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***PROMOTING HEALTHCARE INNOVATION ON THE DEMAND
SIDE***

*REBECCA S. EISENBERG
W. NICHOLSON PRICE II*

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PROMOTING HEALTHCARE INNOVATION ON THE DEMAND SIDE

Rebecca S. Eisenberg[†] & W. Nicholson Price II[‡]

ABSTRACT

Innovation policy often focuses on the incentives of firms that sell new products. But optimal use of healthcare products also requires good information about the likely effects of products in different patients, and it is hard to provide the right incentives for producers to develop and disclose information that could limit future sales. Regulation partially fills this gap by requiring sellers to conduct clinical trials and report adverse events. But it is inherently problematic to rely on producers to supply negative information about their own products.

Healthcare payers, however, can profit from avoiding inappropriate use of costly technologies. Recent technological advances enable insurers to innovate by analyzing their data about healthcare provision and outcomes. The federal government seeks to promote this sort of innovation through a series of initiatives; some picture insurers as passive data repositories, while others provide opportunities for insurers to innovate more directly.

In this paper, we examine the role of health insurers in developing new knowledge about the provision of quality healthcare—what we call “demand-side innovation.” We address the contours of this underexplored area of innovation and describe the behavior of participating firms. We examine the legal rules surrounding privacy and their effects on this research, and consider the effect of market structures and intellectual property rules on incentives for demand-side innovation. Throughout, we highlight the multi-pronged way that government facilitates payer innovation, apart from the traditional tools of innovation policy.

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INTRODUCTION

Policy mechanisms to promote biopharmaceutical innovation often focus on fortifying incentives for firms to develop new products. Pharmaceutical firms favor exclusionary rights that defer competition, allowing them to profit by charging higher prices prior to generic entry. In

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addition to providing patent term extensions for developers of new drugs,¹ Congress has repeatedly provided for periods of regulatory exclusivity to encourage the same firms to collect and submit data about the effects of their products in patients.² Providing better information about these effects is an important form of innovation that distinguishes warfarin as a therapeutic anti-coagulant for use in humans from the same substance as rat poison.³ But it is problematic to rely on product-developing firms to provide this information, because although they might profit from favorable information, they stand to lose from disclosure of negative information about their own products. Regulatory mandates require sellers to produce data from rigorous clinical trials showing that their products are safe and effective as a condition for approval of new drugs.⁴ But side effects are difficult to observe in clinical trials of limited scope and duration. Often the bad news only comes to light after products have been widely used; if the news is bad enough it may lead to the withdrawal of previously approved products from the market.⁵ But the adverse events reporting system⁶ that FDA has long relied upon as its principal source of bad news after approval is haphazard and unreliable.⁷

Healthcare payers,⁸ on the other hand, stand to profit from the bad news. Information that an expensive drug has harmful side effects, or that it does not work for many of the patients currently taking it, could lead to more sparing use of these products, reducing healthcare costs while improving quality of care. The incentives of payers to cut costs could be a

¹ 35 U.S.C. § 156.

² These provisions include five years of regulatory exclusivity for submitting data showing safety and efficacy for a new chemical entity, 21 U.S.C. § 355(j)(5)(F)(ii); three years for submitting data supporting a new use or product change that requires clinical trials, 21 U.S.C. § 355(j)(5)(F)(iv); twelve years for showing safety and efficacy for a new biologic, 42 U.S.C. § 262(k)(7); five years for showing safety and efficacy for a new qualified infectious disease product that targets any of a variety of resistant organisms, 21 U.S.C. § 355f; and six months for submitting data from clinical trials in children, 21 U.S.C. § 355a.

³ Douglas Wardrop & David Keeling, *The story of the discovery of heparin and warfarin*, 141 BRITISH J. HAEMATOLOGY 757–763 (2008).

⁴ 21 U.S.C. §§ 355(b)(1)(A), 355(d).

⁵ 21 U.S.C. § 355(e).

⁶ 21 C.F.R. § 314.80.

⁷ See, e.g., Fontanarosa PB et al., *Postmarketing Surveillance—Lack of Vigilance, Lack of Trust*, 292 J. AM. MED. ASSOC. 2647 (2004). 2007 legislation gave FDA greater powers and duties with respect to monitoring and disclosing postapproval risks, including authority to establish the Sentinel system discussed in greater detail *infra* in Part II.B.2.

⁸ We use the term “payer” to refer to third parties who pay for health treatment. The term includes private insurers, public payers like Medicare and Medicaid, and integrated health systems like Kaiser Permanente that provide both care and insurance.

counterweight to the incentives of product sellers to maximize their own patent-protected profits.

Recent advances in information technology and genomics have put healthcare payers in an excellent position to play a larger role in future innovation to improve healthcare through better understanding of the effects of medical treatment. Insurance companies and integrated healthcare providers have custody of a treasure trove of data about healthcare provision and outcomes that can yield valuable insights about how to improve the quality of healthcare and lower its costs. Some integrated healthcare systems have seized upon this advantage to make notable discoveries about the effects of particular products that have changed the standard of care.

Studying the consequences of past clinical care to improve healthcare practice is an important research frontier with the potential to yield valuable innovations. Although it is easier to recognize innovation when a new product is introduced than when new information leads to more sparing use or even withdrawal of existing products from the market, in both cases new knowledge is put to use to improve the quality of healthcare. Both are socially valuable forms of innovation. But the distribution of benefits from the two forms of innovation is quite different. Much of the social value of new products accrues to product sellers, at least when they are protected from competition by patents and regulatory exclusivity. On the other hand, when further knowledge leads to more parsimonious use of existing products, the benefit is captured on the demand side by payers and by patients who save money and improve health by using less of these products.

Healthcare payers enjoy several advantages that allow them to complement the role of product-developing firms as providers of information about the effects of healthcare products. First, payers have access to large volumes of data from administrative claims and healthcare records that reveal healthcare consequences. Second, payers have an incentive to reduce healthcare costs rather than to increase them, providing a counterweight to the incentives of product-developing firms. Third, the observational studies that payers can pursue are cheaper than the controlled clinical trials that swell the R&D budgets of product-developing firms. Fourth, although randomized, controlled clinical trials have long been considered the gold standard for studying treatment effects free of selection bias, healthcare records may provide much larger datasets and observations over longer periods of time, and can thus shed light on questions that clinical trials leave unresolved.

The standard policy toolkit for promoting biomedical innovation offers little in the way of direct benefits to these “demand side innovators,”

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although the exclusive rights that the legal system awards to developers of new products may give payers an indirect incentive to learn more about whether these products are worth their high costs. Rather than providing payers with their own exclusive rights, the federal government has used a variety of different mechanisms to promote the use of data from healthcare records as a source of ongoing innovation. These mechanisms include agency initiatives to use healthcare records for regulatory and research purposes, such as FDA's Sentinel System and NIH's eMERGE consortium. They also include new legislation to support these initiatives⁹ and agency rulemaking to address obstacles to research use of healthcare records.¹⁰ Although some of these initiatives picture payers primarily as repositories of data that others might analyze, they also provide opportunities for insurers to become more fully engaged as partners in healthcare innovation. Healthcare payers engage in medical innovation to an extent that is largely unrecognized in the legal scholarship on innovation. Nevertheless, they could potentially do much more.

This paper proceeds in three Parts. In Part I, we address the contours of this underexplored area of innovation, and describe the resources and opportunities available to payers. We show how payers are unable to claim rewards for pursuing those opportunities from the usual IP toolkit of patents and trade secrecy. Part II considers technical obstacles to medical innovation by payers, focusing on the challenges of making payer data useful for research, and government initiatives that have helped the industry begin to address those challenges. In Part III, we examine legal privacy barriers to using and assembling information, and administrative and legislative avenues to lowering those barriers. Throughout, we highlight the multi-pronged way that government facilitates payer innovation without relying on exclusionary rights. Although these "demand side innovators" do not directly benefit from the exclusionary rights favored by pharmaceutical firms, they have nonetheless benefited from a variety of government initiatives that have lowered the legal and technical barriers to innovation while building collaborative networks to share information and expertise.

⁹ See, e.g., the Food and Drug Administration Amendments Act of 2007, Pub. L. 110-85, 121 Stat. 823; the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009, enacted under Title XIII of the American Recovery and Reinvestment Act of 2009, Pub. L. 111-5, 123 Stat. 115; the Affordable Care Act of 2010, Pub. L. 111-148, 124 Stat. 119; and the Food and Drug Administration Safety and Innovation Act of 2012, Pub. L. 112-144.

¹⁰ See, e.g., recent HHS modifications to the HIPAA Privacy Rule, discussed *infra* Part III.C.

I. INNOVATION BY HEALTH-CARE PAYERS

While payers may lack the scientific labs of pharmaceutical companies and the front-line patient interactions of practicing physicians, they have access to valuable health data that can shed light on questions about what works in different clinical contexts and in different kinds of patients. These data give payers an advantage in innovation to improve the choice of appropriate treatments. This Part describes the innovation landscape for payers. It begins by giving two examples of payer innovation that fit poorly in a regulatory regime that was designed for the use of product-developing firms. Next, it briefly canvasses the innovation resources and opportunities available to payers, with a focus on research questions that payers might be better positioned to address than product-developing firms. It concludes by considering the standard toolkit of innovation incentives from the perspective of innovating payers.

A. Examples

Two extended examples highlight both the potential benefits of payer innovation and the limited opportunities for payers to inform regulatory decisions in a legal regime designed for innovation by drug-developing firms. The first involves a request by payers to FDA to switch the terms of approval for the antihistamines Allegra, Claritin, and Zyrtec from prescription (Rx) to over-the-counter (OTC) sales. The second tells the story of the painkiller Vioxx, and illustrates the reluctance of FDA to use data from payer records rather than from drug company clinical trials to establish toxic side effects in a previously approved product. It is no coincidence that both involve widely prescribed, patent-protected blockbuster products that were costing payers a lot of money.

1. Rx-to-OTC Switch: Non-sedating antihistamines

The first example illustrates the divergent interests of payers and drug manufacturers in the context of regulatory approval for switching drugs from prescription (Rx) to OTC sales.¹¹ An Rx-to-OTC switch can be a

¹¹ The Food, Drug and Cosmetic Act provides that a drug which “is not safe for use except under the supervision of a practitioner licensed by law to administer such drug” or which is limited by the terms of its regulatory approval to use under the professional supervision of such a practitioner shall be dispensed by prescription only. 21 U.S.C. § 353(b). For a discussion of how FDA implements the distinction between Rx and OTC drugs, see Holly M. Spencer, *The Rx-to-OTC Switch of Claritin, Allegra, and Zyrtec: An*

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significant cost-lowering innovation for at least two reasons.¹² First, it permits patients to treat themselves without incurring the costs and delays associated with seeing a doctor for a prescription. Second, it often leads to a significant price reduction for the drug itself, because health insurance typically covers Rx but not OTC drugs and cost-sensitive patients may be unwilling to pay the high prices that drug companies charge insurance companies.¹³

In 1998, Blue Cross of California (later Wellpoint) submitted a petition to FDA asking it to permit OTC sales of nonsedating antihistamines sold under the brand names Allegra, Claritin, and Zyrtec.¹⁴ Blue Cross/Wellpoint argued that nonsedating antihistamines were safer than older antihistamines, already available OTC, which had significant sedative side effects. According to the petition, the lack of OTC access to the safer nonsedating products “results in a greater incidence of side effects associated with the OTC alternatives adding considerable unnecessary medical costs to the health care system.” Of course, the switch would also save costs for Blue Cross/Wellpoint by allowing patients to purchase their own nonsedating antihistamines out of their own pockets in the OTC market rather than using insurance to pay for doctor visits and prescriptions.

Unprecedented FDA Response to Petitioners and the Protection of Public Health, 51 AM. U. L. REV. 999, 1011-18 (2002).

¹² For an estimate of cost savings from the availability of OTC drugs, see Consumer Healthcare Products Ass’n, *The Value of OTC Medicine to the United States* (2012), <http://www.chpa.org/ValueofOTCMeds2012.aspx> (estimating drug cost savings of approximately \$25 billion per year and clinical visit cost savings of approximately \$66 billion per year). Because drug companies often seek an Rx-to-OTC switch at the same time that they lose patent protection for a drug, it is not always clear how much of a price reduction is a consequence of the switch itself and how much is a result of competition following the loss of patent protection. At a minimum one would expect the lower costs of dispensing OTC products relative to that for Rx products to lead to some price reduction. On the other hand, from the perspective of consumers, the out-of-pocket cost of an OTC drug may exceed the out-of-pocket cost for the co-pay on a prescription drug that is otherwise covered by insurance. See Joshua P. Cohen, Cherie Paquette & Catherine P. Cairns, *Switching prescription drugs to over the counter*, 330 BRITISH MED. J. 39–41 (2005) (concluding that switching drugs to OTC availability reduces insurers’ prescription drug costs but increases the costs for most patients); cf. Peter Temin, *Realized Benefits from Switching Drugs*, 35 J.L. & ECON. 351-369 (1992) (concluding that OTC switches have both reduced costs and increased consumer welfare).

¹³ Cohen et al., *supra* note 12 (noting in survey of 12 managed care organizations “a strong tendency to remove switched drugs from the formulary and raise copayments of prescription drugs in the same class” following an OTC switch).

¹⁴ Letter dated July 21, 1998 from Robert C. Seidman to Dockets Management Branch, Food & Drug Admin., Docket 98P-0610 (1998), <http://www.fda.gov/ohrms/dockets/dockets/98p0610/cp00001.pdf>.

The product manufacturers opposed the switch, arguing that Blue Cross/Wellpoint had failed to submit adequate supporting data to establish the safety and efficacy of the nonsedating products when used without the supervision of a physician.¹⁵ While it may seem odd for product manufacturers to warn regulators about the potential hazards of their products, in this case it was entirely consistent with their own financial interests. Drug manufacturers typically wait to seek approval for an Rx-to-OTC switch until the drug approaches the end of its patent life, when generic competition is about to erode profits. At that point, the firm may seek to mitigate the loss of revenue by invoking a statutory incentive of exclusivity for conducting further clinical trials to support a change in the terms of regulatory approval.¹⁶ If further clinical trials are “essential” to FDA approval of an application for the switch, the manufacturer is entitled to three years of exclusivity before FDA will approve a generic product for OTC sales.¹⁷ This supplemental exclusivity gives the branded product a 3-year head start in the OTC market. A switch prior to patent expiration would surrender more lucrative exclusivity in the Rx market in exchange for less lucrative exclusivity in the OTC market, and would hasten the arrival of full competition by allowing the OTC exclusivity to run during the patent term. But because the statute authorizes further exclusivity only if new clinical trials are essential for approval, and not if it is already apparent that the product is safe for OTC sale without further study, the manufacturers had to persuade FDA that more data were necessary to support the switch. In other words, the Blue Cross/Wellpoint petition not only threatened to end payer coverage of nonsedating antihistamines, but also undermined the case for three years of exclusivity in the OTC market.

¹⁵ See letter dated Jan. 15, 1999 from Alexander R. Jacquinto to Dockets Management Branch, Food & Drug Admin., Docket 98P-0610 (1999), <http://www.fda.gov/ohrms/dockets/dockets/98p0610/c000004.pdf>; Schering Plough Research Institute, Briefing Book (April 12, 2001), http://www.fda.gov/ohrms/dockets/ac/01/briefing/3737b_15_schering-plough.pdf.

¹⁶ 21 U.S.C. § 355(c)(3)(E)(iii)

¹⁷ The statute provides in pertinent part:

If a supplement to [a previously approved new drug application or NDA] is approved after September 24, 1984, and the supplement contains reports of new clinical investigations ... essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, [FDA] may not make the approval of an application submitted under this subsection [i.e., an Abbreviated New Drug Application seeking approval to market a generic version without having to repeat the showing of safety and efficacy in the original NDA] for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement

21 U.S.C. § 355(j)(5)(F)(iv).

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FDA asked an advisory committee whether nonsedating antihistamines “could be used appropriately and safely by consumers without the intervention of a learned intermediary,”¹⁸ and the committee concluded that they could.¹⁹ But although FDA seemed to have the authority to make such a switch on the petition of a payer,²⁰ it was unprecedented and controversial to grant such a petition over the objection of the drug manufacturer.²¹ The more traveled pathway was for the manufacturer to initiate an OTC switch by filing a supplemental new drug application at a time of its choosing. And sure enough, Schering-Plough filed its own application for an Rx-to-OTC switch for Claritin—the first of the nonsedating antihistamines to face patent expiration—eleven months after opposing the Blue Cross/Wellpoint petition on the ground that the data were insufficient to support such a switch.²² FDA approved the Schering-Plough application on November 27, 2002, without ruling on the Blue Cross/Wellpoint petition.²³ The patent protecting Claritin expired three weeks later.²⁴

This episode shows how the interest of payers in reducing healthcare costs diverges from the interest of product manufacturers in maximizing revenues, making payers more eager to pursue a cost-lowering innovation (such as an Rx-to-OTC switch) that a manufacturer would rather defer. The statutory incentive of regulatory exclusivity may eventually motivate a manufacturer to conduct clinical trials and to pursue an Rx-to-OTC switch just prior to patent expiration. But payers might find it worthwhile to pursue this innovation more promptly and without the need for propping up prices

¹⁸ Food & Drug Admin., *FDA Overview of Issues for the Joint Nonprescription Drugs Advisory Committee and the Pulmonary-Allergy Drugs Advisory Committee* (May 11, 2001), http://www.fda.gov/ohrms/dockets/ac/01/briefing/3737b_02_overview.pdf.

¹⁹ *Claritin Approval Marks Significant Shift in Rx-to-OTC Switches*, 666 FOOD & DRUG LETTER, (Dec. 20, 2002), <https://www.rahasia.biz/reading/claritin-approval-marks-significant-shift-in-rx-to-otc-Myvf.html>.

²⁰ The statute provides that FDA “may by regulation remove drugs ... from the [Rx only] requirements when such requirements are not necessary for the protection of the public health.” 21 U.S.C. § 353(b)(3). FDA regulations authorize either the FDA Commissioner or “any interested person” to petition for a switch:

A proposal to exempt a drug from the prescription-dispensing requirements of section 503(b)(1)(C) of the act may be initiated by the Commissioner or by any interested person. Any interested person may file a petition seeking such exemption, which petition may be pursuant to part 10 of this chapter [which governs citizen petitions such as that submitted by Blue Cross/Wellpoint], or in the form of a supplement to an approved new drug application.”

²¹ C.F.R. § 310.200(b).

²² See *id.*; Spencer, *supra* note 11.

²³ Spencer, *supra* note 11, at 1023–24.

²⁴ Melody Peterson, *Claritin to Sell Over the Counter*, N.Y. TIMES (Nov. 28, 2002).

²⁵ *Id.*

through regulatory exclusivity. Moreover, because they do not stand to gain from persuading FDA that costly clinical trials are necessary to support a switch, payers may be willing to show safety at lower cost by consulting their own data generated from clinical experience with the drug without unnecessary clinical trials.²⁵

2. Post-Approval Studies

The second example concerns exposure of a toxic side effect of the blockbuster drug Vioxx through research in health records of the integrated healthcare provider Kaiser Permanente. Vioxx is a selective Cox-2 inhibitive non-steroidal anti-inflammatory drug (NSAID) for relieving pain and inflammation without the gastric side effects of an earlier generation of NSAIDs (such as aspirin and ibuprofen).²⁶ The manufacturer Merck voluntarily withdrew Vioxx from the market in the fall of 2004, at a time when it was selling \$2.5 billion per year, in the face of mounting evidence that Vioxx was causing fatal heart attacks.²⁷

Data from Merck-sponsored clinical trials comparing Vioxx to naproxen (one of the older generation of NSAIDs) had previously shown more heart attacks (as well as fewer gastric side effects²⁸) in patients taking Vioxx²⁹, but Merck had argued that the difference in heart attacks reflected a protective effect of naproxen rather than a toxic effect of Vioxx.³⁰ FDA was not convinced,³¹ and Merck agreed to provide warnings about cardiovascular risks while it continued to monitor cardiovascular safety in

²⁵ The data submitted by Blue Cross/Wellpoint primarily concerned the risks posed by the sedating effects of the earlier antihistamines that were already available in the OTC market, including a study from the National Transportation Safety Board of deaths from traffic accidents involving drivers who had used sedating antihistamines. *Id.* at 1019–1021.

²⁶ See Statement of Sandra Kweder, M.D., Deputy Director, Office of New Drugs, Center for Drug Evaluation and Research, U.S. Food & Drug Admin., before the Senate Comm. On Finance, (Nov. 18 2004) [Kweder testimony], <http://www.fda.gov/newsevents/testimony/ucm113235.htm>.

²⁷ U.S. FOOD & DRUG ADMIN., VIOXX (ROFECOXIB) QUESTIONS AND ANSWERS (Sept. 30, 2004), <http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm106290.htm>.

²⁸ See Claire Bombardier et al., *Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 N. ENG. J. MED. 1520–28 (2000).

²⁹ See Memorandum from Shari L. Targum to Sandra Cook re Consultation NDA 21-042, S-007 Review of cardiovascular safety database (Feb. 1, 2001), http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_06_cardio.pdf.

³⁰ *Id.*, at 1526–27.

³¹ Memorandum from Shari L. Targum, *supra* note 29, at 34–35.

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additional clinical trials of Vioxx for new indications.³² Meanwhile, millions of patients took Vioxx, many of whom were at low risk of gastric side effects and could have received the same benefits at less risk and at lower cost from one of the older nonselective NSAIDs.³³

While Merck's clinical trials proceeded, Dr. David Graham from the FDA Office of Drug Safety began a collaborative study with Kaiser Permanente comparing health records of patients who took Vioxx with those who took other NSAIDs. That study showed significantly more heart attacks in the Vioxx patients,³⁴ leading Kaiser Permanente to reconsider whether to provide coverage of Vioxx.³⁵ But according to Dr. Graham's Congressional testimony, FDA sought to suppress publication of the study.³⁶ Dr. Graham explained that FDA's primary institutional mission is approving new drugs, not re-evaluating already approved drugs. Moreover, FDA has long favored clinical trials over observational studies.³⁷ Both of these factors favor reliance on the data submitted by drug companies over that coming from other sources with different motivations.

In the case of Vioxx, the same cardiovascular effects that showed up in the Kaiser Permanente data were becoming too clear to overlook even in data from ongoing Merck clinical trials.³⁸ Shortly after the Kaiser

³² Kweder testimony, *supra* note 26.

³³ Carolanne Dai et al., *National Trends in Cyclooxygenase-2 Inhibitor Use Since Market Release: Nonselective Diffusion of a Selectively Cost-effective Innovation*, 165 ARCH. INTERN. MED. 171-177 (2005). Merck later paid substantial criminal fines for "misbranding" Vioxx by promoting and marketing it beyond the scope of FDA-approved uses. U.S. Justice Dept. Press Release, U.S. Pharmaceutical Company Merck Sharp & Dohme Sentenced in Connection with Unlawful Promotion of Vioxx (April 19, 2012), <http://www.fda.gov/ICECI/CriminalInvestigations/ucm301329.htm>.

³⁴ Kweder testimony, *supra* note 26; David J. Graham et al., *Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclooxygenase-2 selective and nonselective non-steroidal anti-inflammatory drugs: nested case-control study*, 365 LANCET 475-481 (2005).

³⁵ Anna Wilde Matthews & Scott Hensley, *Big HMO Reconsiders Vioxx After Study Points to Heart Risks*, WALL ST. J. (August 26, 2004), <http://www.wsj.com/articles/SB109346588678101103?cb=logged0.44817835511639714>.

³⁶ Testimony of David J. Graham before the Senate Finance Committee (Nov. 18, 2004), <http://www.finance.senate.gov/imo/media/doc/111804dgttest.pdf>. According to Dr. Graham's testimony, the Director of the FDA Office of New Drugs sent him an email suggesting that "since FDA was 'not contemplating' a warning against the use of high-dose Vioxx, my conclusions should be changed," *id.* at 3.

³⁷ *Id.* at 4.

³⁸ Robert S. Bresalier et al., *Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial*, 352 N. ENG. J. MED. 1092-1102 (2005). The Merck-sponsored study was designed primarily to show that Vioxx was effective in preventing recurrent colon polyps rather than to measure cardiovascular side effects.

Permanente data were presented at an international conference, Merck voluntarily agreed to withdraw Vioxx from the market,³⁹ and under the intense glare of Congressional and media attention, FDA allowed Dr. Graham to publish the Kaiser-Permanente study in a leading medical journal.⁴⁰ Once again, FDA took no action until the drug manufacturer came around to the same conclusion as the payer.

The Vioxx episode showed the potential of large-scale observational studies to illuminate questions that were left ambiguous in data from drug company clinical trials. Healthcare payers have the necessary data for observational studies and face different incentives than drug companies. The availability of data that is not controlled by the drug companies opens the door to analysis that is free of the possible distortions and wishful thinking of a company that is making billions of dollars a year selling a blockbuster product. FDA has long treated data from clinical trials as proprietary information belonging to the drug company that paid for the trials, and has therefore prevented public scrutiny of the data. But data from patient health records are not under the proprietary control of the drug companies and could be analyzed by other parties with different interests, such as Kaiser Permanente and its collaborators.

B. Resources

Payers possess tremendous amounts of valuable health data about individuals. At this time, the longest-term and most readily available form of payer data is administrative claims data. These data include the information necessary to process payment claims, providing a view of medical encounters over time. Administrative claims data typically record diagnoses and treatments for patients, hospital admissions and releases, tests performed and their results, prescriptions filled, and professional services provided, as well as demographic information about patients (such as age, sex, and location) and the identities of providers.⁴¹

Payers also frequently have access to other data sources that can supplement administrative claims data. They typically have prescription payment records that reveal when patients actually pick up and pay for drugs (as opposed to merely getting the prescription), and when they refill

³⁹ Kweder testimony, *supra* note 26

⁴⁰ Thomas H. Maugh II, *Banned Report on Vioxx Published*, L.A. TIMES (Jan. 25, 2005), <http://articles.latimes.com/2005/jan/25/science/sci-vioxx25>.

⁴¹ Sebastian Schneeweiss & Jerry Avorn, *A Review of Uses of Health Care Utilization Databases for Epidemiologic Research on Therapeutics*, 58 J. CLIN. EPIDEMIOL. 323, 323 (2005).

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prescriptions. Payers typically know when patients are referred to specialists and why. They may have access to laboratory test results under contracts with laboratory test providers, especially when tests are performed by major national providers rather than in-house.⁴²

In addition, it is increasingly common for payers to have access to patient medical records generated by doctors and other caregivers. These records can provide richer data on treatment and outcomes than administrative claims data, although analyzing them can be challenging due to variability across providers in what is included and how they are written.⁴³

Integrated health systems that combine the functions of payer, health care coordinator, and health care provider are particularly likely to have access to medical records. Notable examples of integrated health systems include Kaiser Permanente;⁴⁴ Geisinger;⁴⁵ Highmark; Intermountain Healthcare;⁴⁶ and the Departments of Defense and Veterans Affairs.⁴⁷ In the Kaiser system, for example, members pay premiums to Kaiser and see doctors who are Kaiser employees in Kaiser offices or hospitals.⁴⁸ Integrated health systems may have centralized custody of records that are otherwise likely to be dispersed across multiple custodians in other parts of the healthcare system, reducing the need to gather data from multiple sources.⁴⁹ In the overall health system, a relatively small fraction of patients belong to integrated health systems, but these systems have been important participants in research to date using data from electronic health records.⁵⁰ Payers may use these data for their own research, provide them to other

⁴² Conversations with anonymous industry members and consultants.

⁴³ For a more detailed discussion of challenges with patient medical records, *see infra* Part II.A

⁴⁴ *See* www.kaiserpermanente.org

⁴⁵ *See* www.geisinger.org, www.highmark.com

⁴⁶ *See* www.intermountainhealthcare.org

⁴⁷ The Department of Defense's Tricare offers healthcare to 9.2 million eligible military personnel and families. <http://www.tricare.mil/stakeholders/statistics.cfm>. The Veterans Administration provides medical care to veterans and had 8.9 million enrollees in 2013. <http://www.va.gov/HEALTHPOLICYPLANNING/enroll02/Fnl925Doc.pdf>.

⁴⁸ *See* RICKEY HENDRICKS, A MODEL FOR NATIONAL HEALTH CARE: THE HISTORY OF KAISER PERMANENTE (1993).

⁴⁹ In integrated health systems, data formats and the difference between claims data and clinical data may differ from typical payer-only systems since claims data are not needed to actually pay claims, but rather for internal accounting and measurement purposes.

⁵⁰ Integrated health systems are not the only way to integrate; some entities, like Cal INDEX, are allowing payers to overcome barriers to integrate data without working in an integrated system. *See infra* notes 143–149 and accompanying text.

researchers, or enter into collaborations with others to use the data for innovation.⁵¹

C. Opportunities

Payers have the opportunity and incentive to engage in valuable forms of innovation that are under-provided by other innovators. Innovation based on payer data can improve the quality of care and decrease costs, potentially giving innovating firms competitive advantages and increased profits.⁵² In particular, payers stand to benefit from innovation to identify harmful effects of treatment and to compare different treatment options. This includes both traditional comparative effectiveness research and new research in personalized medicine enabled by advances in genomics and information technology. Payer innovation efforts like United Health's Optum⁵³ or Anthem's HealthCore⁵⁴ conduct both internal research and external work for other entities like pharmaceutical companies or other payers.⁵⁵ This innovation offers potential benefits for patients and payers alike.

1. Drug toxicity

Drugs frequently have a wide range of side effects that have not yet been fully identified at the time they are initially approved for sale. Payers are especially well positioned to identify these side effects, which may sometimes change the determination that the drug is safe and effective.

Side effects often go unnoticed before approval because of limitations in the clinical trial process. Clinical trials typically involve only a few thousand patients, and occur over the course of a few months to a few

⁵¹ Payers may either sell their data to nonpayers or enter into research collaborations with them. *See, e.g.*, www.healthcore.com/academic (describing academic collaboration with Anthem's HealthCore innovation unit and potential use of Anthem's data). In addition, Medicare provides a rich dataset of health information about its enrollees, but the scope of research on those data is circumscribed by the fact that Medicare is largely available only to the elderly and some non-elderly with disabilities.

⁵² Elsewhere, we discuss how various factors decrease insurer cost sensitivity, and acknowledge that these factors may decrease the incentive to innovate. *See infra* Part I.D.1.

⁵³ *See* Optum, *About Us*, <https://www.optum.com/about.html> (last visited July 16, 2015) ("As a health services and innovation company, we combine data and analytics with technology and expertise to power modern health care.").

⁵⁴ Healthcore, *Home*, www.healthcore.com (last visited Feb. 22, 2016).

⁵⁵ *See, e.g.*, www.healthcore.com/government, [/academics](http://www.healthcore.com/academics), [/life-science-companies](http://www.healthcore.com/life-science-companies), and [/payersproviders](http://www.healthcore.com/payersproviders) (listing opportunities for research and publications resulting from collaborations in various categories).

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years.⁵⁶ The relatively small test population means that drug developers are unlikely to observe toxicity that occurs only in a small fraction of patients, or in a population not included in the clinical trials.⁵⁷ Enrollment criteria for clinical trials often exclude patients who are pregnant or are taking other medications, for example, and therefore provide no information about the effects of the study drug in these patients.⁵⁸ Similarly the relatively short duration of clinical trials makes it difficult for developers to observe long-term effects of the drug. As a result, one in five approved drugs later receive at least one new “black-box warning”—the strongest type of warning—after approval.⁵⁹ Of the drugs that acquire black-box warnings after approval, it takes an average of 10 years before the effect is confirmed and the warning is added.⁶⁰

Once a drug has been approved and is in clinical use, payers begin to accumulate longer-term observational data that permit them to observe previously unnoticed drug toxicity effects. The Vioxx example illustrates the potential of this type of payer innovation.

Payer records are not the only way to learn of post-approval drug toxicity. Side effects may become apparent in the course of further clinical trials by the seller of the drug, as happened in Merck’s clinical trial of Vioxx for a new indication.⁶¹ Drug manufacturers, doctors, and patients

⁵⁶ In fact, drug developers have strong incentives to complete clinical trials as quickly as possible. Patents on the drug itself are typically filed very early in development, and the limited patent term means that time spent in clinical trials reduces the period of high-profit patent-protected sales. See ERIC BUDISH ET AL., DO FIXED PATENT TERMS DISTORT INNOVATION? EVIDENCE FROM CANCER CLINICAL TRIALS (National Bureau of Economic Research, 2013), available at <http://www.nber.org/papers/w19430> (finding that drug companies disproportionately focus on drugs with shorter clinical trial period times).

⁵⁷ See Jesse A. Berlin et al., *Adverse Event Detection in Drug Development: Recommendations and Obligations Beyond Phase 3*, 98 AM. J. PUBLIC HEALTH 1366 (2008).

⁵⁸ See Marshall Godwin et al., *Pragmatic Controlled Clinical Trials in Primary Care: The Struggle between External and Internal Validity*, 3 BMC MED. RES. METHODOL. 28 (2003); Greer Donley, *Encouraging Maternal Sacrifice: How Regulations Governing the Consumption of Pharmaceuticals During Pregnancy Prioritize Fetal Safety over Maternal Health and Autonomy*, NYU REV. L. & SOCIAL CHANGE 45 (2013).

⁵⁹ Sean Hennessy & Brian L. Strom, *Improving Postapproval Drug Safety Surveillance: Getting Better Information Sooner*, 55 ANNU. REV. PHARMACOL. TOXICOL. 75, 76 (2015).

⁶⁰ *Id.* at 76. Short durations of clinical trials may also obscure the actual health outcomes of interest, Jonathan J. Darrow et al., *New FDA Breakthrough-Drug Category — Implications for Patients*, 370 N. ENGL. J. MED. 1252, 1253–54 (2014), a problem that can also potentially be addressed by innovating payers using longer-term data.

⁶¹ See *supra* Part I.A.2.

may also report side effects to FDA.⁶² But this passive reporting system depends upon someone making a connection between the adverse event and the drug and going to the trouble of reporting it. Such reports are unlikely to provide information on increases in the frequency of otherwise common ailments, such as the cardiovascular side effects among patients who took Vioxx.⁶³

After the Vioxx episode, Congress fortified FDA's authority to require drug manufacturers to conduct postmarket surveillance studies.⁶⁴ At the same time, Congress directed FDA to establish a system for monitoring drug adverse events through use of health records, a mandate that FDA is implementing in its Sentinel program, discussed below.⁶⁵ Other international health agencies have similar programs.⁶⁶

But while these programs give regulators access to data from a network of payers, the data can only answer the queries that are submitted to it. FDA continues to rely primarily on adverse event reports to identify new risks. Payers with an interest in lowering the costs and improving the quality of healthcare have an opportunity to play an active role in identifying appropriate queries by scrutinizing their own data for evidence of drug toxicity, either ahead of regulators or in partnership with them.

2. Comparative effectiveness and cost-effectiveness

Payers are in an excellent position to study the comparative effectiveness or cost-effectiveness of different treatment interventions. Comparative effectiveness research compares health outcomes for

⁶² FDA maintains these reports in a database called the FDA Adverse Event Reporting System (FAERS) that it monitors for evidence of potential safety concerns. Doctors and patients may voluntarily report adverse events directly to FDA at <http://www.fda.gov/Safety/MedWatch/>, but the majority of voluntary information received by FDA comes through reports to drug manufacturers, which in turn must report adverse events to FDA. See 21 C.F.R. § 314.80, 21 U.S.C. § 355(k)(1) (requiring drug manufacturers to submit adverse event reports to FDA).

⁶³ Hennessy & Strom, *supra* note 59, at 77.

⁶⁴ Under the Food and Drug Administration Amendments Act of 2007, FDA was given statutory authority to require postapproval studies or clinical trials if passive and active surveillance will be insufficient to address known or potential serious risks. FDAAA § 901, codified at 21 U.S.C. § 355(o); see also FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: POSTMARKETING STUDIES AND CLINICAL TRIALS—IMPLEMENTATION OF SECTION 505 (O)(3) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT (2011). These provisions are more fully discussed *infra* at Part II.B.2.

⁶⁵ See *infra* Part II.B.2.

⁶⁶ See Hennessy & Strom, *supra* note 59, at 79–81 (listing large government-sponsored adverse-event population-surveillance databases).

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interventions; cost-effectiveness research further considers costs to determine which intervention buys more health for the money.⁶⁷ Comparing the effects of different interventions is a valuable form of research that is often neglected in the premarket stage. Premarket clinical trials typically compare a new drug with a placebo rather than with another intervention, unless the drug developer seeks approval to make specific marketing claims of superiority to alternative treatments,⁶⁸ and consequently provide little information about whether the new drug is better or worse than alternative treatments. Comparative effectiveness studies may involve clinical trials, in which researchers randomly assign patients to receive one drug or the other, or data-based observational studies, in which researchers observe differences in outcomes between matched populations of patients that received each course of treatment.

Payers, both public and private, are in a good position to conduct comparative effectiveness research through observational studies. As previously noted, they have access to large datasets of patient records, including information about diagnoses and drug prescriptions and purchases.⁶⁹ Although administrative claims data may not indicate how well the intervention worked (beyond such crude indicators as hospital readmissions), patient health records may include richer data about outcomes.

Moreover, cost-sensitive payers have strong incentives to perform comparative effectiveness—and especially cost-effectiveness—research. Other performers of comparative effectiveness research face different

⁶⁷ See Alan M. Garber & Harold C. Sox, *The Role Of Costs In Comparative Effectiveness Research*, 29 HEALTH AFF. 1805, 1807–09 (2010) (describing and comparing comparative effectiveness research and cost-effectiveness research). Exactly how to measure “more effective” or “more health” are knotty issues, which have spawned a major literature including the calculation of Quality-Adjusted Life Years (QALYs) and Disability-Adjusted Life Years (DALYs), global surveys of patient preferences, and many other techniques. See, e.g., Marthe R. Gold et al., *HALYs and QALYs and DALYs, Oh My: Similarities and Differences in Summary Measures of Population Health*, 23 ANNU. REV. PUBLIC HEALTH 115 (2002); Franco Sassi, *Calculating QALYs, Comparing QALY and DALY Calculations*, 21 HEALTH POL’Y PLAN. 402 (2006). We do not address these issues here.

⁶⁸ For example, when Merck developed Vioxx, it conducted clinical trials comparing the experience of patients taking Vioxx with those taking the older NSAID naproxen, and used those studies to support the marketing claim that Vioxx had fewer gastric side effects than naproxen. Claire Bombardier et al., *Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 N. ENG. J. MED. 1526–27 (2000). See *supra* Part I.A..

⁶⁹ See *supra* Part I.A.

incentives and constraints. Academic institutions,⁷⁰ nonprofit organizations,⁷¹ and government-created comparative effectiveness institutes focus on public health goals rather than cost control. In fact, the Patient-Centered Outcomes Research Institute created by the Affordable Care Act is prohibited by statute from performing certain types of cost-effectiveness research.⁷² These institutions generally need to partner with payers for access to data. Doctors and hospitals have some access to health data, although they too may find it advantageous to partner with payers to obtain access to larger datasets that include data from different providers. But doctors and hospital may have perverse incentives under a classical fee-for-service model, because they make more money by providing more (and more expensive) treatments.⁷³ Finally, drug companies have the capability to conduct comparative effectiveness research, through both clinical trials and observational studies, and an incentive to demonstrate that their new products are better than older drugs. However, this incentive is biased in one direction; comparative effectiveness research runs the risk of showing that a new drug is worse than existing treatments. Since placebo-controlled trials are generally enough to win regulatory approval, they may decide not to take the risk of demonstrating inferiority rather than superiority for the patent-protected product.

Payers have different incentives, which could make them an important source of comparative effectiveness research and cost effectiveness research. For example, Mayo Clinic researchers used Optum Labs data to

⁷⁰ For example, Harvard's Comparative Effectiveness Research Initiative focuses on "public health and health systems interventions." <http://www.hsph.harvard.edu/comparative-effectiveness-research-initiative/>

⁷¹ For example, the Institute for Clinical and Economic Review's New England Comparative Effectiveness Public Advisory Council, <http://cepac.icer-review.org/>, has produced comparative effectiveness reports on treatments for opioid dependence, type 2 diabetes, and depression, as well as on the use of community health workers and on behavioral health integration into medical care. Comparative Effectiveness Public Advisory Council, *Reports*, <http://cepac.icer-review.org/adaptations/> (last visited July 14, 2015).

⁷² The Patient-Centered Outcomes Research Institute (PCORI) was created by the Affordable Care Act to conduct comparative effectiveness research. However, it is statutorily prohibited from certain types of cost-effectiveness research. PCORI "shall not develop or employ a dollars-per-quality adjusted life year . . . as a threshold to establish what type of health care is cost effective or recommended." ACA § 6301, codified at 42 U.S.C. § 1320e-1(e). *But see* Nicholas Bagley, *Who says PCORI can't do cost-effectiveness?*, <http://theincidentaleconomist.com/wordpress/who-says-pcori-cant-do-cost-effectiveness/> (Oct. 14, 2013) (arguing that PCORI is not actually prohibited from such research, while acknowledging widespread views inside and outside the Institute that it is). Medicare and Medicaid are prohibited from using any such threshold to make coverage determinations. ACA § 6301(e).

⁷³ *See infra* Part I.D.

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determine that newer anticoagulant drugs have a higher risk of gastrointestinal bleeding among older patients.⁷⁴ Despite the greater convenience of the newer—and more expensive—drugs, this risk may make these drugs less appropriate for those older patients.⁷⁵ Overall, the competing incentives of different stakeholders provide counterweights that can provide a more balanced understanding than reliance on data from any one kind of innovator.

3. Off-label use

Payers can also contribute to understanding and supporting off-label use of drugs. Pre-approval clinical trials often focus on relatively narrow indications to simplify the showing of efficacy and safety necessary to get regulatory approval. But once a drug becomes available, doctors are free to prescribe it for other purposes that are not indicated in the FDA-approved label for the product. In some fields, such as oncology, off-label use of products for indications beyond the scope of FDA approval is quite common.⁷⁶ Drug companies have relatively low incentives to conduct costly clinical trials to provide evidence for off-label use, especially once such use enters into widespread practice; firms might benefit from increased drug sales without having to incur the costs and risks of further trials. Many off-label uses are, unsurprisingly, unsupported by rigorous evidence, even when they have become the standard of care.⁷⁷

FDA has long sought to motivate drug companies to conduct further clinical trials of off-label uses by preventing firms from promoting their products for off-label use. FDA takes the position that promotion of a product for off-label uses renders the product “misbranded” in violation of

⁷⁴ Neena Abraham, *et al.*, *Comparative risk of gastrointestinal bleeding with dabigatran, rivaroxaban, and warfarin: population based cohort study*, BRIT. MED. J. 350 (2015).

⁷⁵ See Constantinos Michaelidis, *Risk of GI Bleeding With Use of NOACs for Atrial Fibrillation: Commentary on Two Recent Cohort*, American College of Cardiology : Latest in Cardiology (Jul. 14, 2015), <http://www.acc.org/latest-in-cardiology/articles/2015/07/14/12/14/risk-of-gi-bleeding-with-use-of-noacs-for-atrial-fibrillation>.

⁷⁶ See, e.g., Dominique Levêque, *Off-Label Use of Anticancer Drugs*, 9 LANCET ONCOL. 1102 (2008); Rena M. Conti et al., *Prevalence of Off-Label Use and Spending in 2010 Among Patent-Protected Chemotherapies in a Population-Based Cohort of Medical Oncologists*, 31 J. CLIN. ONCOL. 1134 (2013) (finding 30% off-label use of ten leading patent-protected intravenous chemotherapeutics, and over 50% off-label use for some).

⁷⁷ See Largent EA et al., *Going off-Label without Venturing off-Course: Evidence and Ethical off-Label Prescribing*, 169 ARCH. INTERN. MED. 1745 (2009) (describing different levels of evidence for off-label use).

the Food, Drug & Cosmetic Act.⁷⁸ But recent judicial decisions have held that the First Amendment protects drug companies and their sales force from criminal prosecution for promoting off-label use.⁷⁹ Moreover, once a generic version of the drug is available, the original sponsor has little incentive to invest in costly clinical trials of off-label uses for a product that is no longer profitable.⁸⁰

Payers have the incentive to ensure that off-label uses are effective and supported by evidence, because ineffective uses are wasted money.⁸¹ They also have the data to observe the effectiveness of off-label uses that have already entered into practice. Observational studies in payer health records may provide a more cost-effective alternative for filling the information gap about the effects of off-label uses of drugs.

4. Prevention and long-term effects

Pre-approval clinical trials are necessarily limited in duration, and thus have limited value in determining long-term health effects over an extended period of time. We noted above that clinical trials may fail to reveal toxic side effects that manifest over time.⁸² For some products, such as vaccines and other prophylactic measures to prevent disease or forestall its progression, long-term effects are critical for determining not just safety, but also efficacy.⁸³ In recent decades FDA has adapted its regulatory approach to permit approval of some products on the basis of data on “surrogate markers” rather than requiring that trials continue for years to measure disease endpoints.⁸⁴ This allows products to get to market that

⁷⁸ 21 U.S.C. § 352

⁷⁹ *U.S. v. Caronia*, 703 F.3d 149 (2d Cir. 2012); *Amarin Pharma v. FDA* (No. 2015-cv-03588, Docket No. 73, S.D.N.Y. Aug. 7, 2015) (order granting preliminary relief preventing FDA misbranding action for off-label promotion involving truthful statements).

⁸⁰ See Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL'Y L. & ETHICS 717 (2005).

⁸¹ Cf. Monika K. Krzyzanowska, *Off-Label Use of Cancer Drugs: A Benchmark Is Established*, 31 J. CLIN. ONCOL. 1125, 1126 (2013) (“[I]n the short term, the greatest opportunity to optimize off-label prescribing is likely at the reimbursement level. . . . On the part of payers, there should be greater scrutiny of reimbursement for drugs that are potentially toxic and expensive and are associated with a high proportion of off-label prescribing.”).

⁸² See *supra* Part I.C.1.

⁸³ See INSTITUTE OF MEDICINE, EVALUATION OF BIOMARKERS AND SURROGATE ENDPOINTS IN CHRONIC DISEASE 38–45 (2010) [EVALUATION OF BIOMARKERS].

⁸⁴ See, e.g., Russell Katz, *Biomarkers and Surrogate Markers: An FDA Perspective*, 1 NEURORX 189 (2004); Thomas R. Fleming & John H. Powers, *Biomarkers and Surrogate Endpoints in Clinical Trials*, 31 STAT. MED. 2973 (2012).

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might otherwise not be approvable under a more rigorous application of standards for safety and efficacy. But although it might not be commercially feasible to require that clinical trials continue for many years, the lack of data on clinical endpoints is a significant gap in the information base for determining appropriate clinical use of these products, especially since many surrogate endpoints are eventually found to be poor predictors of clinical outcomes.⁸⁵

Payer data on clinical outcomes can provide a valuable and cost-effective supplement to the limited data available from clinical trials in these circumstances. A recent example that illustrates the potential for payer clinical data to show the long-term value of prophylactic treatment is a study of the pre-exposure prophylactic use (known as PrEP) of anti-retroviral drugs using data from Kaiser-Permanente in San Francisco.⁸⁶ In that study, not a single person using PrEP was infected with HIV.⁸⁷ This study is notable because payer data confirmed that a potentially costly treatment is valuable, rather than indicating that a costly product should be used more sparingly.⁸⁸ When payers may be on the hook for more costly future medical care, they may benefit financially from more extensive use of prophylactic treatment that forestalls the need for that future care.⁸⁹

5. Personalized medicine

Personalized medicine, also known as precision medicine and frequently touted as the future of medicine,⁹⁰ takes the idea of comparative

⁸⁵ See T. R. Fleming & D. L. DeMets, *Surrogate End Points in Clinical Trials: Are We Being Misled?*, 125 ANN. INTERN. MED. 605 (1996); INSTITUTE OF MEDICINE, EVALUATION OF BIOMARKERS, *supra* note 83, at 45–52.

⁸⁶ Jonathan E. Volk et al., *No New HIV Infections With Increasing Use of HIV Preexposure Prophylaxis in a Clinical Practice Setting*, 61 CLIN. INFECT. DIS. 1601 (2015); Carlos F Cáceres et al., *The Promises and Challenges of Pre-Exposure Prophylaxis as Part of the Emerging Paradigm of Combination HIV Prevention*, 18 J. INT. AIDS SOC. (2015).

⁸⁷ Volk et al., *supra* note 86.

⁸⁸ *Id.* The wholesale acquisition cost of Truvada for PrEP is around \$1,300 per month. David Heitz, *Insurers and Medicaid Cover It. So What's Behind the Slow Adoption of Truvada PrEP?*, HEALTHLINE (May 8, 2014), <http://www.healthline.com/health-news/hiv-prevention-truvada-prep-covered-by-most-insurers-050814> (last visited February 11, 2016).

⁸⁹ See James F. Fries et al., *Reducing Health Care Costs by Reducing the Need and Demand for Medical Services*, 329 N. ENGL. J. MED. 321 (1993) (making the case for cost-savings through preventive care); *but see* Joshua T. Cohen et al., *Does Preventive Care Save Money? Health Economics and the Presidential Candidates*, 358 N. ENGL. J. MED. 661 (2008) (noting that some preventive measures save money while others are costly).

⁹⁰ See Barbara J. Evans, *What Will It Take to Reap the Clinical Benefits of Pharmacogenomics*, 61 FOOD & DRUG L.J. 753 (2006); Geoffrey S. Ginsburg & Jeanette J.

effectiveness research to the individual or small-group level. Personalized medicine focuses on providing “the right patient with the right drug at the right dose at the right time.”⁹¹ It responds to the inherent variation among patients, or among groups, by linking that biological variation to differences in the most effective and efficient treatment.⁹² An early success story for personalized medicine is the use of a test to identify those patients that could benefit from the breast-cancer drug Herceptin, a drug that is effective only against tumors that overexpress a particular gene named *HER2/neu*.⁹³ A simple genetic test can measure whether a patient’s tumor overexpresses the gene, allowing providers to give the drug only to patients with tumors that are likely to respond to it, while sparing other patients from exposure to unnecessary side effects.⁹⁴ Personalized medicine may also answer other kinds of questions, such as the appropriate dose of a drug based on patient sex, weight, and genetic makeup⁹⁵ or which patients might benefit more or less from the availability of an inpatient hospital bed.⁹⁶ Research is underway to explore more complex and sophisticated personalized medicine implementations.⁹⁷

A key piece of this research is the use and understanding of genomic data and biomarkers.⁹⁸ An individual’s genome—the sum of his or her

McCarthy, *Personalized Medicine: Revolutionizing Drug Discovery and Patient Care*, 19 TRENDS BIOTECHNOL. 491 (2001); Rachel Sachs, *Innovation Law and Policy: Preserving the Future of Personalized Medicine*, 49 U.C. DAVIS L. REV. ___, (forthcoming 2016), available at <http://papers.ssrn.com/abstract=2596875>.

⁹¹ Food & Drug Admin., *Personalized Medicine*, <http://www.fda.gov/scienceresearch/specialtopics/personalizedmedicine/default.htm> (Jan. 30, 2015).

⁹² *Id.*

⁹³ Isaac S. Chan & Geoffrey S. Ginsburg, *Personalized Medicine: Progress and Promise*, 12 ANNU. REV. GENOMICS HUM. GENET. 217 (2011).

⁹⁴ *Id.*

⁹⁵ For example, consider the voluminous literature on dosing considerations for the blood thinner warfarin based not only on physical patient characteristics but also on which versions of drug-metabolizing enzymes the patient’s genes encode. See, e.g., J.L. Anderson et al., *Randomized trial of genotype-guided versus standard warfarin dosing in patients initiating oral anticoagulation*, 116 CIRCULATION 2563, 2563–70 (2007); Y. Caraco, S. Blotnick, & M. Muszkat, *CYP2C9 Genotype-Guided Warfarin Prescribing Enhances the Efficacy and Safety of Anticoagulation: A Prospective Randomized Controlled Study*, 2008 CLIN. PHARMACOL. THER. 460, 460–70; www.warfarindosing.org.

⁹⁶ I. Glenn Cohen et al., *The Legal And Ethical Concerns That Arise From Using Complex Predictive Analytics In Health Care*, 33 HEALTH AFF. 1139 (2014).

⁹⁷ See, e.g., W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J. L. & TECH. 419 (2015) (discussing complex and opaque medical algorithms).

⁹⁸ A biomarker is a measurable characteristic that indicates a biological state within the body. Kyle Strimbu & Jorge A. Tavel, *What Are Biomarkers?*, 5 CURR. OPIN. HIV AIDS 463 (2010).

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genetic information—represents a tremendous amount of biological variability, including how fast the individual may metabolize certain drugs⁹⁹ and how likely the individual is to develop a certain type of cancer.¹⁰⁰ Aside from a patient's own genetic information, the genetics of viruses, bacteria, and cancerous tumors can inform the treatment of related diseases.¹⁰¹ Other biomarkers, like blood-sugar level, the amount of prostate-specific antigen, or the previously mentioned overexpression of HER2 by a tumor, can similarly be used to direct treatment (for diabetes, prostate cancer, and breast cancer, respectively).

Payers have an opportunity to use their data to contribute to personalized medicine research. They have demographic and health information about patients, including information about treatments and outcomes. Optum, for example, is involved in developing predictive analytics technology to identify high-risk patients based on a combination of administrative claims data and real-time clinical data from multiple sources.¹⁰² These data may reveal patterns of which drugs or treatments work best for which patients, and which patients might be best off avoiding treatment altogether in particular circumstances. Payers may have direct access to tissue samples (or analyses of those samples) to determine biomarker, genetic, and genomic status; if they do not, they may be well positioned to collaborate with other researchers to link health records to tissue samples.¹⁰³ In fact, payers are important participants in the eMERGE network, further discussed below.¹⁰⁴

The incentives of payers to perform personalized medicine research may offer a useful counterweight to the incentives of the drug companies that have become the key drivers of personalized medicine.¹⁰⁵ For drug

⁹⁹ See Chan & Ginsburg, *supra* note 93, at 227 (2011) (describing the use of genetic analysis of two genes, CYP2C9 and VKORC1, to predict metabolism rate of the blood thinner warfarin and prospectively adjust dosage accordingly).

¹⁰⁰ See Y Miki et al., *A Strong Candidate for the Breast and Ovarian Cancer Susceptibility Gene BRCA1*, 266 SCIENCE 66 (1994) (identifying the BRCA1 gene, linked to breast and ovarian cancer); Myriad, BRACANALYSIS, <https://www.myriad.com/products-services/hereditary-cancers/bracanalysis/> (describing commercially available test for breast and ovarian cancer susceptibility based on genetic analysis of the BRCA1 and BRCA2 genes).

¹⁰¹ Chan & Ginsburg, *supra* note 93.

¹⁰² Optum, *Improved Predictive Analytics Better Identify High-Risk Patients*, HEALTH CARE CONVERSAT., <http://healthcare-conversation.com/2015/06/08/improved-predictive-analytics-better-identify-high-risk-patients/> (June 8, 2015).

¹⁰³ The eMERGE network, discussed *infra* in Part II.B.3, aims to facilitate this linking practice.

¹⁰⁴ See Part II.B.3. *infra*.

¹⁰⁵ See Chan & Ginsburg, *supra* note 93 (describing pharmaceutical company

companies, personalized medicine presents a tradeoff between more reliable treatment and smaller market size. If research shows that a particular drug only works for a third of people taking it, and provides a mechanism for identifying those patients, the other two thirds will no longer use the product, and sales will decline.¹⁰⁶ If the company can market a new, targeted drug, and potentially a companion diagnostic, it may be able to charge a higher price for a drug that is more likely to be effective in its targeted group. For payers, on the other hand, broader implementation of personalized medicine could improve healthcare quality and reduce costs. A payer, for example, might save costs by demonstrating that two-thirds of patients currently taking an expensive drug would be better off taking an older generic drug or other less expensive treatment—or no treatment at all.¹⁰⁷ Of course, both drug companies and payers face the risk that observational studies will not yield the results that are best for their bottom lines. But financial incentives are nonetheless likely to inform the research questions that they pursue, and perhaps to influence their analysis of results and their decisions about what results merit publication. The participation of both drug companies and payers as innovators in the field of personalized medicine is thus likely to yield a more balanced and complete picture than would emerge if the field were dominated by the drug companies.

D. Incentives for innovation

Although payers are in a good position to play a larger role in healthcare innovation, their incentives to invest in innovation are constrained by a number of economic and regulatory features of the healthcare market. First, some quirks of health-care markets and tax law directly reduce incentives. Second, because payers typically do not directly control care, they may fail to realize the full cost saving benefits from their innovation. Third,

development of companion diagnostics for drugs). This is not to argue that insurer incentives are perfect, as discussed below. Patients and payers may have different views as to acceptable money-for-health tradeoffs. Moreover, patients can shift between payers over time, giving current payers an incentive to postpone costly treatment to shift the cost to another payer; this happens most clearly as patients age into Medicare and leave private payers.

¹⁰⁶ Firms may have ways to recoup that loss. For example, it may be possible to patent a diagnostic device to guide the choice of treatment, allowing the firm to charge higher prices for personalized medicine. In some cases the identification of a subgroup that benefits from a drug may lead to approval of a drug that would otherwise present an unacceptable balance of safety and efficacy in an undifferentiated patient population.

¹⁰⁷ The opposite could, of course, also be true; a diagnostic test might reveal that an older, cheaper drug is unsuitable for a subsection of the patient population, who might then need to take a more expensive newer drug.

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intellectual property incentives are less available for the innovation opportunities available to payers than they are for other kinds of innovation such as new products.

1. Market quirks and tax preferences

Cost sensitivity should motivate payers to invest in developing or identifying more cost-effective treatments. However, the U.S. market for health care and insurance has complexities and idiosyncracies that blur these incentives.¹⁰⁸ Four features particularly dampen the cost-sensitivity of payers: muted competition, passed-on costs, tax subsidies, and medical loss ratios.

First, payers frequently face muted competition due to industry consolidation, status-quo bias, and product opacity. The industry is highly consolidated, which gives payers some power to dictate the terms of their coverage and the rates they charge.¹⁰⁹ Status quo bias further weakens competition, because employers and individuals have a tendency to stick with the payer they currently use.¹¹⁰ Finally, product opacity may also reduce competition among insurance products.¹¹¹ While these factors

¹⁰⁸ The U.S. health-care market is the subject of a vast scholarly literature that we do not try to summarize or augment here. Instead, we merely highlight a few features of the market that may decrease incentives for payers to innovate.

¹⁰⁹ LEEMORE DAFNY ET AL., PAYING A PREMIUM ON YOUR PREMIUM? CONSOLIDATION IN THE U.S. HEALTH INSURANCE INDUSTRY 3 (National Bureau of Economic Research, Working Paper 15434, October 2009), *available at* <http://www.nber.org/papers/w15434>; MARIKA CABRAL ET AL., DOES PRIVATIZED HEALTH INSURANCE BENEFIT PATIENTS OR PRODUCERS? EVIDENCE FROM MEDICARE ADVANTAGE (National Bureau of Economic Research, Working Paper 20470, September 2014), *available at* <http://www.nber.org/papers/w20470> (finding that concentrated payer markets led to a marked decrease in how much Medicare Advantage premium supports (public funds provided to lower premiums) actually decreased premiums paid by patients).

¹¹⁰ Benjamin R. Handel, *Adverse Selection and Inertia in Health Insurance Markets: When Nudging Hurts*, 103 AM. ECON. REV. 2643 (2013) (documenting plan inertia at a large firm).

¹¹¹ Although the Affordable Care Act has drastically increased the transparency of insurance plans, exactly what services and products are covered by a plan remain challenging to discern and compare, especially for individual purchasers. *See, e.g.*, JEFFREY R. KLING ET AL., COMPARISON FRICTION: EXPERIMENTAL EVIDENCE FROM MEDICARE DRUG PLANS (National Bureau of Economic Research, 2011), *available at* <http://www.nber.org/papers/w17410> (finding low information access in choosing Medicare Part D plans); *cf.* SAURABH BHARGAVA ET AL., DO INDIVIDUALS MAKE SENSIBLE HEALTH INSURANCE DECISIONS? EVIDENCE FROM A MENU WITH DOMINATED OPTIONS 4 (National Bureau of Economic Research, 2015), *available at* <http://www.nber.org/papers/w21160> (describing substantial numbers of employees choosing strictly inferior health plans and attributing this choice to inability to understand plan options).

interact in complex ways far beyond the scope of this Article, they may combine to decrease competitive pressure on payers to innovate to lower costs.¹¹²

Second, the combination of weak market competition and weak oversight of price increases by insurance regulators allow payers to pass on increased costs to their customers with relative ease through increased premiums,¹¹³ although the Affordable Care Act has introduced some limits on the ability of payers to raise premiums in a deliberate attempt to increase cost sensitivity.¹¹⁴

Third, tax subsidies for health insurance have dampened incentives for frugality on the demand side of healthcare. Health insurance premiums paid by an employer are both fully deductible by the employer as a business expense and also excluded from the employee's taxable income.¹¹⁵ In this system the government shares the costs of healthcare, diminishing the interest of patients and their employers in cost-lowering innovation and making it easier for insurers to pass rising costs along to them in the form of higher premiums.

Fourth and finally, the complex dynamics of the Affordable Care Act's medical loss ratio (MLR) provisions may reduce incentives for cost-lowering innovation. Under those provisions, payers must pay 85 cents in

¹¹² The exact mechanics of decreased competition, and its precise effects on innovation incentives, are complex and beyond the scope of this Article or, indeed, our expertise. For instance, decreased competition may decrease the need for intellectual property protection, if competitors are not seeking to appropriate innovations for themselves. Opacity could potentially cut in both directions; it may decrease competition, but may also allow payers to shield potentially controversial cost-cutting innovations from public scrutiny. Teasing out the full effects of these market features requires substantial further study.

¹¹³ See NAIC Health Insurance and Managed Care (B) Committee, Rate Review White Paper (June 27, 2012), http://www.naic.org/documents/committees_b_related_wp_rate_review.pdf.

¹¹⁴ See, e.g., Internal Revenue Service, Notice 2015-16: Section 4980I — Excise Tax on High Cost Employer-Sponsored Health Coverage (2015), *available at* www.irs.gov/pub/irs-drop/n-15-16.pdf (instituting the so-called "Cadillac Tax" of 40% on plans with very high premiums).

¹¹⁵ The staff of the Joint Committee on Taxation estimated value of this tax expenditure in 2014 at \$143 billion. See ESTIMATES OF FEDERAL TAX EXPENDITURES FOR FISCAL YEARS 2014-2018, prepared for the House Committee on Ways and Means and the Senate Committee on Finance by the Staff of the Joint Committee on Taxation (Aug. 5, 2014), at 31 (Table I), <https://www.jct.gov/publications.html?func=startdown&id=4663>. The Congressional Budget Office arrived at a higher estimate of \$250 billion that includes the cost to the government of tax preferences for employee contributions to health insurance premiums. CONGRESSIONAL BUDGET OFFICE, OPTIONS FOR REDUCING THE DEFICIT: 2014-2023 (Nov. 2013) at 243-249, <https://www.cbo.gov/sites/default/files/cbofiles/attachments/44715-OptionsForReducingDeficit-3.pdf>.

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medical expenses for each dollar received in premiums.¹¹⁶ This sets a ceiling on the increase in profits to be gained by lowering costs; it can be no higher than 15% minus administrative expenses. While countervailing factors exist in the MLR regime—increased efficiency may offset other rising costs, and quality improvement research counts as part of the “medical expense” 85%—on the margin, this cap may reduce profit-based incentives for innovation. Overall, these features of the health market likely combine to lower incentives to innovate toward efficiency. The marginal incentive for frugal innovation diminishes to the extent that payers are able to pass on cost increases to employers and patients.

2. Challenges implementing innovation

Payer incentives to innovate are further mediated by the reality that many payers do not actually provide care. For payers to benefit from their innovations around quality, efficiency, and medical targeting, health care providers must actually adopt those innovations. Payers must therefore influence providers to implement changes. In a fee-for-service system, health care providers face perverse incentives to use more and costlier treatments, thereby increasing their own remuneration. Thus, at least some provider incentives are in serious tension with the goals of frugal payer innovation.¹¹⁷ Integrated health systems, which both provide and pay for care, may find it easier to control the behavior of providers.

Traditional payers’ options for influencing caregiver behavior range from direct procedure-setting to collaborative knowledge-sharing. Payers can use utilization review and reimbursement tiering to guide physician behavior, though these practices have had a contentious history.¹¹⁸ Payers

¹¹⁶ Small payers (fewer than 100 subscribers) must meet a MLR threshold of 80%. ACA § 1001. For a summary of this requirement, see Suzanne M. Kirchhoff, *Medical Loss Ratio Requirements Under the Patient Protection and Affordable Care Act (ACA): Issues for Congress* (2014), available at <https://fas.org/sgp/crs/misc/R42735.pdf>.

¹¹⁷ This problem is not unique to health insurers, and indeed may be seen as just another manifestation of principal-agent conflicts. Nonetheless, we mention it here because it potentially decreases the incentive for insurers to innovate and because it may increase their incentive to collaborate with providers.

¹¹⁸ The principal mechanism of relatively direct payer control over physician decisions has long been utilization review, where insurers—and especially managed care organizations—review decisions for medical appropriateness to decide whether to pay for the care; review could be prospective or retrospective. Substantial scholarship has focused on the impact of utilization review. Among many others, see, e.g., Paul J. Feldstein et al., *Private Cost Containment. The Effects of Utilization Review Programs on Health Care Use and Expenditures*, 318 N. ENGL. J. MED. 1310 (1988); Thomas M. Wickizer, *The Effect of Utilization Review on Hospital Use and Expenditures: A Review of the Literature and an*

can also influence provider behavior less directly by, for example, publishing their results and working to establish best practices, which can include clinical guidelines or “critical pathways,” reflecting treatment patterns that are both effective and efficient.¹¹⁹ Treatment pathways are most frequently developed by expert committees—typically well-known physicians—relying on published literature.¹²⁰ Payers may influence these committees by contributing their studies to the published literature. Payers may be more effective in influencing clinical practice when they collaborate with influential clinicians to conduct and publish observational studies, before providing them to expert communities that can then establish standards of care. Such collaborations are a feature of the PCORnet and eMERGE networks. But to the extent that providers resist following new clinical guidelines, the benefit of the innovation is diminished.¹²¹

Payers can also try to align provider incentives with cost-saving goals by using financial incentives or risk-sharing. If providers are compensated on a fee-for-service basis, increased treatment costs mean increased provider compensation, making it difficult to motivate providers to pursue efficiency. This is the subject of a large literature; we note here only that to the extent that incentives are successfully aligned, providers have greater incentives to adopt payer innovations, especially frugal innovation. This should increase the benefit to payers of developing such innovations, and thus the likelihood that they will make the necessary investments.

This may be why integrated providers such as Kaiser Permanente have been more active participants in payer innovation than traditional insurers. It may be easier to implement cost-saving innovations through caregivers

Update on Recent Findings, 47 MED. CARE RES. REV. 327 (1990). However, managed care and utilization review prompted significant backlash around the turn of the millennium. See, e.g., Marc A. Rodwin, *Backlash as Prelude to Managing Managed Care*, 24 J. HEALTH POLIT. POL’Y LAW 1115 (1999); David Mechanic, *The Managed Care Backlash: Perceptions and Rhetoric in Health Care Policy and the Potential for Health Care Reform*, 79 MILBANK Q. 35 (2001).

¹¹⁹ See, e.g., Nathan R. Every et al., *Critical Pathways: A Review*, 101 CIRCULATION 461 (2000).

¹²⁰ See, e.g., P4 Pathways, Protocol Development, <https://www.p4pathways.com/go/p4pathways/program/services/pathway-development.htm> (describing a protocol-development steering committee comprising “locally based academic and community oncologists to ensure pathways reflect both rigorous evidence-based medicine and the clinical expertise in that region”).

¹²¹ See, e.g., Rainer Blaser et al., *Improving Pathway Compliance and Clinician Performance by Using Information Technology*, 76 INT. J. MED. INF. 151 (2007). For an example of a compliance-monitoring schema, see P4 Pathways, Compliance Monitoring, <https://www.p4pathways.com/go/p4pathways/program/services/compliance-monitoring.htm>.

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who are salaried employees with nothing to gain from the provision of costly and excessive care. The Affordable Care Act aims to achieve similar alignment of incentives for frugality through Accountable Care Organizations, coordinated groups of physicians, hospitals, and other providers.¹²² Among other benefits, these structures allow physicians to share in the financial benefits of frugal care, shifting their incentives from those of traditional fee-for-service.¹²³ More broadly, the Affordable Care Act aims to shift a substantial fraction of care away from fee-for-service towards value-based payments or other frugality-focused payment models, which should further align the incentives of payers and providers and enable smoother adoption of demand-side innovation.¹²⁴

Finally, payers could influence the behavior of providers by using data to influence FDA regulatory decisions. They might, for example, use their data to reveal risks to FDA that it should study through the Sentinel System, perhaps leading to future warnings or even withdrawal of product approvals. These regulatory moves might have a greater impact on the behavior of caregivers than the exhortations of payers.

3. Intellectual property incentives

Intellectual property raises a final set of questions about payer incentives. Standard intellectual property incentives for innovation are typically geared toward the producers of new products, although high prices for patent-protected products may have the incidental benefit of motivating payers to invest in learning how to use these products more sparingly. More fundamentally, the excludability at the center of intellectual property is not a viable option for the type of payer innovations discussed above.¹²⁵ But other incentives and subsidies for payer innovation are available and in use to promote payer innovation.

In a familiar story, intellectual property provides legal excludability to

¹²² See Centers for Medicare and Medicaid Services, *Accountable Care Organizations*, <http://cms.gov/aco> (Jan. 6, 2015).

¹²³ *Id.*

¹²⁴ See Sylvia M. Burwell, *Setting Value-Based Payment Goals — HHS Efforts to Improve U.S. Health Care*, 372 N. ENGL. J. MED. 897 (2015) (setting goal of 30% of traditional fee-for-service payments to alternative payment models by the end of 2016, and 50% by the end of 2018).

¹²⁵ See Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 112 YALE L.J. 1923–41 (2013) (describing how patents are ineffective at protecting inventions that are hard to exclude others from using, and describing the specific examples of negative information about drugs, positive information about health-enhancing lifestyle interventions, and health-care quality initiatives).

solve the public goods problem that would otherwise prevent innovators from capturing the full value of their investments. By allowing innovators to exclude competitors from using their information goods, intellectual property permits them to raise prices, thereby increasing *ex ante* incentives to innovate. The forms of payer innovation considered above are pure information goods; there is typically no new physical product that the payer can sell associated with the knowledge gained from observational studies of patient health records, for example.¹²⁶ But intellectual property is a poor fit for appropriating and monetizing the value of this knowledge; secrecy is ineffective and inappropriate, and patents are largely unavailable.¹²⁷

The first and most obvious way to appropriate an information good is to keep it secret; if others do not have the information, they cannot use it. This strategy is ill suited to payer medical information, because payers must at a minimum share the information with doctors and other caregivers before they can put it to use in a clinical setting. Moreover, caregivers are required to obtain informed consent for medical treatment, which may require further disclosure of the information to patients. Broader disclosure may be necessary to bring about a change in the standard of care. For example, if payer studies indicate that caregivers should not continue to provide a form of treatment that is considered the standard of care in the medical community, caregivers may fear potential malpractice liability for withholding the treatment.¹²⁸ Widespread disclosure of the study results may therefore be necessary to facilitate clinical implementation of changes in the standard of care. Secrecy may thus be a serious obstacle to effective use of payer innovations.

Patents on comparative effectiveness research results or personalized

¹²⁶ The patent on the relevant drug—and the higher prices it enables—provide a different incentive, discussed below at note 133 and accompanying text.

¹²⁷ The third major form of exclusivity in the medical world is FDA-mediated regulatory exclusivity, whereby FDA refuses to approve competitor products, or to allow competitors to use the innovator's regulatory data submissions, for a certain period of time to give the first-to-be-approved product a period of lucrative exclusivity. Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345 (2007). This form of exclusivity is inapplicable here.

¹²⁸ Under medical malpractice law, doctors and other medical professionals may be liable for negligently injuring patients; demonstrating that the care provided was within the relevant standard of care serves as a defense against malpractice liability. John C. Drapp III, *The National Standard of Care in Medical Malpractice Actions: Does Small Area Analysis Make It Another Legal Fiction*, 6 QUINNIPIAC HEALTH L.J. 95, 96–100 (2002). Accordingly, doctors have an incentive to follow the current standard of care to avoid liability. If payers aim to guide physician behavior into providing better forms of care—whether more cost effective or more personally effective—demonstrating that the preferred care is a new or developing standard is an important part of that process.

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medicine information are likely unavailable, unenforceable, and impractical. Judicial limitations on what sorts of inventions constitute patentable subject matter under 35 U.S.C. § 101 cast considerable doubt on the patent eligibility of algorithms for selecting medical treatments for patients.¹²⁹ Standard patent law rules about prior art are also likely to prevent the patenting of the treatment options themselves. Because observational studies of health outcomes necessarily involve treatments that are already a part of current practice, those treatments could not be patented because they are already in public use and on sale.¹³⁰ Even if these innovations were patentable, the patents might be difficult to enforce for at least three reasons: first, it would be difficult to observe and police infringing behavior in light of the privacy of health records;¹³¹ second, medical practitioners practicing medical activities have a statutory exemption from patent infringement remedies;¹³² and third, suing doctors to prevent them from practicing medicine more effectively might create a public relations problem for a healthcare payer.

Although intellectual property does not provide the same direct incentives for medical innovation by payers that it provides for product sellers, it may provide an important indirect motivation for payers by increasing the costs they incur in covering patented products. When Kaiser Permanente collaborated with FDA to study the cardiac side effects of Vioxx, payers were collectively paying \$2.5 billion per year for Vioxx, creating a conspicuous opportunity to cut costs by reducing the use of

¹²⁹ See *Mayo Collaborative v. Prometheus Labs.*, 566 U.S. 10 (2012) (holding a diagnostic method patent involving customizing patient dosages unpatentable subject matter as preempting a law of nature); *Alice Corp. Pty. v. CLS Bank Int'l*, 134 S.Ct. 2347 (2014) (holding unpatentable a financial method patent and clarifying that abstract inventions like algorithms are not made patentable by implementing them on a general-purpose computer); see also Rebecca S. Eisenberg, *Prometheus Rebound: Diagnostics, Nature, and Mathematical Algorithms*, 122 YALE L.J. ONLINE 341 (2013) (analyzing *Prometheus* in the context of medical algorithms); Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21 B.U. J. SCI. & TECH. L. 256 (2015).

¹³⁰ Sections 102 and 103 require that inventions be new and nonobvious, respectively, to be patentable. 35 U.S.C. §§ 102, 103. If particular treatments are in use and are known to be medically useful, innovation in comparative effectiveness research demonstrating their relative efficacy may be difficult to bring past the §§ 102/103 bars.

¹³¹ See Kapczynski & Syed, *supra* note 125, at 1938–40 (describing the difficulty in enforcing health-care quality patents). Broader availability of health data, such as access to EHRs, could ease enforcement concerns, though HIPAA limitations may restrict such access. Even with more available data, enforcement still faces challenges. See *id.*

¹³² Under 35 U.S.C. § 287(c), medical practitioners and related health care entities are not liable for infringement for performing any “medical or surgical procedure on a body,” not including the use of patented drugs or biotechnological processes.

Vioxx.¹³³ Payers may be less interested in studying the effects of less costly treatments that are already off patent, except in comparative effectiveness studies that offer the prospect of lowering costs incurred for coverage of a higher-priced alternative. In this indirect sense, the law of intellectual property is likely to structure the incentives of payers towards more scrutiny of the clinical benefits of patented treatments.

Despite these gaps in incentives, some payers are already making notable efforts to advance the use of payer data for medical innovation. We posit that at least three reasons why some level of innovation even without traditional intellectual property incentives. First, as we noted above, for innovation related to costly patent-protected treatment, high costs create an incentive to reduce costs. Second, observational studies are relatively cheap, especially as compared to expensive clinical trials. Third, there are a variety of government initiatives under way that are partnering with payers and helping them to overcome obstacles and kickstart their own research. In the next Parts we discuss challenges in this research and explore how government policies help payers overcome those challenges.

II. TECHNICAL CHALLENGES

The use of payer data for innovation presents substantial technical challenges.¹³⁴ Some challenges involving the storage and analysis of data are not unique to healthcare and therefore benefit from overall improvements in information technology.¹³⁵ Special concerns in the healthcare field revolve around data availability, data quality, data assembly, and data interoperability. The federal government has provided a substantial assist to payer innovation through legislation and agency initiatives targeting these challenges.

¹³³ Barbara Martinez et al., *Merck Pulls Vioxx Off Market After Link to Heart Problems*, WALL ST. J. (Oct. 1, 2004), available at <http://www.wsj.com/articles/SB109654671320932405>.

¹³⁴ For an overview, see Niels Peek et al., *Technical Challenges for Big Data in Biomedicine and Health: Data Sources, Infrastructure, and Analytics*, 9 YEARB. MED. INFORM. 42 (2014).

¹³⁵ For instance, natural language processing of electronic health records—determining what doctors mean when they write narratives—is a very challenging task, but natural language processing in health records builds off of extensive natural language processing efforts in other fields. See, e.g., Prakash M. Nadkarni et al., *Natural Language Processing: An Introduction*, 18 J. AM. MED. INFORM. ASSOC. 544 (2011) (describing natural language processing and how generalist efforts might be applicable to health informatics issues); Lucila Ohno-Machado, *Realizing the Full Potential of Electronic Health Records: The Role of Natural Language Processing*, 18 J. AM. MED. INFORM. ASSOC. 539 (2011) (introducing a special issue on the topic).

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A. Making data useful for research

First, data must be acquired and assembled. As discussed above, payers have direct access to some data, principally administrative claims data and prescription data, and may have indirect access to hospital admissions/releases, laboratory testing data, and provider records of clinical care.¹³⁶ It takes time, money, and technical expertise to bring these data together, link them by patient and demographic information, and structure the data to permit meaningful analyses.¹³⁷ Even when firms have access to data from different sources, the fragmented nature of the health-care system means that those different sources will cover different populations of patients. For example, although Optum's Data Warehouse has health data for over 150 million unique patients, it has the combination of claims, prescription, and clinical records for fewer than three percent of those patients.¹³⁸

For some studies, it is necessary to assemble comprehensive data not only across different patients in a population, but also across different periods in the lives of particular patients.¹³⁹ Longitudinal data—that is, data that follow patients over long periods of time—are useful for measuring preventive treatments, long-term drug effects, interactions between treatments, and other important medical questions.¹⁴⁰ But the records of any one payer frequently only cover a relatively limited span of a patient's life.

¹³⁶ See *supra* Part I.A. Some particularly notable efforts include Optum Labs' Data Warehouse and IBM's Watson Health, which recently acquired Truven Analytics and has at least some form of data for approximately 300 million patients. See Optum, *Data*, <https://www.optum.com/life-sciences/data.html> (last visited Feb. 23, 2016) (describing Optum's Data Warehouse); IBM, Press Release: *IBM Watson Health Announces Plans to Acquire Truven Health Analytics for \$2.6B, Extending Its Leadership in Value-Based Care Solutions*, <http://www-03.ibm.com/press/us/en/pressrelease/49132.wss> (Feb. 18, 2016).

¹³⁷ See, e.g., Barbara J. Evans, *Sustainable Access to Data for Postmarketing Medical Product Safety Surveillance under the Amended HIPAA Privacy Rule*, 24 HEALTH MATRIX 11, 14 (2014).

¹³⁸ Optum, *Optum Research Data Assets*, 2 (2015), <https://www.optum.com/life-sciences/data.html> (click link for "U.S. core data assets at the bottom of the page") (last visited Feb. 23, 2016) (listing cumulative population counts through 2014).

¹³⁹ See, e.g., Optum, *Better Predictive Modeling Requires Bigger, More Varied, Higher Quality Data Sets*, HEALTH CARE CONVERSATION, <http://healthcare-conversation.com/2015/06/22/better-predictive-modeling-requires-bigger-more-varied-higher-quality-data-sets/> (June 22, 2015) (describing the advantage of larger and more varied datasets in developing health predictive analytics).

¹⁴⁰ Weber GM et al., *Finding the Missing Link for Big Biomedical Data*, 311 J. AM. MED. ASSOC. 2479 (2014) (discussing the need to integrate patient records from different data sources).

Patients frequently switch their insurance coverage, whether because they change to a new job with a different set of payer options¹⁴¹ change payers while staying at the same job (perhaps because the employer changes its associated payers), change plans on the individual market, or become eligible or ineligible for Medicaid based on changing income. The largest change comes when patients turn 65 and become eligible for Medicare. In any of these situations, one payer stops collecting data about that patient, and another begins. Some patients, of course, stay with the same payer for decades; in that case the records of a single payer may provide long-term information without the need for aggregation. But this is rare; in one large dataset, only about 15% of patients had administrative claims data for more than five years.¹⁴² For most patients, assembling a longer-term record of information may be necessary to provide useful data for long-term studies.

Some regional efforts are already trying to overcome the challenge of fragmented data to allow caregivers to exchange patient information more readily. One promising example, Cal INDEX, a nonprofit health information exchange,¹⁴³ was founded in California in 2014 with seed money from two major payers, aiming to store centralized, comprehensive patient information for the vast majority of patients in California.¹⁴⁴ Providers choose whether to join the exchange,¹⁴⁵ and their patients

¹⁴¹ Approximately 48% of Americans receive health insurance through their employers. Kaiser Family Foundation, *Health Insurance Coverage of the Total Population*, <http://kff.org/other/state-indicator/total-population/> (2013 data; last visited July 16, 2015)..

¹⁴² Optum, *Optum Research Data Assets*, *supra* note 138, at 3 (noting 63.1 million patients with affiliated administrative claims data for at least 1 day, but only 9.7 million with data for at least 60 months).

¹⁴³ Health Information Exchanges are key players in the field of interoperability and data exchange, helping enable information transfers between providers and payers. Exchanges still face substantial challenges in implementation more than a decade after their promotion, Robert S. Rudin et al., *Usage and Effect of Health Information Exchange: A Systematic Review*, 161 ANN. INTERN. MED. 803 (2014) but show benefits in the provision of care and for the eventual interoperability of health data, Jan Walker et al., *The Value of Health Care Information Exchange and Interoperability*, 24 HEALTH AFF. W5 (2005).

¹⁴⁴ See Cal INDEX, *New California Not-for-Profit to Operate Statewide, Next-Generation Health Information Exchange* (August 5, 2014), <https://www.calindex.org/new-california-healthcare-exchange/> (last accessed July 16, 2015) (“Cal INDEX will securely collect and integrate clinical data from providers and claims data from payers to create comprehensive, retrievable patient-centered records known as longitudinal patient records (LPRs)”).

¹⁴⁵ See Cal INDEX, *Provider FAQ*, <https://www.calindex.org/provider-faq/>. Providers must pay fees to participate in Cal INDEX. For the first three years, patients covered by the two funding sponsors (Blue Shield of California and Anthem Blue Cross) will be included in Cal INDEX free of charge, and patients covered by other providers must pay

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participate unless they opt out.¹⁴⁶ If Cal INDEX can successfully persuade many providers in different payer networks to participate, it may succeed in resolving the problem of cross-provider data fragmentation, at least within California.¹⁴⁷ A patient's single longitudinal patient record will include both clinical and administrative claims data from multiple sources even as the patient shifts providers and payers.¹⁴⁸ Cal INDEX's stated purposes are to improve care and to increase efficiency, but it recognizes its consolidated dataset could also be a useful resource for research.¹⁴⁹

Second, and related, data from different sources must be interoperable—that is, they must be in compatible formats so they can be joined and analyzed together.¹⁵⁰ There is no standard format for electronic health records or administrative claims data, and data from different systems are typically kept in different formats.¹⁵¹ Moreover, some payers have changed from one data system to another over time. This means that any effort to aggregate data must translate data from one proprietary format to

subscription fees; after the initial three-year period, all providers and insurers will pay subscription fees. *Id.*

¹⁴⁶ See Cal INDEX, *Opt Out*, <https://optout.calindex.org/OptOut/optout.html>. Note that federal law requires opting-in for particular types of sensitive information such as substance abuse records, mental health information, and the results of an HIV test. See *infra* notes 233–239 and accompanying text. Thus, some types of data may remain fragmented, even if data sources are integrated.

¹⁴⁷ As described above, health data laws, including those on privacy, can vary from state to state. See *supra id.* Cal INDEX apparently does not currently have infrastructure to capture patient records from other states to account for patient movement. However, other parallel efforts exist in other jurisdictions.

¹⁴⁸ See Cal INDEX, *Provider FAQ*, <https://www.calindex.org/provider-faq/> (describing a Longitudinal Patient Record as “comprehensive, retrievable, patient-centered record that integrates payer and provider data over time, [initially including] payer information (e.g., demographics, medical and Rx information)[, later adding provider-supplied] clinical information from electronic medical records . . . and facility admission, discharge and transfer . . . systems (as examples).”

¹⁴⁹ See Cal INDEX, *Value of Cal INDEX*, <https://www.calindex.org/value-of-cal-index/> (noting that Cal INDEX can “benefit public health by providing de-identified data that can be used for medical research.”)

¹⁵⁰ See, e.g., OFFICE OF THE NATIONAL COORDINATOR FOR HEALTH INFORMATION TECHNOLOGY, *CONNECTING HEALTH AND CARE FOR THE NATION: A SHARED NATIONWIDE INTEROPERABILITY ROADMAP (DRAFT) 10–11* (2015), <http://www.healthit.gov/sites/default/files/nationwide-interoperability-roadmap-draft-version-1.0.pdf>; see also Evans, *supra* note 39, at 14 (citing PRESIDENT'S COUNCIL OF ADVISORS ON SCI. AND TECH., EXEC. OFFICE OF THE PRESIDENT, *REPORT TO THE PRESIDENT: REALIZING THE FULL POTENTIAL OF HEALTH INFORMATION TECHNOLOGY TO IMPROVE HEALTHCARE FOR AMERICANS: THE PATH FORWARD* 39 (2010)).

¹⁵¹ *Id.*

another.¹⁵² Some pieces of information may be present in one system but not another; other information may be coded in different fashions (e.g., numerical versus qualitative judgments) or using different standards (e.g., different ranges indicated by “high” and “low”). Some of these barriers may arise through inadvertence, but there is also evidence that some firms providing electronic health record systems may use proprietary formats to stymie aggregation and use of data from other systems.¹⁵³ Further complicating the interoperability problem, as described below, data about different kinds of conditions may be subject to different privacy regimes because some information is especially sensitive and thus more strongly protected by law.¹⁵⁴

Third, ensuring and maintaining the quality of data is difficult.¹⁵⁵ Especially in administrative claims data, information essential to receiving payment may be coded in ways that reflect financial incentives.¹⁵⁶ Because insurance requires certain diagnoses or procedures to reimburse for physician services, health care providers may have incentives to code those data in marginal or inappropriate situations, leading to biased data.¹⁵⁷ In addition, some health terms are inherently imprecise, such as “overweight” or “high” blood pressure, and may carry different meanings to different practitioners; attempting to distill imprecise categories into numerical variables can introduce errors if not done carefully and consistently. Finally,

¹⁵² See, e.g., Sharona Hoffman & Andy Podgurski, *Big Bad Data: Law, Public Health, and Biomedical Databases*, 41 J.L. MED. ETHICS 56 (2013); Jan Walker et al., *The Value of Health Care Information Exchange and Interoperability*, 24 HEALTH AFF. W5 (2005); W. Ed Hammond, *The Making and Adoption of Health Data Standards*, 24 HEALTH AFF. 1205 (2005).

¹⁵³ See OFFICE OF THE NATIONAL COORDINATOR FOR HEALTH INFORMATION TECHNOLOGY, REPORT TO CONGRESS: REPORT ON HEALTH INFORMATION BLOCKING 11–19 (April 2015), www.healthit.gov/sites/default/files/reports/info_blocking_040915.pdf (defining the technique of “information blocking” as “when persons or entities knowingly and unreasonably interfere with the exchange or use of electronic health information,” describing anecdotal and evidence of its prevalence).

¹⁵⁴ Different legal restrictions on data are discussed in more detail below in Part III, *infra*, but include the Privacy Rule of the Health Insurance Portability and Accountability Act of 1996 (HIPAA), 45 CFR Parts 160 and 164(A) & (E); the Genetic Information Nondiscrimination Act of 2008 (GINA), Pub. L. 110-233, 122 Stat. 881 (2008); and the Federal Information Security Management Act of 2002, 44 U.S.C. §§ 3541–3549.

¹⁵⁵ For an overview of quality challenges in medical data, see Sharona Hoffman & Andy Podgurski, *Big Bad Data: Law, Public Health, and Biomedical Databases*, 41 J.L. MED. ETHICS 56 (2013); Sharona Hoffman, *Symposium, Medical Big Data and Big Data Quality Problems*, 21 CONN. INS. L.J. 289 (2014).

¹⁵⁶ See ROBERT WACHTER, *THE DIGITAL DOCTOR: HOPE, HYPE, AND HARM AT THE DAWN OF MEDICINE’S COMPUTER AGE* (2015).

¹⁵⁷ *Id.*

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even with adequate care and effort, errors exist in all sources of data, and entities using those data for analysis need to account for that error.¹⁵⁸

B. Assistance from federal regulatory initiatives.

Although these challenges are substantial, a number of federal legislative and regulatory initiatives are helping to facilitate the use of health records in research. These efforts include incentives to promote the adoption and use of interoperable health records by caregivers and hospitals, creation of a network of data sources for public health monitoring of postmarket drug safety issues, and research initiatives in the areas of comparative effectiveness studies and personalized medicine.

1. Electronic health records.

The federal government has been actively promoting the use of electronic health records (EHRs) for well over a decade in the hope of reducing medical errors, reducing costs, and improving the quality of care.¹⁵⁹ Policy makers have also touted the potential for research use of electronic health records as part of a “learning healthcare system” in which caregivers continuously adapt their treatment choices in light of ever-expanding knowledge about healthcare outcomes.¹⁶⁰

The healthcare industry has been extraordinarily slow to adopt information technology, lagging far behind the rest of the economy.¹⁶¹ For a variety of reasons, paper records and hard copies dominated health records well into the first decade of the 21st century.¹⁶² President George W. Bush called for computerizing health records in his 2004 State of the Union

¹⁵⁸ Randomly distributed error may be accounted for by using sufficiently large samples, though with subtler or more complex relationships, or with smaller sample sizes, the signal can be swamped in noisy data. Systematic biases in data cannot be accounted for with larger sample sizes.

¹⁵⁹ See Report and Recommendations from the National Committee on Vital and Health Statistics, *Information for Health: A Strategy for Building the National Health Information Infrastructure* (2001), <http://aspe.hhs.gov/sp/nhii/documents/NHIIReport2001/>.

¹⁶⁰ *Id.* at 145–160.

¹⁶¹ Eric G. Poon et al., *Assessing the level of healthcare information technology adoption in the United States: A snapshot*, 6 BMC MED. INFORMATICS & DECISION-MAKING (Jan. 2006), <http://www.biomedcentral.com/1472-6947/6/1>; Gerard F. Anderson et al., *Health Care Spending and Use of Information Technology in OECD Countries*, 25 HEALTH AFF. 819-831 (2006).

¹⁶² Institute of Medicine. *Crossing the quality chasm: a new health system for the 21st century* (2001) [IOM Quality Chasm].

address,¹⁶³ and followed up by creating a new Office of the National Coordinator for Health Information Technology (ONC) to pursue this goal, with a budget of \$42 million.¹⁶⁴ But progress remained slow.

Federal incentives to make use of electronic health records were strengthened considerably in the Obama administration,¹⁶⁵ largely as a result of the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH Act), passed as part of the American Recovery and Reinvestment Act of 2009.¹⁶⁶ The HITECH Act codified the responsibilities and authority of the ONC within the Department of Health and Human Services.¹⁶⁷ It charged the ONC with reviewing standards for health information exchange, coordinating the activities of the federal government concerning health information technology, certifying compliance with applicable standards on a voluntary basis, publishing reports, and disseminating financial assistance. The legislation also established a Health IT Policy Committee¹⁶⁸ to make recommendations to the ONC for implementing a nationwide health information technology infrastructure and a Health IT Standards Committee¹⁶⁹ to recommend standards, specifications and certification criteria for the exchange of health information technology.¹⁷⁰ It directed the Secretary of HHS to “assist health care providers to adopt, implement, and effectively use certified EHR technology that allows for the electronic exchange and use of health information” through support of a research center and regional extension centers to provide technical assistance, disseminate best practices, and allow for the exchange and use of information in compliance with standards.¹⁷¹ And it provided \$30 billion for incentive payments through Medicare and Medicaid to reward the adoption and “meaningful use” of EHRs by

¹⁶³ George W. Bush, State of the Union Address (2004), <http://georgewbush-whitehouse.archives.gov/news/releases/2004/01/20040120-7.html>.

¹⁶⁴ David J. Brailer, *Interview: Guiding the Health Information Technology Agenda*, 29 HEALTH AFF. 586-595, 588 (2010).

¹⁶⁵ *Id.* (noting substantial increase in funding for ONC). The HITECH Act included appropriations of \$2 billion for the operation of the ONC and an estimated \$30 billion in Medicare and Medicaid incentive payments for physicians and hospitals that adopt and make meaningful use of electronic health records. See Melinda Beeuwkes Buntin et al., *Health Information Technology: Laying the Infrastructure for National Health Reform*, 29 HEALTH AFF. 1214-19 (2010).

¹⁶⁶ American Recovery and Reinvestment Act of 2009, Pub. L. No. 111-5, 123 Stat. 115 (Feb. 17, 2009) (ARRA), Div. A, Title XIII, Div. B, Title IV [HITECH Act].

¹⁶⁷ ARRA § 3001

¹⁶⁸ ARRA § 3002

¹⁶⁹ ARRA § 3003

¹⁷⁰ ARRA Div. A Tit. I.

¹⁷¹ ARRA § 3012

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providers and hospitals.¹⁷² Requirements to establish meaningful use increase over time, and after 2015, those who fail to make meaningful use EHRs are subject to penalties.

Use of EHRs increased significantly following the implementation of HITECH payment incentives,¹⁷³ although this has hardly been an unqualified success story.¹⁷⁴ Progress has been much slower in promoting health information exchange among providers. A major focus of the ONC in the years ahead is to achieve “a nationwide, interoperable health IT infrastructure.”¹⁷⁵

HITECH-driven adoption of EHRs offers considerable potential benefits for research users. EHRs provide richer and more complete information than claims data, and are easier to aggregate for use as research data than

¹⁷² ARRA §§ 4101, 4102. See Dept. of Health & Human Serv., Centers for Medicare and Medicaid Serv., Medicare and Medicaid Programs; Modifications to the Medicare and Medicaid Electronic Health Record (EHR) Incentive Program for 2014 and Other Changes to the EHR Incentive Program; and Health Information Technology: Revisions to the Certified EHR Technology Definition and EHR Certification Changes Related to Standards, 79 Fed. Reg. 52910 (Sept. 4, 2014).

¹⁷³ There is some debate about how much of this increase is a result of the resources and incentives put in place by the HITECH Act. Compare C.J. Hsiao et al., *Office-based physicians are responding to incentives and assistance by adopting and using electronic health records*, 32 HEALTH AFF. 1470, 1470–77 (2013) (rapid growth in adoption and meaningful use of basic EHR systems among US ambulatory care physicians from 2010–2012) and Michael F. Furukawa et al., *Despite Substantial Progress in EHR Adoption, Health Information Exchange and Patient Engagement Remain Low in Office Settings*, 33 HEALTH AFF. 1672 (2014) (finding greater progress in EHR adoption than in use of computerized health information exchange and patient engagement) with David Dranove et al., *Investment Subsidies and the Adoption of Electronic Medical Records at Hospitals*, NBER Working Paper No. 20553 (Oct. 2014), <http://www.nber.org/papers/w20553> (finding that HITECH incentives only modestly increased rate of adoption of EHRs by hospitals).

¹⁷⁴ A comparison of survey results in 2012 and 2015 by Accenture show a declining share of US doctors that see EMRs and health information exchange as improving the quality of treatment decisions, reducing medical errors, and improving health outcomes for patients. Accenture, *Doctors Survey 2015, US Report*, slide 14, <http://www.accenture.com/SiteCollectionDocuments/public-service/accenture-doctors-survey-2015-us-infographic.pdf>. For a narrative account of the impact of electronic medical records on providers and hospitals, see WACHTER, *supra* note 156.

¹⁷⁵ Office of the National Coordinator for Health Information Technology, *Connecting Health and Care for the Nation: A 10-Year Vision to Achieve an Interoperable Health IT Infrastructure* (2014), <http://www.healthit.gov/sites/default/files/ONC10yearInteroperabilityConceptPaper.pdf>; Office of the National Coordinator for Health Information Technology, *Connecting Health and Care for the Nation: A Shared Nationwide Interoperability Roadmap* (Draft Version 1.0 April 2015) (hereinafter *Interoperability Roadmap*), <http://www.healthit.gov/sites/default/files/nationwide-interoperability-roadmap-draft-version-1.0.pdf>

the paper records used by providers in the past. Although lack of interoperability is an ongoing problem, ONC is working to promote the development of interoperable EHR products that allow providers to share and access a common clinical data set according to common technical standards across a nationwide network.¹⁷⁶ The networks and infrastructure that promote information exchange in the context of clinical care will also facilitate access and aggregation by researchers, as ONC recognizes.¹⁷⁷ Indeed, for research purposes it may be possible to achieve considerable benefits without nationwide interoperability by using the records of a single large provider.¹⁷⁸ Data quality may prove to be a more persistent problem in making research use of records that some observers claim are optimized for (or distorted by) the purpose of justifying billing.¹⁷⁹

2. Regulatory use of networked data for observational studies

Payer innovators may also benefit from the infrastructure and technology developed to support the FDA Sentinel System, a legislatively mandated network of data sources and tools for post-market monitoring of the safety of FDA-approved products.

A series of high-profile drug safety cases (including the Vioxx episode)¹⁸⁰ provoked members of Congress to ask the Government Accountability Office (GAO) to review FDA's organizational structure and decision-making process for postmarket drug safety.¹⁸¹ The GAO Report was highly critical of FDA's system of postmarket surveillance, noting that it was underfunded¹⁸² and relied too heavily on an unreliable system of

¹⁷⁶ *Interoperability Roadmap*, *supra* note 175, at 13.

¹⁷⁷ *Id.* at 18–19 (noting that interoperability will promote “a learning health system” that improves health “by generating information and knowledge from data captured and updated over time”).

¹⁷⁸ *E.g.*, the Kaiser Permanente study of the effects of Vioxx was limited to the records of one large, integrated provider.

¹⁷⁹ WACHTER, *supra* note 156, at 120 (“Much of the data in EHRs continues to be collected for the purpose of creating a superior bill, and using this waste product of administrative functions for clinical decision making can lead to a GIGO (garbage in, garbage out) problem, even with fabulous analytics.”).

¹⁸⁰ Another contemporaneous controversy involved FDA's delay in notifying the public of risks of suicide risks associated with the use of antidepressants by children. [cite]

¹⁸¹ U.S. Gov't Accountability Off., Report to Requesters: Drug Safety, Improvements Needed in FDA's Postmarket Decision-making and Oversight Process (2006).

¹⁸² *Id.* at 7–8 (noting that in fiscal year 2005 the FDA Office of Drug Safety had expenditures of \$26.9 million and a staff of 107, while the Office of New Drugs had expenditures of \$110.6 million and a staff of 715).

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adverse event reporting.¹⁸³ Although at the time FDA had started working with the Centers for Medicare and Medicaid Services (CMS) to obtain access to data on clinical experience and patient outcomes with drugs provided under the then-new Medicare prescription drug benefit, it was unclear how useful those data would be for surveillance of drug safety.¹⁸⁴ The GAO Report concluded that “FDA will need to continue its efforts to develop useful observational studies and to access and use additional healthcare databases” and recommended that “Congress should consider expanding FDA’s authority to require drug sponsors to conduct postmarket studies, such as clinical trials or observational studies.”¹⁸⁵

Around the same time FDA and the Department of Health and Human Services asked the Institute of Medicine (IOM) to convene a committee of experts to assess the US drug safety system and to make recommendations to improve risk assessment, surveillance, and the safe use of drugs.¹⁸⁶ The IOM Committee report embraced a “lifecycle approach to drug risk and benefit” that would not rely exclusively on FDA and drug companies, but would also engage the healthcare delivery system, the academic research community, and other government agencies in an “ongoing, active reassessment of risk and benefit” throughout the life of the product.¹⁸⁷ In particular, the report recommended an overhaul of FDA’s outdated post-approval adverse event reporting system and an increase in “programs that access and study data from large automated healthcare databases.” Noting that preapproval clinical trials “do not provide adequate information about the balance of risks and benefits of drugs that are used by many people for many years,” the report recommended making more effective use of “increasingly high-quality data and scientific capacity” of other public and private sector institutions through “a public-private partnership with drug sponsors, public and private insurers, for-profit and not-for-profit health care provider organizations, consumer groups, and large pharmaceutical companies to prioritize, plan, and organize funding for confirmatory drug safety and efficacy studies of public health importance.”¹⁸⁸ The IOM report also echoed the recommendations of the GAO Report that Congress fortify FDA’s authorities to take a variety of regulatory actions after drug

¹⁸³ *Id.* at 24-25.

¹⁸⁴ *Id.* at 35 (noting “data quality issues”).

¹⁸⁵ *Id.* at 36

¹⁸⁶ IOM Comm. on the Assessment of the US Drug Safety System, *The Future of Drug Safety: Promoting and Protecting the Health of the Public* at 2–3 (Washington DC: National Academies Press 2007)

¹⁸⁷ *Id.* at 4–5.

¹⁸⁸ *Id.* at 7–8.

approval.¹⁸⁹

The recommendations in these reports did not speak directly to the role of payers in healthcare innovation and regulation. But by highlighting the value of healthcare records and observational studies in the ongoing process of systematic learning from clinical experience, they set a course that would enlarge the role of institutions with stewardship of those records.

Congress responded to the GAO and IOM reports on drug safety by passing the Food and Drug Administration Amendments Act of 2007 (FDAAA 2007),¹⁹⁰ a complex piece of legislation that gave FDA significant new authorities to oversee the safety of drugs after approval.¹⁹¹ This legislation marked a significant shift in the evidentiary basis for FDA decision-making away from sole reliance on data from premarket clinical trials and adverse event reports submitted by drug companies¹⁹² towards new sources of data and expertise.¹⁹³ It directed FDA to collaborate with “public, academic, and private entities” to obtain access to “disparate data sources” and to “develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources.”¹⁹⁴ Once these methods were developed, it directed FDA to “establish and maintain procedures for risk identification and analysis based on electronic health data.”¹⁹⁵

The electronic health data that these provisions direct FDA to monitor are for the most part in the custody of payers. Although the statute charges FDA with the job of developing and using the system for surveillance, it also contemplates that FDA will work in cooperation with other actors and

¹⁸⁹ *Id.* at 10–12.

¹⁹⁰ Pub. L. No. 110-85, 121 Stat. 823 (codified as amended in scattered sections of 21 U.S.C.).

¹⁹¹ Particularly notable are new authorities to require a drug sponsor to conduct postapproval studies or new clinical trials at any time after approval of a new drug application if FDA becomes aware of new safety information, 21 U.S.C. § 355(o)(3); to require labeling changes to disclose new safety information, 21 U.S.C. § 355(o)(4); and to require “risk evaluation and management strategies,” which might include the use of Medication Guides and patient package inserts or other communication with providers, special training or certification requirements for providers that dispense the product, and special monitoring of patients that use the product, if necessary to ensure that the benefits of the drug outweigh its risks. 21 U.S.C. § 355-1.

¹⁹² Data from clinical trials remain necessary as part of a new drug application under 21 U.S.C. §§ 355(b)(1)(A) and 355(d)(1), (5), and (7). Sponsors also have a continuing obligation to report adverse events.

¹⁹³ For a thoughtful analysis of this shift, see Barbara J. Evans, *Seven Pillars of a New Evidentiary Paradigm: The Food, Drug, and Cosmetic Act Enters the Genomic Era*, 85 NOTRE DAME L. REV. 419-524 (2010).

¹⁹⁴ 21 U.S.C. § 355(k)(3).

¹⁹⁵ 21 U.S.C. § 355(k)(3)(C)(i).

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institutions, and explicitly authorizes FDA to enter into contracts with public and private entities to achieve these goals.¹⁹⁶ Indeed, it is difficult to imagine how FDA could carry out its new statutory directives unless it works with the payers who have custody of health data.

With these marching orders, FDA has been working with outside entities, including payers, to establish its Sentinel System for monitoring the safety of drugs. It entered into a 5-year contract with the Harvard Pilgrim health plan to develop a pilot “mini-Sentinel” system, and recently entered into a new contract with Harvard Pilgrim to lead the Sentinel System in partnership with over fifty health care organizations and academic institutions.¹⁹⁷

Mini-Sentinel has already facilitated the development of innovative information using payer data. In 2010, FDA launched a study of the risk of intussusception¹⁹⁸ in infants receiving rotavirus vaccines after ambiguous postmarketing studies conducted by the vaccine sponsors.¹⁹⁹ FDA used Mini-Sentinel to access payer information from Aetna, Healthcore, and Humana relating to over 1.3 million vaccine administrations.²⁰⁰ Researchers found a small but significant increase in intussusception, enough to require labeling changes for the vaccines.²⁰¹ Although this is a success story for Mini-Sentinel, it also highlights the challenge of this type of network: someone must know to ask the question, and currently, the only one asking the questions is FDA.

Sentinel is an important public health initiative to develop and utilize new technology and data sources in a distributed network to monitor safety. Although the purpose of the Sentinel System is to monitor drug safety, this unique resource is currently being used for other public health purposes as well,²⁰² and FDA officials have announced plans to make the Sentinel infrastructure—though not the data themselves—available to other users in the future as part of a national data infrastructure.²⁰³

¹⁹⁶ 21 U.S.C. § 355(k)(3)(C)(v).

¹⁹⁷ See Health Affairs, *Health Affairs Health Policy Brief, The FDA’s Sentinel Initiative*. (June 4, 2015) [Health Affairs Sentinel Brief], http://healthaffairs.org/healthpolicybriefs/brief_pdfs/healthpolicybrief_139.pdf

¹⁹⁸ Intussusception is a serious medical condition in which part of the intestine folds into another section of the intestine.

¹⁹⁹ U.S. FDA, *FDA Releases Final Study Results of a Mini-Sentinel Postlicensure Observational Study of Rotavirus Vaccines and Intussusception* (June 13, 2013), <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ucm356758.htm>.

²⁰⁰ W. Katherine Yih et al., *Intussusception Risk after Rotavirus Vaccination in U.S. Infants*, 370 N. ENGL. J. MED. 503 (2014)

²⁰¹ *Id.*

²⁰² *Id.* at 4.

²⁰³ Janet Woodcock, Another important step in FDA’s journey towards enhanced

More broadly, Sentinel is also a significant research initiative that leverages public resources, public health goals, and legal authorities to support the development of technology that has other uses in biomedical research. The statute explicitly calls for the development and validation of new analytical methods.²⁰⁴ More generally, it sets goals that drive the development of new capabilities. Because this initiative looks to establish a network of data sources, it creates new partnerships among institutions, including payers, that might benefit from other collaborations outside the Sentinel System. By setting ambitious goals for utilizing new technological strategies, it identifies obstacles (such as data quality and interoperability and privacy) and challenges participants to develop strategies to overcome them.²⁰⁵ And it engages in this research effort a set of institutions that have a direct stake in the research, but might not otherwise have taken on such a significant role in health R&D.

3. Government research programs

The federal government has also used its role as research sponsor to establish new research programs that organize, subsidize, and direct research using health records. These programs provide subsidies and training and build networks across public, private, and academic institutions, providing a foundation for future research.

a. Comparative effectiveness research

The Affordable Care Act (2010) authorized the establishment of the Patient Centered Outcomes Research Institute (PCORI) to oversee and set guidelines for comparative effectiveness research. The legislation specifies that PCORI will be a nonprofit, nongovernmental research institute with an initial appropriation from Congress and subsequent funding from a new fee on health insurers until it sunsets in 2019.²⁰⁶

safety through full-scale “active surveillance,” FDA Voice (Dec. 30, 2014), <http://blogs.fda.gov/fdavoices/index.php/2014/12/another-important-step-in-fdas-journey-towards-enhanced-safety-through-full-scale-active-surveillance/>.

²⁰⁴ 21 U.S.C. § 355(k)(3)(B).

²⁰⁵ Health Affairs Sentinel Brief, *supra* note 197, at 4.

²⁰⁶ The choice to set up an organization outside the existing science agencies is interesting, and likely explained by the politics of holding together a fragile coalition to pass the Affordable Care Act in the face of industry anxiety about the likely impact on coverage decisions and prices for their products. The House version of the ACA called for a government entity housed within the Agency for Healthcare Research and Quality (AHRQ), which in turn is a part of the Department of Health and Human Services. The

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PCORI is governed by a 19-member board including patients, caregivers, and representatives of hospitals, insurers and product-developing firms. It is distinctive in its focus on engagement with stakeholders including clinical and patient communities to ensure the relevance and impact of research.

The PCORI provisions of the ACA specifically target the same technical difficulties that payers would confront in their own comparative effectiveness research,²⁰⁷ creating communities to address these difficulties with federal funding. PCORI has awarded \$100 million to establish a national patient-centered outcomes research network, PCORnet, composed of 11 large healthcare organization networks and 18 patient-group-based networks, that will generate interoperable datasets to support multinet network studies, and it is actively funding studies.

PCORI occupies a politically precarious niche in the biomedical innovation system. There have been repeated proposals to eliminate PCORI. Some critics charge that it is redundant to the ongoing efforts of other agencies. But its focus on engaging clinical caregivers and private payers in the research distinguishes it from other more academically oriented research programs, and perhaps offers the prospect of training and engaging a new set of institutions that will continue their involvement in research in the future.

The political compromises necessary to pass the ACA constrained PCORI with the following ambiguous statutory prohibition:

The Patient-Centered Outcomes Research Institute . . . shall not develop or employ a dollars-per-quality adjusted life year (or similar measure that discounts the value of a life because of an individual's disability) as a threshold to establish what type of health care is cost effective or recommended. The Secretary shall not utilize such an

Senate Finance Committee version of the ACA called for a nongovernmental entity, and that is the version that was ultimately signed into law. Kavita Patel, *Health Reform's Tortuous Route to the Patient-Centered Outcomes Research Institute*, 29:10 HEALTH AFF. 1777, 1777–82 (2010).

²⁰⁷ The ACA amended the Public Health Service Act to add a new section 937(f) authorizing the Secretary of HHS to build data capacity for the conduct of comparative effectiveness research:

The Secretary shall provide for the coordination of relevant Federal health programs to build data capacity for comparative clinical effectiveness research, including the development and use of clinical registries and health outcomes research data networks, in order to develop and maintain a comprehensive, interoperable data network to collect, link, and analyze data on outcomes and effectiveness from multiple sources, including electronic health records.

ACA § 6301(b).

adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIII.²⁰⁸

This language reflects concerns by some opponents of comparative effectiveness research that it would lead to rationing or withholding of care from disabled people based on assessments of government bureaucrats that some lives are worth less than others. Some commentators read this language broadly to prohibit consideration of cost-effectiveness in PCORI-funded research.²⁰⁹ Whatever limits the statutory language imposes on PCORI, it does not constrain other institutions outside the government. Thus private insurers could develop their own cost-effectiveness thresholds and use them to make coverage determinations without violating the law. Indeed, the statute explicitly states that “Nothing in this section shall be construed . . . to permit the Institute to mandate coverage, reimbursement, or other policies for any public or private payer”²¹⁰

But the statute directly prohibits use of dollars-per-quality adjusted life years as thresholds for coverage determinations under Medicare. Since private insurers often replicate Medicare coverage determinations, the constraints on “the Secretary” may effectively determine private sector moves as well. These provisions may undermine the potential of PCORI research to drive cost-savings in practice, but should not significantly constrain its research mission.

b. Personalized medicine

Another important source of research funding that is likely to accelerate progress in overcoming technical obstacles to payer innovation is the National Institutes of Health (NIH). NIH is, of course, the largest source of funding for biomedical research, and an important driver of personalized medicine research. Two NIH initiatives particularly stand out: the Precision

²⁰⁸ ACA § 1182, codified at 42 U.S.C. § 1320e-1(e).

²⁰⁹ Professor Nicholas Bagley, while acknowledging that some legislators sought to impose just such a limitation, reads the enacted statutory language more narrowly. In this reading, the statute merely prevents the development or employment of a cost-effectiveness *threshold* based on dollars-per-quality adjusted life years or similar measures. So long as PCORI does not develop or employ such a threshold to establish what type of health care is cost effective or recommended, nothing in the statutory language prevents it from compiling, considering, and comparing costs of the treatments that it evaluates. Nicholas Bagley, *Who says PCORI can't do cost effectiveness?* The Incidental Economist (Oct. 14, 2013), <http://theincidentaleconomist.com/wordpress/who-says-pcori-cant-do-cost-effectiveness/>

²¹⁰ ACA § 6301(a), codified at 42 U.S.C. § 1320e (j)(1)(A).]

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Medicine Initiative, and the eMERGE network.

President Obama announced the Precision Medicine Initiative in his 2015 State of the Union address. The aim of the initiative is to drive personalized medicine forward through public-private partnerships, including work with drug companies on cancer genomics.²¹¹ Eventually, the initiative aims to develop a cohort of at least one million Americans with full genomic and health data to be used for research. The President called for an initial \$215 million in funding to drive this research.²¹² Crucially, the goals of the program included a significant focus on infrastructure for research, including developing the cohort, creating information management and analysis tools, and helping cement relationships between public and private entities in the area.²¹³

Another particularly important NIH initiative in this area is the eMERGE (electronic MEDical Records and GENomics) Network, a consortium of research institutions organized and funded by the National Institute for Human Genome Research that brings together researchers with wide-ranging expertise in genomics, statistics, ethics, informatics, and clinical medicine.²¹⁴

The eMERGE Network aims to combine information from electronic health records with genotype data from DNA biorepositories to identify relationships between genetic variations and health outcomes and to assess the utility of genotype information for clinical use.²¹⁵ To facilitate this research the eMERGE network has had to address a number of issues with legal implications, including developing standardized patient consent language and best practices for sharing patient genetic data, and has formed working groups to address these issues.²¹⁶ eMERGE's sponsor, the National Human Genome Research Institute, has a long history of sponsoring

²¹¹ See Francis S. Collins & Harold Varmus, *A New Initiative on Precision Medicine*, 372 NEW ENG. J. MED. 793, 793 (2015); Nat'l Inst. of Health, *Near-Term Goals*, <http://nihprod.cit.nih.gov/precisionmedicine/goals.htm> (last updated October 13, 2015).

²¹² Press Release, The White House, Fact Sheet: President Obama's Precision Medicine Initiative (Jan. 15, 2015), <https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative>.

²¹³ Collins & Varmus, *supra* note 211.

²¹⁴ eMERGE Network, <https://emerge.mc.vanderbilt.edu/> (last visited Feb. 24, 2016); Catherine A. McCarty et al., *The eMERGE Network: A Consortium of Biorepositories Linked to Electronic Medical Records Data for Conducting Genomic Studies*, 4 BMC MED. GENOMICS 13 (2011).

²¹⁵ eMERGE Network, *About eMERGE*, <https://emerge.mc.vanderbilt.edu/about-emerge/> (last visited Feb. 24, 2016).

²¹⁶ See Laura M. Beskow et al., *Model Consent Language* (2009), http://www.ninds.nih.gov/research/clinical_research/application_process/eMerge_model_language.pdf.

research on ethical and legal issues associated with human genome research and incorporating best practices into research.²¹⁷

The tools and databases created by the eMERGE network have also been used by participating institutions in collaborations outside the network, suggesting spillover benefits in promoting further research outside the immediate scope of sponsored activity. For instance, eMERGE researchers developed the Phenotype KnowledgeBase, or PheKB, a collaborative environment used to collect, validate, and share electronic algorithms for learning about patient phenotype based on health data.²¹⁸ Similarly, eMERGE's model consent form can be used by any organization, including integrated systems, collecting genomic data for future analyses. Finally, eMERGE's privacy-protecting data collection framework offers a pathway for future data-collection endeavors by payers or data aggregators.²¹⁹ This last is a particularly relevant example of the way that federal research initiatives can facilitate payer innovation, because it bears on a large non-technological hurdle to that innovation: privacy rules protecting patient data.

III. LEGAL PRIVACY OBSTACLES: HIPAA AND HITECH

Privacy laws, principally the Health Insurance Portability and Accountability Act of 1996 (HIPAA),²²⁰ present a challenging obstacle to the use of patient health information for research purposes.

HIPAA aimed to facilitate the flow of information for health care and administrative purposes (such as claims processing), while protecting patient privacy by restricting uses and disclosure for other purposes.²²¹ The Department of Health and Human Services has elaborated upon these general statutory provisions in detailed rules,²²² including a Privacy Rule²²³

²¹⁷ See Jean E. McEwen et al., *The Ethical, Legal, and Social Implications Program of the National Human Genome Research Institute: Reflections on an Ongoing Experiment**, 15 ANN. REV. GENOMICS HUM. GENET. 481 (2014).

²¹⁸ See *PheKB*, <https://phekb.org/> (last visited Feb. 24, 2016).

²¹⁹ See Ioana Danciu et al., *Secondary Use of Clinical Data: The Vanderbilt Approach*, 52 J. BIOMED. INFORM. 28 (2014) (discussing data architecture and privacy-protecting collection practices); Abel N. Kho et al., *Design and Implementation of a Privacy Preserving Electronic Health Record Linkage Tool in Chicago*, J. AM. MED. INFORM. ASSOC. ocv038 (2015) (implementing similar system to collect data in Chicago).

²²⁰ Pub. L. No. 104-191, 100 Stat. 2548 (hereinafter HIPAA).

²²¹ See Nicolas P. Terry, *Big Data Proxies and Health Privacy Exceptionalism*, 24 HEALTH MATRIX 65, 67-69 (describing basic architecture of privacy protection under 1996 statute).

²²² Section 264 of HIPAA called for the Secretary of Health and Human Services (the Secretary) to submit detailed recommendations to Congress with respect to the privacy of

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that sets limits on disclosure and use of “protected health information”²²⁴ by “covered entities”²²⁵ and their “business associates.”²²⁶ Health insurance plans, providers, and health care clearinghouses are all “covered entities.”²²⁷ Business associates include anyone who, “on behalf of a covered entity,” receives protected health information from the covered entity to perform “legal, actuarial, accounting, consulting, *data aggregation* . . . management, administrative, accreditation, or financial services.”²²⁸ “Protected health information” includes both medical and billing records.²²⁹ The baseline rule under HIPAA is that all use or disclosure of protected health information is prohibited unless it is specifically allowed.²³⁰ In addition, the Privacy Rule requires reasonable efforts to limit uses or disclosures of protected information to “the minimum necessary” to accomplish the intended purpose.²³¹ The Privacy Rule thus creates substantial hurdles for aggregating data from different sources, and even for internal use of data by

individually identifiable health information within twelve months of the enactment of HIPAA, and further provided that if legislation governing privacy standards were not enacted within three years, the Secretary “shall promulgate final regulations containing such standards” within 42 months after the enactment of HIPAA. HIPAA, *supra* note 220, § 263.

²²³ 45 C.F.R. Parts 160, 164.

²²⁴ The HIPAA Privacy Rule generally defines “protected health information” as “individually identifiable health information.” 45 C.F.R. § 160.103.

²²⁵ “Covered entities” is defined at 45 C.F.R. § 160.103 to include a health plan, a health care clearinghouse, or a health care provider who transmits any health information in electronic form.

²²⁶ 45 C.F.R. § 160.103.

²²⁷ 45 C.F.R. § 160.102. Only providers who transmit health information in electronic form in connection with certain transactions are “covered entities.” *Id.* Health care clearinghouses are entities that engage in the data integration process described above, changing information between different formats to facilitate its use in different environments. 45 CFR § § 160.103, 164.500(b).

²²⁸ 45 C.F.R. § 160.103 (emphasis added).

²²⁹ 45 C.F.R. § 160.103 defines “protected health information” as “individually identifiable health information . . . that is (i) transmitted by electronic media; (ii) maintained in electronic media; or (iii) transmitted or maintained in any other form or medium.” It broadly defines “health information” to mean “any information, including genetic information, whether oral or recorded in any form or medium, that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual.”

²³⁰ 45 C.F.R. §§ 164.502.

²³¹ 45 C.F.R. § 164.502(b) This limitation does not apply to disclosures to providers for the purposes of providing care, or various other purposes required by the statute. *Id.* § 164.502(b)(2).

a covered entity, but it is limited in a number of ways that leave room for some research use of protected information.²³²

Complicating the picture, different kinds of health information are subject to different rules. The Privacy Rule itself provides additional protection for psychotherapy notes²³³ while allowing more stringent privacy protections under various state laws.²³⁴ Some state statutes, for example, provide more stringent additional protections against disclosure of information related to HIV status and treatment.²³⁵ Other federal statutes provide additional protection for genetic information,²³⁶ substance abuse treatment records,²³⁷ and HIV status beyond the HIPAA baseline.²³⁸ This

²³² See 45 C.F.R. §§ 164.502 (general rule prohibiting use or disclosure of protected health information except as permitted or required by the Privacy Rule); 164.508 (defining uses and disclosures for which an authorization is required); 164.512 (defining uses and disclosures for which an authorization is not required).

²³³ 45 C.F.R. § 164.508(a)(2) (prohibiting disclosure without specific written authorization).

²³⁴ 45 C.F.R. § 160.203(b); 42 U.S.C. § 1320d-2(c)(2).

²³⁵ E.g., New York Public Health Law § 2783

²³⁶ Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, 122 Stat. 881 (GINA). The protections of GINA are particularly notable because of the importance of genetic information to researchers seeking to understand the heterogeneous responses of different patients to healthcare interventions. GINA prohibits discrimination in health insurance coverage based on an individual's genetic information. It also states that genetic information is health information under HIPAA contains new privacy protections for genetic information and prohibits insurers from using or disclosing genetic information for underwriting purposes. *Id.* § 105. While GINA does not impose specific restrictions on use or disclosure of genetic information for research purposes, insurers are prohibited from requiring patients to undergo genetic testing. *Id.* § 101(b). In addition, at least one commentator has expressed concern that doctors will keep genetic information out of insurer-accessible medical records to prevent GINA-prohibited discrimination. Eric A. Feldman, *The Genetic Information Nondiscrimination Act (GINA): Public Policy and Medical Practice in the Age of Personalized Medicine*, 27 J. GEN. INTERN. MED. 743, 745 (2012).

²³⁷ Under 42 U.S.C. § 290dd-2(a), "Records of the identity, diagnosis, prognosis, or treatment of any patient which are maintained in connection with the performance of any program or activity relating to substance abuse education, prevention, training, treatment, rehabilitation, or research, which is conducted, regulated, or directly or indirectly assisted by any department or agency of the United States shall, . . . be confidential and be disclosed only for the purposes and under the circumstances expressly authorized under subsection (b) of this section." The only statutory exception is for a "bona fide medical emergency," *id.* § 290dd-2(b)(2)(A), but regulations provide that information can be shared between personnel within a program or its direct administrative supervisor for substance abuse treatment purposes. 42 C.F.R. § 2.12(c)(3). Less protective state laws are preempted, but more protective state laws are not. 42 C.F.R. § 2.20.

²³⁸ For a helpful overview, see Timothy S. Jost, *Constraints on Sharing Mental Health and Substance-Use Treatment Information Imposed by Federal and State Medical Records*

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uneven landscape of privacy restrictions further complicates the challenge of assembling broad, comprehensive, longitudinal health records. Different types of health information are fragmented into different privacy siloes, and the legal privacy protections change as patients move between states or develop new medical conditions.

The Privacy Rule nonetheless allows some room for innovators to use health data. Some uses of protected health information are generally permitted, while specific waiver and authorization provisions enable normally prohibited uses. Moreover, the HITECH Act of 2009 has modified HIPAA to reshape—and hopefully, to reduce—some hurdles to innovation.

A. Normally permitted uses

The wording of the Privacy Rule creates considerable confusion about the extent to which the study of healthcare records to improve future patient care qualifies for the more favorable treatment for “health care operations” rather than falling into the less favored category of “research.” The Privacy Rule permits a covered entity to use or disclose protected health information “for treatment, payment or health care operations,”²³⁹ so long as it makes “reasonable efforts to limit protected health information to the minimum necessary to accomplish the intended purpose.”²⁴⁰ Although the Rule explicitly allows use of protected health information for “quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines,” such studies may not have the primary purpose of “obtaining [] generalizable knowledge.”²⁴¹ These provisions are tough to reconcile, since it would be irresponsible to develop clinical guidelines on the basis of anything short of generalizable knowledge.²⁴² At

Privacy Laws in INSTITUTE OF MEDICINE (US) COMMITTEE ON CROSSING THE QUALITY CHASM: ADAPTATION TO MENTAL HEALTH AND ADDICTIVE DISORDERS (Washington DC: National Academies Press 2006).

²³⁹ 45 C.F.R. § 164.506(a).

²⁴⁰ 164.502(b). The definitions set forth in the Privacy Rule make it clear that the exception for “health care operations” does not cover “research.” “Health care operations” is defined to include “conducting quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines, provided that the obtaining of generalizable knowledge is not the primary purpose of any studies resulting from such activities.” 45 C.F.R. § 164.501.

²⁴¹ 45 C.F.R. § 164.501.

²⁴² See IOM, *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research* (2009) [IOM Beyond HIPAA], 131–39 (discussing “somewhat artificial distinction between health research and some closely related health care practices, such as ... quality improvement activities”); see also Stacey A. Tovino, *The Use and Disclosure of Protected Health Information for Research Under the Hippa Privacy Rule:*

a minimum, one might expect that as the analysis of health outcomes to improve clinical care becomes more scientifically rigorous (and its conclusions therefore more generalizable), it may look less like permissible “health care operations” and more like restricted “research.”²⁴³ Notably, the 21st Century Cures Act, currently under consideration by Congress, would resolve this issue by “revis[ing] or clarify[ing]” that research, “including studies whose purpose is to obtain generalizable knowledge,” falls within the definition of health care operations.²⁴⁴

De-identified data. De-identified data isn’t covered at all by the Privacy Rule. Even for activities that count as “research,” the Privacy Rule applies only to “individually identifiable health information” and not to “[h]ealth information that does not identify an individual and with respect to which there is no reasonable basis to believe that the information can be used to identify an individual.”²⁴⁵ Although advances in information technology have made it increasingly easy to re-identify individuals on the basis of limited information,²⁴⁶ the Privacy Rule nonetheless provides a safe harbor that qualifies data as de-identified if seventeen pieces of identifying information are removed.²⁴⁷ De-identifying data is a key way to navigate HIPAA restrictions even for government entities; when California’s health

Unrealized Patient Autonomy and Burdensome Government Regulation, 49 S.D. L. REV. 447, 450–55 (2004) (discussing the applicability of HIPAA restrictions to research).

²⁴³ “Research” is separately defined as “a systematic investigation, including research development, testing, and evaluation designed to develop or contribute to generalizable knowledge.” 45 C.F.R. § 164.501.

²⁴⁴ 21st Century Cures Act, H.R. 6 (2015), 114th Congress, § 1124, *available at* <https://www.congress.gov/114/bills/hr6/BILLS-114hr6ih.xml>. The Act was approved by the House of Representatives on July 10, 2015.

²⁴⁵ 45 C.F.R. § 164.514(a).

²⁴⁶ See Daniel C. Barth-Jones, “The Re-identification of Governor William Weld’s Medical Information: A Critical Re-examination of Health Data Identification Risks and Privacy Problems, Then and Now” (Working Paper June 4, 2012), http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2076397; *see also* Paul Ohm, *Broken Promises of Privacy: Responding to the Surprising Failure of Anonymization*, 57 UCLA L. REV. 1701, 1716–31, 1736–38 (2009) (describing re-identification generally and in the HIPAA context).

²⁴⁷ 45 C.F.R. § 164.514(b)(2)(i). The list includes names, geographic subdivisions smaller than a state, certain dates directly related to an individual, telephone and fax numbers, email addresses, social security numbers, medical record numbers, health plan beneficiary numbers, and other identifying numbers and codes, biometric identifiers, full-face photographic images, and “any other unique identifying number, characteristic, or code, except as permitted by paragraph(c) of this section.” 45 C.F.R. § 164.514(b)(2)(i)(A)-(R). An exception to the final catch-all item permits the covered entity to assign a non-substantive code to allow the covered entity itself to reidentify the information so long as the covered entity does not use or disclose the code for any other purpose nor disclose the mechanism for re-identification. 45 C.F.R. § 164.514(c).

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exchange marketplace, Covered California, begins collecting payer data on its 1.4 million customers, the data will go to a third-party analytics company, and the state itself will receive only de-identified data.²⁴⁸

However, de-identification brings its own problems. The list of identifiers includes information that may be relevant to researchers, including dates, ages, and biometric identifiers; excluding this information limits the value of the data.²⁴⁹ Moreover, retention of identifiers may be necessary to link data from different sources and over time.²⁵⁰ The most straightforward way to integrate information from different sources—a key technical challenge discussed above—is to use unique identifying information from individual records. If Miles Vorkosigan’s records from different providers and payers are related only by the fact that those records all pertain to Miles Vorkosigan, the easiest way to link those records is through his name.²⁵¹ Removing identifying information prevents this aggregation. There are ways around this problem involving translating identifiable information into unique identifiers through a one-way encoding process, but they add technical complexity and require at least some form of centralized infrastructure.

Limited data sets. The Privacy Rule provides a less restrictive alternative allowing covered entities to use or disclose “limited data sets” without the need for authorization “only for the purposes of research, public health, or health care operations.”²⁵² The list of identifiers that must be excluded to qualify as a limited data is less restrictive than the exclusions required to qualify for the de-identification safe harbor.²⁵³ A covered entity may use or disclose a limited data set only if it enters into a “data use agreement” obliging the data recipient to use or disclose the protected health information only for “limited purposes” permitted by the Rule.²⁵⁴

²⁴⁸ Chad Terhune, *California’s Obamacare Exchange to Collect Insurance Data on Patients*, LOS ANGELES TIMES (June 21, 2015), <http://www.latimes.com/business/la-fi-obamacare-patient-privacy-20150622-story.html>.

²⁴⁹ For example, the requirement for removal of any geographic identifier smaller than a state can significantly limit the assembly of detailed geographic health information. *Id.* § 164.514(b)(2)(i)(B). For a discussion of this problem see IOM Beyond HIPAA, *supra* note 242, at 230–33.

²⁵⁰ IOM Beyond HIPAA, *supra* note 242, at 177–179.

²⁵¹ See LOIS M. BUJOLD, *BROTHERS IN ARMS* (Baen Books, 1989) (discussing the potential consequences of access to uniquely-identified biomedical information and samples).

²⁵² 45 C.F.R. § 164.514(e).

²⁵³ *Id.* § 164.514(e)(2). Unlike a fully de-identified data set, a limited data set may include date, town, state, and zip code; there is also no catch-all category prohibiting “any other unique identifying number, characteristic, or code.” *Id.*

²⁵⁴ 45 C.F.R. § 164.514(e)(4)(i).

The agreement must specify permitted uses and disclosures, require safeguards to prevent further use or disclosure, and prohibit recipients from identifying or contacting the individuals whose health information has been disclosed.²⁵⁵

Public health activities. The Privacy Rule explicitly permits use or disclosure of protected health information for certain public health activities, including disclosure to a public health authority for surveillance purposes.²⁵⁶ This allows disclosures to FDA for postmarketing safety monitoring under the Sentinel Initiative.²⁵⁷ A related provision permits disclosure of information about an FDA-regulated product or activity to its FDA sponsor in order to collect or report adverse events and to conduct post marketing surveillance.²⁵⁸ While this lets drug companies access information about their own products, it does not permit disclosure of data about other treatments that could serve as controls, limiting the possibility of comparative effectiveness research.²⁵⁹

The foregoing limitations²⁶⁰ on the Privacy Rule allow some use of healthcare information in research, although compliance with the conditions necessary to qualify for these limitations may be burdensome and may limit the scope of research.

B. Authorization and waivers

In addition to normally permitted uses, the Privacy Rule enables allows otherwise prohibited uses and disclosures in two circumstances. First, individual patients may authorize any use of their protected health information. Second, researchers may obtain waivers of HIPAA requirements from an Institutional Review Board or a Privacy Board.

The Privacy Rule permits individual patients to authorize the use of their protected health information for any purpose, including use in research

²⁵⁵ 45 C.F.R. § 164.514(e)(4)(ii).

²⁵⁶ 45 C.F.R. § 164.512(b)(i).

²⁵⁷ See Kristen Rosati, Barbara Evans & Deven McGraw, White Paper, *HIPAA and Common Rule Compliance in the Mini-Sentinel Pilot*, http://www.mini-sentinel.org/work_products/About_Us/HIPAA_and_CommonRuleCompliance_in_the_Mini-SentinelPilot.pdf.

²⁵⁸ 45 C.F.R. § 164.514(b)(iii).

²⁵⁹ Barbara J. Evans, *The Ethics of Postmarketing Observational Studies of Drug Safety Under Section 505(o)(3) of the Food, Drug & Cosmetic Act*, 38 AM. J.L. & MED. 577, 588-89 (2012).

²⁶⁰ Other, narrower limitations also exist, such as provisions permitting the use of protected health information to prepare a research protocol and the use of decedents' information if necessary for research, 45 C.F.R. § 164.512(i)(1)(ii)-(iii).

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studies.²⁶¹ The requirements for a valid authorization are exacting. It must include a “specific and meaningful” description of the information to be used or disclosed; identify those using, disclosing, or receiving the information; describe each purpose of the requested use or disclosure; and specify an expiration of the authorization (which, for research uses, may be “none”).²⁶² The authorization must be written in plain language and signed by the individual.²⁶³ It must include statements advising the individual of his or her right to revoke the authorization in writing,²⁶⁴ explaining any consequences to the individual of refusing to sign the authorization,²⁶⁵ and warning of the potential for information to be redisclosed by the recipient and no longer protected under the Privacy Rule.²⁶⁶

Getting authorizations presents practical problems, but those may be surmountable. Unfortunately, the use of individual authorizations presents a different and less tractable problem for research use. There are significant medical differences between patients who are willing to authorize the use of their information and those who are not.²⁶⁷ The need for individual authorizations is thus a source of selection bias that distorts the results of observational studies, making them less informative than they would be if patients did not have the opportunity to remove their health information from the study.

An Institutional Review Board or a Privacy Board²⁶⁸ may waive the authorization requirement for research studies that require such waivers and meet specified criteria.²⁶⁹ This can mitigate the serious problem of selection

²⁶¹ 45 C.F.R. § 164.508.

²⁶² 45 C.F.R. § 164.508(c)

²⁶³ 45 C.F.R. § 164.508(c)(3), (c)(1)(vi)

²⁶⁴ 45 C.F.R. § 164.508(c)(2)(i)(A)

²⁶⁵ 45 C.F.R. § 164.508(c)(2)(ii)

²⁶⁶ 45 C.F.R. § 164.508(c)(2)(iii).

²⁶⁷ IOM *Beyond HIPAA*, *supra* note 242, at 209–214. It may be, for example, that patients with prescriptions for Viagra are less willing to authorize the use of their health records in research than other patients.

²⁶⁸ 45 C.F.R. § 164.512(i)(1)(i)(A), (B). A detailed analysis of the interactions of Privacy Boards (privacy-ensuring entities created by the HIPAA Privacy Rule) and Institutional Review Boards (research oversight entities created under the Common Rule governing human subjects research) is beyond the scope of this Article. For overviews of each, see NATIONAL INSTITUTES OF HEALTH, INSTITUTIONAL REVIEW BOARDS AND THE HIPAA PRIVACY RULE, <http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp> (2004), and NATIONAL INSTITUTES OF HEALTH, PRIVACY BOARDS AND THE HIPAA PRIVACY RULE, http://privacyruleandresearch.nih.gov/privacy_boards_hipaa_privacy_rule.asp (2004), respectively.

²⁶⁹ These criteria include that the use or disclosure involves no more than a minimal risk to privacy of individuals based on an adequate plan to protect from improper use or disclosure, an adequate plan to destroy the identifiers at the earliest opportunity consistent

bias, but the need for Board review imposes costs and delays. Survey data indicate that many researchers have found it very difficult to obtain Privacy Rule waivers.²⁷⁰ Moreover, ambiguity in the waiver criteria creates uncertainty, especially for studies that aggregate data from multiple sources and may therefore require approval from multiple Boards that may interpret the Privacy Rule differently.²⁷¹

C. The HITECH Act and amendments to the Privacy Rule

The HITECH Act fortified the privacy protections of HIPAA in a number of ways, including applying its provisions to a broader set of entities,²⁷² requiring notification to individuals of breaches,²⁷³ and strengthening enforcement provisions.²⁷⁴ It also imposed a new statutory requirement for individual authorization for the sale of protected health information,²⁷⁵ subject to certain exceptions, including sale for research purposes for a price that “reflects the cost of preparation and transmittal of the data.”²⁷⁶

In the course of amending the Privacy Rule to comply with the HITECH Act requirements,²⁷⁷ HHS made a number of changes and interpretations to

with conduct of the research, and adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, and that the research could not practicably be conducted without the waiver and without access to and use of the protected health information. 45 C.F.R. § 164.512(i)(2).

²⁷⁰ IOM Beyond HIPAA, *supra* note 242, at 223.

²⁷¹ IOM Beyond HIPAA, *supra* note 242, at 169–170, 221–227.

²⁷² HITECH Act, *supra* note 166, §§ 13404 (extending provisions of Privacy Rule to business associates of covered entities) and 13408 (requiring that covered entities enter into business associate contracts with organizations such as health information exchanges that provide data transmission of protected health information to such covered entities).

²⁷³ HITECH Act, *supra* note 166, § 13402 (requiring notification to individuals of breaches)

²⁷⁴ HITECH Act, *supra* note 166, § 13410

²⁷⁵ *Id.* § 13405(d)(1).

²⁷⁶ *Id.* § 13405(d)(2)(B). Other exceptions include sales for public health activities, treatment, health care operations, remuneration to a business associate, provision to an individual of the individual’s protected health information, and other similar exceptions to be specified by the Secretary of Health and Human Services. § 13405(d)(2)(A)–(G). *See also* Barbara J. Evans, *Sustainable Access to Data for Postmarketing Medical Product Safety Surveillance under the Amended HIPAA Privacy Rule*, 24 HEALTH MATRIX 11 (2014) (arguing that the cost provisions in HITECH fall short of allowing sustainable access to postmarket surveillance medical data).

²⁷⁷ DEP’T OF HEALTH & HUMAN SERV., MODIFICATIONS TO THE HIPAA PRIVACY, SECURITY, ENFORCEMENT, AND BREACH NOTIFICATION RULES UNDER THE HEALTH INFORMATION TECHNOLOGY FOR ECONOMIC AND CLINICAL HEALTH ACT AND THE GENETIC INFORMATION NONDISCRIMINATION ACT; OTHER MODIFICATION TO THE HIPAA

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facilitate authorizations for use of health records in research.²⁷⁸ HHS clarified that the receipt of grant funding to perform a research study that involves provision of protected health information is not considered a sale of protected health information.²⁷⁹ In another change not explicitly required by the statute, HHS amended the Privacy Rule to permit covered entities to combine authorizations for use and disclosure of health information with related permission to use biospecimens,²⁸⁰ and modified its interpretation of the Privacy Rule to permit use of a single authorization form for multiple future studies.²⁸¹ These changes minimize bureaucratic costs by allowing a single authorization to cover multiple studies, and even to include future health information.

Overall, HIPAA creates substantial legal barriers to innovation by payers.²⁸² In addition to direct legal restrictions, privacy rules also exacerbate technical challenges, as when de-identification makes it harder to integrate information from different sources. Although recent legislation and modifications to the HIPAA Privacy Rule have made research uses easier in some respects, more reform may be necessary to exploit the promise of research using health records.²⁸³

RULES, 78 Fed. Reg. 5566 (Jan. 25, 2013) [2013 HIPAA Modifications].

²⁷⁸ For a critical analysis of these provisions by a noted renowned privacy advocate, see Mark A. Rothstein, *HIPAA Privacy Rule 2.0*, J.L. Med. & Ethics 525-528 (Summer 2013).

²⁷⁹ See 2013 HIPAA Modifications, *supra* note 277, 78 Fed. Reg. at 5606.

²⁸⁰ 45 C.F.R. § 164.508(b)(3).

²⁸¹ The new interpretation is explained at 2013 HIPAA Modifications, *supra* note 277, 78 Fed. Reg. at 5611-13.

²⁸² See Tovino, *supra* note 216, at 450 (Describing HIPAA's restrictions on research as "onerous").

²⁸³ We would be remiss if we did not mention the other side of this argument. Others have argued that the privacy protections are strikingly inadequate to actually safeguard patient privacy in the age of electronic medical records and Big Data.²⁸³ See, e.g., Sharona Hoffman, *Electronic Health Records and Research: Privacy Versus Scientific Priorities*, 10 AM. J. BIOETH. 19 (2010); Sharona Hoffman & Andy Podgurski, *In Sickness, Health, and Cyberspace: Protecting the Security of Electronic Private Health Information*, 48 B.C. L. REV. 06 (2007). Since we focus here on the role of payer innovation, we describe privacy rules as challenges for that innovation. Ideal solutions may be Pareto-superior by maintaining or increasing privacy while facilitating innovation, but may not always be available. One of us has begun to address such potential improvements in the context of medical datasets for complex computational modeling. See Roger A. Ford & W. Nicholson Price II, *Privacy and Accountability in Black-Box Medicine* (draft manuscript on file with authors). We do not here take a position on how best to balance privacy and innovation when they are strictly opposed.

Yet paradoxically these obstacles may enlarge the role of payers as custodians of health records in research as research consortia use distributed networks of data rather than central repositories to avoid triggering HIPAA violations. These arrangements are an opportunity for payers to expand their involvement in health research. At the same time, increased payer participation in innovation may minimize risks to patient privacy by reducing the need to transfer health records to entities that are not bound by the protective constraints of HIPAA.

CONCLUSION

Demand-side innovation by healthcare payers has tremendous potential to improve the healthcare system. Payers have access to large amounts of health data on millions of patients, and have the opportunity to develop new information about drug toxicity, comparative effectiveness of different treatments, and personalized medicine. Just as important, payers have substantially different incentives than the product-developing innovators that are more typically the target of innovation policy. As health costs continue to rise, innovation directed at frugality and efficiency becomes ever more crucial. But encouraging innovation on the demand side may require very different policy tools than the standard exclusionary rights used to motivate firms to develop expensive new products.

The barriers facing payer-innovators are substantial, including technical hurdles that impede aggregation and analysis of data as well as legal obstacles designed to protect patient privacy. The peculiar economic and legal landscape of the health care market may limit the ability of individual firms to capture the benefits of payer innovation, and the standard rewards of intellectual property are unlikely to help. However, a multi-pronged government approach is helping payer innovation move forward. A combination of funding and mandates for the use of electronic health records, engagement of stakeholders in building research networks, and modest changes to privacy rules are helping to make new research initiatives possible. While we applaud these efforts, there is more to be done to take advantage of the incentives and capabilities of payers as innovators. Meanwhile, scholars of innovation law and policy may find a fruitful, if largely unnoticed, target in demand-side innovation.