Pediatrics & Therapeutics
ISSN: 2161-0665

Stefans, Pediat Therapeut 2012, 2:4
DOI: 10.4172/2161-0665.1000e110

Editorial Open Access

Omics and EBM: Towards the Art of Individualization or the Standardization of Science - Which Way is this Train Headed?

Vikki Stefans*

Associate Professor, Department of Pediatrics and PM&R, Arkansas Children's Hospital, USA

Many researchers and commentators in today's world of publication seem to expect that scrupulously conducted multi-center randomized controlled trials with ever larger sample sizes will put an end to unwarranted individual variation and standardize pharmacological and other treatment approaches once and for all. To be sure, most grudgingly acknowledge that men may present and respond differently than women, even post-menopausal women; Inuits may be different from Africans; and pediatric pharmacokinetics, particularly neonatal pharmacokinetics are a different ball game altogether. But surely, small series and case reports should be a thing of the past. Those annoying outliers will just dry up and blow away, won't they? The medical quality metric system becomes in essence a simple matter of our power to persuade the highest possible percentage of patients to do the right thing. For the adults, we just need to see them take those statins, choke down that metformin, get that hemoglobin A1c between 6.1 and 7.3, and have their screening colonoscopies done on time no matter if the preparation for it kills them. As an example, there is a recent proposition that the most cost effective (or at least the cheapest) approach to cardiovascular risk reduction would be simply to put ALL women on statins, and ALL men on ASA, regardless of lipid profile. See http://www.theheart.org/article/1380521.do; it admittedly would save the costs of complex lipid profile testing, though it would expose more people to more side effects, which is particularly of concern since we have also just learned that at least some statins may in fact increase the risk of progression to type II diabetes.

Then, if screening for ovarian and prostate cancer for the entire population is just not cost-effective, and the symptoms are too subtle, well, that's just too bad for a few unfortunate people, right? A few of us old softies, especially in pediatrics, might have a hard time looking straight into the eyes of a young mom or a new grandparent who was saved from a cancer death by a screening program, and telling them and their children how they would not have even qualified for it under current or proposed guidelines; that it does not matter, because those are the guidelines now for everyone, and it won't be covered or approved of any more for anyone. The U.S. Congress is now considering special legislation for pancreatic cancer. (http://www.govtrack.us/congress/bills/112/hr733/text.)

But the answer is not to abandon evidence-based medicine; we actually need to pay more attention to new evidence that moves us all in a very different direction, one that we may be in a unique position to showcase in an Open Access journal. Genomics, exomics, and even the recent debut of "personal-omics" with an "N of 1" is showing us what's really going on behind the scenes [1] (Maybe OMICS is an apter acronym than we ever imagined). Few of us welcome a learning curve that's going to make our first year of medical school look like a picnic in the park, but understanding of the human genome and epigenome could change the way we need to think, study, write, and practice. Sensitivity and specificity of screening tests are going to look a lot different when applied to a population pre-identified as at higher risk genetically. And if it has not happened to you already, one of your patients is going to ask you to take the findings from their direct-to-consumer gene test report under consideration before you start the standard diagnostics and treatment for any medical concern they might have.

Personalized medicine should not be confined to special university programs, as it is now, and regarded as something in the realm of "concierge" or "boutique". Real world examples of well-substantiated individual variation in practice already abound. The list of medications for which we can tell our patients more than "we have to try it and see here are the side effects you might have" is growing. You probably already know that it's not racist for a clinician to avoid giving an Asian patient a trial of carbamazepine; a common HLA type in the Han Chinese makes their likelihood of Stevens-Johnson syndrome dangerously high [2]. For chemotherapeutic regimens, knowing the genome of both the patient and the cancer cell may make all the difference between ineffective or fatal treatment versus a high chance of remission and long-term success. That's not saying we have any excuse for unnecessary variations, such as fewer African than Caucasian patients being offered routine mammograms or TPA when they've had a qualifying stroke, or an adult hospital continuing to admit patients for specialized pediatric procedures where, despite a similar risk and severity profile, the outcomes are far worse than at the other hospital with greater pediatric experience and expertise just down the freeway. Most of us recognize that one size does not fit all under many circumstances. And if the risk of adverse reactions to more commonly used drugs could be predictable in advance, it could reduce the astonishing statistics of deaths and hospitalizations in just the U.S.A. every year. Back in 1994 those numbers may have been around 2 million and 100,000 respectively [3]. The literature suggests the problem is increasing, not decreasing, with only around half of the cases considered preventable with the level of current knowledge and surveillance, for children and adults alike [4,5]. It's almost a catch-22 though; even once we know what to look for, genetic tests as currently priced would cost too much to apply to everyone who is taking, let's say, baclofen, ranitidine, or zolpidem; yet they won't cost less until we do.

What can we do? We can look to our outliers for clues to the underlying realities instead of carefully excluding them both from our research and from our clinical guidelines. We can, like our forebears, astutely notice a clinical characteristic, just as someone must have noticed in China that carbamazepine was a relatively dangerous choice, and then use our most up-to-date tools to find out why. We can ask for funding for the gene tests when it will make a difference as part of our research, and hopefully more and more often, in our practice for

***Corresponding author:** Vikki Stefans, M.D., UAMS College of Medicine, Associate Professor, Department Pediatrics and PM&R, Section of Developmental Medicine and Pediatric Rehabilitation, Arkansas Children's Hospital, 1 Children's Way, Little Rock AR 72202, USA, Tel: 501 364-4374 or 837-8470; Fax: 501-364-6829; E-mail: stefansvikkia@uams.edu

Received April 16, 2012; **Accepted** April 20, 2012; **Published** April 21, 2012

Citation: Stefans V (2012) Omics and EBM: Towards the Art of Individualization or the Standardization of Science - Which Way is this Train Headed? Pediat Therapeut 2:e110. doi:10.4172/2161-0665.1000e110

an individual patient as well. Above all, we can prepare ourselves to get on board this train as it picks up speed. If you don't know, learn what mitochondrial versus nuclear inheritance is, what a SNP is, and what the epigenome is all about [6]. DNA methylation and acetylation make a difference and may be alterable by lifestyle choices, sometimes parental or even prenatal ones. In some cases, individual variation just explains why some children won't eat their broccoli, but sometimes it explains why some people get diabetes in today's society and culture despite their best efforts and lifelong struggles to modify their lifestyle and achieve a healthier body weight, and that may point us in the right direction to make a difference for society as a whole.

Personally, I'm looking for the day when the research gives us all a sound scientific basis for both the standardization and the individualization that real populations and real people actually need. Whether we honestly think everyone should be on one or because we could miss a QI quota, it might not always make sense for us to try to put adults back on statins after rhabdomyolysis or cognitive impairment, or to feel obligated to refer them to the special clinic at Mayo to find out if they really had ADRs after all before letting them consider living statin free. There is a real danger for the field that if we continue to fail to conduct adequate trials of alternative agents for people not taking statins, third party payors and practitioners alike will understandably interpret the available evidence to exclude coverage for other agents which apparently don't do much more when added to statins for the people who do tolerate them. And as you probably know, some folks want us to try those on some of our hyperlipidemic kids; I may be biased, but I think we need to be very careful to find out who is helped and who is harmed first, instead of solely and simply focusing on proving that for the population at large the risks outweigh the benefits. I think this journal may be in an excellent position to help, given its readership, its rapid peer review, and its openness to new ideas.

References

1. Chen R, Mias GI, Li-Pook-Than J, Jiang L, Lam HY, et al. (2012) Personal omics profiling reveals dynamic molecular and medical phenotypes. Cell 148: 1293-1307.
2. Man CB, Kwan P, Baum L, Yu E, Lau KM, et al. (2007) Association between HLA-B*1502 allele and antiepileptic drug-induced cutaneous reactions in Han Chinese. Epilepsia 48: 1015-1018.
3. Lazarou J, Pomeranz BH, Corey PN (1998) Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA 279: 1200-1205.
4. Hakkarainen KM, Hedna K, Petzold M, Hägg S (2012) Percentage of patients with preventable adverse drug reactions and preventability of adverse drug reactions - a meta-analysis. PLoS One 7: e33236.
5. de Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA (2008) The incidence and nature of in-hospital adverse events: a systematic review. Qual Saf Health Care 17: 216-223.
6. Mefford HC, Batshaw ML, Hoffman EP (2012) Genomics, intellectual disability, and autism. N Engl J Med 366: 733-743.