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## Acronym Definitions

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<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality</td>
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<td>ASPE</td>
<td>Office of the Assistant Secretary for Planning and Evaluation</td>
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<td>CATIE</td>
<td>Clinical Antipsychotic Trials in Intervention Effectiveness</td>
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<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<td>CMS</td>
<td>Centers for Medicare &amp; Medicaid Services</td>
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<td>CPIC</td>
<td>Clinical Pharmacogenetics Implementation Consortium</td>
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<tr>
<td>CT</td>
<td>computerized tomography</td>
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<td>DES</td>
<td>drug-eluting stents</td>
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<td>EVIC</td>
<td>economic value of individualized care</td>
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<td>FDA</td>
<td>U.S. Food and Drug Administration</td>
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<td>HAART</td>
<td>highly active antiretroviral therapy</td>
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<td>HCUP</td>
<td>Healthcare Cost and Utilization Project</td>
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<tr>
<td>HHS</td>
<td>U.S. Department of Health and Human Services</td>
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<td>HRS</td>
<td>Health and Retirement Study</td>
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<tr>
<td>ICD</td>
<td>implantable cardioverter defibrillator</td>
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<td>IRIS</td>
<td>Institute for Research on Innovation &amp; Science</td>
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<tr>
<td>IT</td>
<td>information technology</td>
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<td>LDL</td>
<td>low-density lipoprotein</td>
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<td>MEPS</td>
<td>Medical Expenditure Panel Survey</td>
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<td>NIA</td>
<td>National Institute on Aging</td>
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<td>NICHD</td>
<td>Eunice Kennedy Shriver National Institute of Child Health and Human Development</td>
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<tr>
<td>NIH</td>
<td>National Institutes of Health</td>
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<td>PCORI</td>
<td>Patient-Centered Outcomes Research Institute</td>
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<tr>
<td>PDMP</td>
<td>prescription drug monitoring program</td>
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<tr>
<td>PM</td>
<td>personalized (or precision) medicine</td>
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<tr>
<td>PPACA</td>
<td>Patient Protection and Affordable Care Act</td>
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<td>PRICES</td>
<td>Personalized Risk Information in Cost Effectiveness Studies</td>
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<td>PriMER</td>
<td>Personalized Medicine Economics Research</td>
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<tr>
<td>R&amp;D</td>
<td>research and development</td>
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<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
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<td>RIGHT</td>
<td>Rational Integration of Genomic Healthcare Technology</td>
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<td>RWD</td>
<td>real-world data</td>
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<td>RWE</td>
<td>real-world evidence</td>
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<td>VA</td>
<td>U.S. Department of Veteran Affairs</td>
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<td>VisTA</td>
<td>Veterans Health Information and Technology Architecture</td>
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<tr>
<td>VBID</td>
<td>value-based insurance design</td>
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<tr>
<td>VOI</td>
<td>value of information</td>
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Executive Summary

The Health Economics Common Fund Program at the National Institutes of Health (NIH) has supported research to understand how innovations in treatments, diagnosis, and preventive strategies can be most effectively deployed to improve health and well-being. Research supported by this program identifies factors determining adoption of effective health technologies, innovations, and discoveries, so that past and future investments by NIH may have greater public health impact.

In recognition of its last year, the Health Economics Common Fund Program sponsored a research symposium titled *Turning Discovery into Health: The Contributions of Economic Research* on September 28-29, 2017, on the NIH Main Campus. The goals of this event were to highlight results from Common Fund–supported projects and to stimulate ideas for future contributions of economic research to NIH and Institute-specific missions. Health economics research continues to have a significant role in the missions of multiple agencies at the U.S. Department of Health and Human Services (HHS). Greater accessibility to federal and state data is important, as real-world data will be vital in studying population health.

Participants included investigators conducting research funded under the auspices of the Health Economics Common Fund Program, other NIH-funded investigators working on related health economics topics, and NIH staff. As the final meeting of the seven-year program, the workshop was designed to showcase how the field of economics is useful and important to the NIH mission. The workshop consisted of brief research presentations and discussant remarks grouped in panels moderated by NIH leadership on relevant topics: life cycle of innovations, value of information from and for health research, precision medicine, changing health behavior, and understanding health outcomes. The workshop also featured a roundtable discussion of HHS research priorities. Each set of presentations was followed by a group discussion. The entire meeting was live videocast to the public, and the recording is archived on the NIH Videocast website.¹

Life Cycle of Innovations in the Health Sector

Incentives play a role throughout the life cycle of innovations in the health sector, which includes patents for new technology, the diffusion of technology among providers, gradual reduction in use of outdated technology. Financial incentives, however, are only one component. Expertise, knowledge, and other provider and practice characteristics appear to be important. Furthermore, fast diffusion may not always be desirable, particularly if it leads to overuse of low-value therapies. The research highlights the need for more information to understand the variation in diffusion of high-value technologies and exnovation of low-value technologies before appropriate incentives can be identified and implemented. The current

patent, regulatory, and insurance systems are blunt instruments for rewarding innovation, particularly for prevention.

**The Value of Information from (and for) Health Research**

Presenters shared research on the different ways that information analysis can support cost-effective solutions. Value of information (VOI) analysis is a method to value proposed medical research. Uncertainty plays a critical role, both in determining the VOI and in projecting results from a trial population to the general population. A key assumption underlying VOI calculations is that new evidence can change behavior; thus, the estimates are affected by diffusion of technology. Findings from VOI studies can help NIH as it makes investment choices, designs new trials, and supports translation efforts. Real-world data present the opportunity to project the real-world impact of a new therapy based on existing trial data without requiring extensive and time-consuming research, for example, by using propensity score weighting methods. Advances in data science have generated unprecedented opportunities to rigorously analyze the value of innovation and how to support high-value innovation. Health economics research provides methods for thinking about how to conduct and use those analyses.

**Economic Analysis and Precision Medicine**

If implemented cost-effectively, precision medicine (PM) presents opportunities to improve outcomes for individuals. The expected value of individualized care (EVIC) framework, which couples economic modeling with stakeholder preferences, informs understanding of how and when patients, providers, and payers will use or reimburse a PM test. The Rational Integration of Genomic Healthcare Testing project’s simulation model will estimate the value of using genetic information to inform pharmacological treatment decisions. Presenters noted that existing tests, such as the Oncotype DX, do not provide the expected benefits if patients are unaware that they have been tested or if the information does not influence patient or physician decisions; providing clinicians with tools to better use information and convey it to patients would be beneficial. Benefits may also be improperly estimated when relative risk is used rather than stratified risk in analysis when there are heterogeneous treatment effects. Risk modeling may provide better information on the cost-effectiveness of a treatment and may enable prioritization of treatment or testing.

**Economic Approaches to Changing Health Behavior**

Neo-classical economics and behavioral economics can inform interventions to improve health outcomes. Presenters shared research in which nudges influenced physicians (e.g., writing fewer opioid prescriptions, choosing less aggressive treatments when appropriate) and patients (e.g., getting flu shots, signing up for automatic prescription refills). Financial incentives encouraged individuals to participate in a wellness program and to take initial steps to cease smoking. Patient incentives may need to be combined with physician incentives when the desired outcome requires both parties to act.
Economic Approaches to Understanding Health Outcomes

Presenters used detailed data and subgroup analysis to uncover trends in mortality rates that are often missed. Reduced health inequality among children indicates that insurance expansion in the 1980s had positive effects. In-depth analysis of increased mortality rates among middle-aged whites with no more than a high school education led to a model of cumulative deprivation that point to the need for social and economic interventions. State policies, such as prescription drug monitoring programs and laws to increase medical access, offer tools in fighting the opioid epidemic. Underlying the research findings is the recognition that the United States spends trillions of dollars on health care and has made significant medical advances, yet segments of the population are experiencing high rates of mortality and morbidity. Participants discussed the need for more comprehensive interventions and preventions requiring continued multidisciplinary research and approaches.

Conclusion

Dr. James Poterba (Massachusetts Institute of Technology and the National Bureau of Economic Research) and Dr. Richard Hodes (National Institute on Aging [NIA]) offered concluding remarks about how health economics research can be used to support the NIH mission of turning discovery into health, as well as the missions of multiple individual Institutes and Centers. The Health Economics Common Fund Program will formally end in fiscal year 2018, but its activities, workshop, and portfolio of funded research from the past 7 years has spurred trans-NIH conversations about how health economics research can strengthen the integration of economic research into NIH’s mission and has provided a body of work on which the Institutes and Centers can build.
Meeting Summary

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Life Cycle of Innovations in the Health Sector

**How Incentives Determine What Gets Developed at All**

*Bhaven Sampat, Columbia University*

Technological change in health care markets is driven by not only scientific advances, but also economic incentives. The patent system is a particularly important government-provided source of economic incentive. This Health Economics Common Fund–supported award aimed to develop new data and empirical methods to examine how patents shape the development and diffusion of medical technologies. Patents provide 20 years of exclusivity from the time of filing, but the long time from discovery to commercialization reduces the value of the patent term. Open questions include whether strengthening patents generates incentives for innovation, and whether patents on existing technologies affect subsequent research investments.

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Cancer treatment by organ and by stage provides an opportunity to categorize observed and potential R&D. Survival time provides a good predictor of commercialization lag. An analysis of the number of clinical trials for three different stages of cancer (metastatic, regionalized, localized) over a 5-year survival period showed a negative relationship: metastatic cancers have low survival rates and many trials. Analysis of blood cancer trials supported the findings: with shorter commercialization periods, other available scientific opportunities would be pursued. Rough calculations suggest the value of missing R&D is $90 billion (three times the budget of NIH). Patents may not be the only factor, and lengthening the patent period may not be the only answer. Public funding of trials or development of better surrogate endpoints may contribute to additional R&D.

Many innovations are cumulative; thus, patents could hinder follow-on innovation. Williams and colleagues examined DNA sequences that can be linked with patents, publications, diagnostic test data, and clinical trials, all of which are measures of follow-on research. The analysis found no difference between successful and unsuccessful applications, while scientific publications were much lower for genes not claimed in a patent application.

Results of this work indicate that there is no impact (one way or another) of patents on follow-on research. In addition, results suggest that for the case of human genes, the traditional patent tradeoff is sufficient to analyze patent policy. This work has supported new data and empirical techniques that have enabled progress in understanding how patents affect research and innovation in medicine.

What Affects the Diffusion and Use of New Technology?

Haiden Huskamp and Sharon-Lise Normand, Harvard University

Advances in technology and its diffusion into practice are key drivers of health care spending growth. With new delivery and payment models focusing accountability on provider organizations and the amalgamation of small practices into larger practices, we need to better understand how organization-level characteristics relate to diffusion patterns. In their Health Economics Common Fund–supported project, Huskamp and Normand examined three types of technologies: biologics, devices, and drugs.

Bevacizumab is a high-cost, targeted therapy with minimal survival benefit for most cancers. The diffusion curves showing time to first use and time to 10 percent use of Bevacizumab were most rapid for colorectal cancer, likely because it was the first type of cancer for which the drug was approved in 2004. Different relationships were visible based on how use was characterized. Variation in diffusion rates was observed between oncology practices. Diffusion was faster at independent practices, larger practices, and practices with a higher ratio of oncologists to all medical practitioners.

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Turning Discovery into Health: The Contributions of Economic Research

physicians. Less variation occurred among practices for Food and Drug Administration (FDA)-
approved uses and for higher value uses for the drug.

Drug-eluting coronary stents (DES) were approved for cardiovascular interventions in April 2003
and rapidly diffused throughout the United States. The researchers found that from April 2003
to March 2005, 74 percent of the treatments used DES compared to the bare metal stent. In
2006, concern emerged about delayed adverse events including stent thrombosis. By 2008,
operators could choose among bare metal stents, first-generation DES, and second-generation
DES. An analysis of the period February 2008 to February 2015 found a dampening of DES
overall, from 74 to 68 percent, but within all DES, operators chose the second generation.

Second-generation antipsychotic medications consist of reformulations, new brands, and
generic entries. An initial analysis of prescriptions of antipsychotics by 64,005 prescribers from
2006 to 2015 found generics quickly diffused, while newer brands have lower diffusion. Analysis
of how rates vary by prescriber and over time is under way.

Future research will look at practice, clinician, and patient characteristics associated with
diffusion, as well as diffusion by medication type, formulation type, and approved versus non-
approved indications.

The Difficulty of Getting Rid of Ineffective Technology

Jonathan Skinner, Dartmouth College and Geisel School of Medicine

Skinner’s work focuses on the “other side of innovation,” or how ineffective technologies are
phased out and at what pace, or what he terms as “exnovation.” His work integrates multiple
files and literatures and borrows terminology from other disciplines, including the terms
abandonment/de-adoption, exnovation, and de-implementation.5 Abandonment or de-
adoption is when providers drop the use of a procedure entirely. Exnovation is when providers
scale back on use of a procedure. De-implementation is when a health system discourages use
of a procedure. There is unwarranted variation in de-adoption/exnovation, which can lead to
disparities in care and unproductive expenditures.

Skinner examined variation in exnovation using data on carotid endarterectomies and
implantable cardioverter defibrillators (ICDs) for congestive heart failure and found large
regional differences. The use of ICDs, for example, increased nationally from 2002 to 2005, then
declined. A comparison of ICD use in six cities (San Francisco, CA; Miami, FL; Savannah, GA;
Munster, IN; McAllen, TX; and Seattle, WA) found diffusion was fastest in Munster, while other
areas, such as Seattle, did not become as invested in ICDs. The data suggest that cardiologists
scaled back and became more selective in prescribing ICD use. Faster adopters exnovated most
rapidly, but remained above average in usage. The places where diffusion occurred most
rapidly had the lowest risk-adjusted outcomes, suggesting that the link between innovation and
exnovation may be more complicated than initially thought.

5 Data from dartmouthdiffusion.org are publicly available to examine issues of diffusion and exnovation.
Improving the processes of de-adoption, exnovation, and de-implementation of inefficient or ineffective medical technologies provides a major opportunity to reduce waste. Little is known about early and late exnovators. The fiscal implications could be important, especially as new innovations are developed.

**Discussant Remarks: Innovation in Medical Technology: A Story of Average versus Marginal Benefit**

*Dana Goldman, University of Southern California*

Innovation in health care is an issue of average versus marginal benefit. In the short run, unfettered access to new treatments is desired, yet high prices limit access. In the long run, innovators are needed to develop new treatments.

The treatment of HIV provides a good example. Advocates protested the high cost of highly active antiretroviral therapy (HAART) when the therapy was first introduced. Incremental technologies developed to treat HIV, improved the survival curve from 1984 to 2000, by which time innovation had added 15 years to life expectancy. Over decades, these incremental improvements have had a large effect, resulting in $1.4 trillion in patient health benefit from life-years gained and 5 percent of the return was captured by the innovators. For the most successful drugs, innovators capture only a modest share of the value, and therefore helping to finance innovation is an important public role.

Skinner and colleagues have repeatedly and convincingly revealed inefficiencies in the health care system. Huskamp and Normand demonstrated that much of the inappropriate use comes from outlier physician practices. Work from Williams and Sampat shows that the playing field is tilted in the wrong direction. Reimbursement is tied to treatment, which creates incentives to overtreat in traditional, fee-for-service medicine. The regulatory process rewards treatment, not prevention. The patent system rewards R&D that can manage, rather than eliminate, a chronic illness, while the FDA approval process makes it difficult to get drugs for “healthy” people approved.

The United States underinvests in preventing disease and disability. For example, it would be worth more than $7 trillion to society if we can successfully prevent disease and disability from Alzheimer’s disease. A 5 percent chance of success would justify R&D investments of $350 billion. Our patent, regulatory, and insurance systems are very blunt instruments for rewarding innovation, particularly for prevention, which is where the value lies.

**Panel 1 General Discussion**

**Reimbursement and Diffusion**

It is typically assumed that reimbursement rates drive diffusion. Research supported by the Health Economics Common Fund Program presented in this panel demonstrates that other factors are also important. In Skinner’s research, reimbursements were the same in Seattle and Munster, yet providers responded differently. Similarly, there was no payment difference in the DES study; variation in use was related to the practice. Rates of diffusion and exnovation can
differ for drugs, biologics, and procedures, because there are big differences in the contexts in which they operate. For example, two biosimilars for Bevacizumab received FDA approval in summer 2017. The Gates Foundation is making HIV treatments using generics available at modest cost ($75 per year). Labor-intensive procedures such as ICDs and DES are associated with increasing wages, thus raising the cost of failure to exnovate. Traditionally, the reimbursement system rewards volume rather than health outcomes, although there is some evidence of movement toward value-based care.

Huskamp and Normand’s research looked at the date of FDA approval for DES, which included statements of care following 2006. More generally, they incorporated the timing of newly released information into their analysis, demonstrating that the role of new information on the rate of diffusion can be quantitatively evaluated.

**Demand for Innovation**
The demand for innovation differs based on patients and the disease course. Ken Warner wrote of the desperation-reaction model of medical diffusion. With chemotherapy, adoption is faster for acute than for chronic disease. For children at risk of dying, parents might demand extraordinary measures. With cancer clinical trials, participating patients have different motivations. NIH has an opportunity to consider how to design trials that account for these differences.

In addition to the life cycle of innovation, the life cycle of the population needs to be considered. Diffusion of medical technologies and innovation should be examined separately for the aging population and for the pediatric population. For example, data on devices in children remain limited. Trials involving children have different approval pathways and are understudied. The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) includes a focus on device development for children and pregnant women. Additionally, the 21st Century Cures Act, enacted in December 2016, mandates that NIH consider inclusion across the lifespan, covering children and older adults.

**Barriers to Exnovation**
Participants discussed whether high innovation costs create a “lock-in” effect in health care, making exnovation of older technologies more difficult. Stents are an example of when switching from first to second generation is not cost prohibitive. With imaging and other big equipment investments, the provider will want to recoup costs, which can make coverage rules and payment policies important. Patients have an incentive to pay more attention and prevent lock-in from happening.

Expertise and learning costs may play a role in the exnovation rate. A clinician who invested in training for a procedure or device will be less incentivized to exnovate that procedure, particularly if there are no obvious alternatives. The older technology should not be exnovated too quickly because operators need experience with the new device. Yet, some evidence suggests that skills do not always improve. With ICDs, it was expected that surgeons would get better over time, but they did not. Preferably, those with worse outcomes would exnovate the practice, but a surgeon often does not know where he or she stands in comparison to others.
Joint replacement is a particularly interesting example. The metal-on-metal implants were found to release chromium and cobalt particles into the blood and tissue over time and cause adverse effects; these have since been recalled but the process of exnovating was slow. Knowledge of the problem with metal-on-metal implants diffused more quickly outside the United States, particularly in Australia and the United Kingdom.

**Future Research**

We need to better understand the variations in diffusion of innovation and exnovation. It would be helpful to have better access to cardiology registry data. More information that defines the provider and device codes would be beneficial. Clinicians in practices identified as rapid innovation adopters could be surveyed with vignettes to explore the reasons for their behavior; they may not realize they are rapid adopters.

**The Value of Information from (and for) Health Research**

**Value of Information Analysis as a Guide to Research Investment**

*David O. Meltzer, The University of Chicago*

With finite funds available for health research, topics must be prioritized. Value of information (VOI) analysis can provide quantitative estimates of the value of research. Cost-effectiveness analysis has long been used to assess the value of medical treatments and the information from diagnostic tests. Newer VOI techniques have extended these analytic tools to assess the value of medical research. The VOI is the difference between the expected outcome with information and the expected outcome without information.

Calculating the VOI requires information on the burden of illness and priors and posteriors for the subject of research; typically, not all this information is available. VOI is a sum over time of the value of information to individual patients adjusted by the number of patients, extent of implementation and rate at which the value of information depreciates. VOI estimates become more precise as more information is available. VOI can be conducted using full modeling (e.g., Peter Neumann’s work on Alzheimer’s disease), limited modeling (e.g., the Clinical Antipsychotic Trials in Intervention Effectiveness (CATIE) trial), or no modeling (e.g., sinusitis medication, where complete resolution can be observed). Another option is a conceptual VOI. Because the equation is multiplicative, if any of the three factors is zero—no one has the problem, no one listens, or better data are available immediately—there is no value to conducting the study.

VOI principles and methods may help inform research priorities. Conceptual VOI aligns with peer review efforts. The simplest way to integrate VOI may be through a two-stage prioritization process, using a conceptual VOI first and then performing the practical quantitative calculations for expensive potential investments.

VOI analysis should complement judgement of research priorities. The expected value of perfect information is the upper bound. VOI analysis will not be equally informative among studies. Future work needs to test use of VOI analysis in priority-setting processes for research
to determine how it impacts decision-making, and to determine the health impact and monetary value of decisions influenced by VOI results.

**Promise of Real-World Data**  
*Anirban Basu, University of Washington*

In this era of big data and data science, real-world data (RWD) and real-world evidence (RWE) have become buzzwords. From many definitions, Basu defined RWD as “an overarching term applied to data obtained in the naturalistic setting, not collected in conventional RCTs.” RWE involves the aggregation and synthesis of RWD to inform health care decision-making. RWD and RWE enable discussion of the distinction between efficacy and effectiveness as well as treatment-effect heterogeneity. RWD are also useful for making projections of randomized controlled trials (RCTs), informing VOI analysis, and use in predictive analytics with biomarkers.

RWD present the opportunity to project the real-world impact of a new therapy based on existing trial data without requiring extensive and time-consuming research, for example, by using propensity score weighting methods. Basu applied this method to project results from three RCTs on the use of antipsychotics to treat patients with schizophrenia in a managed Medicaid population. He compared characteristics of the trial population with the Medicaid population using RWD and found the proportions were not the same. These findings suggest that considering how the trial population compares to the overall population is important when structuring trials. Measuring more baseline characteristics and collecting more biomarkers in RCTs to fully describe the target population could improve projection methods. Additionally, the control arm in RCTs should have some resemblance to standard care in the population.

Projections introduce more uncertainty, which has implications for VOI analysis. For example, a new drug may not appear cost-effective in RCT data, but the increased uncertainty of the projection data may produce an error rate that shows it is cost-effective. One of the key assumptions underlying VOI calculations is that new evidence has the potential to change behavior; thus, the estimates are affected by diffusion of technology. Predictive analytics are being used more widely, but may provide less value for comparative effectiveness, where causality is still key. One promising development is continuous biomarker monitoring.

There are many challenges to using RWD, including the implications for privacy and satisfying requirements associated with the Health Insurance Portability and Accountability Act (HIPAA). As a researcher, the biggest challenges to using RWD are access and cost. Data curation, data cleaning and quality management, and data maintenance are costly. Lack of competition in the data market keeps data assets expensive. Patients, who own their data, do not have a way to contribute to a national data registry. It would be tremendously helpful if NIH could facilitate easier and no-cost access to Centers for Medicare & Medicaid Services (CMS) data to its awardees who need these data for their funded projects.
Adverse Effects of Information in Health Information Technology

David Chan, Stanford University

Information plays a crucial role in how clinicians diagnose and treat patients on a daily basis. To improve patient health outcomes, we must understand how clinicians receive and produce information. Clinicians must deal with uncertainty and must use judgement. They are subject to heuristics, biases, and limited attention. Health information technology (IT) is becoming increasingly important to the practice of medicine. Most agree that health IT is key to clinicians’ ability to provide quality, population-based medicine. However, there is conflicting evidence on the overall effect of HIT on patient health outcomes, particularly because there are many implementation approaches. Health IT may provide useful information to clinicians; it could also contribute to information overload or alert fatigue.

Chan conducted a proof-of-concept study of health IT using the U.S. Department of Veterans Affairs (VA) Veterans Health Information and Technology Architecture (VistA) system, which provides electronic reminders to clinicians. Electronic reminders are a common way to alert physicians to patient-specific recommendations, such as to screen for smoking, to counsel a smoker against smoking, or to remind a diabetic to have an annual foot or eye exam. The VA’s VistA platform is similar across locations, but there is variation in the electronic reminders across location and time. The study tracked clinical care for a cohort of diabetic patients over a 6-year period at the 25 largest VA locations to see whether the burden of non-diabetic electronic reminders negatively impacted diabetic control. Results indicate potential evidence of a negative effect of health IT on clinical care due to limited clinical attention (i.e., information overload). This type of research has the potential to change how the VA health system delivers care as VistA is redesigned.

There are many more opportunities for future research to learn about the characteristics of practices and systems that use health IT effectively to improve patient outcomes.

Discussant Remarks

Bruce Weinberg, Ohio State University

Common themes that emerged from the second panel included how information can be optimally acquired and delivered; what can be learned from RWD; and how to incorporate VOI analysis and innovations accounting for dynamic optimization. Weinberg presented preliminary work producing data for the research community and analyzing what investments in research produce the most value, where transformative work is happening, what kinds of people produce it, and results-based suggestions for funding high-value research.

Analyzing the best value of NIH investments—or its marginal product—involves many considerations such as whether value in investments is increasing or decreasing, time lags, variation by activity code, how productivity should be measured (e.g., publications, more funding), impact of multiple versus one award, and how investigators spend award dollars. These types of questions attempt to identify the scientific production function.
To get the most “bang per buck” from NIH investments, one needs to consider how to support work. How much more does one get from investing an extra dollar? Is the relationship concave? How do we measure productivity? How does money get spent? The availability of UMERICRIS data makes it possible to see just how research funding translates into output from a project. Advances in data science have also generated unprecedented opportunities to rigorously analyze the value of innovation and how to support high-value innovation. Health economics research provides methods for thinking about how to conduct and use those analyses.

**Panel 2 General Discussion**

**Population Effects**

RCTs allow for better controlling of covariates, but even large RCT samples are unlikely to reflect the general population. This may be in part because of unequal access to trials. The NIH All of Us Research Program\(^6\) cohort is being designed, and what will be collected is in flux. All of Us could provide an opportunity to focus on data collection decisions and how to balance the strengths and weaknesses of observational and RCTs.

It is tempting to assume that RCT results apply in the general population; however, studies have demonstrated this to be inaccurate. For example, a study on carotid endarterectomies found complication rates to be low in RCT populations, higher in the general population at the hospitals participating in the RCTs, and even higher in general hospitals not participating in the RCTs. Registry data, which provide information on the treated only, may be useful to make inferences on the quality of the outcomes across institutions, by volume, and by other factors.

With real-world experiences, the weighting method is based on estimated conditional treatment effects and the baseline characteristics from the RCT. The quality of the match depends on how many baseline characteristics are collected. Matching can be more efficient than conducting a large study. Integrating VOI analysis with matching techniques would be a good way to decide where to invest.

Future research that assesses how clinicians and other decision-makers respond to evidence from RCTs compared to observational studies would be useful.

**Application of Economics**

Economic theory needs to consider real-world clinical practice. When a trial takes 10 or more years, the population and disease can change, and new drugs are developed. Carefully constructed VOI analysis can provide a framework to think through these real-world issues. VOI analysis is only as good as the ability to tie the treatment to outcomes within the study, and there are many steps between basic research and demonstrating an impact on outcomes.

Other items that need to be considered with respect to VOI analysis are market failure and crowd-out. The value of information is relative to what others are doing. There are market failure issues with VOI analysis. NIH research funding priorities need to be considered in the

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\(^6\) See [https://allofus.nih.gov](https://allofus.nih.gov)
context of other investments; market failure in terms of return on investment has not been examined. Investment should be considered from multiple perspectives, not only the societal perspective, which if reflected in VOI analysis, could provide a rich tool for strategic decision-making. An understanding of how value is appropriated by different stakeholders could inform decisions about public investments.

The Patient-Centered Outcomes Research Institute’s (PCORI) conducted a pilot study using VOI analysis in the research setting. Researcher clinicians can be trained in VOI analysis techniques and their incorporation into the decision-making process. However, VOI analysis is not yet fully accepted in the research community. Factoring the costs of technology into decisions, particularly with oncology, has received some pushback. Researchers believe they are being penalized for conducting research on high-cost drugs.

**Data and Model Access**

Cost is a barrier to both data and model development. Several participants suggested that NIH require awardees to share models developed through NIH-funded work. When data are required to be made public, the investments in data collection and maintenance might need to be further incentivized. There are high fixed costs associated with data collection and maintenance, which are barriers to entry.

**Economic Analysis and Precision Medicine**

**Demand for Personalized Medicine and Implications for Research Prioritization**

David Veenstra and Josh Carlson, University of Washington

The University of Washington’s Personalized Medicine Economics Research (PriMER) program examines the drivers for the uptake of personalized medicine (PM). The Health Economics Common Fund Program–funded project has three specific aims: (1) develop a coherent economic model for PM; (2) assess societal, provider, and payer preferences; and (3) create a pragmatic framework for PM policy development.

The conceptual framework describes the relationship between research evidence and decision-making by physicians, payers, and patients. The expected value of individualized care (EVIC) incorporates the use of the information for diagnosis or treatment, the level of uncertainty, and trajectories of adoption over time. The research team conducted a mixed-methods study on genetic tests for screenings and treatment change to develop a predictive model to inform population-level estimates for the EVIC, particularly on which attributes are most important, the marginal rates of substitution relating to risks and costs, and the probability that entities will use, recommend, or reimburse a given test with a given expected outcome.

Focus groups and interviews were conducted to understand the key attributes driving the decisions of physicians, payers, and patients. The resulting list of attributes and attribute levels was used to create a quantitative survey in the format of a discrete choice experiment. For patients, significant decreased demand was associated with low medical expert agreement on changing the treatment based on genetic markers, little to no change in patients’ quality or
quantity of life and increasing cost. Increased demand was associated with tests that could guide treatment or had a higher probability of having an informative marker. Respondents were willing to pay more for certainty even when the life expectancy gains were less. Predicted uptake for the Oncotype DX diagnostic test increased from 24 to 63 percent, which correlates with observed uptake.

The predictive model, when completed, can be linked to VOI analyses for use in research prioritization. For example, the relationship between time as evidence accumulates and the maximum value of research indicates that as time goes on, the value decreases. This study provides an example of how VOI analysis can be used to prioritize research and get a better understanding of evidence thresholds in genomics.

**Oncotype Testing as a Case Study for Personalized Medicine**

*Jeanne Mandelblatt, Georgetown University*

Oncotype DX is the most common gene-expression profile test used in the United States. It is marketed as helping patients and their doctors estimate the risk of recurrence, inform and increase confidence in therapy decisions, and lower costs by avoiding unnecessary chemotherapy. The test is validated in early stage, hormone +, HER2-, and breast cancer that has spread to the lymph nodes. This Health Economics Common Fund Program–supported research involved examining multilevel influences on test use, cost-effectiveness analysis, the effects of the test on patient-reported outcomes, and physician discussion of the testing.

Results of a multilevel analysis of the determinants of gene-expression profile test use indicate wide variation in use of breast cancer multigene testing, even without financial barriers. The variation is associated with oncologist gender and perceptions and with practices of the chief oncologist. Results also suggest variation may relate to a lack of data on the meaning of intermediate-risk test results.

Cost-effectiveness modeling yielded several conclusions: (1) Oncotype DX testing has a high cost-effectiveness ratio; (2) changes in key drivers of results could yield lower cost-effectiveness ratios; (3) results are most sensitive to test accuracy; and (4) the consideration of the value of reassurance and worry is important. Sensitivity analyses indicate the test would be more cost-effective if the price were less than the reimbursement rate, if the test were more accurate, and if there were greater adherence to the test recommendations.

The team’s patient-reported outcomes study points to several lessons learned and recommendations for future work. Nearly 30 percent of patients did not know whether they had received a gene-expression profile test. Older and less educated patients were less likely to be aware they had been tested. Comparing those who knew they were tested versus those who knew they were not tested, gene-expression profile testing did not improve confidence in a woman’s decisions about her chemotherapy. The intermediate risk group had the least confidence in treatment decisions. These results imply a need for greater physician-patient communication about the option of gene-expression profile testing, the implications of results for chemotherapy decisions, and accuracy of the test and risk of recurrence.
The researchers surveyed oncologists on the variables that influence their discussions of the tests with patients. Practice-level variables (e.g., time, practice policies, and reimbursement) were not influential, whereas oncologist-level variables (e.g., confidence and experience with the testing) were somewhat influential. Patient-level variables (e.g., a patient’s pre-testing preferences for treatment and their performance status) were most influential. When asked which decision tool features would assist in these discussions, oncologists favored a tool that would provide them with a risk algorithm, integrating information such as the risk for recurrence and the benefits of treatment. They also wanted patient education materials about testing and a treatment decision tool they could provide to patients.

Adoption of new genomic tests does not follow a prescribed, structured path; rather it is influenced by multilevel factors and may vary by region. Adoption is influenced by many factors, not all of which we understand. Genomic tests may not be as cost-effective as initially predicted. Genomic tests may not lead to the anticipated patient-reported benefits (e.g., confidence in treatment decisions). To optimize use, the effects and cost-effectiveness of new genomic tests should be reassessed post-introduction. Results need to be translated into tools that clinicians and patients can use to improve outcomes.

Heterogeneity of Treatment Effects

*David Kent, Peter Neumann, and David Kim, Tufts Medical Center*

In this Health Economics Common Fund–supported study, Kent and colleagues conducted Personalized Risk Information in Cost-Effectiveness Studies (PRICES). Clinical evidence comes from groups of patients, yet treatment decisions are made for individuals. Applying the overall results of clinical trials to all patients might not lead to the best outcomes. Achieving optimal outcomes requires an understanding of individualized treatment effects; however, clinical trials measure effects at a group level and do not typically indicate which subgroup(s) benefited from or were harmed by treatment. Conventional subgroup analyses that consider one variable at a time inadequately account for the true heterogeneity of individual patient characteristics. These analyses lead to multiplicity and spurious false-positive results.

An alternative approach is to use risk models to understand the variability of treatment effects in clinical trial populations. The premise is to assign risk scores to patients and to stratify analyses based on the resulting risk distribution. A treatment might benefit high-risk patients greatly but will not benefit, or might harm, low-risk patients.

With funding from PCORI, the team previously found risk heterogeneity in clinical trials with positive results. It examined the treatment effect in relation to relative risk and found, when looking at absolute risk reductions, that the treatment effect was higher in higher-risk patients. Examples from the Diabetes Prevention Program and National Lung Screening Trial demonstrate that treatment effects are, indeed, heterogeneous across risk percentiles. Relative risk reductions frequently, but not always, tend to be similar across the entire distribution, whereas absolute risk reductions are much greater for high-risk than low-risk groups.
To estimate risk-based cost-effectiveness, variables such as life expectancy, utility, and cost need to be modeled at the same level of granularity as risk. Multistate regression modeling using detailed empirical data is a useful method to jointly model the risks of multiple transitions for these analyses.

Combining personalized information and policy-based incentive programs can inform a risk-targeted pay-for-performance strategy and risk-targeted value-based insurance design (VBID). An example is the Patient Protection and Affordable Care Act (PPACA) requirement for lung cancer screening without cost sharing to be included as an essential health benefit. Personalized information can identify individuals who should be prioritized for this screening, even among those considered to be high risk.

Different rates of technology adoption can occur with heterogeneity in treatment effects. Policies can influence adoption behavior, such as through cost-sharing. New metrics could be used for policy evaluation by weighting cost-effectiveness ratios after adjusting for subgroup-level adoption rates and heterogeneous effects.

The Cost-Effectiveness of Pharmacogenetic Panel Testing

Josh F. Peterson and John Graves, Vanderbilt University

Vanderbilt University's Rational Integration of Genomic Healthcare Testing (RIGHT) project, funded by the Health Economics Common Fund Program, seeks to maximize the value of testing large populations with a pharmacogenetic panel, calculate the long-term value of pharmacogenomic panel testing, and discover influential scientific, financial, and behavioral determinants of cost-effectiveness.

Pharmacogenetic testing strategies include no testing, serial single gene testing, reactive multiplexed testing, and preemptive multiplexed testing. Peterson and Graves found that universal preemptive multiplexed testing is not cost-effective, and therefore their research focuses on how to better target high-risk patients for this type of testing.

Using a retrospective cohort of Medical Home patients, the research team developed a Discrete Event Simulation for three drugs—warfarin, clopidogrel, and statin—to select the population for genotyping, determine the rate of development of drug indications, and compare outcomes between a genotyped and non-genotyped population. In the simulation both reactive single gene and reactive panel were cost-effective over a lifetime. Simulation was feasible and accurate for small pharmacogenetic panels; however, designing and debugging the Discrete Event Simulation was time intensive and computationally challenging.

It is relatively inexpensive to add another gene to a multiplex test. However, the addition can be methodologically challenging as more complicated panel results are used to inform decisions and to model the value of the genetic information. The research team modeled a healthy population of patients being exposed to any of these three drugs over their lifetime using a

7 See the Clinical Pharmacogenetics Implementation Consortium for more information, https://cpicpgx.org/.
canonical scenario for pharmacogenomics testing. The model assumes a patient has an indication for a drug over time and would receive standard treatment unless the patient is genotyped as a poor metabolizer, and that information is used to provide an alternative pharmacogenomics test-guided therapy. This simplified model can be converted into a scalable delay differential equation that can be solved to provide a numerical solution for a given pharmacogenomics testing strategy.\(^8\)

Another part of the project evaluated the cost-effectiveness of Clinical Pharmacogenetics Implementation Consortium (CPIC) Level A recommendations using Discrete Event Simulation modeling converted to delay differential equations. The team identified the value of genomic information by CPIC drug category (e.g., drug frequency, adverse event frequency, adverse event severity). Reactive multiplexed testing was found to be more cost-effective over a 10-year period and over the lifetime (the latter by a lesser degree) than pre-emptive multiplexed testing. Peterson and Graves found that with few exceptions, reimbursement for genetic testing is inconsistent and often focused on serial single gene testing for specific pharmacogenetic testing scenarios, which is in part a result of lack of evidence on the value of genomic information. This project was designed to overcome key methodological challenges by jointly modeling cost-effectiveness of multiplex strategies. The metamodel provides a powerful tool for examining sensitivity of results and key thresholds.

**Discussant Remarks**

*Ernst Berndt, Massachusetts Institute of Technology*

A common theme among the presentations in the third panel is an interest in the effects on adoption, utilization, and patient outcomes as uncertainty is transformed to more precise risk. Game theory provides insights into personalized medicine.

Precision medicine involves the combination of a therapy and a companion diagnostic, which relies critically on the ability *ex ante* to distinguish treatment responders from nonresponders, because many drugs prove efficacious for a subset of patients. Precision medicine indications typically possess relatively small numbers of patients; they are more likely to be “niche busters” than “block busters.” The small markets will attract few entrants, making the situation appropriate for game theory.\(^9\) It is an “information pharms race” between drug developers who want to create scientific foundations for differentiating their medicines and payers who want to minimize that differentiation and instead create a lowest price bidding war among the developers. The primary issue is selection of the cutoff values for the companion diagnostic, which affects clinical outcomes and the market size of potential treatment subpopulations.

Berndt illustrated how the selection of different cutoff values affect the sensitivity and specificity of the test and determine the size of the population. The innate drug performance is

\(^8\) The simulation model is open source and is available online at [https://rightsim.org/RIGHT/](https://rightsim.org/RIGHT/).

the same; the observed differences are driven by the imperfect biomarker creating choices of whether to use a companion diagnostic, and if so, what cutoff to choose. This result, consistent with the prisoner’s dilemma\textsuperscript{10} outcome, has implications for pricing.

**Panel 3 General Discussion**

Differences between the initial economic studies supported by companies and the Mandelblatt et al. project reflect that the original research assumed Oncotype DX would be used 100 percent of the time, would be 100 percent accurate, and patients were 100 percent compliant. It is highly effective under those circumstances. Mandelblatt et al. incorporated into their analysis RWD on how clinicians use the test and how patients make choices, which captures the incremental value of the test in addition to clinicians’ opinions and patients’ decisions about whether to undergo chemotherapy. Reflecting on whether these results could be useful for reviewers or regulators, participants noted that regulators do not have input into how modeling is conducted for cost-effectiveness studies. Reviewers could consider more realistic scenarios rather than optimal use. The studies based on ideal circumstances provide a starting point; however, adoption and diffusion of technology in real-world settings involve many additional factors.

VBID or reimbursement changes are often thought to be important, but Ramsey and Mandelblatt’s study on Oncotype DX testing showed differences between health maintenance organization sites, where the costs and payments are uniform, suggesting reimbursement is not the only factor.

The reporting of clinical trials results must consider how clinical decisions are made. It might be preferable for clinical trials to use stratified risk rates rather than relative risk. One could decouple the metric in which results are reported from how they are analyzed. The primary analysis for the main effect of the trial could be retained, but using a simple risk-stratification method would help a doctor or patient better understand the risk reduction for that patient. The challenge is that clinical trials are underpowered to reflect the heterogeneity across patient populations. The assumption that the proportional risk reduction will be similar across risk groups is not necessarily valid.

There continues to be a disconnect between the traditional goal of producing hazard ratios from trials and clinical decision-making based on different data. Research needs to produce outcomes that feed into clinical decision-making tools. Studies that examine the implementation of technology and that replicate trial results would be beneficial.

\textsuperscript{10} See www.econlib.org/library/Enc/PrisonersDilemma.html.
Economic Approaches to Changing Health Behavior

Present Bias, Behavioral Science, and Health

David Laibson, Harvard University

Behavioral economics posits that economic incentives matter, but psychological factors matter too. Our choices reflect limited rationality, imperfect self-control, and social preferences. Behavioral nudges targeted at the psychological roots of self-defeating behavior can be highly effective. Laibson presented examples to demonstrate time-inconsistent preferences, present bias or quasi-hyperbolic discounting, procrastination, and effective behavioral nudges for these problems, such as default enrollment (i.e., opt out versus opt in).11

Individuals and society have many aligned goals, such as to improve individual health and to control social costs. Individuals also want behavior change, although not “right now,” such as improved diet, increased physical activity, smoking cessation, medical regimen adherence, and wellness program participation. Interventions that lower barriers and increase desired behavior can also be applied to health. The challenge is to align intentions and actions.

Laibson presented studies of three nudges that improved the alignment of intention and action: commitment devices, proximity, and active choice. The simple strategy of prompting individuals to make a concrete plan to follow through on their intended behavior, by selecting a date and time, promoted the desired outcome in a study to increase workplace flu shot adherence.12 Employee proximity to the location of the flu shot clinic, and whether it fell within the employee’s normal route through the office influenced who obtained flu shots. Home delivery of prescription medicines is less costly for consumers and employers, saves time, raises medication adherence, and improves safety. Requiring employees in a large firm to make an active choice between home delivery and standard pickup increased enrollment from 100,000 to almost 300,000 in a pilot study. This led to substantial savings for both employees ($820,000 in the first year) and the employer health plan ($350,000).

Researchers are gaining a better understanding of the mechanisms underlying these self-regulation problems using functional magnetic resonance imaging (fMRI). Three brain regions appear to be involved: frontal cortex, medial prefrontal cortex, and dopamine reward system. For example, maintaining a diet involves executive function in the analytic cortex, and falling off the diet (eating a donut) involves impulsivity in the dopamine reward system.

Behavioral economics helps explain why people often fail to act in their own best interest: costs come early and benefits come late. Self-defeating behavior can be changed using choice-preserving nudges and choice architecture to dramatically shift behavior. Studies have shown

that many of these interventions are inexpensive and scalable. Research has demonstrated the effectiveness of defaults and other nudges in savings behavior; these same types of interventions can be applied to health behaviors.

**Discouraging Smoking by Low-Income Populations: Applications to Food Choices**  
*Jody Sindelar, Yale University*

To change the behavior of low-income individuals related to use of addictive goods, such as tobacco, illicit drugs, and food requires the development of effective, scalable, low-cost approaches. With smoking cessation, both neo-classical economics (financial incentives) and behavioral economics (how to structure those dollars) can play a role. Counseling services can increase both short- and long-run effectiveness by helping individuals develop new habits and internal motivation. The challenge is creating financial incentives for a no- to low-cost approach. Possibilities include motivating individuals to recognize they could pay themselves to not smoke, informing them about the opportunity cost of smoking, and using pre-commitment devices such as betting they can quit.

The researchers examined financial and health motivations to reduce smoking among low-income residents in New Haven, Connecticut, by providing two messages (“Kick the Habit and Get Healthy” and “Kick the Habit and Save Money”) at three location types: health clinics (health prime), grocery stores (neutral), and check cashing premises (financial prime). Results indicate that more individuals picked up the financial message flier than the health message fliers, particularly in the check cashing setting.

To study the use of a pre-commitment device, the researchers conducted an online discrete choice experiment on cigarette pack size and willingness-to-pay to stick with the smaller pack. Smokers who wanted to quit were willing to pay a relatively large premium for a smaller pack size, suggesting structural approaches may help smokers quit. Even with a small effect, such an approach could have a large impact on the overall population of smokers.

A randomized study of Medicaid enrollees examined financial incentives to use cessation clinics and to quit smoking. The small, quickly paid incentives of $5 provided the potential for a large cumulative incentive ($350 to $450). There was a significant increase in cessation at 3 months, but it was insignificant at 12 months. Use of services was significant at both 3 and 12 months, with a four-fold increase, perhaps implying a desire to quit. A study designed to combine incentives with use of a pre-commitment device was unable to recruit enough participants, because it required people to bet their own money on their ability to quit. Additionally, the Medicaid population was not comfortable with the internet and texting requirements.

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The next steps are to apply these techniques to obesity and nutrition. Using economic insights to change health behaviors provides opportunities to reach a wider population in nonclinical settings in low-cost, scalable ways.

**Encouraging Guideline-Appropriate Treatments**

*Jason Doctor, University of Southern California*

It is estimated that one-third of health care expenditures do not improve health. Behavioral insights can inform policies to improve the quality of decisions that are produced in health care. Doctor presented a series of studies focused on reducing inappropriate antibiotic and opioid prescribing. These studies suggest that tools are available to assist physicians in providing guideline-concordant care. Six types of behavioral nudges that can affect physicians’ decision making were tested:

1. decision fatigue: decision-making gets worse with repeated decisions
2. choice partitioning: choices are spread over salient consumption options
3. public commitments: commitments bind our future self to desires our present self wants to fulfill
4. social norms: we look to others for how we should act
5. justifications: we want others’ approval of our behavior
6. availability: the more easily we can call some scenario to mind, the more probable we will find it to be

Doctor presented several studies examining how these concepts and strategies can be used to improve care and health outcomes. These studies suggest that tools are available to assist physicians in providing guideline-concordant care.

In a study examining antibiotic prescribing behavior, Doctor and colleagues found evidence of decision fatigue; 26 percent more prescriptions were written at the end of the shift. Another study assessed choice partitioning by asking providing physicians which drugs they would choose to treat patients with acute respiratory disease in vignettes. Physicians chose an aggressive treatment more often when four aggressive treatments were presented in a list form and the less aggressive, over-the-counter treatments were grouped on one line.

In a study of public commitment devices, a publicly visible poster informing patients that the doctors in the practice would avoid prescribing antibiotics when they are likely to do more harm than good was associated with a reduction in antibiotic prescriptions compared to control practices without the poster. Based on this research, the Centers for Disease Control and Prevention (CDC) funded replications of the commitment device in New York and Illinois.

A large cluster RCT to reduce antibiotic prescriptions in three health systems using three different EHR systems evaluated the use of social norms and justifications. In one condition, salient alternatives were recommended by a pop-up screen in the EHR. In another condition, physicians were asked to justify their clinical action after a pop-up noted that antibiotics are typically not used for the condition. In the third condition, a peer comparison was provided via
monthly emails (e.g., top performer versus not a top performer) indicating the number of prescriptions written for cases that did not warrant antibiotics. Results indicate that justification led to a decrease in prescriptions that lasted as long as the nudges continued. The peer comparison had a longer-term effect.

In a study of the availability heuristic, physicians were sent a nonjudgmental letter that a patient of theirs had died and prescription drug overdose caused or contributed to the death. The letter included information on how to prevent opioid deaths by adhering to CDC guidelines. An analysis of prescriptions before and after receiving the letters found the letter reduced opioid prescriptions.

**Applying Behavioral Economics to Improve Health**  
*Kevin Volpp, University of Pennsylvania*

For many diseases, there is great potential to improve population health through behavior change, and behavioral economics can provide a framework for intervention program design. Although people may be irrational, they are irrational in predictable ways: present-biased preferences, loss aversion, goal gradients, overweighting of probabilities, and inertia. By taking advantage of these typical decision-making errors, individuals can be steered toward more healthful behaviors. Volpp suggested that advances in wireless technologies, understanding of behavioral economics, and shifts in financing create new opportunities to improve population health by allowing physicians to monitor and impact behavior outside of the clinic setting through choice architecture enhancements, incentives for health improvement, and behavioral science and wireless technologies.

Volpp presented studies to demonstrate the benefits of implementing lessons learned from behavioral science. Technological changes, such as switching the default from brands to generics, can immediately change prescription rates for generics. Using an opt-out system for participation in a remote monitoring program for people with diabetes increased participation by three-fold, even with a required in-person visit. Active choice for enrollment in an automatic refill program doubled the rate of enrollment. Synchronizing medication refills improved adherence.

A study on smoking cessation among General Electric employees published in the *New England Journal of Medicine* found that a $750 incentive tripled long-term smoking cessation rates. This led to a benefit design change implemented among all General Electric employees nationwide. The findings are also important because PPACA rules allow employers to use increasingly large portions of premium dollars for outcome-based incentives. A follow-up study using incentives and a pre-commitment device among CVS employees funded by the National Cancer Institute, also published in the *New England Journal of Medicine*, replicated the tripling in long-term smoking cessation rates and showed some promise of an approach that involved employees putting some of their own money at risk. The employees’ initial deposits of $150 were matched 4:1, and the total would then would be lost if the employee was not successful in quitting smoking. This led to a program implemented nationwide by CVS for its employees in 2015 called “700 good reasons to quit.” The framing of incentives can affect outcomes. A program to
increase physical activity for overweight employees by using a 7,000-step goal was most effective with a loss framing than with a gain or lottery framing.

Wireless technology provides exciting new opportunities to scale up behavior change. The Penn Way to Health is a software platform originally funded by an NIH American Reinvestment and Recovery Act-funded grant that collects individual-level information from different devices, sends the information to a secure server, and then provides automated feedback to participants that can be customized based on the study design. It supports different incentive models, integrates with a range of devices and many biomedical measures, and is used in a wide variety of clinical conditions in dozens of studies that have included participants in 45 states.

An RCT focusing on incentives for physicians and patients found all groups experienced a reduction in low-density lipoprotein (LDL) at 12 months, including the control group, which received wireless devices to monitor adherence and was paid participation incentives. Only the shared incentive group performed better than the control group, reflecting the need for providers to initiate prescribing and intensify therapy as appropriate and for patients to take the medication to obtain positive results. This study won the AcademyHealth Article of the Year award in 2016, and the shared incentive approach between patients and providers represents a potential new paradigm for thinking about health improvement for chronic diseases.

Another important area of current inquiry is examining the role of incentives for habit formation, again looking at changes in LDL. In one condition, the participant receives the full incentive if he or she takes the medication before receiving the reminder and receives half the incentive if he or she takes it after the reminder. Another area of study compares the effectiveness of process incentives, outcome incentives, and combined process and outcomes incentives. Although the economic perspective suggests one should provide incentives for outcomes and let the individual determine how to reach the goal, process incentives may be more effective because they are more tangible and can be used to give more immediate feedback. As another example, a combination of technologies and behavioral science engagement strategies are being tested to keep congestive heart failure patients from being readmitted to the hospital.

Volpp was optimistic that future efforts to improve population health can be more effective due to three recent developments: behavioral economics has expanded our understanding of human behavior; social media and wireless devices create new possibilities for engagement; and health care financing shifts create economic motivation to connect with people outside of medical settings.

15 See https://www.waytohealth.org.
Many studies focus on individual decision-making and health outcomes to assess how individuals respond to incentives for healthy behavior and what types of individuals are most likely to benefit from health interventions and why. However, there are other key actors: firms face incentives regarding employee or consumer health; health outcomes are further affected by market-level forces and equilibrium; and government policies may improve health or create unintended barriers to health improvement. Jones demonstrated these dynamics in the context of workplace wellness programs.17

Workplace wellness programs have become increasingly popular among U.S. employers. Such programs aim to reduce health care costs, improve employee health, and increase productivity. The industry has grown rapidly from $1.8 billion in 2011 to $8.0 billion in 2016. More than 47 million workers in 83 percent of large firms are covered by workforce wellness programs. However, the effectiveness of workplace wellness programs is unclear, and further research is needed to investigate questions such as

1. Can workplace wellness programs improve the health and well-being of employees?
2. Do the effects of these programs vary across different time horizons?
3. What types of workers are most likely to participate/benefit from these programs?
4. Are there impacts beyond health outcomes, including productivity and health care spending?
5. Do the benefits for firms outweigh the costs of implementation?

The current evidence for the effects of wellness programs is mixed and suffers from empirical challenges such as selection bias from nonrandom participation, the potential for publication bias, and issues of measurement, scope, and power. While prior studies have looked at average benefits and average costs, marginal analyses are necessary to determine the scale and level of intensity for implementation. A specific experimental design is needed to estimate the marginal costs and benefits to distinguish between average costs (cost per program participant) and marginal costs (cost of adding one more participant).

Jones and colleagues designed the Illinois Workplace Wellness Study, which is a large-scale field experiment involving more than 12,000 employees at the University of Illinois at Urbana-Champaign.18 The study design involved individual, random assignment to control or treatment groups in a population with minimal campus-based wellness options outside of the study. Although workplace wellness programs vary widely across employment settings, most contain one or more components: biometric screening, health risk assessment, and wellness activities. The University leadership–approved Illinois Workplace Wellness Study program was designed

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18 See study pre-registration at https://www.socialscienceregistry.org/trials/1368.
to be broadly representative of gold-standard wellness program and included all three components and financial incentives tied to participation.

The study yielded rich data linked at the individual level—administrative employer data, health insurance claims data, and baseline survey on health status, behaviors, and utilization—which allows for a comprehensive evaluation. Of those who completed the baseline survey (N=4,834), 1,534 were randomized to the control group, and 3,300 were randomized to one of six treatment arms that represented combinations of screening rewards (nothing, $100, or $200) and activity rewards ($25 or $75). Variable program costs included the monetary incentives, health screening ($78 per person), and wellness activities ($26 per person per activity).

Jones discussed the variations in results by screening incentive levels. Health screening participation was highest for the $200 incentive group (62.5 percent) compared to 58.5 percent participation for $100 screening incentive and 46.9 percent participation in the no screening incentive group. The average variable cost per participant (N=1,900) was $265, and the average variable cost per employee (N=3,300) was $153, ranging from $79 per employee in the no screening incentive group to $224 per employee in the $200 screening incentive group. The difference in marginal cost between the no screening incentive group and the $200 screening incentive group was $1,750. The marginal cost increases more sharply as the incentive increases. The marginal cost curve demonstrates that once about 50 percent participation is achieved, it becomes increasingly expensive to draw more participation. Optimal design of workplace wellness programs can be informed by marginal cost analyses to help decide whether a $200 versus $100 incentive is worth the additional participation it would yield.

The next steps in the Illinois Workplace Wellness Study are to evaluate the 1-year impact on health care spending, productivity, and other health behaviors using administrative data, health insurance claims, and participation in the Illinois marathon and 5K race. Data will be collected through 2020 to examine long-term impacts. Forthcoming research from Katherine Baicker and colleagues will examines the firm-wide impact of wellness programs. Future research is needed to determine market-level impacts of wellness programs.

**Discussant Remarks**

*Donald Kenkel, Cornell University*

The body of inventive research presented by this panel focused on behavioral economic approaches and demonstrates that health economics research is making a large contribution to the NIH mission. The economics of health behaviors is different from behavioral economics of health. A neoclassical economics approach, which continues to have a role in health research, assumes rational maximizers, which involves using traditional tools such as taxes on alcohol or the effects of advertising on e-cigarettes. The panel presentations demonstrated that incentives matter. Insights about health behaviors are driven by not only individual behavior, but also market forces.
Kenkel asserted that research supporting the development and testing of behavioral economics–informed interventions to improve health, such as several of the low-cost nudges presented by the panel members, contributes to the NIH mission. Such behavioral nudges can be integrated with traditional economic tools to scale up interventions and have a greater effect.

Methods commonly used in traditional econometric research and behavioral economics research using RCTs and field experiments provide many opportunities. To support rigor, reproducibility, and transparency of research, Kenkel stressed the importance of a registry of RCTs, replication of results in varied populations, and commitment of high-impact journals to publish nonsignificant results.

Panel 4 General Discussion
Participants suggested that more research, and more nuanced research, is needed to determine how to optimize various nudges to increase healthful behavior and improve health outcomes in the real-world, including the need for cost-benefit analysis to understand the marginal cost of the desired effect.

Participants suggested that future behavioral economics research explicitly address aging-related issues and health disparities. Predictive analytics can be used to identify which subgroups or populations are most likely to experience the biggest marginal benefits. Multiple coordinated nudges may be needed to address a problem. Older adults are being asked to make increasingly complex decisions about their health, finance, and living arrangements, and are increasingly staying in the workforce. The aging working population might have unique needs with respect to interventions such as workplace wellness programs.

Economic Approaches to Understanding Health Outcomes

Inequality in Mortality Over the Life Course: Why Things Are Not as Bad as You Think
Janet Currie, Princeton University

Currie presented research on changes in age-specific mortality rates to provide additional perspective on the relationship between economic inequality and health inequality. There has been a great deal of recent research and publicity about increases in inequality in life expectancy and mortality over the past 20 years, most of which focuses only on adults of middle age and older and not on children or young adults. Currie and colleagues analyzed 3-year mortality rates by race and gender at the county level for all age groups for 1990, 2000, and 2010. From age 0 to 4, the results show large declines in mortality between decades, particularly for black children. Decreases were much larger in the poorest counties, showing a decrease in inequality for infants and children. Infant and child mortality is an important and sensitive indicator of population health. Furthermore, declining mortality rates in childhood implies that these cohorts are likely to be healthier into the future. Similar results were found for ages 5 to 19. For ages 20 to 49, mortality rates improved for white men, but not for white women. For ages 50 and older, increasing inequality in mortality is evident among whites.
Among African Americans, there were large decreases in mortality at all ages, which were most concentrated in the poorest places.

The results of these analyses suggest that research focused on middle-aged and older adults presents an incomplete picture of trends at the population level. There may be no necessary relationship between income inequality and mortality inequality: income inequality increases for all groups, but health inequality increases for the old and decreases for the young. Past policy initiatives, such as Medicaid expansion in the late 1980s to 2000s, may have been effective at improving the health of the younger population.

In order to provide further evidence about whether policies affecting children are responsible for the decrease in inequality in mortality among the young, Currie and colleagues compared trends in mortality and mortality inequality between Canada and the United States. Canada is an appropriate comparison because many factors (e.g., technology access, smoking, driving, product safety) are similar to the United States, but the policy environment is different. Specifically, Canada provided universal health insurance for children throughout the period of study.

The comparison suggests that the mortality profile for U.S. children approached that of Canadian children, which supports the idea that expansions of health insurance have been an important factor. While the U.S. mortality rates are higher at every age group, there was a larger decline in child mortality in the United States in the poorest places, with convergence between U.S. and Canadian children in the period following Medicaid expansion. Compared to Canada, 40- to 44-year-old U.S. adults showed few improvements in mortality in the United States, particularly in poorer counties, again suggesting that there is no necessary relationship between changes in economic inequality and changes in health inequality.

These analyses suggest health insurance expansion has been important to improving children’s health. Because health in early childhood has long-term effects, Currie and colleagues expect sustained improvements in the health of current younger cohorts as they age, all else being equal. Conversely, disparities at older ages, particularly in heart disease and cancer, may reflect changes that happened much earlier in the cohort’s life span. Even in times of increasing economic inequality, health inequality can be reduced by policy.

Worsening Health and Mortality in Middle Age

Anne Case, Princeton University

Case presented work supported by NIA through a grant to the National Bureau of Economic Research (NBER). Over the 20th century, there was a remarkable decline in mortality rates for middle-aged and older adults in the United States, the United Kingdom, and across Europe, as

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well as declines in morbidity, even among the increasingly long-lived elderly. In many countries in Europe and for Hispanics and blacks in the United States, that trend continued from 1990 to 2010. For non-Hispanic whites in the United States, life expectancy declined between 2013 and 2014, and in 2015 life expectancy declined for the entire U.S. population, despite the trillions spent on medical care. Economic models of mortality by cause, country, sex, education, and race can help identify possible drivers of these outcomes.

Analyses by Case and Deaton found that the differences lie in what they term “deaths of despair.” In every state, suicide rates rose for non-Hispanic white prime-aged adults (ages 24-64) between 1999 and 2015. Similarly, with the exception of New Jersey and Maryland (where death rates were flat), alcohol-related liver mortality rates rose in this group. Accidental or intentional undetermined drug or alcohol poisoning also increased in every state over the same time period. The results are consistent for non-Hispanic whites across all age cohorts between 30 and 64.

Analysis of gender and education level showed the increases in drug, alcohol, and suicide mortality are mostly among people with less education. This trend precedes the Great Recession. Although the increase is seen with each age cohort, younger cohorts are at greater risk. In addition, these trends are seen in central cities, rural areas, and areas in between.

The difference between black and white mortality has been decreasing according to the CDC’s annual reports. Among men and women with no more than a high school education, black mortality rates have fallen while white mortality rates have risen, contributing to the convergence. A recent increase in black mortality rates, particularly from drugs, continues to be a concern.

Morbidity follows a similar pattern. An analysis of sciatic pain found differences by education and birth cohort; a greater fraction in the younger cohorts with an education level less than a BA reported pain at any given age. A self-report survey on physical health similarly showed fewer young people reporting their health as excellent or very good from 1993 to 2011, while older people have increasingly reported good health. Results for serious mental distress were similar.

These analyses suggest that research is needed to identify causes of these trends that affect men and women in about equal proportions; affect non-Hispanic whites in the United States, but not blacks and Hispanics; have larger effects in later born birth cohorts; disproportionately affect adults with less education; affect both morbidity and mortality; may be related to slowdown in progress in heart disease; and have not had the same effects on mortality in other rich countries.

Case proposed a model of cumulative deprivation to explain these trends. There has been a long-term process of decline for individuals without an undergraduate degree, including a steady deterioration of job opportunities, beginning with those leaving high school in the early 1970s, and labor force participation has been falling for men without college degrees. Further, the social and economic structures have been weakened: marriage rates have fallen and out-of-
wedlock parenting has increased. Health problems may be an outcome of the labor market, particularly for those at the bottom half of the income distribution. These trends have impacted health and mental health outcomes and mortality.

Case hypothesized that this process was unfolding before the current opioid epidemic, which has made circumstances worse. These cumulative effects are unlikely to disappear at retirement. European countries have not suffered in the same way. She suggested focusing future research on the labor market and health insurance costs.

The Opioid Epidemic and State Intervention Strategies  
Dhaval Dave, Bentley University and the National Bureau of Economic Research

Dave provided a detailed analysis of the role of opioids in mortality rates and the potential for state interventions to reduce overdose deaths. Opioid mortality rates are an order of magnitude higher than those of heroin in the 1970s and crack cocaine in the 1980s and 1990s. More than 64,000 drug overdose deaths occurred in 2016, which is more than American deaths in Vietnam, Iraq, and Afghanistan combined. Overdose mortalities affect all states but are worse in the rustbelt and southern mountain states. Whites have been impacted more than blacks, and males more than females. In 2000, deaths were more likely among 40-year-olds; by 2015, younger people were dying more.

Opioids are a class of drugs that act on the nervous system to relieve pain, create a sense of euphoria, and can be highly addictive. There are natural (e.g., poppy) and synthetic (e.g., fentanyl) opioids. Opioids include illicit drugs (e.g., heroin) and prescription pain killers such as hydrocodone, oxycodone, morphine, and codeine.

The opioid crisis originated in the health care system. Variability in prescribing rates persists even after controlling for hospital fixed effects; the lowest-prescribing quartile of doctors prescribed opioids to just 7 percent of patients, while the highest prescribed opioids to 24 percent—more than three times as often. Patients who saw a high-intensity prescriber were about 30 percent more likely to end up with a long-term opioid prescription lasting at least 6 months within a year following their hospital visit. Physician network effects, training, and information asymmetry may contribute to the differences. The role of payment incentives has not been fully explored, including the importance of high patient satisfaction scores and low readmission rates. Illicit supply is also a factor as individuals get multiple doctors to prescribe opioids and then sell them on the street. As policy interventions have been introduced to reduce the availability of prescription opioids, users have switched to heroin and fentanyl.

A state prescription drug monitoring programs (PDMP) is a policy intervention to collect dispensing information to track prescribers and patients. Initially designed for law enforcement, these databases are now being used to provide information to physicians and pharmacists. Every state but Missouri has implemented a PDMP, and 29 states currently mandate that prescribers use the database. Use of the database is low in states where it is voluntary. Research on the effect of mandatory PDMP regulations on opioid use found evidence of a 10 to 30 percent decline in treatment admissions for prescription drug abuse and a 5 to 10 percent
decline in opioid mortality about 2 years after the law took effect, reflecting the time needed for learning and diffusion of practice.

Another opportunity to reduce overdoses and mortality is through state policies on access to treatment. Naloxone Access Laws provide greater access to overdose-reversing naloxone by permitting its prescription to third parties or making it available without a prescription. Naloxone Access Laws have been found to reduce opioid-related deaths by 9 to 11 percent. Good Samaritan Laws provide immunity from prosecution for drug possession to anyone who seeks emergency medical assistance, which can encourage bystanders or victims to call 911 in the event of an overdose.

The complexity of the epidemic is compounded by the fact that many drugs are prescribed for a legitimate purpose. Additionally, the epidemic is not monolithic. It requires a combination of approaches to address the root causes such as the factors that lead to deaths of despair, prevent new generations of opioid addicts, treat current addicts and limit the transition to addiction of current legitimate users, and limit access both from overprescribing and through illicit supply channels. Health economics research can inform future interventions by helping to quantify which approaches, and combinations of approaches, are effective and efficient for whom.

**Discussant Remarks**
*Kosali Simon, Indiana University*

This panel of presentations together present good and bad news about the past and cautions about the present and future. Despite continuing medical breakthroughs, advances in the evidence base in public health, rising average incomes, and higher health care spending, the United States continues to have worsening life expectancy, primarily among the low-educated non-Hispanic white population. Understanding the causes and the role of policy to address these issues is a national research priority in economics and will require a multidisciplinary approach to solving health outcomes puzzles. A collaborative approach that engages states, communities, and academia is needed.

Currie’s research presented good news about improvements in children’s health inequality. Other evidence finds that social safety net programs beyond Medicaid, such as the Earned Income Tax Credit and Supplemental Nutrition Assistance Program, have been positive for families with children. Yet welfare reform has brought about a contraction of some insurance programs, leading to more support for the working population and less of a safety net for the nonworking poor. The environment, including mothers’ stress during pregnancy, affects child development and health. As shown in Dave’s presentation, the opioid crisis is affecting people of parenting ages, making it important to consider the impact on the next generation.

Economics provides a framework for understanding the evolution of health outcomes. Through this framework, one can trace policy effects and unintended consequences of factors such as job opportunities, social capital, and feedback loops. Insights from other fields, such as psychology, sociology, and medicine, should be integrated with health economics.
economics can help us understand and change patient and provider behaviors. Health care systems do not always act according to rational behaviors. Economic research methods provide ways to estimate what improves health outcomes, especially when RCTs are not possible. Economists have developed many methodological tools that can inform causal inference and natural experiments. As we tackle these national priorities, economics has much to offer in a mixed disciplinary approach.

**Panel 5 General Discussion**

The theory of cumulative deprivation described by Case includes reduced employment and lower labor force participation rates; yet, blacks suffer greater unemployment than whites. Cumulative deprivation would seem to be relevant for blacks, particularly with the high rates of incarceration. Because the higher mortality rates are driven by suicide, Case hypothesized that people in the white community lost hope in their futures. The theory of cumulative deprivation suggests the need for comprehensive prevention efforts and interventions as we develop a better understanding of how variables come together.

Some evidence suggests that the epidemic among whites may result from physicians’ greater likelihood of providing an opioid to a white patient presenting with pain than a black patient. Technology also plays a role. In the past, attempted suicides failed because the available drugs were weak. Today, some opioids are strong enough that 15 pills are sufficient to cause death. Technology is interacting with despair to enable unintended outcomes.

The differences in mortality rates between adults and children by subgroups are significant. Mortality may not be a sufficiently sensitive indicator for children or children may be more resilient. Another hypothesis is that cumulative deprivation takes time to develop. An increasing amount of money is spent on programs for children, and the programs make a difference at the margin. For example, children who benefited from health insurance were more likely to get a college education. Investments in health take a long time, so we need to invest in effective programs for young children to have better outcomes 30 years later.

**Health Economics Research Priorities at HHS**

*Roundtable Discussion Moderated by Marie Bernard, National Institute on Aging*

_Sharon Arnold, Agency for Healthcare Research and Quality (AHRQ)_

AHRQ’s intramural and extramural research priorities are to improve health care quality; make health care safer; increase accessibility; and improve health care affordability, efficiency, and cost transparency. AHRQ focuses on bringing together those topics in supporting organizations so that they can become “learning health organizations,” organizations that use their internal and external data to improve quality and safety.

AHRQ’s interests in economic research include demand and supply issues, such as those related to insurance, disparities, the impact of market and organizational structures, medical malpractice, and public reporting. All payers—Medicare, Medicaid, private health insurance, States, and the VA—are of interest.
In 2016, $100 million in grants were awarded to extramural researchers; half of which were investigator-initiated and half of which were agency-directed. Over the past 3 years, congressionally directed AHRQ investigator-initiated research funding levels have been steady, while other funding has decreased.

AHRQ funds training opportunities, including a new program designed for embedding health services researchers in health systems to drive learning at the health system level. AHRQ also maintains and shares data, including the Medical Expenditure Panel Survey (MEPS) and the Healthcare Cost and Utilization Project (HCUP). Through HCUP, AHRQ makes state-level data available and produces a nationally representative sample. Although it currently charges a small fee for use of the national database, each state determines the price for use of its data. AHRQ is developing a compendium of all health systems in the country, identifying hospitals and associated physicians, which will be enhanced over time.

John Graham, Office of the Assistant Secretary for Planning and Evaluation (ASPE), U.S. Department of Health and Human Services

HHS has a broad interest in health economics research that goes beyond health to include human services. Economic analysis can play an important role in many of the activities at HHS, including allocation of health care resources, reducing the burden of the insurance exchanges, and a new direction for the CMS innovation center. More opportunities for economic analysis will develop as states take advantage of the Section 1115 waiver authority and consider greater alignment between Medicare and commercial health insurance features. The PPACA’s effects on consumer choice, pricing, employment, and job growth are among issues HHS will continue to research. HHS is implementing two executive orders to reduce the number and cost of regulations.

Recognizing that innovation is important and that FDA is taking steps to speed drugs to market, publish an orphan drug modernization plan, and look at where its rules may delay the timely entry of generic formulations, HHS welcomes economic analysis on issues such as incentives for new therapies when market incentives are not adequate, such as with rare diseases, medical countermeasures, and other threats to public health.

Mark McClellan, Duke University

The leveling off in age-adjusted mortality rates for middle-aged whites is a worrisome trend. More work on understanding these trends in population health and what is driving them is fundamentally important for the United States.

Nonmedical factors affecting health are important. The country’s spending on social services, education programs, infrastructure, and job training has been reduced through bipartisan consensus over the past 30-40 years. The increase in health care entitlement comes at the expense of other programs. We need to better align resources with what we learn about population health. CMS will spend more than $1 trillion this year. The entire federal budget on

homeland security and national security is only $600 billion and 10 percent of that is attributed to health care costs.

Other important research topics are to identify incentives to turn biomedical insights into products that are safe, effective, and reliable for patients, and to increase the value of biomedical investments generally. FDA is working to improve development science, including more clearly showing the connection between basic science and health. More knowledge on the impact of treatments on subpopulations is needed for precision medicine. Research design issues can use techniques from health economics research.

State research opportunities should be pursued, including how state health policies vary. This work could link with more support for access to RWD sources as states take advantage of Section 1332 state innovation waivers and Medicare waivers. States need to play a larger role in improving population health, such as by combining Medicare with nonmedical programs, behavioral health programs, and social services.

General Discussion
Dr. Marie Bernard invited questions, comments, and recommendations for future NIH research priorities. Participants discussed the disconnect between life-improving research and negative population health trends. The NIH mission includes “turning discovery into health,” yet the relationship between discovery and health needs to be better understood.

The United States spends trillions of dollars on delivering services annually and a small amount on trying to understand the mismatch between expenditures and poor outcomes. Nonmedical studies are not high profile, and research on nonmedical determinants can be challenging. RWD may be useful in constructing meaningful populations for tracking.

The HHS proposed strategic plan includes a goal of reducing health disparities. AHRQ has always been interested in health disparities and is working to better understand barriers to high-reliability care, ensure evidence is spread to all patients, and ensure equal treatment. Engaging underrepresented patients in research should be a priority.

Suggested research priorities include the following:

- Develop new methods for disseminating new technology and exnovating ineffective or inefficient practices
- Develop alternative methods to assess health and well-being and use these data to assess outcomes
- Articulate and fund a seamless path of research from basic to intervention development to translation
- Conduct research to address health disparities that considers linkages to non-health factors, such as housing, transportation, and secure environments

• Develop new research designs to study the social determinants of health

Closing Remarks

NIH and Health Economics
James Poterba, Massachusetts Institute of Technology and the National Bureau of Economic Research

The research presented over the past 2 days is a testament to the contributions of NIH-funded health economics research over the past several decades. NIH research funding has impacted the study of economics and the economics profession. NIA supported economics research in the context of the study of aging Americans beginning in the mid-1980s, and this changed how economists behave and what they study. A sustained commitment from NIA and a level of research support commensurate with the important problems being addressed were key factors in the successful contributions of economics research to the NIH mission. Over the past 30 years, we have seen a remarkable advance in the level and quality of the NIH-funded health economics research.

The field of economics research is well-positioned to contribute to the mission of NIA and several other Institutes and Centers because it incorporates a life-course approach. NIH’s support for team science has been a powerful engine for economic research. Economists had to learn how to build teams and harvest capacity in a productive and powerful way. One component of this was NIH’s early support for postdoctoral training to support talented economists in the formative phase of their career, leading to a denser network of postdocs today.

NIH has also been willing to recognize new tools and techniques. NIA’s continued support for the Health and Retirement Study (HRS) is one example. The HRS features an interdisciplinary study design with multiple disciplines contributing to determining priorities and identifying the tradeoffs. The HRS is used in hundreds of publications because a dense network of researchers can process the information as soon as it becomes available.

The NIH program officers pushed economists to work with researchers in different disciplines. A quick look at the list of coauthors on NIH-funded research shows how different groups come together to meld their insights to address problems. Economic analysis has been integrated into clinical research, and clinicians have learned to incorporate economists and economic methods. Economic research might not yield a new treatment, but it can contribute to favorable health outcomes through behavior change interventions. The recognition of simple tradeoffs that are second nature to economists has made its way to core parts of the U.S. medical world. Victor Fuchs’ comment, “The economic perspective alone is rarely sufficient for good policy-making, but it is usually necessary. To neglect it, to assume that resources are unlimited or that human behavior is insensitive to changes in incentives and constraints, is often an invitation to disaster,” shows how far we have come. The NIH deserves great credit for the transformation of the field.
The Health Economics Common Fund Program

Richard Hodes, National Institute on Aging

NIA has come to appreciate the value of health economics over the past 25 years, and it is now integral to what the Institute supports. The Health Economics Common Fund Program was conceived during a meeting in May 2010 on NIH research priorities for health care reform, in which the role of health economics was a controversial topic. NIH staff across multiple Institutes and Centers were galvanized by this opportunity to recognize the importance of health economics as part of NIH’s core mission. The ability to analyze health outcomes and health-relevant parameters and to identify causalities and translate them into insights and interventions is vital to the NIH research enterprise, now and into the future. The Health Economics Common Fund Program will formally end as all Common Fund programs do, but it has left a legacy of strengthened integration of economic research into the NIH mission as well as the mission of several individual Institutes and Centers.
## Appendix A: Agenda

### Thursday, September 28, 2017

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<th>Time</th>
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<td>9:00 a.m.</td>
<td>Welcome                                                                 Sarah Q. Duffy</td>
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<tr>
<td>9:10</td>
<td><strong>PANEL 1: LIFE CYCLE OF INNOVATIONS IN THE HEALTH SECTOR (Chair: John Haaga)</strong></td>
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<tr>
<td>9:10</td>
<td>How Incentives Determine What Gets Developed at All                      Bhaven Sampat</td>
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<tr>
<td>9:30</td>
<td>What Affects the Diffusion of New Technology?                           Haiden Huskamp Sharon-Lise Normand</td>
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<td>9:50</td>
<td>The Difficulty of Getting Rid of Ineffective Technology                  Jonathan Skinner</td>
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<td>10:10</td>
<td>Panel 1 Discussant Remarks                                              Dana Goldman</td>
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<td>10:20</td>
<td>Panel 1 General Discussion</td>
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<td>10:40</td>
<td><strong>BREAK</strong></td>
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<td>10:55</td>
<td><strong>PANEL 2: THE VALUE OF INFORMATION FROM (AND FOR) HEALTH RESEARCH (Chair: Robert Carter)</strong></td>
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<tr>
<td>11:15</td>
<td>The Promise of Real World Data                                          Anirban Basu</td>
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<td>11:35</td>
<td>Adverse Effects of Information in Health IT                              David Chan</td>
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<td>11:55</td>
<td>Panel 2 Discussant Remarks                                              Bruce Weinberg</td>
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<tr>
<td>12:05 p.m.</td>
<td>Panel 2 General Discussion</td>
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<td>12:25</td>
<td><strong>LUNCH</strong></td>
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<td>1:25</td>
<td><strong>PANEL 3: ECONOMIC ANALYSIS AND PRECISION MEDICINE (Chair: Doug Lowy)</strong></td>
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<td>1:25</td>
<td>Demand for Personalized Medicine and Implications for Research Prioritization  David Veenstra Josh Carlson</td>
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<td>1:45</td>
<td>Oncotype Testing as a Case Study for Personalized Medicine             Scott Ramsey Jeanne Mandelblatt</td>
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<td>2:05</td>
<td>Heterogeneity of Treatment Effects</td>
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<td>2:45</td>
<td>Panel 3 Discussant Remarks</td>
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<td>2:55</td>
<td>Panel 3 General Discussion</td>
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<tr>
<td>3:15</td>
<td><strong>BREAK and Demonstrations of Data Resources</strong></td>
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<td><strong>Supported by the Common Fund Program</strong></td>
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<td>Diffusion of Medical Procedures and Technology</td>
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<td>RIGHT Simulation Web Tool</td>
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<td>PM-specific Diffusion Estimates</td>
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<td>State Health Practice Database for Research</td>
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<td>3:45</td>
<td><strong>ROUNDTABLE DISCUSSION: Health Economics Research Priorities at HHS</strong></td>
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<td>5:00</td>
<td><strong>ADJOURN</strong></td>
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**Friday, September 29, 2017**

<table>
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<tr>
<th>Time</th>
<th>Session Title</th>
<th>Presenter(s)</th>
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<tbody>
<tr>
<td>8:30 a.m.</td>
<td>Welcome</td>
<td>John Haaga</td>
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<tr>
<td>8:40</td>
<td>Present Bias, Behavioral Science, and Health</td>
<td>David Laibson</td>
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<tr>
<td>9:00</td>
<td>Discouraging Smoking by Low-income Populations: Applications to Food Choices</td>
<td>Jody Sindelar</td>
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<td>9:20</td>
<td>Encouraging Guideline-appropriate Treatments</td>
<td>Jason Doctor</td>
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<td>9:40</td>
<td>Applying Behavioral Economics in Health Improvement Programs</td>
<td>Kevin Volpp</td>
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<td>10:00</td>
<td>Workplace Wellness Promotion</td>
<td>Damon Jones</td>
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<td>10:20</td>
<td>Panel 4 Discussant Remarks</td>
<td>Donald Kenkel</td>
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<td>10:30</td>
<td>Panel 4 General Discussion</td>
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10:50          BREAK

PANEL 5: ECONOMIC APPROACHES TO UNDERSTANDING HEALTH OUTCOMES (Chair: Della Hann)

11:00          Declining Inequality in Mortality Among the Young           Janet Currie
11:20          Worsening Health for the Middle Aged                         Anne Case
11:40          The Opioid Epidemic and State Intervention Strategies         Dhaval Dave
12:00 p.m.     Panel 5 Discussant Remarks                                  Kosali Simon
12:10          Panel 5 General Discussion

CLOSING REMARKS

12:30          NIH and Health Economics                                   James Poterba
12:45          The Health Economics Common Fund Program                   Richard Hodes
1:00           ADJOURN
Appendix B: Participant List

Health Economics Common Fund Working Group Chair and Coordinators

Richard J. Hodes, National Institute on Aging, Chair
Sarah Q. Duffy, National Institute on Drug Abuse, Co-coordinator
John G. Haaga, National Institute on Aging, Co-coordinator

Invited Speakers

Sharon Arnold, Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services
Anirban Basu, University of Washington
Marie Bernard, National Institute on Aging
Ernst Berndt, Massachusetts Institute of Technology
Josh Carlson, University of Washington
Robert Carter, National Institute of Arthritis and Musculoskeletal and Skin Diseases
Anne Case, Princeton University
David Chan, Stanford University
Janet Currie, Princeton University
Dhaval Dave, Bentley University and the National Bureau of Economic Research
Jason Doctor, University of Southern California
Dana Goldman, University of Southern California
Patricia A. Grady, National Institute of Nursing Research
John Graham, Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services
John Graves, Vanderbilt University
Della Hann, Eunice Kennedy Shriver National Institute of Child Health and Human Development
Haiden Huskamp, Harvard University
Damon Jones, University of Chicago
Donald Kenkel, Cornell University
David Kent, Tufts Medical Center
David Kim, Tufts Medical Center
David Laibson, Harvard University
Douglas Lowy, National Cancer Institute
Jeanne Mandelblatt, Georgetown University
Mark McClellan, Duke University
David O. Meltzer, University of Chicago
Peter Neumann, Tufts Medical Center
Sharon-Lise Normand, Harvard University
Josh Peterson, Vanderbilt University
James Poterba, Massachusetts Institute of Technology and the National Bureau of Economic Research
Scott Ramsey, Fred Hutchinson Cancer Research Center
Bhaven Sampat, Columbia University
Kosali Simon, Indiana University
Jody Sindelar, Yale University
Jonathan Skinner, Dartmouth College
David Veenstra, University of Washington
Kevin Volpp, University of Pennsylvania
Bruce Weinberg, Ohio State University

National Institutes of Health Staff

Susan Azrin, National Institute of Mental Health
Partha Bhattacharyya, National Institute on Aging
Gregory Bloss, National Institute on Alcohol Abuse and Alcoholism
Cheryl Boyce, National Heart, Lung, and Blood Institute
Nancy Breen, National Institute on Minority Health and Health Disparities
Regina Bures, Eunice Kennedy Shriver National Institute of Child Health and Human Development
David Chambers, National Cancer Institute
Juanita Chinn, Eunice Kennedy Shriver National Institute of Child Health and Human Development
Rebecca Clark, Eunice Kennedy Shriver National Institute of Child Health and Human Development
Leslie Derr, Office of the Director
Prisca Fall, National Institute on Aging
Michelle Hamlet, National Institute of Nursing Research
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