Proposal for

Health Care Compact for Europe

2015

Contents

A. Executive Summary

Where do we want to go?

We are all patients of the future and tax payers of today. In both roles we critically depend on European health care systems to provide optimal support for disease prevention, diagnosis and treatment at an affordable cost. Technical progress in a number of areas now makes it possible to redesign our current health care system, to make it more personalised, more preventive, and more cost effective, an enormous chance not only for us as individuals but also as societies.

Here we propose a *Health Care Compact for Europe*, a data and computational model driven strategy that can offer European citizens new, tangible options for their quality of life: a revolutionary improvement of their health care based on a more sustainable approach. The *Heath Care Compact for Europe* has the potential to be as successful as Schengen or Erasmus. It is not predominantly about more money, rather a new legislative and investment framework. Fruits are harvested from previous and on-going European Union (EU) and global research initiatives; technological possibilities are harnessed and new infrastructures created to enable the intelligent combination and exploitation of personal molecular data and health care data; EU citizens are informed, educated and engaged. The effects will be Copernican. Europe will extend and increase its scientific excellence and competitiveness, driven forward through the creation of a cost-effective, sustainable, equitable and truly personalised pan-European health care system. The benefits offered by the *Health Care Compact for Europe* could be felt by each European by 2025.

Why now?

This new concept has become possible through the intersection of at least three major developments, which also form key objectives for the future: (i) improved understanding of disease and drug mechanisms through basic and applied research, generating an accumulating knowledge-base, (ii) continuing dramatic improvements in the (energy) efficiency of computing, communications and sensing, enabling Internet-of-Everything (IoE) applications and, most recently, (iii) technological advances that are essential for the detailed molecular characterisation of every individual patient, the inherent basis of any truly personalised medicine, prevention and wellness strategy. This wealth of information will, in particular, allow development of individual 'guardian angel' models, enabling the doctors treating us for serious diseases to test and optimise their individual treatment strategy on a detailed computer model of our individual biology. Just like the 'Food Taster' who protected kings of past times against poisons, such 'guardian angel' models can, with increasing sophistication, help guard against incompatibilities between the drugs we take, the foods we eat, and even the exercises we do (or don't do). We routinely use sophisticated computer models to guard against catastrophic mistakes in designing skyscrapers, cars or planes; it is high time we used similar techniques to reduce the risk of mistakes in medical treatment, prevention and wellness.

The idea and the related goals of this proposal find support in previous FET Flagship initiatives: 'ITFoM: IT Future of Medicine', led by Prof. Hans Lehrach (Max Planck Institute for Molecular Genetics, Berlin), and 'Guardian Angels for Smarter Life', led by Prof. Adrian Ionescu (Ecole Polytechnique Fédérale de Lausanne). The technological roadmaps and the networks of partners generated by these two flagships create a unique opportunity for implementing a joint concept proposed here in the *Health Care Compact for Europe*.

In this way partners from medicine, science and engineering, industry, finance, health care funders, patient organisations, regulators, administrators and the general public will join to develop a stepwise, global, coherent and integrated path towards truly personalised medicine and prevention in Europe.

What can be done?

The *Health Care Compact for Europe* is based on four pillars:

- **TECHNOLOGY**: Development and implementation of new technologies for a much deeper characterisation of every patient by clinical, molecular, imaging and multi-parameter sensor based analyses as the basis of truly personalised prevention and treatment models (e.g. 'virtual patients' to explore effects and side effects of drug therapies without potentially harming real patients);
- **INFRASTRUCTURE**: Development of new health care infrastructures ('hospitals without walls, health care without borders') to bring the benefits of these new (and even already existing) technologies to most or all European citizens; also, new models of engagement between professionals and other citizens to enable citizens to engage in greater self-management and to contribute to policy discussions on ethics and the use of patient data;
- **LEGAL & REGULATORY**: Further development of the legal, regulatory and reimbursement framework in Europe to take maximal advantage of the new technologies and infrastructures, while also respecting individuals' rights regarding the use of data about them;
- **EDUCATION & ENGAGEMENT**: Education of medical personnel as well as the public (from early childhood onwards) in the new possibilities for patient treatment, prevention and wellness and the new options to improve their own health and wellbeing. Creation of a multi-disciplinary educational framework, highly interactive between traditional engineering education and health care. This will create a unique strength in Europe for diversity, promotion of young scientists and enhancing innovation at this boundary, generating new jobs and businesses.

Why do we have to act at the EU level?

EU level action is needed to:

- Shape the legal and regulatory framework concerning data protection of personal medical records and leading the public discourse regarding benefits and threats of acquiring and sharing data, creating a cross-border data sharing platform controlled by the individual citizen;
- Provide EU level legal and regulatory frameworks and incentivise national investment strategies in health care systems to develop in an optimal, mutually compatible manner across Europe;
- Provide financial support for research, technology transfer and infrastructure development.

Who will benefit?

- **EU citizens**, through a radical improvement of their health care (up to 50% improvement in treating serious diseases, halving the negative side effects of today´s generic medicine methods) and through a new quality of life, in which preventive medicine could induce a long-term paradigm change;

- **The European economy**, through new job and employment opportunities. Formation of a new vibrant economic ecosystem bridging traditional engineering, computer sciences and health care, with unique opportunities for production in Europe. Reductions in sick leave and health related early retirement;
- **Public finances**, by curbing the uncontrolled increase in health care spending (potential savings of hundreds of billions of euros);
- **Europe**, in enhancing its performance legitimacy and its excellence.

Funding

The *Health Care Compact for Europe* is not primarily about public money. Nevertheless, public funding from the EU of €10 billion over 12 years would be necessary (€0,83/year).

Existing EU financing tools (e.g. Horizon2020, regional funds, Juncker Plan) will be leveraged, supplemented by private funding sources once the EU expresses its political will and creates the required legal environment. It is expected that the private sector would top-up the EU funds at a ratio of minimally 1:5 (public/private).

Next steps

The Coordinators are available to provide further clarification. In an ideal situation a *Communication* can be launched by the EU Commission in order to consider putting the *Health Care Compact for Europe* into practice.

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B. Report

1. Background

Significant advances in health care have dramatically improved the health and wellbeing of European citizens over the last decades. Despite this progress, our health care systems are still failing millions of European citizens.

Every day 4000 Europeans die of cancer,[1] not only causing untold misery for patients and families but also exerting a huge financial demand - €126 billion in 2009 alone.[2] By 2025 more than 20% of Europeans will be 65 or older,[3] with many in ill health and dependent on the work of others. Our health care systems therefore not only need to deal with our increasing longevity, and the associated burden of chronic and degenerative diseases but also identify ways in which citizens stay healthy, active and productive for longer (also a current priority for the European Innovation Partnership on Active and Healthy Ageing[4]). The cost of meeting such challenges is spiralling. Every day European Union (EU) member states collectively spend close to €4 billion on health care,[5] an amount likely to rise with the demographic transition, raising doubts concerning the sustainability of our current health care systems. The EU is calling for a long-term vision that will provide sustainability of health care systems through 'better spending' and initiatives that are capable of improving competitiveness as well as the quality of public services and peoples' quality of life.[6]

Currently, the general approach taken in much of health care is a 'one-size-fits-all'. In the case of drug based therapies, patients are given treatments that have been found statistically to be the best option for a similar group of patients. But this does not mean that the majority of patients benefit. Some will respond positively, while others may actually become sicker or might even die, due to the severe side effects of a chosen therapy. Available estimates suggest between 38% and 75% of patients are unresponsive to drugs selected in this manner,[7,8] resulting not only in unnecessary suffering for both patients and families but also representing an enormous economic burden on European health care systems. Drugs (often expensive) that are not effective for the patient receiving them, not only delay recovery but can potentially trigger detrimental effects, requiring additional treatments, possibly long-term care, and potentially a reduction in the productive life-span.

At the basis of these varied responses is the fact that we are all very different from one another. We inherit different (forms of) genes, have different diseases, different lifestyles and are exposed to different environments. It is therefore not surprising that we often react very differently to the drugs we take. Tumours, for example, are not only dissimilar because our genomes are distinct. They arise by a combination of changes in their own genome and epigenome (i.e. chemical changes to the genome that affect gene activity), which make each tumour absolutely unique. The vast molecular diversity exhibited by tumours means that each one has never existed before or will ever exist again. Even subpopulations of cells from the same tumour can react differently to the treatment a patient receives. Our current view of biology underestimates this irreducible complexity

[1] http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/data-and-statistics
[2] Luengo-Fernandez et al. (2013). Economic burden of cancer across the European Union: a population-based cost analysis. Lancet Oncol. *14*, 1165–1174.
[3] http://ec.europa.eu/health/population_groups/elderly/index_en.htm
[4] http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing
[5] WHO (2010): Tackling chronic diseases in Europe Observatory Studies Series No 20
[6] https://ec.europa.eu/digital-agenda/en/news/communication-data-driven-economy
[7] Spear et al., (2001). Clinical application of pharmacogenetics. Trends Mol. Med. *7*, 201–204.
[8] Emerging Technologies: From Hindsight to Foresight. UBC Press 2009. Edited by Edna F. Einsiedel

of the 'biological system' that each human being is. In particular, we do not know the full extent to which various components interact, such as the genetic makeup of individuals, environmental and lifestyle factors, and microbiomes (i.e. the microbial residents in the gut and other bodily surfaces).

Approaches to our health and wellbeing that address the true complexity of every single individual and their diseases (and potential diseases) to provide more tailored solutions are therefore essential. This is only possible through a detailed (and ideally continuous) characterisation of every individual, down to the minute details which make us respond differently to therapy and prevention. In turn, this enormous amount of detailed information on every individual has to be translated into predictions. Predictions can be made using detailed (mechanistic) computer models; analogous in a sense to those we use to predict the weather, the behaviour of car designs in a crash scenario, or the response of a plane to a flight manoeuver. In situations where this is not (yet) possible, due to a lack of information, sophisticated statistical/machine learning models will be employed. In all areas of medicine, prevention and wellness, truly personalised selection of therapies as well as disease prevention measures will be required, in a new data and model driven health care '*forged in the white heat of technology*'.[9] An integral part of this new approach will also be engagement with the patient as an individual who has a role in shaping their own care. People will be empowered to engage in self-management of health, based on a greater understanding of their own health parameters and of causal relations between behaviours and outcomes. Through technologies such as non-invasive and non-intrusive wireless sensors embedded in everyday objects and/or as wearables, one can perform long-term quasi-continuous multi-parameter sensing of physiological signals and, following appropriate data mining, identify new biomarkers for early detection of the onset of diseases and/or prevent their evolution to a chronic state. Moreover, such smart sensing could be used for a quick and personalised assessment of the efficacy of drugs and therapies, saving costs and reducing the duration of the disease as well as the recovery period.

The ideal of a truly personalised therapy choice is already close to being fulfilled in many areas of medicine (e.g. surgery), in which the cause of a disease can be visualised, and the effect of an intervention can be easily anticipated; however, when it comes to treating patients with drugs such an approach is currently not feasible. The complex molecular networks and corresponding drug interactions occurring in an individual patient cannot be observed as easily as, for instance, the exact location and type of fracture in a patient with a broken arm. At best, we are able to use biomarkers to subdivide the patients into (typically few) subgroups more or less likely to respond similarly to a specific therapy. To date, however, really useful biomarkers have been very hard to find. While roughly 150,000 publications on biomarkers have been published, only around 100 biomarkers have proven useful in clinical practice. An essentially unsolvable problem is also posed by trying to predict the likely response of the patient from a specific combination of biomarker results. It quickly becomes technically impossible to test these robustly in clinical trials. We need new ways of thinking about how we conduct more effective clinical trials. More holistic, systems-orientated approaches are required.[10]

In all other situations in which we are faced with similar complex situations, with dangerous or expensive consequences, e.g. designing buildings or cars, training pilots or predicting the weather, we use computer models to predict the behaviour of these systems. At the basis of these models is a detailed characterisation of the situation at the start, knowledge of the rules governing its further development, and sufficient computing power. This strategy enables us to plan ahead (e.g.

[9] Rt Hon Harold Wilson, MP. Labour's Plan for Science. Reprint of Speech at the Annual Conference, Scarborough, October, 1963.

[10] http://www.nature.com/nature/journal/v469/n7329/full/469156a.html

according to the weather), optimise the design of a system (e.g. designing safe cars based on the results of virtual crash tests) and adapt our response to a system (e.g. in a flight simulator). This general approach of using computer models to define the optimal response in complex situations, allows us to make unavoidable mistakes in the computer rather than in reality, ultimately improving designs, accelerating developments, reducing risks and saving lives. Computer models provide the only way of using the large amounts of information necessary to define a complex situation in sufficient detail to predict how one system will evolve in contrast to a superficially similar system. Application of such a strategy to the extremely complex, highly interactive biological networks acting in us to keep us alive and healthy or make us sick may also reap comparable benefits in the context of our health and wellbeing.

This data and computational model driven strategy therefore offers the only real hope for a true personalisation of therapy and prevention in most, if not all, areas of medicine. A strategy that is supported by the enormous increase in our general knowledge of the biological processes involved, our rapidly increasing power to characterise every individual by a range of clinical, molecular and sensor based techniques, and the continuous increases in computing power.[11] Today we have the chance to calibrate and personalise such models based on clinical data provided through future Electronic Health Records (EHR), regular deep molecular analyses, and an abundance of sensor information, e.g. through on-body sensor networks. Such a modelling system has the potential to become incredibly powerful due to its self-learning capacity. Treatment results gained in a health care system that ultimately comprises 500 million Europeans, as well as many 'pre-clinical' experimental results and citizen generated data, would be used to continuously improve an integrated system, enabling an evolution akin to that of human beings themselves. To make use of the data generated within this integrated health care system, we need a General Data Protection Regulation which enables access to that data for the benefit of current and future patients, while ensuring a robust governance framework which can provide appropriate technical and ethical safeguards to protect people's personal data.

To make this reality, we propose here a *Health Care Compact for Europe* to develop the technology, the required infrastructure, and the legal, regulatory and educational environment for a sustainable health care system that will offer truly personalised medicine, prevention and wellness for European citizens.

2. Vision

We propose a vision of a truly individualised health care and disease prevention system in Europe, based on a detailed characterisation (e.g. clinical, molecular and sensor based) of the patient/individual and their wellness, health and disease course, in which the individual is engaged in self-management as appropriate.

A pan-European approach that will enable us to: (i) directly address the enormous (and almost certainly irreducible) complexity of the biological differences between every patient and every disease, (ii) to use this information to improve efficacy of drug development, reducing costs, time and risk, and the need for animal experiments, (iii) acquire, store and redistribute the ever-accumulating amounts of data per patient required to fulfil this goal, within a strong governance framework which protects personal data from misuse and which ensures privacy, (iv) develop (self-learning) computer models of every patient and disease state that allow physicians to test the consequences of all possible therapies in a virtual rather than the real patient, and (v) develop the

[11] http://www.top500.org/statistics/perfdevel/

future energy efficient technologies for on-body and implantable sensors, as key components of the Internet-of-Everything (IoE), featuring highly secure data management.

To achieve this vision, an infrastructure is required that will ensure all EU citizens can securely access their medically (or otherwise) relevant data on a Europe-wide basis, and be able to provide this information to a relevant medical professional in a secure, ethical and citizen-orientated manner. The developed infrastructure will ensure an intelligent linking, management and evaluation of data across borders and help to generate new models of engagement between professionals and other citizens, promoting greater self-management of data. Combined with the development of powerful IT and accumulating knowledge, aiding the construction of sophisticated modelling systems, and integrating environmental and lifestyle factors, this rich information base will provide a range of truly personalised disease prevention and treatment options for all European citizens, triggering a revolution in the quality and cost effectiveness of health care and health maintenance in Europe.

An important feature of this system will be the establishment of 'virtual patient/virtual individual' models of every patient/individual, able to act as 'guardian angels' throughout our lives. Through such personal models, effects and side effects of all possible therapy (and prevention) options could be tested without risk to us, and without significant cost for health care systems. Such 'guardian angel' models could warn us (and our doctor) of developing health risks and guard against unanticipated effects of the drugs we receive or the food we eat. Where possible, such 'guardian angel' models should be based on a deep understanding of the relevant biological processes, the molecular mechanisms of the disease and the possible therapies. In situations where knowledge is lacking, we can use less powerful (but still applicable) machine learning/statistical models. The models developed will also be able to learn from mistakes and use sophisticated mathematical algorithms to address knowledge gaps. As our diagnostic capabilities increase, and more and more disease and therapeutic mechanisms are unravelled, we can expect this data driven modelling approach to be used in an increasing number of disease areas, as well as in prevention and wellness applications.

Although models are still far from perfect, they are in many cases (particularly in oncology) likely to perform better than current clinical practice. As information on biological networks improves, and disease mechanisms and parameters become increasingly well defined, based on a systematic comparison of predicted and actual therapy response, overall accuracy will improve asymptotically. This continuous 'reverse engineering' of biological mechanisms built into a future pan-European health care system will, in addition, provide valuable input for hypothesis driven basic research, ultimately providing as much (or more) information on disease mechanisms in humans as other sources of information.

This 'big data' modelling based analysis strategy is closest to clinical use in oncology due to typically straightforward access to tissue samples (surgical specimens, biopsies, or even 'liquid biopsies'), the often dramatic (causal) changes in the genome, transcriptome, proteome and/or metabolome of the tumour and the wealth of information on disease (and therapy) mechanisms in different forms of cancer.

As part of the *Health Care Compact for Europe,* pilot projects will be established in specific disease areas, including ageing related and gender specific diseases (e.g. oncology, metabolic and rare diseases, and ophthalmology) for which we are closer to establishing mechanistic models of disease processes. These projects will develop and validate this approach for a truly personalised therapy choice, and following validation in clinical trials, will be expanded into general use, with on-going

monitoring through the EU's Pharmacovigilance mechanism.[12] In addition, pre-pilot projects will be supported for disease areas/therapies, for which basic information on disease and drug mechanisms is still missing, relying instead on other strategies not requiring mechanistic information.

Although a leader in science and technology, Europe as a whole has often not succeeded in completing the innovation chain from new discovery to its ultimate use in society. There are numerous examples where innovations originating in Europe return to the European citizen only when they purchase American or Japanese products. The Internet was originally developed at CERN (European Organization for Nuclear Research), then licensed to MIT (Massachusetts Institute of Technology), but returned basically as a US development to dominate the lives of Europeans (as much as anybody else's). Initial seminal work was conducted on the human genome by European researchers at Genethon (France) and the MRC Laboratory of Molecular Biology (UK), including the first large-scale sequencing analysis. With few exceptions, these concepts were only developed further in Europe once they returned as US-dominated projects. Similarly, the major technological breakthroughs pivotal for next generation sequence analysis were developed in Europe at Solexa, an SME that was taken over by Illumina, a leading US company.

Within the field of Information and Communications Technology (ICT), Europe has an important role to play in Embedded Systems as part of future IoE and Cyberphysical systems. The health care, automobile and aeronautical industries are key for European leadership; however, the role of new smart sensing technologies for health care is seen as much more revolutionary due to the significant societal impact and through the direct connection to a more sustainable model for health care costs. It will therefore be important to further develop the fundamental infrastructure that will enable scientific discovery and progress, in tandem with the political mechanisms in Europe that will support the translation of innovation. This will not only ensure maximal benefits for European citizens through improvements in the health care system but also provide economic benefits due to the development of a vibrant economy that links medicine and IT.

The *Health Care Compact for Europe* will provide a strong European perspective, creating a platform for key technological advances, pushing European innovation into the spotlight and opening up new avenues of opportunity, stimulating growth and development of regional economies and a cultural shift that enables the potential of such technologies to be fully realised.

3. Benefits

The *Health Care Compact for Europe* could be part of a new vision for the EU, providing major benefits to the regions 500 million citizens within one of the most important aspects of their lives – health care.

Every year Europe spends more than one trillion euros on health care. Roughly one fifth of this amount is being spent on drugs, half or more in treating patients who will not respond to the drug they receive, at a cost of €100 billion or more per year. Available estimates suggest that only between one quarter (oncology) and one half (many other areas of medicine) of patients respond positively to prescribed drugs.[7,8] In addition, millions of euros are wasted on medication that people don't take (€125 million annually), also a contributing factor to the premature deaths of 200,000 Europeans annually.[13] A truly personalised health care system in Europe, in which patients only receive drugs they actually respond to, would therefore not only substantially reduce current expenditure on drugs but would also avoid many downstream costs, such as extended care, the

[12] Pharmacovigilance Directive 2010/84/EU, and Regulation (EU) No 1235/2010

[13] European Council Policy makers Debate. An EU response to medication non-adherence. Brussels, 2010

need for additional therapy to counteract the side effects of the original treatment, as well as illness related absence from work; the latter currently costing European nations approximately 2.5% of their gross GDP per year.[14]

The *Health Care Compact for Europe* will provide the technologies and the data required to help identify the right drug(s) for the right patient(s), through a data driven approach combining 'virtual patient' models with other techniques (statistics, machine learning) to predict, which available drug or drug combination would have the most positive impact on individual patients. The latter likely to be an important factor in improving adherence rates, a growing priority as prevention and care increasingly move beyond the confines of the hospital.

This same set of technologies and the data generated would also help to accelerate the drug development process through virtualising major parts of the process. Large scale 'virtual clinical trials', comprising all patients (potentially millions) previously analysed in the 'personalised medicine' arm of the health care system, would provide a test-bed for new drugs. This would facilitate identification of patient groups most likely to respond to a new drug or drug combination, as well as potential biomarkers to identify sub-groups of responding patients in small, quick, and low-cost clinical trials, for rapid approval; however, as model-based therapy selection gains approval for routine clinical use, this inherently less powerful biomarker based selection of responders could be replaced by model-based therapy optimisation. Virtual trials also have the potential to reduce or even abolish the requirement for animal testing in pre-clinical drug developmental stages and ensure only patients who are most likely to respond positively to a drug will be enrolled in real-life clinical trials. Aligning with EU initiatives that are calling for improvements in the competitiveness and quality of public services and people's lives,[15] such a 'pre-screening' stage using virtual clinical trial technology is likely to become a future prerequisite for any clinical trial, helping to protect patient welfare and increase cost-efficiency. To allow large scale virtual clinical trials, the General Data Protection Regulation will need to include a provision permitting re-use of data through broad consent. The requirement for specific consent for every use of data introduced in the European Parliament's adopted revision of the General Data Protection Regulation would hinder beneficial research and slow down the EU's ability to provide innovative and improved health care to its citizens. The Regulation must encourage the protection of personal data through technical and ethical safeguards already in place in medical research instead of restricting access to useful data which can generate knowledge for the benefit of society.

A focus on prevention within the *Health Care Compact for Europe* would also provide numerous benefits for European citizens. Through the proposed developments in technology and infrastructure, implementation of home-based monitoring concepts ('hospital without walls') could very quickly make a real difference to the health of the European population, growing into more sophisticated 'virtual patient/virtual individual' based monitoring schemes ('guardian angels') over time. As part of such a program, daily or weekly self-observation with specialised devices, including 'home-OTC' (over the counter) or smartphone 'apps' would help to detect early disease signs and increase patient compliance. These new IT-based forms of care will also be of relevance for older and less mobile patients (in particular within rural areas), and may help to compensate for the shortage of skilled workers in the medical as well as nursing fields. Application of such apps in the eye disease field, for instance, would not only reap financial benefits but also has the potential to significantly impact patient welfare, preventing blindness in millions of Europeans,[16] benefitting

[14] http://www.eurofound.europa.eu/observatories/eurwork/comparative-information/absence-from-work

[15] https://ec.europa.eu/digital -agenda/en/news/communication-data-driven-economy

[16] Prof. Antonia Joussen, Charite Berlin, *pers comm.*

society as a whole. Integral to the success of this approach, however, is an active focus on patient engagement.

Under our current model of personnel intensive, statistics driven health care, costs will inherently continue to rise in tandem with our ageing societies, leading sooner or later to some form of health care rationing. In contrast, data and computational model driven health care will continue to become more cost effective, driven by significant progress in computational and analytical techniques, and an exponentially increasing information base flowing back into an evolving, self-learning system. The information generated will therefore further improve the performance of the 'virtual patient/virtual individual' models, and lead to unprecedented gains in knowledge regarding human biology. This will not only serve to accelerate improvements in health care and drug development but also represents a high-level intellectual challenge akin to (and for most Europeans far more relevant) understanding the composition of matter; the latter a current topic of investigation at CERN with an **annual** budget similar to the anticipated **total** costs of the *Health Care Compact for Europe.*

The development of a new European high-tech industry uniting health care and IT will also be catalysed, providing a platform to exploit key technological advances and commercial opportunities that will stimulate the growth and development of regional economies. Although difficult to quantify completely, we can expect long-term economic benefits many orders of magnitude higher than the anticipated costs of the proposed concept.

Through the deployment of personalised medicine, prevention and wellness strategies proposed by this program as well as the incentives provided for European companies to form, develop and prosper as part of the new ecosystem created, there is huge potential to alleviate the suffering and improve the health and wellbeing of the EU's 500 million citizens, whilst strengthening the economic outlook of Europe as a whole.

4. EU Actions

For the *Health Care Compact for Europe* to succeed, we need significant progress in four major areas:

a. **TECHNOLOGY:** to develop, improve and validate techniques for precision monitoring and data analytics in health care. This will be based on two pillars: (i) a detailed characterisation of every patient, comprising an intermittent clinical/imaging/molecular survey (genome, epigenome, transcriptome, proteome, metabolome, immune status etc.), complemented by potentially continuous sensor based monitoring; (ii) self-learning IT models translating this information into predictions on the future development of diseases (prevention) and the likely response to specific therapies. The combined pillars providing the individually best therapy to every patient. In this field the role of nanosensor arrays for advanced biomarker detection and the role of multi-parameter sensor nodes to generate uniquely structured data (and allow even real-time reconfigurability of data collection) will become crucial to support the development and validation of new therapies. This would allow personalised therapy, early disease detection, prevention and wellness applications, for an increasing number of disease and disease prevention areas.

b. **INFRASTRUCTURE:** to develop a pan-European, potentially federated health care infrastructure based on these technologies. This should initially focus on hospitals, but

ultimately include doctors in hospitals and private practice, as well as private citizens, generating 'hospitals without walls, health care without borders'. Such an infrastructure would allow the entire wealth of data generated to deeply characterise the patient and his/her disease status to be acquired, stored and effectively used to optimise patient health care; currently a serious problem for hospital IT systems. The performance of these systems representing a critical bottleneck to optimal medical care. The infrastructure should be citizen-centric, allowing each individual to control access to their own health data regardless of location within Europe, employing a similar range of security measures (password, pin, tan) as used for banking. Individuals/patients would decide who sees their data; whether data can be given to doctors for treatment optimisation and /or fed back (in a secure, pseudoanonymised form) into the system to further improve predictions for future patients. Individuals could decide to use sensors linked into such a system to continuously monitor their health and wellbeing: Routine check-ups carried out at home (e.g. personal metabolomes, smartphone apps to deliver early warning signs for specific disease areas), with data being checked automatically, notifying patients and doctors if further measures should be taken. Doctors, pharmacies, but also patients themselves, should be able to use the patient 'guardian angel' models to test whether a newly prescribed drug(s) could have unexpected side effects in the context of the patient's biology as well as their current therapeutic regime. Overall this will also help to cater for increasingly mobile European populations, and redress the remaining, still very significant inequalities in health care across Europe.[17] Beyond the medical infrastructure, the creation of such highly technologized hospitals is a unique economic opportunity for the design and production of the necessary hardware for sensing systems (made in Europe) to be embedded in the new smart infrastructure. This is expected to strongly enhance European innovation and leadership in smart sensors and be positively mirrored by the creation of jobs within Europe.

c. **LEGAL AND REGULATORY FRAMEWORK:** to address the legal and regulatory hurdles and accompany developments in technology. A relevant and harmonised legal framework (European and national, based on a coordinated approach) is required for data storage, protection and use. The legal and regulatory framework should align with the newly developed infrastructure to ensure citizen centric access to their own information. EU citizens will determine who is allowed to access their information, e.g. for doctors to help them identify the individually best treatment option, or for research projects to aid development of better treatment options. Data on a particular person are as much that individual's property as the money in his/her bank account. It is up to an individual to decide what they want to do with their information. Accordingly, it is up to the health care system to provide that individual (and their authorised doctor) with guaranteed, completely secure access to all available data as and when required. The legal and regulatory framework concerning data protection of personal medical records should protect the patient, his/her health and autonomous decisions rather than the data *per se*.

   To enable European citizens to benefit from the *Health Care Compact for Europe,* special attention will be given to current European legislative proposals for basic data protection regulation, which are strengthening and modernising the principles enshrined in the EU's 1995 Data Protection Directive[18], bringing them into the digital age. Further legislative

[17] United Nations' global development network: Human Development United Nations' global development network: Human Development Report (access 2013)

[18] Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of

proposals[19,20] are currently being discussed in the Council and the European Parliament. In addition, the *Health Care Compact for Europe* could help to implement *Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare*.[21] In this directive many elements are contained such as National Centres of Reference in a European Network of Centres of Reference or data sharing across internal European borders through the EHR. Most recently, an EU proposal for a Regulation on the *protection of individuals with regard to the processing of personal data and on the free movement of such data* (General Data Protection Regulation) has been made.[22] This existing legislation will help to provide a legal framework for the personalised knowledge base generated from "omics" data. The Regulation should aim to harmonise data protection rules for health research to facilitate cross-border research and sharing of data. The Council General Approach, adopted on 15 June 2015, provides derogations to Member States to regulate some aspects of data use in research, thereby maintaining the status quo. Harmonised rules are essential to the realisation of the *Health Care Compact* and should be ensured in the trialogue negotiations on the text of the Regulation. The Regulation could be adopted as early as the end of 2015, but it will take two years for the Regulation to take effect.

d. EDUCATION and ENGAGEMENT: to develop and adapt medical education and health literacy to the rapid changes in technology. During working careers of approximately 40 years, doctors who are currently in training will experience an enormous increase in the amount of individual information available on every patient, based on the generation and analysis of terabytes to petabytes of data per patient. Medical professionals will require an enhanced skill set that will align them with the accelerated pace of data generation, data integration and analyses via computational models, as part of routine clinical practice. Medical education therefore has to equip the doctors of tomorrow not only with the knowledge they will need when they enter the medical environment but also with the tools (and the mind-set) to deal with a seemingly endless series of technology revolutions throughout their working lives. Moreover, as patients become increasingly empowered and take more responsibility for their own health, access to education for European citizens would encourage 'non-medical' uses of the new possibilities (e.g. 'wellness', individual fitness training), helping to boost health levels on a general level, positively impacting health care and health associated costs throughout Europe. This could involve building these (life-course) concepts into the curriculum from early childhood, but also engaging people of all ages in the discourse of what is desirable for them, as well as what is technologically possible.

To achieve these goals the following actions by the EU would be critical:

General measures

The EU could publish a *Communication* inviting Member States to cooperate on the *Health Care Compact for Europe*. The *Communication* should highlight: (i) alignment with ongoing EU calls to support 'lighthouse' data initiatives that are capable of improving the competiveness and quality

individuals with regard to the processing of personal data and on the free movement of such data

[19] http://ec.europa.eu/justice/newsroom/data-protection/news/120125_en.htm

[20] http://europa.eu/rapid/press-release_MEMO-14-186_de.htm

[21] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN

[22] REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)

of public services and people's lives;[23] (ii) initiation of secondary legislation to harmonise the legislative and regulatory environment for health IT standardisation, exchange of information and data protection; (iii) the forging of stronger links between policy actions and EU-funded research in areas such as genomics; (iv) a renewed effort in optimising and rebalancing different areas of health-care expenditure, to take maximal advantage of the new possibilities and (v) an active effort to leverage synergies between similar initiatives worldwide, including the 100K Wellness Project (Leroy Hood; http://research.systemsbiology.net/100k/), the Personal Genomes Project (PGP) (George Church; http://www.personalgenomes.org/), which is pushing forward the concept of 'open consent' for personal data, and most recently, the new Precision Medicine Initiative (http://www.nih.gov/precisionmedicine/) by the US government.

Funding

The *Health Care Compact for Europe* is not primarily about public money. Nevertheless, public funding from the EU of €10 billion over 12 years would be necessary (€0,83/year).

EU financing could come from the existing tools, such as Horizon2020 and the Innovative Medicines Initiative (IMI). Consultation with the relevant strategic groups, e.g. the IMI2 Strategic Governing Groups (SGGS), will be integral to leveraging these funding mechanisms. The Commission can also incentivise Member States to use Structural Funds as well as the European Fund for Strategic Investment (EFSI) for this project.

Private funding sources would supplement the funding needs once the EU expresses its political will and creates the required legal environment. It is expected that the private sector would top-up the EU funds at a 1:5 ratio (public/private).

Types of action and budget estimated for EU funding:

- **TECHNOLOGY**: Development of the required technology, driven primarily by public research and medical centres in conjunction with SMEs. Clinical/imaging/-omics analyses combined with dedicated smart sensing and computing systems, as input for 'virtual patient/virtual individual' models and related systems to predict effects and side effects of therapeutic or preventative measures. Complementary resources and information can also be provided by a number of on-going European and International initiatives, such as the 100,000 Genomes Project (UK) and the International Cancer Genomes Consortium, as well as relevant existing guidelines and standards, e.g. Declaration of Rome 2012.

  Budget: €1,6 bn/12 years

- **INFRASTRUCTURE**: Infrastructure development driven by industry and SMEs. Seed funding by the EU through different mechanisms will trigger a much larger investment volume, financed through the enormous cost-savings that are anticipated on all levels.

  Budget: € 5 bn/12 years

[23] https://ec.europa.eu/digital -agenda/en/news/communication-data-driven-economy

- **LEGAL AND REGULATORY ASPECTS**: Administrative capacity building support for governmental and regulatory agencies, health care funders and medical organisations. Specific EU instruments can be leveraged, e.g. ERA-Net.

  Budget: € 0,4 bn/12 years

- **EDUCATION & ENGAGEMENT**: Development of new curricula to train new generations of medical personnel in new concepts, providing multi-disciplinary training at the interface between medicine and engineering, with high potential for innovation. Targeting a 'life-course' approach, through introduction of new concepts into the curriculum from early childhood, and actively supporting engagement of citizens of all ages and persuasions in the new developments occurring, e.g. through crowd-sourcing and citizen science mechanisms.

  Budget: €1 bn/12 years

- **SME/INDUSTRY, PRIVATE & PUBLIC PARTNERSHIPS:** Support to enable already developed research and development of finance tools that support late-stage finance of start-up companies to translate technological and clinical research into practice.

  Budget: €2 bn/12 years

5. Boards

5.1 Project Board

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