Systems Approach in Multifactorial Chronic Diseases with Co-Morbidities

1- Chronic diseases: the global health priority
Chronic diseases

- Pathogen
- Host
- Infectious disease
- Socio-economic determinants
- Ageing
- Life style - environment
  *Risk and protective factors*
  - Tobacco smoking, Pollutants
  - Allergens, Nutrition, Infections
  - Physical exercise, Others
- Genetic disease
Total deaths in each WHO Region
(all countries)

Source: WHO estimates 2008

- **Group I** – Communicable diseases, maternal, perinatal and nutritional conditions
- **Group II** – Other deaths from NCDs
- **Group II** – Premature deaths from NCDs (below 60 years), which are preventable
- **Group III** - Injuries
## Common risk factors of major NCDs

<table>
<thead>
<tr>
<th></th>
<th>Tobacco use</th>
<th>Unhealthy diets</th>
<th>Physical inactivity</th>
<th>Harmful use of alcohol</th>
<th>Biomass fuel combustion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular diseases</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Diabetes</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Cancer</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Chronic respiratory diseases</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Ageing and co-morbidities of NCDs

Barmett et al, Lancet 2012
Chronic diseases cluster in co-morbidities

Barmett et al, Lancet 2012
Systems Approach in Multifactorial Chronic Diseases with Co-Morbidities

1- Chronic diseases: the global health priority

2- Systems biology to understand the complexity of chronic diseases
<table>
<thead>
<tr>
<th>Socio economic determinants</th>
<th>Life style - environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk and protective factors</td>
<td>Tobacco smoking, Pollutants</td>
</tr>
<tr>
<td></td>
<td>Allergens, Nutrition, Infections</td>
</tr>
<tr>
<td></td>
<td>Physical exercise, Others</td>
</tr>
</tbody>
</table>
Genes

Biological expression of chronic diseases
- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

Life style - environment
Risk and protective factors
- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Socio economic determinants

Gender
Genes

Biological expression of chronic diseases
- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

Clinical expression of chronic diseases
- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment

Life style - environment
Risk and protective factors
- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Socio economic determinants

Sex

Socio economic determinants

Gender

Life style - environment
Risk and protective factors
- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Genes

Biological expression of chronic diseases
- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

Clinical expression of chronic diseases
- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment
Genes

Life style - environment
Risk and protective factors
Tobacco smoking, Pollutants
Allergens, Nutrition, Infections
Physical exercise, Others

Socio economic determinants

Gender

Genes

Biological expression of chronic diseases
Transcripts, proteins, metabolites
Target organ local inflammation
Systemic inflammation
Cell and tissue remodelling

Clinical expression of chronic diseases
Co-morbidities
Severity of co-morbidities
Persistence, remission
Long-term morbidity
Responsiveness - side effects to treatment

Age
Systems biology on precise phenotypes

Life style - environment
Risk and protective factors
- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Genes

Biological expression of chronic diseases
- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

Clinical expression of chronic diseases
- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment

Socio economic determinants

Age

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}

Systems biology on precise phenotypes

Sex

Socio economic determinants

Risk and protective factors

Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

Gender

Clinical expression of chronic diseases
}
**Personalized medicine**

**Primary prevention**

- **Risk and protective factors**
  - Tobacco smoking, Pollutants
  - Allergens, Nutrition, Infections
  - Physical exercise, Others

**Integrated care for stratified phenotypes**

**Health promotion**

- Primary prevention

**Genes**

**Biological expression of chronic diseases**

- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

**Clinical expression of chronic diseases**

- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment

**Socio economic determinants**

**Life style - environment**

**Age**

**Gender**

**Risk and protective factors**

- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

**Personalized medicine**

- Primary prevention
- Secondary prevention
- Tertiary prevention
- Treatment

**Biological expression of chronic diseases**

**Clinical expression of chronic diseases**

**Health promotion**

**Integreated care for stratified phenotypes**

**Gender**

**Risk and protective factors**

- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

**Biological expression of chronic diseases**

- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

**Clinical expression of chronic diseases**

- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment

**Socio economic determinants**

**Life style - environment**

**Age**

**Gender**

**Risk and protective factors**

- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

**Biological expression of chronic diseases**

- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

**Clinical expression of chronic diseases**

- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment

**Socio economic determinants**

**Life style - environment**

**Age**

**Gender**

**Risk and protective factors**

- Tobacco smoking, Pollutants
- Allergens, Nutrition, Infections
- Physical exercise, Others

**Biological expression of chronic diseases**

- Transcripts, proteins, metabolites
- Target organ local inflammation
- Systemic inflammation
- Cell and tissue remodelling

**Clinical expression of chronic diseases**

- Co-morbidities
- Severity of co-morbidities
- Persistence, remission
- Long-term morbidity
- Responsiveness - side effects to treatment
Systems Approach in Multifactorial Chronic Diseases with Co-Morbidities

1- Chronic diseases: the global health priority

2- Systems biology to understand the complexity of chronic diseases

3- Integrated approach to re-define and stratify chronic diseases
Combattre les maladies chroniques pour un vieillissement en bonne santé

Le Languedoc Roussillon porteur d'un projet innovant, intégré et en réseau

Centré autour de tous les patients de la Région

En partenariat avec les acteurs publics et privés de la Région (et au delà)

Pour réduire les hospitalisations pour maladies chroniques de 30% en 2020 chez les sujets de plus de 65 ans

Avec un fort impact socio-économique régional

En liaison avec le EIP-AHA (UE)
Classical phenotypes

Hypothesis-driven

Patient with chronic disease

CVD  COPD  Diabetes

Assessment of co-morbidities and severity

Classical phenotypes in patients with severe defined diseases and co-morbidities

Responsiveness to treatment
Follow up
Classical phenotypes

Hypothesis-driven

Patient with chronic disease

CVD
COPD
Diabetes

Assessment of co-morbidities and severity

Classical phenotypes in patients with severe defined diseases and co-morbidities

Responsiveness to treatment
Follow up

Novel phenotypes

Discovery-driven

Co-morbidities
(standardized assessment)

Severity of co-morbidities
(standardized assessment)

Novel phenotypes in individual patients with severe co-morbidities of chronic diseases

Responsiveness to treatment
Follow up
Definition of severe asthma
(Geneva, 6-7 April 2009)

Workshop summary

Uniform definition of asthma severity, control, and exacerbations: Document presented for the World Health Organization Consultation on Severe Asthma

Jean Bousquet, MD, PhD, a,b Eva Mantzourani, MD, PhD, d Alvaro A. Cruz, MD, a Nadia Ait-Khaled, MD, PhD, 1 Carlos E. Baena-Cagnani, MD, 9 Eugene R. Bleecker, MD, h Chris E. Brightling, MRCP, PhD, i Peter Burney, MA, MD, FRCP, FFPH, FMedsC, j Andrew Bush, MD, FRCP, FRCPCH, k William W. Busse, MD, n Thomas B. Casale, MD, o Moira Chan-Yeung, MD, g Rongchang Chen, MD, a Badrul Chowdhury, t Kian Fan Chung, DSc, MD, l Ronald Dahl, MD, DrMedSci, a Jeffrey M. Drazen, MD, f Leonardo M. Fabbri, MD, u Stephen T. Holgate, MD, DSc, y Francine Kauffmann, MD, b,c Tari Haahela, w Nikolai Khaltaev, x James P. Kiley, PhD, y Mohammad R. Masjedi, aa Yousser Mohammad, MD, bb Paul O’Byrne, MB, FRCPI, FRCP(C), FRCPE, FRCP(Glas), cc Martyn R. Partridge, MD, m Klaus F. Rabe, dd Alkis Togias, MD, z Christiaan van Weel, MD, PhD, ee Sally Wenzel, f Nanshan Zhong, MD, q and Torsten Zuberbier, gg Montpellier, Villejuif, and Paris, France, Geneva, Switzerland, Brazil, Cordoba,
Asthma severity

Based on NAEPP, 2007

Asthma severity

Control
- Symptoms
- Functional limitation over 2-4 weeks
- Exacerbations over 6-12 mo

Future risks
- Risk of asthma exacerbations
- Lung function loss (lung growth)
- Adverse reactions to meds

Level of treatment
- Inhalation technique
- Compliance

Responsiveness to treatment
<table>
<thead>
<tr>
<th></th>
<th>Asthma</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Underdiagnosis</strong></td>
<td>Risk of acute exacerbation</td>
<td>Risk of coma and death</td>
</tr>
<tr>
<td><strong>Effective treatment</strong></td>
<td>ICS, β2 agonists</td>
<td>Insulin, oral drugs</td>
</tr>
<tr>
<td><strong>No treatment available/affordable</strong></td>
<td>Risk of acute exacerbation</td>
<td>Risk of coma and death</td>
</tr>
<tr>
<td><strong>Incorrect diagnosis</strong></td>
<td>COPD (adults)</td>
<td>Weight loss</td>
</tr>
<tr>
<td></td>
<td>CF (children)</td>
<td></td>
</tr>
<tr>
<td><strong>Difficult-to-treat disease</strong></td>
<td>Compliance</td>
<td>Compliance</td>
</tr>
<tr>
<td></td>
<td>Inhaler misuse</td>
<td>Complications</td>
</tr>
<tr>
<td></td>
<td>Risk factors</td>
<td>Risk factors</td>
</tr>
<tr>
<td><strong>Controlled treatment dependent disease</strong></td>
<td>Risk of exacerbation when treatment stopped</td>
<td>Risk of death when treatment stopped</td>
</tr>
<tr>
<td><strong>Uncontrolled treatment resistant disease</strong></td>
<td>Treatment resistant asthma: Risks</td>
<td>Insulin-resistant diabetes Risks</td>
</tr>
</tbody>
</table>
Chronic disease clinic

- Chronic Respiratory diseases
- Cardio-vascular diseases
- Diabetes Metabolic Kidney diseases

Common questionnaire (risk factors, diseases)
Specific questionnaires
Exam (clinical, biological, EKG, FEV1, Echocardiogram)
Screening of co-morbidities
Chronic disease clinic

Common questionnaire (risk factors, diseases)
Specific questionnaires

Exam (clinical, biological, EKG, FEV1, EchocardioG)

Screening of co-morbidities

QOL, depression, anxiety (questionnaire)

Frailty, risk of falls > 65 yrs

Severity - Control

Risk assessment

Falls prevention
Frailty Prevention
Treatment
Specialist advice
Physicians in rural areas

Le Monde 7 avril 2012
Dépistage de Proximité des Pathologies Associées aux maladies chroniques

- Département de médecine générale de MTP-Nîmes
- CHU de Nîmes
Systems Approach in Multifactorial Chronic Diseases with Co-Morbidities

1- Chronic diseases: the global health priority
2- Systems biology to understand the complexity of chronic diseases
3- Integrated approach to re-define and stratify chronic diseases
4- Across the life cycle
Prevention and control of childhood asthma and allergy in the EU from the public health point of view: Polish Presidency of the European Union


1Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland; 2Ministry of Health, Warsaw, Poland; 3National programs against asthma and the Polish national asthma program – Polasthma, Medical University of Łódź, Łódź, Poland; 4European Academy of Allergy Clinical Immunology (EAACI), Swiss Institute of Allergy and Asthma Research (SIAF), Christine Kühne-Center for Allergy Research and Education, Davos, Switzerland; 5Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain; 6Imperial College London, UK; 7Imperial College and Royal Brompton Hospital, London, UK; 8Department of Respiratory Diseases, Aarhus University Hospital, Aarhus, Denmark; 9European Federation of Allergy and Airways Diseases Patients’ Associations (EFA), Brussels, Belgium; 10WHO Europe, Copenhagen, Denmark; 11Department of Clinical Immunology, Wroclaw Medical University, Wroclaw, Poland; 12Department of Immunology, Rheumatology and Allergy, Medical University of Łódź, Łódź, Poland; 13Department of Allergy, European Academy of Allergy Clinical Immunology (EAACI), 2nd Pediatric Clinic, University of Athens, Athens, Greece; 14European Public Health Alliance, Brussels, Belgium; 15University Children’s Hospital, Munich, Germany; 16Silvermedia, Sp. z o. o. Sp. k., Krakow, Poland; 17The Allergy & Asthma Institute, Islamabad, Pakistan; 18Department of Dermatology and Allergy, Charité, Berlin; 19University Montpellier-1 and Inserm CSEP 1018, WHO Collaborating Center for Asthma and Rhinitis, Montpellier, France

NEWS AND COMMENTARIES

Impact of early diagnosis and control of chronic respiratory diseases on active and healthy ageing

A debate at the European Union Parliament

J. Bousquet\textsuperscript{1,2,3}, C.C. Tanasescu\textsuperscript{4}, T. Camuzat\textsuperscript{5}, J.M. Anto\textsuperscript{6,7,8,9}, F. Blasi\textsuperscript{10,11}, A. Neou\textsuperscript{12}, S. Palkonen\textsuperscript{13}, N.G. Papadopoulos\textsuperscript{14,15}, J.P. Antunes\textsuperscript{16}, B. Samolinski\textsuperscript{17}, P. Yiallouros\textsuperscript{18}, T. Zuberbier\textsuperscript{12,19,20}
The role of developmental determinants of chronic diseases and frailty in ageing: From science to value creation and policies

Région Languedoc Roussillon (MACVIA-LR, EIP on AHA Reference Site)  
University Montpellier 1  
CHRU Montpellier and Nîmes  
MedALL (Mechanisms of the Development of Allergy, FP7)

European Innovation Partnership on Active and Healthy Ageing: DG Sanco and DG CONNECT  
Framework Programme 7, DG Research  
National Institute of Allergy and Infectious Diseases (NIH)

Proposal following the recommendations of the EU Council of the Polish (2011)  
and Cyprus (2012) Presidencies

Montpellier, 2-3 December 2013
1- Chronic diseases: the global health priority

2- Systems biology to understand the complexity of chronic diseases

3- Integrated approach to re-define and stratify chronic diseases

4- Chronic diseases tackled across the life cycle