

### ● STRATEGY ∽ CHANGE

# Innovation for Personalized Health Care

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#### Introduction

In 2003, the co-founder of Seattle's Institute for Systems Biology (ISB), Leroy Hood, coined the term 'P4 Medicine', a systems approach to health and disease.<sup>1</sup> It aims to make health care more *Predictive, Preventive, Personalized* and *Participatory*. Advances in genomics and molecular diagnostics have enabled the development and use of *predictive* information to *prevent* diseases.<sup>2</sup> In case a patient is already subject to a disease, individual genetic information is then used to *personalize* treatments. The *participatory* nature of the approach is also important, involving individuals in managing their own health.<sup>3</sup>

This Issue Brief takes a closer look at the element of **personalization**.

#### 1. Personalization: a response to health challenges in Europe

Personalization in health care is an emerging approach that could greatly benefit the financial sustainability of health-care systems, and improve health outcomes. It is believed to be more adapted to the emergence of new disease patterns and the growing prevalence of certain chronic illnesses (e.g., cancers, obesity), caused by trends like aging and unhealthy behaviors. Currently, most treatments are being developed based on randomized clinical studies testing drug effects on large groups of patients. And many new drugs are normally tested on men only.<sup>4</sup> But one size does not always fit all: these current assessments do not reflect how medicines apply to each individual.<sup>5</sup> Injury or death are increasingly caused by adverse drug reactions, and certain drugs do not effectively cure all patients as each individual genome is unique.<sup>6</sup>

Personalization is reflected in more 'customized' or 'individualized' drug treatments and medical care. As they improve knowledge on the specific needs of various patient groups, research advances and population-based studies allow for such 'tailor-made' processes to be increasingly implemented in health care. This is expected to lead to a more effective development and administration of medicines, therefore a better quality of life.<sup>7</sup>

It is worth mentioning here that concepts such as patient empowerment and self-management (the *participatory* element of the 'P4 medicine') can be associated with personalization. Both aim to afford individuals a more central place in health-care systems, with more responsibility and control over their own health and wellness. This has much to do with the integration of new and innovative technologies into health care. For example, individual health data could be collected and controlled by patients themselves with personal devices. Such a development may increase the effectiveness of health-care supply and reduce costs, but also change the dynamics of our health-care systems with, in particular, increased participation and self-knowledge.<sup>8</sup>

## 2. The role of scientific and technological innovation in personalization

A number of innovations in genetics – particularly genomics – and technologies such as mobiles or bioprinting are progressively incorporating more approaches of personalization in health care.

#### Genomics

Genomics information from individuals allows for much more targeted intervention (medicines and treatment). These strategies may be aimed at individuals, but more often will address the specific characteristics of a subset of the population. The 'stratification' of the population in relevant subgroups (according to their biological phenotype e.g., based on blood groups, gender, cell type, age, or other variables) and with targeted care can be seen as an intermediate step in treatment processes, between the traditional one-size (or drug)-fits-all approach and a more integrated approach with fully personalized diagnoses and treatments.<sup>9</sup>

#### Personal genome information

Recent advances in genome science research (through the growing availability of genomic data, new technologies, etc.) have led to several initiatives transforming genetic testing from single gene analyses to comprehensive genome scanning and studies. Clinical applications based on genome risk profiling are expanding. Genomic profiling perfectly fits the approach of personalization, as it consists of *individual* reports of estimated genomic ancestry, genotype information and possible disease associations (e.g., a predisposition to cancer).<sup>10</sup>

#### **Personalized medicine**

Individualized genetic testing is expected to predict and assess an individual's predisposition to health risks and diseases. With the translation of pharmacogenomics into clinical practice, personal genomics could anticipate a patient's potential reaction to certain medications, thereby ensuring the safety and efficiency of medicines for each patient.<sup>11,12</sup>

For instance, although a number of clinical studies have shown the benefit of Herceptin (trastuzumab) in women diagnosed with breast cancer, some patients have not all been responsive or have developed cardiotoxicity (e.g., heart failure). Before administrating the drug, a personalized test through a risk-benefit analysis and cardiac monitoring assessing potential risk factors and side effects (both positive or negative) could be performed on each patient.<sup>13</sup>

Regarding prediction, depression is an example of a chronic disease that may originate from both personal histories and risk genes. Researchers at the Max Planck Institute of Psychiatry are investigating methods aiming to identify the genes involved and to detect a process of depression before the symptoms manifest (the predictive element of the 'P4 medicine'). Such advances may enable targeting the disease earlier and preventing it more effectively.<sup>14</sup>

The evolution of stem-cell treatments<sup>15</sup> may increasingly lead to their increased use in the personalized treatment of neurodegenerative disorders.<sup>16</sup> For example, Alzheimer's disease is commonly treated with standardized drugs administrated to all patients, whereas there are multiple factors behind the development of this illness – genes, but also environmental factors, or diets.<sup>17</sup> According to the Personalized Medicine Coalition, 70% of Alzheimer's drugs would be ineffective on the patient population today.<sup>18</sup>

#### **Personalized nutrition**

We have become increasingly aware of the linkages between disease and dietary habits. With the progress of science and technology in the field of genomics, molecular medicine and food science, a personalized approach to nutrition is expected to play a more important role in health care. Using a patient's genetic information could help better define individual genotypes, risk profiles and metabolites, thereby supporting recommending diets based on more specific, more adapted food components.<sup>19</sup> Personalized nutrition would lead to better quality of life and positive physiological effects by improving chronic disease management and mitigating health risk factors. This is likely to highly benefit a society confronted with the increased prevalence of cardiovascular diseases, diabetes or obesity.

Functional foods include "conventional foods; fortified, enriched or enhanced foods; and dietary supplements" and aim to prevent or mitigate nutrient deficiencies. Examples include supplements in minerals, essential fatty acids (e.g., retinoic acid, eicosanoids, calcium-fortified juices to strengthen bones), phytosterol/stanol-fortified foods that lower cholesterol and reduce the risk of heart disease,<sup>20</sup> or essential vitamins such as in folate-enriched foods that help prevent neural tube defects. Other benefits of functional foods may be the enhancement of mental alertness, the improvement of sleep, the increase of energy, and tailor-made diets adapted to the medical needs of different ages. Several food manufacturers are developing alternatives to foods that are high in saturated fat in order to reduce undesirable fatty acids. For example, Calgene has developed Laurical, a high lauric acid canola which can be used in confectioning cocoa butter, and is a substitute for coconut and palm oils. Others are introducing additional sources of omega-3 fatty acids: these are associated with many health benefits, but are lacking in current Western diets.<sup>21</sup>

Although much of it remains to be explored, the potential of functional foods is promising.<sup>22</sup> For example, some could play a significant role in preventing diseases like cancer.<sup>23</sup> New technologies could lead to new opportunities to determine the efficacy and effects of bioactive food components. In addition, they would facilitate patients' control over their own health and wellness.<sup>24</sup> Beyond, the democratization of personalized nutrition is expected to change the way we look at food and diets in relation to health.

#### **Digital health**

As they empower patients, new technological devices are viewed as a factor of behavioral change which would be more efficient than the encouragements of medical personnel. The ubiquity of these technologies could enable tailor-made, more efficient treatments and health-care delivery. Instant information may help practitioners keep track of patients' conditions more easily, and support more accurate recommendations.

#### Wireless health

Personalization is expected to be increasingly fostered by internet-based and mobile technologies and more generally, supported by the development of initiatives that use 'big data' in health care. Information about customers of these initiatives can be collected, registered, and exchanged; users can measure their performance and evaluate their behaviors with their smart phone applications or other devices.<sup>25</sup> Telemedicine technologies could ensure a more robust collection of patient information and data-sharing and help identify and target different levels of individual needs. A number of innovations may enable the continuous monitoring of patients' vital signs. There are for

instance hopes to develop a medical mobile device on the basis of the 'Tricorder' (from the fictional Star Trek universe), which would scan signs such as body temperature, chemical composition of the blood, heart and breathing rate, and diagnose diseases such as pneumonia or diabetes.<sup>26</sup>

A number of firms have already developed technologies that support personalization in health care. Regarding diabetes, risk assessment processes are becoming more customized. The Leibniz Association (Germany) has developed a Risk Score calculating an individual's proneness to diabetes and detecting it at an early stage.<sup>27</sup> A more general example is the tailor-made solution developed by the UMC Utrecht and Harvard University through a computer model, with which physicians could calculate how much patients benefit from a treatment.<sup>28</sup> The first bedside monitor was recently created by Medtronic; it helps parent track blood sugar levels of children with diabetes while they sleep.<sup>29</sup> HealthMedia (Johnson & Johnson) implements online tools as a chronic disease management and prevention system: the 'Digital Health Coaches' help patients deal with diabetes or lose weight.<sup>30</sup> GE Healthcare and GE's technology development branch, Global Research, have developed a Body Sensor Network, a wireless device that collects and monitors patient data (e.g., body temperature) which medical personnel can access in real time.<sup>31</sup> The platforms 23andMe and Pathway Genomics go further, by providing customers with personal genetic information based on their DNA sample. Customers can access a diversity of services, including personal DNA analysis with reports on their disease risk and response to treatments.<sup>32</sup> Further, the online social networks of Virgin HealthMiles support good health practices by allowing fellow employees or family members to communicate with and encourage patients that are exercising or aiming to lose weight. Online communities or forums can be created by patients themselves, e.g., through phone applications.<sup>33</sup>

#### **Bioprinting technologies**

Traditionally, 3D printing or 'scan-to-print technology' is used in manufacturing to create "three dimensional solid objects from a digital model".<sup>34</sup> Each device could be made individually due to a fast process, allowing for customization. 3D printing is predicted to be increasingly incorporated to the health-care industry – and to become less expensive, faster, and more precise.<sup>35</sup> Current examples include "medical models, surgical guides, dental applications and implantable devices",<sup>36</sup> but also custom hearing aids and prosthetic limbs.<sup>37</sup> Customized medicines could also be increasingly developed through this process, expected to be used by the general public within twenty years. Practitioners, and later patients could download drug recipes and tailor these to individual needs.<sup>38</sup> A future field of implementation for 3D printing could be medical research and regenerative therapies, with the creation of human tissue for organ replacement.<sup>39</sup> In addition, the technology may lead to better cost-efficiency within health-care systems by, for instance, cutting drug testing costs.<sup>40</sup>

Examples of customized medical applications of 3D printing include orthopaedic devices, such as those commercialized by 3D Systems and Bespoke Innovations. In 2012, this company created a new generation of custom-made hand brace devices which are "adaptive and personalized to fit the lifestyle and condition of each individual patient".<sup>41</sup> Skin or kidney cells printer to heal wounds quicker are being developed by the Wake Forest University in North Carolina and the Armed Forces Institute for Regenerative Medicine.<sup>42</sup> And researchers at Cornell University are testing ways to print synthetic knee cartilage, heart valves and bone implants.<sup>43</sup>

#### 3. Assessing the costs and benefits of personalization in health care

By reducing trial-and-error prescribing, personalization could solve a number of challenges. Economically, it may help reduce costs. One way would be to assess which expensive treatment may or may not be beneficial to one's health before prescribing it. In addition, health benefits for individuals are not negligible. Several studies have shown that the access to genetic risk profiling helps in promoting positive health behaviors, such as an increase of screenings for cancer detection and the uptake of drugs preventing Alzheimer's disease.<sup>44</sup> According to the Personalized Medicine Coalition, 34% less chemotherapy use would occur if women with breast cancer were to receive a genetic test before starting a treatment. The same organization estimates that the costs of generating genomic sequences have decreased quite rapidly and significantly, from \$300.000.000 in 2001 to \$5.000 in 2011.<sup>45</sup>

However, many challenges must be addressed by all stakeholders before personalization becomes fully integrated in our health-care systems.

First, the clinical validity of genome risk profiling, and its utility and limitations are yet to be fully understood. Genomic profiling may reduce the eligibility of patients for certain treatments. Relevant studies are based on data that can be considered as ambiguous and insufficient, and as a result, the extent to which the knowledge of risk information can actually improve health outcomes remains to be defined.

Second, although advocates suggest that targeted treatments and genetic information may decrease costs through the reduction of waste or the avoidance of adverse reactions,<sup>46</sup> personalization as an alternative to one-size-fits-all drugs policies may be economically ambitious. The intervention scope of preventive drug therapy or preventive scanning would be too expensive to implement on a large scale. Personalized care also suggests a higher volume of high tech material, with significant investments in equipment and infrastructure. In addition, the overall cost impact of personalized medicine is unclear – and prospective trials aiming to support the validity of genomic profiling and analyze the costs and benefits of its application could prove very costly.<sup>47</sup> Some expect validation tests to become as expensive as bringing new drugs to the market.<sup>48</sup> What is more, studies have shown that new technologies are responsible for a large share of yearly cost increases,<sup>49</sup> and that the cost savings generated by new treatments are limited in the long run.<sup>50</sup>

Third, further research on the societal and policy implications of its use by individuals and health-care providers needs to be conducted.<sup>51</sup> Challenges that call for new and carefully implemented regulations include approval processes for pharmacogenic testing, reimbursement policies for genetic profiling, enhanced medical education to support the incorporation of personalization into health care, the use and control of reliable technology systems for data sharing and decision-making, and sufficient R&D funding for genetic and genomic studies.<sup>52</sup>

#### Conclusion

As the developed world is facing a growing prevalence of chronic diseases, the increasing use of treatments comes with concerning consequences that include non-responsiveness to medicines and adverse drug reactions. Current treatments are mostly tested on large population groups. As a result, their adequacy and efficiency are questioned.

There is an increasing consensus that one way to address this challenge is to base health-care provision on the approach of personalization. Scientific advances could enable an increased access to genomic profiling, leading to the development of nutritional foods adapted to individual diets, and of personal pharmacogenomics preventing diseases or detect predispositions or symptoms. New technologies such as wireless devices or bioprinting are increasingly customized; they could help in establishing a more personalized model of care, and translate into more cost-effectiveness.<sup>53</sup>

More research on the associated economic benefits and limitations of this approach appears necessary, and a number of policy and ethical issues must be dealt with. In particular, specific attention must be paid to the ethics of genomics and the issue of genetic privacy, which will have to be tackled through ambitious regulations. With data sharing, concerns are raised about transparency, trust among stakeholders, the ownership of personal genetic information,<sup>54</sup> and potential discrimination by health insurances.<sup>55</sup> Furthermore, if a (perhaps paradoxical) pre-condition to personalized health care is the availability of 'big data' (as suggested by Hood<sup>56</sup>), the exploration of individual genetic information may only be possible if significantly large sets of patient data are collected.

To conclude, an increased participation of the population to its own health management, more efficient treatments and a better quality of life appear to be the main benefits of the approach, while the challenge of affordability and ethical issues that may arise cannot be overlooked.

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