AUDIT, RESEARCH AND GUIDELINE UPDATE

Developmental determinants in non-communicable chronic diseases and ageing


ABSTRACT
Prenatal and peri-natal events play a fundamental role in health, development of diseases and ageing (Developmental Origins of Health and Disease (DOHaD)). Research on the determinants of active and healthy ageing is a priority to: (i) inform strategies for reducing societal and individual costs of an ageing population and (ii) develop effective novel prevention strategies. It is important to compare the trajectories of respiratory diseases with those of other chronic diseases.

Prenatal and peri-natal events play a fundamental role in health, development of diseases and ageing (Developmental Origins of Health and Disease (DOHaD)). Research on the determinants of active and healthy ageing (AHA) is a priority to: (i) inform strategies for reducing societal and individual costs of an ageing population and (ii) develop effective novel prevention strategies.

The European Union (EU) leads a global effort to understand the early determinants of ageing. The Polish Presidency of the EU Council (2011) targeted chronic respiratory diseases in children to promote AHA.1 The developmental determinants of chronic diseases in ageing were reinforced during the Cyprus Presidency of the EU Council (2012). Several projects of the EU Sixth and Seventh Framework Programme for Research and Technological Development (FP6 and FP7) were funded to understand the mechanisms of prenatal and early life events on the development of chronic diseases. One of the action plans of the European Innovation Partnership on AHA is devoted to integrated care for chronic diseases, and chronic respiratory diseases have been selected as the model for chronic diseases.

As part of this research initiative, a meeting in Montpellier on 2 and 3 December 2013 attempted to better understand the early life events that may impact ageing in health and disease, with a particular focus on respiratory diseases. The results of the FP6 and FP7 projects on population-based cohorts in adults and old age were reviewed to propose novel research, policies and value creation. The full report is in the online supplement and on the MACVIA-LR website (macvia.crlanguedocroussillon.fr).

IMPORTANCE OF LIFE COURSE MODELS TO UNDERSTAND HEALTHY AGEING AND DISEASE
Biological ageing is the progressive deterioration of function that occurs in the postmaturity phase and can be assessed at the individual, physiological systems and cellular levels.2 Cross cohort comparisons of British birth cohorts show that social and biological factors from early life onwards can affect ageing, in particular respiratory function and disease.

In order to detect health-promoting factors, the early life events of diseases such as COPD need to be understood (European COST action BM1201: Developmental Origins of Chronic Respiratory Disease3). Susceptibility to COPD is associated with markers of foetal growth and early childhood disadvantage. Lung function at birth is determined by in utero processes.

Future research needs to develop a life course model of ageing that integrates the rather separate research on specific diseases or clinical conditions, functional ageing and well-being and should include socio-economic characteristics.

BIRTH COHORTS FOCUSING ON CHRONIC RESPIRATORY DISEASES IN THE GENERAL POPULATION
Asthma and allergic diseases begin early in life. Birth cohort studies are relevant to investigate environmental and lifestyle determinants of asthma and IgE-associated diseases or the absence of such
Nutrition is vital to understand the development of chronic diseases and the promotion of healthy ageing.

**ADULT COHORTS IN CHRONIC DISEASES**

The French prospective cohort (E3N), the EPIC-France cohort, is composed of women who were under a health insurance plan, the *Mutuelle Générale de l’Education Nationale*, for schoolteachers and coworkers. In 1990, about 100 000 women (40–65 years) were recruited. Epidemiological research in nutrition, hormones and chronic diseases (asthma, diabetes or osteoporosis) studied the risk factors for developing these diseases.

Two large European epidemiological cohorts, recruited in the early 1990s and followed up for 20 years, have been carried out in respiratory health: (i) the European Community Respiratory Health Survey (ECRHS; http://www.ecrhs.org/), including 18 668 individuals aged 20–44 years at baseline and (ii) the Epidemiological study of the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy (EGEA; http://egeanet.vjf.inserm.fr), a French case-control and family study of adults and children at baseline, including 2120 individuals aged 7–70 years at baseline. Combined analyses between these cohorts have been performed.

COPACETIC, a cohort of the lung cancer screening trial with over 2200 individuals with lung function and CT scans, identified genes associated with lung function decline in interaction with smoking, CT scan-based emphysema and coronary calcifications.

LifeLines (The Netherlands) is a three-generation cohort of 165 000 individuals followed annually by questionnaire and, every 5 years, by extensive functional screening of the five prime research areas: (1) metabolic/hormonal, (2) heart/vessel/kidney, (3) lung/respiratory/allergy, (4) psychiatric and (5) musculoskeletal.

**OLD AGE COHORTS**

Neuropsychiatric disorders of old-age (eg, depression, Alzheimer’s disease) may be determined by earlier risk exposure. The DEVELAGE consortium (FP7) aims to characterise shared molecular pathways between the early developmental processes in the brain and brain ageing.

This example underlines the limits of old age cohorts in the study of chronic neuropsychiatric disorder in the elderly.

Integrated research on DEvelopmental determinants of Ageing and Longevity (IDEAL; http://www.ideal-ageing.eu, FP7) examines the role of epigenetic regulation and transmission to next generations. A unique human cohort and animal studies are studied to discover novel longevity pathways and the links between development and ageing.

The Three-City Study (3C Study) is a population-based longitudinal study of the relation between vascular diseases and dementia in persons aged 65 years and older. A total of 9294 participants of both sexes were recruited from three French cities.

CONSTANCES, a large general-purpose epidemiological population-based cohort, aims to provide public health information. The cohort is a representative sample of 200 000 French adults, aged 18–69 years at inception.
Cohorts in middle and old age adults can be intertwined with earlier cohorts to understand the mechanisms of AHA and diseases in ageing.

Recommendations for future research are reported in the online supplement and the MACVIA-LR website on (i) integration of omics in epidemiological studies across the life cycle, (ii) performance of longitudinal studies assessing chronic diseases and (iii) value of European birth cohorts to study chronic diseases and AHA. Cohorts with an initial focus on chronic respiratory diseases could be expanded to understand the trajectories of chronic diseases and AHA.

Cohorts across the life cycle are essential to understand AHA. Lifelong birth cohorts give an overview of the problem and are complemented by cohorts carried out at different ages. Birth cohorts initially focusing on chronic respiratory diseases offer highly valuable additive information to understand chronic diseases and AHA.

Author affiliations
1 University Hospital, Montpellier, France
2 Inserm U 1168, Paris, France
3 Centre les Maladies Chroniques pour un Vieillissement Actif en Languedoc Roussillon, Site de Reference de l'EIP on AHA, Montpellier, France
4 MeDALL, Mechanisms of the Development of Allergy, FP7, Amsterdam, Groningen, the Netherlands
5 Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
6 IMM (Hospital del Mar Medical Research Institute), Barcelona, Spain
7 Universitat Pompeu Fabra (UPF), Barcelona, Spain
8 CIBER Epidemiología y Salud Pública (CIBERESP), Barcelona, Spain
9 Deputy Head of Unit for Medical Research and the Challenge of Ageing, DG Research & Innovation, European Commission, Brussels, Belgium
10 National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA
11 European Commission, Directorate General for Health and Consumers, Brussels, Belgium
12 University Montpellier 1, France
13 Région Languedoc Roussillon, France
14 Montpellier Medical School, France
15 Department of Physiology, Montpellier University Hospital, France
16 University Montpellier 1, France
17 Nîmes University Hospital, France
18 Montpellier University Hospital, France
19 Swiss Institute of Allergy and Asthma Research (SIAF), Davos and University of Zurich, Switzerland
20 David Hide Asthma and Allergy Research Centre, Isle of Wight, UK
21 Inserm, Research Unit U1061, University Montpellier I, Montpellier, France
22 Department of Paediatric Respiratory Medicine, Royal Brompton Hospital and National Heart and Lung Institute, Imperial College, London, UK
23 Institute of Human Genetics, CNRS, Montpellier, France
24 Equipe 10 UMR Inserm-Université Paris-Sud (Centre de recherche en Epidémiologie et Santé des Populations, CESP), Villejuif, France
25 Nutrition, Hormones and Women’s Health Team, INSERM UMR-S 1018, Paris-South University, Villejuif, France
26 Obesity Prevention Program, Department of Population Medicine, Harvard Medical School/Harvard Pilgrim Health Care Institute, Boston, Massachusetts, USA
27 Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, USA
28 Channing Division of Network Medicine, Department of Medicine, Brigham and Women’s Hospital, Harvard Medical School, and Harvard School of Public Health, UK
29 Population-Based Epidemiological Cohorts, INSERM-UVSQ UMS 011, Villejuif, France
30 Human Development & Health, Faculty of Medicine, University of Southampton, Southampton, UK
31 Institute of Clinical Physiology, National Research Council (CNR), Pisa, Italy
32 Horba, Montpellier, France
33 Department of Geriatrics, University Hospital, Montpellier, France
34 CESP—Team of Respiratory and Environmental Epidemiology INSERM UMR-S 1018, University Paris-Sud, Villejuif, France
35 Institute of Social Medicine, Epidemiology and Health Economics, Charité—Universitätsmedizin, Berlin, Germany
36 Institute for Clinical Epidemiology and Biometry, Julius Maximilian University of Wuerzburg, Germany
37 Department of Pediatric Pulmonology and Pediatric Allergology, University of Groningen, University Medical Center Groningen, Beatrix Children’s Hospital, Groningen Research Institute for Asthma and COPD, Groningen, The Netherlands
38 Comprehensive Pneumology Center, Ludwig Maximilians University and Helmholtz Zentrum Muenchen, Member of the German Research Center for Lung Research, Großhadern, Germany
39 MIRC Unit for Lifelong Health and Ageing at UCL, London, UK
40 Institut de Médecine Régénérative et de Biothérapie (I.M.R.B.), University Hospital, INSERM U1040, Montpellier, France
41 Department of Paediatrics, University of Oslo and Oslo University Hospital, Oslo, Norway
42 Biomax Informatics AG, Planegg, Germany
43 Institute of Environmental Medicine, Karolinska Institutet and Sachs’ Children’s Hospital, Stockholm, Sweden
44 Aix-Marseille University (AMU), Research Unit 912 AMU/INSERMIRD Social and Economic Sciences Applied to Health (SESSIM), France
45 Department of Public health and biostatistics, Descartes University, Paris, France
46 Municipal Department of social action, childhood, and health, Paris, France
47 SATT AuR, Montpellier, France
48 Department of Pulmonology, University Medical Center Groningen, University of Groningen, GRIAC Research Institute, Groningen, The Netherlands
49 Inserm U1061 Neuropsychiatrie, Montpellier and Faculty of Medicine, Imperial College London, London, UK
50 Inserm Research Unit 988, Paris, France
51 Inserm Research Unit 710, Montpellier, France
52 École Pratique des Hautes Etudes (EPHE), Paris, France
53 Department of Prevention of Environmental Hazards and Allergology, Medical University of Warsaw, Warsaw, Poland
54 Team of Environmental Epidemiology applied to Reproduction and Respiratory Health, University Grenoble Alpes, IAB, Grenoble, France
55 Team of Environmental Epidemiology applied to Reproduction and Respiratory Health, INSERM, IAB, Grenoble, France
56 Team of Environmental Epidemiology applied to Reproduction and Respiratory Health, CHU de Grenoble, IAB, Grenoble, France
57 Section of Molecular Epidemiology, Leiden University Medical Center, Leiden, the Netherlands
58 Consortium for Healthy Aging, Leiden University Medical Center, Leiden, the Netherlands
59 Julius Center of Health Sciences and Primary Care, University Medical Center Utrecht, University of Utrecht, Utrecht, the Netherlands
60 Division of Immunopathology, Department of Pathophysiology and Allergy Research, Center for Pathophysiology, Infectiology and Immunology, Medical University of Vienna, Vienna, Austria
61 University Hospital and INSERM U 1058, Montpellier, France
62 EPHE, Section des Sciences de la Vie et de la Terre, Paris, France
63 UMR 5 710, University Montpellier 2, Montpellier, Paris, France
64 Institut Transdisciplinaire d’Études du Vieillissement, Montpellier, France
65 Cyprus International Institute for Environmental & Public Health in Association with Harvard School of Public Health, Cyprus University of Technology, Limassol, Cyprus
66 Director of Population-Based Epidemiological Cohorts, INSERM-UVSQ UMS 011, Villejuif, France

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