Published in final edited form as:

Lancet. 2015 May 23; 385(9982): 2118–2119. doi:10.1016/S0140-6736(15)60722-X.

Aligning incentives to fulfill the promise of Personalized Medicine.

Victor J. Dzau, MD[1],
Institute of Medicine, 500 5th Street, NW, Washington, DC 20010, 202-334-3300

Geoffrey S Ginsburg,
Duke Center for Applied Genomics and Precision Medicine, 101 Science Drive, Room 2111, Ciemas Building, Durham, NC 27708

Karen Van Nuys,
Precision Health Economics, LLC, 11100 Santa Monica Blvd., Suite 500, Los Angeles, CA 90025, (310) 984-7711

David Agus, and
University of Southern California Keck School of Medicine and Viterbi School of Engineering, 9033 Wilshire Blvd, Suite 300, Beverly Hills, CA 90211

Dana Goldman
University of Southern California Schaeffer Center for Health Policy and Economics, University Gateway 100C, Los Angeles, CA 90089

Personalized medicine has generated global policy interest in the past few years. In 2012, the European Union established the European Alliance for Personalized Medicine with the aim to accelerate the development, delivery, and uptake of personalized health care, broadly defined. In the same year, the UK's Medical Research Council and National Institute for Health Research funded the National Phenome Centre to deliver broad access to a world-class capability in metabolic phenotyping for biomarker discovery and validation, improved patient stratification, and early identification of drug efficacy and safety. In the USA, President Obama recently proposed to invest US$215 million in a Precision Medicine Initiative, with the goal to further research into patient genetics and customized treatments.

There are reasons to be optimistic about these kinds of initiatives. The sequencing of the human genome and rapid advances in technology have catalyzed the development of personalized medicine—so much so that reliable and affordable genetic analysis is well

[1]Corresponding author: address: 500, Fifth Street, NW, Washington, DC 20001; vdzau@nas.edu.

The views expressed in this article are those of the authors and do not necessarily represent the views of the Institute of Medicine.

Declaration of interests

The World Economic Forum provided a grant for this work. GSG has acted as a consultant for US Diagnostic Standards, has participated in advisory boards and holds stock options for Omicia and CardioDx, has participated in advisory boards for Interleukin Genetics, Pappas Ventures, Q-CROC/PMPC/PreThera, TheHeart.org, Medscape/WebMD, has received grants from Novartis and Merck, acts as Editor at Large for *Genome*, is a consultant for Third Point and TGEN Health Ventures, and receives royalties from Elsevier, outside the submitted work. KVN is an employee of and DG is a partner at Precision Health Economics, a company providing consulting services to the life-sciences industry. DA co-founded Navigenics in 2006, but has had no financial interest in the company since February, 2010. VJD declares no competing interests.

within reach of many patients and payers.[1] Much of the research and development to date has focused on genetic mutations commonly found in cancer tumors or rare genetic diseases, and the development of targeted therapies. Indeed, the majority of personalized therapies currently on the market are indicated for slowing tumor growth or orphan diseases. However, the promise has spawned a rapidly growing industry where genetic markers of disease and treatment responses are searched on a larger scale.

Indeed, the full promise of personalized and precision medicine (PPM) – as healthcare innovations involving molecular diagnostics and pharmacogenomics are called – extends beyond targeting therapies for patients who are already sick. It also includes the ability to identify healthy individuals at elevated risk of disease, enabling preventive measures to be targeted towards those who could benefit most. While applications of PPM aimed at prevention have the potential to generate significant value for society, the present reimbursement environment, characterized by near-term budget pressures on national health systems and private payers alike, discourages their development in favor of PPM treatments that may generate less value overall, but provide greater short-run returns.

On the other hand, the potential social benefits from prevention in the PPM context can be enormous. We used an existing health simulation model to consider the benefits (and costs) of PPM innovations to improve screening and risk-factor stratification technologies that identify pre-symptomatic individuals at high risk for acquiring certain diseases. The model — The Health Economics Medical Innovation Simulation, or THEMIS — was developed with funding from CMS, NIH, and the MacArthur Foundation, and has been used to assess the long-term consequences of medical innovation in many settings, including cardiovascular disease, diabetes, cancer, and obesity.[2]

Our scenarios mirror the current research and development pursuit of PPM technology to identify patients at highest risk of high prevalence disease. These patients are then administered targeted prophylactic therapy to prevent or delay disease onset. The preventive therapy itself need not be innovative--for example, the multi-center Diabetes Prevention Program trial identified patients at high-risk for Type 2 diabetes (prediabetes), and showed that early intervention with existing therapies reduced risk of subsequent Type 2 diabetes.[3] In our scenarios, the PPM innovation permits identification of the subset of patients for whom intervention is most valuable. So, for example, although diet and exercise interventions may lower the risk of heart disease among the population in general, adherence to such programs is notoriously poor among the general population. However, aggressive preventive and interventional strategies targeted to patients whose genetic tests identify them as having extraordinary risks of developing cardiovascular disease have a much greater likelihood of success.

In our analysis, these preventive PPM interventions are assumed to permanently reduce the incidence of six diseases (cancer, diabetes, heart disease, hypertension, lung disease, and stroke) by some fixed percentage starting in 2012. Interventions are assumed to have efficacy—and costs — similar to the Diabetes Prevention Program, meaning that they need to be sustained over a lifetime. Benefits are computed by looking at life expectancy and

quality-adjusted life expectancy gains over the subsequent 50 years. Values are expressed in dollars using a very conservative $100,000 per quality-adjusted life year.

Figure 1 summarizes the value of health generated from 2012 to 2060 by PPM innovations that reduce incidence of six diseases in the US by 10% and 50%. Depending on the disease, a PPM innovation that reduces incidence by as little as 10% generates anywhere from $33 to $114 billion in the form of longer, healthier lives enjoyed by the US population. A PPM innovation that reduces disease incidence by more generates commensurately larger benefits, for example a 50% reduction in heart disease incidence would generate $607 billion in improved health over 50 years. Among the six diseases studied, PPM innovations aimed at reducing heart disease have the greatest impact on public health because heart disease is highly prevalent and has relatively large impact on life expectancy. Other diseases such as stroke or lung disease are much less prevalent and offer more modest opportunities for creating value from incidence reduction.

Despite their potential for generating significant social value, PPM innovations aimed at prevention have generally lagged behind those aimed at treating patients who already have disease.[4] Outside the US, severe healthcare budget pressures have led to coverage policies that favor technologies with short payback periods. In the US, reimbursement for diagnostic tests is based on costs, rather than value. Unlike reimbursement for personalized cancer therapies, which is based in part on the demonstrated value of the drug in terms of increased survival, reimbursement for diagnostic tests is typically determined according to a clinical laboratory fee schedule which does not distinguish between traditional diagnostics such as basic metabolic panels and PPM diagnostics that may have similar production costs but very different clinical value.[4] As a result, companies contemplating development of PPM diagnostics to facilitate disease prevention have limited incentives to do so; predictably, such diagnostics, despite their potential for generating significant social value, have been slow to appear on the market.

The policy implications of these findings are clear. First, the potential social benefits of preventive PPM innovations — and prevention more generally — can be quite large, but the incentives to develop them are weak. While we do a good job reimbursing for therapeutics, we do a much worse job reimbursing for diagnostic tests. In particular, more consistent coverage decisionmaking processes across payers, as well as reimbursement based on a test's value, rather than cost, could strengthen manufacturers' incentives to bring preventive PPM diagnostic tests to market more quickly.

Second, while PPM holds significant promise for reducing the total burden associated with some diseases, the scenarios investigated here demonstrate that different types of PPM innovations may have very different health benefits. For a health policy maker deciding how to invest finite resources across different innovations and disease areas, these results may help prioritize among different options. The future health benefit to reducing disease incidence even 10% can be significant in areas such as diabetes and heart disease—with health gains among the US population worth $96 and $114 billion respectively. By contrast, for a disease like stroke, PPM would need to reduce incidence by a larger amount to generate similar health benefits. Thus, value is tied to prevalence.

Third, it is important to realize that risk stratification is not enough. We need to have effective and sustainable interventions that can be implemented at reasonable cost, which may include diet and exercise. Otherwise, society is just increasing the prevalence of disease at additional cost to the entire system.

Finally, we need to consider which conditions for which generous coverage of PPM would be optimal—from both society and payers' perspectives. In the US, private insurers' incentives favor interventions with near-term benefits and short payback periods, since plan member turnover can be high, and the realized benefits would need to be returned in a few short years. But the real benefits of PPM innovations accrue over much longer horizons, as individuals live longer, healthier lives. Covering these interventions may not generate positive returns for private US payers, but could do so in single-payer systems such as those in Europe. PPM innovations with the shortest payback periods may thus enter the marketplace first, but they may not generate the largest social returns. Figuring out a model that might generate positive returns for private payers could benefit everyone.

REFERENCES

1. Feero WG, Guttmacher AE, Collins FS. Genomic Medicine — An Updated Primer. New England Journal of Medicine 2010;362:2001–11. [PubMed: 20505179]
2. Michaud PC, Goldman D, Lakdawalla D, Gailey A, Zheng Y. Differences in health between Americans and Western Europeans: Effects on longevity and public finance. Social Science & Medicine 2011;73:254–63. [PubMed: 21719178]
3. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. New England Journal of Medicine 2002;346:393–403. [PubMed: 11832527]
4. Goldman D, Gupta C, Vasudeva E, et al. The Value of Diagnostic Testing in Personalized Medicine. Forum for Health Economics & Policy 2013;16:121–33.

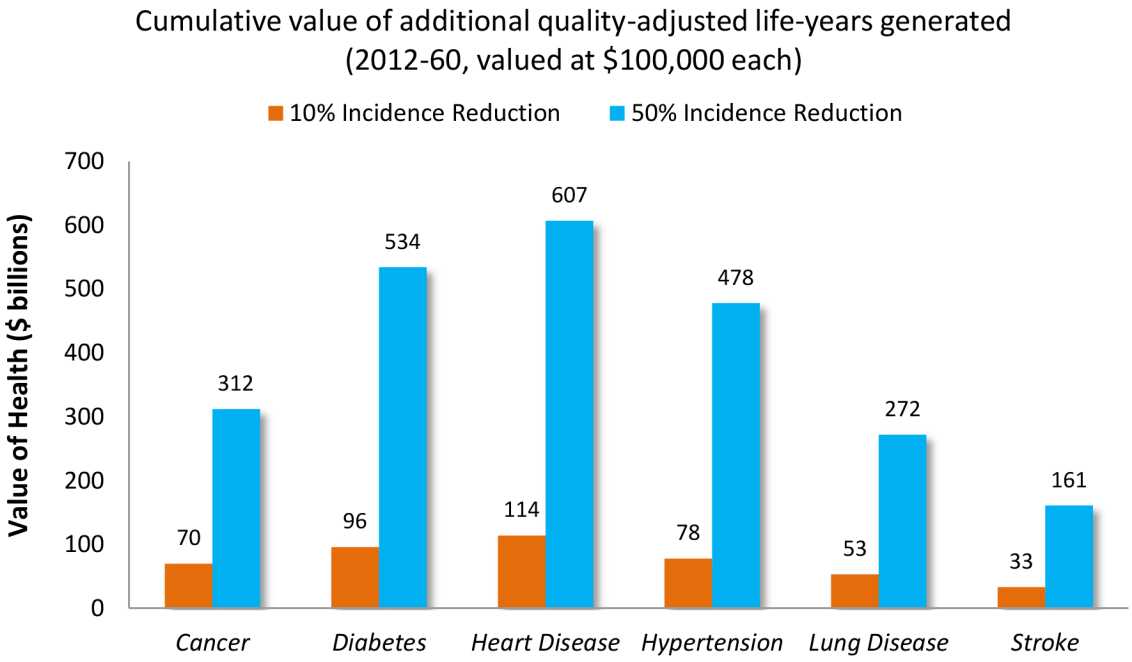

Figure 1:
Value of Health from Hypothetical PPM Prevention Innovation at Two Levels of Incidence Reduction in Six Diseases in the US ($ billions)