The True Meaning of Personalized Medicine

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I am not my genome. You cannot understand my desires or preferences, the trajectory of my life, nor my plans for the future from my DNA. Yes, in time more of what will be offered to treat me with will be shaped by my molecular biology, and for that I am profoundly thankful. But personalized medicine is not defined in the base pairs of my double helix, nor in the methylation pattern of my epigenome. It is defined, as it always was, by my choices and my needs.

Somehow we have allowed the idea of personalized medicine to be colonized by molecular biology, by the promise of therapeutic magic bullets [1, 2]. The promise is that a molecular understanding of individual variation will lead to targeted molecular therapies. Personalization is reduced to a molecular match with the individual, to a crafting of a molecule rather than an engagement with a person.

Modern medicine is sometimes criticized for inventing diseases that can then be treated by new medicines, or leaning too heavily on drug therapy when a more holistic assessment of patients would lead to non-pharmacological interventions. Consider for example the choice between prescribing a cholesterol lowering agent, or asking a patient to exercise, change their diet and lose weight. The pill is easier to prescribe than embarking on the journey of partnering with an individual to realign the way they conduct their lives, and the reasons that shape their behaviors. Personalized molecular medicine can similarly be criticized for diverting our attention from the traditional meaning of personalized medicine, where the care of an individual is shaped by an understanding of their entire context, and an engagement with their wishes and needs.

There will, we all hope, come a day when much of medicine is bespoke, and medicines are purpose-built an atom at a time for the individual. But even when that happens, there will be other choices that need to be made, trade-offs to be considered; there will be preferences and decisions about care that have nothing to do with molecules or survival curves. The choice to be treated, or how to be treated, is much more complicated than that. Consider for example, the difficulty in making end-of-life decisions. Classical decision making theory is often derided for being too abstract, but at its core, the notions of individual preference and utility are quantified, and the equation for making a decision is truly personal [3]. So, no one is saying the grand endeavor of molecular medicine has failed to deliver, or that is misguided. It is however time to reclaim the meaning of personalized medicine in the name of the whole individual, and not just our molecular biology.

Informatics is not blameless in the retreat from the personal. In the early days of AI in medicine, generic models of clinical knowledge were soon replaced by the idea of patient-specific models, where knowledge about diagnosis and treatment was adapted and modified computationally to create models about the individual [4]. That notion has somehow been lost. Indeed the technologies that informatics concerns itself with have in the main moved in the opposite direction, searching for generic instead of individual approaches.

Clinical decision support systems in routine clinical use today might reflect the practices of individual institutions, but not the needs of the individual, even thought there are well-known mechanisms for modifying trigger values based on individual measurements [5, 6]. Treatment plans, whether they be paper or computational constructs, often reflect national or local consensus guidelines. Yet every clinician knows co-morbidity and personal choice often lead to deviations from recommended care. The problem here is that this deviation from practice is often not evidence-based, and can in some cases lead to suboptimal care. Indeed when one looks at whether patients receive care recommended by professional experts, only about half of them receive care that meets basic quality indicators [7].

What has been lost now needs to be found. Perhaps the next informatics challenge is to formalize the personal - to create formal and robust methods to help patients and their caregivers to make the most evidence-based decisions they can, as they craft individual decisions. Rather than building generic technologies that try to force patients to meet cookie-cutter treatment plans, we should be building technologies shaped around the individual. Where there is no evidence, there soon will be data from electronic medical records. It is now becoming possible to create 'virtual' patient cohorts from past health records of others that match a new patient, to help inform treatment decisions [8]. By knowing the choices others made in similar circumstances, and the outcomes of those choices, we have access to crucial evidence that shapes what is decided next. The data stored in electronic records (including genomic data) should help in bridging the gap between 'on average' treatment captured in randomized controlled trial data, and 'n of 1 ' treatments [9, 10] . We are seeing real progress now in mining electronic records, still mainly focusing on looking for general relationships [11]. Harnessing data mining to

support individuals rather than cohorts is a tremendously exciting frontier.

In healthcare, quality initiatives often strive to turn our hospitals into Toyota factories or Formula-1 racing pits [12], and there is great merit in that endeavor. The more efficient, safe and effective healthcare delivery is, the better. The problem is that this lens sees all aspects of care fall under the same regime. Yet what we are learning from implementation science is that because of its complex and socio-technical nature, healthcare is local. Interventions in one institution can have very different uptake and outcomes in another [13]. And so it is with the individual. There is a need to work out which clinical decisions are best suited for generic standardization [14], and which are best left for personal customization. There is no strong theoretical underpinning here to help us make such choices yet, but the idea of defining the formalizabilty of clinical processes is not new. The notion of 'common ground' or shared models is one theoretical approach to thinking about the choice to generalize or leave tasks to individualized decision making [15, 16].

Consumer informatics may be a rich source of new models to support the new personalized medicine. For most of us, the personal is deeply influenced by the social. We are shaped by how others feel, experience, or value the things in our lives. Consumer informatics researchers are actively engaged in understanding how online social engagement shapes individual decision processes [17], and how we can use social engagement to support individual decision making. Apomediation, the replacement of the traditional information gatekeeper (for example a doctor), with peer group engagement and collaborative filtering, may soon become the norm [18]. Where there is no crowd to help, we can still use data from those that have come before to help in making our own decisions. Tools to help consumers visualize decisions and risks are likely to become

increasingly important. We know from cognitive studies that patients are often challenged in interpreting information, and are subject to biases, and information overload [19, 20], and these biases persist online [21]. Informatics tools not only can help consumers better interpret the implications of information [22], they can help them interpret it in relation to their own situation. For example, rather than being rigidly encoded, care plans can be structured in a more skeletal form around generic options [23], leaving the choice to follow one option over another to the individual. The risks and benefits can be calculated by population level data but visualized in a way that is understandable by the patient because it reflects their personal context [24, 25].

So, personalized medicine is indeed a 'grand' challenge for informatics, given that it currently occupies so little of our research or our practice. We have left personalized medicine in the hands of biologists and bioinformaticians, and not yet grasped that a greater set of problems remain to be solved. When the focus moves from genes, biology, models of disease, or even models of clinician workflow, and shifts to the consumer, we by definition start with the personal. We start with the 'I'.

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