Conference Scene

Is personalized medicine ready for prime time?

The Duke Center for Personalized Medicine 2012 Symposium: 'At the Interface of Clinical Research and Clinical Medicine'

29 March 2012, Durham, NC, USA

This article provides a meeting report from the Duke Center for Personalized Medicine 2012 Symposium, which took place in Durham, NC, USA, on 29 March 2012. The event titled 'At the Interface of Clinical Research and Clinical Medicine', focused on many of the issues that arise as personalized medicine becomes integrated into clinical care. In particular, we summarize presentations on various topics: the future of genomic medicine, opportunities in pharmacogenomics and genetic testing; challenges in the clinical implementation of personalized medicine; systems medicine and biomedical informatics; the policy and education strategies for adopting personalized medicine; the common bond between comparative effectiveness and personalized medicine; and the value of personalized medicine.

The Duke Center for Personalized Medicine (NC, USA) brought together faculty, invited guest speakers, panelists and clinicians for a 1-day symposium titled, 'At the Interface of Clinical Research and Clinical Medicine'. The event was the first of its kind to be organized by the Duke Center for Personalized Medicine, an interdisciplinary center created in 2010 to bring the benefits of personalized medicine to patients at Duke University Health System and beyond. The 1-day symposium centered on discussions around pharmacogenomics, clinical implementation, and policy and education outcomes and the value of personalized medicine.

Advances in genomic and molecular medicine hold the potential to radically transform human health by enabling more precise prediction, prevention and treatment of disease on an individual level. However, realizing this potential requires a revolution in how healthcare is delivered, from designing new models of care that incorporate unprecedented technologies and a greater focus on prevention, to changing financial reimbursement to support these models, to empowering patients to play a leading role in their care. Symposium participants shared their experiences with bringing personalized medicine into the clinic, and debated how best to provide the evidence and infrastructure needed for this burgeoning field to reach its full potential. As Victor Dzau (Duke University, NC, USA) noted in his opening remarks, one of the biggest challenges facing personalized medicine will

be to define a path to implement clinical evidence into practice.

"The diligent collection of information at the point of care, coupled with the appropriate use of informatics and bio-statistics can produce predictions to help clinicians act on complex information," said Robert Califf (Duke University). As an example, he described how pilots in the airline industry make decisions based on an array of information that is ordered and integrated in ways they do not necessarily understand, but which produces enough knowledge to steer the plane. Geoffrey Ginsburg (Duke University) explained how the Duke Center for Personalized Medicine is taking a variety of approaches to personalize care, including family health histories, pharmacogenomics, comparative effectiveness research, genetic risk information and behavior modification, and diagnostic sequencing. He called the current iteration of the field 'Personalized Medicine 1.0', a provider-driven scenario that focuses on parameters such as possible allergies or aberrant laboratory values only after a medical issue has arisen. Ginsburg predicted another iteration, 'Personalized Medicine 2.0'; a truly personalized, proactive situation where patient participation in the healthcare process is critical. He then framed further discussion by giving a broad definition of the field: personalized medicine is an integrated evidence-based approach to individualizing patient care across the continuum (from health to disease), using multidisciplinary teams to promote health and wellness, patient

William E Kraus¹, Susanne B Haga¹, Howard L McLeod¹, Judd Staples¹ & Geoffrey S Ginsburg^{*1}

¹Duke Center for Personalized Medicine, Duke University School of Medicine, Duke University Health System, 101 Science Drive, DUMC Box 3382, Durham, NC 27708, USA

^{*}Author for correspondence:

Tel.: +1 919 668 6210

Fax: +1 919 668 6202

geoffrey.ginsburg@duke.edu

education and satisfaction, and customized disease prevention, detection and treatment [GINSBURG GS, UNPUBLISHED DATA].

Genomic medicine & pharmacogenomics: the challenges ahead

Eric Green (National Human Genome Research Institute, MD, USA) stated that: "In the 3273 days that had passed since the completion of the Human Genome Project, great progress has been made toward applying genomics to medical problems." Driving this progress has been a surge in technology bringing the cost of sequencing the human genome down from the original US\$1 billion price tag to approximately US\$1000. Green predicted these new sequencing technologies will be used to further understand the molecular basis of rare and complex genetic diseases. He cautioned that expanded use of sequencing raises a number of challenges that need to be addressed, such as how sequencing may be used in routine newborn screening, how it can influence medication choice and dosing through pharmacogenomics, and how to communicate complex science to healthcare providers and, ultimately, patients.

Deepak Voora (Duke University) expressed that the field of pharmacogenetics is faced with a rapidly expanding evidence gap that will continue to grow as new pharmacogenomic markers are discovered. He suggested a new evidentiary framework for pharmacogenetic testing, one that does not rely solely on randomized controlled trials. Voora said that in some cases observational data may be sufficient, especially when tests are commercially available and can guide dosing, monitoring or choice of equivalent agents. More complex decisions such as novel indications of existing drugs, however, may warrant randomized controlled trials. A panel of experts then outlined some of the challenges of using personalized medicine in their everyday professional lives. For example, Howard McLeod (University of North Carolina at Chapel Hill, NC, USA) highlighted the challenge of interpretation of tests, with a paucity of clinical expertise including 11 states that do not have a single genetic counselor to help distill complex genomic testing results.

The partnering of personalized medicine & clinical medicine: making it happen

Marc Williams (Geisinger Health System, PA, USA) mentioned a common misconception that medical care today is safe, when in fact 88,000 people die in hospitals every year because of medical mistakes. Williams argued that personalized medicine is an effort to make a very risky system safer. Culture often trumps evidence in the clinical decision-making process. Williams suggested that a rational system be built to manage processes in a way that includes personalized information. To do so, he stated that additional expertise is needed in quality improvement, dissemination and implementation science, outcomes research, economics and value constructs.

Invited panelists gave their perspectives as clinicians trying to incorporate personalized medicine tools into their medical practice. Lori Orlando (Duke University) said that the advantage of personalized medicine is that it celebrates variability in individuals and their responses to interventions instead of considering all patients to be identical. Ruth Wolever (Duke University) cautioned that many discussions around personalized medicine neglect to consider that how the individual processes and acts on information a patient receives from their doctor has a lot to do with adherence and outcome. Peter Ubel (Duke University) seconded that opinion, saying that medical care will only improve once researchers understand how patients make decisions when faced with complex information and unclear choices.

Isaac Kohane (Harvard Medical School, MA, USA) explained that important lessons in personalized medicine are hidden within the healthcare system, but investigators cannot find them because the data are too rough and disorganized. To illustrate his point, he described work by his team demonstrating adverse responses to the drug Vioxx®, which may have been withdrawn from the market earlier if clinicians had been looking at patient data prospectively, rather than retrospectively. Kohane introduced the 'Informed Cohort', a controversial idea that makes patients partners in discovery, letting them hear about their own personal results in a study as the research progresses.

Adopting personalized medicine: identifying the policy & education strategies

Amy McGuire (Baylor College of Medicine, TX, USA) stated that the drop in the cost of genome sequencing has made it possible for the technology to become integrated into daily medical practice. However, she cautioned that the wealth of information in sequencing data raises a number of ethical and policy issues. For example, how much information is a clinician expected to disclose? Is there a duty to look back as knowledge of deleterious variants increases and update patients on their risks? McGuire outlined a number of other challenging areas that need to be studied, including interpretation of test results, access and reimbursement for genetic assays, informed consent and privacy concerns.

Symposium panelists discussed how a lack of knowledge and understanding can be an impediment to the adoption of personalized medicine. Amy Abernethy (Duke University) noted that when concepts are complex for a physician, it is hard to expect patients to understand them. She suggested that researchers develop a language to convey how personalized medicine improves care without making the current system sound dangerous. Aimee Zaas (Duke University) agreed, stating that her own informal survey of colleagues across the country indicated that no internal medicine program possessed more than a 1-h noon conference on personalized medicine. Laura Beskow (Duke University) suggested the same degree of scientific rigor be brought to the consent process as is clinical trials, to identify what types of information participants deem most important, as well as uncover areas prone to misinterpretation. McGuire proposed that researchers create an unbiased decision support tool for both physicians and patients.

Abernethy then introduced the notion that comparative effectiveness research is an iterative step toward personalized healthcare. She gave an overview of the field's evolution, first from evidence-based medicine, to evidence-based practice, to comparative effectiveness research and finally to personalized care. Abernethy referred to an Institution of Medicine model of 'Learning Health Care', whereby

data routinely collected through patient care are fed into an ever-growing databank. The system learns by routinely analyzing captured information, iteratively generating evidence, and constantly implementing new insights into subsequent care that benefit both the individual patient and the entire population.

Personalized medicine: what is the value?

Bob Kocher (Venrock, CA, USA) expressed that personalization creates value for consumers and suppliers, an approach successfully used by companies such as Amazon (WA, USA), Apple (CA, USA) and Starbucks (WA, USA) to expand their market and promote brand loyalty. He explained that personalization can unlock productivity, requiring less work by treating fewer illnesses, causing less rework through better outcomes, and promoting better processes through the standardization of personalized approaches. Kocher listed three policies that will make it easier to promote personalized medicine: the Health Care Reform Act, the Health Information Technology for Economic and Clinical Health (HITECH) Act, and the Health Data Initiative. He stated that investors are looking for applications of personalized medicine that substantially save money and change outcomes.

Another panel of experts stated that successes in personalized medicine are hard to come by because of cultural resistance to change, shortfalls in implementation science, lack of accepted methods to communicate that knowledge, need for improvement in preparedness of healthcare workforce and difficulty interpreting data sets. David King (LabCorp, NC, USA) expressed that 'individualized medicine' may have been a more effective term to describe the field, as 'personalized medicine' makes the care sound expensive and superfluous. Kyle Cavanaugh (Duke University) explained that the Health Care Reform Act has brought a sense of urgency for providers to redesign the care paradigm, perhaps incorporating personalized medicine. Turner Jenkins (Pappas Ventures, NC, USA) said it can be difficult to get a return on investment for complex diagnostic tests such as those from Genomic Health (CA, USA), which could cost over

US\$100 million for discovery and validation. Carolyn Carpenter (Duke University) explained it is difficult to quantify minimal improvements in cost avoidance through personalized medicine, particularly when it is layered on top of a healthcare system that is growing 8% a year.

Acknowledgements

The authors would like to thank MV Broadfoot for writing and editorial assistance and T Rakhra-Burris and R Chambers for their role in symposium logistics and execution.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing assistance was utilized in the production of this manuscript. This was supported by the Duke Center for Personalized Medicine (NC, USA).