

Lean Personalized Medicine?

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Summary

This dissertation aims to shed light on translational aspects to move from genetic reductionism toward holistic systems thinking in personalized medicine (PM). Summarized the approach will shed light on (1) the development of societal awareness and ethical argumentations to inform political decision making, (2) the integration of Big Data and ICT in the development of PM, (3) practical applications investigated in the context of chronic complex disease, (4) the inclusion of lifestyle and its preventive potential when applied in a personalized manner and (5) the overall challenges on the path towards a sustainable health care system.

According to the definition of the European Commission Horizon 2020 Advisory Group for Societal Challenge, “Health, Demographic Change and Wellbeing” PM refers to “a medical model using characterization 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 to determine the predisposition to disease and deliver timely and targeted prevention.”

Current first success stories are mainly reported in the field of oncology. Targeted testing for specific genetic abnormalities has been transforming the classification and treatment. However, development and implementation of PM approaches for other diseases and many aspects of health care delivery are still far from being reality. Genetics are just one of a suite of personalized tools to achieve healthier living, rather than an almighty method to reliably predicts future disease. Despite various calls for a more holistic view of PM, this term or alternatively system medicine remain proxies for the application of genetics to individualized therapies. In the present dissertation, the five SRIA of challenges have been chosen as a frame of orientation and horizontal guideline. The aim is to fill the challenges with scientific investigations, original data and specific examples, to shed light on translations aspects in order to move from a genetic focus towards more holistic systems thinking in PM.

Developing Awareness and Empowerment: Case of Personal Genomics

Given the overall need for genomic data to receive further insights into the complex system of health and disease, the first objective was to investigate the societal perception of research participation, the value people attribute to genetic research and the types of trade-offs between privacy and utility that people are willing to accept.

In Part 1, attitudes of Swiss older adults towards personal genomics and peoples’ willingness to engage and share their genetic data for research have been explored. The study indicated a positive overall attitude towards personal genomic testing among older Swiss adults, a group not typically represented in

studies about personal genomics. Main drivers were the possibility to access their personal disease risk and the opportunity to contribute to scientific research. Based on Part 1 we can conclude, that an increased focus on general public engagement, especially of older adults, in scientific research activities known as “citizen science” initiated by public research institutions may further strengthen the uptake of PM.

Big Data

Part 2 illustrates how to integrate the infinite amount of emerging data, known as Big Data to support the development the specific cases of policy making. For effective, high quality policy making in the context of public health we need to reshape the process of policy making using continuous, real time data inflow. In detail, the objective of Part 2 was to investigate the potential of Big Data as a support tool for making innovative decisions in public health policy making. Based on the findings, it has been concluded that the value and necessity of a pan-European data sharing platform or (Health) Data Cooperatives is its function as a tool to tap into the potential of all existing and rapidly emerging data sources. Such a Data Common would enable to leverage all the data required to overcome computational, algorithmic and technological challenges that characterize today’s highly heterogeneous data landscape, as well a host of diverse regulatory, normative, governance and policy constraints.

Translating Basic to Clinical Research and Beyond: Chronic Complex Disease

A majority diseases is caused by lifestyle issues: Nutrition, exercise and environment. However, medicine has not yet tapped into this potential. The need for PM derives from the realization that today’s most challenging medical conditions are chronic complex diseases with multiple pathogenic components that interact with each other. Currently, complex diseases cannot properly be controlled and much less cured by modulating single components at sporadic time points in the course of the disease or administering the same treatment to all patients. Lifestyle interventions namely physical activity have been tested as a promising intervention in a large variety of chronic inflammatory diseases to improve inflammation along with sleep quality, mental well-being, fitness and daily physical activity. Therefore, objective 3 was to explore the influence of a lifestyle intervention including regular physical activity on inflammation, fitness, depression and sleep among pediatric patients with IBD. In summary, the four articles showed that participants with IBD

in an active state of the disease (IBD-AD) showed higher markers of inflammation, had lower psychological functioning, impaired objective sleep and lower PA (average steps per day) compared to participants with IBD in remission (IBD-RE) and healthy controls (HC). After an 8-week physical activity intervention exercise capacity improved in all participants, self-reported fitness and daily physical activity increased in IBD-AD, but not in IBD-RE and HC. No improvements were observed for psychological functioning, depressive symptoms or subjective sleep. Objective sleep improved, deep sleep increased, light sleep decreased, and in the IBD-AD group the number of arousals after sleep onset also decreased. Finally, after a single bout of exercise inflammation markers strongly increased in all three groups, while after a long-term AET intervention, inflammation significantly decreased.

In conclusion, the integration of lifestyle into medical practice is one step to add and provide additional treatment options and recognize the importance of lifestyle and behavior change as an integral part and opportunity to increase treatment effectiveness and reduce costs. The increased efficacy through personalization will lead to empowerment, feeling of self-efficacy and regaining of control for chronically ill patients to improve health outcomes based on individual health metrics and personal preferences.

Bridging Innovation to the Market: mHealth and Business opportunities

A crucial tool in terms of innovation and development towards the notion of PM is mobile health (mhealth). The convergence of wearable electronics, miniaturized sensor technologies, and mobile phone penetration provides novel opportunities for personalized lifestyle interventions and support of health care practice. For example, the positive effects of regular physical activity are well known, yet many people do not comply with physical activity guidelines. General practitioners and other medical professionals often don't have time to encourage inactive patients or personalize their lifestyle advice to the patient's needs. As soon as people start moving, it is important to maintain this behavior, a second barrier many people fail. Physical Activity Behavior is highly dynamic, momentary and embedded in context. With a business plan, Part 4 will propose a tool to translate scientific evidence on behavior change into a personalized program to support GPs and empower patients to start a physically active life. Aiming towards holistic PM, MoVit is a concrete example on how to empower patients and health care professionals to integrate evidence based lifestyle advices into clinical practice. MHealth again, produces data that might improve patient self-efficacy, health literacy and may contribute towards decision making in the health care context.

Shaping Sustainable Healthcare: Discussion and Future scenarios

With the promise of PM to improve outcomes by providing treatment to the right patient, at the right dosage, at the right time and avoiding the trial and error based traditional “one-size fits all” approach, new opportunities emerged to reach the health care systems goals. Understandably, this development is expected to reduce the economic burden health care systems are facing due to adverse treatment effects, incomplete benefits or misdiagnosis. At the same time, the changing medical model will create new demands on the health care system. Objective 5 was to investigate the role of health care systems and policy making, when shifting focus from traditional disease categorization towards unique disease profiles.

In conclusion for Part 5, as well as overall, the implementation of PM will need a paradigm shift from multiple stakeholders and the health care system towards holistic systems thinking to realize truly PM. Technology will be the main driver in the fast development. However, patient-centeredness should be the ultimate goal of personalization. Therefore, the paradigm of PM should remain flexible and dynamic to integrate exponentially growing technology, incorporate lifestyle and environmental medicine and place the patient at center: *Lean Personalized Medicine*.