Priorities for Horizon Europe's Health Cluster

The Guild
of European Research-Intensive Universities

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Introduction

The EU is one of the most prosperous regions in the world, with a healthy population and long average life expectancy. However, despite significant medical and technical advances achieved in the past decades we still face many challenges. Non-communicable diseases, many of which could be preventable, lead to the premature death of more than 550,000 people of working age each year across EU countries, resulting in the loss of 3.4 million potentially productive life years. This amounts to an annual loss of €115bn for EU economies.[1]

Risk factors associated with overweight and obesity – largely life-style related – are also increasing at a rapid rate in most of the EU Member States, with estimates of 51.6% of the EU's adult population being overweight in 2014.[2] And this is only an example. Confronted with this, our understanding of population based preventive measures and the development of improved, often personalised treatment and intervention strategies, are insufficient.

For the EU to effectively tackle these challenges and improve people's health and well-being, funds allocated to health research within Horizon Europe must be commensurate with the impact the EU aspires to achieve. A higher budget (or at least a more equitable budget share among the clusters composing pillar II) is therefore needed to capture the pressing health challenges our societies face today. At the same time, it is crucial that the expected impact remains realistic and targets citizens' greatest areas of concern.

The Health cluster must achieve a proper balance between research and innovation. Opportunities for fundamental research in collaborative parts of Horizon 2020 have been limited and require more attention in Horizon Europe. Fundamental research is a key driver for innovation, not antithetic to it. Fundamental and/or early-stage collaborative research should therefore complement close-to-market activities. The Health cluster should also strike a balance between topics related to public health and medical research, as both are equally important for improving health outcomes and promoting healthy living.

It is extremely important that societal aspects are taken into account in each health intervention area and in each phase of development. This is to ensure that societies benefit from discoveries, to avoid negative side effects and to counter citizens' distrust and misconceptions. Cross-sectorial and interdisciplinary aspects must also be taken into account and facilitated by the projects funded under this cluster.

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[1] OECD/EU (2016). *Health at a Glance - Europe 2016: State of health in the EU cycle*. Paris, FR: OECD Publishing, p.3. Retrieved from https://doi.org/10.1787/9789264265592-en.

[2] EUROSTAT (Dataset 2014). *Overweight and obesity – BMI statistics.* Retrieved from https://ec.europa.eu/eurostat/statistics-explained/index.php/Overweight_and_obesity_-_BMI_statistics.

Finally, we reiterate our call for the voice of the scientific community to be heard in the implementation of Horizon Europe in a structured and sustained manner. This is a pre-condition for the quality and impact of Horizon Europe as well as for the quality of the programming.[3]

This document presents priority areas for the Horizon Europe's Health cluster identified by The Guild's academic communities. These are articulated around six key challenges affecting European societies in the coming decades and highlight areas where future research will help to significantly improve people's health and quality of life.

1. Health throughout the life course and the role of environmental and social health determinants

One of the focus areas for Horizon Europe's Health cluster should be the promotion of a healthy lifespan and disease prevention. Whereas processes and events in the various stages of life (from conception, through childhood, adolescence, and adulthood) are major determinants of the ageing process, individual healthcare budgets are largely consumed during the late phase of life. Investing in health throughout the life cycle will help build a healthy and active population for the future.

The most appropriate option to promote a healthy lifespan is the implementation of health literacy, thereby increasing citizens' awareness of what constitutes a health-determining lifestyle. This concerns, among other things, nutrition, physical activity and early prevention based on identifying personal risk factors using assessment or self-assessment methods, tools and models.

Furthermore, it is widely acknowledged that environmental factors have a profound impact on health, both in terms of negative effects (stressors) and positive effects (promoters). Clear examples of stressors are smoking, and air and water pollution, for which successful prevention programmes have been developed. However, there is a huge knowledge gap in our understanding of the mechanisms of the integrated and complex relationships between multiple stressors (physical, biological, socio-economical, physiological, etc.) and health in specific contexts, as well as in how this would translate into individualised or context specific prevention and interventions.

Expected impact

Promoting health literacy will contribute to the increase of a healthy lifespan. This will ensure the following results:

- Better control of the health care budget in European countries (thereby contributing to sustainable health systems);

- Maintenance of the European workforce in terms of health and productivity;

- Reduced inequalities in health and life expectancy;

- Healthier societies throughout the entire life course (from conception to adulthood) and prolongation of independent living of the elderly.

By studying environmental and social determinants, R&I will also provide knowledge on multi-causal mechanisms involved in the interaction of multiple environmental stressors leading to health dysfunction syndromes in specific contexts (geographical area, urban versus rural areas, age, individual susceptibility, etc.) and its relation to and use of health promoters. This knowledge can translate into individualised, targeted and population-based approaches to create healthy environments in Europe. New knowledge from research will also allow us to develop new guidelines and policies, which will be more effective and cost-effective than non-targeted generic programmes.

However, we highlight that impact in these areas will not be subject to the same timescale. While the impact deriving from a health literacy-based intervention could potentially be seen in the short term,

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the impact of understanding unknown associations between environmental/social stressors and specific health-related outcomes is likely to become visible only over the long term.

Key R&I orientations

Projects should be supported at the level of (preas well as postnatal) prevention, nutrition, lifestyle, and use of big data resources. We also need epidemiology (understanding of determinants), and mental, social and environmental stressors long-term intervention studies. Clearly, both fundamental research and applied clinical research activities are required to achieve the desired impact.

Key collaborative, multi-disciplinary and cross-sectoral R&I endeavours should also aim to analyse the mechanisms by which the balance between environmental stressors (as mentioned above) and facilitators translate into health states (spectrum from normal function to dysfunction). This would require:

- The integration of available data at the molecular, individual (lifestyle) and population level, and;

- The development of experimental models at these respective levels such as human exposure models with a wide range of techniques involved (e.g., epigenetics and functional genomics studies).

2. Non-communicable and chronic diseases, including rare diseases

Non-Communicable Diseases (NCDs), and in particular chronic NCDs, currently constitute the largest portion of total burden of disease in Europe. According to the IMHE 2017 analysis[4] of the global burden of disease, in Europe, the first 13 conditions per burden of disease measured with DALY are non-communicable. Compared to the same analysis in 2012, cardiovascular, musculoskeletal, neurological, mental, digestive and respiratory disorders showed no improvement, while the burden of diabetes disorders has increased.

In part this is due to lifestyle and environmental conditions that may be affected by prevention and risk management. But in large part, these diseases have in common a complex, multifactorial etiopathology for which the traditionally reductionist approaches have failed to provide reliable knowledge of the mechanisms of disease. This framework of complexity translates into a wide (and frequently fragmented) range of experimental models, which result in a poor integration and overall interpretation of the scientific results available. As a result, the management of these patients is still largely based on empirical evidence, which might be lifesaving, but leaves considerable residual burden of disease.

The main challenges related to tackling NCDs and reducing their burden include:

- Discovering disease mechanisms for NCDs, providing new targets for prevention, diagnosis and intervention;

- Tackling inherited and acquired resistance to drugs beyond infections;

- Improving accessibility to treatments: methods to reduce the costs of developing and assessing new diagnostics and interventions;

- Lowering the barriers to sharing sensitive medical data on NCDs. In order to foster the identification and standardisation of analytical reference methods, and to improve the definition of successful experimental models through multifactorial approaches, reflecting the complexity of NCDs etiopathology through data interoperability;

- Tackling unmet health needs of patients with rare diseases.

Expected impact

The goal of R&I actions in this area will be to increase the understanding of disease mechanisms, thereby contributing to the improved management of NCD and rare disease patients. Actions in this

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[4] See http://www.healthdata.org/gbd/gbd-2017-resources.

area will also lead to a reduction of inherited and acquired resistance to treatment.

This will ultimately reduce costs for health systems, as today NCDs amounts to an annual loss of €115bn for EU economies.[5]

We also note that, especially in this area, the usual project timeframe of 3-4 years is insufficient in order to obtain results with an adequate statistical power to make a real impact. A longer follow up timeframe must be allowed to achieve relevant impact.

Key R&I orientations

To tackle the challenge of NCDs, a more systematic and holistic investigation of disease mechanisms is required, which leverages 'state-of-the-art' technologies (e.g., genome sequencing, medical imaging, biomedical instrumentation), and modelling and simulation, in conjunction with pre-clinical and clinical experimentation. Analysis on the onset of diseases are also needed to help prevent later chronicity.

Another issue is drug resistance. While there is great attention on antibiotic resistance, NCDs also face serious drug resistance issues in two forms. Intrinsic drug resistance refers to sub-groups of patients for which the first line of care is ineffective; here there is a need for more advanced methods to stratify patients by response to treatment. Acquired drug resistance is more subtle, but very important for many chronic NCDs: it indicates the progressive loss of efficacy or the insurgence of adverse effects associated with long-term therapies. Here again there is need for advanced stratification methods, but also research on ways to reverse resistance, as well as how to best manage these forms of resistance when they manifest.

NCDs are in general characterised by a considerable financial burden of disease, largely due to the high costs of state-of-the-art treatments, whether drugs or medical devices. A major component of these costs is the very high cost of development

and regulatory assessment, which has been growing exponentially in the last years. Thus, the best way to improve access to treatments is to develop new methods to reduce the cost of development and assessment of new diagnostics and interventions, using in vitro and/or in silico alternatives to animal and human experimentation, and developing more advanced approaches to safety and efficacy assessments of new medical products.

In a number of diseases, therapeutic progress using advanced methods, such as machine learning, is impaired because of the growing difficulties in composing large collections of detailed clinical data, too detailed to expect anonymisation. A systematic investigation of all legal, regulatory, and technological barriers that prevent the formation of such large collections is required, followed by research on innovative methods to overcome these barriers without compromising privacy, medical data ownership, and other ethically sensitive areas. This is a horizontal topic, and a similar challenge is also faced in the area of communicable diseases (see point 3 below).

Finally, on rare diseases it is crucial that European Reference Networks (ERNs) – which gather cutting edge research expertise in this area – are further supported by Horizon Europe in their collaborative research endeavours.

3. Communicable diseases

Diseases have no borders. Although EU countries have successfully fought against infectious diseases and managed to significantly reduce their rates, we are facing today further challenges due to new and re-emerging communicable diseases such as measles, and diseases caused by the Ebola and Zika viruses. Vaccinations against infectious diseases have been one of the most important medical measures developed in the 20th century, but they are being challenged by growing levels of mistrust. Additionally, according to the WHO, antimicrobial resistance (AMR) has already reached alarming levels in many parts of the world.[6] High levels of resistance are encountered in bacteria linked to

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[5] OECD/EU (2016). *Health at a Glance - Europe 2016: State of health in the EU cycle*. Paris, FR: OECD Publishing, p.3. Retrieved from https://doi.org/10.1787/9789264265592-en.

[6] World Health Organization (2014). *Antimicrobial resistance: global report on surveillance*. Geneva: WHO Press.

numerous common infections, while resistance to antivirals is also increasing.

In light of this, the main challenges related to communicable diseases consist of:

- Tackling infectious diseases and the spread of antimicrobial resistance (AMR) that puts global health security at risk;
- Lowering the barriers to sharing sensitive medical data on communicable diseases;
- Developing new antiviral and other antimicrobial interventions (preventive and treatment-based).

Expected impact

Collaborations in this area will help achieve better accessibility to new treatment for infectious diseases. It will also contribute to the development of improved strategies to reduce the impact of antimicrobial resistance (AMR) and to improve vaccination coverage.

Key R&I orientations

A number of infectious diseases can be considered neglected, both for prevention and treatment; for example, because the pharmaceutical industry is not targeting its R&I investments toward these areas. Thus, it is imperative that the development of new vaccines, as well as antiviral and other antimicrobial interventions for these conditions is sustained by public funding, including Horizon Europe.

4. Innovative, sustainable and accessible health systems

Universal access to public healthcare services in the EU requires a patient-centric organisation of the health systems. A multi-informant perspective is needed, covering the views of patients, but also carers and health professionals, and it should be the main driver for studies of new healthcare models that improve equality and equity. Citizens should benefit from a continuum between the different levels of care (from primary to secondary and tertiary), as well as between regions and countries within the EU.

To optimise and maintain the accessibility and sustainability of health systems, and also deliver high quality care, systems must be able to attract, retain and provide continuous education for their workforces. Yet, there is a lack of research evidence to inform management on what is needed to develop a competent and stable health workforce. This is echoed by initiatives like the EU Joint Action on European Workforce Planning and Forecasting, which recommended further EU research in this area.[7]

Expected impact

By establishing models for healthcare organisations, R&I can identify optimal systems and provide best practice for implementation in the EU. The goal is the creation of a service that continuously improves by learning from wrong treatment decisions, prevents reoccurrence and thereby diminishes adverse events, and limits excessive administration of drugs (polypragmasy) and unnecessary hospitalisation. This will improve the efficiency of health systems while keeping them financially sustainable.

Key R&I orientations

The key collaborative R&I orientations in order to achieve these goals are to design healthcare models that consider patients' perspectives and examine how health systems can incentivise the promotion of health throughout the entire life course. Evidence-based studies are needed to compare different health systems and approaches including patient outcome, use of resources and health economy, and to study how systems can deliver high quality care. In addition, R&I programmes developed to secure workforce recruitment and retention and continuous education will be vital in order to avoid drop-out from the profession and

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[7] Health Workforce (2016). "Final Guide of the Joint Action on Health Workforce Planning and Forecasting." http://healthworkforce.eu/wp-content/uploads/2016/11/WP2_FINAL_GUIDE_final_version.pdf, p. 53.

increasing differences between the private and public sectors.

Data sharing will be important in order to facilitate learning and diminish adverse events. This requires interoperability between systems and the development of common standards. Surveillance systems can be established to identify, monitor and understand drug interactions and optimal use of e.g. antibiotics, hypnotics, sedatives and antidepressants. Data sharing will enhance the benefits of Artificial Intelligence and machine learning. However, data has to be reliable, based on how the patients are phenotyped, the standards used and the quality of the data.

Finally, knowledge is needed about the degree to which vulnerable sub-groups in the population access local and national healthcare, to avoid increasing the gap between social and economic groups in accessing and using healthcare services.

5. New tools, technologies and digital solutions, including predictive technologies

Big data and digitalisation have the potential to transform the way in which healthcare is delivered, such as by supporting the understanding of health and disease parameters and helping to stratify populations. However, there are still many barriers to the full exploitation of this potential, such as access to data, global 'FAIRification' (making data Findable, Accessible, Interoperable, and Reusable) especially for secondary use of data, development of technologies such as encryption, and blockchain. We also need to promote interoperability to understand how to bring together individual data into a unique system and link these through electronic personal health records. Enabling the generation and/or curation of large medical data collections for the development and validation of predictive technologies will be crucial for managing the benefits and risks of Artificial Intelligence, Digital Twins, and other new predictive technologies, and to translate these innovations into health policies, health systems, and clinical practice. Finally, unlocking the potential of new digital tools depends also on the clarification of legal requirements for collecting, aggregating, and processing data. This includes ethical aspects such as data donation and data ownership. It is also important to ensure widespread adoption by authorities, healthcare professionals and patients.

Expected impact

Research in this area will contribute to removing barriers in access to and re-use of data, improving (among other things) cross-border healthcare and individual health data portability, and the ability to integrate new technologies into medical practice. The successful exploitation of digital technologies will ultimately make various processes (within or between health systems) quicker and more reliable, reduce costs by helping to avoid duplication in diagnostic procedures, and enable the more effective use of "real-life data" that is already available. This will help tackle major health challenges and benefit citizens and health systems.

Key R&I orientations

Increased access to large databases in many countries represents progress in research. However, big data technologies must be further developed to cope with specific requirements that emerge from their application.

Collaborations in this area should support studies on legal and technological methods to simplify the generation of large medical data collections as well as their curation for the development and validation of predictive technologies. It should facilitate the use of Artificial Intelligence, Digital Twins and other innovative tools, and contribute to the development of Personal Health Forecasting (i.e., technologies to support the patient-centric, supervised self-management of chronic disease).

To develop and to robustly confirm the credibility of such predictive technologies, it is essential to create well-curated collections of clinical data that can bring together electronic personal health records, genome sequencing, medical imaging, biomedical instrumentation measurements, and medication history under a common language and ontology including reliable outcomes, against which to validate new predictors. The formation of such curated collections of identifiable clinical data is being pursued at a smaller scale by some Member

States. We advocate funding pilot projects aimed to form such precious collections at the EU scale, while finding innovative ways to overcome the legal, organisational and technological barriers that currently make difficult to establish such initiatives.

Finally, R&I should help manage the benefits and risks created by these new technologies and identify methodologies that would help overcome barriers to adoption.

6. Better health systems through academia-industry collaboration

Universities provide skilled professionals necessary for the development, innovation, and implementation of solutions into the clinic or market and the industrial production of new diagnostic methods, treatments, therapies and pharmaceutical drugs. They should therefore be recognised as essential actors contributing to the competitiveness of the European health-related industry. Academia and medical researchers are essential for defining the value chain for industrial product development, which covers: (1) identification of needs, (2) development, (3) production and (4) implementation of solutions.

Collaborations between academia and industry may address research areas in which present industrial activities are insufficient to meet societal demands, which would benefit from public-private partnerships (such as in the development of therapeutics for mental disorders and antibiotics). Such collaborations may also address fundamental scientific challenges that are not receiving enough interest and funding, and which often need multi-disciplinarity.

Clarification on the ownership of health data is also needed, to avoid conflicts between regulating bodies, healthcare, companies, universities, researchers and patients/citizens.

Expected impact

Strong early-stage research (at low TRLs) will provide attractive environments for innovation, start-up companies and the localisation of industry, which will increase Europe's competitiveness (and will ultimately contribute to economic growth). Enhanced academic involvement will also provide the essential innovations needed for creating an efficient ecosystem that facilitates the development of start-ups and SMEs.

Clarifications as regards to the ownership of data will promote the creation of systems/organisations for partner collaborations protecting intellectual data, both for researchers and companies. This will facilitate access to high quality health register data and biobank samples.

Key R&I orientations

Horizon Europe's support for the competitiveness of the health-related industry should aim at promoting more collaboration and stronger partnerships with academia, as this is an essential pre-requisite for Europe's industrial competitiveness.

The Innovative Medicines Initiative (IMI) has been a very successful example of a public-private partnership facilitating collaborations among industry and universities. In Horizon Europe we advocate for the continuation of this initiative with a stronger focus on promoting university-industry collaboration by involving academics in setting research priorities and supporting the development of models for sustainable university-industry long-term collaborations.

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