Advice 2016 of the Horizon 2020 Advisory Group for Societal Challenge 1, "Health, Demographic Change and Well-being"

Executive Summary

In recent years Europe has faced major challenges from migration, financial crises and other disruptions. For Europe to successfully tackle these challenges, research, innovation, education and knowledge generation are essential.

Within this context, health research is crucial to ensure the continuing health and well-being of all European citizens.

We have rising healthcare costs, an ageing population, migration and other disruptions at the heart of our societies. We see new emerging serious infectious diseases, climate change is influencing health and well-being, and there is a reduction in general security within many sections of society, including problems with inequality and even issues of food security. At the same time, technology continues to develop at an accelerating pace alongside societal attitudes marked by ever greater demands. We need smart solutions to overcome these challenges and we must grasp every opportunity for European leadership.

The recommendations in this Advisory Group report were developed at the request of DG Research and Innovation, in response to "Health, Demographic Change and Well-being", which is Societal Challenge 1 under the Horizon 2020 Research and Innovation Programme. These recommendations are for the end of the period 2018–2020. The report is a collective effort with all authors being members of the Advisory Group.

The main research priorities are the following:

VERTICAL themes
1. Personalised medicine
2. Rare diseases
3. Infectious diseases
4. Non-communicable diseases
5. Paediatrics
6. Public health and prevention including migration
7. Active and healthy ageing

HORIZONTAL themes
8. Big data
9. eHealth, mHealth, ICT
10. Integration of care
11. Environment and health, green solutions and sustainability including climate change

CROSS-CUTTING issues
12. Social Sciences and Humanities, integration, inequalities, migration and ethics
13. Sex and gender differences in medicine
14. Commercialisation within "Health, Demographic Change and Well-being"
15. Encouraging stronger and successful involvement of EU-13

VERTICAL THEMES

Personalised medicine

We need continued insight in both etiologies and underlying mechanisms that modulate progress of many diseases across the full course of the disease. Translation of such knowledge and technological innovation into the clinic and healthcare systems in general is the key challenge to be addressed to implement personalised medicine (PM). Europe has unique relevant strengths in this regard, including large collections of omics-derived biomarkers, established prospective clinical cohorts and scientific leadership in specific disease areas. A holistic approach is needed to synergise and capitalise on these strengths, and interoperability of health-related data will need to be addressed to develop valid PM solutions and products for Europe.

Rare diseases

Rare diseases represent a health and social burden to be investigated in depth and breadth, and they serve as research models. Research on molecular causes and mechanisms is warranted to identify, test and develop new therapies and biomarkers and will also bring new insights into common diseases. Clinical trials need to be tailored to disease rarity by new methodological approaches; patient engagement will contribute to building trial readiness and defining significant outcome measures. Coordinating efforts across funding instruments and research infrastructures is needed. New treatments and cures, including advanced therapies and repurposed drugs, will require strong partnerships between academia and industry to be translated into therapies available on the market.

Research and innovation for infectious diseases

Three priority research questions remain: 1. Vaccines against infectious diseases affected by anti-microbial resistance (AMR) (e.g. *S. aureus*) and against emerging diseases (e.g. Lassa fever); 2. Novel diagnostics (e.g. tests for multiple agents and for differential diagnoses and surveillance), anti-infective therapeutics (e.g. antibacterial agents to tackle AMR, antivirals, immune modulators, and host-directed therapies) and exploration of the role of host genetic factors on disease severity, and of modalities for controlling sepsis; 3. Improving standards to support innovation (e.g. to improve quality of medicines through process development and standardisation, combat sub-standard products, encourage public acceptance for vaccines).

Non-communicable diseases

There is increasing recognition of the burden of the main non-communicable diseases (NCDs) and their shared risk factors and determinants. Collectively, NCDs present a substantial burden in terms of morbidity and mortality, particularly amongst the poorest in our society. The overall goal of the chapter on NCD in this report is to highlight areas that would benefit from research investment so that policy decisions for addressing NCDs will be grounded in evidence-based research. A comprehensive approach that is patient-centered is needed across disciplines to address the complexity of multi-morbidity and NCDs.

Paediatrics

Many diseases starting in childhood persist throughout life (e.g. allergies, autoimmune diseases, neuropsychiatric disorders, obesity). Their early diagnosis and treatment will impact on health throughout life. Data linking analyses of multiple types of big data (in particular genomics) with clinical studies is of paramount importance. Childhood cancer and chronic diseases need personalised medicine for overcoming drug supply inequalities and offering better quality cures. European Reference Networks need strengthening to capitalise on their research capacity. eHealth- and mHealth-based health record and surveillance instruments are needed to facilitate this transition and to empower young people.

Public health and prevention including migration

The identification of personal, social and environmental risk factors and processes responsible for health and well-being in society will form the science base for improving health in Europe. This will include Social Sciences and Humanities, causal understanding of non-communicable diseases, access to large amounts of data and consideration of sex and gender issues as well as minorities and recent migration. Evaluation of individual and population-based intervention strategies, both retrospectively and prospectively, is needed to guide future prevention programmes. Research "from genes to greens" will allow the unravelling of their link to neurodevelopment and neurodegeneration.

Active and healthy ageing

The increase in chronic diseases and the ageing of the population are placing high demands on healthcare services. To maintain high quality of care and to help citizens to remain active and independent, a paradigm shift is necessary, focusing on health promotion, disease prevention, and early diagnosis. More coordinated and sustainable healthcare systems are needed to realise the 'Triple Aim' of better health, better use of resources, patient satisfaction and citizen empowerment. We propose building an evidence-based roadmap to enable faster adoption of new technologies and new care models (such as ICT, big data and artificial intelligence), aimed at overcoming current barriers to change.

HORIZONTAL THEMES

Big data

Future health research will increasingly rely on integration of large datasets to provide the evidence base for realisation of personalised medicine and future health policies. Such datasets range from high-throughput 'omics' analyses of human specimens to electronic health records, personal monitoring devices, population and patient cohorts and registries, and data on environmental exposure, nutrition, lifestyle, socioeconomic status, and so forth. Efficient use of big data requires interoperability and standardisation of different datasets, and requires public acceptance based on assurance of the protection of the privacy of individuals. Big data is our overarching theme for health research and it is also relevant for the other societal challenges.

eHealth, mHealth, ICT

The following 'ICT for Health' innovations must be adopted and scaled up: Information governance (best practices in legal and ethics issues, privacy protection policies, data sharing arrangements and validation of semantic interoperability assets) for patient care, clinical research and learning health systems; eHealth and mHealth solutions for improving safe and participatory continuity of care (including for persons with multi-morbidity); Integration of high quality Electronic Health Record data with other big data (e.g. molecular data, lifestyle and environmental data, microbiome, etc.) in order to deliver precision medicine and better treatment decision support.

The above should be accelerated by the public sector by stimulating public confidence about health data governance.

Integration of care

Integrated care (IC) is a precondition for the economic sustainability of our health and social care systems. Lack of care coordination between primary, community, social, and hospital settings and the specific needs of the patient, is detrimental to care quality, to care efficiency, and to patient safety. Current state-of-the-art Electronic Health Records (EHRs), decision support systems, diagnostic tools, clinical guidelines and care pathways are still insufficient to cope with the challenges of IC across the different tiers. Building on the experience from existing experiments, as documented by the B3 Action Group (Innovation Union, A European 2020 Initiative) we call for the EU to support an umbrella programme on IC, which is sustainable in terms of funding and allows for resolution of remaining challenges, as elaborated in the chapter on IC later in this report.

Environment and health, green solutions and sustainability including climate change

European urban environments undergo transformation due to technological innovation and external drivers such as climate change. Three main research aims to establish health as a major driver for technological and environmental needs are: (a) the impact of green housing solutions and increased economic pressures on health, considering indoor environments and future city planning, (b) the health benefits and costs of green solutions to mobility, focusing on electric mobility, and (c) the role of urban environments on active and healthy ageing employing the exposome as a biomedical approach jointly with social, spatial and economic aspects.

CROSS-CUTTING ISSUES

Social Sciences and Humanities, integration, inequalities, migration and ethics

Good research cannot take place in the absence of ethical and scientific integrity and as researchers we have a duty to respect the rights and dignity of research participants and to protect them from harm – symbolic or actual. The synergistic benefits of multi-disciplinary research with the inclusion of Social Sciences and Humanities (SSH) and participatory action research enrich datasets enabling a more holistic approach to the design of studies. Health care research is strengthened when it is expanded to include the relevant scientific study of

behavioural, cultural, and social phenomena, in fields ranging from anthropology, economics, psychology, political science and sociology to literary studies and education research.

Sex and gender differences in medicine

Attention to sex and gender in biomedical, health and clinical research is an important quality and safety issue. Women and men have different sex- and gender-related risks for developing certain conditions. Robust sex, gender and age analysis must be conducted in research to fill the knowledge gaps and promote more targeted citizen-centred healthcare. These challenges overlap with other societal challenges that influence health, including but not limited to ageing, socio-economic status, education status, ethnicity and sexual orientation. A multi-sectoral and multidisciplinary commitment is needed to effectively integrate sex and gender in research.

Commercialisation within "Health, Demographic Change and Well-being"

Horizon 2020 aims to catalyse "breakthroughs, discoveries and world-firsts by taking great ideas from the lab to the market." What are the barriers to bringing new ideas to the marketplace? Early investment is needed to transform an idea into a minimum viable product, together with practical measures to integrate EU-funding for scaling-up (mobile phones, company registration, tax and banking) and to facilitate the interaction between entrepreneurs and corporate decision makers. We recommend measuring the impact of Horizon 2020 in commercialisation, on the basis of interviews, online research and Horizon 2020 progress data analytics as project results become available.

Encouraging stronger and successful involvement of EU-13

In order to encourage stronger involvement of EU-13 countries in Horizon 2020 the method of defining the salaries for young researchers should not refer to their current, very low, salary levels. Using a unified method, such as for example the Maria Curie Skłodowska rules, would significantly increase the attractiveness of the programme for young researchers from EU-13 who, after all, are the future innovation leaders. EU-15 countries should be motivated to involve partners from EU-13. Call topics should be defined in accordance to challenges in all EU countries, including specific problems faced by the EU-13. An effective awareness campaign on Horizon 2020 funding possibilities is needed for EU-13 countries.

The big picture

Big data is an important common denominator for the research area "Health, Demographic Change and Well-being", and impacts on all the other societal challenges.

Big data are large in volume, diverse, dynamic and often comprise distributed and unstructured information. The large and complex nature of big data requires radically new approaches to data processing, which can underpin the steps towards the necessary solutions of the health-related Grand Challenges. As the nature of evidence becomes increasingly grounded in a wide range of measurements, from physical measurements

through biomarkers and human behaviour to government statistics, the value lies not so much in the data itself, but in insights that can be derived.

We need developments in ICT infrastructure, data science, governance and standards, all of which are challenges that share methodology with research in most other areas: climate, energy, transportation, secure societies, urbanisation and migration, food and health, the 'blue world', space and Earth. We propose to future-proof European "big data" science, from infrastructure to methodology and use, to secure Europe as the research leader of this area. The goal is to secure the European economy in the future. We recommend a major push towards exploitation of big data in health research and across the other societal challenges to establish European leadership in this major field. Europe has the potential for the world leading role here, and with an open approach we can build on already existing European Strategy Forum on Research Infrastructures (ESFRI) big data infrastructures. Huge impact will result from a step-up in common standards of interoperability and data sharing, alongside advances in algorithms to derive actionable information through large-scale data linkage, real-time processing of streamed data and deep learning from unstructured data, once these are predicated on practical solutions to real problems within the timescale of H2020.

Personalised medicine is growing in importance. It offers the prospect of tailor-made solutions together with companion diagnostics and stratified medicine, with "red pills for patients with red tumour genes and blue pills to patients with blue tumour genes" to use a simplistic metaphor. Personalised medicine is important for cancer diseases, but also for immunology, infections, and other disease areas, for prevention and for early diagnosis, and as a model when applied to rare diseases. Personalised medicine is also important in paediatrics.

Europe has a comparative advantage, with a long tradition of epidemiology, registers, biobanks and cohorts. The use of already existing cohorts, databases and biobanks is important, as is the continued and strengthened use of ESFRI.

New emerging, serious, infectious diseases that are rapidly spreading around the world are a challenge: "Bugs respect no borders". Microbial antibiotic resistance is a very important area, and in spite of efforts in previous programmes under the European Commission and much effort across the world, antimicrobial resistance continues to be a huge global problem. It is important therefore that we focus on this challenge, to develop new principles, new drugs and entirely new solutions. Vaccines are of course the preference here. The concept of "One health" with a united perspective on food, animal, plant and human health is not obsolete. The cover of the journal Nature on May 12th 2016 read: "Superbugs Rising. Inadequate sanitation promotes transmission of antimicrobial resistance". Migrant health will create new challenges and disease patterns we have not seen for a long time in Europe.

In some areas in Europe the healthcare system is coherent and well-functioning; in other areas it is not. Evidence-based exploitation of "best practice examples" in integrated healthcare is of great importance for better healthcare in Europe. One electronic patient health record or at least one DICOM-like standard for all Europeans is recommended, together with the most creative and proactive use of ICT, eHEALTH and mHEALTH.

In Europe we spend about 10% of GDP on hospitals and healthcare, and only a small fraction of this on prevention. Prevention strategies together with the promotion of a healthy life style is crucial for the well-being of Europe's citizens, for the reduction of healthcare costs and for the welfare of society at large. It is a difficult area to research, and is closely

intertwined with national Member State politics. Bad habits cannot be changed by research alone, and the crucial research questions are how to change behaviour to produce a healthier life style, especially among those who are less well educated. This provides a critical opportunity to address certain issues of inequality that persist. It will require new methodologies for design and evaluation of trials, combing quantitative measures of health benefit with individual reported outcomes. Gaining engagement at scale will build on expertise from Social Sciences and Humanities (SSH).

Patients and citizens must be involved in the entire process, from the design of research programmes to the dissemination and implementation of results relating to wellbeing, health, social care, public health, and society. Tailoring of user-centred interfaces, decision supports and interventions based on user needs and capabilities are important, with investigation of models and community engagement to ensure inclusiveness, equity, relevance, and timeliness of efforts. Investigation is needed into the balance between personal contact and fully automated smart solutions: digital to physical.

Research integrity and ethics must be secured through Codes of Conduct leading to robust and valid data and which are respected throughout the whole research process. This is mandatory for all research themes. For big data, the issue of data security is even more complex, as it is important to ensure that it is possible to carry out research and at the same time maintain individual patient and citizen security. At the same time, access to data is essential for research and innovation purposes while respecting individual data confidentiality.

The gender aspect must be addressed throughout the research programme. Researchers should be both males and females, in all areas and at all levels. For research subjects, the gender balance must also be considered: for animal studies, for studies in volunteers and for clinical studies patients of both sexes should be involved (where relevant). Research must be carried out along the whole life course from conception, early development, children, adolescents, through to adults, the ageing and the oldest old. It is not enough to focus research on young healthy males, neither for volunteers, patients or those who perform the research.

We recommend transnational collaboration with a focus on the use of EU funds for research where Member States cannot solve problems alone and where collaboration is needed. The programme needs to focus on international collaboration with researchers outside Europe, and we need to focus on mobility of both young and senior researchers both across the ERA and out of the ERA and back again.

Medical research includes basic, translational and clinical research, and implementation in clinical practice after new research results are proven by the principles of evidence-based medicine. Medical research also includes well-being, public health and prevention. It is not a linear model, but a multidimensional model with a high level of complexity. The group recommends linking research to education and innovation and to use research results as basis for political decision making.

Innovation is a broad concept that includes new products: drugs, diagnostics, tools, surgical procedures, software and hardware for imaging, medical technology and devices. It also includes the new, large area of ICT solutions and big data. ICT solutions will be relevant throughout the chain from prevention, screening, early diagnosis, treatment, rehabilitation and everyday life, including the growing number of patients with long-term, chronic diseases.

The potential for industry and SME involvement is huge for all themes in this societal challenge area, not only for obvious new products, but also for new solutions and ways of organising health and care. This will inevitably lead to new products not even yet thought of. We challenge the present handling of innovation in Europe: we are not doing well enough.

Interdisciplinarity is crucial and links exist between all our themes. ICT can help to address challenges in all areas and personalised medicine may provide the underlying explanation for disease mechanisms in many research areas. In public health, the programme needs to focus on a holistic integration with other research areas. Both mental health and mental disorders influenced by physical health should be viewed in cohort studies, in interventions and with big data approaches. Tobacco, alcohol consumption, healthy food, healthy lifestyle with physical exercise and interactions with the natural environment with a sustainable approach to societal life should be the focus for the future. We need to re-think the future and let new, intelligent, sustainable, and if possible green sustainable approaches, provide the solutions to create better lives and enhanced well-being for our citizens. The crucial research question is not what is healthy, but how to make all citizens live a healthy and happy life, including those citizens who are less well educated and less privileged.

Interdisciplinarity among scientific disciplines such as the life sciences, natural sciences, technical sciences, social sciences and humanities is crucial. Well-being, health and healthy living is relevant to all the societal challenges. If the populations of Europe are healthy, happy, and thriving, Europe will be a better society and for all the other societal challenges we recommend that well-being, health and healthcare aspects are considered as integral.

In a world of rapid environmental changes that have potential impacts on health and well-being, "environment and sustainable solutions", are overarching keywords of high importance for all research themes in this report and for the other societal challenges. An open collaboration with interdisciplinary approaches with focus on both disruption and exploitation and continuation of already initiated relevant and high quality research is recommended.

Conclusions

These are the recommendations from the Advisory Group for the potential strategic priorities for the work programme 2018–2020 and beyond for the Horizon 2020 Societal Challenge 1: "Health, Demographic Change and Well-being".

Recommendations will also come from the other stakeholder groups, from the Member States, Associated Countries and Programme Committees, from conferences, workshops, the healthcare sector, researchers, patient organisations and society. The development of the programme is the result of a melting pot, where we all must strive to make the most out of scarce public research monies.

The overarching big theme of all the Horizon 2020 Societal Challenges is "Big Data" – both for health and for all the other societal challenges. Here Europe is leading and can with a realistic effort be a spearhead – for the benefit of Europe as well as for the rest of the world.