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Research gaps, patient needs and innovative solutions: a forward look on lung health research

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Specific Aims of the Presentation

The presentation focuses on the major open questions in respiratory health research to understand the effects and public health relevance of air quality. After a brief view on the current state and related open issues, inputs will be given to the discussion on how to fill the gaps of knowledge through research. The need for better balance between investments in only the –omics space of respiratory health versus all other and most relevant co-determinants (including research on phenotypes, environmental, cultural and socio-economic factors) will be emphasized.

Summary

INTRODUCTION, STATE AND GAPS

In Europe, the most important health-relevant exposures to air pollution occur at home, during commute, and at work. The most prevalent sources of air pollution amenable to policy relate to transport media (scooters, cars, trucks, diesel trains, ships, planes, construction and farming related off-road vehicles), point-sources (industry, power plants including small-scale mobile power generators), and consumer products and occupational processes. These sources contribute to exposure to a broad range of pollutants, including particulate matter (PM) of various sizes, primary and secondary gaseous and semi-volatile pollutants. Knowledge about the respiratory health effects of the most prevalent emissions, pollutants, and sources has progressed fast and despite open questions and uncertainties, rigorous and decisive regulatory action is strongly supported by science [1-3]. The EU regulatory process lags behind this evidence and is weak in setting ambient air quality standards [4, 5] where the WHO guidelines should unambiguously be the point of reference [6].

There are a range of open research questions and gaps of knowledge. Important ones will be summarized in the WHO project REVIHAAP (soon online in final version - http://www.euro.who.int/en/what-we-do/health-topics/environment-and-health/air-quality/publications/2013/review-of-evidence-on-health-aspects-of-air-pollution-revihaap). The list is long and one way to prioritize may be related to the potential size of the public health problem (thus, number of people exposed and the frequency of related respiratory health problems) and emerging trends in exposure changes. Let me emphasize a few points:

- Exposure to transport related sources of pollution is extremely prevalent among European citizens as a very large fraction of the population lives within a few meters from heavily trafficked roads [7]. Changes in fuel formulation and engine technology result in substantial changes in the level and mix of these pollutants, thus exposure. Uncertainties remain with regard to the acute and long-term effects of near-road traffic related exposures (e.g. nano-sized ultrafine particles, black carbon, larger fractions of non-exhaust particles originating from abrasion and re-suspension etc.) [8].

- With the now required diesel particle filter technology and emerging “alternative” fuels, research is needed to anticipate trends in exposure (e.g. increase in gaseous pollutants, nano-sized ultrafine PM, PAH etc.) and to investigate related health effects. Trends in consumer products, occupational production processes, and combustion and engine technology highlight the need for research to understand consequences of exposure to nano-particles [9].
Due to various reasons, including economic hardship, trends toward home-based combustion for heating is seen in many parts of Europe. This needs high attention on all levels of air quality and health research and close exchange with policy makers as it can be a new source of indoor exposure and a major contributor to ambient air quality.

There is a lack in understanding how air pollution exposure from outdoor, indoor, and work related sources interact with the most important and prevalent co-factors that people are exposed to, under real live (including work) conditions. The role of potentially modifying factors is not well known, thus, limiting the ability of a more targeted “personalized” approach to prevention. Environmental laws and standards are set to protect the health of all people. It is thus essential to also identify those at highest risk to pursue policies profitable to these people as well. A few key factors that may determine susceptibility may be age (intrauterine; infancy; childhood and adolescence; adulthood; pre- and post-menopause; the elderly), sex, body weight (in particular obesity), diet, co-morbidities, life-styles, social stress including poverty as well as endogenous factors (such as genetic variants).

**POTENTIAL RESEARCH DIRECTION**
The funding of complementary atmospheric science, epidemiological, controlled human exposure and toxicological studies is needed to advance understanding of the most relevant harmful sources of emissions, its distributions, the physico-chemical composition of the pollution and biological mechanisms leading to adverse health effects. To address a range of questions, European respiratory research on air pollution needs fully standardized large-scale population based studies and sustained investment in phenotype and exposure assessment research. Support for research collaborations with those countries where air quality problems are most serious should be enforced. Also to be considered:

- While understanding the long-term effects of air pollution is of particular relevance, there is a clear need to further develop methods and update research on the acute effects of air pollution on death and hospital admissions. European researchers developed world-renowned models on how to promote multi-city research relevant to policy making [10]. A next generation of studies is needed on the European scale to understand whether and how acute effects may change in light of the substantial changes in the air quality mixture (as a result of progress in policy and technology) and in the underlying susceptibility patterns which are also subject to changes due to migration, adaptation in life styles, and the economic crisis as a strong driver of health determinants and modifier of environmental conditions (e.g. use of wood and trash for heating as electricity bills become unaffordable). Acute effect research provides results in due time, thus, can be used as early indicators to identify changes in effects and possibly new patterns of public health relevance.

- As a starting point, EU did support research making better use of existing epidemiological studies (e.g. www.ESCAPEproject.eu). This has further advanced knowledge in the field. However, the experience also highlights the limits of such approaches, related primarily to the inherent lack of standardization in how “existing studies” collected data on health and crucial co-factors. The proper definition of respiratory phenotypes is essential to advance the understanding of the role of air pollutants and its interactions with modifying endogenous and exogenous factors as these relationships may substantially depend on the specifics of the phenotypes and endotypes [11]. Thus, in the absence of standardized health data, the most informative research is often related to well-defined mortality despite the fact that morbidities ultimately affect health, the health care systems, and work absenteeism in Europe. The strong focus on genetic factors analysed in pooled but very heterogeneous “existing studies” exemplifies these limitations. The relevance of genetic factors is heavily dependent on phenotypes and fundamentally interlinked with environmental exposures and other endogenous and exogenous factors that orchestrate susceptibility and effects [12].
Advancement in knowledge relevant for respiratory prevention and treatment depends on research that is fully integrating all health relevant dimensions and interactions (i.e. air quality, biologic, life-style and socio-economic factors). This underscores the need for population based cohort studies where all key factors – not only genes and other endogenous -omics actors – are assessed with cutting edge methods. European research funds must more equally be assigned to all health relevant domains to understand effects of air quality on respiratory health, namely better characterization of phenotypes, long-term environmental (source specific) exposure assessment, the socio-economic, life-style, and cultural environment (e.g. in migrants) as much as the molecular and genetic makeup. Large resources get invested in the -omics part of respiratory health whereas the other equally important domains remain underfunded, thus, rely on (too) simple methods to characterize phenotypes and environmental exposure. [Research on the health effects of near-road traffic related air pollution gives a vivid example where dozens of asthma studies relying on a primitive proxy of exposure, namely “residential distance from busy roads” [13] with the definition of the complex asthma phenotype being based on very simple questionnaire data [2, 14].

The misbalance in resource allocation (-omics versus all other determinants) jeopardizes advancement of science in this field. This is odd in light of the very large and often immediate and sustained potential for prevention through policies that adapt environmental conditions or life styles. Environmental factors are very well amenable to highly efficient (and often affordable) preventive solutions for entire populations. Effective interventions on the -omics level are far from reach, inherently expensive, and unable to target the strongest determinants of respiratory health (i.e. environmental, life-styles, poverty and co-morbidities). Personalized approaches that emphasize the -omics level alone will amplify inequalities in access to prevention and cure.

More research is needed to demonstrate how interventions to improve air quality affect public health in the long term. Very few studies were able to address these questions directly (and usually coincidentally) capitalizing on policy driven trends in air quality (such as in the SAPALDIA study [15]). To accomplish this goal, methods to estimate exposure on the individual level, over years and decades are required to understand changes in exposure over time.

Research to advance atmospheric modeling, in conjunction with validation studies using targeted monitoring campaigns and cutting-edge e- and m-tools may provide an efficient way forward in health effects research. Increasing instead the number of single components measured in routine monitoring networks, at a few locations, may not be the most efficient way to advance knowledge in this field. The studies should include better characterization of the pollution mix and improved (also source specific) exposure assessments.

European research should facilitate collaborations with scientists from countries where air quality problems continue to be much worse and even deteriorating [16]. Air quality ranks among the “top three” killers in many countries in Asia and Africa and among the “top ten” in Eastern and Southern Europe [17]. Due to differences in sources and underlying susceptibilities respiratory effects may differ. To advance local policy making there is a need to have sustainable research capacity present in these countries as well.

For occupational air pollution related research needs, the Jack Pepy Workshop conclusions can give excellent guidance. The last discussion was in May 2013. Work absenteeism, presenteeism, promotion and early retirement should all be better investigated in relation to work related respiratory health [18]. This includes research on the socio-economic consequences of chronic respiratory diseases and related co-morbidities.
REFERENCES

9. Particles, H.R.P.o.U., Understanding the Health Effects of Ambient Ultrafine Particles. , in HEI Perspectives 32013, Health Effects Institute