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# Opportunities in the Economics of Personalized Health Care and Prevention

**Abstract:** Personalized medicine is best viewed from a broad perspective of trying to use information about a patient to improve care. While “personalized medicine” often emphasizes the value of genetic information, traditional clinical approaches to personalizing care based on patient phenotype, provider and system-level factors should not be neglected. As these diverse approaches to personalization are examined, tools such as cost-effectiveness analysis can provide important insights into the value of these approaches, strategies for their implementation and dissemination, and priorities for future research. Such analyses are likely to be most insightful if they recognize that patient and provider behaviors are essential determinants of the value of treatments and that patient factors in particular may have large effects on the value of treatments and the need for interventions to improve decision making. These comments suggest three major areas of opportunity for economic analyses of personalized medicine: (1) traditional clinical approaches to personalized medicine, (2) multi-perspective studies of the benefits and costs of personalized medicine, and (3) the role of behavior in the value of personalized medicine.

**Keywords:** cost-effectiveness analysis; health economics; personalized medicine.

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## 1 Introduction

The idea of personalized medicine has generated a great deal of interest for at least the past decade. The field of personalized medicine has surely benefitted from this interest for several reasons. First, certain types of personalization – especially those based on new genetic and molecular markers – have been the subject of increased basic and clinical research interest and funding. The rationale for such work is fairly clear – the exploding knowledge of the genetic and molecular basis of clinical heterogeneity should make it possible to more reliably predict the likely outcomes of alternative approaches to treatment for specific individuals and therefore what course of action is likely to be best for any given patient.

Ideally, this will improve both outcomes and costs, or at least provide information that is needed to balance them cost-effectively. Second, enthusiasm over the potential benefits of personalized medicine has led to significant investments of resources in the translation of applications of personalized medicine into practice, whether through regulatory means [such as Food and Drug Administration (FDA) labeling for warfarin] or through commercial development of genetic tests. Finally, many hope that personalized medicine will play an important role in national efforts to control costs and improve the cost-effectiveness of care. Key to this has been the belief that comparative effectiveness research (CER) is an important component of an effective and efficient health care system. Increased interest in personalization has arisen from this interest in CER for two reasons. One is the belief that many efficacious treatments are not efficacious for a significant fraction of individuals, so research that could identify those individuals would be of great value in eliminating wasteful spending. Second, there is concern that CER could be used to ration care, which has led to efforts to undercut CER, with inter-individual variation and a resulting imperative for personalization highlighted as a major rationale for caution in the use of CER. Consequently, efforts to develop a CER research institute in the United States resulted in the establishment of the Patient-Centered Outcomes Research Institute (PCORI), with a strong mandate to focus on personalization of care that places a great deal of emphasis on variability at the patient level and on the related, though not identical, idea of the importance of patient engagement.

However, these same forces that have promoted interest in personalized medicine have also limited the concept in some ways compared to what one might imagine the concept to be based on its name. Indeed, taking its name literally, personalized medicine can be understood as an approach to medicine that bases medical decision making for persons on more information about the person than other approaches to medical decision making. From this perspective, a given approach to medical decision making can be defined as personalized only in comparison to some other approach to medical decision making. In contrast, the National Cancer Institute (NCI) has defined personalized medicine more specifically as “A form of medicine that uses information about a person’s genes, proteins, and environment to prevent, diagnose, and treat disease.”<sup>1</sup> The NCI definition has the advantage of not requiring that personalized medicine be defined in relative terms. It also has the advantage of more closely reflecting the emphasis on genetic and proteomic markers that has been the focus of most recent research in personalized medicine. However, it is limiting in neglecting the potential importance of other forms of information

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1 See <http://www.cancer.gov/dictionary?cdrid=561717>.

about the patient in personalized medical decision making, such as phenotype, which can be understood to include patient preferences and behaviors. To the extent that it is desirable to use all available forms of information to achieve desired outcomes of medical decisions, the broader definition of personalized medicine based on the use of more detailed information about the individual may be a better starting point for a discussion of opportunities for further research in personalized medicine.

One reason that a broader definition of personalized medicine may be useful is that clinical decision making and research that emphasizes one set of factors may result in de-emphasis of clinical decision making and research that emphasizes other factors. For example, enthusiasm about the importance of our increased understanding of the biological basis of clinical variability may have distracted attention from older biological approaches to identifying heterogeneity in treatment benefits and phenotypic indicators. Enthusiasm over the potential clinical value of personalized medicine may have inhibited careful analysis of the effectiveness, costs, and cost-effectiveness of specific approaches to personalized medicine and the economic returns to investments in developing those technologies. Likewise, increased attention to the potential adverse effects of restrictive payment policies in the context of clinical variability may have drawn attention away from studies of the benefits of payment policies that encourage individuals to behave selectively in choosing care and factors that may influence the effectiveness of such choices.

These comments suggest three major areas of opportunity for economic analyses of personalized medicine: (1) traditional clinical approaches to personalized medicine, (2) multi-perspective studies of the benefits and costs of personalized medicine, and (3) the role of behavior in the value of personalized medicine. The key to defining research priorities for economists is to identify: (1) opportunities for economic research to lead to greater efficiency in the degree of personalization and in the development, translation, and diffusion processes that lead to use of more highly personalized interventions; (2) key research questions that must be addressed to capitalize on these opportunities; and (3) research strategies that hold the greatest promise for addressing these key questions.

## 2 Traditional Clinical Approaches to Personalized Medicine

The concept of personalized medicine is, to a great degree, not novel. Indeed, the term “personalized medicine” seems to imply that there is a form of medicine

that is not personalized, yet essentially all medicine is personalized to the extent it is targeted based on patient attributes. For example, prostate exams and pap smears are never administered without consideration of gender, pain relievers without symptoms of pain, and red blood cell transfusions without hemoglobin levels that suggest anemia. Such forms of personalization are based on the idea that individuals with those attributes will tend to benefit from one or another alternative; it is recognized that any given individual may have other attributes that can cause the best decision for them to differ. Another form of personalization focuses on the idea that an individual's past responses to a treatment may predict future ones. N of 1 trials are the classic approach for formally evaluating such effects, but simple trial and error is far more commonly applied. Whether based on patient symptoms, standard clinical markers, or a history of past response, these traditional clinical approaches to decision making are all examples of personalization of medicine and present great opportunities for research.

Examples of types of research questions within this broad rubric of clinical and traditional approaches to personalized clinical decision making include:

*Under what conditions are genetic predictors of heterogeneity in clinical response more useful than traditional biomarkers or phenotypic markers?*

**Patient factors:** While specific genotypic markers may be very important predictors of outcome and treatment response, many genes, as well as environmental factors, may factor into such outcomes. In such cases, traditional biomarkers and/or phenotypic markers may be more useful than genetic markers. Warfarin dosing for patients who have been stable on warfarin for some time is an easy example of a case in which traditional biomarkers are superior to genetic markers.

**Intervention factors:** Choices about interventions that are reversible and have little toxicity may be strong candidates for personalization approaches based on phenotype, whereas choices about irreversible, toxic interventions may be especially likely to be improved by identifying genetic or other predictors of treatment benefit. This may be one reason why the NCI and others interested in cancer treatment have placed so much emphasis on genetic and other molecular markers rather than phenotype in defining personalized medicine.

*Under what conditions do clinicians tend to seek the guidance of indicators of clinical heterogeneity? How, if at all, are predictors of the use of indicators different for phenotypic, traditional clinical biomarkers, and genetic biomarkers? How do clinicians use and integrate available risk markers, whether genetic or traditional, in decision making?*

Questions here may focus on which markers clinicians perceive as most useful, and the extent to which clinicians make clinical decisions based on

some of the factors noted above that might affect patient benefit, or implicit or explicit bias that cause them to place more or less emphasis on certain types of indicators of risk. We also know very little about how physicians integrate multiple risk factors into clinical decision making. The use of pharmacogenetic testing for warfarin in practice may be an excellent area for studies of these questions.

*To what extent do approaches to clinical data collection, such as the use of electronic health records, affect personalized decision making and to what extent can they be used to increase personalization of care?*

With the increasing use of electronic health records and techniques to improve the collection and use of electronic health data, such as computer adaptive testing, natural language processing, and distributed computing models, there are myriad opportunities to advance the evidence base for and implementation of personalized medicine. This is also a strong area of interest for the PCORI and potential area for partnership.

*How do clinicians and patients reflect the probability and magnitude of alternative outcomes in their decision making? Do their decisions correspond with normative models of decision making? If no, is that a concern, and what can and should be done to improve decision making?*

A large literature bridging economics and psychology suggests that decision makers may overemphasize low probability events, or be influenced by changes in risk relative to a baseline or relative risk, instead of changes in absolute risks, as would be suggested by normative models of decision making. To the extent that personalized medicine is intended to provide information on risk, understanding how these biases will influence decision making is essential. The National Science Foundation has supported research in decision making frequently, but much more rarely related to medical decision making.

*When are within-subject approaches to therapeutics based on treatment response, such as formal N of 1 trials or simple trial and error, most likely to be applied? If they are applied, then are they likely to be applied effectively? What are the conditions under which within-subject approaches to therapeutics are most likely to be valuable? What barriers exist to their greater use of such approaches?*

Though many interventions may lend themselves to within-subject designs such as these, we know almost nothing about when or how clinicians use such approaches to guide care. We do not know whether therapeutic trials in individu-

als are typically appropriate in length or how they are monitored. There has been no systematic analysis of the attributes of therapeutic approaches that make them well or poorly suited to such empirical approaches to personalize care based on treatment response, or how treatment approaches might be altered to make them more amenable to personalized approaches based on treatment response. There also seems to be little known about the role of medical-legal concerns in within-subject approaches to therapeutics.

*There is a surprisingly strong literature on the value of a positive and durable relationship between clinicians and patients in improving costs and outcomes. How is this related to the idea, and value of, personalization of care?*

Studies suggest that a strong doctor-patient relationship that is characterized by trust, a positive interpersonal relationship, good communication, and a detailed knowledge of the patient by the doctor, can improve patient outcomes and reduce costs (Sharma et al. 2009). Rigorous randomized studies show that interventions to enhance continuity in the doctor-patient relationship can decrease unnecessary hospitalization and intensive care unit (ICU) use at the end of life (Wasson et al. 1984). It seems likely that studying the value of a personal relationship between the doctor and patient may provide valuable insights into approaches to the personalization of care more generally.<sup>2</sup>

### 3 Multi-Perspective Benefits and Costs of Personalized Medicine

Approaches to personalized medicine will be socially useful only if they offer aggregate benefits in excess of their costs and if they are used. Because the implementation of interventions, including personalized medicine, often requires the willing participation of multiple parties (e.g., patients, clinicians, payers, and regulators) understanding the distribution of benefits and costs across these entities is also important. Tools of cost-effectiveness analysis could provide answers to a rich range of relevant questions, including:

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<sup>2</sup> See, for example, the University of Chicago project on the use of Comprehensive Care Physicians, funded by the Centers for Medicare and Medicaid Innovation, <http://www.uchospitals.edu/news/2012/20120710-innovation-grant.html>.

*What are the effectiveness, cost, and cost-effectiveness of specific personalized medicine interventions from societal, patient, clinician, and payer perspectives?*

Especially important here is emphasis on multiple perspectives, providing insights into not only whether the use of an approach would be socially desirable, but also what sort of barriers might need to be overcome to implement the approach. This has implications for when regulation or other public policy interventions may be required.

*What factors of approaches to personalized medicine affect the extent to which they are useful and to what extent they can be altered to increase their use?*

For example, the timeliness of test results may be an important concern for some applications of personalized medicine, and little is known about the extent to which rapid receipt of results is important or whether prospective approaches to testing can be effective and cost-effective. The rapidly increasing level of knowledge about pharmacogenetics also creates almost unique challenges in performing rigorous randomized studies with meaningful outcomes. The advantages and disadvantages of practical approaches to clinical trials, observational analyses, and simulation models need to be examined. Sensitivity analysis in medical decision analysis can be an especially important tool to address questions such as these.

*Can value of information analysis be useful in informing priorities for research in personalized medicine, including selection of study design?*

Value of information (VOI) analysis is an increasingly accepted approach to prospectively estimate the expected population value of health research. Questions here might include which personalized care interventions are most important to evaluate through further research and what study designs will be most effective and efficient. Newer “minimal modeling” approaches for the application of VOI analysis that do not require decision models may make VOI practical for a larger number of questions (Meltzer et al. 2011).

*What business models for personalized diagnostics and treatments are likely to be most profitable and to produce the greatest societal benefits?*

Personalized medicine may alter the price, quantity used, and revenue from medical innovations, and encourage price discrimination that could have effects on access to therapies, costs, and innovation. These are all areas that may be amendable to empirical and theoretical analysis.

## 4 Role of Behavior in the Value of Personalized Medicine

The benefits and costs of personalized medicine interventions are likely to be altered by the behaviors that govern the use of treatments. Patients may already selectively choose treatments they prefer, effectively personalizing their care. Some patients (e.g., more educated ones) may do this more effectively than others. Some providers may be more effective than others in helping their patients receive treatments concordant with their preferences. Interventions, such as decision aids, may enhance the ability of behaviors to improve the personalization of care. The value of such interventions may vary depending on patient and system-level factors. For example, a decision aid might be more or less effective in individuals that vary in educational level depending on the extent to which their care is already highly personalized or they are able to productively engage in an intervention to improve decision making. Accordingly, personalized medicine interventions might increase or decrease health disparities, and personalized medicine interventions may need to be tailored to specific patient groups (e.g., low literacy patients) to minimize potential adverse effects on health disparities. System-level factors, such as coverage policy, may also affect the value of efforts to personalize care. The effects may be complex. High copayments could reduce the value of efforts to personalize care if patients cannot afford options even when they determine they would prefer them in the absence of costs (Basu and Meltzer 2007). On the other hand, low copayments could cause patients to select costly options of limited value because they do not bear the full cost of the choice. Examples of specific classes of questions in this domain include:

*How does patient self-selection affect the value of treatments?*

Little is known about whether patients who are more likely to benefit from treatments are more likely to choose them. If such effects are important, clinical trials with high compliance rates and modeling studies that fail to account for selection may be highly misleading as to the true benefits of treatments. Intensive therapy for diabetes care may be an excellent example, where standard modeling studies of the effects of intensive therapy among all older persons and some randomized controlled trials (RCT) suggest intensive therapy may be harmful, but modeling studies we have done that account for self-selection suggest intensive therapy is beneficial and cost-effective because people who would suffer adverse effects of treatment reject it (Meltzer et al. 2002). Research into these effects could have

very important implications for the design of clinical studies as effectiveness or efficacy trials and for the conduct of modeling studies of the value of medical interventions.

*How do patient characteristics (e.g., education, literacy) affect the extent of self-selection?*

Some of our studies of diabetes treatments suggest that educated patients are more successful at selecting therapies they will benefit from than are less educated patients. Better ability to access information could be one reason for this, and better access to insurance coverage or other financial resources could be another. It is possible that such differences in self-selection could play an important role in the existence of health disparities and potential approaches to reduce them.

*How do biologically oriented approaches to personalized medicine (e.g., pharmacogenetics) and behaviorally oriented approaches to personalized medicine (e.g., decision aids) differ in effectiveness by patient characteristics (e.g., education, literacy)?*

To the extent that personalization of care occurs spontaneously through self-selection, it may reduce the value of some approaches to personalization. On the other hand, self-selection may increase the value of approaches to personalization if it makes information about potential treatment benefits more likely to be acted upon. This may differ by educational status. For example, it is possible that less educated patients might benefit more from decision aids than more educated patients would benefit if the more educated patients are already making the best possible decisions given available information. In contrast, more educated patients might benefit more from additional information about biological markers of treatment response. Maximizing the benefits of new prognostic information for less educated patients could require additional support in decision making, and interventions to increase the ability of such vulnerable groups to utilize complex medical information might be an important area for research to ensure that the benefits of that information are broadly realized.

## 5 Conclusion

Personalized medicine is best viewed from a broad perspective of trying to use information about a patient to improve care. While there is an impressive expansion of genetic information that should and will become an increasingly impor-

tant component of that information about individual patients, traditional clinical approaches to personalizing care should not be neglected. These traditional clinical approaches to personalization are influenced by patient, provider, system, and intervention factors, all of which are promising areas of study. As these diverse approaches to personalization are examined, tools such as cost-effectiveness analysis can provide important insights into the value of these approaches, strategies for their implementation and dissemination, and priorities for future research. Such analyses are likely to be most insightful if they recognize that patient and provider behaviors are essential determinants of the value of treatments and that patient factors in particular may have large effects on the value of treatments and the need for interventions to improve decision making, especially among less educated patients.

In a period of highly limited research funding, there is always a danger that research in one area may be viewed as in competition with research in another. While research funds spent on traditional approaches to personalized medicine may be viewed as competing with research on novel biological approaches, work in the two areas is far more likely to be complementary, increasing the likelihood that the growing body of biological information relevant to personalized medicine is translated into measurable clinical benefit.

## References

- Basu, A. and D. O. Meltzer (2007) "Value of Information on Preference Heterogeneity and Individualized Care," *Medical Decision Making*, 27:112–127.
- Meltzer, D. O., E. Huang, L. Jin, M. Shook and M. Chin (2002) "Effects of Self-Selection on Medical Cost-Effectiveness Analysis: Impact in Intensive Therapy for Type 2 Diabetes Mellitus Among the Elderly," *Medical Decision Making*, 22:535.
- Meltzer, D. O., T. Hoomans, J. W. Chung and A. Basu (2011) "Minimal Modeling Approaches to Value of Information Analysis for Health Research," *Medical Decision Making*, 31:E1–E22.
- Sharma, G., J. Freeman, D. Zhang and J. S. Goodwin (2009) "Continuity of Care and Intensive Care Unit Use at the End of Life," *Archives of Internal Medicine*, 169:81–86.
- Wasson, J. H., A. E. Sauvigne, R. Mogielnicki, W. G. Frey, C. H. Sox, C. Gaudette and A. Rockwell (1984) "Continuity of Outpatient Medical Care in Elderly Men: A Randomized Trial," *Journal of The American Medical Association*, 252:2413–2417.