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# Chronic respiratory diseases and lung cancer research: a perspective from the European Union

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## The mounting burden of chronic respiratory diseases

Chronic respiratory diseases (CRDs) are chronic diseases of the airways and other structures of the lungs. Major CRDs are asthma and respiratory allergies, chronic obstructive pulmonary disease (COPD), occupational lung diseases, sleep apnoea syndrome and pulmonary hypertension. Globally, they affect 1 billion people and account for 7% of all deaths worldwide (4.2 million deaths) [1]. Lung cancer adds to this number another 1.4 million deaths annually (2.4%) [2]. Of the communicable lung diseases, tuberculosis is by far the most important. In 2012, 1.3 million people were killed by tuberculosis and 8.6 million new cases required treatment [3].

The 2010 Global Burden of Disease (GBD) study estimated that COPD was the third leading cause of death, accounting for 2.1% of total adult deaths [4]. Global deaths from COPD are projected to increase by more than 30% in the next 10 years [5]. Approximately 150 000 adults aged 40 years or older die of COPD each year in the European Union [2]. In addition, total COPD costs are estimated to amount €141.4 billion annually [2].

In 2010, in the 28 European Union member states, approximately 1.0% of children aged up to 14 years and 3.2% of the population between 15 and 44 years had asthma [2]. The estimated economic burden of asthma is approximately €72.2 billion annually [2].

According to the 2010 GBD study, lung cancer was the fifth leading cause of death [4]. It is predicted that it will cause over 20% of total cancer deaths (close to 280 000 deaths) in Europe in 2015. It has the highest predicted death rates in men: 36 deaths per 100 000. In women, mortality from lung cancer is rising and, with a predicted death rate of 14.24 per 100 000, will overtake breast cancer mortality (with 14.22 per 100 000) [6]. In 2008, costs of lost productivity due to premature lung cancer-related mortality in Europe were an estimated €17 billion [7].

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Apart from genetic traits, major risk factors for CRD include tobacco exposure and second-hand tobacco smoke; indoor and outdoor air pollutants; allergens; occupational agents; diet, nutrition and socioeconomic factors; and pathogens [8]. Prevalence, morbidity and mortality of CRD generally increase with age. Although not fully reversible, COPD and asthma are partially preventable.

### **A look into the future: bridging the gap by focusing on translational research and innovation in the European Union**

Further research and innovation activities are warranted to ensure knowledge development and subsequent applications in the area of CRD. However, translational research is specialised, multidisciplinary and costly, and requires a “critical mass” to undertake large-scale, high-value projects. Besides, research and innovation activities are fragmented in Europe. Therefore, the European Union adds value by facilitating, coordinating and monitoring multinational, multidisciplinary, world-class research.

There is a great need to increase the understanding of (epi)genetic, unique and common disease mechanisms [9] and risk factors, either natural or anthropogenic environmental determinants, to develop targeted interventions and more effective drugs, including prevention and quality of life improvement. A consensus has been established on major research areas and gaps that would require further investments such as new diagnostic technologies [10]; new treatments aiming to restore pulmonary function or enabling personalised [11] and regenerative medicine; deepening of intrinsic and extrinsic health determinants such as lifestyle, ageing, environment and climate change [12]; more effective prevention and treatment of respiratory infections; involvement of patients in disease self-management and in research initiatives; or new healthcare approaches such as telemedicine [13, 14] and remote monitoring of CRD.

The Seventh Framework Programme for Research and Technological Development (FP7) [15] has displayed a comprehensive approach to nurturing research and innovation on CRD, tuberculosis and cancer [16]. During this programme, 194 relevant projects (table 1) related to CRD, lung cancer and infections with an impact on CRD have been funded for an amount of over €350 million, of which over €246 million focussed on disease research, mainly on chronic inflammatory airway disease (COPD and asthma) and lung cancer (figure 1).

The majority of the projects constitute multidisciplinary collaborations between academia, clinicians and industry. They represent a total of 737 organisations (figure 2), of which 21% are small and medium-sized enterprises (SMEs), offering opportunities for synergy between the private and public sectors (figure 3). Overall, the 29 closed FP7 projects on CRD and lung cancer from the Health Directorate filed nine new patent applications on diagnostics, vaccines and drug candidates, and produced more than 500 peer-reviewed papers with an average 23 publications per project. Although most participants are located in Europe, participants from outside Europe, particularly in the Asian region (receiving some €2.5 million), Latin America (€1.5 million) and the Mediterranean partner countries (€1.0 million) also contributed.

### **The European Union CRD and lung cancer major research priorities and initiatives** *Understanding CRDs*

Collaborative research has particular added value for this area, unveiling the interactions between genotype and environment that lead to respiratory diseases. Epidemiological studies to deepen knowledge of the aetiology and pathogenesis of childhood and adult asthma and COPD, clinical management of cases and exacerbations, and prevention are part of this portfolio.

Long-term cohort studies are crucial to understanding the life course, early predictors, risk and protective factors of diseases. They also provide important insights into the determinants of health, wellbeing and disease, and have contributed to public health policy and changes in clinical practice.

Since 2002, the European Union has supported the integration and analysis of large cohorts in the field of CRDs with a view to produce evidence on CRD determinants, risk factors and socioeconomic implications. Two particular areas of sustained efforts have been allergy and asthma as well as environmental health.

The FP6-funded project Ga<sup>2</sup>LEN (The Global Allergy and Asthma European Network) [17] set the foundations for building a competitive international network of excellence of 26 centres aiming at overcoming the fragmentation of allergy research in Europe, creating durable research structures and application of research results into clinical practice, policy development, and integration of the public and private sectors. A European database of comparable, longitudinal epidemiological studies has been completed. More than 500 papers have been published by the Ga<sup>2</sup>LEN members, including 80 position papers, practical guides or task force papers.

Long-term population-based birth cohort studies have proven instrumental in developing European and national policies for CRD. The FP7 long-term birth cohort study MeDALL (Mechanisms of the

TABLE 1 Examples of European Union (EU)-funded projects on chronic respiratory diseases

Project acronym	Project title	Project EC contribution € million	Project total budget € million	Targeted disease or determinant	Current major achievements	Website
<b>Ga<sup>2</sup>LEN</b>	Global Allergy and Asthma European Network	14.4	14.4	Allergy/asthma	Database: longitudinal studies of genetic and environmental factors for asthma and allergy 80 position papers Guideline on urticaria Active partner of GARD	<a href="http://www.ga2len.net/index.html">www.ga2len.net/index.html</a>
<b>MEDALL</b>	Mechanisms of the Development of Allergy	11.9	15.7	Allergy/asthma	Database: 14 longitudinal birth cohorts on allergy-related phenotypes Contribution to redefinition of classical phenotypes of allergic diseases	<a href="http://medall-fp7.eu/">http://medall-fp7.eu/</a>
<b>PreDICTA</b>	Post-Infectious Immune Reprogramming and its Association with Persistence and Chronicity of Respiratory Allergic Diseases	5.9	7.9	Allergy/asthma	Preschool-aged asthmatic children cohort (n>200) Rhinovirus serological test	<a href="http://www.predicta.eu">www.predicta.eu</a>
<b>U-BIOPRED</b>	Unbiased Markers for the Prediction of Respiratory Disease Outcomes	8.9	20.7	Asthma	Clinical trial adult and children cohorts (n>1000) Biobank (n=100 000) Development of a Patient Input Platform	<a href="http://www.europeanlung.org/en/projects-and-research/projects/u-biopred/">www.europeanlung.org/en/projects-and-research/projects/u-biopred/</a>
<b>AmbuLung</b>	Ambulatory Bio-Artificial Lung	5.6	7.4	COPD	Bioartificial mobile lung prototype Preclinical testing ongoing	<a href="http://www.ambulung.com">www.ambulung.com</a>
<b>COPACETIC</b>	COPD Pathology: Addressing Critical Gaps, Early Treatment and Innovative Concepts	2.9	4.0	COPD	GWASs for COPD, chronic bronchitis and emphysema GWAS results on COPD found approximately 350 DNA variations (SNPs)	<a href="http://www.copacetic-study.eu">www.copacetic-study.eu</a>
<b>EVA</b>	Markers for Emphysema versus Airway Disease in COPD	2.9	3.9	COPD	COPD phenotypes and genetic markers (n>800)	<a href="http://www.eva-copd.eu">www.eva-copd.eu</a>
<b>HEMOCARE</b>	Clinical Continuity by Integrated Care	2.2	2.7	COPD	Guide for integrated homecare in stroke, heart failure and COPD Systematic review on the evidence of telefacilities in relation to integrated homecare Health economic evaluation	<a href="http://www.integratedhomecare.eu">www.integratedhomecare.eu</a>
<b>PRO-active</b>	Physical Activity as a Crucial Patient Reported Outcome in COPD	6.8	16.7	COPD	Telecoaching to enhance physical activity in COPD Trials of innovative tools to assess impact of physical activity on COPD	<a href="http://www.proactivecopd.com">www.proactivecopd.com</a>
<b>AIRPROM</b>	Airway Disease Predicting Outcomes through Patient Specific Computational Modelling	11.7	15.5	COPD/asthma	NOX4 as a potential novel target for asthma therapy	<a href="http://www.europeanlung.org/en/projects-and-research/projects/airprom/">www.europeanlung.org/en/projects-and-research/projects/airprom/</a>
<b>CHILD-EU</b>	Orphans Unite: Child Better Together – European Management Platform for Childhood Interstitial Lung Disease	3.0	3.9	ChILD	European ChILD database and biobank (n>70) Check list for diagnostics Observational trial on incident and prevalent cases ongoing	<a href="http://www.klinikum.uni-muenchen.de/Child-EU/en/index.html">www.klinikum.uni-muenchen.de/Child-EU/en/index.html</a>
<b>IMPACTT</b>	Immunoglobulin IgY <i>Pseudomonas</i> : a Clinical Trial for Cystic Fibrosis Treatment	5.4	7.0	Cystic fibrosis	Anti- <i>Pseudomonas aeruginosa</i> IgY proof of concept CT recruitment in 8 EU countries (n>80)	<a href="http://impactt.eu/">http://impactt.eu/</a>

Continued

TABLE 1 Continued

Project acronym	Project title	Project EC contribution € million	Project total budget € million	Targeted disease or determinant	Current major achievements	Website
<b>MM4TB</b>	More Medicines for Tuberculosis	11.0	16.7	TB	Target identification and preclinical development of new TB drugs	<a href="http://www.mm4tb.org">www.mm4tb.org</a>
<b>NEWTBVAC</b>	Discovery and Preclinical development of New Generation Tuberculosis Vaccines	12.0	18.9	TB	4 vaccine candidates to phase I CT 17 biomarkers characterised and validated, and 18 new biomarkers identified.	<a href="http://www.tbvi.eu/projects/">www.tbvi.eu/projects/</a>
<b>ORCHID</b>	Open Collaborative Model for Tuberculosis Lead Optimisation	5.4	8.5	TB	Identification of compounds for sensitive and resistant TB	<a href="http://projectorchid.org/">http://projectorchid.org/</a>
<b>STOPLATENT-TB</b>	Latent Tuberculosis: New Tools for the Detection and Clearance of Dormant <i>Mycobacterium tuberculosis</i>	2.7	3.6	TB	Advancements in drug combinations for latent TB	<a href="http://cordis.europa.eu/result/rcn/52850_en.html">http://cordis.europa.eu/result/rcn/52850_en.html</a>
<b>SYSTEMTB</b>	Systems Biology of <i>Mycobacterium tuberculosis</i>	10.6	13.8	TB	Data storage platform Dynamic <i>M. tuberculosis</i> metabolic model	<a href="http://www.systemtb.bio">www.systemtb.bio</a>
<b>TB PAN-NET</b>	Pan-European Network for the Study and Clinical Management of Drug Resistant Tuberculosis	11.0	14.1	TB	New platform and tools to manage drug resistant TB	<a href="http://www.tbpannet.org">www.tbpannet.org</a>
<b>ACTRIS</b>	Aerosols Clouds and Trace Gases Research Infrastructure Network	7.8	11.6	Air pollution	Proposal for world-class European RI on the next ESFRI roadmap for RIs	<a href="http://www.actris.net">www.actris.net</a>
<b>ECLAIRE</b>	Effects of Climate Change on Air Pollution Impacts and Response Strategies for European Ecosystems	7.0	10.9	Air pollution	Prediction of climate warming worsening air pollutants of European ecosystems	<a href="http://www.eclairer-fp7.eu">www.eclairer-fp7.eu</a>
<b>ESCAPE</b>	European Study of Cohorts for Air Pollution Effects	5.9	8.2	Air pollution	Cohort study (n=900 000) and database air pollution exposure	<a href="http://www.escapeproject.eu">www.escapeproject.eu</a>
<b>SANOWORK</b>	Safe Nano Worker Exposure Scenarios	3.4	4.8	Occupational exposure	Risk Remediation Strategies and evaluation for nanomaterials	<a href="http://sanowork.eu">sanowork.eu</a>
<b>NANO-HVAC</b>	Novel Nano-Enabled Energy Efficient and Safe HVAC Ducts and Systems Contributing to a Healthier Indoor Environment	2.9	4.2	Indoor air quality	Antimicrobial and antiallergic solutions for indoor air quality	<a href="http://www.nanohvac.eu">www.nanohvac.eu</a>
<b>PULMOSTENT</b>	Development and Evaluation of a Viable Stent Device for the Treatment of Bronchotracheal Cancer	3.2	4.1	Lung cancer	New type of stent made of mesh covered with cells and releasing drugs.	<a href="http://www.pulmostent-project.com">www.pulmostent-project.com</a>
<b>ARTFORCE</b>	Adaptive and Innovative Radiation Treatment for Improving Cancer Patients Treatment Outcome	6.0	8.0	Lung cancer	Radiotherapy clinical trial ongoing Potential prognostic marker identified	<a href="http://www.cancerartforce.eu">www.cancerartforce.eu</a>
<b>LUNGTARGET</b>	New Approaches for the Targeted Therapy of Non-Small Cell Lung Cancer	3.0	4.0	Lung cancer	Identification of several potential therapeutic targets in KRAS-dependent NSCLC, development of EGFR family targeting DARPins.	<a href="http://www.lungtarget.eu">www.lungtarget.eu</a>

Continued

TABLE 1 Continued

Project acronym	Project title	Project EC contribution € million	Project total budget € million	Targeted disease or determinant	Current major achievements	Website
<b>CURELUNG</b>	Determining (Epi)genetic Therapeutic Signatures for Improving Lung Cancer Prognosis	3.0	3.8	Lung cancer	Establishing molecular screening network for lung cancer (NGM) identifying aurora B kinase as a potential therapeutic target.	<a href="http://www.curelung.eu">www.curelung.eu</a>
<b>JBIR-23</b>	Nature's First Lead in the Fight against Mesothelioma: the Total Synthesis and Biological Evaluation of JBIR-23 and Related Compounds	0.2	0.2	Mesothelioma	Synthesis of JBIR-23 analogues and <i>in vitro</i> testing of their antimesothelioma activity.	<a href="http://cordis.europa.eu/project/rcn/98735_en.html">http://cordis.europa.eu/project/rcn/98735_en.html</a>

EC: European Commission; COPD: chronic obstructive pulmonary disease; TB: tuberculosis; CHILD: childhood interstitial lung disease; GARD: Global Alliance against Chronic Respiratory Diseases; GWAS: genome-wide association scan; SNP: single-nucleotide polymorphism; CT: clinical trial; RI: Research Infrastructure; ESFRI: European Strategy Forum on Research Infrastructures; NSCLC: non-small cell lung cancer; EGFR: epidermal growth factor receptor; DARPIn: designed ankyrin repeat protein; NGM: Network Genomic Medicine.

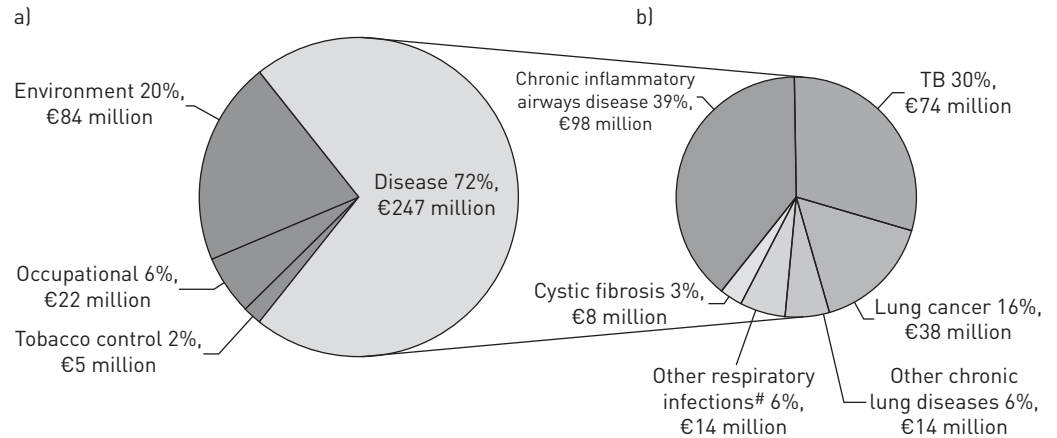


FIGURE 1 Distribution of Seventh Framework Programme for Research and Technological Development projects related to chronic respiratory diseases and lung cancer by a) research area (n=194) and b) disease focus (n=140). TB: tuberculosis. #: projects on respiratory infections with direct impact on chronic respiratory diseases.

Development of Allergy) aimed to generate novel knowledge on the mechanisms of initiation of allergy from early childhood to young adulthood, in order to propose early diagnosis, prevention and targets for therapy. It has achieved significant results, such as the building of a pooled and harmonised database of 14 European longitudinal birth cohorts (44 000 children at birth, 22 000 at 4 years and 19 000 at 8 years) on classical and novel allergy-related phenotypes [18]. The project has also contributed to the development of a new allergen microarray technology [19] and a novel classification of allergic diseases [20]. MeDALL supported the development of the Finnish Allergy Programme 2008–2018 [21].

Similarly, the ENRIECO project (Environmental Health Risks in European Birth Cohorts, [www.enrieco.org](http://www.enrieco.org)) demonstrated the association between a mouldy home environment in early life and an increased risk of asthma and allergy [22] among other findings.

Air quality and climate change are approached by projects such as ACTRIS (Aerosols Clouds and Trace Gases Research Infrastructure Network), ECLAIRE (Effects of Climate Change on Air Pollution Impacts and Response Strategies for European Ecosystems) and ESCAPE (European Study of Cohorts for Air Pollution Effects) [23] that focused on long-term effects on human health of exposure to air pollution in Europe.

Occupational exposure to nanomaterials in SANOWORK (Safe Nano Worker Exposure Scenarios) and indoor air quality in NANO-HVAC (Novel Nano-Enabled Energy Efficient and Safe HVAC Ducts and Systems

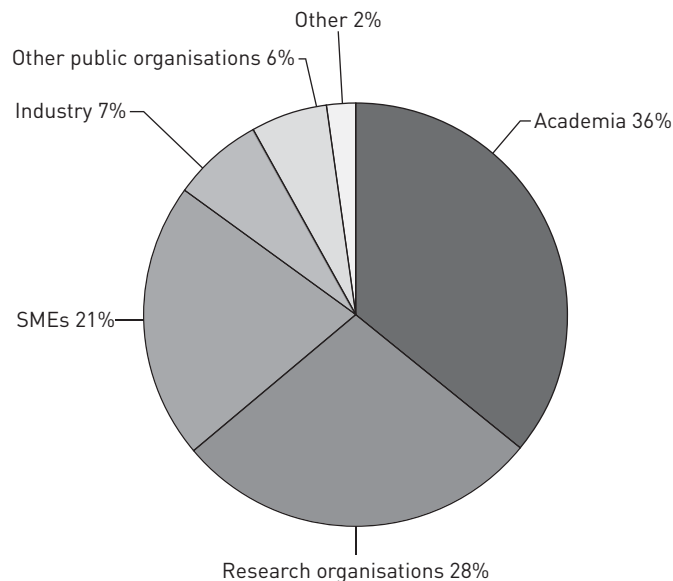


FIGURE 2 Seventh Framework Programme for Research and Technological Development participation in chronic respiratory diseases and lung cancer projects by organisation type. SME: small and medium-sized enterprise.

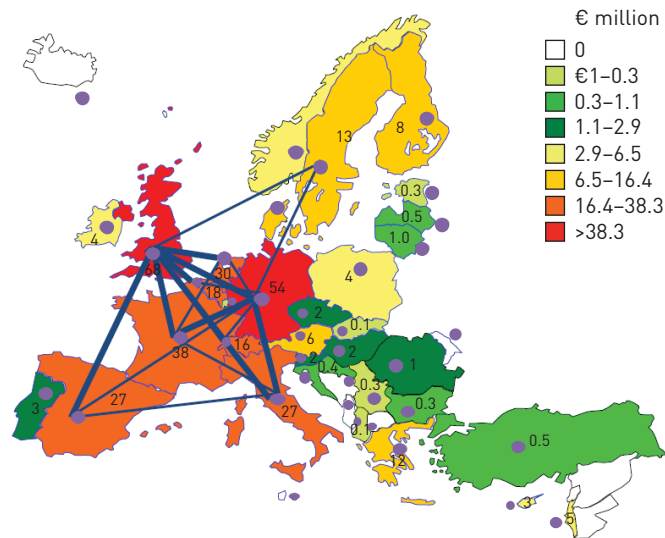


FIGURE 3 European Union Seventh Framework Programme for Research and Technological Development (FP7) contribution to research in chronic respiratory diseases and lung cancer by member state and associated countries. Lines represent major connections between partners of collaborative projects between countries. Line width is proportional to the number of connections. The colour scale represents distribution of FP7 funding among member states and associated countries.

Contributing to a Healthier Indoor Environment) are also research subjects within FP7. COPACETIC (COPD Pathology: Addressing Critical Gaps, Early Treatment and Innovative Concepts) has collected genetic material from thousands of people in various European countries to elucidate which genes and what aberrant lung physiology underpin the development of COPD. In a complementary effort, EVA (Markers for Emphysema *versus* Airway Disease in COPD) addresses COPD phenotypes and the identification of specific genetic markers to stratify them into subgroups and inform about progression of the disease.

EPIC (The European Prospective Investigation into Cancer and Nutrition) (<http://epic.iarc.fr/>), a prospective cohort study with more than 521 000 participants, was also cofinanced by the European Commission. EPIC produced a wealth of information on lifestyle factors influencing lung cancer risk (smoking, occupational exposure and diet) and on genetic variants that modulate lung cancer risk and survival. Finally, a large number of Marie Skłodowska-Curie (Marie Skłodowska-Curie Actions, <http://ec.europa.eu/research/mariecurieactions/>) training grants, such as NCRNALUNGCANCER (Function of Non-coding RNAs in Lung Cancer) or NO-CANCER (Protein S-Nitrosylation in Inflammation and Cancer), are dissecting molecular pathogenesis of lung cancer.

The European Union has also pioneered research infrastructures in Europe with the European Strategy Forum on Research Infrastructures (ESFRI) ([http://ec.europa.eu/research/infrastructures/index\\_en.cfm?pg=esfri](http://ec.europa.eu/research/infrastructures/index_en.cfm?pg=esfri)), consisting of networked research facilities to develop the scientific integration of Europe and to strengthen its international outreach and innovation potential. ESFRI supports BBMRI (Biobanking and Biomolecular Resources Research Infrastructure, <http://bbmri-eric.eu/>) (European Union contribution €170 million), providing access to human biological samples [24] that can be used in research on CRD and lung cancer. Another infrastructure of interest, EATRIS (European Infrastructure for Translational Medicine, <http://eatris.eu/>), supports researchers and funders in developing biomarkers and health products, providing key expertise in molecular imaging and tracing, vaccines, biomarkers, small molecules, and advanced therapeutic medicinal products [25].

#### ***Towards personalised medicine: modelling, biomarkers and innovation in drug development***

CRD and lung cancer are usually referred to as “complex diseases”. Therefore, there is a need for integrating information coming from different sources (biological, environmental, clinical, radiological, *etc.*) to make a proper diagnosis and determine the best intervention for each patient.

The consortium AirPROM (Airway Disease Predicting Outcomes through Patient Specific Computational Modelling) has designed multiscale computational models of airways to disentangle pathophysiological mechanisms in asthma and COPD, and a platform to translate these patient-specific tools into personalised management of airway disease [26]. As a result, pharmaceutical companies are currently translating the platforms results into usable applications in joint projects.

FP7 has funded biotechnology projects with high potential for innovation, such as AmbuLung (Ambulatory Bio-Artificial Lung) to assist COPD patients with chronic lung failure. Innovative solutions to lung cancer are also being researched. PULMOSTENT (Development and Evaluation of a Viable Stent Device for the Treatment of Bronchotracheal Cancer) focuses on developing a new kind of pulmonary stent based on a combination of stent technologies and tissue engineering. Similarly, Lung Card ([www.lungcard.eu](http://www.lungcard.eu)) is developing a simple point-of-care chip device combining blood sample processing and detection of epidermal growth factor receptor (*EGFR*) mutations in tumour DNA in order to predict patients' drug responses.

Innovative pharmacological research and innovation mean a shift of the current paradigm towards science and high-technology collaborative projects, and capitalising on a knowledge-based economy by translating new ideas into targeted diagnosis and drugs, while reducing red tape and development costs. In this context, the European Union has created a joint undertaking with the pharmaceutical industry association EFPIA (European Federation of Pharmaceutical Companies and Associations, [www.efpia.eu](http://www.efpia.eu)), the Innovative Medicines Initiative (IMI) ([www.imi.europa.eu](http://www.imi.europa.eu)), the world's largest public-private partnership in life sciences to date with a total budget of more than €5 billion between 2008 and 2024 [27].

As part of enabling personalised medicine, the development of clinical biomarkers has become an essential core activity to allow early prediction of drug efficacy and safety, to inform treatment decisions, and to bring personalised medicine into clinical practice, thus shortening drug development, avoiding ineffective treatment and toxicity, and decreasing costs. IMI has fostered two projects in the realm of CRD: U-BIOPRED (Unbiased Markers for the Prediction of Respiratory Disease Outcomes) that uses biomarkers to stratify patients and, thus, speed up the development of targeted treatments for severe asthma [28]; and PRO-active (Physical Activity as a Crucial Patient Reported Outcome in COPD), aiming at developing new tools for patients, doctors and researchers to assess disease status [29].

Under FP7, the European Commission has devoted over €1.4 billion to support a multitude of personalised cancer medicine projects aimed at improving cancer prevention, diagnosis, treatment and care. The lung cancer research project ARTFORCE (Adaptive and Innovative Radiation Treatment for Improving Cancer Patients Treatment Outcome) is running a randomised phase II clinical trial on stratified patients validating the potential of a radiation boost to the radiation-resistant parts of the tumour, based on a pre-treatment fluorodeoxyglucose positron emission tomography scan of the patient. Likewise, LUNGTARGET (New Approaches for the Targeted Therapy of Non-Small Cell Lung Cancer) aimed to develop novel drug targets and EGFR-targeting therapies for patients with *KRAS* mutations, while CURELUNG (Determining (Epi)genetic Therapeutic Signatures for Improving Lung Cancer Prognosis) established (epi)genetic targets for therapies and (epi)genetic response markers to targeted therapies. Following up on previous European Union lung cancer prevention research, biomarkers in lung cancer patients' breath and the devices to identify them are a focus of projects such as BREATH (Characterization of Biomarkers in Breath of Lung and Breast Cancer Patients) or LCAOS (A Nanoscale Artificial Nose to Detect Lung Cancer) ([www.lcaos.eu](http://www.lcaos.eu)).

### ***Preventing infectious diseases with a direct impact in CRDs***

More effective diagnosis, prevention and treatment of respiratory infections have been among the priorities in FP7. Tuberculosis, considered a CRD, has received more than €90 million from the FP7 Cooperation Health Programme.

The funding has focused on understanding host-pathogen interaction, on managing drug-resistant tuberculosis, and on developing better diagnostics, drugs and vaccines. Systems biology of *Mycobacterium tuberculosis* (SYSTEMTB), latent tuberculosis (STOPLATENT-TB; Latent Tuberculosis: New Tools for the Detection and Clearance of Dormant *Mycobacterium tuberculosis*), multidrug-resistant tuberculosis (TB PAN-NET; Pan-European Network for the Study and Clinical Management of Drug Resistant Tuberculosis), new-generation tuberculosis vaccines (NEWTBVAC; Discovery and Preclinical development of New Generation Tuberculosis Vaccines) and new drug development (MM4TB (More Medicines for Tuberculosis) and ORCHID (Open Collaborative Model for Tuberculosis Lead Optimisation)) are but a few examples. Furthermore, PreDiCT-TB (Model-based Preclinical Development of Anti-tuberculosis Drug Combinations) ([www.predict-tb.eu](http://www.predict-tb.eu)) is an IMI-funded initiative focused on tackling preclinical research barriers to the discovery and development of new tuberculosis drug combinations. PreDiCT-TB has established an alliance with the US Critical Path Institute (<http://c-path.org/>) to combine forces in the fight for better tuberculosis treatments.

The modelling of repeated lung infections and their impact on developing persistent inflammatory patterns that lead to allergy (asthma and rhinitis) is covered by PreDiCTA (Post-Infectious Immune Reprogramming and its Association with Persistence and Chronicity of Respiratory Allergic Diseases)



([www.predicta.eu](http://www.predicta.eu)). The ultimate and more ambitious objective of PreDICTA is to establish diagnostic and therapeutic strategies to predict and, if possible, avoid respiratory allergy persistence [30]. In addition, FP7 has sponsored drug development through IMPACTT (Immunoglobulin IgY *Pseudomonas*: a Clinical Trial for Cystic Fibrosis Treatment) [31], which will complete a clinical phase III trial of a pioneering intervention therapy for the fatal chronic infection of *Pseudomonas aeruginosa* in cystic fibrosis patients.

In the area of collaboration with developing countries, the European and Developing Countries Clinical Trials Partnership (EDCTP) ([www.edctp.org](http://www.edctp.org)), a public–public partnership, aims to accelerate the clinical development of new medical products by financially supporting clinical trials and capacity building for poverty-related diseases in sub-Saharan Africa. EDCTP has supported 48 projects aiming at improved diagnostics, vaccine development and treatment for tuberculosis.

### ***Providing patient-centred integrated care***

The use of health information technologies to enhance home-based care of long-term conditions allows a quick and more integrated approach to health services, and enables patients to participate in the management of their own conditions. The European Union is supporting such initiatives through different instruments.

The FP7 HOMECARE (Clinical Continuity by Integrated Care) project aims to find better ways to ensure continuity in clinical care for elderly rehabilitation patients with frequent chronic conditions such as stroke, COPD and heart failure, structured in a platform for remote monitoring of patients with chronic diseases. A health technology assessment report from the project has concluded that integrated homecare leads to improved health and reduces costs [32].

CHILD-EU (Orphans Unite: Child Better Together – European Management Platform for Childhood Interstitial Lung Disease) fosters research in childhood interstitial lung diseases, in order to produce accepted evidence-based and consensus-agreed diagnostic and management clinical guidelines to improve lives of children with these incurable diseases.

Several projects focus on patients' quality of life. For example, REQUITE (Validating Predictive Models of Radiotherapy Toxicity to Improve Quality-of-life and Reduce Side-effects in Cancer Survivors) ([www.requite.eu](http://www.requite.eu)) seeks to identify biomarkers of radiotherapy toxicity in lung (and other) cancer patients, whereas ACTION (Advance Care Planning: an Innovative Palliative Care Intervention to Improve Quality of Life in Cancer Patients – a Multi-Centre Cluster Randomized Clinical Trial) ([www.action-acp.eu](http://www.action-acp.eu)) looks at advanced care planning in lung and colorectal cancer patients.

### **The European Union's political framework for curbing CRDs**

The European Union's commitment to guarantee European citizens' respiratory health and wellbeing encompasses an orchestrated series of actions translating its political support.

The backbone strategy to curtail damage caused by tobacco exposure consists of legislative acts, such as various directives and council recommendations [33] on tobacco control. The European Union has also legislated in the environmental and air quality fields, with impact in respiratory health through actions such as the Environment Action Programmes [34].

The conclusions of the conference on “Chronic respiratory disease-exploring solutions in the EU” (October 2010, Belgian presidency) [35] and further discussions by the Ministers of Health of all 28 European Union member states resulted in the Council conclusions on chronic diseases [36], inviting the European Commission to integrate chronic diseases as a priority in current and future European research and innovation programmes. The Council conclusions on “Prevention, early diagnosis and treatment of chronic respiratory diseases in children” [37, 38] invite the member states to develop research for better understanding of increase in prevalence of CRD in children, and to tackle the disparities between regions and throughout Europe, among other actions.

Lately, the Council conclusions on healthy ageing [39] have recognised the mounting burden of CRD and advocated for a cross-sectorial approach to achieve active and healthy ageing. The importance of lifestyle choices, including tobacco use, and screening in cancer prevention is emphasised in the European Code against Cancer, a set of recommendations aiming to reduce cancer risk, produced by the International Agency for Research on Cancer ([www.iarc.fr](http://www.iarc.fr)) and co-financed by the European Commission's Health Programme [40].

### **Trends and opportunities for European Union-funded research on CRDs in Horizon 2020**

CRDs and lung cancer are, to a large extent, preventable, and prevention costs are less than treatment costs. Therefore, education and legislative actions supporting better lifestyle choices and helping to eliminate risk factors will be crucial in reducing CRD burden. Future actions will need to adapt to an ageing population,

putting in the centre the patients and their quality of life; make use of innovative technologies and large cohorts to improve disease and risk factors understanding; and capitalise on the advances in knowledge to provide better screening methods and stratified therapies. The future of multidisciplinary research lies in collaboration, both in a geographical sense and between multiple stakeholders (researchers, healthcare professionals, patients, policymakers and regulators); for example, *via* public-private partnerships.

Horizon 2020 [41], the Framework Programme for Research and Innovation (2014–2020; overall budget €80 billion), provides a wealth of opportunities to address unmet research and innovation needs in CRD within the theme “Health, demographic change and wellbeing” (budget €7.6 billion) and elsewhere in Horizon 2020. Besides continuing the support of multidisciplinary, international collaborative research, whilst applying an integrated and cross-cutting approach, Horizon 2020 is designed to systematically address current challenges in the field of medical respiratory research, such as promotion of healthy lifestyles, prevention of environmental and occupational exposures, early detection and diagnosis, new treatments and care, and translation of findings into clinical practice in the context of age-related comorbidities. IMI2 (European Union contribution €1.6 billion, total budget €3.3 billion), building on the achievements of its predecessor, will assemble companies, academia, public laboratories, SMEs, patient representatives and regulators to collaborate on projects for better, affordable drugs for major respiratory diseases, among others.

Interestingly, a novel, dedicated SME instrument (budget €3 billion) will provide funding for early-stage, high-risk research and breakthrough innovation by SMEs, with the aid of the tool Fit for Health 2.0 ([www.fitforhealth.eu](http://www.fitforhealth.eu)) to assist SMEs to deliver effectively their projects’ outputs to end users. Also under Horizon 2020, with a more ambitious strategic research agenda and budget (European Union contribution €683 million) than its precursor, EDCTP2 will underpin the clinical development of new or improved diagnostics, drugs and vaccines against tuberculosis and other poverty-related diseases (malaria, HIV, *etc.*).

An innovative initiative, GTBVP (The Global Tuberculosis Vaccine Partnership), convening the European Commission, the European Investment Bank ([www.eib.org](http://www.eib.org)), the Bill and Melinda Gates Foundation ([www.gatesfoundation.org](http://www.gatesfoundation.org)), the South Africa Department for Science and Technology, the French Ministry of Research, EDCTP, AERAS (Advancing Tuberculosis Vaccines for the World, [www.aeras.org](http://www.aeras.org)) and TBVI (Tuberculosis Vaccine Initiative, [www.tbvi.eu](http://www.tbvi.eu)), is jointly working to develop a global portfolio management of tuberculosis vaccine candidates and to improve utilisation of available financial resources to develop and commercialise new effective and affordable tuberculosis vaccines. Moreover, the European Commission, as member of the GACD (Global Alliance for Chronic Diseases, [www.gacd.org](http://www.gacd.org)) has recently launched an action on lung diseases with a focus on implementation research in low- and middle-income countries and/or vulnerable populations in high-income countries. Also, in the battle to prevent antimicrobial resistance, the Horizon Prize for Better Use of Antibiotics (€1 million) (<https://ec.europa.eu/research/horizonprize/index.cfm?prize=better-use-antibiotics>) will be awarded for a point-of-care test for patients with upper respiratory tract infections.

Horizon 2020 will capitalise on previous framework programmes, strengthening the capabilities of a vibrant research community. The knowledge and concrete outputs generated by former, current and future European Union research actions will be an essential guide for decision-making, informing policy and practice to improve the quality of life of citizens with CRDs.

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