

PERSONOMICS AND PRECISION MEDICINE

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ABSTRACT

The importance of knowing patients as individuals has been highlighted throughout the history of medicine. However, shorter visits, electronic documentation, reliance on technology, and increasing linguistic and cultural differences between patients and physicians create more challenges to effective communication than ever before. Perhaps more concerning is the greater emphasis on aspects of care considered more precisely measurable and quantifiable, the sum of which is sometimes felt to represent the patient better than knowledge of the patient himself. While genomics, proteomics, pharmacogenomics, metabolomics, and epigenomics promise enhanced diagnostics and therapeutics, understanding the unique circumstances of the person — what may be called *personomics* — is at least as critical to patient care. Such an understanding can only be developed when the relevant psychological, social, cultural, behavioral, and economic factors are obtained. Personomics determines how a disease reveals itself phenotypically and the way that disease and the individual with the disease respond to treatment.

INTRODUCTION

From 2008–2011, Gallup called 1,000 Americans each day and asked them about various quality-of-life indicators. Based on the data from these interviews, they developed a description of the happiest person in America. That composite person is a tall, Asian-American man more than 65 years old who is married with children, lives in Hawaii, runs his own business, earns more than \$120,000 a year and also happens to be an observant Jew. It turns out that *The New York Times* found such a person, a man by the name of Alvin Wong. Upon learning of this, Mr. Wong noted, “This is a practical joke, right?” (1).

Over the last several decades, appropriate medical practice has often been described by clinical practice guidelines that are based on the

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treatment of composite patients, individuals who share a common phenotype. At times, if care were based on those guidelines it would result in nonsensical treatment that would be impractical at best, and potentially even hazardous to individual patients. The failure of clinical practice guidelines to take into account individual variability is perhaps most obvious when considering an older patient with multiple comorbidities. Following disease-specific clinical practice guidelines for such a patient would, in many cases, result in the need for complex medical regimens that consist of multiple, different medications, typically cost significant amounts of money, need to be taken many times a day, and could expose vulnerable patients to adverse drug-drug interactions and undesirable side effects (2). Such a hypothetical patient, if approached with such a list of medications based on disease-specific clinical practice guidelines might well note, “This is a practical joke, right?”

INDIVIDUAL VARIABILITY AND PRECISION MEDICINE

The last several years have seen a renewed emphasis on the individual variability of patients. It is important to note that this is not a new phenomenon. It can be traced back many years, certainly to the time of Sir William Osler. Osler emphasized that knowledge of the patient based on obtaining a thorough and informed history and careful observation was critical, and he noted that “it is much more important to know what sort of a patient has a disease than what sort of a disease a patient has” (3).

The recent emphasis on knowing and treating patients as individuals has focused primarily on characterizing patients by their biological uniqueness defined by a variety of so-called “-omics” (4). Genomics, metabolomics, epigenomics, proteomics, pharmacogenomics, transcriptomics, microbiomics, and a number of other -omics each define a part of our biological identity that can be used to individualize diagnostics and treatment (4,5). This approach, known as precision medicine, was highlighted in President Barack Obama’s State of the Union address on January 20, 2015. Commenting on the President’s initiative in the *New England Journal of Medicine* several weeks later, Collins and Varmus noted, “The concept of precision medicine...has been dramatically improved by the recent development of large-scale biologic databases (such as the human genome sequence), powerful methods for characterizing patients (such as proteomics, metabolomics, genomics, diverse cellular assays, and even mobile health technology), and computational tools for analyzing large sets of data.” (6).

THE UNIQUE CIRCUMSTANCES OF THE INDIVIDUAL: PERSONOMICS

While using the information provided by these -omics in the diagnosis and care of patients has enormous potential to improve human health, the concept of precision medicine has not typically taken into consideration aspects of individual variability related to the life experiences of the person himself or herself. The importance of developing an understanding of the unique circumstances of the individual has been largely absent from the discussion. This concept has been termed “personomics” (7) to indicate that these issues are just as important and their description and study just as rigorous as the -omics that have heretofore had a seat at the precision medicine table. Personomics takes into account the social, psychological, cultural, behavioral, and economic factors that affect the patient’s health beliefs, the way he or she approaches illness, and the patient’s interactions with the medical system. It considers the patient’s personal preferences, his or her values and goals, and the support the patient receives from family and friends. It is only by understanding and appreciating these factors that one can develop an understanding of the patient as an individual.

THE ELEMENTS OF PERSONOMICS

A reasonable question that has emerged from the personomics discussion is whether there is a particular method that clinicians should use to develop an understanding of the patient as an individual. Is the idea simply to spend as much time with the patient as possible, hoping that these critical elements of the individual will be appreciated? That strategy seems doomed to failure given the time pressures clinicians face today. Moreover, it is not consistent with the systematic approach most clinicians use when obtaining a patient history in other areas. In fact, the personomics approach to the medical history may be broken down into key elements that can be taught, learned, and incorporated into medical practice. These key elements are perhaps best captured in a National Institute for Health and Clinical Excellence (NICE) guideline document (8) that outlines the elements of knowing the (adult) patient as an individual (p. 48). The guideline notes that “... there is an important need for health services to recognize that individuals are living with their condition(s), experiencing it in a unique way, and that family and broader life need to be taken into account.” (p. 48). The key features of knowing the patient outlined in the document can be

grouped into five areas: 1) the patient as an individual, 2) the patient's life circumstances, 3) the patient's concerns, 4) the patient's needs, and 5) an admonition to clinicians not to make assumptions about the patient. Areas of the patient history that can be explored during the interview to address these five areas are shown in Table 1 (8).

In a separate report, Hanyok et al surveyed physicians recognized for their clinical excellence and asked them how they get to know patients as individuals (9). The list of areas defined by these clinically excellent physicians has many features in common with the recommendations in the NICE guidelines. Six major themes were derived from a qualitative analysis of the questions or phrases these clinicians use to know their patients. These areas are 1) the patient's concerns, 2) personal relationships, 3) hobbies and pleasurable activities, 4) open-ended questions to learn about the patient, 5) work, and 6) the patient's perspective on the patient-physician relationship. Similar to the NICE guidelines, the results from the work of Hanyok et al focus mostly on the adult patient.

TRAINING THE NEXT GENERATION

For precision medicine to realize its potential, practicing physicians need to understand and incorporate the knowledge derived from the application of -omics to individual patients. So too, practicing physicians

TABLE 1.
Getting to Know the Patient as a Person

| Elements of knowing the patient | Questions to consider in the patient's history |
|----------------------------------|---|
| The patient as an individual | How does the condition affect the person? How do the person's circumstances and experiences affect his or her condition and treatment? |
| The patient's life circumstances | How do the person's domestic, social, and work situations and his or her previous experience of healthcare impact his or her condition, affect willingness to engage with healthcare services, and/or affect self-management and lifestyle choices? |
| The patient's concerns | How do the person's health beliefs, concerns, and preferences affect how and whether he or she engages with treatment? |
| The patient's needs | How does the patient's need for psychological, social, spiritual and/or financial support affect his or her condition and treatment? |
| Don't make assumptions | Avoid making assumptions about the patient based on appearance or other personal characteristics. |

Adapted from the National Clinical Guideline Centre (8).

must understand and incorporate the elements of personomics into patient care. There is also a need to teach the next generation how to understand and apply information from genomics, pharmacogenomics, metabolomics, and other -omics alongside the information obtained from personomics. Modifying residency training so that it incorporates the fundamental principles of personomics as well as the tools of precision medicine will be challenging given the extreme time limitations faced by today's trainees. Indeed, time motion studies conducted in two different internal medicine residency programs found that residents spend only a small percentage of their time in direct patient care, less than 10% in a 2010 study (10) and 12% in a study conducted in 2012 (11).

In October 2007, an experience was developed and implemented in the internal medicine residency program at Johns Hopkins Bayview Medical Center that focuses on knowing each patient as an individual. The program, known as the Aliko Initiative (named for philanthropist Aliko Perroti), involves a specific curriculum (12,13), and a focused approach to teaching and patient care rounds that address the principles of personomics. The Aliko Initiative emphasizes the importance of evidence-based diagnosis and treatment tailored to each patient. Residents make telephone calls to patients after discharge from the hospital and they make home visits and visits to subacute rehabilitation centers on selected patients. The experience has demonstrated benefit in many areas. There is evidence that it enhances the joy of practicing medicine (14). The Aliko Initiative is highly rated by residents and students, and faculty find greater fulfillment in teaching on this team (15). There is also evidence that patient satisfaction is improved by care focused on knowing them as individuals. Patients rate doctors on this team in the 97th percentile on Press Ganey patient satisfaction surveys (15). The more patient-centered approach is associated with reduced hospital readmissions, especially for patients hospitalized with a primary diagnosis of congestive heart failure, a diagnosis where patient self-management plays a critical role (16). Knowing patients as individuals may also reduce diagnostic error because critical elements of the patient's story may be revealed that might otherwise go unrecognized (17).

SUMMARY

The potential for precision medicine to define specific treatments and outline individualized care plans based on patient's biological uniqueness is extraordinary. However, that potential can only be realized if

clinicians are able to apply the information from the -omics to each person they treat with an appreciation of the unique circumstances of the individual. Personomics should be placed alongside other -omics, each critical to deliver on the promise of precision medicine.

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DISCUSSION

Hellmann, Baltimore: Roy, congratulations...not only a terrific presentation but I applaud the work that you have been doing. I was wondering if you would comment on — what you suggest occurs when people are trained in both personomics and precision medicine. How should the information be recorded or shared with concerns about privacy. What are most places recording using electronic medical records? Any idea about how to keep the information obtained from questions you asked? How should it be recorded or shared?

Ziegelstein, Baltimore: I am not sure that I will give this a good answer David, and you may want to comment because I am sure you have thoughts about it. But I see nothing about either the -omics, the traditional -omics, or the personal information that we get in the medical record, that should not be shared. I recognize that in some cases, including for example gun ownership in some states, that people have been advised that this should not be something that is shared. But I believe that since the medical record is protected information, that there is actually not a reason not to share such information. But in fact I believe that to not do it is doing a disservice to the patient, but also impedes the ability to be a physician or other healthcare provider of that patient. We need to know our patients and share what we know with other providers. I don't know if you had other ideas David.

Thibault, New York City: Thank you Roy for that. Great work and for the example you are setting. Thank you for taking care of our Macy faculty scholars there. But even at Hopkins, the Aliko service is only one service. Can you talk about what the barriers are to make this the way we will teach everybody?

Ziegelstein, Baltimore: Yes, it's a terrific question and its one we grapple with a lot. We are beginning to make inroads. Dr. Dover is in the audience somewhere, I saw him earlier, and he has really championed the spread of the Aliko initiative to our pediatric residency program, also in Johns Hopkins All Children's Hospital in Florida. There is an interest now in spreading some of the Aliko initiative to the Osler residency program at Johns Hopkins Hospital. It has spread to the United States Air Force residency programs, for example. I think, to be honest, almost any new paradigm including traditional precision medicine will be challenging to incorporate into a very traditional practice of educating residents. And one that now is much more challenging because of all the pressures of rapid patient turnover and all the pressures of documentation. I think that in addition to focus on education, we've got to take back the medical record, for example, and reduce the need to document so much just for the sake of documentation and meaningful use.

Hasday, Baltimore: So, for us the problem is business and geometry. We have to check all those boxes in the electronic medical record otherwise we get messages from our dean that we are endangering our Medicare reimbursement rate. And then the question is where do you put the computer so you can do that and still talk to the patient in the traditional way?

Ziegelstein, Baltimore: So I think it's very difficult. What I do in the outpatient area is something that probably is not generalizable to medical residents and to busy practitioners. I actually have the computer screen facing me and the patient and as part of the visit we actually go over it together. The parts that are important. And then I do a lot of my documentation afterwards. Again, it's hard to generalize. I think that we do have to make sure that our trainees and our practicing physicians are engaging with the patients rather than the computer screen. And I also believe that there is room for customizing the electronic medical record to put the patient's story right up front. That's what we've done on our Aliko initiative. We have actually customized Epic, if you believe that that can be done, to actually have the patient's story right up front.

Bodenheimer, New York City: Thank you very much for your concepts and presentation. One of the areas that you pointed out is a challenge in training residents. One of the challenges of training residents is communication but it's also the challenge of physical examination and I think that physical examination is a very powerful form of communication—looking at a person's hands and discussing their lifestyle, nutrition, and disease entities with them. This is a way we can facilitate that. Perhaps the training and improvement in physical examination skills could parallel improvement in communication skills. I'd like your thoughts.

Ziegelstein, Baltimore: I agree 100%; in fact, I believe that the way that we teach our medical students and residents about the history and, you know, the history of present illness followed by the social history and so on and so forth, and then the physical examination as separate entities, is misguided. I think that with the history and the physical examination there should be a smooth transition. One informs the other, and so I would say that it is absolutely important to teach bedside history and physical examination skills. I completely agree with what you said.

Ludmerer, St. Louis: Thanks Roy, do you have any data on what happens to Aliko residents after they go into practice and how they...the nature of their practice?

Ziegelstein, Baltimore: Yes, we have done a graduation questionnaire that specifically addresses the impact of the Aliko experience. We are actually writing this up for publication. It looks like there is a long-lasting effect. In fact, I would say — now this may shock some of you, and if you have difference of opinion let me know — I am actually not aware, this is a bold statement, of any evidence that anything that we teach residents has a long-term effect. Now, we believe that it does but I am not aware of any publication. We are having our librarians and informationists actually search this right now. This may be the first time that there is actually evidence that what we teach our residents has long-term effects.

Ludmerer, St. Louis: This could be a key to changing the system because it's not just the electronic record, it's the way medical care is financed with the prevailing myth that what matters most is doing things quickly rather than doing things well. And that's at the root of our dilemmas. That was the title of my last book, "A Time to Heal." We need time to heal.

Wolf, Boston: I think it's a HIPAA violation because I'm from Boston, but I'm going to quote Osler who said, "The good physician treats the disease; the great physician treats the patient who has the disease."

Schwartz, Denver: First of all, I just want to congratulate you on the work that you are doing. I think that it's fantastic. I think it really gets to the fundamental nature of the patient/physician interaction, which in many cases we've lost in terms of our educational efforts and also our practicing efforts. What I wanted to ask is if you could talk more about the challenges that you faced in terms of expectations and incentives that go against spending as much time as it takes to really get to know the patient, and understand the drivers that are behind the disease and behind the patients desires, in terms of being taken care of in an individualized way.

Ziegelstein, Baltimore: I thank you for asking that. I actually do not think that it takes considerably longer to do the things that we are doing, the exception being the patient's home visit, for example. I actually think that in many instances it shortens the amount of time because it provides much more targeted and focused care of the patients, so we are not doing a lot of extraneous things. What I will say is that this has to be embedded in the actual care of the patient and the teaching of the house staff so that it's not something extraneous. That would add time. But I actually do not believe that getting to know the patient as an individual takes additional time.

Hook, Birmingham: Roy, thank you for reminding us about medicine as a calling and the connection of us to our patient, but as so many of the comments suggest we're losing. I was wondering if you thought the firm system at Hopkins facilitated the connections you are talking about?

Ziegelstein, Baltimore: I think that any time that you put a group of patients together with a group of residents with a group of faculty it offers the possibility to create more meaningful interactions. I think that the key though is to figure out how to make those meaningful interactions focused on what you believe they should be focused on. So, I believe that an important part is not to focus on getting patients out of the hospital quickly and fast patient turnover, but on precision medicine and personomics. So, I think that yes, it provides a vehicle, a substrate if you want to call it that, but it's how you actually use that vehicle that is critical.