Advice for 2018–2020 of the Horizon 2020 Advisory Group
for Societal Challenge 1,
"Health, Demographic Change and Well-being"

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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

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.

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.

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". The main themes are:

VERTICAL themes
1. Personalised medicine
2. Rare diseases
3. Research and innovation for 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
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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.

Forewords

Foreword of the Chair and co-Chair of the Advisory Group

We would like to thank the European Commission for a fine collaboration and helpful guidance with our Advisory Group. In this Advisory Group for the Societal Challenge 1, "Health, Demographic Change and Well-being" we worked closely together to compile the chapters in the report through small focus groups. As chair and vice chair we would like to say thank you for the great job done by our Advisory Group members and thank you so much to our rapporteur Professor Anne I.H. Borge from Norway. The Advisory Group met for the first time January 2016, and the report was finished in early summer 2016. We would like to say thank you to the European Commission Directorates General "Research and Innovation" and "Connect" for their excellent collaboration and for their support in terms of information and professional sparring. Thank you so much to Simon Hadlington for language editing. From our Advisory Group we recognise the importance of interdisciplinary collaboration with the other societal challenges and we see big data as the common denominator – and a solution to some of the questions and problems.

Europe needs to maintain and strengthen its position as a knowledge-based society through research, innovation and open sharing of valuable ideas, publication and data. The challenge is at present large and serious and we need to collaborate in order to secure future health and prosperity in Europe.

Prof. Liselotte Højgaard, Chair and Prof. Paulo Lisboa, co-Chair

June 2016

Foreword from the European Commission

This 2016 Advisory Group report for the 'Health, Demographic Change and Well-being' Societal Challenge of Horizon 2020 provides an excellent starting point for deliberations on the Horizon 2020 strategic programming exercise for 2018-2020.

The added value of research and innovation funded under Horizon 2020 is the scale and scope of co-operation between excellent teams, representing European and global diversity. The membership of this Advisory Group reflects this diversity and we are indebted to them for their commitment to delivering such a high quality and thought-provoking document. We look forward very much to receiving the views of the broader stakeholder community, and to continuing to work with this Advisory Group, such that Societal Challenge 1 can deliver its promise of better health and quality of life for all.

We are very grateful for the excellent co-operation with and within the Advisory Group for providing such a high level advice to helping us to reach the aims of this societal challenge.

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Brussels, June 2016

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The list of members of the Advisory Group is also available on the following website:
http://ec.europa.eu/transparency/regexpert/index.cfm?do=groupDetail.groupDetail&groupID=2942

Introduction and working method

This document provides the second specific advice of the Horizon 2020 Advisory Group (AG) for Societal Challenge 1 (SC1), "Health, Demographic Change and Well-being" towards defining potential priorities for EU research and innovation funding in the work programme 2018–2020.

The Commission services have been consulting this AG as a first step in the process towards preparing the next SC1 work programme. The consultation has been organised around meetings of the group taking place on 22 January, 2 March and 27 April 2016.

The AG organised 15 working groups, taking into account the different activities of the specific programme. The challenges and related working groups were identified in the AG meeting on 22 January 2016.

For consistency of the analyses of the challenges (see full working group reports) the groups used the same set of questions (see Annex 1) based on the consultation paper provided by the Commission (see Annex 2).

For consistency the challenges are described by the same matrix.

Full working group reports

VERTICAL THEMES

Personalised medicine

Matej Oresic (Chair), Catherine Larue, Mikael Benson, Orla Sheils (Anders Olauson and Paula Marques Alves), Marta Cascante, Janis Klovins

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In order of importance, which three main research questions should be addressed by 2020?

1. **Building cases for implementation of personalised medicine (PM).** Better understanding of disease etiologies at the system level (including their co-morbidities and sex-related differences) across a full course of disease development, leading to better diagnostic re-classification, novel biomarkers and targets. Focus on disease areas where such knowledge would create biggest impact in the context of PM and where Europe has unique strengths in the study of non-communicable diseases (NCDs), e.g. in established prospective clinical cohorts and research leadership, including immune-mediated diseases, neurodegenerative and psychiatric disorders.

2. **Focus on specific disease areas for successful implementation of PM.** Pilot and implement PM in specific cases, building on new disease knowledge and utilising innovative technologies (e.g. diagnostics, ICT, therapies). Primary focus on disease areas where significant advances in PM approaches have already been made in Europe; for example, but not exclusively, rare diseases, oncology, and cardiometabolic disorders. Testing of PM against the established clinical practice will also require innovative clinical trial designs, considering both health benefits and health economics as outcomes for such serious diseases.

3. **Wider acceptance of PM and facilitating development of European market for PM.** Advance governance, semantic interoperability and scalability of electronic health records (EHR) across Europe. Focus on supporting development of novel tools for semantic integration of EHRs across different healthcare system (short term goal) and harmonisation of EHRs across different EU states (long term goal).
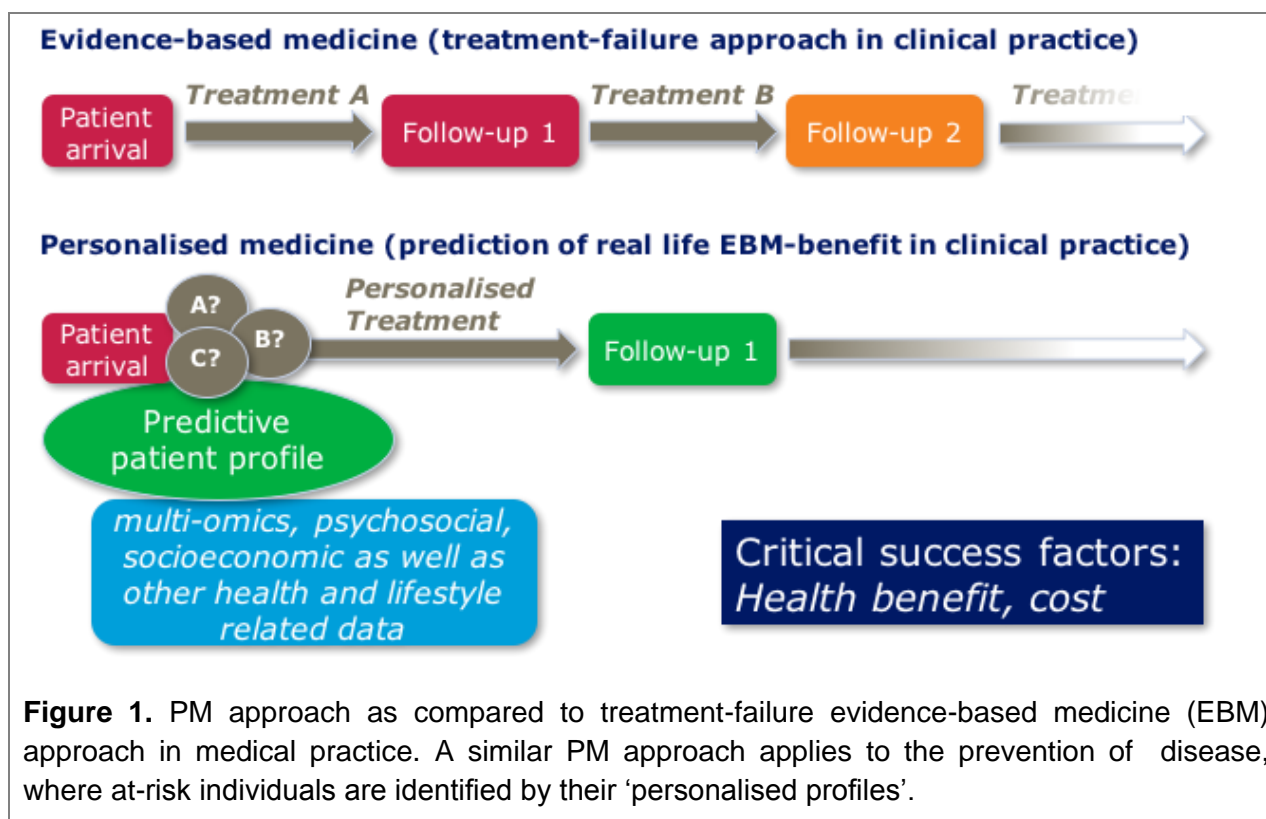

Introduction

A large number of patients do not respond to treatment. This causes patient suffering and enormous costs for healthcare systems, as well as impairing innovation in the development of new therapies. Two important reasons for the lack of treatment response are (a) the individual variations in disease mechanisms and (b) that treatment is generally started late in disease processes, which may last for years or even decades. These problems can be addressed by PM, which is based on characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.

Despite the many advances in research on different diseases over the years, there is still a general lack of knowledge on both etiologies and underlying mechanisms that modulate progress of many diseases (including their co-morbidities and sex-related differences) across the full course of the disease. Translation of such knowledge, i.e. moving scientific discoveries and technological

innovation into the clinic and healthcare systems in general, is the key challenge to be addressed if one is to implement PM. In particular the use of the latest technological innovations (e.g. diagnostics, ICT) is currently still poorly integrated into translational research. Europe has unique strengths relevant to implementing PM, such as established prospective clinical cohorts and research leadership in specific disease areas. These strengths need to be exploited if Europe is to maintain global leadership in PM. Interoperability of health-related data also needs to be addressed if one is to develop a European market for PM solutions and products.

Comment on terminology

Different synonymous terms have been used alongside 'personalised medicine', most commonly 'precision medicine' and 'stratified medicine'. While there may be subtle differences in the literal meanings of these terms, they usually refer to the same concept when applied in practice. **Stratified medicine** (mainly used in the UK) is more treatment-dependent, while **precision medicine** (mostly used in US) has a relatively broad meaning as it refers to 4P (predictive, preventive, personalised and participatory) medicine. We use the term **personalised medicine**, because the term best reflects the ultimate goal of effectively tailoring treatment based on an individual's 'personal profile', as determined by the individual's genotype and phenotype data. Based on individuals' profiles, PM aims to identify the optimal treatment regime by avoiding the treatment-failure approach commonly used in current evidence-based medicine (**Figure 1**).

Figure 1. PM approach as compared to treatment-failure evidence-based medicine (EBM) approach in medical practice. A similar PM approach applies to the prevention of disease, where at-risk individuals are identified by their 'personalised profiles'.

1. What are the challenges in the field concerned that require action under the Work

1.1. What are three main challenges in the field concerned?

To expedite access to healthcare and allow for community care where this is needed, in the most cost effective manner, the main challenges are:

1. **Accelerating medical research** to create new knowledge and related intellectual property (IP) needed to develop new medical products, solutions and business models.

2. **Advancing technologies for PM** to translate outcomes from medical research (including big data) and ICT to facilitate piloting and implementation of PM in healthcare settings.

3. **Advancing ICT platforms and semantic interoperability of the Digital Health Framework** in order to create a vital business environment for industry, including SMEs, to operate across Europe and internationally.

1.2. Give three research orientations to resolving these challenges:

1. Accelerating medical research

- Acceleration of research on early disease detection and (primary and secondary) prevention in healthy or at-risk individuals. Holistic understanding of disease etiologies and pathophysiologies by integrating big data (including environmental profiling, e.g. biomonitoring), functional studies, and computational modelling. By doing so, build cases for early detection/screening and disease prevention, with strong emphasis on validation of existing or novel biomarkers. Based on this, support piloting and implementation of PM in specific disease areas, as well as evaluate the benefit of PM over established practice with respect to health benefit and health economics (**Figure 1**).

- Acceleration of research on tertiary prevention and disease management, including prevention of disease-related complications and co-morbidities:

  o Design of predictive, multi-scale models enabling the discovery of new algorithms and biomarkers for disease, the stratification of patients based on their unique profiles (genetic, phenotypic, environmental), and the prediction of treatment response (including drug resistance). Strong emphasis should be put on validation platforms of existing or novel biomarkers and decision support tools.

  o Systems medical approaches to study disease progression and development of specific co-morbidities and complications.

  o Build cases to identify at-risk individuals early, to predict patients' responses to specific treatments, and ultimately to develop optimal treatments based on patients' profiles. Based on this, support piloting and implementation of PM in specific disease areas.

- Testing of PM against the established clinical practice will require innovative clinical trial designs, considering both health benefits and health economics as outcomes. New clinical trial paradigms are also needed by optimising utilisation of existing data and biobanks. The power of such studies would increase if such prior information and resources could be successfully incorporated into study designs. The clinical trials should include two aspects:

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(a) *in silico* modelling; and, (b) based on real healthcare scenarios (for Phase III and IV trials – not biased through stringent inclusion/exclusion criteria using a disease-oriented approach exclusively). Moreover, the potential of the Digital Health Framework should be used.

- A group of top-level EU scientists has proposed the establishment of an EU-wide cohort of ERASMUS students (who cover both the widening and the mobility aspect) and make this a showcase of big data collection and its usage in healthcare setting towards interoperability of the systems. Similarly, establishment of an EU-wide birth cohort should be supported, which will prospectively collect health-related data, including environmental exposure data. Given the track record and infrastructure for setting up large prospective studies, Europe is in a unique position to be the leader in this area and thus develop the clinical setting needed for innovation in PM.

- Despite the ERIC–BBMRI (http://bbmri-eric.eu/) initiatives, biomedical researchers must deal with a paucity of access to human bioresources and well-annotated data. How to improve this is the key to our approach.

2. Advancing technologies for PM

- Acceleration of technological innovation in biotechnology and sensor/detector biomarker technologies (including biomonitoring) for PM. Bridging outcomes from medical research (including big data) and ICT to facilitate piloting and implementation of PM in healthcare settings. There is a need for inexpensive or accessible technologies, which can capture key relevant information from big data and thus be applicable in healthcare settings without significant loss of precision.

- There remains a substantial step between true translational medicine and *in vitro* studies or animal models and validation in human subjects. New technologies such as "organ-on-a-chip" (and/or "human-on-a-chip") should be made available for use by researchers in order to decrease the time taken from discovery to market and to circumvent the toxicology and safety issues often seen in phase I clinical studies.

- Miniaturisation of diagnostic/imaging/connected technology will directly and positively help researchers (in biospecimens or in use of human materials, as well as nano-cameras, nano-robots, and nano-sensors in the body) and patients (connected devices to receive direct feedback from patients under severe conditions).

3. Advancing ICT platforms and semantic interoperability of Digital Health Framework

- Governance, semantic interoperability and scalability of EHRs across Europe. This is essential if one is to scale-up applicability of innovative solutions and services for PM across Europe (e.g. ICT solutions). By contrast, limiting interoperability to individual EU countries will also limit the business models in the PM domain for European companies. A mechanism should be implemented that ensures broader participation of groups represented by EU countries with underdeveloped EHR systems.

- Semantic interoperability of sensor-generated data, including individuals' health monitoring and environmental data. This is essential if one is to develop a Europe-wide market for innovative medical products supporting the implementation of PM.

- A systems-oriented approach of EHRs should be implemented. This involves management by clinical processes following an adaptive case management approach (ACM) (instead of current management by clinical episode or by disease). Moreover, the ICT architecture should support both collaborative work across healthcare tiers and data analytics from distributed datasets.

- Visualising and modelling personal health data. Build decision support tools (based on EHR and other relevant health-related data such as lifestyle, environmental exposure, etc.) and visualisation solutions which facilitate monitoring individuals' health, based on high-dimensional health-related and environmental data.

- Building public trust in PM. Solutions are needed for privacy protection of EMR data across Europe, for research, individuals' use and for healthcare systems. This should be facilitated without harming innovation, i.e. the solutions should also support public deposition of big data for research purposes. Furthermore, a shift towards patient ownership of the data is needed.

The Innovative Medicines Initiative (IMI) is a public–private partnership between the European Union (EU) and the pharmaceutical industry association EFPIA that aims to speed up the development of better and safer medicines for patients (http://www.imi.europa.eu/content/home). With the EU funding for IMI coming from H2020 Societal Challenge 1, potential synergies between IMI and collaborative research projects can be ensured and potential overlaps avoided.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

With respect to research, there may be synergies with the Societal Challenge 5 (Climate action, environment, resource efficiency and raw materials). Environmental causes are linked to several non-communicable diseases, but the underlying mechanisms that could lead to better prevention or treatment in the context of PM are still poorly understood. Exposome research is one such research area on the interface of the Societal Challenges 1 and 5.

2. The Leadership in Enabling and Industrial Technologies?

The challenge 2 listed above in section 1.2 may overlap with and in particular benefit from the FET programme, which may provide novel technological solutions to be developed for PM. Technological platforms must accelerate R&D transfer to both industry and healthcare providers. Moreover, connected tools will also contribute to the well-being of European citizens.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Better understanding of disease etiologies at a system level (including complications and co-morbidities). This will contribute to the identification of novel biomarkers and therapeutic targets, as well as diagnostic re-classification, all of which can be used clinically for PM. This in turn will lead to understanding in advance how patient will respond to specific therapy. Using biomonitoring and ICT tools at home or in the community will minimise unnecessary visits to clinicians and empower patients to have input into their own disease management rather than be passive participants in a clinician-driven process. Ultimately this will establish true patient-centred treatment.

2. Established practices, governance and privacy protection of EHRs across Europe, still allowing the access and sharing of data. Increased trustworthiness and interoperability of medical data (e.g. big data, sensor-generated data).

3. Increased utilisation of personal health data by individuals and wide acceptance of the PM approach by healthcare professionals. Quicker/safer decisions (thanks to sharper algorithms and tools) for medical staff and therefore better health management of European citizens (healthy or not). Evidence of health and economic benefit of PM approach in specific disease areas.

2.2. What are the new trends and disruptive innovation in health and care?

- Rapid advancements in understanding of disease etiologies in multiple medical domains based on big data (e.g. multi-omics, psychosocial, socioeconomic as well as other health and lifestyle related data), leading to innovation in predictive and preventive medicine.

- Technological advances, allowing more accurate and non-invasive screening/monitoring of patients. Connected devices and miniaturisation of diagnostic/imaging/connected technology will directly and positively help researchers and patients.

- Availability of ICT solutions which may facilitate effective health monitoring and data exchange.

2.3. Which innovations which could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Medical innovation and thus creation of knowledge and related IP needed to develop new medical products and solutions.

2. Developments of technological solutions bridging the gap between medical research and implementation of PM in healthcare settings (e.g. connected devices, miniaturisation of diagnostic/imaging technologies). The first successful examples of PM are likely to reach the clinic within 5–7 years. Quicker time from discovery to market for innovative drugs/products.

3. Put the patient at the centre (invite them to H2020 preparation meetings).

Propose three business models that could mobilise these changes:

1. New therapies – Innovative biotech and pharmaceutical companies exploiting the latest

medical and technological innovation.

2. New diagnostic/screening tools – Innovative diagnostics based on the latest medical and technological innovation, including for use by patients themselves.

3. ICT Health – Integrative solutions for health monitoring and disease risk detection based on multi-modal patient data, for healthcare professionals as well as for patients.

Have you seen any market trends in your field in recent years?

- Diagnostic companies emerging which aim to transform and democratise current laboratory testing procedures, e.g. by Point of Care (POC) testing or with novel diagnostic assays.

- ICT Health companies emerging aiming to exploit patient health data, including genetic and multi-omics data.

- New virtual platforms with different companies (coming from different businesses) to assess and set up tomorrow's devices by gathering the best talents for new medical nano-engineering.

- Move of biotech/pharma industry away from one-size-fits-all drug development towards more personalised approaches in specific indication areas, particularly in oncology.

2.4. How would you envisage the support across various funding instruments?

Complementarity should be sought across other relevant and partly overlapping programmes, such as IMI (which is part of SC1) and FET (which may complement SC1 by providing new technological solutions). The use of existing European research infrastructures should be optimised.

3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

We first need to remember to put the patient (via patients' associations) in the centre of the debate by inviting them to participate in these initiatives.

3.1. What are the research gaps at the levels of:

1. *Science and technology?* Need for strengthened translational research – to expedite the transfer of key scientific discoveries and technological innovation into the clinic. There is also need for assuring sustainability of projects funded by EC.

2. *Innovation?* Gaps in knowledge of disease etiologies (including their co-morbidities and sex differences) across the full course of the disease, which would be needed for developing new solutions for predictive and preventive medicine. Innovation may also come by gathering different medical and biotechnological companies/competences that are not yet used to working together.

3. *Market?* Fragmented market due to lack of data interoperability across different European

healthcare systems as well as across different technologies.

4. ***Policy?*** Engagement of stakeholders (EU states, funding agencies, citizens, healthcare professionals, researchers) to reach wide acceptance of PM as well as by the shift towards patient ownership of the data.

3.2. What are the three main potential game changers:

1. Integrated care solutions across Europe, leading to a vital business environment for industry, including SMEs, to operate across Europe and internationally. Shift towards patient ownership of the data.

2. Breakthrough innovation in medicine, leading to new medical products, solutions and services.

3. Engagement of stakeholders (EU states, funding agencies, citizens, healthcare professionals, researchers) to promote semantic interoperability of EHRs and other related data. Wide acceptance of PM by key stakeholders, by demonstrating its health and economic benefit, as well as by assuring privacy protection.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Accelerating medical research (section 1.2, challenge 1) and assuring sustainability of EC funded projects, e.g. by appropriate data/model deposition and knowledge transfer.

2. Advancing technologies and their implementation for PM (section 1.2, challenge 2), as well as advancing ICT platforms and semantic interoperability of the Digital Health Framework (section 1.2, challenge 3).

3. Creating a forum which engages key stakeholders in PM and promotes the concept of PM as a solution for the emerging crisis of healthcare systems.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

In the sense of widening participation (EU-13) one should recognise the existing gaps in many countries within areas of their health systems, especially in the field of ICT and molecular diagnostics. Where possible this should be taken into account by defining the calls that concern interoperability and other issues.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

Widening participation can most easily and directly be addressed in the context of building semantic interoperability of EMRs and other data platforms across Europe. Furthermore, regional partnership projects could be encouraged which involve EU-13 members as well as other Member States.

Establishment of EU-wide prospective cohorts (see section 1.2, challenge 1) is also another step towards engaging participation of the EU-13.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

The key issues are wide accessibility and affordability of healthcare, as well as interoperability of EMRs across different European countries.

What practical research steps could be taken to improve the health and well-being of European migrants?

In the context of migration, implementation of PM should also promote its wide accessibility and affordability.

4.3. Sex and gender

Over the years, scientific knowledge has increasingly demonstrated that some treatments affect men and women differently. However, the proportion of treatments for which men and women respond differently is yet unknown. Many physiological and pathological functions are influenced by sex-based differences in biology. Recent research on cardiovascular disease, osteoporosis and depression has identified significant differences among women and men with respect to the distribution of these diseases. Women and men have different sex- and gender-related risks for developing certain conditions and respond differently to treatment.

These sex and gender differences have important implications for health and healthcare. It is imperative to target medicines to these patient population sub-groups by utilising the correlation between sex and the incidence, prevalence, symptoms, age at onset and severity of disease as well as the reaction to medicines.

Calls should therefore include more specific cohorts to build evidence-based medicine in certain specific areas. After all, PM is all about research at a population level and outcomes. Personalised medicine should be a truly integrated approach.

Rare diseases

Lucia Monaco (Chair), Anders Olauson, Ruth Ladenstein, Paula Marques Alves

Gene therapy for a rare genetic disease

This image represents the outcome of a gene therapy trial for the severe inborn neurodegenerative disease metachromatic leukodystrophy. The therapy is based on extensive engineering of the patient's hematopoietic stem cells and homing of their progeny to the nervous system where they deliver therapeutic enzyme and halt disease progression. The picture is an artist's view of the therapy. It shows a machine that engineers HIV viruses which are then shuttled to the affected brain by a rollercoaster, which represents both the vasculature routing the genetically engineered hematopoietic cells to the brain as well as the DNA helix into which the virus inserts its therapeutic genetic cargo. The choice of objects, background colour and the intense stare of the treated boy communicate a sense of wonder as well awareness of the implications of the bold new gene therapy attempt.

Digital composition by Günter Pusch, a German-born architect and painter who works in Milan. http://www.gunter-pusch.com.

In order of importance, which three main research questions should be addressed by 2020?

For any particular rare disease:

1. What is the molecular etiology and pathophysiological mechanism?

2. Which therapeutic approach(es) could be tested to treat or cure the disease?

3. How can a clinical trial be effectively conducted, leading to impactful outcomes?

Note: these questions are not in order of importance, but reflect the progression of research from disease cause to solution. Any particular rare disease will need to be addressed starting from the relevant level of advancement along the research pipeline.

Introduction

Rare diseases affect fewer than five people in every ten thousand in the European Union and are estimated to number between 6,000 and 8,000, affecting more than 30 million people in the EU; most of the diseases have a genetic origin. Onset may occur at any age, but in most cases these are paediatric diseases. Any or multiple organs may be affected, and vital functions are often severely or fatally impaired.

The extreme diversity in molecular causes and mechanisms makes rare diseases a vast and complex field to be investigated in the search for treatments and cures. The rarity of patients challenges traditional paradigms for clinical trial design and therapy development and makes natural history studies all the more difficult. Most rare diseases are neglected by researchers and investors: this is why the key research questions are not original, and will be reiterated over and over again. Fortunately, today omics technologies, systems biology approaches and advanced therapies provide powerful tools to tackle rare diseases.

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1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. Identifying novel patho-physiological pathways in appropriate disease models leading to targets for therapeutic interventions and preventive medicine.

2. Developing therapies: scoping possible therapeutic approaches leading to pharmacological or advanced therapies; developing novel therapies in the academic setting, including target validation, toxicology and biodistribution studies; development of scalable and cost effective processes for the production of GMP grade advanced therapeutic medicinal products; gaining proof-of-concept at preclinical and clinical level.

3. Building trial-readiness by supporting patient registries and natural history studies; defining clinical endpoint, clinical trial design and patient-relevant outcome measures for those rare diseases for which these have not yet been developed.

1.2. Give three research orientations to resolving these challenges:

1. Big opportunities are offered by the new genomic era:

   a. The genome editing technology based on the CRISPR/Cas9 system is deeply influencing the design of basic studies and somatic gene therapeutic approaches for rare as well as common diseases.

   b. Genomic data acquired by next generation sequencing technologies bear the promise of an increasing number of molecular diagnostic tools for rare genetic diseases.

   c. Epigenetic medicine based on modulation of chromatin accessibility offers a promising avenue for treating rare diseases.

2. Systems biology approaches allow the complexity of rare diseases to be addressed by aiming to unravel major pathways and mechanisms underlying families of related diseases, leading to the identification of new targets for rare disease drugs.

3. Research on treatment strategies and protocols to optimise clinical practice will allow greater exploitation of existing knowledge, products and methods, in order to elaborate broad guidelines for the management of complex diseases and conditions with unmet medical needs, such as most rare diseases, covering all aspects of patients' care, beyond and in addition to product development and drug treatment (e.g. paramedical treatments, use of medical devices, physiotherapy, nutrition, surgery, complementary treatments, etc.).

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

Europe in a changing world – inclusive, innovative and reflective societies

A European health system aimed at reducing inequalities needs to face the challenge of rare diseases. Patients and families affected by rare diseases are often isolated, and have limited or no access to diagnostic tools and care/therapeutic opportunities.

Developing diagnostics, treatments and therapies for rare diseases requires the involvement of patients and their families at multiple levels. Patients are not only the key stakeholders of rare disease research, but also relevant actors in key activities aimed at collecting complete and accurate clinical data in patient registries and precious biological materials in research biobanks, defining clinical trial outcome measures, setting the ethical and legal framework for personal data handling, and so on. Patient empowerment makes such processes more accurate and more effective, and reduces the risk of errors.

2. The Leadership in Enabling and Industrial Technologies?

Public–private partnerships (PPPs); seizing the ICT opportunities

- Increasingly, research on rare diseases up to proof-of-concept for new therapies takes place in academia; there is a requirement for the development of an effective collaborative model to allow translation and development of these results into the industrial setting, up to product development and commercialisation.

- New therapies for rare diseases include in particular gene and cell therapeutic approaches that require new process development research and industrial production settings by biotech and pharma companies, ranging from small start-ups and SMEs, to big pharma. Such a development stage is key to transforming research results into available therapies and should be facilitated at all levels, taking into account the limited commercial attractiveness of rare diseases.

- Most rare diseases, however, will probably be treatable with small molecules. Enabling research and industrial development by SMEs and library screening from large pharma could have a significant impact.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Basic and translational studies will produce new knowledge to feed the research and development pipeline leading to new therapies and treatments for rare diseases, with a potentially tremendous impact on the lives of affected individuals and families.

2. Such knowledge will also have an impact on research and development of therapies for common diseases: rare diseases allow mechanistic insights into fundamental biological processes involved in common diseases.

3. Targeted specific approaches to the development of new therapies will lead to increased and faster translation of biomedical research into better quality and more effective therapies.

2.2. What are the new trends and disruptive innovation in health and care?

Significant innovation in healthcare management will be brought about by the establishment of the European Reference Networks (ERNs). After two years of life, in 2018 the first ERNs will be solidly established for well-identified disease groups and will have also shown their ability to become clusters for research development, beyond care (e.g. quality assurance mechanisms for laboratory testing; development of good practice guidelines for diagnosis and care; support to cross-national clinical trials; registries and links to other European research infrastructures, etc.).

On these grounds, specific calls for European Clinical Research Networks – embedded in ERNs – should be launched to exploit in full the research potential of experts' networking and clustering by disease areas. Such networks could be piloted (as was the case of the Pilot Network of Excellence under previous Framework Programmes) in the first call. Research and Innovation Actions seem the most suited type of actions for this call.

2.3. Which innovations could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Advanced therapies, such as gene therapy, are starting to deliver on their promise to provide effective therapies for rare diseases. The field is ripe for an increasing number of these therapies to reach the market in the coming years. In parallel, neonatal screening for those paediatric rare diseases for which advanced therapies are effective if delivered at the pre-symptomatic stage should be developed and widely applied.

2. Deeper understanding of physio/patho-mechanisms underlying rare diseases is leading to more and more instances of drugs already tested or approved for common diseases that can be repurposed for the effective treatment of rare diseases. This new scenario must be appropriately developed, including through the direct involvement of regulatory authorities, to allow fast access to these repurposed drugs.

3. Similarly, the growing knowledge on rare diseases will bring new and more effective biomarkers and surrogate endpoints that will need to be rapidly developed through the R&D process for fast impact and fruition.

Propose three business models that could mobilise these changes:

1. The involvement of private companies is key to the effective development of therapies for rare diseases and streamlined regulatory approval paths. Pharma companies are increasingly relying on discovery from academic laboratories. This calls for a collaborative model between academia and industry that matches the knowledge, competence and independence of academic research with the resources, development and marketing capabilities of companies. Supporting development of the late pre-clinical and early clinical stages in academic laboratories where appropriate disease models and expertise exist and facilitating transition to the industrial setting would streamline the process.

   Of note, the sustainability of the often prohibitive costs of therapies for rare diseases, for both healthcare services and insurance companies, is a crucial issue that needs to be addressed at a higher and transversal level, in order to allow people affected by rare diseases to benefit from the fruition of research outcomes.

2. Repurposing/repositioning of medicinal products for their potential in rare indications requires a direct commitment by companies and must be driven by funding agencies and patient advocacy associations.

3. Financing patient registration of quality data that are embedded in European Reference Networks with a coordinated approach and shared tools would create a significant operational change to build trial-readiness and enhance clinical development.

Have you seen any market trends in your field in recent years?

An increasing number of pharma companies are addressing rare diseases with dedicated programmes and units, as is evident by the participation of several of them in the IRDiRC consortium.

2.4. How would you envisage the support across various funding instruments?

- Funding of rare diseases research is not streamlined or optimised across the number of many existing rare diseases. An overview of unmet needs across the board is currently lacking and research/funding efforts are unevenly distributed across diseases. Therefore, supporting a gap analysis of unmet medical needs that could potentially be addressed by 2020 is warranted.

  Examples include:

  – rare diseases for which there are no currently available treatments but that do have orphan designations from different agencies;

  – rare diseases from a cluster in which a novel type of therapy has shown therapeutic benefit for another disease of the same cluster and the therapy could be adapted to the other members;

  – rare diseases with registries and active patient groups, to identify and promote research development of those designated compounds.

  Such a gap analysis recommended by the IRDiRC (Therapeutic Scientific Committee Recommendations) needs yet to be funded.

- Several European research infrastructures and platforms that support health research activities in general also benefit rare diseases research (to name a few: BBMRI-ERIC for biomaterials, ELIXIR for biological information, EATRIS for translational research, the JRV EU Platform on RD Patient Registries, etc.). Developing streamlined and coordinated access for rare disease research would ensure optimisation of services, reduce redundancies, and allow maximum exploitation of such resources by the rare diseases community at large. Other platforms are being developed specifically for rare diseases, for example RD-Connect, aimed at connecting and managing omics data, registries and biobanks for rare diseases. In all cases, support mechanisms for long-term development and maintenance of these infrastructures are required to ensure full exploitation, the expansion of existing models to all ERNs, and return of investment.

- Access to existing European research infrastructures should be encouraged in the calls, and access and service fees should be included in eligible costs, thus contributing to the infrastructures' long-term sustainability.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. *Science and technology?*

Given the large number and the vast complexity of rare diseases, the first gap to be filled is the knowledge gap between the discovery of the disease cause and the understanding of the disease mechanism.

Next, a development gap exists for therapies that have gained proof of concept in the laboratory setting, due to the scarcity of competences and resources for clinical and product development and because of the rarity of patients.

2. *Innovation?*

3. *Market?*

Fostering public–private partnerships, in particular committing universities, infrastructures and SMEs, for the development of therapies for rare diseases based on results of academic research is key to this goal.

4. *Policy?*

The rarity of these diseases limits market development and therefore makes them unattractive to pharmaceutical companies (although some rare diseases allow insights into common diseases). The Regulation on Orphan Medicinal Products, by creating economic incentives for sponsors, was able to foster translation of science into therapies for rare diseases. Yet despite this progress, advances in medical research still fail to be translated with sufficient speed into approved therapies that effectively reach patients, and unmet medical needs are still insufficiently addressed (e.g. those of rare diseases for which there are no treatments or no satisfactory ones).

With approximately 5% of patients benefiting from an orphan drug therapy available, protocols of treatments (covering all aspects of patients' care, beyond and in addition to product development and drug treatment) are essential for people living with rare diseases. Currently such guidelines for the management of complex diseases and conditions with unmet medical needs are almost non-existent. Supporting the development of such "protocol of treatments" is therefore essential (as explained above in point 3 under 1.2 on key research orientations).

3.2. What are the three main potential game changers:

1. Research into rare diseases increasingly relies on the production of huge amounts of data from genomics, proteomics and other omics approaches, which call for high-level and high-volume data storage and management and for interoperability of mathematics and informatics tools, as well as for shared principles for data security, ethical data handling and controlled data sharing.

2. Supporting new methodological and statistical approaches (e.g. adaptive design, adaptive statistical methods) for clinical development in small populations. These new methodological and statistical approaches may help to register medicines faster with a much lower cost of R&D.

3. Encouraging, supporting and developing patient-reported outcome measures as an essential step to gather more successful outcomes at the time of benefit–risk assessment. Guidelines of patients' relevant outcomes for specific diseases are especially useful for those diseases where

product development is advanced at pre-clinical phase or phase 1, but for which the endpoints are not yet well identified or are too limited.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. A dedicated Unit on Rare Diseases within the Commission would ideally serve the scope of overseeing and steering the rare diseases scenario at both the European and global level and would be extremely effective in coordinating and managing the diverse initiatives, investments and efforts on rare diseases in Europe, by optimising resources, building synergies and avoiding duplications of effort. A possible solution could entail expanding and reinforcing eRare to coordinate research policies on rare diseases of Member States and the European Commission, linking them to research infrastructures servicing ERNs, with an integration of actions in support of knowledge and capacity building for involved actors (information, training, education, etc.).

2. Supporting trans-national informatics facilities and services for mathematically driven systems biology using high performance computing and ensuring access to such services by the rare disease research community. In this regard, efforts at standardisation of data from genomics and other omics research is regarded as a top priority.

3. Encouraging, supporting and establishing early and continuous dialogue on clinical development strategy and wide evidence generation (e.g. natural history, registry, clinical trial design, clinical endpoints, surrogate endpoints, patient relevant outcomes, regulatory strategy, medical practice, public health strategy) with all relevant stakeholders such as patients' representatives, medical experts, researchers, scientific societies, regulators, health technology assessors, payers and sponsors when appropriate.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

What practical steps could be taken to encourage the participation of the EU-13 in calls?

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

What practical research steps could be taken to improve the health and well-being of European migrants?

We do not feel able to provide specific advice on these topics, as we believe they are overarching themes that would be better addressed in more general contexts. Any suggestion would go beyond the rare disease perimeter and would certainly overlap with other working groups' indications.

Research and innovation for infectious diseases

Marie-Paule Kieny (Chair), Marcel Tanner, Paula Marques Alves
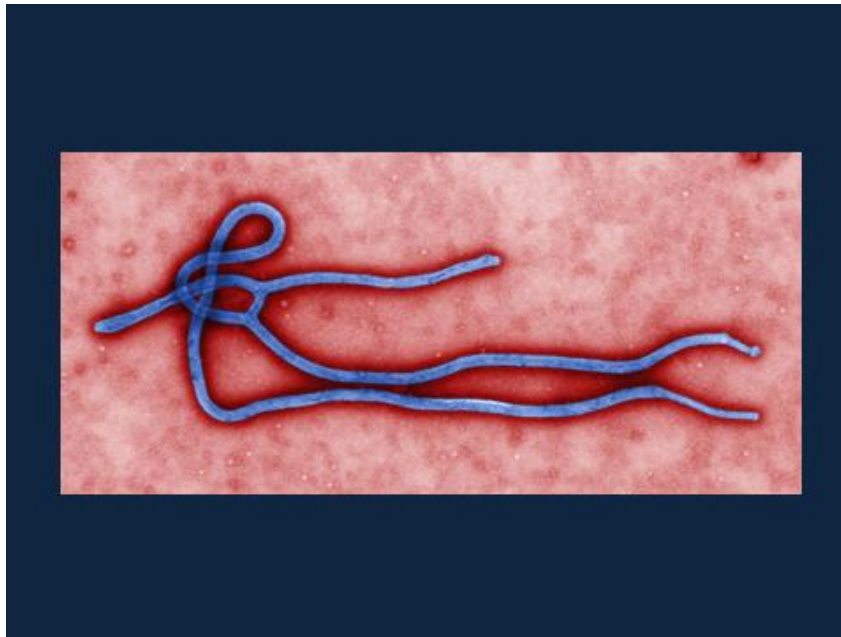
Electronic microscopy picture of Ebola virus

(credit: http://www.cdc.gov/vhf/ebola/modules/flexslider/about-ebola.jpg)

Three priority research questions:

1. Vaccines against infectious diseases affected by antimicrobial 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-standards products, encourage public acceptance of vaccines).

Three main research questions below, to be addressed by 2020:

1. <u>Vaccines against</u>:

- **Infectious diseases affected by AMR**, e.g. *S. aureus*, gonorrhoea, as well as vaccines against diseases currently treated with antibiotics (e.g. S. group A, Borrelia) so as to reduce the overall use of antibiotics;
- **Specific emerging and remerging diseases** (e.g. Ebola, Marburg, Lassa, Congo-Crimea, Rift Valley, Nipah, Zika, SARS- and MERS-CoVs, potentially pandemic influenza), as well as broadly cross-protecting influenza vaccines.

<u>2. Diagnostics, anti-infective therapeutics and exploration of means to control host–microbial interactions</u>:

- Point of care (POC) diagnostic tests for multiple agents and capable of enabling differential diagnoses (Prize as the instrument);
- POC diagnostics/diagnostic strategies for the surveillance and identification of antimicrobial resistance dynamics (Prize as the instrument);
- Novel antibacterial agents to tackle the growing AMR threat and against diseases such as tuberculosis and gonorrhoea, or infections with *S. aureus* and multi-drug-resistant Enterobacteriaceae (Prize as the instrument).
- Antivirals, immune modulators, and host-directed therapies for the treatment of respiratory syncytial virus, Flaviviruses (esp. dengue and Zika viruses), Herpesviruses (esp. HSV and CMV), influenza virus.
- Exploration of modalities for controlling sepsis through a more comprehensive understanding of signalling pathways, both for diagnosis and for intervention.
- Exploration of the role of host genetic factors on disease severity for e.g. influenza, RSV, and flaviviruses.

3. Improving processes and standards to support innovation:

- Development of standards to support public acceptance of medicines and the manufacture and sale of safe and effective medicines, vaccines and health technologies;
- Development of strategies to inform the public and counteract anti-vaccination lobbies (Prize as the instrument);
- Development of standards and methods to support surveillance for falsified, falsely-labelled, sub-standard, spurious or counterfeit medical products (Prize as the instrument).

Introduction

Diagnostics, vaccines and anti-infectives are essential for controlling infection, but much more is needed. It is critical to assess infectious disease within the broader health context to determine which integrated approaches entail the most effective mix of curative and preventive strategies that can be deployed effectively in a given health and social system, meeting public acceptance and in line with public health policies and strategies. Research collaborations for public health infectious priorities should be based on strong partnerships across different cultures and systems to yield maximal utility and to contribute to the establishment of a research ecosystem of wider reach and benefit.

While the EC has already invested substantially in research on infectious diseases in various Framework programmes and in Horizon 2020 calls, more investment is needed in view of the increasing threat to health and security due to infectious diseases.

1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. Resistance dynamics taking new dimensions without adequate surveillance approaches being in place. Unnecessary or prolonged use of anti-infective treatments adds to societal costs and

resistance, which could be addressed by better diagnostics prior to treatment, as well as prevention rather than treatment.

2. Specific disease or infectious pathogen-generated threats, in particular linked to zoonotic and emerging/re-emerging infectious diseases. The emergence of new diseases demands a capacity for research readiness and the ability rapidly to integrate findings from multiple disciplines and approaches.

3. Inefficient or maladapted research and development policies and processes. The current R&D pipeline for anti-infectives and vaccines has a high attrition rate due to the need for elaborate pre-clinical development, costly clinical trials, and the rapid development of resistance to new antimicrobials once they enter into use. Moreover, current business models for investing in research and innovation are failing for diseases for which return on investment is assessed by the private sector as insufficient (diseases of poverty, emerging diseases, antimicrobial agents).

1.2. Give three research orientations to resolving these challenges:

1. Concerted and focused R&D bringing together academia, public health institutions, SMEs and industry, and with input from regulators, policy makers and civil society. Increase of translational research capacity is essential to enhance European competitiveness in this area.

2. Improved down selection of products under development, in particular late stage clinical trials, would assist in reaching development decisions earlier (concept of "kill early"). This can be achieved through better understanding of animal models, development of advanced "human cell based" in vitro models; pharmacokinetic–pharmacodynamic (pk/pd) modelling at the preclinical and clinical level, innovative bioinformatics, and analytical approaches using big data and genetics.

3. Public sector stewardship and financial investment is indispensable in areas where the market fails to drive innovation.

1.3 Do these challenges overlap with:

1. Other Societal Challenges?

2. The Leadership in Enabling and Industrial Technologies?

Research and innovation in the infectious diseases area should be commissioned and performed with a prospect of application in view, and should build the necessary collaboration between disciplines from the outset, across the Societal Challenges and the Leadership in Enabling and Industrial Technologies. Private sector industry and biotechs are major players in innovation for infectious diseases.

- Food security, sustainable agriculture and forestry, marine and maritime and inland water research, and the bioeconomy, as it very closely related to the challenges of antimicrobial resistance;

- Emerging and re-emerging diseases and the development of antimicrobial resistance require research, R&D and public health action guided by the One-Health approach.

- Climate action, environment, resource efficiency and raw materials, as it related to the challenge of new emerging infectious diseases.

2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

Three main achievements expected:

- Creation and validation of new products and strategies for the applications identified above;

- Building of effective partnerships across Europe in terms of type of achievement and time;

- Better global public health security through solutions to the AMR and emergent epidemic diseases threats.

2.2. What are the new trends and disruptive innovation in health and care?

New ways of getting multiple industry and SMEs to collaborate openly with academia so that results are shared and leads are rapidly identified and taken forward – new collaborative designs for mixed research campuses involving academia and industry in joint research and shared benefits. Real-time data sharing to accelerate the pace of innovation. Encouragement of further development and penetration of pre-competitive collaboration models for R&D. Potential of synthetic and systems biology and the convergence of disciplines to accelerate the development of new products. Exploration of the microbiome as a source of new therapeutic approaches. Potential of improved production technologies and technology platforms (e.g. improved, high yield culture systems) to reduce production infrastructure footprint and costs.

2.3. Which innovations which could reach market deployment within 5–7 years?

- Diagnostic tests and standards to support innovation could reach the market within 2–3 years, as well as products derived from microbiome exploration;

- Anti-infective therapeutics and modalities for controlling sepsis could reach the market within 3–5 years;

- Vaccines would most likely need more than 5–10 years to reach the market.

List three changes in the market that you would like to see by 2020:

1. Review by the Commission on how management of intellectual property and business interest might be best addressed in research consortiums' contracts, to avoid these becoming bottlenecks in the future for equitable access to new products developed through public funding.

2. Increased use of truly innovative open-innovation and R&D models.

3. Real-time sharing of data between all stakeholders.

Propose three business models that could mobilise these changes:

1. Increase current EC investment of public funds to leverage private sector funding, especially in areas where the market fails to drive innovation and in the so-called "death valley" of innovation for new medical technologies.

2. An innovation model which enables collaboration while providing reasonable business interest, at the same time ensuring an affordable price for new products. Pre-competition collaborative models are one pathway to be further developed, but later-stage approaches must also be conceived, tested and developed.

3. Science parks should be considered as more than merely a collection of start-ups. Investment in product development partnerships with complementary skills and mandates could help address priority questions (e.g. AMR, emerging diseases)

Have you seen any market trends in your field in recent years?

Very high prices of new innovative patented products (e.g. for hepatitis C treatment), which are challenging health systems even in Europe, while the price of some generic medicines is becoming so low that it threatens their future availability as producers exit the market.

2.4. How would you envisage the support across various funding instruments?

Some areas could be supported through Prizes under Priorities for 2018–2020 (see first section above) as well as well-designed, milestone-based investment bonuses when new innovation and R&D models are pursued.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. Science and technology?

More public sector investment in academic fundamental and translational research to stimulate and support future innovation.

2. Innovation?

New enabling translational research environments such as science parks with the appropriate complementary skills and sets of interrelated, cross-stimulating start-ups, SMEs and PDPs

3. Market?

Review by the EC of newly proposed business models for areas where the market fails to provide incentives for innovation and R&D.

4. Policy?

Stronger and coherent support to open-innovation, data sharing and fair partnerships.

3.2. What are the three main potential game changers:

1. Weak and fragmented translational research capacity in Europe has been a bottleneck to translating innovative ideas into products. The <u>strengthening of existing science parks and the creation of new environments</u> for academia, SMEs and industry to collaborate closely will facilitate leverage of private capital to translate public-sector research into anti-infectives, vaccines, other health products and interventions.

2. Within such collaborations positive determinants include <u>broadly acceptable Intellectual Property Rights solutions</u> which allow for preservation of value and for access in line with need. The EC could play a pioneering role in exploring such solutions.

3. Integrated therapeutic approaches which could not be overcome by mutations conferring resistance in the pathogen as well as therapeutic vaccines to resolve major chronic infections, and preventive vaccines for priority diseases.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. The public sector is inextricably involved in research and development for infectious diseases:

- in identifying the problems through surveillance and response to health events within a given health and social system,

- in participating meaningfully in funding research and innovation processes,

- in contributing to many aspects of healthcare or public health in countries, so is a contributor, user and a provider of solutions and interventions.

2. The public sector can, and does, affect research outcomes by defining infectious diseases' control and elimination priorities and needs, generation of research questions and active participation in research consortia. It can promote policies and strategies to ensure effective application of research findings and products, and in more affluent countries, in public funding of research and incentivising cooperation and inclusion of the private sector.

3. Regulatory agencies have the responsibility to develop new standards to assess benefits and risks of novel regulated health products. European regulatory agencies are acknowledged world leaders in this context.

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4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

Calls that are overly specified and structured and that do not create an atmosphere conducive to attract dynamic and innovative minds. The way calls are currently formulated sometimes stimulates applicants to "sell" already established work rather than engaging in innovation and translational research.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

A more attractive (non-administrative) way of describing the areas of need, demand and investment needed to attract innovative, dynamic minds.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

Infectious disease (endemic, emerging, re-emerging) calls for a particular and great emphasis on surveillance and surveillance response systems within a national and regional public health approach, including beyond EU-13. It will also be important to establish links to even higher population dynamics (climate change, refuges, asylum seekers besides traditional migration).

What practical research steps could be taken to improve the health and well-being of European migrants?

Research on how migrants/asylum seekers can best become part of any health and social system which not only allows timely immunisation but timely preventive and curative actions based on surveillance–response systems.

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Glossary:

AMR: Antimicrobial resistance
CMV: Cytomegalovirus
EC: European Commission
HSV: Herpes simplex virus
MERS-CoV: Coronavirus responsible for Middle East respiratory syndrome
PDPs: Product Development Partnerships
POC: Point of care
R&D: Research and Development
RSV: Respiratory Syncytial Virus
S. aureus: *Staphylococcus aureus*
S. group A: *Streptococcus group A*
SARS-CoV: Coronavirus responsible for severe acute respiratory syndrome
SMEs: Small and Medium Size Enterprises

Non-communicable diseases

Orla Sheils (Chair), Elisabete Weiderpass, Mizi Làszlò, Annette Peters, Matej Oresic, Paula Marques-Alves

In order of importance, which three main research questions should be addressed by 2020?

1. Intervention studies that will bend the curve of morbidity and mortality in non-communicable diseases (NCDs). We need a concerted effort to develop preventive/therapeutic approaches, including lifestyle interventions that examine behavioural sciences' role in tailoring interventions to change risk profiles/risk behaviour, (including obesity, smoking, alcohol consumption, dietary habits). There is strong synergy here with personalised medicine strategic thematic advice to pilot and implement the PM approach to tackle NCDs.

2. Understanding the pivotal role of co-morbidities in NCDs. Few diseases occur in isolation, in particular in the elderly, and the effects on a person's health may be multiplicative. To develop better therapeutic strategies, one needs better understanding of the synergistic effects of disparate patho-biology, host immune system and metabolism, lifestyle, and environment. We strongly recommend adopting a systems approach to identify the risk factors of NCDs and associated co-morbidities.

3. Resilience in NCDs. Why do some people not develop disease despite being at risk (e.g. based on their genetic, phenotypic or environment profiles)? We need a strategic approach to identify resilience among individuals at high risk of specific NCDs and/or their co-morbidities to determine and study individuals' unique profiles based on multi-omics, environmental and other health-related data, with the ultimate **aim of identifying new approaches for disease prevention based on this knowledge.**

Introduction

Non-communicable disease (**NCD**) is a medical condition or disease that is *non-infectious* or *non-transmissible*. NCDs often refer to chronic diseases which last for long periods of time and progress slowly. NCDs are the leading cause of death globally. In 2012 they caused 68% of all deaths (38 million) up from 60% in 2000, with a worryingly disproportionate number of people from poor or low income countries affected.

NCDs are driven by forces that include ageing, rapid unplanned urbanisation, environmental exposure, chronic inflammatory stimuli and the globalisation of unhealthy lifestyles. Every year, at least 5 million people die as a direct consequence of tobacco use and about 2.8 million die from being overweight. High cholesterol accounts for roughly 2.6 million deaths and 7.5 million people die because of high blood pressure. Most worryingly, NCDs rarely occur in isolation and patients frequently display several co-morbidities.

A comprehensive approach is needed to ameliorate the effects of NCDs on individuals and society that will of necessity involve research that cuts across myriad disciplines and will recognise the complex interplay between these diseases which rarely occur in isolation and which have multiplicative effects when present in tandem.
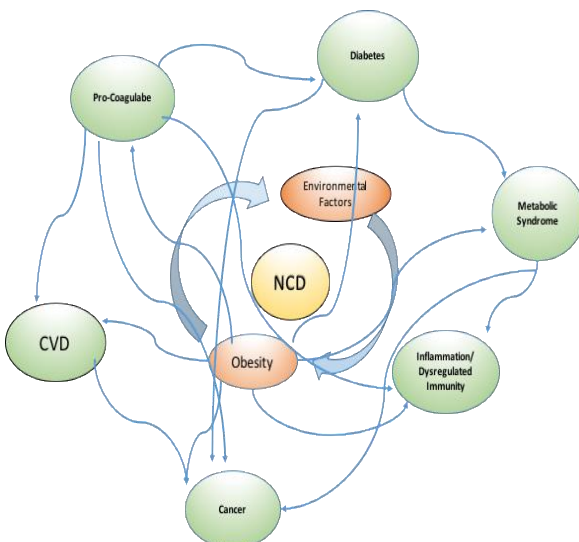
Fig. 1 Emphasis on Complex interplay between NCD and multiple factors/morbidities

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1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. While Europe has been a leader in personalised therapeutic approaches in the area of oncology, we lack the same strategic emphasis on PM approaches in NCDs to deliver proof of principle of efficacy, improve health outcomes and reduce healthcare costs.

2. Europe has an ageing workforce. It is imperative we intervene to maintain a healthy workforce, particularly if they have longstanding chronic illness (NCD) or have developed a NCD consequent to survival of another disease (e.g. cancer) or have concurrent multi-morbidity.

3. There is a lack of systemic knowledge and understanding of the roles of multiple risk and protective factors (biological, environmental, lifestyle, socioeconomic, etc.) contributing to NCDs and their co-morbidities, or promoting resilience. We need a more holistic, truly multidisciplinary approach to provide comprehensive answers to the multiple causes and drivers of NCDs.

1.2. Give three research orientations to resolving these challenges:

1. Europe has the advantage of having a strong tradition and related infrastructure for setting up large prospective studies in multiple NCDs. These unique resources and knowledge could be exploited in performing NCD prevention trials or screening programmes targeting risk factors that have an impact across multiple NCDs including but not limited to:

1. **Mental health**, including alcohol and drug dependencies

2. **Cardiovascular diseases**

3. **Chronic respiratory diseases**

4. **Diabetes**

5. **Inflammatory diseases**

6. **Neurological diseases**

7. **Chronic degenerative diseases**

8. **Multi-morbidity and its exacerbative effect in**

   a. **Cancer**

   b. **Immunological diseases/inflammatory/auto immune/microbiome**

   c. **Diabetes**

   d. **Metabolic syndrome**

   e. **Fatty liver diseases**

Such programmes should include all populations and all age groups, and address issues such as lifestyle interventions on weight control, physical activity, healthy diet and reduction of exposure to environmental toxins, stress and unsocial working hours. In particular vulnerable populations such as new migrants must be included. Such personalised approaches should be tested against established practices, for example in randomised controlled trial settings.

2. Maintaining an independent ageing population. Solutions are needed to maintain an ageing workforce and retain older people in the workforce (even if they have chronic disease or multimorbidity). Focus should be on identifying optimal workplace strategies and supports (therapeutic, lifestyle, health promotion, psychosocial) for health maintenance or management of diseases.

3. A comprehensive systems approach is needed to identify and study (1) the risk factors associated with NCDs and their co-morbidities and (2) resilience, i.e. why some individuals do not develop specific NCDs despite having many risk factors. The factors may include, among others:

- o Socio-economic factors: vulnerable and socially disadvantaged people get sicker and die sooner than people of higher social positions
- o Exercise, dietary prescription, overweight and obesity or underweight and malnourished
- o Psychosocial factors: the role of behavioural sciences in tailoring interventions that are effective
- o Environmental exposure – urban areas, workplace, role of social inequalities
- o Metabolic–physiological factors (e.g. blood pressure, hyperglycemia, hyperlipidemia)
- o Microbiome – e.g. role in obesity and its co-morbidities
- o Post-traumatic stress disorders as a major burden in migrants
- o Ageing – impact of immune-senescence in the context of multi-morbidity

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

There are synergies with the Societal Challenge 5 (Climate action, environment, resource efficiency and raw materials). Environmental causes are linked to several NCDs, but the underlying mechanisms that could lead to better prevention or treatment are still poorly understood. Exposome research is one research area at the interface between Societal Challenges 1 and 5.

2. The Leadership in Enabling and Industrial Technologies?

The FET programme provides the technological innovation that would benefit development of solutions for monitoring/managing NCDs and their co-morbidities (or risk thereof). The new technology could be tested in healthcare settings in the proposed trials aimed at tackling NCDs.

2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

- Patients are the sum of multiple pathologies, life events and exposures. Previous research has failed to take into consideration the synergistic effect of these and to perform holistic research incorporating complex omics, systems biology, social sciences and environmental biology.

- Influencing policy to identify modifiable risks, resilience factors and prevention of NCD development.

- Democratising healthcare delivery to be inclusive for vulnerable, poor and at-risk citizens including migrants, new Europeans and those most at risk in our society for developing NCDs.

2.2. What are the new trends and disruptive innovation in health and care?

1. Increased incorporation of wearable devices and biomonitoring into healthcare delivery, measuring therapeutic utility, diagnosis and prevention of NCDs.

2. True patient-centred research that translates discovery into meaningful changes in diagnosis, treatment and care of patients.

2.3. Which innovations could reach market deployment within 5–7 years?

1. Routine NGS genomics and multiplex omics analyses that are affordable and may be reported using easy-to-use and understand algorithms

2. Widespread environmental monitoring including patient monitoring for known risk factors (such as sedentary lifestyle, poor sleep patterns, etc.)

3. Increased use of near patient or POC devices to provide cheap diagnostic and monitoring tools to our citizens and to empower them in the management of **their** disease.

List three changes in the market that you would like to see by 2020:

1. Despite high expectations of economic returns, large investments in biomedical research have yet to materialise, partly due to a lack of proven business and investment models, regulatory hurdles, and a greater focus on cost-effectiveness for reimbursement decisions by payers.

2. Adoption of new economic modelling methods will better link investment decisions to value-based criteria of health systems.

3. Increased incorporation of implementation science to investigate and address bottlenecks (social, behavioural, economic, management) that impede effective implementation to improve health programming and to define causal relationships between intervention and impact.

Propose three business models that could mobilise these changes:

1. New therapies for tackling NCDs – innovative biotech companies and pharmaceutical companies exploiting the latest medical and technological innovation.

2. New diagnostic/screening tools – innovative diagnostics based on the latest medical and technological innovation. Development of apps and monitoring tools for use by patients and thus involving them as autonomous players in their own disease management.

3. Integrative ICT solutions for health monitoring and disease risk detection based on multi-modal patient and environmental data, for healthcare professionals as well as for patients.

Have you seen any market trends in your field in recent years?

2.4. How would you envisage the support across various funding instruments?

Areas of common interest should be consolidated into thematic programmes encompassing disparate instruments such as ERC, FEC, IMI and across complementary areas of different SCs etc.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. *Science and technology?*

   Greater focus on true translational research and medicine which is about the patient and for the patient, whatever their socioeconomic status or geographical location.

2. *Innovation?*

   Holistic research that incorporates effects of genetic susceptibility, co-morbidities and lifestyle, environmental drivers of disease.

3. *Market?*

   Need to manage expectations and have realistic expectations of research outcomes. Biomedical research is more complex than device engineering for example, requiring clinical validation and regulatory approval before implementation.

4. *Policy?*

Engagement with society and recognition of resource implications. Consider democratic voting on research areas to be pursued.

3.2. What are the three main potential game changers:

1. Integrated care Europe-wide. Common electronic patient records which are transferrable.

2. Opening of bioresources and datasets to EU-wide consortia to expedite research translation (cognisant of ethical challenges); this is particularly important for rare diseases.

3. Our research should aspire to minimise health inequalities and inequity particularly with regard to NCDs.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Support for maintenance of extant bio- and data resources

2. Proactive fostering of multidisciplinary research efforts through suggested matching of research groups from different backgrounds.

3. Funders and scientists must start to engage with the public from the outset of any popular conversation, and not arrive late to the discussion or try to impose their ideas on society.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

Identification of the tangible benefit that researchers from new Member States may bring. We should not patronise researchers by 'allowing' them to participate in funded projects. They must be *bona fide* participants. This means project calls must be tailored to identify the strengths of countries that are poorly represented or to be targeted. This might refer to particular skill sets in certain countries or perhaps the over representation of certain NCDs among the citizens of these countries.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

1. Increase success rate by making the calls more targeted.

2. Simplify application procedures, in particular simplify budget

3. Remove mandatory requirement of inclusion of industries/enterprises

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

Mental health (in its broad sense, including integration aspects) and prevention of NCDs

What practical research steps could be taken to improve the health and well-being of European migrants?

Performing studies aimed at understanding:

- NCD risk profile of migrant populations to Europe in particular in terms of lifestyle, exposome, stress, etc., and also on migrants' use of healthcare systems.

- How to make healthcare and prevention services targeted to ´new Europeans' in an inclusive way (these may include NCDs population prevention trials, as well as screening trials, amongst others).

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Three main research questions equally important should be addressed by 2020:

For non-communicable paediatric diseases including childhood cancer:

1. **Molecular characterisation and pathophysiological mode of actions (MOA) mechanism** coupled with standardised preclinical testing procedures to greatly expedite the development of more precise and efficacious drugs for children (**delivery of personalised medicine in paediatrics**) via proven efficacy and safety in appropriate clinical trial settings (**fostering pan-European innovative clinical research settings in rare diseases**).

2. **Systems paediatrics for early detection and prevention of non-communicable diseases.** Recent advances in systems medicine and omics point towards inflammatory responses as key mechanisms in the development of complex and common non-communicable diseases such as inflammatory, cardiovascular and malignant diseases. Thus, understanding of inflammatory responses will provide important keys to personalised medicine.

3. **Long-term health surveillance instruments ("HEALTH meets RESEARCH")** by using eHealth and mHealth solutions to improve safe and participatory continuity of care from childhood throughout adulthood for young patients expecting a life-long disease and treatment burden to enable management of the transition phase, patients self-care and to cover the needs of a moving European population. Instruments should provide surveillance and support for the individual patient's needs and serve equally via eHealth record linkage long-term observational studies (registries) to generate outcomes-oriented evidence with insight to late effects related to treatments given.

Introduction

Many diseases that start in childhood persist throughout life. These diseases include allergies, autoimmune disorders, neuropsychiatric disorders and obesity. Despite improved treatments these diseases have become more common, and affect 20–40% of children. Not only do these diseases persist throughout life but they are also linked to other common diseases that affect the healthy ageing, such as heart and lung diseases. This leads to a simple question with great potential for health in Europeans: Can life-long, chronic diseases be predicted and prevented in childhood? There are already successful examples, such as early diagnosis and treatment of asthma and screening of newborns. If these examples can be generalised this would significantly improve health in Europe. The keys may already be available from research prioritised by Horizon 2020: Big data, such as population-wide electronic medical records, quality registers and genome-wide analyses of most human diseases, may be co-analysed to find how diseases are linked to environmental, lifestyle and molecular changes. Ideally, such analyses can guide clinical studies aimed at preventative measures in childhood. These measures may consist of drugs, as well as lifestyle, societal or environmental changes.

Major inequalities still exist in healthcare capabilities and children´s well-being in European countries. There is still a big need to improve access to high quality, timely and accurate diagnosis, care, treatment and long term follow up strategies across Europe. Cross-border and within-border interoperability of electronic health records remains limited, and nearly non-existent for personal health records and systems. Although the EU Paediatric Regulation has improved the situation of

medicines for children, the pipeline of paediatric medicines continues to be limited and the access to new innovative drugs remains unsatisfactory.

Cancer in young people is rare with 12,000 being newly diagnosed in Europe each year. At least 60 different types of cancer are recognised in a population ranging from new-borns to teenagers, and even more when biological markers are considered. In spite of largely improved overall outcomes, more than 6,000 young people still die of cancer in Europe each year. Improved treatments are needed for children with Cancer with poor prognosis, because their survival reached a plateau many years ago. Today there are more than 300,000 European childhood cancer survivors (by 2020, there will be nearly half a million): two-thirds of these people have some late treatment side effects which impact on daily life in half of those affected.

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1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. Recent advances in systems medicine and omics point towards inflammatory responses as key mechanisms in the development of complex and non-communicable diseases such as inflammatory, cardiovascular and malignant diseases. Several of these are linked to diseases that start in childhood. An important challenge is to identify such links and the underlying mechanisms. This may help to find biomarkers and drugs to prevent diseases already in childhood. Integrated programmes between basic and translational biology and clinical research are needed to foster preventive and personalised medicine in paediatric populations. A wide range of inflammatory diseases in childhood is suitable for inclusion in such programmes, including allergies, diabetes, coeliac disease, rheumatic disease and inflammatory bowel disease.

2. Poor prognosis of childhood cancer is still a reality in particular in advanced disease stages or in the presence of unfavourable biological marker profiles. Patient survival for difficult-to-treat cancers has plateaued over many years, which calls for innovative treatments with new mechanisms of action (MOA) to control resilient and resistant diseases. Of particular concern are entities of brain tumours, neuroblastoma, bone and soft tissue sarcomas, very rare paediatric tumours as well as AML. Teenagers and young adults (TYA) do have specific needs and carry a special risk for poor cancer treatment outcome. Inflammatory immune-mediated diseases (IIMD) may be associated with significant tissue destruction without evident adaptive immune responses and are designated as autoinflammatory due to distinct immune-pathologic features. This is of clinical relevance, because IIMD may respond to cytokine antagonism whereas autoimmune-mediated diseases respond better to anti-T and B cell therapies. Poorly defined "autoimmune" diseases need enhanced research.

3. There are still considerable disparities in Europe not only for access to standard care but in particular for highly specialised treatment interventions in conditions where the number of cases at the hospital treatment sites is low. There is the potential for cross-border healthcare paediatric networks to deliver in the large arena of research (clinical, translational and basic) as well as care needs. These networks could be largely enhanced by adequate means and appropriate compensation mechanisms for advisory board functions. There is potential for cross-border

provision of the latest diagnostics as well as well-structured patient referral schemes embedded in visionary eHealth models, including links to research platforms.

1.2. Give three research orientations to resolving these challenges:

1. **Big data,** such as population-wide electronic medical records, quality registers and genome-wide analyses of most paediatric diseases may be co-analysed to find how diseases are linked to environmental, lifestyle and molecular changes. Ideally, this will lead to identification of preventive measures in childhood. These may consist of drugs that are effective for more than one disease, as well as lifestyle, societal or environmental changes. In summary, co-analysis of different forms of existing big data can be used as a starting point for clinical studies of children with different diseases, in order to find biomarkers and treatments to prevent disease during and after childhood. The use of big data analyses may identify "optimal diseases" to demonstrate the potential of preventative treatments. Proposals are needed for developing, testing, and validating inflammation biomarkers as early childhood prognostic factors for common diseases in childhood, adolescence, and adulthood that predispose for age-related disease. Such markers should also be tested for personalised medicine, and be derived from multi-omics analyses, and integrated with relevant information about sex, heredity, disease history, ethnicity, geographic origin, cultural factors, and socioeconomic status, including family.

2. Another factor, whose importance is increasingly recognised, is the bacteria that colonise the human body **(the microbiome).** Changes in the microbiome may cause diseases, but also potentially cure diseases. Analysis of microbiome data is therefore another example of how co-analyses of multiple types of big data may provide clues for prediction and preventive treatment of common diseases. An important advantage of population-wide records is that associations between common and rare diseases may be found. The advantage lies in that rare diseases often have known molecular mechanisms, which may be shared with the common diseases with which they co-occur. Thus, those mechanisms can be used to find new biomarkers for early diagnosis and treatment.

3. Individuals after paediatric life-threatening cancer and/or disabling diseases deserve the best possible long-term care. Surveillance and early intervention may reduce the frequency, severity and impact of late treatment side effects. Long-term follow up and risk-based prevention programmes for individuals with diseases at a young age require a **Health Surveillance Passport and associated Research Platforms ("Health meets Research")**. Healthy ageing programmes should also embrace paediatric populations. Two-thirds of cancer survivors have some late side effects impacting on daily life in half of them. Accumulated health data provided by eHealth-based patients' records and platforms may provide "self-generating long-term surveillance". This may allow early signals to be detected and timely interventions to secure the best possible quality of life as well as preventing secondary cancer. In addition, this provides patient empowerment that fosters self-care.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

A European health system that aims to reduce inequalities needs to face the challenges of diseases in the paediatric age groups and recognise the importance of cross-border healthcare. Patients and families affected are often isolated, have limited or no access to diagnostic tools and care/therapeutic opportunities.

The involvement and empowerment of patients and their families are key at multiple levels: collections of complete and accurate clinical data in patient registries and precious biological materials in research biobanks, defining clinical trial outcome measures, setting the ethical and legal framework for personal data handling, and so on.

2. The Leadership in Enabling and Industrial Technologies?

A concept for improved cross-country cooperation and communication between institutes dealing with rare paediatric diseases using newly developed ICT-tools is a clear need. An **efficient European IT infrastructure** to support integrated e-Health/m-Health and research strategies should facilitate cross-border healthcare, access to expertise and long-term follow up serving outcome research. This builds on the European Cross Border Health Care Directive aiming to implement European Reference Networks (ERN) where highly specialised healthcare networks will meet the needs of rare, complex diseases or conditions.

Digestion of Big Data based on international collaboration to overcome small volume sample sizes is required in order to investigate disease mechanisms but also to promote functional studies. Many areas of health ICT innovation require greater capacity.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. **Personalised medicine** using biological disease profiling and patient characteristics (such as molecular and immunological factors) will impact on outcomes and will be monitored for long-term consequences.

2. **Strengthening of partnerships of patients, parents, medical care teams, researchers** and industry in 'intelligent and transparent' public–private partnerships. Enabling research and industrial development by SMEs and library screening from large pharma could have much impact.

3. **A Health Surveillance Passport for paediatric diseases** with long-term effects will provide a concise, standardised treatment summary, outlining potential long term risks and linked to guiding tools to risk-based prevention screening. Explicit consent will ensure patients' autonomy and mastery over their own health data. Such data would inform about disease history and treatments, special risks and potential needs. Standardised e-Health applications will facilitate the transfer of information between relevant healthcare providers and concerned individuals. Enhanced health monitoring in individuals with identified risks together with paediatric disease and cancer ERN networks, as well as expert long-term follow up ERN, will contribute to improved outcomes. Better quality and more interoperable health data in priority health and care areas are key!

2.2. What are the new trends and disruptive innovations in health and care?

Technologies that allow simultaneous analyses of all genes and their products, together with increased skills in big data analysis, will facilitate "fingerprinting" of individual disease characteristics in all diseases that affect children. Translation into personalised medicine approaches require expert advice and access to new drugs corresponding to relevant pathways. Related costs may be prohibitive for this innovation and need to be addressed to overcome current inequalities. Tools are needed to empower former patients to manage their later well-being.

Integrated solutions of healthcare, informatics and research aspects are warranted. This calls for common actions combining previous efforts from DG SANTE, DG Research and DG connect.

The establishment of European Reference Networks (ERNs) will bring innovation to European healthcare management and will allow for enhanced research development beyond care (e.g. quality assurance mechanisms for laboratory testing; development of good practice guidelines for diagnosis and care; support for cross-national clinical trials; registries and links to other European research infrastructures, etc.). Specific calls for European Clinical Research Networks – embedded in ERNs – should be fostered to exploit in full the research potential of experts' networking and clustering by disease areas.

eHealth and mHealth tools will change the traditional landscape of patient care.

2.3. Which innovations could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Young people could benefit from drug developments based on mechanisms of action (MOA) rather than disease diagnosis. Such a new drug strategy could impact quickly on improved access to innovative drugs for paediatric diseases. Also the field of advanced therapies, such as gene therapy, are starting to deliver effective therapies for rare paediatric diseases.

2. Innovative compatible eHealth tools, improved tools for conferencing platforms (virtual case consultation system, virtual tumour boards).

3. Health surveillance record applications for long-term patient follow-up (Health Surveillance Passport) with mobile App functions and links to research data bases to produce together informative guidance have the potential to be broadly applicable ("Health meets Research").

Propose three business models that could mobilise these changes:

1. Public–private partnership are key models to foster these developments.

2. New Member State compensation systems for advice and diagnostics in CBHC care settings compensating for hours spend in advisory function of experts at ERN sites.

3. Long-term follow up registries via the Healthcare Health Surveillance Passport Forum supported by industry as long-term follow up data may be provided.

Have you seen any market trends in your field in recent years?

EnpreEMA as a European Network of Paediatric disease or national networks have started to foster relationships between academia and industry.

Some pharma companies have started dedicated paediatric programmes to support and foster paediatric drug development.

2.4. How would you envisage the support across various funding instruments?

1. All of the above are important stakeholders include DG Sante, DG Research, DG Connect and the pharmaceutical industry.

2. The pharmaceutical industry hopefully will provide support to future ERN systems (unrestricted grants, etc.)

3. EEIGs could be promoted for academia consortia as one possible option.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. Early detection and prevention of the most common diseases in childhood, which despite improved treatments have increased during the last decades. Examples include allergies, autoimmune, and neuropsychiatric diseases and obesity. All these diseases tend to persist throughout life and increase the risk for other, age-related diseases. Systematic big data analyses of existing electronic medical records, quality registers and genome-wide analyses are needed to identify molecular, environmental and societal causes for the increased incidence of these diseases. The results can guide clinical studies for early and individualised medicine.

2. Despite progress made over the past two decades in the treatment of paediatric cancer and largely improved outcomes, results clearly fall short of society's expectations with 6000 children still dying from cancer each year in the EU and around 70% of the survivors suffering serious long-term side effects due to therapy.

3. Today, the development of specific drugs for paediatric tumours finds important limitations. Incomplete understanding of molecular mechanisms of disease, fragmented or deficient integration of currently available knowledge, insufficient datasets (clinical, molecular, histopathological, etc.) for many tumours, and limited availability of adequate in vivo and in vitro preclinical models, represent major obstacles which need to be removed in order to accelerate the development of specific paediatric cancer therapies. Efforts towards the removal of these limitations, however, face additional challenges. Firstly, tumours diagnosed in children and adolescents differ from adult cases in many critical aspects, and yet therapies for children are mainly transposed from adult oncology practice. Secondly, even the most common paediatric cancers can be considered rare diseases. Third, developing drugs for small patient populations is financially challenging from an industry perspective and there is currently little incentive for companies to specifically develop drugs for paediatric cancers.

3.2. What are the three main potential game changers?

1. Health Care Surveillance passports (end of treatment summaries) and Patient Reported Outcome Measures (PROMs), associated research platforms.

2. Active ERNs.

3. Interoperability of systems to facilitate advisory functions including semantic aspects.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Interoperability of digital applications is key to ensure broad applicability throughout Europe. Supporting trans-national informatics facilities and services for mathematically driven systems biology using high performance computing and ensuring access to such services.

2. The application of a European unique patient identifier (EUPID) may enhance research capacities particularly in view of the possible secondary use of data.

3. Efforts at standardisation of data from genomics and other omics research is a top priority.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

What practical steps could be taken to encourage the participation of the EU-13 in calls?

1. Research into rare diseases increasingly relies on the production of huge amounts of data from genomics, proteomics and other omics approaches, which call for high-level and high-volume data storage and management and for interoperability of mathematics and informatics tools, as well as for shared principles for data security, ethical data handling and controlled data sharing.

2. Digital technologies like case consultation systems, registries and long-term follow-up applications will give valuable insights in clinical research questions for rare paediatric diseases.

3. Treatment innovation through patient empowerment in rare diseases. Ethical issues regarding patient privacy of personal data in biomedical research at large requires particular attention. Engagement of the research community in ethical issues should be encouraged and facilitated at all levels.

4. An 'Ethics and Social Science and Humanities' focus is needed to address the special needs of minors in research and drug development. Education, training and support programmes should ensure adequate training of paediatric health professionals and train parents, patients and respective stakeholder associations towards active engagement on multiple levels.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

What practical research steps could be taken to improve the health and well-being of European migrants?

Health Surveillance Passport and associated research platforms ("Health meets Research") are fundamental to overcome these current circumstances.

Public health and prevention including migration

Annette Peters (Chair), Roza Adany, Peggy Maguire, Marie-Paule Kieny, Anne I.H. Borge

In order of importance, which three main research questions should be addressed by 2020?

1. How to promote well-being and prevent health problems and social exclusion. Mechanisms and causes.

- The identification of personal, social and environmental risk factors and processes responsible for health and disease in society. This spans from considering social sciences and humanities (SSH) expertise, understanding the mechanisms of the development of disorders, access to large amounts of data about many people and complex research designs.

- The interplay between the person and the environment needs elaboration. Determining the causes of psychosocial and health difficulties throughout the lifespan for increasing the mental, physical and social capital of the populations of Europe, will lead to improved prevention because understanding the causes of health problems is the key to promote health and well-being.

- Europe is facing challenges ensuring the health of minor ethnic groups and migrants. Integrating these aspects into comprehensive research programmes will provide the means for future action.

2. How effective were already implemented preventive programs on individual and population level? How to improve preventive programmes on evidence-based approaches?

- Assessments of already implemented programmes of individual and population health promotion will create an evidence-based approach for future initiatives for prevention and public health.

- Evidence shows that investing money in early interventions leads to lower cost of treatment later, but many programmes are almost ineffective when tested in the real world; and why do few programmes succeed when the burden of disease and mental health problems are so huge?

- A systematic evaluation and testing of programme packages for prevention in trials needs to be conducted to arrive at evidence-based public health.

3. From genes to greens. Future research needs to span inclusion of information from neurons to neighbourhood.

- Examining the individual in the larger context will reveal environmental protective factors against health problems and reduced well-being.

- Future research needs to span from analyses of the individual's genetic make-up to family harmony and interactions, peer relationships, social institutions (day-care, school, work) and neighbourhoods.

- Integration of disease understanding spanning from neurodevelopmental processes to neurodegeneration will allow public health and prevention to be advanced.

Introduction

A healthy workforce, early intervention, prevention, integration of information and communication technologies (ICT) throughout the lifespan are all virtues that are often broadcast. Nobel laureate in economy James Heckman has produced data indicating that the return of investment in human capital is more effective the earlier in life the money is spent, and that investment in preschool children is more effective than investments in later life. We have only scant knowledge about how efficient the social and health services are in implementing new technologies to promote better citizen-centred well-being and identifying disadvantaged groups. Large scale studies utilise transdisciplinary expertise and databases that enable researcher to follow the individual from cradle to grave. Examining positive functioning and resilience in spite of an adverse environment gives insight into protective processes for well-being across phases of the life course of vulnerable groups of people, ethnic minorities and migrants, and gives clues about why there is different susceptibility to environmental risk in various cultures and societies.
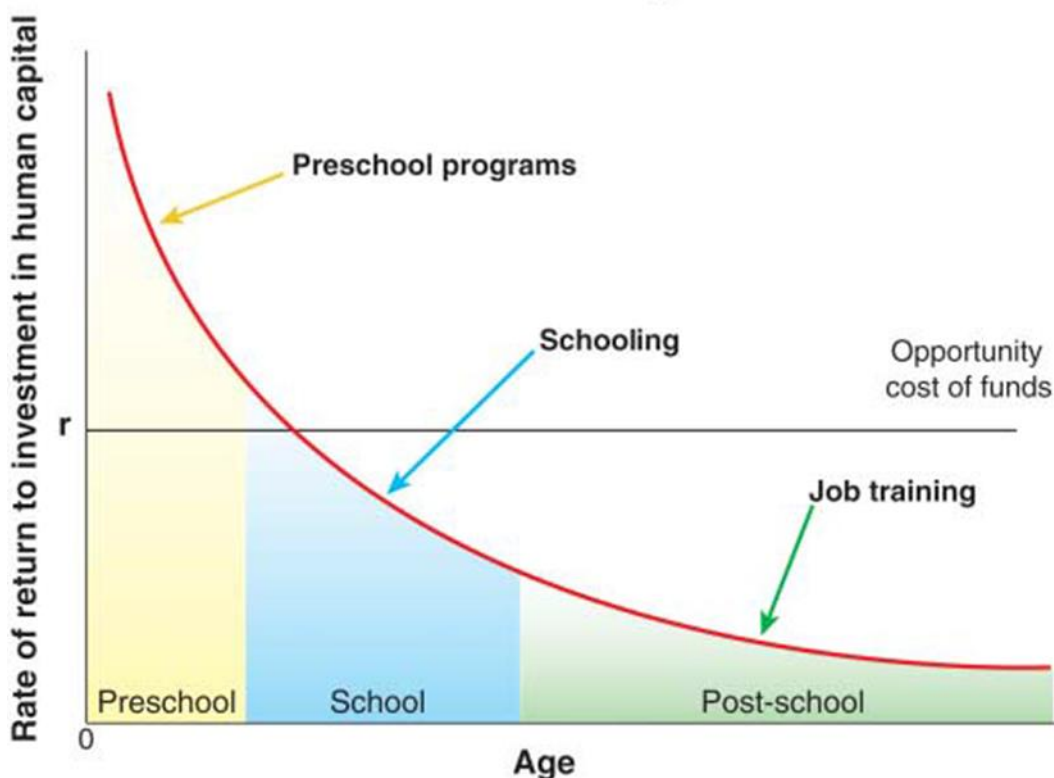
Rates of return to human capital investment

Figure 1: Highlighting the role of early development for health and well-being. James J. Heckman (2008)

The case for investing in disadvantaged young children. In: Big Ideas for children: Investing in our nation's future (pp. 49–58) (Figure 1a, page 52). Washington, DC: First Focus

> **1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?**

What are three main challenges in the field concerned?

1. *The future workforce of Europe. Health promotion and* **social inclusion**: *building mental, physical and social capital of the citizens.*

Transdisciplinary research across the societal challenges includes the necessary expertise. We need predictive research to deal with the unforeseen future. Social inclusion will be a future main challenge.

Social inclusion is complicated and we need to understand the determinants of personal health and well-being as well as the dynamics of society. Future research will capitalise on the effectiveness of better use of health data, big data, health registers, and databanks. New knowledge is needed for efficient prevention and how to promote an individual's control over his or her own well-being and behaviour change including application of relevant ICT. Identification of relevant factors in individuals and society for reducing malfunctioning in society is needed for behaviour change that results in a healthier lifestyle. We need more research on bio-psycho-social mechanisms of behaviour change. We need to examine how and why criminality among citizen gangs of adolescents and young adults is associated with genes, family processes, peer relationships, overcrowding, bad physical surroundings and cultural attitudes.

2. *Health promotion and prevention: The* **best of prevention** *programmes*

A main challenge is how to achieve efficient population-based prevention and how best to document past successes to arrive at that aim. A future challenge is to understand how and why this can be done in a cost-effective and user-friendly way. Many prevention programmes that have been proven moderately effective during efficacy trials become almost ineffective when they are tested in the real world (i.e. during effectiveness trials). Examining personal and environmental factors involved might increase or decrease their effectiveness. There is also a need to test the effects of evidence-based interventions in various social systems across societies, ethnic groups and cultures. We need extensive research about anxiety, personality disorders, hyperactivity and attention disorders, affective disorders and suicide.

It is critical that all inhabitants of the community participate in the development of modern health Apps, such as reading web-based information, participate in developing a personal health web journal, apply Apps and follow recommendations. We have to avoid gaps in competence in the application of eHealth and mHealth in the population across the lifespan.

3. *Health in cities and rural environments. Investigate* **determinants of malfunctions** *in health and well-being under varying social and environmental conditions.*

A future challenge is examining why people are differently susceptible to risk exposure in different social and physical environments. Governance and public policy for changing behaviour to produce a healthier lifestyle affects individuals differently and we need to understand why. A central issue is to tackle the hurdles to behaviour change for better health and well-being in varying social contexts. In city centres, social selection is a problem with extensive numbers of groups of disadvantages people. Thus, we need knowledge about the dynamics of individuals and neighbourhoods and the dynamics of peer groups for understanding what leads to mental and somatic problems. Research for new causal findings will need to include various SSH disciplines, epidemiology, psychology, sociology, and so forth. Furthermore, a challenge is associated with the interplay between mental and somatic health and well-being, co-morbidity and how new technology can bridge the gap and strengthen functioning.

1.2. Give three research orientations to resolving these challenges:

1. Need to study large and diverse populations. To do this, research should build on merging data from various registries, data- and bio-banks, population-based cohort databases, etc., for establishing evidence for developing strategies to promote health, well-being, and human capital.

2. We need longitudinal studies for developing preventive strategies and to evaluate long-term effectiveness. We need natural experiments about why various lifestyles affect the onset of mental health problems differently.

3. Need to start early in life. It is best to start before conception for detecting causal mechanisms of risk and malfunctions throughout the lifespan and to include participants across various contexts, such as cities and rural environments. Investment in research in early human development that aims at following the same individual over a long time leads to knowledge about protective processes that can be used for age-appropriate interventions, which might lead to impressive decreases in healthcare costs.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

SC 1, SC 5 and SC 6: Some issues should engage social and humanities researchers and some issues are fundamentally social but need health expertise.

2. The Leadership in Enabling and Industrial Technologies?

User-friendliness is a key challenge in health issues. The population is heterogeneous in attitudes towards technologies and leadership in enabling and industrial technologies is relevant for developing user-friendly technologies. One challenge is to be at the forefront for children's use and exposure, for example to build in protection and prevent cyber-bullying among children and other vulnerable groups. Research ethical challenges with respect to storage of personal information, and age-appropriate devices, are other important issues.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. New understanding of how to combat mental and physical ill-health in an efficient approach. Replicate original programmes in different socioeconomic contexts, for both genders and cultures to identify their limits.

2. Provide evidence-based data for promoting prevention programmes and public health and to start novel initiatives targeting individuals as well as populations.

3. To provide hard evidence for debates that are too often dominated by unsubstantiated assertion and to build up what is currently an underdeveloped academic discipline.

2.2. What are the new trends and disruptive innovation in health and care?

- Enabling people to increase control over their health and its determinants and thereby increase their well-being.

- Age should not matter in learning how to engage with new technologies. Recent research into the plasticity of the brain during the lifespan shows that learning something new, even when the brain is chronologically old, improves cognitive functioning. The whole population should be motivated to try new things.

- The introduction and use of new Apps, technological devices and investment in smart homes contribute to cognitive good functioning in light of their usefulness and effectiveness for health and well-being.

- One disruptive innovation is the extensive struggle when getting started on new electronic devices.

- Social selection might be disruptive. Social selection occurs if unemployed citizens with no or little education and of a minority status fall behind the rest of the population in the implementation of current health technologies developed for the whole population.

- The risk that the social equality gap widens instead of closing must be avoided.

2.3. Which innovations which could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Improve user-friendliness and age appropriateness of technological devices

2. Equal distribution of the new products to all, avoiding social selection

3. Online and mobile technologies, ICT, social media that can improve dissemination and implementation, collect data in population-based studies, linked to registers and bio-bank data which can be used to monitor or estimate dissemination/implementation, effectiveness, cost-utility/ cost-effectiveness, and user satisfaction.

Propose three business models that could mobilise these changes:

1. Create debate, and capture the attention of young people and other target groups, empower citizens to monitor the success of population-based interventions.

2. Provide research and scientific training services for policy teams and civil staff.

3. Provide services for implementation and monitoring of policy options and individual prevention programmes.

Have you seen any market trends in your field in recent years?

The trend is strong because the population level implies huge market value.

2.4. How would you envisage the support across various funding instruments?

A healthy workforce is in the interest of all, and avoiding absenteeism from work and productivity loss from 'presentism' – decreased productivity while being ill at work. Establishing Prizes could play a role.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. ***Science and technology?*** A substantial reduction of mental disorders and NCDs in Europe.

2. ***Innovation?*** Education of local health authorities about innovation to practice and develop incentives for participation in innovation because there is resistance to change behaviour and social systems.

3. ***Market?*** Tele-medicine for example can benefit from innovative products such as online and mobile technologies, ICE and diagnostics.

4. ***Policy?*** Resistance against change has to be addressed and discussed; economic benefits need to be visualised.

5. ***Other?***

3.2. What are the three main potential game changers:

1. Mental health problems, anxiety and depressive disorders cause more than half of the illness cost from disorders in Europe and are also the easiest and most cost-effective to prevent.

2. By early intervention, individual resilience and lifelong mental well-being is a realistic goal and of special importance for ethnic minorities and migrant families.

3. Child health and non-communicable diseases (NCD) constitute a major burden on society and any substantial progress in understanding the underlying causal mechanism or identifying effective interventions will be a game changer for society.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Promotion of preventive measures at the population scale integrated with collection of high quality data. The role of public sector, universities, hospitals, schools, institutions, prisons and so forth, is to contribute with precise and up-to-date data.

2. Mental health disorders are one of the main causes of sick leave and contribute significantly to the work environment and productivity.

3. When it comes to migration issues, integrating adolescents and young adults engaging in activities with and for minority members. This can speed up integration, language competence and motivation for work and treatment, and they like to participate in research studies.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

Very little, because public health problems are present in all countries and address the population.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

Pilot projects for evaluating the validity and reliability before starting larger programmes. Collaborate with national research councils which have bilateral programmes supporting EU-13 and build on experience from previous collaborations.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

- Promotion of mental health and prevention of mental disorder is a matter of social integration.

- To develop social integration, we need to understand how environments provide people with a sense of identity and self-respect, meaning in life, mastery, belonging, social networks and support.

- Research about the importance of well-being and health, mental health and social inclusion is not new. It is a long tradition in ethnicity research of multicultural societies, such as the UK, USA, Canada and Australia, and therefore new initiatives should build on previous research findings from other cultures beyond Europe.

- In Europe we know next to nothing about the mental, physical and social resilience of the new migrants, refugees and asylum seekers. It is recommended to apply a resilience perspective with focus on strong personal characteristics and positive experiences in intellectual, emotional, social and behavioural functioning.

- In addition, conducting research screening for experiences and post-traumatic stress disorders (PTSD), torture, violence and human rights is essential.

- The research should apply a multi-informant design, collecting data from migrant children themselves, adolescents, adults and older people, as well as staff and organisations. This would provide a better understanding of current problems and would combine information from different perspectives.

What practical research steps could be taken to improve the health and well-being of European migrants?

- Peer education is efficient. Local adolescent boys and girls should be included in tasks aimed at improving social inclusion for their newly arrived peers. This could be done on a daily basis through leisure activities, language education and social support.

- These practical efforts can be monitored and combined with collecting data, which is difficult among minority groups due to language problems and a general anxiety to reveal information about oneself. Thus research through the peer method avoids asking direct questions to the young immigrant; one should rather ask about their peers. This is recommended ethically, and research ethics is important.

- Create a longitudinal programme across countries, to monitor and improve the social integration of migrant children and adolescents. Canada is already doing this for Syrian immigrants.

- Experiment with integration strategies for avoiding ghetto day care and ghetto schools.

Active and healthy ageing

Sylvie Bove (Chair), Agnieszka Cieśla, Peter Saraga, Luc Thijs

In order of importance, which three main research questions should be addressed by 2020?

1. What <u>prevention strategies</u> can be applied to ensure active and healthy ageing of our population.
2. Building an <u>evidence-based roadmap to enable faster adoption</u> of new technologies and new care models for the elderly citizen, overcoming current barriers to change.
3. How can the latest Information & Communication Technology (ICT) and Artificial Intelligence (AI) <u>technology</u> better support <u>independent living and active engagement of the elderly citizen in society</u>.

Introduction

The ageing population of Europe is placing more demands on healthcare services. The burden of morbidity and disabilities caused by chronic diseases (cancer, respiratory disease, cardio- and neurovascular disease, diabetes and mental illness, musculoskeletal diseases, problems related to visual, hearing and cognitive impairment) is far reaching. <u>Healthcare, long-term care and social care services</u> will need <u>to be managed more efficiently to be sustainable</u>. But healthy ageing is a continuous process throughout life. Next to better management of existing long-term health conditions in the community, <u>health promotion, disease prevention and early diagnosis</u> are equally important to help citizens remain active and independent for as long as possible and to improve their quality of life. Last but not least, there is a need for a <u>more age-friendly environment</u> which encourages and supports active engagement, social inclusion and well-being of the elderly citizen. We call for the H2020 programme to pursue innovative and multi-disciplinary research in the above-mentioned domains, making use of the newest technologies and latest know-how, combined with the most recent experience from existing experiments and programmes.

1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. **Maintaining health:** preventing and managing age-related conditions with a more empowered (elderly) citizen.

   - Ageing and ageing processes in the human body, including age-related chronic diseases.
   - Rise of the burden of chronic diseases, mental illness, degenerative diseases and co-morbidities in view of the ageing population.
   - Increased awareness of risk factors through early diagnosis.
   - Patient involvement and citizen empowerment, including education on self-care and on prevention, enabling people to more actively manage their own health.
   - Concepts for more structural involvement of patients in research.
   - Workplace intervention models to prolong active living.

2. Effective and sustainable care

- Care systems are to realise the 'Triple Aim' of better health, better use of resources and patient/citizen satisfaction.

- Access to healthcare for all, including opportunities of telemedicine and eHealth to overcome age-related and geographic barriers such as mobility, visual, hearing, cognitive limitations and low doctor density.

- Business and payment models, in particular for prevention strategies and for better care coordination.

- Management of medical information generated and used by all stakeholders in the care process, including patients, medical professionals, social care and informal care givers. Ensuring that this information is accessible for medical research and that the knowledge derived is reintegrated in the care process.

- Fragmentation of healthcare, leading to slow and partial adoption of new technologies and services.

3. Enabling independent living

- Maximising opportunities for independent living of senior citizens by creating a more age-friendly environment: Smart cities that are aware of the special needs of the elderly population in terms of housing, transport, social participation and inclusion, healthcare, communication and community support services, leisure and culture. Purposely designed individual dwellings (smart homes), integrated with public spaces and enabled with adapted technology.

- Improved usability of ICT tools, leading to better adoption and therefore inclusion of the elderly, maximising opportunities for their active participation in society, including employment, healthcare and social interaction in general. Proactively addressing social isolation and loneliness, avoiding both spatial and digital exclusion, are recognised as important contributors to maintain physical and emotional health, as well as cognitive function.

- A more participatory approach of the elderly citizen in the development of an age-friendly environment: in design of ICT tools, in urban development, in design of (smart) housing, etc.

1.2. Give three research orientations to resolving these challenges:

Before listing the research orientations, we wish to explicitly stress that involvement of the elderly citizen is key in each:

1. Prevention strategies for lifestyle-related diseases and the ageing process.

2. Evidence-based roadmap for implementation and adoption of new technologies and better (coordinated) care models, overcoming current barriers to change.

3. Maximising opportunities for independent living of elderly citizens by creation of a more age-friendly environment, including physical, technological and organisational dimensions.

Do these challenges overlap with:

1. Other Societal Challenges?

- Smart Transportation in SC4 and Inclusive Society in SC6 should address some age-friendly environment issues.

- Sustainable development: adaptability of the physical environment to the changing needs of the ageing population.

- Integrate social, behavioural science with care, therapy and well-being; effectively address adoption of tools, compliance to care plans, coaching to well-being and health literacy of elderly, as well as payment and reimbursement models.

- The ageing of the workforce in healthcare.

2. The Leadership in Enabling and Industrial Technologies?

- Technologies such as 'the internet of things', big data, artificial intelligence, human–computer Interfaces and robotics are already being applied in this area and are expected to be very significant. Their deployment should contribute to industrial leadership in these areas.

2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Better health in old age (important for the labour market), more active years and better quality of life, as well as slowing down of chronic disease "epidemics".

2. A more effective, coordinated and sustainable care system in which the elderly easily find their way. Focus on investments for prevention rather than costs of diseases.

3. A better living environment for the elderly, enabling them to stay independent for as long as possible, also with medical conditions, thus freeing resources in the care system and enhancing their well-being.

2.2. What are the new trends and disruptive innovation in health and care?

- Further advances in artificial intelligence, big data, the internet/cloud of things, robotics, nanotechnology (sensors, portable devices, smartphones as medical device), and applications (social networks, telecom, tele-care, tele-education, tele-shopping) will no doubt offer new opportunities and make a significant contribution to resolve the challenges of active and health ageing.

- At the same time, the above-mentioned advances are very likely to disrupt industries, care systems and have an important influence on society overall. We need to recognise that disruptive change is not inherently desirable and a better understanding of the disruptive impact of innovations is needed, including mitigation of major risks and adverse consequences.

- Experiments with care coordination are ongoing in North America as well as in several Member States. These are quite disruptive for they require fundamental changes in governance, in reimbursement, and in the willingness to exchange information and coordinate care activities among healthcare professionals, social care providers, informal care givers and patients themselves.

- Advances in personalised medicine, tailoring the right therapeutic strategy for the right person at the right time, determining predisposition of disease and delivering timely and targeted prevention.

2.3. Which innovations which could reach market deployment within 5–7 years?

- The internet of things, big data, artificial intelligence, smart human–computer interfaces, robotics, smart homes in smart(er) cities which connect the elderly citizen.

- In view of the adverse demographic trend (baby boomers retiring) and the ageing-related health burden, the redesign of healthcare systems (towards outcome-based reimbursement, care coordination) is very likely to happen at a much faster and wider scale in the upcoming 5 to 7 years.

List three changes in the market that you would like to see by 2020:

1. New business models leading to an informed and empowered citizen/consumer/patient, who actively manages his/her own health in an efficient and sustainable care setting, with more investment in prevention therapies.

2. Successful deployment of health prevention strategies and of new technologies which create an age-friendly environment, through a better understanding of good practices in uptake of those technologies.

3. Active participation of elderly citizens in research, including user ideation and use of living labs.

Propose three business models that could mobilise these changes:

1. Value-based healthcare provision (and outcome-based reimbursement rather than current volume-based 'fee-for-service').

2. A business model that rewards and motivates prevention.

3. Private insurance models.

Have you seen any market trends in your field in recent years?

- Care providers are reaching out to patients and patient engagement in the care process is steadily increasing.

- Initiatives with outcome-based reimbursement (bundle payments, episode-based payments) are ongoing in several Member States.

- Initiatives around 'elderly smart city services' and 'sustainable planning for housing in an ageing population' which take into account health.

- Life Sciences (J&J) and tech companies (IBM, Samsung, Philips, Siemens), reaching out to healthcare in order to both influence how care is applied and be able to access data for medical research.

2.4. How would you envisage the support across various funding instruments?

- Connection to other active H2020 and EU programmes (e.g. EIP AHA, AAL, EIT Health): show fit, complementarity, value added and avoidance of duplication.

- This H2020 programme should focus on the longer term, enabling shorter term innovation programmes to develop real products and services. This would support a coherent programme from research to market and foster job creation.

- Joint calls – better information (avoid confusion) H2020/DG SANTE's health programme, one-stop-points to guide interested parties to the right programme.

- Interdisciplinary research e.g. medical research and health system analysis or health economics.

- Link to other Societal Challenges such as smart cities/age-friendly environments.

3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. *Science and technology?*

- EU-wide coordination and vision at the EU level for biomedical, eHealth, mHealth and medtech research is lacking. Move from parallel, fragmented and specific to a long-term, comprehensive strategy with frequent reviews, shared among different actors/stakeholders.

- Complemented by a stronger interplay of European and national research and health funding schemes, leading to synergies and more efficient use of resources. A stronger link to DG SANTE Joint Actions (driven by MS) is desirable.

- Need for stronger alignment of research funding with Structural Funds; '*smart specialisation*' is key to enabling SMEs to come up with innovative bottom-up solutions.

2. *Innovation?*

- The main issue with innovation is market adoption: if not adopted, new ideas remain inventions, but not innovations. Research into good practices of the public sector empowering innovation (e.g. innovative procurement in practice). Sound regulatory and legal frameworks (ethical guidelines, privacy, data protection, etc.) are also key to market adoption.

- Also, the impact of innovation deserves attention:
  a. Broader issues such as ethics, integrity, making ICT technology accessible to older people.
  b. Sufficient attention to the impact of innovation on people, roles, processes in the care setting. Change management is required to fully benefit from technology.

c. Public sector should examine/look into potential social risks. Balance between automation (economic optimisation) and social effects of a dehumanised environment.

3. *Market?*

- See comment above on the market adoption of innovation.

- Regions could be a key player in adoption/deployment of innovation and should therefore be involved in the innovation process at an early stage.

- Another aspect of market needs is the role of private players in the future delivery of healthcare.

4. *Policy?*

- Improve legislative and financial frameworks for research- and innovation-oriented SMEs, in particular in the 'medtech' area.

- One regulatory framework and harmonised security and privacy standards facilitating healthcare data liquidity, both for healthcare (primary use) and research (secondary use) purposes.

3.2. What are the three main potential game changers:

1. A paradigm shift in the healthcare domain from 'healthcare technologies' to 'well-being and prevention technologies': society needs not only technologies to help elderly persons recover, but rather technologies that support a better lifestyle and a socially included and active elderly person.

2. True market adoption of technology and best-practice, making sure invention becomes innovation and thus that real impact is achieved.

3. Attention to and drive for outcomes, and for the transformation of health systems towards being more coordinated, outcome-oriented and patient-centred.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Stimulate Member States to adopt best practice in care models and supporting technologies, founded on the evidence-based roadmaps derived from funded experiments over the last five years.

2. Stimulate citizens to engage in managing their own health and creating awareness that healthy ageing starts at birth, linked to incentives for prevention and lifestyle changes.

3. Stimulate one regulatory framework and harmonised security and privacy standards facilitating healthcare data liquidity, both for healthcare (primary use) and research (secondary use) purposes. Subsequently reassuring public opinion.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

- The EU-13 countries have lower scores in the Active Ageing Index as a consequence of the older segment of their population being more passive and less willing to take part in economic activities. In general, the idea prevails that elderly are less fit for work and not easily employed. This perception needs to change to increase interest for topics regarding active and healthy ageing.

- The EU-13 countries are facing unprecedented rapid ageing in the coming years, and lack of action to address these issues will be detrimental to their economies.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

- In general, the newer Member States have less "entrenched" health systems and are therefore quite open to new approaches and best practice dissemination between member states and regions.

- Increasing technical accessibility not only through better infrastructure but also through education on internet use among the elderly.

- To widen participation, there needs to be full use of resources made available by the structural funds (ESIF). Member states to prioritise investment in research infrastructures.

- Need specific solutions for regions with structural disadvantages but high potential.

- Financial support made available by the ESIF to be channelled more into research (and the health sector).

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

- Continuity of care is already a challenge within a Member State, let alone in case of travel or migration outside of the home country. With few exceptions, citizens today are seldom in possession of their own Personal Health Records.

- On top of the above, access to care and its affordability still varies widely among Member States.

What practical research steps could be taken to improve the health and well-being of European migrants?

- Migrants' health – spread of certain diseases – a potential new threat to EU healthcare systems?

- Better data exchange between healthcare systems of the country of origin and destination.

Big data

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In order of importance, which three main research questions should be addressed by 2020?

1. Nearly all future health research will be based on analysis of increasingly large datasets ("big data") leading towards stratification of diseases, personalised medicine and systems medicine. While the concept of big data integration into useful knowledge and better healthcare (from prevention to improved diagnostics and therapies, and to innovations) is clear, **a new innovative and integrated research approach is needed to develop existing and future data resources in a harmonised/standardised manner and make them interoperable across the different disciplines**. Focus should shift from data generation to data integration and interpretation.

2. Progress towards use of big data in health research requires **better understanding of disease mechanisms, physiology and pathophysiology, disease co-morbidities and contributing environmental, psychological, socioeconomic, nutritional and lifestyle information at the systems level**. Research should focus on disease areas where such knowledge would create the biggest impact in the context of personalised/systems medicine and where Europe has unique strengths and where large sample collections and datasets are available (e.g. in biobanks, established prospective clinical cohorts, health records and registries). Thus, systematic characterisation of pathophysiology of selected human diseases, including analysis of co-morbidities and disease trajectories, are seen as the next steps for introduction of big data into healthcare and to lead the way to innovations. Examples of diseases where Europe has demonstrated research leadership include cancer, diabetes, and other chronic, non-communicable diseases, as well as immune-mediated and rare diseases.

3. **Medical informatics.** Widespread introduction of personalised/systems medicine into clinics cannot be envisaged without totally new solutions for translating the big data into meaningful information in the actual healthcare settings. Development of innovative tools and decision support systems is a major multidisciplinary challenge requiring participation of all parties/stakeholders concerned.

Introduction

Most aspects of health research currently involve generation of big data from laboratory analysis of human samples by various high-throughput omics techniques and from electronic health records incorporating digitised images and other relevant information. Combined with data on environmental exposure, nutrition, lifestyle, socioeconomic indicators, etc. future medicine will truly be based on generation and analysis of big data. Diseases will be stratified using biomarkers and other datasets into molecularly distinct subtypes which will form the basis for their prediction, prevention, diagnosis and treatment, referred to as personalised medicine or systems medicine. Individual monitoring devices are likely to increase the amount of data available about personal health status and lifestyle. Intelligent exploitation of big data will drive research progress in all research areas, not only in medicine but will also provide new approaches to all of the Grand Challenges covering marine, space, Earth, climate, urban societies, food, energy and transport.

1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. The challenges to realise the full potential of big data are immense. Europe currently lacks a well-functioning, standardised and interoperable ICT (information and communication technology) infrastructure capable of linking the databases of basic and clinical research with different registries (including those from environmental, food and social sciences and humanities) addressing at the same time both legal and ethical frameworks to maintain public trust. The role of Research Infrastructures established under the ESFRI process in providing new possibilities for storage, annotation and distribution of biological samples and big data has not yet been fully realised. In respect of big data and health research the most important infrastructures are ELIXIR (European life-sciences Infrastructure for biological Information), BBMRI-ERIC (biobanking and biomolecular resources) and EMBL/EBI (European Molecular Biology Laboratory/European Bioinformatics Institute), but the other life science research infrastructures also contribute to big data production and storage in their fields. The possibility of the European Open Science Cloud to provide such a storage service should be explored.

2. On a more practical side, the current European healthcare systems are very heterogeneous in almost every aspect (including legal and ethical environments and use of national languages) and oriented towards national or regional healthcare with little tradition of international co-operation. Against this background, development of medical informatics to realise the potential of big data for personalised medicine faces major challenges. All Europeans should have DICOM (Digital Imaging and Communications in Medicine)-type patient records, as will be discussed below.

3. Large-scale introduction of integrated big data solutions into healthcare (prevention, prediction, personalised/systems medicine, mHealth, eHealth, etc. as well as re-use of samples and data for further research purposes) requires public acceptance. Solving ethical and data protection issues in a publicly acceptable manner is obviously a major challenge, which has to be adequately solved before analysis of big data can realise its full medical and research potential. True interdisciplinary social sciences are of major importance here.

1.2. Give three research orientations to resolving these challenges:

1. European research in all societal challenge domains and in ICT continues to suffer from fragmentation. Results (data, samples, software) from projects are often not deposited into public repositories (databases and biobanks) of Research Infrastructures (see above) which would allow their effective re-use by other investigators and thus assure the sustainability of the results of the funded projects. Furthermore, the data produced still suffer from lack of standards and lack of interoperability. There should be an obligation for all publicly funded research projects to store the samples and data in a manner that allows them to be accessed and re-used by other researchers. This requires clear rules on ownership and custodianship of samples and intellectual property (IP).

Research efforts should focus more on a well-functioning, standardised and interoperable ICT infrastructure capable of linking the databases of basic and clinical research with different registries (including those from environmental, food and social sciences and humanities) towards a digital European health framework with sustainable funding. **Both researchers and funders overlook the importance (and funding) of long-term storage and re-use of large sample and datasets collected during research.**

2. To demonstrate the usefulness of big data usage in health research and development of personalised medicine, the next steps of research should focus on systematic analysis of selected human diseases in areas where existing samples, databases, registries and electronic health records facilitate progress. Big data-based research should contribute to early disease detection and prevention, to systematic characterisation of disease etiologies, pathophysiologies, co-morbidities and disease trajectories, towards holistic understanding of human diseases by integrating big data from environmental profiling (e.g. biomonitoring) with data relating to lifestyle, nutrition, socioeconomic status, psychological factors, etc. Combining these data with functional studies and computational modelling will build cases for early detection/screening and disease prevention, with strong emphasis on validation of existing or novel biomarkers. The final goal is of course better treatment resulting in better quality of life and survival in patients, and with proven outcomes.

3. Governance, semantic interoperability and scalability of electronic health records across Europe (DICOM standard for the whole EU). This also includes efficient text mining of health records in different languages. This is essential if one is to scale up applicability of innovative solutions and services for personalised medicine across Europe.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

Big data in the SC1 domain has obvious overlaps with essentially all other Societal Challenges. Understanding human health, demographic change and well-being overlaps with, contributes to, and benefits from big data coming from areas such as food security, agriculture ("one health"), marine environment; secure, clean and efficient energy; smart transport; climate and environment; secure societies, urbanisation and migration. Indeed, big data is the overarching topic that applies across all Societal Challenges. The biomonitoring initiative is an excellent example of such an overarching approach. By linking separate datasets into a strong evidence base, new knowledge will be created to drive applications and decision making with significant potential for huge practical and commercial value. The time is right for a push to exploit the use of linked data as a driver for more efficient solutions to societal challenges. True interdisciplinary research with convergence is crucial for this to happen.

2. The Leadership in Enabling and Industrial Technologies?

Big data in the SC1 domain overlaps with, contributes to, and benefits from Key Enabling Technologies and ICT, and to some extent also Space. Europe is still in a leading position to implement personalised healthcare based on its long-term tradition of systematically and prospectively collecting health-related data, samples and cohorts at population level. Currently this high potential suffers from fragmentation of activities, insufficient communication and lack of

interoperability and generic solutions, but Europe has considerable strengths in ICT and other enabling technologies (e.g. public–private partnerships, contributions to solving societal challenges and cross-cutting aspects, international cooperation and responsible research and innovation). To maintain a leading position, Europe must move from the current national or regional (even hospital-based) systems towards a single market and an open European standard for health informatics, which – with involvement of industrial participants and SMEs – offer great potential for global market leadership. To remain competitive, Europe must act now adding an open health informatics standard (DICOM) to its existing list of successful examples of standardisation (e.g. standard gauge of railways, as well as mobile phone and credit card systems throughout the World).

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Based on efficient use of existing cohorts, bio-banks and databases, better understanding of disease mechanisms and aetiologies at a systems level will be achieved (including complications, sex/gender-differences and co-morbidities). This will contribute to identification of novel biomarkers, therapeutic targets and treatments, as well as diagnostic re-classification, including clinical realisation of personalised medicine with disease prediction and prevention.
2. Established practices, governance and privacy protection of electronic health records across Europe, still allowing the access and sharing of data. Increased trustworthiness and interoperability of medical data (e.g. big data, sensor-generated data).
3. Increased utilisation of personal health data by individuals and wide acceptance of personalised/systems medicine approach by healthcare professionals. Quicker/safer decisions for medical staff and therefore better health management of European citizens and patients. Evidence of health and economic benefit of personalised/systems medicine approach in specific disease areas.

2.2. What are the new trends and disruptive innovation in health and care?

- Healthcare as such, accounting currently for approximately 10% of global gross domestic product (GDP), must be considered an emerging megatrend. Citizens pay more attention to their health than their wealth; life expectancy and occurrence of age- and life style-related illnesses are increasing. While rising costs of healthcare are a major economical challenge and unequal distribution of health benefits persists, the current situation is also an opportunity to renew, transform and innovate in the healthcare domain. These issues are gaining importance in the present situation of migration and instability.

- Technological development is likely to continue to be the facilitator of big data production: more data is produced more effectively for less money. Production of DNA sequence and

other high-throughput omics data serves as excellent example of this development. This necessitates development of bigger and more efficient data handling and storage facilities and supercomputing centres. Energy consumption is becoming an increasing concern of data production and storage and also requires new technological solutions.

- At personal level, miniaturisation of sensor/detector technology has rapidly increased the possibilities for monitoring of an individual's health status noninvasively by mobile Apps (mHealth). Such physiological monitoring systems will help to pilot and implement personalised medicine in actual health care settings, as they can detect signals of ill health and indications of disease progression in diagnosed patients. Already today Apps are increasingly used for well-being monitoring. These data are often unstructured, irregularly sampled, noisy, sometimes poorly calibrated, streaming and also potentially combining multiple modalities including contextual measurements such as movement data from accelerometers and even environmental data such as temperature and humidity. While such data are likely to increase rapidly, their interoperability and medical use have to be critically evaluated. For research purposes it is important that new monitoring devices must be used for a purpose, rather than just for the use of a product.

- In silico medicine, which involves the analysis of large datasets collected for an individual patient. The data in this case are mainly anatomical and physiological imaging which are processed with image segmentation and then coupled with modelling of tissue functionality, blood flow, etc. This area of work relates to what in FP7 was called Virtual Physiological Human. The limitation of this method can be the difficulty in assimilating data from one individual into complex models and decision support systems. The potential is to create a functional simulation of the individual's biology pathophysiology linked to the DICOM patient record.

2.3. Which innovations which could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Achieving interoperability of big data (from electronic health records to research and registry data) for development of personalised/systems medicine across Europe will lead to medical innovations and related IP, and will open the European market to several SMEs and large companies for innovative medical products (drugs and devices), biomarkers and services.

2. Developments in medical informatics, innovative tools and decision support systems will be available for translating big data into meaningful information in actual healthcare settings. Training of medical professionals in understanding the use of big data is part of their curriculum.

3. Steps should be taken towards creating a truly pan-European system of health records (DICOM) and healthcare allowing EU citizens to used their identity card together with a secure identification system to access their medical records across different Member States and get medical care based on their medical history. Such a system would be particularly important for individuals migrating within EU, or from outside. This development also relates to a shift towards the patient's (an individual's) ownership of the data.

Propose three business models that could mobilise these changes:

1. New diagnostic/screening tools, biomarkers and treatments towards innovative diagnostics and treatment based on the latest medical big data and technological innovation.

2. European Research Infrastructures should have a much more pronounced role as facilities for storage, curation, annotation and distribution of big data for re-use both in academic settings and for commercial purposes. For the latter purpose new types of public–private partnerships will be established allowing the data to remain in the publicly-funded infrastructures and the metadata to be used by commercial enterprises for development of innovative medical products (drugs and devices) and biomarkers. The "Expert Centre" concept has been developed by BBMRI-ERIC to allow analysis of biobanked samples and data in academia and the subsequent transfer of metadata to industry for innovation.

3. Integrative ICT Health solutions for health monitoring and disease risk detection based on multi-modal patient data, for healthcare professionals as well as for the patients.

Have you seen any market trends in your field in recent years?

A persistent and alarming market trend is development of ICT systems for healthcare at national level often with little or no interest in interoperability at EU level nor with other sources of big data even at national level. This obviously greatly limits the business models of European companies in big data usage for health research and care. Programmes are needed for standardisation, e.g. in digital pathology, telemedicine, and outcome studies demonstrating their value.

2.4. How would you envisage the support across various funding instruments?

Complementarity should be sought across other relevant and partly overlapping programmes, such as IMI (which is part of SC1), EDCTP (European and Developing Countries Trials Programme) and FET (which may complement SC1 by providing new technological solutions for big data including the relevant ICT infrastructure). The use of existing European research infrastructures for big data generation should be optimised and harmonised.

3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. ***Science and technology?***

   European research suffers from lack of sustainability of projects and suboptimal re-use of the results of such projects (cohorts, samples and databases). Better use must be made of research infrastructures for data deposition, exchange and integration. Need for strengthened translational research – moving the key scientific discoveries and technological innovations into the clinic.

2. ***Innovation?***

Lack of knowledge on disease etiologies and pathophysiologies (including co-morbidities) across the full course of the disease prevents development of personalised healthcare and use of big data to supplement it.

3. *Market?*

Overall fragmentation of the health market due to lack of European standards resulting in data interoperability across different European healthcare systems as well as across different technologies. Product developers should also consider the development of robust cheap products for less-privileged groups for patients, including migrants.

4. *Policy?*

Europe needs better and more widespread engagement of stakeholders (EU Member States, funding agencies, citizens, healthcare professionals, researchers) to reach acceptance of big data usage, by demonstrating its health and economic benefit, by assuring privacy protection, as well as by the shift towards patient ownership of the data.

3.2. What are the three main potential game changers:

1. The time is right for a major push towards exploitation of big data in and across societal challenges to establish European leadership in this major field – something that is needed for the future. In this particular field Europe is recognised as having the potential for being a true world leader. A cross-cutting systems approach with intelligent exploitation of big data to drive research in all areas. this can be extrapolated to marine, space, Earth, climate, urban societies, food, health, energy, transport, each with specific combinations of infrastructure, privacy and service requirements. Underpinning basic research will lead to a holistic approach based on big data science and SSH methodologies, using rigorous and robust mathematical methodologies and timely models from SSH. In the SC1 domain this could result in breakthrough innovations in medicine, leading to new medical products, solutions and services. The aim is to develop a competitive edge in emerging markets reliant on data-driven infrastructure, algorithms and evidence-based services, which is forecast to have a compound annual growth rate of 23% during 2014–19.

2. Integrated care solutions (including DICOM-type health records) across Europe, leading to a vital business environment for industry including SMEs to operate across Europe and internationally. Shift towards patient ownership of the data.

3. Engagement of stakeholders (EU states, funding agencies, citizens, healthcare professionals, researchers, research infrastructures) to promote semantic interoperability of EMRs and other related data. Wide acceptance of PM by key stakeholders, by demonstrating its health and economic benefit, as well as by assuring privacy protection.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Securing the legal framework to conduct research, to advance technologies and to use big data for implementation for ICT platforms and semantic interoperability of a digital health framework.

2. Creating a forum which engages the key stakeholders in personalised medicine and big data usage, and promotes big data and personalised/systems medicine as solutions for the emerging crisis of healthcare systems. Documentation of the economic and clinical value of big data is needed.

3. Assuring sustainability of publicly funded projects, such as by requiring public deposition of the data and creating solutions and a legal framework for efficient exploitation of such data. This also includes the need to follow up projects that have ended.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

In the sense of widening participation (EU-13) one should recognise the existing gaps in many countries within areas of health system, especially in the field of ICT. Where possible this should be taken into account by defining the calls that concern interoperability and other issues.

Pan-European agreement on standards and efficient use of research infrastructures are seen as ways to achieve participation throughout the EU.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

Research infrastructures, particularly those established under the ESFRI process since 2006, are becoming increasingly important for the production, storage and distribution of big data arising from multinational research projects. Owned and supported by participating Member States they perform a truly pan-European function in harmonisation and standardisation, as well as in the development and provision of technical solutions and services for better (semantic) interoperability of big data across all disciplines. Many research infrastructures and also EMBL/EBI (European Molecular Biology Laboratory/European Bioinformatics Institute) have special provisions to recruit EU-13 countries to join these infrastructures. A major attempt should be made to bring all EU-13 countries to become members of these infrastructures/organisations as this would also bring national research in close contact with big data. Interoperability of health data and other big data across Europe would benefit EU-13 countries as their current systems are underdeveloped. Regional partnerships between Widening countries and older Member States should also be encouraged in specific fields.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

Migration within Europe. For many EU citizens the current healthcare situation is a major concern: they live a mobile life (for work and leisure), but their health records remain national. There is little interoperability of medical records and healthcare systems across different Member States and the situation is even more difficult for those migrating to Europe from elsewhere.

Migration into Europe. This is not yet a big data issue.

What practical research steps could be taken to improve the health and well-being of European migrants?

The goal should be set high: every European citizen should be able to have access to his/her medical records wherever he/she is seeking medical assistance within the EU. Having such a

functioning (DICOM-type) system would naturally also help migrants elsewhere to integrate into the EU healthcare system.

Finally a proposal for addressing issues under item 4 in the context of big data and health and care research: a group of top-level EU scientists has proposed **establishment an EU-wide cohort of ERASMUS students** (who cover both the Widening and the mobility aspect) and make this a showcase of big data collection and its usage in health research and care settings towards interoperability of systems.

eHealth, mHealth, ICT

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In order of importance the three main research questions that should be addressed by 2020:

1. eHealth and mHealth solutions for improving safe and participatory continuity of care (including for example elderly persons with multi-morbidity) and also for personalised medicine.

2. The development of best practices in information governance (legal, ethics and privacy protection policies, data sharing arrangements) and in privacy enhancing techniques (privacy and security by design and by default approaches).

3. Closing the knowledge gap on how molecular medicine can best deliver precision medicine through stratified clinical care pathways and treatment decision support by integrating electronic health record data with other big data (e.g. large scale molecular data).

Introduction

The state-of-play (see also diagram at the end)

1. Most care pathways are for single diseases, and thus poorly manage multi morbidity. Cross-border and within-border interoperability of electronic health records remains limited, and nearly non-existent for personal health records and systems. Patient-centred care is an aspiration primarily realised in pilots, but not yet scaling up. There is a need to grow the evidence base of best practice in combining and coordinating multiple care pathways, to improve semantic interoperability including personal health and mobile health systems, and for health systems to learn how best to engage patients more productively in partnership models of self-care.

2. Big data is starting to become a feasible vision for healthcare, with many projects federating data sources across Europe. Most big data research focuses on the technical aspects of integration, or on using combined datasets for very specific research questions. Learning health systems, clinical research and adaptive pathways all need to leverage large scale data resources to enrich our pool of outcomes-oriented evidence, and to classify the extent of trust that big data analyses should play in real-world decision making.

3. Molecular (genetic) profiles and biomarkers are only applied in very narrow diagnostic and therapeutic areas; existing and successful examples should be scaled up. There is a need for large-scale population profiling using fine-grained clinical, lifestyle, environmental and other data (e.g. microbiome) which are increasingly available but not combined or used for population sub-profiling and stratification, which is urgently needed to enable molecular discoveries to find an appropriate place in routine healthcare.

> **1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?**

1.1. What are three (here four) main challenges in the field concerned?

1. Governance and privacy protection when integrating EHR and PHR data across Europe for patient care, research and learning health systems.

2. The quality and semantic interoperability of health data, including patient-created and accessed data, device- and sensor-generated data, and environmental data such as weather and pollution.

3. Developing methods to integrate analyses of EHRs with other types of big data such as environmental, molecular and microbiome.

4. Accelerated adoption and scale up of innovations in health ICT, including methods to demonstrate the quality, interoperability and trustworthiness of novel products and pre-products arising from EC research.

1.2. Give three research orientations to resolving these challenges:

1. The development of best practices in information governance (legal, ethics and privacy protection policies, data sharing arrangements) and in privacy enhancing techniques (privacy and security by design and by default approaches).

2. The participatory design and promotion of interoperability assets and standards for EHR data, care pathway rules, personal health data, life-sciences data, predictive simulations and analysis queries.

3. Developing methods to integrate analyses of EHRs with other types of big data like environmental, molecular and microbiome.

4. Developing and integrating evidence of outcomes and value from better integrated and reused health data, including quality labelling and business modelling for sustainability.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

a) These research areas, and the initiatives that will be needed to overcome the above-listed challenges, will contribute to the capacity of European health systems to respond to an ageing society.

b) They align with the need for winning greater trust from society, as the envisaged best practice solutions will require a better informed public dialogue, networked with decision-making bodies. These should be facilitated at a European level through the creation of one or more virtual fora for discussion on strategy and policy relating to the uses of health data.

c) These research areas may help respond to the challenge facing the adoption of eHealth innovations due to the lack of synergy between the European dimension (the Digital Agenda for Europe, the Digital Single Market, European project results, etc.) which strengthen the "supply side" of health ICT, and subsidiarity on health, leaving Member States to determine the "demand side" through control of public procurement.

2. The Leadership in Enabling and Industrial Technologies?

If yes, how? (provide some details)

There are many important areas of health ICT innovation that require greater capacity building in terms of thought leadership, product development and commercialisation of R&D innovations, market stimulation and evidence of value, including:

- Internet of things

- Cloud computing

- High performance computing

- Signal processing

- In silico modelling and trials

- Smart connected medical devices

- Medical and assistive robotics, 3D printing, humanoid companions

- Soft mechatronic technologies and solutions

- Wearable and collaborative robotics

- Wireless sensors networks, cloud robotics and automation

- Natural language processing, multilingual systems

- Big data tools (data mining, smart data aware storage systems, preservation and archiving, and so on)

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Widely established best practices in governance, controls and privacy protection of health data at a European scale.

2. Better quality and more interoperable health data in priority health and care areas, including long-term conditions, rare diseases and some aspects of prevention.

3. Convincing evidence base of trustworthiness and benefit from combining, using and re-using health data at a European scale.

2.2. What are the new trends and disruptive innovation in health and care?

Demand modelling is needed to find out where people turn to for care. For young people this may no longer be relatives, family doctors or traditional healthcare leaflets, or even the web. It may be peer-led, mediated through social networks and underpinned with self-monitoring Apps developed with crowd sourcing and marketed via consumer marketing linked to entertainment channels. For the chronically ill this might involve an affordable hospital-in-the-home, using cheap instruments to

monitor, report and motivate compliance. The highest impact disruptive innovations are therefore likely to be:

- Social media and social platforms.

- Big data tools and platforms for the re-use of health data for research, including personalised evidence.

- Mobile health and personal health systems (Apps, bio-sensing, tele-monitoring, ambient assisted living solutions, integrated PHR–EHR systems, self-collected patient data, participatory medicine systems).

- Learning health systems, applied to outcomes optimisation and patient co-production of health.

- Precision medicine software, patient molecular profile integration.

- Smart connected medical technology: portable point of care devices, implantable devices, mechatronic devices for minimally invasive diagnostics and therapy, bioengineered tissues and artificial limbs, wearable and assistive devices.

2.3. Which innovations which could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Growth and de-fragmentation of the European market for health ICT products and services favouring innovation, scaling up new developments more rapidly.

2. Growth of patient-centred and patient-empowering ICT tools, for well-being optimisation, prevention, self-management and contribution of data to research.

3. Sophisticated and intuitive improvements in usability including the real-time capture of computable data from clinicians and patients, multi-lingual support, and proactive (smart) analytics giving "just-in time" recommendations.

Propose three business models that could mobilise these changes:

1. Innovative ICT procurement models for co-operating eHealth and mHealth systems.

2. Value demonstration that ICT investments generate quantifiable organisational and outcomes benefits.

3. Public–private partnerships, not just in ICT but in innovative healthcare delivery models.

Have you seen any market trends in your field in recent years?

- No visible de-fragmentation of the eHealth market.

- Very conservative large scale procurements of monolithic solutions that do not favour innovative SMEs nor market agility in response to changing needs and opportunities.

2.4. How would you envisage the support across various funding instruments?

Firstly there is an inevitable tension that must be recognised between

a) the research agenda of most funding instruments, which seek to bring together best of breed European researchers to develop ground-breaking and highly visible research results;

b) the needs of perhaps one or two SMEs within each research consortium who have to struggle with resolving issues of intellectual property across the consortium before they can exploit the results, the challenges in attracting any further funding to integrate the results of multiple partners and projects, to make the end result robust enough for operational use, to have to develop deployment-supporting resources such as contractual instruments and training materials, all of which are on the basis of a very uncertain market because the solution is – inevitably – highly innovative.

The EC needs to play a stronger role in ensuring that a project's final results are well documented, easily discoverable and that their sustainability is promoted. Innovative SME products should have an easy and subsidised way of obtaining a quality label, to help them to be more convincing to procurers.

There should be a competitive route to access single organisation grants of two kinds:

a) for SMEs to scale up and develop products from the results of EC projects, including legal and capacity building support;

b) for non-profit institutions that have been set up through European projects and provide tangible support to the research and innovation agenda of the EC, as structural funding. It is not appropriate for such organisations to be sustained through competing in future research proposals, nor is it the appropriate way to use research grant funds.

There must be a greater obligation placed on future projects to build on research results rather than reinventing them from scratch. At present, proposals only need to demonstrate an awareness of other projects as part of "state-of-the-art", and reviewers seem not to put much weight on projects that really will use and extend prior results, nor necessarily on projects that are targeting near products rather than only proof of concept.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of: Where are the greatest improvements most likely to come from by 2020 through the use of ICT? (added as question)

1. Patient care:

i) Better understanding of pathophysiology for targeted therapies (e.g. reduce waste from ineffective care)?

ii) Better integration of hospital and community care (e.g. early interception of chronic diseases for targeted interventions incl. patient follow-up)?

iii) Better understanding of interactions between multiple morbidities (e.g. rationalisation of medication/integrated care)?

2. Lifestyle management:

i) Trajectories leading to long-term health or disease (e.g. link between deprivation and health indicators including influence of mental state/inequality of access)?

ii) Influence of environmental exposure in the real-life context of care and disease: how different environments impact on health and well-being – physical, working conditions, social media?

3. European leadership in decision support:

i) Data sharing between hospitals/countries?

ii) Meeting consumer demand: m-health, peer networks?

1. Science and technology? See points under 2

ICT product and tools will be scaled up and should be affordable for all citizens

2. Innovation? See points 1.3.1 c) and 2.3

The innovations should respond to an ageing society. In addition, innovations aimed at the youngest individuals in the market, "intelligent babies", preschool and school devices. Innovations might be developed in studies characterised by a transdisciplinary team with high research ethical standards. eHealth, mHealth and ICT can be part of increased well-being.

3. Market? See point 2.3

A European market grows rapidly and so does the global market. In a sustainable international market, reuse of tools should be stimulated to improve equity and development of ICT for all.

4. Policy? See points 2.4 and 4.2

The research agenda should attract the best researchers. Innovative products should have a quality label and regulations of intellectual property should be clear and practised. Quality criteria should be defined.

5. Other?

All data should be accessible and we need to be additive. Researchers need to interact with society and guidelines are under development. There is a need for validation beyond a randomised controlled approach.

3.2. What are the three main potential game changers?

1. In the large framework of an ageing population, the big challenge is the need for a paradigm shift in the healthcare domain from "healthcare technologies" to "well-being technologies". We need not only technologies to help elderly persons to recover a better quality of life once they are affected by co-morbidities: rather we need "consumer" ICT technologies (e.g. companion robots and smart connected medical devices) promoting the establishment of a better lifestyle, which will then promote the improvement of quality of life. In short, we need to move from

'eHealth' to 'eWell'. This also requires an integrated approach with other sectors of life, such as sports medicine and nutritional science.

2. Pressure from society, insurers and politicians is growing for transparency of outcomes, and for the transformation of health systems towards being more outcomes-oriented and patient-centred.

3. The emerging area of Patient Reported Outcome Measures (PROMs) is gaining traction among healthcare providers and may in the near future inform therapeutic decisions and resource allocation.

4. Evidence and guidance to redirect public procurement towards integrated care solutions, favouring innovation and standards adoption, multi-SME solutions.

5. Co-ordinated European (EC plus MS) stimulus and funding of multi-stakeholder engagement (especially clinicians, patients, research) in defining and promoting semantic interoperability.

6. Governance models for European-scale large health data repositories including protection of privacy, IP and public–private exploitation rules.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Stimulate market growth and procurement practices towards innovative, integrated solutions, making better use of standards and favouring SMEs.

2. Stimulate public confidence about health data governance.

3. Stimulate more patient engagement in self-management and prevention.

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4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

*What practical steps could be taken to encourage the participation of the EU-13 in calls?*

This challenge should not be seen as a volume game. Many call topics are already heavily oversubscribed and with a low success rate. The strategy for widening participation should not result in even more proposals of a low quality, which will impact negatively on the review process but not change the end result. It is more important to look critically at the reasons why proposals led by, or strongly contributed to by, certain EU countries are less successful than others, which means re-examining the unsuccessful proposals scientifically rather than only looking at high level application metrics.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)? What practical research steps could be taken to improve the health and well-being of European migrants?

All of the responses to this template will strengthen Europe-wide and especially cross-border health services, through eHealth and mHealth solutions. All of the research- and innovation-supporting recommendations here are therefore relevant to the situation facing the health needs of migrants and of the health and care systems in their host countries. However, given that a proportion of migrants do not originate from within the EU, some of the challenges raised here, such as interoperability, need to be tackled globally rather than only at a European level.
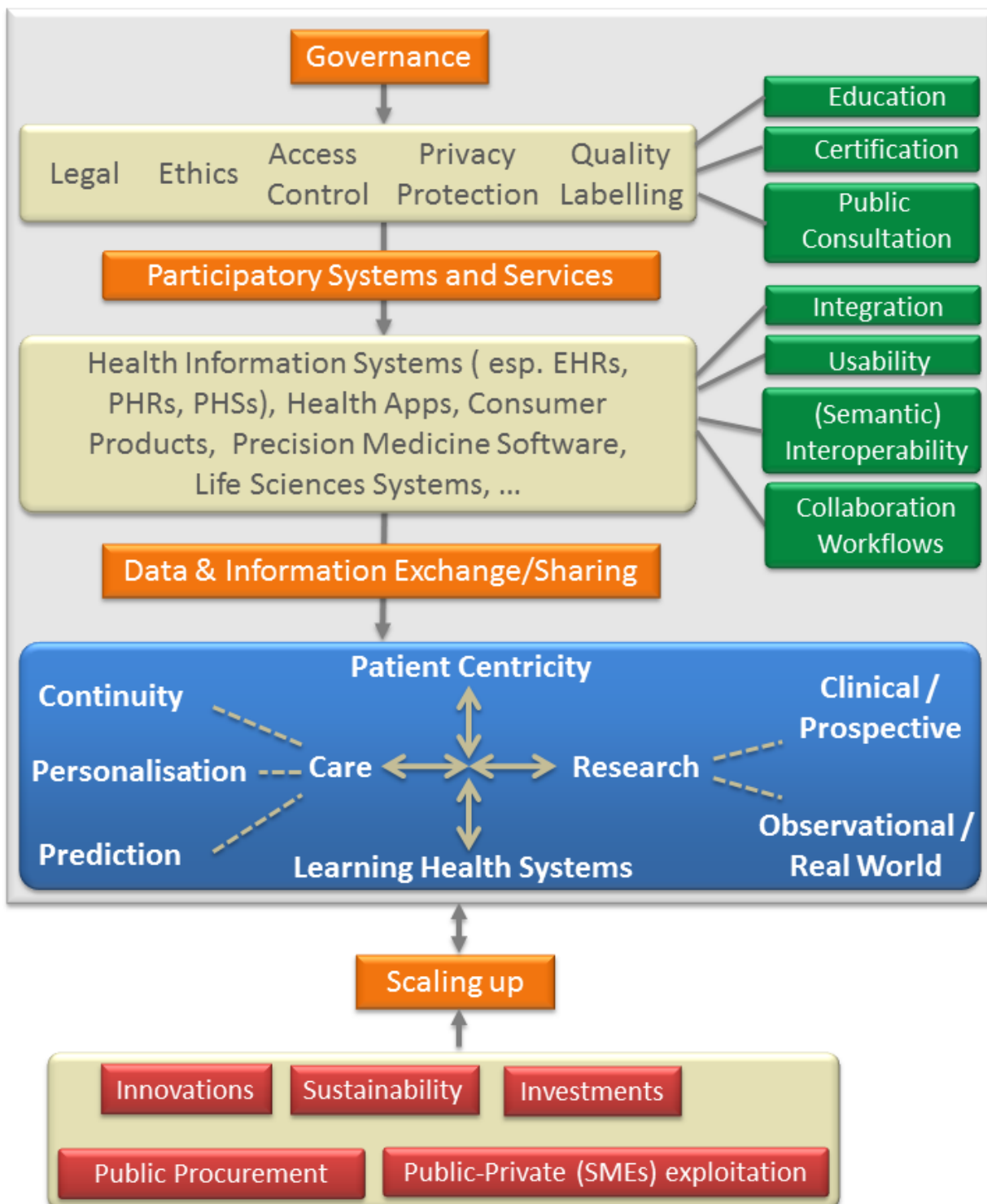
Integration of care

Luc Thijs (Chair), Marta Cascante, Matej Oresic

In order of importance, which three main research questions should be addressed by 2020?

1. How can we foster cross-fertilisation between healthcare and medical research in a coordinated care setting?

Healthcare professionals observe patients and act. By doing so, new data is created which can be analysed so as to create new medical knowledge. This knowledge can be re-injected to steer future activities in healthcare.
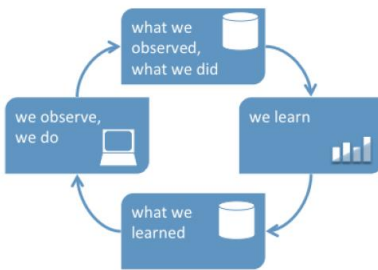
To a large degree, this is still theory, even more so in a coordinated care environment, which extends beyond the walls of the hospital and includes all other stakeholders in the care process, including physicians, specialists, social care givers and patients. How can we make use of advanced analytics to learn from data in this expanded care process and generate new medical knowledge? How can we feed this knowledge back with the necessary clinical decision support and dynamic workflows across the coordinated care setting?

2. How can we capture, organise and visualise distributed health data to enhance care in a coordinated care setting?

Contrary to Electronic Medical Records (EMRs), which focus on the patient in the hospital, Electronic Health Records (EHRs) are longitudinal records, spanning across multiple information sources and across multiple care tiers with the patient at its centre. The architecture of the future EHR still needs to address following questions:

- How will bi-directional interaction with other information systems (e.g. existing GP information systems, existing EMRs, etc.) take place?

- How will the EHR do smart analytics and clinical decision support?

- How will services like patient consent management and identity management be solved across distributed systems?

- How will usability be ensured for the specific needs of the different stakeholders in the care process?

- How can the existing IT systems of individual stakeholders be visually, semantically and operationally integrated with cross-boundary processes, potentially running on multiple platforms?

- How can we ensure that all stakeholders can participate in the care process, while continuing to use their own day-to-day IT system?

3. How to achieve complete semantic interoperability in a coordinated care setting?

Realistically, one can expect <u>multiple</u> standards to co-exist for a long time across the different healthcare tiers relevant to a coordinated care setting. What tools will allow us to achieve interoperability between these standards, terminologies and ontologies themselves, facilitating care coordination, smart analytics and clinical decision support?

Introduction

Better care coordination is increasingly accepted as a precondition for the economic sustainability of our healthcare systems. Lack of care coordination between primary, community, hospital, specialty care, social care and the patient, has, moreover, been documented to be detrimental to care quality, to care efficiency, and to patient safety. While duly recognised, care coordination or 'Integrated Care' (IC) does not evolve naturally and still requires a fundamental transformation of care delivery mechanisms: a shift in focus from acute, hospital-based care to early prevention and population management; a much stronger participation of citizens in their own care process; new governance models between payers, providers and consumers of care, incentivising and organising the coordination of care. Last but not least, fundamental progress is needed in semantic interoperability and in eHealth as essential 'enablers' of IC. Today, current state-of-the-art of deployed EHRs, decision support systems, diagnostic tools, clinical guidelines and care pathways are not able to cope with the challenges of IC. We call for the EU to support an umbrella programme on IC which is sustainable in terms of funding and offers a continuity of topics and eco-system.

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1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. **Governance and business models <u>to incentivise</u> better coordination of care are not yet in place**

   - Current financial models, governance and/or policies do not incentivise proactive sharing of patient information, let alone better coordination between stakeholders in the care process. Citizens/patients today still have to navigate through disconnected healthcare and social care systems.

2. **No <u>overarching redesign programme and template</u> for care coordination.**

   - There seems to be no overarching redesign programme for care coordination, which feeds the knowledge gained from ongoing experiments into an evidence-based roadmap that can serve as guidance to Member States.

   - A review of experiments and pilots in Europe shows that very few projects thus far combine all relevant stakeholders in the care process and all relevant co-morbidities. Existing solutions are often disease-specific, touch certain stakeholders but exclude others, and have not yet succeeded in achieving deep semantic interoperability, or in embedding smart decision support and dynamic workflows across the relevant care tiers. Few have resolved the usability challenge for the very different type of stakeholders. New

research should combine and complement past experiments, focusing precisely on the above to obtain a more <u>comprehensive</u> template.

3. **<u>Better performing eHealth platforms</u> and <u>strong semantic interoperability</u> to allow for care coordination and translational medicine are not yet established.**

- We still need to close the loop between healthcare, informal care and biomedical research: identifying patterns from the big data produced over many information sources, formalising findings and re-injecting them into operational applications in the form of decision support.

- Decision support is still not used at large scale and not connected to the workflow. Both are barely integrated with operational systems, often only take into account the clinical perspective and are not adapting to an ever-changing context. They often have a narrow clinical scope with the result that a 'real' patient, never fits the profile. Current clinical pathways are often in contradiction with personalised and person-centric medicine.

- IT applications still need to be made more 'kind to people': the large majority of medical information generated today is consumed by clinically trained individuals and is therefore presented in a format which is not necessarily meaningful to patients or to informal care-givers. Since patients are expected to play an ever-increasing role in their care process, and since informal caregivers are increasingly to be included in the execution of care plans, this poses a significant challenge which still needs to be resolved. The citizen, actively engaged in digital health, cannot become a reality without significant and sustained attention to this topic. Even professional stakeholders today 'struggle' with the user interface of current health IT systems, claiming they generate more 'work' rather than immediate 'value'.

- Data liquidity in healthcare is still quite limited. True interoperability between IT systems still needs to be established. Far beyond the mere exchange of patient data between IT systems, what is needed is complete contextual information at the point of care, allowing for shared clinical decisions and follow-up. Open platforms are needed which support collaborative adaptive case management across healthcare tiers, built on top of existing proprietary health information systems. An interoperable healthcare system following a distributed architecture needs reflection and research on the relation and interaction between the EMR (covering the patient at the institution), EHR (covering the patient across healthcare tiers), PHR (personal health folder) and more and more, well-being related, social and societal data sources and applications. Full interoperability is needed to facilitate patient engagement, to ensure appropriate linking between informal care and healthcare and support care coordination. This is one of the key elements of the Digital Health Framework (DHF).

1.2. Give three research orientations to resolving these challenges:

1. **<u>Governance and business models incentivising</u> better care coordination.**

- Over the last five years, experiments with IC models have been conducted both in the USA and in several European Member States. It is increasingly becoming clear that outcome-based reimbursement, which provides a payment envelope covering actions by

all stakeholders in the care process (also called bundle payment) and which penalises waste (readmissions, preventable adverse events), is more likely to incentivise care coordination than volume-based reimbursement ever has.

- While reimbursement systems remain the prerogative of individual European Member States, other essential preconditions for success of IC have meanwhile become more apparent. To name a few:

  o Governance around teleconsultation, around the role of informal care-givers and social care-givers, around patient access to medical information, around accountability in a distributed care process.

  o Skillsets required from healthcare workers in a coordinated care setting, as well as from social and informal care givers.

- Meanwhile, we should also have a better understanding of what can be expected from IC and what remains a myth. After several years of experimentation, the time has come to connect the knowledge gained from these experiments and pilots into an evidence-based roadmap and template for IC, as explained in 1.1.2.

2. **Better performing eHealth platforms**, **strong semantic interoperability** and smart applications to allow for care coordination and translational medicine.

- Closing the loop between advanced analytics, smart decision support and adaptive workflows:

  a. Analyse routine world data, extract knowledge (secondary use) and apply this knowledge in smart operational systems (primary use) and decision support.

    o Solutions to convert the results of research and clinical trials into computer readable evidence and generic medical knowledge, to be used in clinical decision support.

    o Solutions to make this knowledge available across relevant IT systems.

    o Solutions to describe provenance and evidence level (quality) of medical knowledge.

    o Solutions to collaboratively curate and validate research outcomes to be used by clinical decision support systems.

    o Solutions for prescriptive analytics: how to apply the outcome into operational systems.

    o Solutions to build patient cohorts across different sources by issuing source-independent queries.

  b. Multi-source analytics deriving information from the combination of clinical data, images, genomics and phenomics, as well as from environmental, psychosocial, and socio-economic data, covering the spectrum of acute and chronic care, but also lifestyle.

    o Solutions to combine multiple types of analytical and deep learning approaches.

- o Solutions to extract features from images and other non-structured data and semantically describe them.

- o Solutions to semantically harmonise data from different sources.

- o Solutions to do 'streaming' reasoning (on device data).

c. Clinical decision support which works in a federated multi-stakeholder flow and is adaptive to the specific and ever-changing clinical and social contexts of patients.

- Enhanced usability:

a. The representation of rich medical data and clinical thinking in dashboards and decision support systems: techniques to summarise, filter, and present large amounts of information, revealing underlying patterns and relationships. These techniques should be applicable to datasets ranging from the individual patient record up to global populations.

b. Smart and friendly user interfaces which dynamically adapt themselves to their user and their specific context.

c. Visual integration of integrated care processes within the existing IT systems of the different stakeholders used day-by-day.

- Architecture of EHRs:

a. Current EMRs lack the capability to capture not only facts but also the clinical thinking and temporal as well as causal relationships between them. This issue will be exacerbated at the level of the EHR, which covers the entire care process across institutions and touches also non-clinically-trained care-givers and patients.

b. EMRs (typically limited to the institution) and EHRs (longitudinal patient-centric, multi-source across healthcare tiers) are converging. Research is still required on the following themes:

- o Advantages and disadvantages of the EHR as a physical depository of data, rather than a virtual data source allowing for just-in-time data access from distributed sources.

- o Solutions to keep track of provenance of information. Solutions to resolve conflicting data entries, etc.

- Better semantic support of current communication standards (HL7, Open EHR): Existing standards lag behind, do not cover all use cases and have poor semantic underpinning. Solve the problem that not only a standard will be used, but that interoperability between standards is needed. Likewise, solve the problem that not only one platform will survive and that the platforms themselves must be interconnected.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

Not to our knowledge.

2. The Leadership in Enabling and Industrial Technologies?

Not to our knowledge

2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. **Faster adoption of IC thanks to an evidence-based roadmap and template**

   - Research on past experiments will consolidate fundamental obstacles to change, successful and unsuccessful methods to overcome them, as well as necessary incentives and business model changes to scale and exploit benefits: an evidence-based roadmap and template to coordinated care which can guide Member States and ultimately lead to faster adoption of new sustainable care delivery models.

2. **Stronger interoperability**

   - Better data liquidity among healthcare providers, strongly facilitated rather than encumbered by technology, policy and behavioural barriers.

   - Interoperability beyond the mere sharing of data but also allowing for collaboration and shared workflows.

3. **Better performing eHealth platforms, leading to better care**

   - Improved usability of IT tools will lead to better adoption of such tools. Expected benefits are better communication and understanding between clinicians, patients and informal care-givers and, for instance, better hand-offs, or better adhesion to care plans. Ultimately, this should also enable a better inclusion of citizen-patients in digital health.

   - Enabling clinical analytics, biomedical research and translational medicine and thus enabling a fast adoption in healthcare of medical research.

   - Better integration of care between the stakeholders, with more focus on prevention and integration into the daily living environment of people.

2.2. What are the new trends and disruptive innovation in health and care?

1. Patient-generated health data are expected to proliferate. The challenge will be to capture and act upon these data in a meaningful way – an extra challenge of interoperability, but also a new source of information. The adoption of smartphones as healthcare devices, with or without add-on sensors and applications, will play a key role in this respect.

2. Advances in personalised medicine, tailoring the right therapeutic strategy for the right person at the right time, determining predisposition of disease and delivering timely and targeted prevention.

3. Computing capacity has dramatically increased, allowing for deep machine learning.

2.3. Which innovations could reach market deployment within 5–7 years?

List three changes in the market that you would like to see by 2020:

1. Achieving strong interoperability of EMRs, EHRs and other relevant IT systems for care coordination.

2. A universal EU data privacy and security framework which motivates advances in care coordination rather than limits them. The US environment is moving fast(er) in this direction.

3. An evidence-based roadmap for care coordination from the EU, listing key success factors and pitfalls to avoid.

Propose three business models that could mobilise these changes:

1. Even if it is the prerogative of EU Member States, outcome-based reimbursement (with bundle payments) is probably the single most important business model which will drive healthcare redesign towards much stronger care coordination. The US environment is moving fast(er) in this direction, boosted both by the increasing economic pressure to reduce the cost of healthcare (now already reaching 18% of GDP) and by political initiatives (Meaningful Use, Hitech Act, etc.), combined with appropriate large scale funding and legislation.

2. Higher co-payments and exclusions in insurance coverage, combined with frustration with current disconnected care systems, are likely to mobilise a number of changes driven by patients, rather than by providers.

3. Data as an asset. The willingness of providers to share data (in a safe mode) in exchange for the use of clinical information/applications, such as benchmarks versus peers, adverse event detection and risk stratification may become an opportunity for data-driven companies.

4. Financing of health care innovation. Today innovation is mainly funded by companies and public subsidies. We need to create more demand (e.g. providers, regions, etc.) for innovation of sufficient scale with a higher return. Current procurement mechanisms do not yet allow this to a sufficient degree.

Have you seen any market trends in your field in recent years?

1. Care providers are reaching out to patients and patient engagement in the care process is steadily increasing.

2. Initiatives with outcome-based reimbursement (bundle payments) are ongoing in several Member States.

3. Life sciences (e.g. J&J) and tech companies (e.g. IBM, Samsung), reaching out to healthcare in order to both influence how care is applied and to be able to access data for medical research.

2.4. How would you envisage the support across various funding instruments?

While experiments with care coordination exist, current initiatives are quite fragmented. We still seem to miss an overarching redesign programme for care coordination

- Few integrated care pilots today are multi-agency, multi-disease related, multi-technology enabled and comprehensively cover all facets of a care redesign programme. Most pilots are quite focused on a specific use case, a specific care pathway, a specific technology.

- Knowledge gained from ongoing pilots should be connected, subsequently providing the basis for new projects, ultimately leading to larger scale implementation and exploitation.

- The transformation needed in comprehensively redesigning the care process is so fundamental that a sustained multi-year, multi-disciplinary research programme is required, across different funding instruments.

This calls for an eco-system with all value chain stakeholders, including small and large industry players, universities, care providers and patients.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. Science and technology?

- Need for strengthened translational research to expedite the transfer of key medical discoveries and technological innovation into healthcare systems.

2. Innovation?

- Better reconciliation between pure research and the economic development imperative, as highlighted in the EU Digital Health Agenda.

- More attention to innovation of care delivery processes and business models, not only to technology innovation.

3. Market?

- The fragmented European market, fragmented industry and lack of interoperability.

- Unequal adoption of IT in healthcare-related processes across Member States.

4. *Policy?*

- A dedicated redesign programme for integrated care, providing an evidence-based roadmap to Member States. Care coordination today seems to be a small attention point in Active and Health Ageing. Is it receiving the attention it deserves?

- The disconnect between healthcare and social care in several Member States, fragmentation of care financing and lack of outcome based reimbursement.

3.2. What are the three main potential game changers:

1. A sustained research programme with critical mass which builds on the iterative results of past experimentation, all the way until large-scale implementation of care coordination is accomplished

- There is a need for continuation of past research and innovation programmes, especially when needs are not sufficiently addressed: Electronic medical records have been a prime topic of research in the nineties, but are not retained any more in the scope of H2020 today. While interoperability was an important topic in 2000, big data and mobile health are now the prime areas of focus. One might be mistaken in thinking that effective

adoption of EMRs is now a fact in Europe and that the large interoperability challenges of our times have been resolved. This is not the case.

- There is a need to build a permanent eco-system of stakeholders around the care coordination theme, which survives the research project or the pilot scope and ultimately drives product development, scaling up and exploitation of the targeted benefits. Academia, major industry players, SMEs, health and social care partners need to participate.

2. Strong guidance on evidence-based best practices in addressing better care coordination:

- Sharing of evidence-based roadmaps to coordinated care: organisational models, change management needed, incentives and obstacles to overcome, supporting tools, etc.

- Political leadership endorsing a comprehensive strategic vision for better care coordination. Encouragement of multi-agency partnerships across the health and social care eco-systems to facilitate the cultural shift needed and develop a common understanding of long-term goals, implementation approaches and solutions.

3. Implementation of a harmonised interoperability framework, ideally based on global standards, and, if needed, on interoperability between regional standards.

4. One regulatory framework and harmonised security and privacy standards facilitating healthcare data liquidity.

3.3. What are the three main actions the public sector could do to accelerate changes?

Putting game changers in place as mentioned in 3.2.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

- Gaps in IT adoption (e.g. EMRs) may today limit participation.

What practical steps could be taken to encourage the participation of the EU-13 in calls?

- Not being burdened with legacy systems; however, new Member States may actually have a unique opportunity to leapfrog to the latest standards and further build on best practice achieved, whereby EU provides guidance.

- Encouraging new Member States to participate in regional projects involving several Member States and build on semantic operability.

- Impelling H2020 to work more in sync with other EU instruments such as structural and cohesion funds for IC purposes. One roof could help capacity building in the required arenas.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

- Continuity of care is already a challenge within a Member State, let alone in the case of travel or migration outside of the home country.

- With few exceptions, citizens today seldom are in possession of their own Personal Health Records.

- Moreover, lack of semantic operability between relevant IT systems within a country, let alone between countries, again is a limiting factor.

- On top of the above, access to care and its affordability still varies widely among Member States.

What practical research steps could be taken to improve the health and well-being of European migrants?

- Research on portable Personal Health Records. Success in this domain has so far been limited.

- Research on semantic operability, as already mentioned above.

Environment and health, green solutions and sustainability including climate change

Annette Peters (Chair), Agnieszka Cieśla

In order of importance, which three main research questions should be addressed by 2020?

1. What are the health impacts of technological innovations in response to climate change: healthy indoor environments and cities?

2. Electric mobility: what are the benefits and costs of green solutions to mobility?

3. How to promote active and healthy ageing in urban areas? How can environmental, spatial, economic and social drivers effectively encourage elderly to stay longer active and healthy?

Introduction

The majority of European citizens live in urban areas, which undergo transformation due to technological innovation and external drivers such as climate change. Environmental exposures are changing in response to these drivers, but their impact on health is difficult to assess without targeted research activities. Sustainability of technological innovation from a health perspective is an emerging field of research need. In particular, measures for energy conversion and electric mobility are considered technological innovations that potentially have tremendous potential to improve the health and well-being of populations. Furthermore, the number of elderly citizens is rapidly growing in Europe. This process poses a great challenge in the social, spatial and economic dimensions. In order to ensure sustainability in the future we need to tackle the consequences of the demographic change in relation to the environment jointly with these three dimensions.

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1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. Cities and indoor environments are changing due to technological innovations; in particular, means for energy consumption in the housing sector and improved city planning. However, there are in many regions increased housing needs, and economic pressures may impact the technological solutions. As a result, environmental exposures in indoor spaces may change. These changes include but are not limited to air pollution concentrations, allergen loads, noise, and microclimates. **The challenge is to conduct research that ensures healthy cities and indoor environments for future generations.**

2. Electric mobility has the potential to bring about huge health benefits by reducing ambient air pollution and noise on the one hand and to enable active mobility in otherwise sedentary subpopulations. **The challenge is to conduct research that adequately captures these benefits and costs of electric mobility.**

3. Research on health and well-being concerning environmental exposures has in the past focused on individuals in early life or middle-age. However, little is known about the role of environmental exposures on aged individuals. **The challenge is to conduct biomedical research to inform**

decisions on how to adjust the environment to meet the changing needs of an ageing population.

1.2. Give three research orientations to resolving these challenges:

1. Research on air quality improvement both in outdoor and indoor spaces. Well-being and healthy standards are not keeping pace with rapidly growing energy standards. In particular, energy savings do not necessarily lead to well-being and health, e.g. excessively compact thermal insulation in buildings may cause high humidity levels and reduce the air flow inside the building. This in turn can result for example in the growth of mould, exposure to which can contribute to the development and exacerbation of asthma, allergies and even cancer. Exposure assessment in the future will use emerging technologies including Apps and small devices for personal sensing, up to innovative approaches involving remote sensing for characterising environmental exposures. Comprehensive research is needed to evaluate the consequences and benefits of current and future innovations in this sector. Research needs to consider impacts over the life-course, from in utero exposures, childhood exposures, up to exposures in aged individuals. This would require potentially building and expanding existing cohort studies. Environmental exposures could be responsible for a wide range of non-communicable diseases (NCDs) and impacts on general well-being is to an extent not yet known. Innovative approaches such as exposome research offer novel tools for studying jointly internal doses of environmental exposures and markers of accelerated crucial developmental processes in early life and childhood, development of subclinical states of NCDs in adulthood, and processes of ageing.

2. Studying the impact of electric mobility on health is an interdisciplinary challenge that needs to integrate knowledge from engineering, mobility research, environmental sciences and various fields of medicine including but not limited to environmental medicine and sports medicine. Novel approaches integrating small personal studies, modelling approaches, assessments in large populations and the tools of citizen science will enable the collection of innovative data.

3. Research on people's changing needs towards spatial arrangements resulting from the process of ageing. This should consider in particular compact city growth, avoiding urban sprawl, difficulties in provision of health care in remote, poorly accessible areas. Here, integrated approaches involving city planners, architects and researchers from the social sciences and humanities offer tremendous potential, especially for developing novel approaches to characterise living conditions.

1.3. Do these challenges overlap with:

Other Societal Challenges?

There is an overlap with SC3, SC4, SC5 and SC6.

The Leadership in Enabling and Industrial Technologies?

Yes, it will provide research for developing sustainable solutions within Europe and will provide an advantage in highly developed as well as emerging markets.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. A cleaner, healthier environment.

2. An environment that is more age-friendly and designed for all.

3. People will remain in their homes for longer as they age.

2.2. What are the new trends and disruptive innovation in health and care?

1. ICT solutions that allow for energy savings, and thus contribute to decreasing environmental damage.

2. Consolidation of medical care in space.

3. New energy concepts

4. New mobility concepts.

2.3. Which innovations which could reach market deployment within 5–7 years?

Three changes in the market we would like to see by 2020:

1. Development of well-being standards for the indoor environment particularly for public/social housing, adjusted to the needs wider age group users.

2. New dwelling solutions, including not only constructional aspects (such as age-friendly design and materials) but also social models (co-housing) and spatial aspects (more compact city development).

3. Sustainable options for transportation and mobility in urban areas.

Propose three business models that could mobilise these changes:

1. Competitions for healthy and green buildings

2. Novel mobility concepts to be marketed; partnerships between cities and private companies

3. Mobility concepts for senior citizens deriving

Recent market trends in this field:

There are innovative measures that have been taken, however these remain isolated and in particular e-mobility is only slowly picking up.

2.4. How would you envisage the support across various funding instruments?

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Integrated cross-disciplinary research projects are needed that support both innovative research as well as knowledge transfer.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. Science and technology?

Considering health as a major component in research conducted in areas overlapping with SC3, SC4 and SC5, but housed in SC1.

2. Innovation?

Testing of the utility of novel technological solutions in small samples of the population and future consumers considering aspects of health in innovative ways.

3. Market?

Developing solutions that come from the consumer and not from the technology.

4. Policy?

Participatory approach regarding design of the built environment.

3.2. What are the three main potential game changers:

1. Integrative interdisciplinary research
2. European efforts learning from emerging solutions in individual countries or sub-populations.
3. Evidence-based approaches for evaluating innovations.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Consider health as a major driver for environmental and technology needs.
2. Enforce environmental laws which require cleaner and healthier technologies.
3. Create opportunity for competitions on healthy buildings and healthy urban environments.

4. In the context of health and care research how to address best the following issues

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

Participation may be limited due to an unmet need for capacity building. In addition, more pressing economic, financial and social needs may be overriding research priorities in these areas. Nevertheless future innovative approaches need to take into account the local and regional situation

with a strong need for integration. The inclusion of all European countries in the area of environment and health is essential to avoid isolation in countries where no such research is conducted.

Practical steps that could be taken to encourage the participation of the EU-13 in calls

Calls for proposals are suggested for medium sized projects focussing on research needs in EU-13.

4.2. Migration

Key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)

Migrants are often facing living conditions with environmental challenges, and therefore, may experience higher environmental health impacts. In addition, there is the strong suspicion that interactions between stress and environmental exposures may augment the impact on health and well-being. Little knowledge is currently available on the vulnerability of migrants given the presence of additional stresses.

Practical research steps that could be taken to improve the health and well-being of European migrants

Future research needs to be inclusive and consider the special situation of migrants in Europe.

CROSS-CUTTING ISSUES

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

Orla Sheils (Chair), Peggy Maguire, Agnieszka Ciesla, Anne I.H. Borge, Lucia Monaco, Anders Olauson, Jan Sedlak

In order of importance, which three main research questions should be addressed by 2020?

1. Consent as an enabler or impeder of access to big data and longitudinal datasets.

2. Social issues and their medicalisation.

3. Equitable resource distribution and social determinants of health throughout the life course.

Introduction

Research needs social science expertise: health economics, psychology, sociology, ethics and research integrity bring substantial synergistic value to research programmes. Scientists in behaviour, computing, physics, engineering, and mathematics are also relevant to SC1. There is a need to highlight societal autonomy versus individual autonomy. Can we legitimise the use of data or collective resources for new (ethically approved) use on the basis of 'the greater good'? Important questions to be asked include: Is unemployment hereditary? How can we reduce income disparity in treatment success and susceptibility to NCDs and multi-morbidities? How do we change cultural and social norms where for example violence against women or homophobia are acceptable?

We need to understand effective mechanisms to incentivise healthy lifestyles and reduce dependence on 'medicine' to cure self-caused morbidities.

Ethical considerations and social science contribute to research on the whole human being, beginning in pregnancy and following the individuals throughout their life course. A more inclusive approach to ethics and Social Sciences and Humanities (SSH) will allow us to really put the patient/participant at the centre of our research and treatment endeavours, to close the circle of our aspirations for personalised medicine and ensure we address research questions for the wider community holistically.

1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

Informed consent and expertise in SSH are needed for most research in health, demographic change and well-being. The three main challenges are:

1. Accelerating genetics, research ethics and SSH

Practical interpretation of risk using genetic data;

Distinguishing actionable from non-actionable mutations;

Issues of ensuring privacy protection in handling/sharing personal data;

Understanding the interaction between environment/exposome and genes/their expression.

2. **Advancing risk research for understanding developmental changes across the lifespan**

Algorithms to predict risk of disease and disorders based on environmental, psychosocial, genetic and lifestyle risk factors.

3. **Expanding knowledge about resilience and repair**

Processes that foster improved coping, algorithms for predicting the impact of particular drugs, psychosocial adversities, stress and treatments on some, but not all individuals

1.2. Give three research orientations to resolving these challenges:

1 **Accelerating** genetics, research ethics and SSH

We need more knowledge about how to study the impact of disease survivorship (cancer, for example). What are the long-term effects of treatment and survivorship on well-being? By doing this, we also gain insight into resilience. The perspective should be wide and include behavioural genetics and epigenetics. Design of approaches to examine whether informed consent actually exists when dealing with big data. Ethical considerations and psychosocial issues are contingent on sexuality, intersex and transgender. Additional issues pertain to ensuring genetic/genomic data are shared across international platforms while protecting privacy and how to address hurdles and bottlenecks in national/international legislation on data protection.

2 **Advancing risk research for understanding developmental changes across the lifespan**

We need studies about how childhood experiences impact on adult well-being. How are early experiences biologically embedded? This could have an impact on clinical practice and well-being. New knowledge can expand the content of educational and training programmes and thereby improve public health, access to high quality health care and better patient outcomes. In Europe today, risks are associated with migration, exploitation, human trafficking, slavery and gender issues. How do we change cultural and social norms where for example violence against women or homophobia are acceptable? Violence particularly against women is acceptable in some cultures and can pose difficulties for integration of migrants. In addition research is needed about domestic violence and its effects on the health and psychological functioning of victims and children. We need to accelerate studies of child witnesses. Care models of dependent/vulnerable persons, particularly the elderly, should be examined.

3 **Expanding our knowledge about resilience and repair**

In Europe today, we need studies on how and why some individuals are able to cope with man-made and natural catastrophes, psychosocial adversity and co-morbidities. Resilience is a response to all types of adversity. Resilience is a cross-disciplinary topic that spans many challenges, such as nutrition, climate change, political systems and the development of secure and sustainable societies.

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

Social sciences and humanities, integration, inequalities, migration and ethics might have central roles to play across all seven SCs; food, energy, transport, secure societies, space, ocean, etc. Disparities and inequity in resource allocation are significant contributors to the manifest broad spectrum of healthcare for our citizens. Moreover, inequity is promoted where research resources are diverted away from mental disorders and somatic diseases affecting the poorest in our communities. In the context of Societal Challenge 5 (climate action, environment, resource efficiency and raw materials) environmental causes are linked to chronic disease and poorer socio-economic strata.

2. The Leadership in Enabling and Industrial Technologies?

The FET programme may provide the technological innovation that would benefit development of solutions for creating more democratic access to healthcare facilities – through wearable monitoring devices or more rapid access portals for service users, for example.

Decision making, social norms and individual behaviour are parts of LEIT. The interface and user perception of the relationship between him/herself and technology is of paramount importance.

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2. What are the outputs/impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5–7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

- How can research contribute to avoid increasing social inequalities in Europe?
    - Inclusion of participatory research can improve "research visibility and usefulness" in society. Participatory research as an instrument can improve responsibility/cohesion (healthy but potentially at-risk populations; healthy and sick family members) and patients' dignity (self-management).
- SSH can examine which are the *protective* resilience factors against reduced well-being across age groups, cultures and societies.
- Ethical issues relating to merging data from registers, cohorts, biobanks, social media, big data: addressing ethical issues pertaining to data protection and security at European level would facilitate research on common as well as rare diseases based on personal data from genomic/genetic studies across countries.
- Understanding why what were once considered normal human events and common human problems – birth, ageing, menopause, alcoholism, and obesity – are now viewed as medical conditions, and we need to understand the huge heterogeneity in coping with these events.

   o Drugs now used to ameliorate 'poor' lifestyle choices, rather than exercise or diet for example. Why do we continue to spend monies that medicalise conditions instead of trying to change lifestyle choices or modifiable risks? We need improved targeted and intended interventions reducing the cost of sick-leave, and improving well-being in the workplace.

2.2. What are the new trends and disruptive innovation in health and care?

- Social media and Apps.

- Wearable monitoring devices.

- ICT for health.

- Near-patient testing/monitoring to democratise healthcare delivery.

- Improved interfaces for all ages, from intelligent babies to wise elders.

2.3. Which innovations which could reach market deployment within 5–7 years?

- Social media and Apps.

- Wearable monitoring devices.

- ICT for health.

List three changes in the market that you would like to see by 2020:

1. A more inclusive approach to incorporating ethics and SSH into calls.
2. Understanding how to use daily social media to inform the population about the ordinary magic of social, humanistic and mental resilience.
3. Convey hope and avoid media's strong focus on adversities.

Propose three business models that could mobilise these changes:

Have you seen any market trends in your field in recent years?

Apps are used for various studies of diabetes in pregnancy, treating depression, preventing suicidal thoughts.

2.4. How would you envisage the support across various funding instruments?

Areas of common interest should be consolidated into thematic programmes encompassing disparate instruments such as ERC, FEC, IMI and across complementary areas of different SCs, etc.

Cross-cutting suggestions:

- Integrate SSH into personalised medicine, public health and ICT development.

- Integrate SSH in studies of age/gender variations in coping with mental and somatic diseases, from pre-school to adult ageing.

- How can research contribute to avoid increasing social inequalities in Europe?

- Does active healthy ageing (AHA) lead to stable well-being or does enhanced well-being lead to AHA?

- Does unemployment lead to NCD or does NCD lead to unemployment?

Social Context for ICT

- Who are the end-users?

- Is there a social selection among them?

- Is there a gender specific behaviour?

- Is there an age gradient?

- When does ICT behaviour start?

- With intelligent babies, in families, group day-care, schools, work places?

We need research in various social contexts in addition to research within service healthcare and institutions.

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3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

Science and technology? Innovation? Market? Policy? Other?

Embracing the importance of ethical reflection and incorporation of SSH into our research programmes can change the way we set research questions and measure outcomes.

- Combating disease, injustice, poverty and climate change as well as managing large-scale migration.
  - o Infant mortality
  - o Antibiotic/emerging disease resistance and phenotypes
  - o Emerging concepts in combined anthropology–global health and cultural differences

- Workplace health promotion interventions
  - o Prevention of non-communicable diseases related to the workplace

- Nosocomial or healthcare-acquired infection (HCAI)
  - o Poor surveillance, weak laboratory support, and other factors are hampering our efforts to control antimicrobial resistance.

- Sex and gender issues

o   Enforced disambiguation of intersex individuals to comply with societal 'norms'

o   Impact of IVF and surrogacy as social determinants of health and potential for exploitation.

o   Research on evolving concepts of gay and lesbian relationships, parenting and well-being

3.2. What are the three main potential game changers:

1. Workplace health promotion interventions**.** The prevention of non-communicable diseases largely revolves around the promotion of a healthy diet and increased physical activity. Although the workplace is a potentially important setting to influence such health behaviours, given that some individuals can spend up to two-thirds of their waking hours at work, current evidence on effective interventions is limited.

2. Identification of resilience factors and correlation with well-being.

3. Democratising healthcare and research across resource-poor and rich areas:

* Achieve through well-matched partners in resource varied settings.

* Tangible outputs include expertise, policy change, partnership, advocacy and foresight.

3.3. What are the three main actions the public sector could do to accelerate changes?

1.   Workplace health promotion interventions – prevention of NCD/exposure-related disease in the workplace and an emphasis on mental health issues related to workplace.

    a.   How to effectively incentivise healthy lifestyles (particularly: physical activity, balanced diet, alcohol, tobacco)? Exercise prescription.

    b.   Solutions that make healthy lifestyles the default and easiest option for the individual? Lifestyle interventions: behavioural sciences role in tailoring interventions to change risk profiles/risk behaviour, including smoking, alcohol consumption, dietary habits and mental health problems.

        -   Focus on early childhood and effects of kindergarten and school with social media on life choices later.

    c.   Tobacco: novel ways to reduce tobacco smoking to zero.

        -   Recreational drug use among wealthy and influence on social competence.

    d.   Alcohol: novel ways of addressing excessive alcohol use? Comparative studies between culturally or religiously disparate groups for example.

2.   Expanding role for complementary medicine (in its broadest sense) in healthcare.

    a.   Alternative or integrative health?

    b.   Impact on personalised medicine.

    c.   Cultural perspective on complementary medicine, e.g. acupuncture is considered mainstream in China but not in the West.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

What practical steps could be taken to encourage the participation of the EU-13 in calls?

It remains a truism that large health inequalities exist between and within EU Member States. Sex and gender (S&G) are recognised as important determinants of health for both women and men, influencing access to health services and how health systems respond to their different needs. Also important are age, socio-economic background, education, religious orientation and ethnicity.

The EU-13 demonstrate divergent levels of research capacities, and based on previous calls it might be assumed that they suffer from the lack of relevant experience and knowledge, low competitiveness, and insufficient national funding for research. However, this may in fact be due to a failure to appreciate the potential strengths of these members and to design calls wherein they may be competitive.

A critical analysis of inherent strengths might help fashion more competitive calls.

Adopting a more proactive approach that facilitates networking with researchers from other countries **and** other disciplines would be helpful. A programme to strategically and specifically target young researchers from EU-13 countries would help build human capital.

Some targeted infrastructure support would be beneficial in enhancing research capacity and physical capital.

Research on the broad skills and competences of adults Europe-wide could raise awareness and drive increased investment in adult learning. This would lead to enhanced competences and social and civic participation. Ultimately, this approach has the potential to increase not just competitiveness and employability but also democracy, inclusion, health and well-being.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

What practical research steps could be taken to improve the health and well-being of European migrants?

The health problems of refugees and migrants are similar to those of the rest of the population, but they are exacerbated by the consequences of stress, and the risks associated with population movements. Such risks include psychosocial disorders, reproductive health problems, higher newborn mortality, importation of infectious diseases, anti-microbial resistance, drug abuse, nutrition disorders, alcoholism and exposure to violence.

Long exhausting journeys to uncertain futures accompanied by poverty ensure these people are more prone to accidental injuries, hypothermia, burns, gastrointestinal illnesses, cardiovascular events, pregnancy- and delivery-related complications, diabetes and hypertension.

Risk of exploitation is high and the vulnerability of refugees (male and female) renders them susceptible to sexual and reproductive health issues and violence. Female refugees and migrants face additional challenges with regard to maternal, newborn and child health.

Practical research questions might include:

    a. Exploitation, human trafficking and slavery associated with migration.

    b. How do we change cultural and social norms where for example violence against women or homophobia are acceptable? Violence, particularly against women, is acceptable in some cultures and may cause difficulties for integration of migrants.

    c. Domestic violence and its effects on the health and psychological welfare of victims and children.

Sex and gender differences in medicine

Peggy Maguire (Chair), Orla Sheils, Anne I.H. Borge

In order of importance, what are the three main research questions should be addressed by 2020 as priorities for 2018–2020?

1. In order to improve standards of care and health policy broadly, intervention and therapies must be studied on how they affect women and men differently. A sex and gender (S&G) balance must be promoted throughout all stages of research, including integration into the training and education of healthcare professionals. Translating the evidence from S&G research into practice will lead to more targeted, effective opportunities for prevention, treatment and care.

2. Robust sex, age and gender analysis of data is often lacking, resulting in important gaps in evidence-based medicine and research. Data and results from H2020 projects should be disaggregated by age and analysed both within and between both sexes in order to examine and understand the causal mechanisms behind development of health conditions and reduced well-being across the lifespan.

3. Research needs to explore how women and men experience health and healthcare from a multi-dimensional perspective across the lifespan. Particular attention should be devoted to differences within groups of individuals, such as migrants and asylum seekers as well as intersex, lesbian, gay, bisexual, transgender (LBGT) people.

Introduction

Sex and gender (S&G) integration into research must be improved. In a just society, women and men must have equal opportunity to benefit from research. Over the years, scientific knowledge has increasingly demonstrated that some treatments affect men and women differently. However, the proportion of treatments for which men and women respond differently is as yet unknown.

Many physiological and pathological functions are influenced by sex-based differences in biology. Recent research on cardiovascular disease (CVD), osteoporosis and depression has identified significant differences among women and men with respect to the distribution of these diseases. Women and men have different sex- and gender-related risks for developing certain conditions and respond differently to treatment. For example, biological differences between males and females can affect how a medicine works in the body. Additionally, patterns of gene expression differ between males and females.

Analyses between and within groups of male and females should be encouraged. Research must comprehensively explore S&G differences in science, research, health promotion, disease prevention and medical interventions/therapies. Other health influences – such as education, socioeconomic status, culture and employment – must also systematically utilise S&G analysis. A firm commitment to a multi-sectoral approach is needed to achieve optimal health for all population groups throughout Europe. S&G affects all aspects of development through the lifespan for girls and boys, women and men so research must consider the interaction of S&G in order to deliver the best care to European citizens.

1. What are the challenges in the field concerned that require action under the Work Programme 2018–2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1. Sex and gender differences have not been systematically integrated into research and medicine. Some S&G considerations are integrated into medical and health professional education; however, many gaps continue to persist and require immediate intervention.

2. More research is needed to better understand how S&G affects causal mechanisms in health promotion and prevention, progression, diagnosis, treatment and care. Many factors that influence health lie outside the health sector, so research in these areas must also include education, socioeconomic status, and culture and employment considerations. The inclusion of S&G impact assessments in all research areas will lead to better policy and contribute to the reduction of inequities in society.

3. Research in life course issues should include studies of how and why gender identity issues develop. Limited research is currently available on the developmental pathways of health and well-being of intersex individuals from birth, after surgery and during childhood and adolescence to adulthood. At birth, surgeons and parents try to decide for the baby in as optimal a way as possible an identity as either female or male and medical treatment (such as hormones) may be provided to reinforce the sex identity that has been decided upon. The impact of such interventions on an intersex individual's physical, mental and social development and any future adverse (or positive) ramifications need more careful research.

1.2. Give three research orientations to resolving these challenges:

1. A multi-sectoral and interdisciplinary commitment to routinely include sex and gender considerations into all research programmes.

2. Improved research that includes data disaggregation based on sex, age and gender.

3. Efforts to ensure that subjects and researchers reflect the diversity of the EU population, including sex and gender diversity.

1.3. Do these challenges overlap with:

1. *Other Societal Challenges?*

   Sex and gender differences in health and well-being overlap with the other societal challenges. Many of the themes of these SCs influence health, such as food, energy, transport, social and family affairs, education, employment, finance, environment and law. A firm commitment to a multi-sectoral approach is needed to achieve optimal health for all population groups.

2. *The Leadership in Enabling and Industrial Technologies?*

   Excellence in future scientific and technological development will be strengthened by the consideration and systematic incorporation of sex and gender in the research and

development processes for new technologies. The integration of S&G factors will help to make society more equitable.

2. What are the outputs/impacts that could be foreseen? Which innovation aspects could reach market deployment within 5–7 years? In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

1. Research in the S&G area will lead to a better understanding of the causes of health problems and reduced well-being. This knowledge can be used to develop improved and targeted interventions, diagnostics and treatment strategies. The inclusion of S&G considerations will create opportunities to increase healthy life expectancy by improving on the previous "one-size-fits-all" approach.

2. A better understanding of how S&G-related causal mechanisms – both biological and social – impact upon risk factors, prevention, development, diagnosis, progression and treatment of various health conditions and diseases.

3. Good research results in more effective health promotion programmes that allow for varying S&G factors and that target individuals at different ages.

2.2. What are the new trends and disruptive innovation in health and care?

Digital technologies are altering healthcare delivery. Digital tools allow the citizen to take a more proactive role in her/his own healthcare decisions. Social media and mobile platforms are becoming increasingly important channels for health information, resulting in the expansion of the digital health-tracking market. These developments must not perpetuate or increase existing inequalities nor exclude vulnerable groups in society. The emergence of personalised medicine holds great promise for patient treatment. However, personalised medicine can only be effective if sex and gender is fully integrated into biomedical and health research.

2.3. Which innovations could reach market deployment within 5–7 years?

- S&G-targeted and efficient prevention, diagnostic and treatment strategies.

- An understanding of how S&G-related causal mechanisms impact health and well-being.

- Improvements on existing strategies and treatments through the integration of S&G considerations.

- Increased participation of women in research and science.

- Improved knowledge about surgical and psychological issues.

List three changes in the market that you would like to see by 2020:

1. The recognition of S&G as important determinants of health and well-being.

2. Consideration of important biological differences between the sexes and data analysis by sex, age and gender, which would result in improved prevention strategies, more targeted and effective treatments and care.

3. Promotion of S&G in all stages of research, including the integration of S&G into healthcare professional training and education.

Propose three business models that could mobilise these changes:

Difficult to apply to this topic.

Have you seen any market trends in your field in recent years?

Difficult to apply to this topic.

2.4. How would you envisage the support across various funding instruments?

The interaction of S&G is relevant and should be supported across various funding instruments including technology and public–private partnerships (PPP):

- Additional for funding for projects that are exemplary in their efforts to address S&G.

- Funding for projects focused primarily on S&G differences.

- Requirement to disaggregate data based on S&G.

3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

Science and technology? Innovation? Market? Policy? Other?

- Lack of data disaggregated by sex and gender.

- Lack of an understanding of the full impact of S&G on health and well-being.

- Treatments and programmes developed that do not account for or address S&G differences, resulting in inefficient, and potentially harmful, use of limited resources.

- The perpetuation and, in some cases, worsening of inequities based on sex and gender.

3.2. What are the three main potential game changers:

1. Explicit requirements in Horizon 2020 to incorporate S&G consideration into all research projects and programmes.

2. The inclusion of S&G considerations in the list of top priorities.

3. Funding of projects and programmes specifically devoted to S&G.

3.3. What are the three main actions the public sector could do to accelerate changes?

1. Drawing attention to the importance of sex and gender considerations. Funding of research that improves the understanding of the impact of sex and gender on health and well-being.

2. Ensuring data collection includes disaggregation of sex and gender to allow the monitoring of trends and developments.

3. Reducing inequities resulting from the interaction of sex and gender.

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation.

What is limiting the participation of the EU-13 in calls? What practical steps could be taken to encourage the participation of the EU-13 in calls?

Research should be conducted in all European countries, particularly in newer Member States. Cultural and societal influences on S&G should be further studied and better understood.

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)? What practical research steps could be taken to improve the health and well-being of European migrants?

The current refugee crisis has large repercussions for public health promotion and prevention as migrants have complex health needs, especially for women, young girls and single adolescent boys. The number of women and children refugees coming in the EU is drastically increasing in 2016, with women and children now outnumbering men in countries like Greece.

However, there is a lack of appropriate support for female refugees, many of whom have been subjected to sexual and domestic abuse. Some women and young girls have been forced to marry for security as those traveling alone are often subject to abuse. Many refugees also struggle to find employment. Some have also had to resort to prostitution in order to support themselves, subjecting them to many risks.

These issues must be better understood and systematically addressed. Better co-ordination is needed between Member States. Improve assessment of incoming migrants' health, vaccination uptake and their specific health needs.

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

Mitzi László, Catherine Larue

Despite leading research, Europe lags behind the USA on bringing innovation into the market. For example, Europe has 16 unicorns[1], while America has 163.

Aim

Identify why Europe is lagging behind the USA in bringing ideas from the lab to the market

Methodology

Interviewing entrepreneurs who have worked in the EU and USA and online research.

Results: What limits bringing innovation into the market in Europe?

1. There is a **lack of investment in the idea to market phase**.

    a. Public money focuses on basic research but does not invest in the idea to minimum viable product phase.

    b. There is a risk-averse culture that is hesitant to invest in ideas and would rather invest in existing products.

    c. Entrepreneurs are hesitant to apply to H2020 calls because the application procedure is offputtingly long, expensive and confusing.

    d. Entrepreneurs are hesitant to apply to H2020 calls because they are unlikely to be successful.

    e. Entrepreneurs often do not know how to access other missing partners to form a successful consortium.

2. It is practically difficult to scale up ideas across Europe because of:

    a. Fragmented mobile contracts with high roaming charges (being fixed).

    b. Fragmented company registration, which means that to operate in multiple countries you need multiple sister companies.

    c. Fragmented banking system, meaning that international transfers are expensive and slow.

    d. Fragmented tax system, meaning that taxes are either over- or underpaid.

3. Investment is often country-specific, meaning that accessing all European funds is impossible without having multiple companies and local representatives.

4. Social networks are very local so it is difficult for innovative groups with ideas to reach decision makers.

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[1] A Unicorn is a start-up company valued at over $1 billion.   https://en.wikipedia.org/wiki/Unicorn_(finance)

Conclusion: How can we incentivise more efficient transition from innovation to the market in Europe?

Strategic Objectives	Expected deliverables
Focus on long-term outcomes	Creates more sustainable and stable systems
Focus on initial risk investment	Brings more ideas to an industry-ready stage
Support initiatives because of viable content and reasoning	Gives innovation a chance
Consider smaller entities being more nimble and therefore more capable to innovate	Faster innovation cycle
Detach investment from being country-dependent, as well as making it attractive for private investors to be country-independent	Faster scaling potential
Facilitate meeting of people with ideas and talent and decision makers in large corporations	Knowledge transfer and linking of new products to existing structures
Invest in initiatives that provide practical solutions to integrate Europeans, for example, integrated mobile banking, tax systems, company registration	Facilitate Europe-wide business
Publicly declare what tax large corporations are paying, where and why, to avoid them weaving in and out of Europe's fragmentation to their advantage	Assure that tax money is not being lost
Invest in market gaps that will probably never be properly covered by the private market; for example rare diseases and infectious diseases	Encourage innovation
Invest in bringing socially beneficial products to a private investment ready stage. For example driving business models for preventative medicine	Stimulate social entrepreneurship
Privacy laws should practically protect citizens. Internet and technical services and multinationals operate between countries so the law becomes obscure. For example, if the company is American, the server is in Iceland and the user is Spanish – under which laws does this fall? Also, laws change quickly, meaning you get long terms and conditions sheets that are practically unreadable and constantly changing. People are giving consent without really fully understanding what they are consenting to	To empower consumers to choose what they do with their data and services. Currently the default is to give up your privacy to be able to use very basic tools. It is difficult to use the internet and keep privacy, but you need internet services and mobile phones to be an operational member of society
Create entities for the proof-of-concept to minimum-viable-product stage, particularly for SMEs	Faster innovation cycle and therefore more nimble (i.e. quick to understand, clearly contrived, faster to adapt, moves with ease, agile, active, rapid)
Stimulate the appetite of bigger industries to acquire more robust technical projects/ideas	Encourage research to more quickly move into the market

that can be more quickly transformed into products and revenues	
Set up small infrastructures and platforms that will help academic researchers, spin-offs/SMEs to go more quickly to the market	Increase interest of industry for academic research; accelerate market launch and economical ROI
Funding pump-priming levers to help spin-offs/SMEs to better transform ideas into prototypes	Accelerate market launch and economical ROI
Matchmaking service where institutions can state what they can contribute and what attributes or skills they would seek in ideal partners for a consortium	More successful consortiums
Integrating service that gives individuals information and services around setting up company registration, mobile communication, banking, taxes across the 28 EU countries	Faster EU-28 scale-up channel

Horizon 2020 Impact on Commercialisation

The Horizon 2020 fund aim is to catalyse "*breakthroughs, discoveries and world-firsts **by taking great ideas from the lab to the market**.*" – Horizon 2020 website.

So Horizon 2020 wants to accelerate the process from discovery, through development to launch in order to get to European market earlier, and to stimulate IP, employment and the economy.

Fund Value €80 billion.

Fund Timeline 7 years (2014 to 2020); i.e. we are one-third of the way through.

Aim

To quantify the impact of Horizon 2020 on taking great ideas from the lab to the market.

Methodology

Analyse H2020 data to provide data-driven insights and advice.

Available raw data:

- All previous calls

- All successful applications for each call

- Follow up results (for example, leads to market translation, number of patients who received resulting treatment)

- Number of applications to each call and feedback to rejected calls

Results

A third of the time has elapsed and a lot has been spent on a number of calls.

Graphs from the data analysis shows the following insights:

- Number/percentage of consortiums that led to a marketable product

- Number of Europeans impacted by Horizon 2020 products

- List of products

- Profile of consortiums that led to marketable products

- Profile of consortiums that did not lead to a marketable product

- Number of applications per call, main reasons why applicants were rejected and suggestions on how to reduce these reasons

- Number of products that scaled up across multiple European countries

Encouraging stronger and successful involvement of EU-13

Agnieszka Cieśla (Chair), Roza Adany, Mitzi László,

In order to encourage stronger involvement of EU-13 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 Europe's 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 peculiar problems faced by the EU-13. An effective awareness campaign on Horizon 2020 funding possibilities is needed for EU-13 countries.

Most research institutions in EU-13 lack dynamics. There is almost no change in their structure proceeding. Current structures in many academic institutions militate against advancement and opportunities for female academics. Furthermore there are huge discrepancies between salary levels of older and younger academics. Young academics are being severely underpaid and they cannot survive from the salary of academic activities. Their scientific career is also limited. These people want to participate in projects which will provide them both: opportunity to fulfill themselves as scientists and a financial stability.

Women form the majority of the research staff in EU-13. Female scientists should be given support to allow them to develop a career that fits with EU values. They should be encouraged to apply for bilateral grants in many countries. When evaluated for positions, time spent on maternity leave should be taken into account when their professional productivity is evaluated in comparison with male applicants. Female applicants could be preferred in cases when male and female applicants for academic positions have equal qualifications. If younger female scientists would be given job opportunities with more decision-making power, this would contribute to a change in the status quo.

Player	Limitation	Incentive
EU-13 academic institution management	Horizon 2020 does not change their month salary	• Ensure that H2020 funds an increase in their personal salaries (the reference for defining financial support for programme participants should be an independent index (e.g. Big Mac index) not current remuneration • This will also mean it is less attractive to migrate because of decreased east–west wage gap
EU-13 academics and entrepreneurs	Do not want to threaten their stable job; easier to get structural funds The EU-13 are not as	• Combine H2020 and structural funds at least to make them equally accessible • Some broad call topics are

	technologically advanced as the EU-15. Many calls in Horizon 2020 require higher knowledge and skills that are not yet present in EU-13.	recommended, particularly among those related to SMEs (bottom up approach) – they give a possibility to produce an innovation effectively responding to the market's needs.
EU-15 institutions	EU-13 not prestigious, and relatively weak social network links	• Offer more capital to EU-15 institutions that cooperate with EU-13 • Give preference to applications with EU-13 and EU-15 cooperation • Make a matchmaking service to identify potential partners with specific skill sets
EU-13 businesses	Bureaucratic, slow co-operation procedure with academic institutions	• Offer more capital to EU-13 academic institutions that cooperate with local businesses • Give preference to applications with EU-13 academic and business cooperation • Make a matchmaking service to identify potential partners with specific skill sets

Other incentivisation strategies:

1. Consider funding up-and-coming institutions that demonstrate potential, rather than only established institutions.

2. Ensure that EU-13 evaluators are appropriately represented.

3. Introduce a quota for middle-aged male applicants to actively reduce the gender pay gap.

4. Support national, regional and online courses explaining the application procedure (Coursera and EdX are excellent MOOC platforms):
   https://youtu.be/eW3gMGqcZQc
   https://www.coursera.org
   https://www.edx.org

For title pictures:

ANNEX 1 - Template

In order of importance, which three main research questions should be addressed by 2020?

Introduction

Summarise the state-of-play (10 lines)

1. What are the challenges in the field concerned that require action under the Work Programme 2018-2020? And would they require an integrated approach across the Societal Challenges and the Leadership in Enabling and Industrial Technologies?

1.1. What are three main challenges in the field concerned?

1.2. Give three research orientations to resolving these challenges:

1.3. Do these challenges overlap with:

1. Other Societal Challenges?

2. The Leadership in Enabling and Industrial Technologies?

If yes, how? (provide some details)

2. What are the outputs / impacts that could be foreseen?

Which innovation aspects could reach market deployment within 5-7 years?

In particular, what are new trends and disruptive innovation in health and care; and how to capture and support this across various funding instruments?

2.1. What are the three main achievements that can be expected from the proposed research actions?

2.2. What are the new trends and disruptive innovation in health and care?

2.3. Which innovations which could reach market deployment within 5-7 years?

List three changes in the market that you would like to see by 2020:

Propose three business models that could mobilise these changes:

Have you seen any market trends in your field in recent years?

2.4. How would you envisage the support across various funding instruments?

3. Which gaps (science and technology, innovation, markets, policy) and potential game changers, including the role of the public sector in accelerating changes, need to be taken into account? How can these be addressed?

3.1. What are the research gaps at the levels of:

1. Science and technology?

2. Innovation?

3. Market?

4. Policy?

5. Other?

3.2. What are the three main potential game changers:

3.3. What are the three main actions the public sector could do to accelerate changes?

4. How can the following issues be best addressed in the context of health and care research

4.1. Widening participation

What is limiting the participation of the EU-13 in calls?

What practical steps could be taken to encourage the participation of the EU-13 in calls?

4.2. Migration

What are the key health and well-being problems for European migrants (both those migrating internally within Europe and those travelling from outside of Europe)?

What practical research steps could be taken to improve the health and well-being of European migrants?

ANNEX 2 - Scene setter

CONSULTATION OF THE HORIZON 2020 ADVISORY GROUPS - PROVIDING ADVICE ON POTENTIAL PRIORITIES FOR RESEARCH AND INNOVATION IN THE 2018-2020 WORK PROGRAMME

1.   Introduction

Horizon 2020 Advisory Groups are consultative entities set up by the Commission to provide strategic advice for the preparation of the work programmes, with respect to the different challenges/parts of the Horizon 2020 Specific Programme.

Advisory Groups represent the broad constituency of stakeholders including both industry and research actors as well as representatives of civil society, providing expertise on the research and innovation fields covered by Horizon 2020 and the potential priorities and investments that are needed.

This paper provides the basis for the consultation of the Horizon 2020 Advisory Groups with respect to the preparation of the Horizon 2020 work programme covering 2018-20.

The Horizon 2020 Specific Programme sets the scope and content for the implementation of the Framework Programme for research and innovation (2014-2020). Providing the legal base as politically agreed with the Member States and the European Parliament, it determines the specific objectives for Union support to the research and innovation activities for each Horizon 2020 challenge/part. On this basis, the Commission services prepare multiannual work programmes of which the first Horizon 2020 work programme covering 2014-2015 was adopted on 10 December 2013 and the second covering 2016-2017 was adopted on 13 October 2015.

This consultation is the first step in the work programme preparation process. The work programme 2018-20 will be the final Horizon 2020 work programme.

The consultation of the Advisory Groups is carried out on the basis of a series of questions (provided in Part 4 of this document) organised around meetings of the groups taking place from January 2016 until end-May 2016. Other main stakeholders such as European Technology Platforms, European Innovation Partnerships, Joint Programming Initiatives, contractual Public-Private Partnerships and other representatives from professional organisations and civil society will be consulted in parallel, where relevant. The Commission will have discussions with the Member States on overall priorities for the 2018-2020 work programme in the third quarter of the year. The interim evaluation of Horizon 2020 is due to be published in the summer 2017. The Commission expects, on the basis of the priorities identified through these consultations and on the basis of the recommendations in the interim evaluation of Horizon 2020, to develop the content of the 2018-2020 work programme in the last quarter of 2016 and the first three quarters of 2017 with the adoption and publication of the calls for proposals not earlier than autumn 2017.

The Horizon 2020 work programme comprises 19 sections, which set out the funding opportunities under the different parts of the programme. Each part is self-contained, and describes the overall objectives, the respective calls, and the topics within each call. The Horizon 2020 work programme

is complemented by the separate work programmes for the European Research Council, Euratom, the Joint Research Centre, the strategic Innovation Agenda for the European Institute of Innovation and Technology (EIT), as well as the Article 187 Joint Technology Initiatives with industry and Article 185 Public-Public Partnerships with Member States.

2. Policy priorities in the work programmes for 2014-2015 and 2016-2017

This consultation is about helping to identify the potential areas and actions which could be rolled-out in the next Horizon 2020 work programme.

The first Horizon 2020 work programme which covered the years 2014-2015, had as overriding priorities the need to boost competitiveness and support the creation of jobs and new sources of growth. Strong emphasis was placed on addressing societal challenges with high potential for sustainable competiveness, innovation and growth; thus reflecting the strong challenge-based approach of Horizon 2020, inviting applicants to come up with innovative solutions and attracting more multi-disciplinary and multi-sectoral proposals.

In the second Horizon 2020 work programme which covers 2016-2017, the overriding priority continues to be the boosting of competitiveness and supporting the creation of jobs and new sources of growth in the context of the Commission's 10 priorities. The chosen focus calls includes Industry 2020 in the Circular Economy; Sustainable Food Security – Resilient and resource-efficient value chains; Energy Efficiency; Digital Security; Blue Growth - Demonstrating an ocean of opportunities; Internet of Things; Competitive Low-carbon Energy; Smart and Sustainable Cities; Automated Road Transport – The New Frontier.

In the second work programme, further efforts are also made to ensure cross-cutting issues (e.g. social sciences and humanities, gender, international cooperation) are integrated in each of the different parts of the Work Programme, ensuring an integrated approach.

3. Policy priorities for the work programme 2018-2020

Although there are positive signs, the EU still has a long way to go before it overcomes the effects of the economic crisis, and the high unemployment rate especially amongst young people, remains the biggest concern and challenge in many Member States. The five point strategic agenda for the Union in times of change set by the European Council and followed up by the Commission's agenda for jobs, growth, fairness and democratic change is a strong response to the challenges we face. Namely by strengthening our global competitiveness, stimulating investments from both public and private sources, promoting growth and creating new and sustainable jobs for the benefit of the economy and citizens.

The Juncker Commission sets out ten policy areas on which the EU needs to focus its efforts over the five year period. This includes maximising the opportunities and assets of the EU by fully exploiting the potential of the single market as well as of international markets and reinforcing its global attractiveness as a place of production, investment, education and living, thus delivering benefits for all by promoting a climate of entrepreneurship, job creation and social fairness. Migration is also a policy priority. The 10 Juncker priorities can be found here: http://ec.europa.eu/priorities/index_en.htm

Research and innovation represent major drivers to both stimulate and leverage investment, providing new solutions and the knowledge which will help to deliver the new Commission's agenda.

Commissioner for Research, Science and Innovation Carlos Moedas has emphasised the importance of 'Open innovation', 'Open science' and of being 'Open to the world'. In general, Horizon 2020 is fully open to participation of entities from across the globe. Challenges in areas like energy, health, food and water are global challenges, and Europe should be leading the way in developing global research and innovation partnerships to address these. To remain competitive Europe needs to engage more with partners in global value chains and in new and emerging markets.

Open innovation is characterised by the combined power of ideas and knowledge from different actors (whether private, public, third sector) to co-create new products and find solutions to societal needs. Creating and supporting an Open Innovation ecosystem encourages dynamic knowledge circulation and facilitates the translation of that knowledge into socio-economic value.

Open Science describes the on-going transitions in the way research is performed, researchers collaborate, knowledge is shared, and science is organised. It is enabled by digital technologies, and driven by the enormous growth of data, the globalisation and enlargement of the scientific community including new actors (e.g. citizen science), and the need to address societal challenges. In the short term, Open Science may offer more transparency, openness, inclusiveness and networked collaboration. In the long term, it may make science more efficient, reliable and responsive to the grand challenges of our times as well as foster co-creation and Open Innovation.

The speed and scale of digitalisation are accelerating and transforming the way we design, develop and manufacture products, the way we deliver services, and the products/services themselves. It is enabling new innovation processes and new ways of doing business, introducing new cross-sector value chains and infrastructures. Horizon 2020 actions can play an important part in merging the physical and digital worlds, notably by maximising the synergies between digital technologies and innovative solutions to societal challenges. Many synergies are already in place, but there are growing opportunities and challenges.

Climate change and sustainable development are important cross-cutting priorities for the whole of Horizon 2020, as evidenced by the expenditure targets linked to these objectives[2]. In an evolving political context – the Juncker Commission's priorities of growth and jobs, the agreement at the climate change conference in Paris in December 2015, the adoption in September 2015 of the UN's 2030 Sustainable Development Agenda with its related Sustainable Development Goals (SDGs), EU policies such as the Commission's new Circular Economy Package or the 2030 Climate and Energy Framework, and the current context of migration – there is a clear and timely political imperative for research and innovation to support and drive forward on these key issues.

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[2] The Horizon 2020 Regulation states: *"Climate action and resource efficiency are mutually reinforcing objectives for achieving sustainable development. The specific objectives relating to both should be complemented through the other specific objectives of Horizon 2020. As a result it is expected that at least 60% of the overall Horizon 2020 budget should be related to sustainable development. It is also expected that climate-related expenditure should exceed 35% of the budget, including mutually compatible measures improving resource efficiency."*

4. **Questions**

For the next work programme key questions are what challenges under each programme part should be addressed considering opportunities and challenges. As was the case for the work programmes for 2014-2015 and 2016-2017, the Commission intends to establish calls for the work programme 2018-2020 cutting across the various programme parts. Furthermore, horizontal policy objectives like integration of social science and humanities, international cooperation and gender aspects remain important. Furthermore, the current policy objectives of the Commission should also be taken into consideration.

The questions to be considered by each Advisory Group, in what concerns their areas of expertise, are set out in the following box.