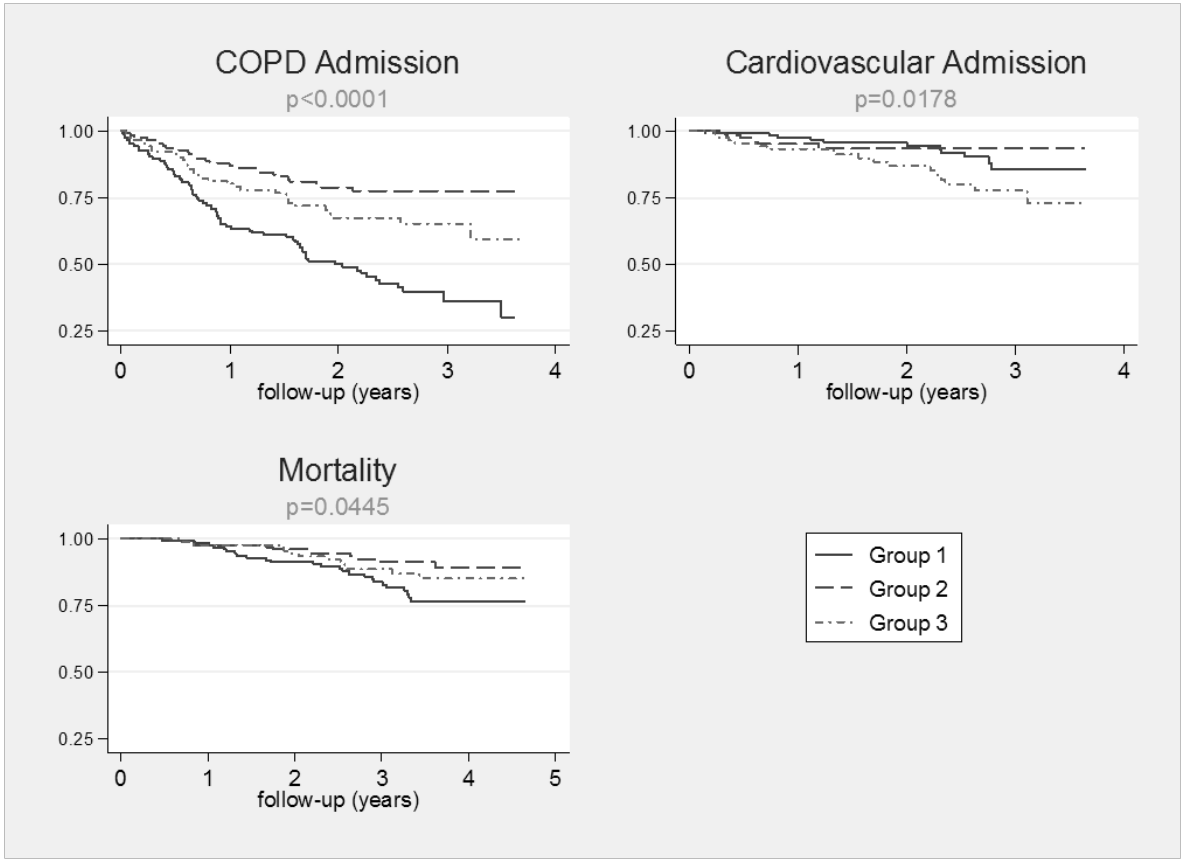
Group 2 - Moderate Respiratory COPD

(n=125, 69 yrs, FEV1 63% pred)
with emphysema

Group 3 - Systemic COPD

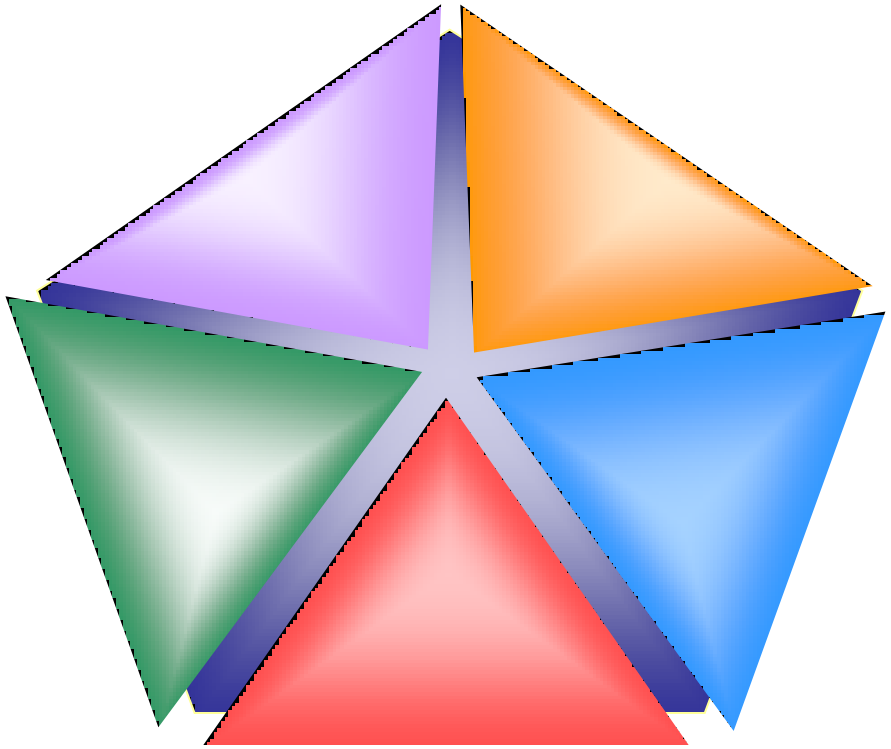
(n=91, 67 yrs, FEV1 58% pred)
with obesity
cardiovascular disorders,
diabetes, and
systemic inflammation.

Patterns of hospital admissions and mortality during follow-up, according to the three COPD groups identified by cluster analysis



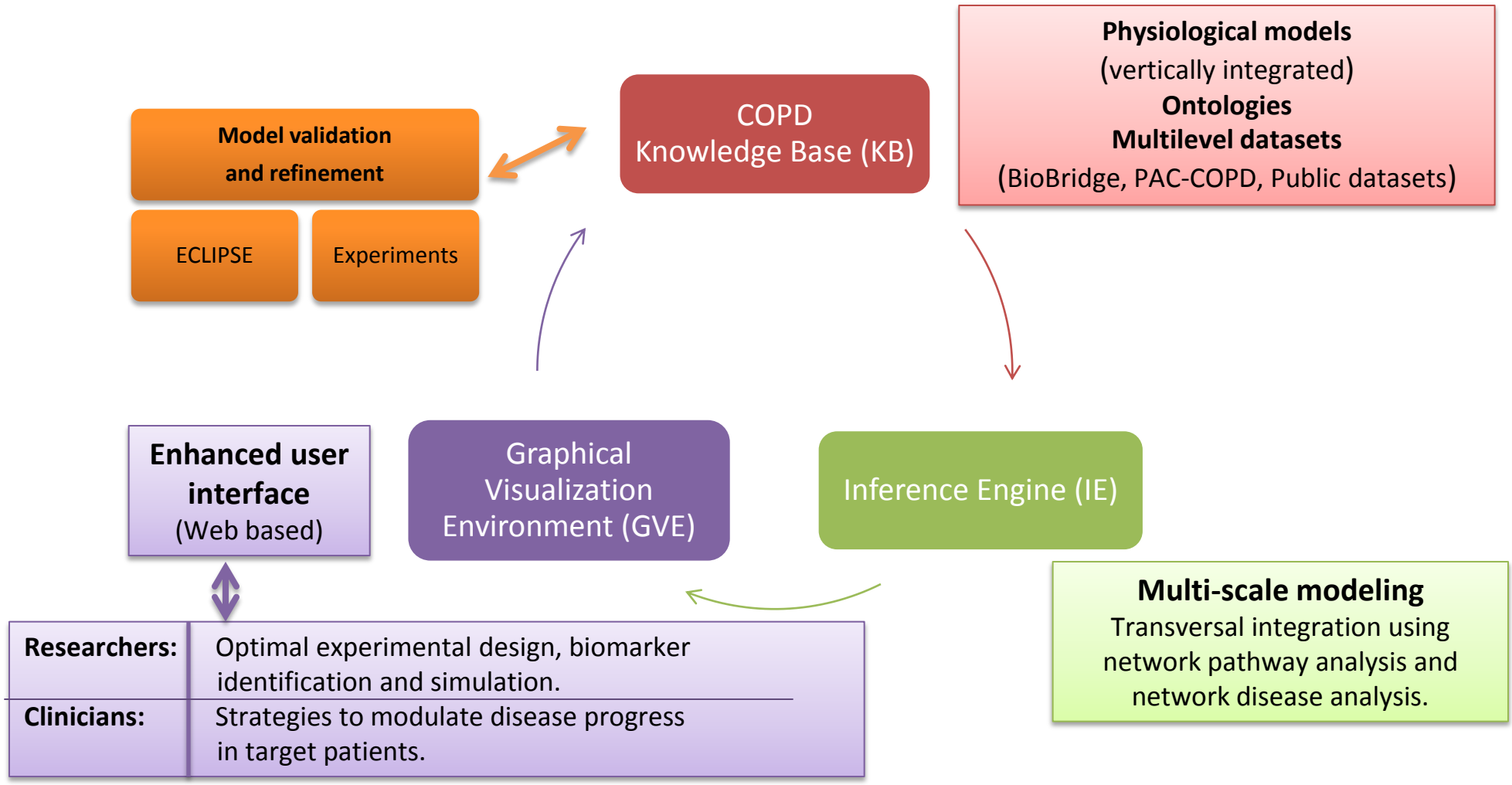
Group 1 had more frequent hospitalizations due to COPD (HR 3.28, p<0.001) and higher all-cause mortality (HR 2.36, p=0.018) than the other two groups
Group 3 had more admissions due to cardiovascular disease (HR 2.87, p=0.014).

Health & COPD



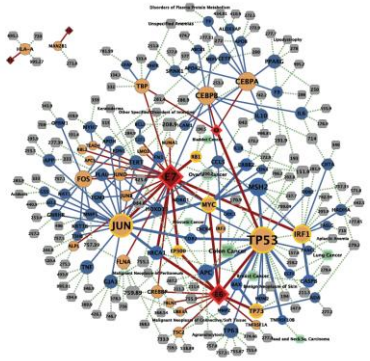
Next steps

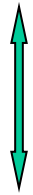
Synergy (COPD) – Systems Medicine



Predictive Analytics

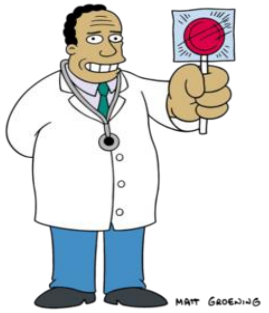
(recognition of patterns & inference analysis)





Clinical Decision Support Systems (CDSS)

(clinical application)



Need for interoperability at Systems level

Health service providers

MULTICENTER INTEROPERABILITY

Clinical Data

Patient

Professional

INTEGRATED CARE SERVICES FOR CHRONIC PATIENTS

Accessibility
Support
Education

Remote Monitoring

Clinical Decision Support Systems

Research Data

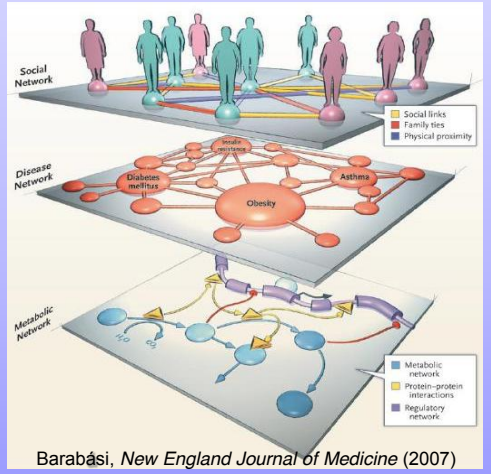
Clinical and Environmental Data

Semantic Interoperability

Data Query and database integration

Data Entry and semantic mapping

NETWORK ANALYSIS PROBABILISTIC MODELLING



Barabási, *New England Journal of Medicine* (2007)

Predictive Modelling

Interoperability between formal and informal healthcare