



# Promoting healthcare innovation on the demand side

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## ABSTRACT

Innovation policy often focuses on fortifying the incentives of firms that develop and sell new products by offering them lucrative rights to exclude competitors from the market. Regulators also rely on these same firms—and on similar incentives—to develop information about the effects of their products in patients, despite their obvious conflict of interest. The result may be a distorted understanding that leads to overuse of expensive new medical technologies. Recent technological advances have put healthcare payers in an excellent position to play a larger role in future innovation to improve healthcare and reduce its costs. Insurance companies and integrated healthcare providers have custody of treasure troves of data about healthcare provision and outcomes that can yield valuable insights about the effects of medical treatment without the need to conduct costly clinical trials. 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. Moreover, to the extent that healthcare payers can profit from reducing costs, they will seek to avoid inappropriate use of costly technologies. Greater involvement of payers in healthcare innovation thus offers a potential counterweight to the incentives of product sellers to promote excessive use of costly new products. In recent years, the federal government has sought to promote innovation through analysis of healthcare records in a series of initiatives; some picture insurers as passive data repositories, while others provide opportunities for insurers to take a more active role in innovation. In this paper, we examine the role of health insurers in developing new knowledge about the provision and effects of healthcare—what we call ‘demand-side innovation’. We address the

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contours of this underexplored area of innovation and describe the behavior of participating firms. We examine the effects of current legal rules on demand-side innovation, including insurance regulation, intellectual property rules, privacy protections, and FDA regulation of new healthcare technologies. Throughout, we highlight many policy tools that government can use and is using to facilitate payer innovation outside the traditional toolkit of patents and exclusive rights.

**KEYWORDS:** FDA, insurers, health innovation, intellectual property, pharmaceuticals, precision medicine

## INTRODUCTION

Policy mechanisms to promote biopharmaceutical innovation often focus on fortifying incentives for firms to develop new products. Biopharmaceutical firms favor exclusionary rights that defer competition, allowing them to profit by charging higher prices prior to generic entry. In addition to providing patent term extensions for developers of new drugs,<sup>1</sup> 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.<sup>2</sup> Providing better information about these effects is an important form of innovation that distinguishes warfarin as a human therapeutic anticoagulant from the same substance as a rat poison.<sup>3</sup> 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 money 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.<sup>4</sup> 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.<sup>5</sup> But the adverse events reporting system<sup>6</sup> that FDA has long relied upon as its principal source of bad news after approval is haphazard and unreliable.<sup>7</sup>

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<sup>1</sup> 35 U.S.C. § 156 (2012).

<sup>2</sup> These provisions include 5 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); 3 years for submitting data supporting a new use or product change that requires clinical trials, 21 U.S.C. § 355(j)(5)(F)(iv); 12 years for showing safety and efficacy for a new biologic, 42 U.S.C. § 262(k)(7); 5 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 6 months for submitting data from clinical trials in children, 21 U.S.C. § 355a (2012).

<sup>3</sup> Douglas Wardrop & David Keeling, *The Story of the Discovery of Heparin and Warfarin*, 141 *BRIT. J. HAEMATOL.* 757–763 (2008).

<sup>4</sup> 21 U.S.C. §§ 355(b)(1)(A), 355(d) (2012).

<sup>5</sup> 21 U.S.C. § 355(e) (2012).

<sup>6</sup> 21 C.F.R. § 314.80 (2012).

<sup>7</sup> See eg Phil B. Fontanarosa, Drummond Rennie & Catherine D. DeAngelis, *Postmarketing Surveillance—Lack of Vigilance, Lack of Trust*, 292 *JAMA* 2647 (2004). The 2007 legislation gave FDA greater powers and duties with respect to monitoring and disclosing post-approval risks, including authority to establish the Sentinel system discussed in greater detail *infra* part III.B.

Healthcare payers,<sup>8</sup> 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, though sometimes problematic in isolation, could be a corrective counterweight to the incentives of product sellers to maximize their own patent-protected profits.

Recent technological advances 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 treasure troves 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. These potential savings could create an incentive for innovation on the demand side by institutions that pay for healthcare.<sup>9</sup>

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. 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 data sets and observations over longer periods of time, and can thus shed light on questions that clinical trials leave unresolved. 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

<sup>8</sup> 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.

<sup>9</sup> We acknowledge that others have discussed a different idea of innovation on the demand side, describing the use of changing payment incentives to drive innovation. See eg Jakob Edler & Luke Georghiou, *Public Procurement and Innovation—Resurrecting the Demand Side*, 36 RES. POL’Y 949 (2007); Charles Edquist & Leif Hommen, *Systems of Innovation: Theory and Policy for the Demand Side*, 21 TECH. SOC’Y 63 (1999); Rachel Sachs, *Prizing Insurance: Prescription Drug Insurance as Innovation Incentive*, 30 HARV. J. L. & TECH (forthcoming). We use the term ‘demand-side innovation’ to describe innovation undertaken by those on the demand side (ie payers), rather than innovation driven by incentives shaped on the demand side.

are cheaper than the controlled clinical trials that swell the R&D budgets of product-developing firms.

The standard policy toolkit for promoting biomedical innovation offers little in the way of direct benefits to these ‘demand side innovators’, 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. But the standard toolkit is not the only way to promote innovation. The federal government has used a variety of different mechanisms to promote the use of data from healthcare records in ongoing innovation. These mechanisms include agency initiatives to use healthcare records for regulatory purposes, such as FDA’s Sentinel System, and for research purposes, such as the NIH-sponsored Precision Medicine Initiative and eMERGE network. They also include new legislation to support these initiatives<sup>10</sup> and others, such as the establishment of the Patient Centered Outcomes Research Institute under the Patient Protection and Affordable Care Act of 2010<sup>11</sup> and agency rulemaking to address obstacles to research use of healthcare records.<sup>12</sup> Although some of these initiatives picture payers primarily as repositories of data that others might analyse, they also provide opportunities for insurers to become more fully engaged as partners in healthcare innovation. Healthcare payers participate in medical innovation to an extent that is largely unrecognized in the legal scholarship on innovation. They could potentially do much more.

This paper proceeds in three parts. In part I, we outline the contours of this under-explored area of innovation. We describe the incentives, resources, and opportunities available to payers, as well as technical obstacles to medical innovation by payers, focusing on the challenges of making payer data useful for research. Part II considers economic and legal obstacles to payer innovation, including features of the market for health insurance and healthcare, regulation of health insurance and health technologies, limitations on intellectual property protection, and privacy protections for health information. In part III, we describe government initiatives that have helped the industry begin to address those challenges and identify further opportunities to assist this emerging area of research through law and policy. Throughout, we highlight the multipronged 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.

## I. INNOVATION BY HEALTHCARE 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

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<sup>10</sup> See eg the Food and Drug Administration Amendments Act, Pub. L. No. 110-85, 121 Stat. 823 (2007); the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009, enacted under Title XIII of the American Recovery and Reinvestment Act, Pub. L. No. 111-5, 123 Stat. 115 (2009); the Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010); and the Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144 (2012).

<sup>11</sup> *Id.*

<sup>12</sup> See eg recent HHS modifications to the HIPAA Privacy Rule, discussed *infra* part III.D.

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 efforts 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 reviewing technical challenges to payer innovation.

### A. Early Efforts and Regulatory Obstacles

Two extended examples highlight the incentives for and potential benefits of payer innovation, while also showing challenges payers face in implementing their innovations in a regulatory 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 involves the use of data from payer records rather than from drug company clinical trials to establish toxic side effects of the painkiller Vioxx, and illustrates the reluctance of FDA to rely on those data. 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.<sup>13</sup> An Rx-to-OTC switch can be a significant cost-lowering innovation for at least two reasons.<sup>14</sup> 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

<sup>13</sup> 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) (2012). 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 Unprecedented FDA Response to Petitioners and the Protection of Public Health*, 51 AM. U. L. REV. 999, 1011–18 (2002).

<sup>14</sup> For an estimate of cost savings from the availability of OTC drugs, see Consumer Healthcare Products Association, *The Value of OTC Medicine to the United States* (2012), <http://www.chpa.org/ValueofOTCMeds2012.aspx> (accessed Oct. 28, 2016) (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 copy 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 BRIT. 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).

Rx but not OTC drugs and patients are likely to be more cost-sensitive than insurance companies.<sup>15</sup>

In 1998, Blue Cross of California (later Wellpoint) submitted a petition to FDA asking it to permit OTC sales of non-sedating antihistamines sold under the brand names Allegra, Claritin, and Zyrtec.<sup>16</sup> Blue Cross/Wellpoint argued that non-sedating 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 non-sedating 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 non-sedating antihistamines out of their own pockets in the OTC market rather than using insurance to pay for doctor visits and prescriptions.

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 non-sedating products when used without the supervision of a physician.<sup>17</sup> In warning regulators about the potential hazards of their products, the product manufacturers were also advancing 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 will soon erode profits. At that point, the firm may seek to mitigate the loss of revenue by claiming a statutory reward of exclusivity for conducting further clinical trials to support a change in the terms of regulatory approval.<sup>18</sup> If further clinical trials are ‘essential’ to FDA approval of an application for the switch, the manufacturer is entitled to 3 years of exclusivity before FDA will approve a generic product for OTC sales.<sup>19</sup> This supplemental exclusivity gives the branded product a 3-year head start in the OTC market. A switch prior to patent expiration would be less attractive to the firm because it would have to surrender more lucrative exclusivity in the Rx market in exchange for less lucrative exclusivity in the OTC market; an early switch would also hasten the arrival of full competition by allowing the OTC exclusivity period to run during the patent term. To maximize profits, drug companies would

<sup>15</sup> Cohen et al., *supra* note 14, at 40 (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).

<sup>16</sup> Letter dated July 21, 1998 from Robert C. Seidman to Dockets Management Branch, Food & Drug Administration, Docket 98P-0610 (1998), <http://www.fda.gov/ohrms/dockets/dockets/98p0610/cp00001.pdf> (accessed Oct. 28, 2016).

<sup>17</sup> See letter dated Jan. 15, 1999 from Alexander R. Jacquinto to Dockets Management Branch, Food & Drug Administration, Docket 98P-0610 (1999) <http://www.fda.gov/ohrms/dockets/dockets/98p0610/c000004.pdf> (accessed Oct. 28, 2016); Schering Plough Research Institute, Briefing Book (Apr. 12, 2001), [http://www.fda.gov/ohrms/dockets/ac/01/briefing/3737b\\_15\\_schering-plough.pdf](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3737b_15_schering-plough.pdf) (accessed Oct. 28, 2016).

<sup>18</sup> 21 U.S.C. § 355(c)(3)(E)(iii) (2012).

<sup>19</sup> 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) (2012).

ordinarily prefer to delay the modest innovation of an Rx-to-OTC switch until the end of the patent term. Moreover, the law gives these companies a perverse incentive to persuade FDA that they must conduct costly clinical trials before the switch, because the statute authorizes further exclusivity only if new clinical trials are essential for approval, and not if FDA agrees that the product is safe for OTC sales without the need for further study. The manufacturers thus had to persuade FDA that more data were necessary to support the switch in order to get additional years of exclusivity. The Blue Cross/Wellpoint petition not only threatened to end payer coverage of non-sedating antihistamines before the manufacturers found the switch commercially advantageous, but it also undermined the case for 3 years of exclusivity in the OTC market.

The scientific question presented by the petition was more straightforward than the regulatory moves. FDA asked an advisory committee whether non-sedating antihistamines ‘could be used appropriately and safely by consumers without the intervention of a learned intermediary’,<sup>20</sup> and the committee concluded that they could.<sup>21</sup> But although this seemed sufficient to give FDA the authority to approve OTC sales on the petition of ‘any interested person’,<sup>22</sup> it was unprecedented and controversial to grant such a petition over the objection of the drug manufacturer.<sup>23</sup> The more traveled pathway was for the manufacturer itself to initiate an OTC switch by filing a supplemental new drug application at a time of its choosing. And sure enough, Schering-Plough soon filed its own application for an Rx-to-OTC switch for Claritin—the first of the non-sedating antihistamines to face patent expiration—11 months after opposing the Blue Cross/Wellpoint petition.<sup>24</sup> FDA approved the Schering-Plough application on November 27, 2002, without ruling on the Blue Cross/Wellpoint petition.<sup>25</sup> The patent protecting Claritin expired 3 weeks later.<sup>26</sup>

This episode shows how the interest of payers in reducing healthcare costs diverges from the interest of product manufacturers in maximizing revenues, giving payers an interest in accelerating a cost-lowering innovation (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, as Schering-Plough did in the case of Claritin. But payers might find it worthwhile to pursue this cost-lowering innovation more promptly

<sup>20</sup> Food & Drug Administration, *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](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3737b_02_overview.pdf) (accessed Oct. 28, 2016).

<sup>21</sup> *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> (accessed Oct. 28, 2016).

<sup>22</sup> 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) (2012).

<sup>23</sup> See *Id.*; Spencer, *supra* note 13.

<sup>24</sup> Spencer, *supra* note 13, at 1023–24.

<sup>25</sup> Melody Peterson, *Claritin to Sell Over the Counter*, NEW YORK TIMES (Nov. 28, 2002).

<sup>26</sup> *Id.*

and without the need for propping up prices 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 are motivated to show safety at lower cost by consulting their own data from clinical experience with the drug without conducting potentially unnecessary clinical trials.<sup>27</sup> But even motivated payers may need regulatory approval in order to implement cost-lowering changes in healthcare, and the FDA regulatory regime was not designed with payer participation in mind. Even with the support of an FDA advisory committee, Blue Cross/Wellpoint was unable to get FDA to approve the switch until the product manufacturer submitted its own petition in its own time. This limit on the ability of payers to implement innovations could dampen the incentive to conduct studies in the first place.

### 2. Post-approval studies: selective COX-2 inhibitors

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).<sup>28</sup> The manufacturer Merck voluntarily withdrew Vioxx from the market in the fall of 2004, at a time when it had sales of \$2.5 billion per year, in the face of mounting evidence that Vioxx was causing fatal heart attacks.<sup>29</sup>

Data from Merck-sponsored clinical trials comparing Vioxx with naproxen (one of the older generation of NSAIDs) had previously shown more heart attacks (as well as fewer gastric side effects<sup>30</sup>) in patients taking Vioxx,<sup>31</sup> but Merck had argued that the difference in heart attacks reflected a protective effect of naproxen rather than a toxic effect of Vioxx.<sup>32</sup> FDA was not convinced,<sup>33</sup> and Merck agreed to provide warnings about cardiovascular risks while it continued to monitor cardiovascular safety in additional clinical trials of Vioxx for new indications.<sup>34</sup> 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 non-selective NSAIDs.<sup>35</sup>

<sup>27</sup> 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.

<sup>28</sup> See Statement of Sandra Kweder, M.D., Deputy Director, Office of New Drugs, Center for Drug Evaluation and Research, U.S. Food & Drug Administration, before the Senate Commission On Finance (Nov. 18 2004) [Kweder testimony], <http://www.fda.gov/newsevents/testimony/ucm113235.htm> (accessed Oct. 28, 2016).

<sup>29</sup> U.S. FOOD & DRUG ADMINISTRATION, VIOXX (ROFECOXIB) QUESTIONS AND ANSWERS (Sept. 30, 2004), <http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm106290.htm> (accessed Oct. 28, 2016).

<sup>30</sup> See Claire Bombardier et al., *Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis*, 343 *NEW ENG. J. MED.* 1520–28 (2000).

<sup>31</sup> 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](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2.06_cardio.pdf) (accessed Oct. 28, 2016).

<sup>32</sup> *Id.* at 1526–27.

<sup>33</sup> Memorandum from Shari L. Targum, *supra* note 31, at 34–35.

<sup>34</sup> Kweder testimony, *supra* note 28.

<sup>35</sup> 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



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 records of patients who took other NSAIDs. That study showed significantly more heart attacks in the Vioxx patients,<sup>36</sup> leading Kaiser Permanente to reconsider whether to provide coverage of Vioxx.<sup>37</sup> But according to Dr. Graham's Congressional testimony, FDA sought to suppress publication of the study.<sup>38</sup> 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.<sup>39</sup> Both of these factors favor reliance on the data submitted by drug companies over that coming from other sources with different motivations.

The same cardiovascular effects that showed up in the extensive Kaiser Permanente data eventually became too clear to overlook even in the data from the smaller number of patients enrolled in the ongoing Merck clinical trials.<sup>40</sup> Shortly after the Kaiser Permanente data were presented at an international conference, Merck voluntarily agreed to withdraw Vioxx from the market,<sup>41</sup> and under the intense glare of Congressional and media attention, FDA eventually allowed Dr. Graham to publish the Kaiser Permanente study in a leading medical journal.<sup>42</sup> 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 not controlled by 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

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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 (Apr. 19, 2012), <http://www.fda.gov/ICECI/CriminalInvestigations/ucm301329.htm> (accessed Oct. 28, 2016).

<sup>36</sup> Kweder testimony, *supra* note 28; 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).

<sup>37</sup> Anna Wilde Matthews & Scott Hensley, *Big HMO Reconsiders Vioxx After Study Points to Heart Risks*, WALL STREET JOURNAL (Aug. 26, 2004), <http://www.wsj.com/articles/SB109346588678101103?cb=logged0.44817835511639714> (accessed Oct. 28, 2016).

<sup>38</sup> Testimony of David J. Graham before the Senate Finance Committee (Nov. 18, 2004), <http://www.finance.senate.gov/imo/media/doc/111804dgttest.pdf> (accessed Oct. 28, 2016). 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.

<sup>39</sup> *Id.* at 4.

<sup>40</sup> Robert S. Bresalier et al., *Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial*, 352 NEW 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.

<sup>41</sup> Kweder testimony, *supra* note 28.

<sup>42</sup> Thomas H. Maugh II, *Banned Report on Vioxx Published*, LOS ANGELES TIMES (Jan. 25, 2005), <http://articles.latimes.com/2005/jan/25/science/sci-vioxx25> (accessed Oct. 28, 2016).

of data that drug companies submit to it.<sup>43</sup> But data from patient health records are free of the proprietary rights of the drug companies and could be analysed by other parties with different interests, such as Kaiser Permanente and its collaborators.

These two stories raise issues discussed in more depth throughout this paper. Payers have the ability to innovate, and crucially have different resources and different incentives than product developers. But they face substantial barriers in implementing their innovations. The regulatory and intellectual property systems are both geared to innovation by product developers, not to innovation by payers. Nevertheless, the role of payers in healthcare innovation is growing.

## B. Resources

Payers enjoy one striking advantage as potential innovators: they possess tremendous amounts of valuable health data about treatments and consequences. So far, the longest term and most readily available form of payer data is administrative claims data used for billing and payments. Looking to the future, widespread utilization of electronic health records (EHRs) could provide payers with access to richer and more extensive data.

Administrative claims data, which include the information necessary to process payment claims, provide a view of medical encounters over time. These data could potentially answer many questions. Administrative claims data typically record diagnoses and treatments, hospital admissions and releases, laboratory test 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.<sup>44</sup>

Payers also frequently have access to other data sources that can supplement administrative claims data. Prescription payment records typically reveal when patients actually pick up and pay for drugs (as opposed to when a doctor writes the prescription), and when they refill prescriptions. Payers typically know when physicians refer patients to specialists and why. They may have contracts with laboratory test providers that give them access to laboratory test results, especially for tests performed by major national providers rather than in house.<sup>45</sup>

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 analysing them can be challenging due to variability across providers in what is included and how they are written.<sup>46</sup>

Integrated health systems that combine the functions of payer, healthcare coordinator, and healthcare provider are particularly likely to have access to medical records. These integrated systems include Kaiser Permanente,<sup>47</sup> Geisinger,<sup>48</sup> Highmark,

<sup>43</sup> Proprietary control of clinical trial data is changing as calls for data disclosure are met by journal, corporate, and regulatory action. See eg INSTITUTE OF MEDICINE, SHARING CLINICAL TRIAL DATA: MAXIMIZING BENEFITS, MINIMIZING RISK (National Academies Press 2015) <http://nap.edu/18998> (accessed Oct. 28, 2016).

<sup>44</sup> 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).

<sup>45</sup> Conversations with anonymous industry members and consultants.

<sup>46</sup> For a more detailed discussion of challenges with patient medical records, see *infra* part I.D.

<sup>47</sup> See [www.kaiserpermanente.org](http://www.kaiserpermanente.org) (accessed Oct. 28, 2016).

<sup>48</sup> See [www.geisinger.org](http://www.geisinger.org), [www.highmark.com](http://www.highmark.com) (accessed Oct. 28, 2016).

Intermountain Healthcare,<sup>49</sup> and the Departments of Defense and Veterans Affairs.<sup>50</sup> In the Kaiser system, for example, members pay premiums to Kaiser and see doctors who are Kaiser employees in Kaiser offices and hospitals.<sup>51</sup> Integrated health systems may have centralized custody of records that are likely to be dispersed across multiple custodians in the case of patients covered by traditional health insurance plans.<sup>52</sup> In the US 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 EHRs.<sup>53</sup> Single payer healthcare systems outside the USA may provide additional aggregated data sources to illuminate some research questions.<sup>54</sup> Payers may use these data for their own research, provide them to other researchers, or enter into collaborations with others to use the data for innovation.<sup>55</sup>

Payers are not passive recipients of data; they can control the content of the data that become available to them through coverage determinations that lead caregivers to document diagnoses, treatments, and outcomes of interest. In the past, public and private insurers have often sought to exclude experimental technologies and to limit coverage to services that are ‘reasonable and necessary for the diagnosis or treatment of illness or injury’.<sup>56</sup> Declining to cover new technologies may save costs in the short run, but could be a missed opportunity to collect data on the effects of these technologies in clinical practice. But payers are changing their behavior to capitalize on this opportunity. Medicare, for instance, has expanded coverage of some experimental technologies in order

<sup>49</sup> See [www.intermountainhealthcare.org](http://www.intermountainhealthcare.org) (accessed Oct. 28, 2016).

<sup>50</sup> The Department of Defense’s Tricare offers healthcare to 9.2 million eligible military personnel and families. <http://www.tricare.mil/stakeholders/statistics.cfm> (accessed Oct. 28, 2016). The Veterans Administration provides medical care to veterans and had 8.9 million enrollees in 2013. <http://www.va.gov/HEALTHPOLICYPLANNING/enroll02/Fnl925Doc.pdf> (accessed Oct. 28, 2016)

<sup>51</sup> See RICKEY HENDRICKS, *A MODEL FOR NATIONAL HEALTH CARE: THE HISTORY OF KAISER PERMANENTE* (1993).

<sup>52</sup> 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.

<sup>53</sup> 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 133–140 and accompanying text.

<sup>54</sup> See eg Gillian C. Hall et al., *Guidelines for Good Database Selection and Use in Pharmacoepidemiology Research*, 21 *PHARMACOEPIDEMIOL. & DRUG SAFETY* 1–10 (2012), <http://onlinelibrary.wiley.com/doi/10.1002/pds.2229/epdf> (accessed Oct. 28, 2016); Surasak Saokaew et al., *Healthcare Databases in Thailand and Japan: Potential Sources for Health Technology Assessment Research*, 10 *PLOS ONE* e0141993 (2015); Dominique Milea et al., *A Review of Accessibility of Administrative Healthcare Databases in the Asia-Pacific Region*, 3 *J. MARKET ACCESS & HEALTH POL’Y* 28076, <http://dx.doi.org/10.3402/jmahp.v3.28076> (accessed Oct. 28, 2016).

<sup>55</sup> Payers may either sell their data to non-payers or enter into research collaborations with them. See eg [www.healthcore.com/academia](http://www.healthcore.com/academia) (accessed Dec. 15, 2016) (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.

<sup>56</sup> The quoted language in text is from § 1862(a)(1)(A) of the Social Security Act, codified as amended at 42 U.S.C. § 1395y(a)(1)(A), which limits permissible payments for Medicare, but private insurers often either copy Medicare coverage determinations or use similar exclusions in their policy terms for experimental procedures. See eg *Pitman v. Blue Cross & Blue Shield of Okla.*, 217 F.3d 1291 (10th Cir. 2000) (excluding coverage of high-dose chemotherapy with autologous bone marrow transplantation); *Shumake v. Travelers Insurance Co.*, 383 N.W.2d 259 (Mich. Ct. App. 1985) (excluding coverage of Laetrile) (2012).

to facilitate assessment of their appropriate use and effectiveness.<sup>57</sup> In 2000, Medicare began covering routine healthcare costs for Medicare patients enrolled in clinical trials, though it did not cover the cost of the investigational item or service itself.<sup>58</sup> In 2006, Medicare formalized an approach called ‘coverage with evidence development’ (CED) that it had used in a handful of prior cases to provide coverage of experimental procedures for the purpose of generating data to assess their appropriateness.<sup>59</sup> Other healthcare systems have used similar coverage determinations linked to participation in research studies.<sup>60</sup> Studies supported by CED produced data that saved both costs and lives by preventing promising but unproven (and ultimately harmful) treatments from becoming the standard of care.<sup>61</sup> Private payers have also sometimes chosen to cover certain technologies for the purpose of collecting data to assess clinical validity, utility, and cost-effectiveness.<sup>62</sup>

### C. Opportunities

The opportunities and incentives of payers could make it profitable for them to engage in valuable forms of innovation that are underprovided by other innovators. Payers could use their data to improve the quality of care and to decrease costs, thereby potentially gaining competitive advantages.<sup>63</sup> In particular, payers stand to benefit from identifying harmful effects of treatment and from comparing the effects of different treatment options. Their data could be useful for both traditional comparative effectiveness research and new research in precision medicine enabled by advances in genomics and information technology. Payer innovation efforts like United Health’s Optum<sup>64</sup> or Anthem’s HealthCore<sup>65</sup> include both internal research and work for other entities like

<sup>57</sup> The Department of Health and Human Services claims statutory authority to support such research under § 1142 of the Social Security Act, 42 U.S.C. § 1320b-12 (authorizing the Secretary of HHS, through the Administrator for Healthcare Policy and Research, to conduct and support such research); see also 42 U.S.C. § 1395y(a)(1)(E) (authorizing Medicare payments for research conducted under this authority) (2012).

<sup>58</sup> See Medicare Coverage, Clinical Trials, Final National Coverage Decision (2000), <https://www.cms.gov/Medicare/Coverage/ClinicalTrialPolicies/downloads/finalnationalcoverage.pdf> (accessed Oct. 28, 2016).

<sup>59</sup> GUIDANCE FOR THE PUBLIC, INDUSTRY, AND CMS STAFF, NATIONAL COVERAGE DETERMINATIONS WITH DATA COLLECTION AS A CONDITION OF COVERAGE: COVERAGE WITH EVIDENCE DETERMINATION (July 12, 2006), <https://www.cms.gov/Medicare/Coverage/DeterminationProcess/Downloads/ced.pdf> (accessed Oct. 28, 2016) (describing the purpose of CED as generating data so Medicare can evaluate the appropriateness of the item or service’s use under current coverage, potentially make future coverage changes, and ‘generate clinical information that will improve the evidence base on which providers base their recommendations to Medicare beneficiaries regarding the item or service’).

<sup>60</sup> See Louise Longworth et al., *When Does NICE Recommend the User of Health Technologies Within a Programme of Evidence Development? A Systematic Review of NICE Guidance*, 31 PHARMACOECONOMICS 137–149 (2013).

<sup>61</sup> Penny E. Mohr & Sean R. Tunis, *Access with Evidence Development: The US Experience*, 28(2) PHARMACOECONOMICS 153–162 (2010). But see Lars Noah, *Coerced Participation in Clinical Trials: Conscripting Human Research Subjects*, 62 ADMIN. L. REV. 329–366 (2010) (arguing that requiring patients to become research subjects as a condition of healthcare coverage is coercive and unethical).

<sup>62</sup> CENTER FOR MEDICAL TECHNOLOGY POLICY ISSUE BRIEF, COVERAGE WITH EVIDENCE DEVELOPMENT (CED) IN THE PRIVATE SECTOR: LESSONS IN DESIGN AND IMPLEMENTATION (July 2010), <http://www.cmntnet.org/docs/resources/CED-in-the-Private-Sector.pdf> (accessed Oct. 28, 2016).

<sup>63</sup> Elsewhere, we discuss how various factors decrease insurer cost sensitivity, and acknowledge that these factors may decrease the incentive to innovate. See *infra* part II.A.1.

<sup>64</sup> See Optum, *About Us*, <https://www.optum.com/about.html> (accessed Oct. 28, 2016) (accessed July 16, 2015) (‘As a health services and innovation company, we combine data and analytics with technology and expertise to power modern health care’).

<sup>65</sup> Healthcore, *Home*, [www.healthcore.com](http://www.healthcore.com) (accessed Oct. 28, 2016) (accessed Feb. 22, 2016).

pharmaceutical companies or other payers.<sup>66</sup> This innovation offers potential benefits for patients and payers alike.

### *I. Drug toxicity*

Drugs frequently have a wide range of side effects that have not yet been fully identified when 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 years.<sup>67</sup> The relatively small test population means that drug developers are unlikely to observe toxic effects that occur in only a small fraction of patients, or in a population not included in the clinical trials.<sup>68</sup> Enrollment criteria for clinical trials often exclude patients who are pregnant, elderly, children, or taking other medications, for example, and therefore provide no information about the effects of the study drug in these excluded groups.<sup>69</sup> Similarly, the relatively short duration of clinical trials makes it difficult for developers to observe long-term effects. As a result, for one in five approved drugs FDA eventually requires at least one new ‘black box warning’—the strongest type of warning—after approval.<sup>70</sup> Of the drugs that add black box warnings after approval, it takes an average of 10 years before the effect is confirmed and the warning is added.<sup>71</sup>

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 conducted by the seller

<sup>66</sup> See eg [www.healthcare.com/government](http://www.healthcare.com/government) (accessed Oct. 28, 2016), /academics, /life-science-companies, and /payersproviders (listing opportunities for research and publications resulting from collaborations in various categories).

<sup>67</sup> 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 Firms Underinvest in Long-term Research? Evidence from Cancer Clinical Trials*, 105 AM. ECON. REV. 2044 (2015) (finding that drug companies disproportionately focus on drugs with shorter clinical trial period times).

<sup>68</sup> 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).

<sup>69</sup> 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*, 39 N. Y. U. REV. L. & SOC. CHANGE 45 (2013).

<sup>70</sup> Sean Hennessy & Brian L. Strom, *Improving Postapproval Drug Safety Surveillance: Getting Better Information Sooner*, 55 ANNU. REV. PHARMACOL. TOXICOL. 75, 76 (2015).

<sup>71</sup> *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 NEW ENGL. J. MED. 1252, 1253–54 (2014), a problem that can also potentially be addressed by innovating payers using longer-term data.

of the drug, as happened in Merck's clinical trial of Vioxx for a new indication.<sup>72</sup> Drug manufacturers, doctors, and patients may also report side effects to FDA.<sup>73</sup> But this passive reporting system depends on 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.<sup>74</sup>

After the Vioxx episode, Congress fortified FDA's authority to require drug manufacturers to conduct postmarket studies.<sup>75</sup> 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, as discussed below.<sup>76</sup> Some foreign health agencies have similar programs.<sup>77</sup>

But while these programs give regulators access to data from a network of payers, the data can only answer the queries that someone thinks to ask. 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 additional appropriate queries for the Sentinel System by scrutinizing their own data for evidence of drug toxicity, either ahead of regulators or in partnership with them. Although in the past FDA showed reluctance to rely upon Kaiser-Permanente data to demonstrate the cardiovascular side effects of Vioxx, since that time Congress has given FDA a legislative mandate to use such data for safety monitoring, opening the door to a larger payer role in informing post-approval regulatory decisions.

## 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 different interventions whereas cost-effectiveness research further considers costs to determine which intervention buys more health for the money.<sup>78</sup> Comparing the effects of different interventions is a valuable form of

<sup>72</sup> See *supra* part I.A.2.

<sup>73</sup> 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/> (accessed Oct. 28, 2016), 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) (2012).

<sup>74</sup> Hennessy & Strom, *supra* note 70, at 77.

<sup>75</sup> 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 ADMINISTRATION, 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* part III.B.

<sup>76</sup> See *infra* part III.B.

<sup>77</sup> See Hennessy & Strom, *supra* note 70, at 79–81 (listing large government-sponsored adverse-event population-surveillance databases).

<sup>78</sup> 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

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,<sup>79</sup> unless the drug developer seeks approval to make specific marketing claims of superiority to alternative treatments.<sup>80</sup> As a result, they 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 data sets of patient records, including information about diagnoses and drug prescriptions and purchases.<sup>81</sup> 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. Payers pay for care, and paying more for the same care, or the same for worse care, is bad for their bottom lines. Cost-effectiveness research can help make care cheaper and better. For example, Mayo Clinic researchers used Optum Labs data to determine that newer anticoagulant drugs have a higher risk of gastrointestinal bleeding among older patients.<sup>82</sup> Despite the greater convenience of the newer—and more expensive—drugs, this risk may make these drugs less appropriate for older patients than older, safer products.<sup>83</sup>

Other performers of comparative effectiveness research face different incentives and constraints. They generally need to partner with payers for access to data. Doctors and hospitals have some access to health data, although they still may find it advantageous to partner with payers to obtain access to larger data sets that include data from different providers. But doctors and hospitals may have perverse incentives under a classical fee-for-service model, because they make more money by providing more (and more

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major literature including the calculation of quality-adjusted life years (QALYs) and disability-adjusted life years, global surveys of patient preferences, and many other techniques. See eg Marthe R. Gold, David Stevenson & Dennis G. Fryback, *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.

<sup>79</sup> Robert Temple & Susan S. Ellenberg, *Placebo-Controlled Trials and Active-Control Trials in the Evaluation of New Treatments Part 1: Ethical and Scientific Issues*, 133 ANN. INTERN. MED. 455 (2000).

<sup>80</sup> 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 NEW ENG. J. MED. 1526–27 (2000). See *supra* part I.A.

<sup>81</sup> See *supra* part I.B.

<sup>82</sup> Neena Abraham et al., *Comparative Risk of Gastrointestinal Bleeding with Dabigatran, Rivaroxaban, and Warfarin: Population Based Cohort Study*, 350 BRIT. MED. J. h1857 (2015).

<sup>83</sup> See Constantinos Michaelidis, *Risk of GI Bleeding With Use of NOACs for Atrial Fibrillation: Commentary on Two Recent Cohorts*, AMERICAN COLLEGE OF CARDIOLOGY: LATEST IN CARDIOLOGY (July 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> (accessed Oct. 28, 2016).

expensive) treatments.<sup>84</sup> Drug companies could also conduct comparative effectiveness research, through both clinical trials and observational studies, and have an incentive to demonstrate that their new products are better than older drugs. However, 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, drug companies may decide not to take the risk of demonstrating inferiority rather than superiority for the patent-protected product. Academic institutions,<sup>85</sup> non-profit organizations,<sup>86</sup> 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 arguably prohibited by statute from performing certain types of cost-effectiveness research.<sup>87</sup>

Payers have different incentives which could make them an important source of comparative effectiveness research and cost effectiveness research to balance the research of other research performers with different interests. Considered in isolation, payers' cost-cutting incentives may seem problematic; they may have hesitate to demonstrate that a new, more expensive drug is better or safer than cheaper alternatives. But considered alongside the incentives of drug manufacturers to demonstrate the superiority of costly new products, payer innovation could provide a healthy corrective. Overall, the competing incentives of different stakeholders provide counterweights that may yield a more balanced understanding than reliance on data from any one kind of innovator.

### 3. Off-label use

Payers can also contribute to evaluating (and perhaps 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 product label. In some fields, such as oncology, off-label use of products for indications beyond the scope of FDA approval is quite common.<sup>88</sup> Drug companies may have little incentive to conduct costly clinical trials to provide evidence for off-label use, especially once such use enters into widespread practice; at this point, firms already benefit from increased drug sales without having to incur the costs and

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<sup>84</sup> See *infra* part II.

<sup>85</sup> 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/> (accessed Oct. 28, 2016).

<sup>86</sup> For example, the Institute for Clinical and Economic Review's New England Comparative Effectiveness Public Advisory Council, <http://cepac.icer-review.org/> (accessed Oct. 28, 2016), 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://icer-review.org/materials> (accessed Dec. 15, 2016).

<sup>87</sup> See *infra* part III.C.

<sup>88</sup> See eg 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 per cent off-label use of 10 leading patent-protected intravenous chemotherapeutics, and over 50 per cent off-label use for some).



risks of further trials. Many off-label uses are, unsurprisingly, unsupported by rigorous evidence, even when they have become the standard of care.<sup>89</sup>

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 has taken the position that promotion of a product for off-label uses renders the product ‘misbranded’ in violation of the Food, Drug & Cosmetic Act.<sup>90</sup> But recent judicial decisions have questioned this statutory interpretation and held that the First Amendment protects drug companies and their sales force from criminal prosecution for promoting off-label use (so long as they make no false statements).<sup>91</sup> 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.<sup>92</sup>

Payers have an incentive to ensure that off-label uses are effective and supported by evidence, because ineffective uses waste money.<sup>93</sup> 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. We noted above that clinical trials may fail to reveal toxic side effects that manifest over time.<sup>94</sup> 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.<sup>95</sup> 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.<sup>96</sup> This allows products to get to market that might otherwise not be approvable under a more rigorous application of standards for proving safety and efficacy prior to approval. 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

<sup>89</sup> See Emily A. Largent 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).

<sup>90</sup> 21 U.S.C. § 352 (2012).

<sup>91</sup> *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).

<sup>92</sup> See Rebecca S. Eisenberg, *The Problem of New Uses*, 5 YALE J. HEALTH POL’Y L. & ETHICS 717 (2005).

<sup>93</sup> 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’).

<sup>94</sup> See *supra* part I.C.1.

<sup>95</sup> See INSTITUTE OF MEDICINE, EVALUATION OF BIOMARKERS AND SURROGATE ENDPOINTS IN CHRONIC DISEASE 38–45 (2010) [EVALUATION OF BIOMARKERS].

<sup>96</sup> See eg 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).

use of these products, especially since many surrogate endpoints are eventually found to be poor predictors of clinical outcomes.<sup>97</sup>

Payer data on clinical outcomes can provide a valuable and cost-effective supplement to the limited data available from clinical trials. 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 antiretroviral drugs using data from Kaiser-Permanente in San Francisco.<sup>98</sup> In that study, not a single person using PrEP became infected with HIV.<sup>99</sup> 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.<sup>100</sup> 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 future care.<sup>101</sup>

### 5. Precision medicine

Precision medicine, also known as personalized medicine and frequently touted as the future of medicine,<sup>102</sup> aims to provide ‘the right patient with the right drug at the right dose at the right time’.<sup>103</sup> It identifies biological variation among patients and correlates that variation to differences in the most effective and efficient treatment.<sup>104</sup> An early success story for precision medicine was 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 called *HER2/neu*.<sup>105</sup> 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.<sup>106</sup> Precision medicine may also help determine the appropriate dose of a drug based on patient sex, weight, and

<sup>97</sup> See Thomas R. Fleming & David L. DeMets, *Surrogate End Points in Clinical Trials: Are We Being Misled?*, 125 ANN. INTERN. MED. 605 (1996); INSTITUTE OF MEDICINE, *supra* note 95, at 45–52.

<sup>98</sup> 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. 19949 (2015).

<sup>99</sup> Volk et al., *supra* note 98.

<sup>100</sup> *Id.* The wholesale acquisition cost of Truvada for PrEP is around \$1300 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> (accessed Feb. 11, 2016).

<sup>101</sup> See James F. Fries et al., *Reducing Health Care Costs by Reducing the Need and Demand for Medical Services*, 329 NEW 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 NEW ENGL. J. MED. 661 (2008) (noting that some preventive measures save money while others are costly).

<sup>102</sup> 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. 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. 1881 (2016).

<sup>103</sup> Food & Drug Administration, *Personalized Medicine*, <http://www.fda.gov/scienceresearch/specialtopics/personalizedmedicine/default.htm> (accessed Jan. 30, 2015).

<sup>104</sup> *Id.*

<sup>105</sup> Isaac S. Chan & Geoffrey S. Ginsburg, *Personalized Medicine: Progress and Promise*, 12 ANNU. REV. GENOMICS HUM. GENET. 217 (2011).

<sup>106</sup> *Id.*

genetic makeup,<sup>107</sup> or predict which patients might benefit more or less from hospital admission.<sup>108</sup> Research is underway to explore more complex and sophisticated precision medicine implementations.<sup>109</sup>

Much of this research uses genomic data and biomarkers.<sup>110</sup> An individual's genome—the sum of his or her genetic information—represents a tremendous amount of biological variability; understanding genomic variations may allow individualized predictions of how an individual may metabolize certain drugs<sup>111</sup> or how likely the individual is to develop a certain type of cancer.<sup>112</sup> Aside from the DNA in a patient's own normal cells, the genetics of viruses, bacteria, and cancerous tumors can inform the treatment of related diseases.<sup>113</sup> Other biomarkers, such as blood-sugar level, the amount of prostate-specific antigen, or the previously mentioned overexpression of HER2 by a tumor, can also be used to direct treatment (for diabetes, prostate cancer, and breast cancer, respectively).

Payers are using their data in precision medicine research. 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.<sup>114</sup> These data may reveal patterns that suggest which drugs or treatments work best for which patients, and which patients should avoid 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 or caregivers to link health records to tissue samples.<sup>115</sup> In fact, payers are essential participants in the eMERGE network, further discussed below.<sup>116</sup>

<sup>107</sup> 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 eg Jeffrey L. Anderson et al., *Randomized Trial of Genotype-Guided Versus Standard Warfarin Dosing in Patients Initiating Oral Anticoagulation*, 116 CIRCULATION 2563, 2563–70 (2007); Yoseph Caraco, Simha Blotnick & Mordechai Muszkat, *CYP2C9 Genotype-Guided Warfarin Prescribing Enhances the Efficacy and Safety of Anticoagulation: A Prospective Randomized Controlled Study*, CLIN. PHARMACOL. THER. 460, 460–70 (2008).

<sup>108</sup> 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).

<sup>109</sup> See eg W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J. L. & TECH. 419 (2015) (discussing complex and opaque medical algorithms).

<sup>110</sup> 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).

<sup>111</sup> See Chan & Ginsburg, *supra* note 105, at 227 (2011) (describing the use of genetic analysis of two genes, CYP2C9 and VKORC1, to predict metabolization rate of the blood thinner warfarin and prospectively adjust dosage accordingly).

<sup>112</sup> See Yoshio 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/> (accessed Oct. 28, 2016) (describing commercially available test for breast and ovarian cancer susceptibility based on genetic analysis of the BRCA1 and BRCA2 genes).

<sup>113</sup> Chan & Ginsburg, *supra* note 105.

<sup>114</sup> 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/> (accessed Oct. 28, 2016) (June 8, 2015).

<sup>115</sup> The eMERGE network, discussed *infra* part III.C., aims to facilitate this linking practice.

<sup>116</sup> See *infra* part III.C.

Payers could further contribute to precision medicine research, and potentially reap further benefits, by providing coverage of genetic diagnostic tests that make their data more informative. The selection of appropriate treatments for particular patients requires the use of validated markers for distinguishing those patients who will benefit from a particular treatment. Validation of tests requires data, but many payers decline to cover genetic tests that have not yet been validated as clinically useful. This Catch-22 may stymie the development of new diagnostic tools.<sup>117</sup> By covering the cost of promising new tests while collecting data to test their validity, payers could accelerate the development of diagnostic products that might eventually guide more appropriate use of costly therapies but that would otherwise never become available for lack of validation.<sup>118</sup>

The incentives of payers may offer a useful counterweight to the incentives of the drug companies that have become key drivers of precision medicine.<sup>119</sup> For drug companies, precision medicine presents a trade-off 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.<sup>120</sup> Precision medicine research on existing drugs may therefore be an unattractive proposition for drug sponsors.<sup>121</sup> For payers, on the other hand, broader implementation of precision 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.<sup>122</sup>

Of course, payers and drug companies face the risk that observational studies will not yield the results that are best for their bottom lines. In both cases, financial incentives are 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 payers as innovators in the field of precision medicine is thus likely to

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<sup>117</sup> Diagnostic test developers could validate their tests through clinical trials prior to marketing them, and in some cases FDA may require that they do so. See Sachs, *supra* note 102, at 1894–99. But premarket clinical trials could be an unaffordable burden for diagnostic laboratories and firms that are unable to obtain valid patents. Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21 B.U.J. SCI. & TECH. L. 256 (2015).

<sup>118</sup> See *supra* part II.B (discussing how payers can drive data generation through coverage decisions).

<sup>119</sup> See Chan & Ginsburg, *supra* note 105 (describing pharmaceutical company 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.

<sup>120</sup> On the other hand, firms that develop a diagnostic test to guide the choice of treatment may be able to get FDA approval for the use of a drug in an identified subgroup even though the same product would otherwise present an unacceptable balance of safety and efficacy in an undifferentiated patient population. Moreover, it may be possible to charge more per patient for a niche product with a small market without provoking resistance from payers, who are more likely to scrutinize outlays for more widely prescribed products that are more noticeable in their overall budgets.

<sup>121</sup> If, however, the company can market a new, targeted drug, perhaps alongside 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. Indeed, this is the focus of drug-company sponsored precision medicine research.

<sup>122</sup> 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.

yield a more balanced and complete picture than would emerge from a field dominated by drug companies alone.

#### D. Technical Challenges

The use of payer data for innovation presents substantial technical challenges.<sup>123</sup> Some challenges involving the storage and analysis of data are not unique to healthcare and therefore benefit from overall improvements in information technology.<sup>124</sup> Particular concerns in the healthcare field revolve around data availability, data quality, data assembly, and data interoperability.

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.<sup>125</sup> It takes time, money, and technical expertise to bring these data together, to link them by patient and demographic information, and to structure the assembled data to permit meaningful analyses.<sup>126</sup> Even when firms have access to data from different sources, the fragmented nature of the healthcare 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 per cent of those patients.<sup>127</sup>

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.<sup>128</sup> Longitudinal data—that is, data that follow patients over long periods of time—are useful for measuring the effects of preventive treatments, long-term drug effects, and interactions between treatments, and for answering other important

<sup>123</sup> For an overview, see Niels Peek et al., *Technical Challenges for Big Data in Biomedicine and Health: Data Sources, Infrastructure, and Analytics*, 9 Y. B. MED. INFORM. 42 (2014).

<sup>124</sup> For instance, natural language processing of EHRs—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 eg 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).

<sup>125</sup> 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*, [www.optum.com/solutions/data-analytics.html](http://www.optum.com/solutions/data-analytics.html) (accessed Dec. 15, 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> (accessed Feb. 18, 2016).

<sup>126</sup> See eg 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).

<sup>127</sup> Optum, *Optum Research Data Assets*, 2 (2015), [www.optum.com/content/dam/optum/resources/productSheets/5302\\_Data\\_Assets\\_Chart\\_Sheet\\_ISPOR.pdf](http://www.optum.com/content/dam/optum/resources/productSheets/5302_Data_Assets_Chart_Sheet_ISPOR.pdf) (accessed Dec. 15, 2016) (listing cumulative population counts through 2014).

<sup>128</sup> See eg 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/> (accessed June 22, 2015) (describing the advantage of larger and more varied datasets in developing health predictive analytics).

medical questions.<sup>129</sup> But the records of any one payer frequently cover only a relatively limited span of a patient's life. Patients frequently switch their insurance coverage, whether because they change to a new job with a different set of payer options,<sup>130</sup> change payers while staying at the same job (perhaps because the employer changes the plans it offers), change plans on the individual market, or become eligible or ineligible for Medicaid based on fluctuating 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 data set, administrative claims data for more than 5 years were available for only about 15 per cent of patients.<sup>131</sup> 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 example, Cal INDEX, is a non-profit health information exchange<sup>132</sup> founded in 2014 with seed money from two major payers to store centralized, comprehensive patient information for the vast majority of patients in California.<sup>133</sup> Providers choose whether to join the exchange,<sup>134</sup> and their patients participate unless they opt out.<sup>135</sup> So far Cal INDEX has had difficulty persuading providers to participate,<sup>136</sup> perhaps because payers are reluctant to share data with competitors.<sup>137</sup> If Cal INDEX can overcome this

<sup>129</sup> Griffin M. Weber et al., *Finding the Missing Link for Big Biomedical Data*, 311 JAMA 2479 (2014) (discussing the need to integrate patient records from different data sources).

<sup>130</sup> Approximately 49 per cent 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/> (2015 data; accessed Dec. 15, 2016).

<sup>131</sup> Optum, *supra* note 127, 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).

<sup>132</sup> 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. WS (2005).

<sup>133</sup> See Cal INDEX, *New California Not-for-Profit to Operate Statewide, Next-Generation Health Information Exchange* (Aug. 5, 2014), <https://www.calindex.org/new-california-healthcare-exchange/> (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)').

<sup>134</sup> See Cal INDEX, *Provider FAQ*, <https://www.calindex.org/provider-faq/> (accessed Oct. 28, 2016). Providers must pay fees to participate in Cal INDEX. *Id.*

<sup>135</sup> See Cal INDEX, *Opt Out*, <https://optout.calindex.org/OptOut/optout.html> (accessed Oct. 28, 2016). 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* note 196 and accompanying text. Thus, some types of data may remain fragmented, even if data sources are integrated.

<sup>136</sup> See Beth Kutcher, *Insurers Build Broad Data Exchange in California, but Providers are Slow to Join*, MODERN HEALTHCARE (Mar. 6, 2016), <http://www.modernhealthcare.com/article/20160305/MAGAZINE/303059948> (accessed Oct. 28, 2016).

<sup>137</sup> Cf. W. Nicholson Price II, *Patents, Big Data, and the Future of Medicine*, 37 CARDOZO L. REV. 1401, 1432–35 (2016) (discussing the incentives to keep health data secret); *Id.* at 1439–44 (describing government-centralized data collection to overcome this problematic non-sharing of data).

obstacle, it may succeed in resolving the problem of cross-provider data fragmentation, at least within California.<sup>138</sup> A patient's single longitudinal patient record would include both clinical and administrative claims data from multiple sources even as the patient shifts providers and payers.<sup>139</sup> Cal INDEX's stated purposes are to improve care and to increase efficiency, but it recognizes its consolidated data set could also be a useful resource for research.<sup>140</sup> Data consolidation could arise as a side effect of industry consolidation.<sup>141</sup> As payers merge their operations, they may also merge their data. Although industry consolidation has arguably detrimental effects for consumers,<sup>142</sup> data consolidation could be an unexpected benefit.<sup>143</sup>

Second, and related, data from different sources must be interoperable—that is, they must be in compatible formats so they can be joined and analysed together.<sup>144</sup> There is no standard format for EHRs or administrative claims data, and data from different systems are typically kept in different formats.<sup>145</sup> 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 another.<sup>146</sup> Some pieces of information may be present in one system but not another; other information may be coded differently (eg numerical versus qualitative judgements) or using different standards (eg signifying different ranges as 'high' or 'low'). Some of these barriers may arise through inadvertence, but there is also evidence that some developers of EHR systems may

<sup>138</sup> As described below, health data laws, including those on privacy, can vary from state to state. See *infra* part II.D. 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.

<sup>139</sup> See Cal INDEX, *Provider FAQ*, <https://www.calindex.org/provider-faq/> (accessed Oct. 28, 2016) (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)').

<sup>140</sup> See Cal INDEX, *Value of Cal INDEX*, <https://www.calindex.org/value-of-cal-index/> (accessed Oct. 28, 2016) (noting that Cal INDEX can 'benefit public health by providing de-identified data that can be used for medical research').

<sup>141</sup> See eg Leslie Picker & Reed Abelson, *U.S. Sues to Block Anthem-Cigna and Aetna-Humana Mergers*, NEW YORK TIMES (July 22, 2016), [http://www.nytimes.com/2016/07/22/business/dealbook/us-sues-to-block-anthem-cigna-and-aetna-humana-mergers.html?\\_r=0](http://www.nytimes.com/2016/07/22/business/dealbook/us-sues-to-block-anthem-cigna-and-aetna-humana-mergers.html?_r=0) (accessed Oct. 28, 2016) (describing two large insurance mergers).

<sup>142</sup> See *Id.* (noting consumer-harming anticompetitive effects of proposed insurance mergers).

<sup>143</sup> The movement of patients between payers can also complicate incentives, as described below in part II.A. Payer consolidation might similarly decrease these complications.

<sup>144</sup> See eg 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> (accessed Oct. 28, 2016); see also Evans, *supra* note 39, at 14 (citing PRESIDENT'S COUNCIL OF ADVISORS ON SCIENCE AND TECHNOLOGY, EXECUTIVE 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)).

<sup>145</sup> *Id.*

<sup>146</sup> See eg Sharon 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); William E. Hammond, *The Making and Adoption of Health Data Standards*, 24 HEALTH AFF. 1205 (2005).

use proprietary formats to stymie aggregation and use of data from other systems.<sup>147</sup> Further complicating the interoperability problem, as described below, data about different kinds of conditions may be subject to different privacy regimes, with some especially sensitive information covered by special laws.<sup>148</sup>

Third, ensuring and maintaining the quality of data is difficult.<sup>149</sup> Especially with administrative claims data, information essential to receiving payment may be coded in ways that reflect financial incentives.<sup>150</sup> Because insurance requires certain diagnoses or procedures to reimburse for physician services, healthcare providers may have incentives to code those data in marginal or inappropriate situations, leading to biased data.<sup>151</sup> 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, 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.<sup>152</sup>

None of these obstacles are insurmountable. They do, however, suggest targets for the attention of policymakers who want to facilitate use of healthcare records in research.

## II. ECONOMIC AND LEGAL OBSTACLES

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 healthcare markets and tax law directly reduce incentives to control costs. Second, because payers typically do not directly control care, they may fail to realize the full cost-saving benefits from their innovation. Third, intellectual property rewards are less available for the innovation opportunities available to payers than they are for new therapeutic product innovations. Fourth and finally, privacy laws restrict access to and use of health information in research.

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<sup>147</sup> See OFFICE OF THE NATIONAL COORDINATOR FOR HEALTH INFORMATION TECHNOLOGY, REPORT TO CONGRESS: REPORT ON HEALTH INFORMATION BLOCKING 11–19 (Apr. 2015), [www.healthit.gov/sites/default/files/reports/info.blocking\\_040915.pdf](http://www.healthit.gov/sites/default/files/reports/info.blocking_040915.pdf) (accessed Oct. 28, 2016) (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).

<sup>148</sup> Different legal restrictions on data are discussed in more detail below in *infra* part II.D, but include the Privacy Rule of the Health Insurance Portability and Accountability Act of 1996 (HIPAA), 45 C. F. R. Parts 160 and 164(A) & (E); the Genetic Information Nondiscrimination Act (GINA), Pub. L. No. 110-233, 122 Stat. 881 (2008); and the Federal Information Security Management Act, 44 U.S.C. §§ 3541–3549 (2002).

<sup>149</sup> For an overview of quality challenges in medical data, see Hoffman & Podgurski, *supra* note 146; Sharona Hoffman, *Symposium, Medical Big Data and Big Data Quality Problems*, 21 CONN. INS. L.J. 289 (2014).

<sup>150</sup> See ROBERT WACHTER, *THE DIGITAL DOCTOR: HOPE, HYPE, AND HARM AT THE DAWN OF MEDICINE’S COMPUTER AGE* (2015).

<sup>151</sup> *Id.*

<sup>152</sup> 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.



### A. Market Quirks and Tax Preferences

Cost sensitivity should motivate payers to invest in developing or identifying more cost-effective treatments and in curtailing overuse of costly products. However, the US market for healthcare and insurance has complexities and idiosyncrasies that blur these incentives.<sup>153</sup> We note four features in particular: muted competition, passed-on costs, tax subsidies, and medical loss ratios (MLRs).

First, payers may face muted competition for a number of reasons. Industry consolidation may give payers some power to dictate the terms of their coverage and the rates they charge.<sup>154</sup> Moreover, employers and individuals may tend to stick with the payer they currently use rather than shopping for competing products.<sup>155</sup> Finally, purchasers may have difficulty understanding the differences among insurance products, further diminishing effective competition.<sup>156</sup> The complexities of this market are beyond the scope of this paper, but it stands to reason that diminished competition in the health insurance market would decrease competitive pressure on payers to invest in cost-lowering innovation.<sup>157</sup>

Second, the combination of weak market competition and weak oversight of price increases by insurance regulators may allow payers to pass on increased costs to their customers with relative ease through increased premiums,<sup>158</sup> although the Affordable

<sup>153</sup> The US healthcare 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.

<sup>154</sup> 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 No. 15434, Oct. 2009), <http://www.nber.org/papers/w15434> (accessed Oct. 28, 2016); MARIKA CABRAL ET AL., DOES PRIVATIZED HEALTH INSURANCE BENEFIT PATIENTS OR PRODUCERS? EVIDENCE FROM MEDICARE ADVANTAGE (National Bureau of Economic Research, Working Paper No. 20470, Sept. 2014), <http://www.nber.org/papers/w20470> (accessed Oct. 28, 2016) (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).

<sup>155</sup> 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).

<sup>156</sup> 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 eg JEFFREY R. KLING ET AL., COMPARISON FRICTION: EXPERIMENTAL EVIDENCE FROM MEDICARE DRUG PLANS (National Bureau of Economic Research, Working Paper No. 17410, 2011), <http://www.nber.org/papers/w17410> (accessed Oct. 28, 2016) (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, Working Paper No. 21160, 2015), <http://www.nber.org/papers/w21160> (accessed Oct. 28, 2016) (describing substantial numbers of employees choosing strictly inferior health plans and attributing this choice to inability to understand plan options).

<sup>157</sup> The exact mechanics of decreased competition, and its precise effects on innovation incentives, are complex and beyond the scope of this paper 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. One could also argue that decreased competition merely makes it easier to capture gains as profits, and that incentives to innovate remain. Teasing out the full effects of these market features requires substantial further study.

<sup>158</sup> 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](http://www.naic.org/documents/committees_b_related_wp_rate_review.pdf) (accessed Oct. 28, 2016)

Care Act has introduced some limits on the ability of payers to raise premiums in a deliberate attempt to make payers more cost-sensitive.<sup>159</sup>

Third, tax subsidies for health insurance may dampen 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 excluded from the employee's taxable income.<sup>160</sup> 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 MLR provisions may reduce incentives for cost-lowering innovation. Under those provisions, payers must pay 85 cents in medical expenses for each dollar received in premiums.<sup>161</sup> This sets a ceiling on the increase in profits to be gained by lowering costs; the total of profits plus administrative expenses can be no higher than 15 per cent of total insurance premiums. Cost-lowering innovation may still be profitable if increased efficiency in one area offsets other rising costs. Moreover, expenditures on quality improvement research count as part of the 'medical expense' and may thus help bring that total up to 85 per cent. On the margin, however, this cap may reduce incentives for innovation. Overall, these features of the health market likely combine to lower incentives to innovate toward efficiency.

### B. Complexities Implementing Innovation

Another factor that makes it challenging for payers to profit from innovation is that many payers do not actually provide care—they just pay for the care that others provide. For these payers to benefit from innovations around quality, efficiency, and medical targeting, they need to influence healthcare providers to actually adopt those innovations. Integrated health systems, which both provide and pay for care, may find it easier to control the behavior of providers. But in a fee-for-service system, providers face perverse incentives to use more and costlier treatments, thereby increasing their own remuneration. These incentives are in serious tension with the goals of frugal payer

<sup>159</sup> See eg Internal Revenue Service, Notice 2015-16: Section 4980I — Excise Tax on High Cost Employer-Sponsored Health Coverage (2015), [www.irs.gov/pub/irs-drop/n-15-16.pdf](http://www.irs.gov/pub/irs-drop/n-15-16.pdf) (accessed Oct. 28, 2016) (instituting the so-called Cadillac Tax of 40 per cent on plans with very high premiums).

<sup>160</sup> 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> (accessed Oct. 28, 2016). 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> (accessed Oct. 28, 2016).

<sup>161</sup> Small payers (fewer than 100 subscribers) must meet an MLR threshold of 80 per cent. 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) <https://fas.org/sgp/crs/misc/R42735.pdf> (accessed Oct. 28, 2016).

innovation.<sup>162</sup> Payers have several potential mechanisms to address this tension, including direct incentives, knowledge-sharing, contracts with product developers, and regulatory influence.

### 1. Direct control and incentives

Traditional payers might in theory require caregivers to follow prescribed procedures or use utilization review and reimbursement tiering to guide physician behavior, though these practices have had a contentious history.<sup>163</sup> Payers can also try to align provider incentives with cost-saving goals by using financial incentives or risk sharing. When providers are compensated on a traditional fee-for-service basis, the interests of providers are opposed to those of payers: increased treatment costs mean increased provider compensation, and providers have little motivation to pursue efficiency. On the other hand, when the incentives of providers are aligned with those of payers, providers have greater incentives to adopt payer innovations, which in turn gives payers greater incentives to invest in innovation.

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 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.<sup>164</sup> Among other benefits, these structures allow physicians to share in the financial benefits of frugal care, rather than rewarding them for providing costly care under a traditional fee-for-service system.<sup>165</sup> More broadly, the Affordable Care Act aims to shift a substantial fraction of care away from fee-for-service toward value-based payments or other frugality-focused payment models, which should further align the incentives of payers and providers and enable smoother implementation of demand-side innovation.<sup>166</sup>

<sup>162</sup> 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.

<sup>163</sup> 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 eg Paul J. Feldstein et al., *Private Cost Containment. The Effects of Utilization Review Programs on Health Care Use and Expenditures*, 318 *NEW 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 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 eg 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).

<sup>164</sup> See Centers for Medicare and Medicaid Services, *Accountable Care Organizations*, <http://cms.gov/aco> (accessed Jan. 6, 2015). To the extent that vertical or horizontal consolidation of providers results in organization-wide shared incentives, it may have similar effects, a potential benefit to be weighed against other negative effects of such consolidation. See Laurence C. Baker et al., *Vertical Integration: Hospital Ownership of Physician Practices Is Associated with Higher Prices and Spending*, 33 *HEALTH AFF.* 756 (2014) (describing such negative effects).

<sup>165</sup> *Id.*

<sup>166</sup> See Sylvia M. Burwell, *Setting Value-Based Payment Goals—HHS Efforts to Improve U.S. Health Care*, 372 *NEW ENGL. J. MED.* 897 (2015) (setting goal of 30 per cent of traditional fee-for-service payments to alternative payment models by the end of 2016, and 50 per cent by the end of 2018).

## 2. Knowledge sharing

Payers can also influence provider behavior less directly through collaborative sharing of knowledge. They can publish the results of their studies and work to establish best practices, including clinical guidelines or ‘critical pathways’ reflecting treatment patterns that their research shows to be both effective and efficient.<sup>167</sup> Within the medical community, expert committees—typically well-known physicians—rely on published literature to develop treatment pathways.<sup>168</sup> 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.<sup>169</sup> Nonetheless, to the extent that providers resist following new clinical guidelines, they diminish the benefit to payers from investments in innovation.<sup>170</sup> Moreover, if payers must change the standard of care in order to realize the benefits of their investments in innovation, they will necessarily share those benefits with competitors who did not share their costs.<sup>171</sup>

## 3. Contracts with product developers

Another new strategy, increasingly popular with payers and drug companies, involves private agreements for drug companies to pay a rebate to a payer if a new product fails to meet specified performance targets.<sup>172</sup> For example, Harvard-Pilgrim recently entered into a ‘pay-for-performance’ agreement with Amgen to provide coverage of Amgen’s new cholesterol drug Repatha at an undisclosed discounted price.<sup>173</sup> Harvard-Pilgrim agreed to exclude from its formulary (ie its list of reimbursable drugs) other drugs in the same class of PCSK9 inhibitors, while Amgen agreed to pay rebates if the drug fails to reduce cholesterol to specified target levels for different patient groups and if total payments exceed a target.

Such agreements may stimulate private innovation by leading the parties to invest resources in measuring future health outcomes and analysing the data to determine whether the targets have been met. At the same time, they could confine cost-saving benefits to the particular firms that are parties to the agreement, without changing

<sup>167</sup> See eg Nathan R. Every et al., *Critical Pathways: A Review*, 101 CIRCULATION 461 (2000).

<sup>168</sup> See eg P4 Pathways, *Protocol Development*, <https://www.p4pathways.com/go/p4pathways/program/services/pathway-development.htm> (accessed Oct. 28, 2016) (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’).

<sup>169</sup> See *infra* part III.C.

<sup>170</sup> See eg Rainer Blaser et al., *Improving Pathway Compliance and Clinician Performance by Using Information Technology*, 76 INT. J. MED. INFORM. 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> (accessed Oct. 28, 2016).

<sup>171</sup> This creates the potential free-riding dynamic that intellectual property is designed to help solve. See *infra* part II.D.

<sup>172</sup> See Peter J. Neumann et al., *Risk-Sharing Arrangements That Link Payment for Drugs to Health Outcomes Are Proving Hard To Implement*, 30 HEALTH AFF. 2329–37 (Dec. 2011).

<sup>173</sup> Robert Weisman, *Harvard Pilgrim Strikes ‘Pay-for-Performance’ Deal for Cholesterol Drug*, BOSTON GLOBE (Nov. 8, 2015), <https://www.bostonglobe.com/business/2015/11/08/harvard-pilgrim-strikes-pay-for-performance-deal-for-cholesterol-drug/iGIV7rBie4K20HNbKORsPJ/story.html> (accessed Oct. 28, 2016).

prices to other payers and without changing the standard of care to bring about more widespread changes throughout the healthcare system.

According to a recent industry analysis, these agreements face legal obstacles under federal and state fraud and abuse laws, the federal Anti-Kickback Statute, and Medicaid rebate provisions.<sup>174</sup> Apart from these legal obstacles, implementing these agreements may be challenging in that they require parties with competing financial interests to agree on appropriate criteria and procedures for measuring performance and to cooperate in sharing and interpreting data.<sup>175</sup> If successfully implemented, these agreements could do a better job of motivating drug companies to optimize health outcomes rather than to maximize total sales, at least for patients who are covered by payers who have entered into such agreements.

The net effects of these agreements on payer innovation incentives are less clear, not least because they are quite new. Perhaps the prospect of recovering rebates would cause some payers to invest resources in tracking health outcomes that they would otherwise ignore, generating valuable knowledge about the effects of drugs in patients. On the other hand, payers and drug companies would both stand to benefit from keeping this knowledge and any resulting payments secret. Secrecy would reduce the social value of the knowledge relative to a system in which payers can only profit by publishing the results and changing the standard of care. Agreements with drug companies may also distort the kinds of research questions that payers ask. For example, if payers like Optum agree to put only one PCSK9 on their formulary of preferred drugs, they may be unable to use their data to do comparative effectiveness studies of different drugs in the same class. The overall impact of these agreements on incentives for payer innovation is thus a complex question.

#### 4. Regulatory influence

Payers might also influence the behavior of providers by using their data to influence regulatory decisions. FDA decisions, for example, determine what products may be sold and what indications and warnings appear on product labels. These determinations in turn influence provider behavior. The Center for Medicare and Medicaid Services (CMS) further influences provider behavior through its determinations about what products and services Medicare will cover. Private payers often follow Medicare coverage determinations in their own policies. But they could play a more active role in influencing which treatments or tests Medicare covers as they accumulate data from clinical experience.

Initially, only product developing firms have information about the effects of their unapproved new products. FDA new drug approval decisions thus inevitably rely heavily on data from product sponsors to show safety and efficacy. As clinical experience accumulates, however, payers may have a larger role to play. Data from clinical experience may show product risks that call for fortified warnings or even withdrawal of

<sup>174</sup> For a review of these obstacles and a call for safe harbors or new legislation in order to encourage 'value-based contracting', see Eli Lilly and Company and Anthem, *Promoting Value-Based Contracting Arrangements* (Jan. 29, 2016), <https://lillypad.lilly.com/WP/wp-content/uploads/LillyAnthemWP2.pdf> (accessed Oct. 28, 2016).

<sup>175</sup> Bob Herman, *Insurers, Drug Makers Wrestle With How to Build Value-Based Contracts*, MODERN HEALTHCARE (Feb. 20, 2016), <http://www.modernhealthcare.com/article/20160220/MAGAZINE/302209963> (accessed Oct. 28, 2016).

product approvals, as in the Vioxx case. On the other hand, they might indicate that a product currently available by prescription only is safer than substitutes that are already available over the counter, as in the case of non-sedating antihistamines. These examples revealed a regulatory regime that gave product sellers substantial control over the information available to regulators while making it difficult for other stakeholders to influence regulatory decisions.<sup>176</sup>

In the future, however, payers might 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. Legal changes after the Vioxx incident strengthened FDA's ability to take precisely this type of data into account. Payers could also provide information about off-label use of drugs that could eventually be used to win FDA approval for those uses.<sup>177</sup> Such regulatory moves might have a greater impact on the behavior of caregivers than the exhortations of payers.

### C. Intellectual Property Incentives

Payers also face diminished intellectual property incentives for innovation relative to the incentives of product-developing firms. In a familiar story, intellectual property provides legal excludability to 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 incentives to innovate. Intellectual property incentives work reasonably well for the producers of new products. But patents, trade secrecy, and regulatory exclusivity offer few direct benefits to demand-side innovators (although high prices for patent-protected products may have the indirect effect of motivating payers to invest in learning how to use these products more sparingly). The forms of payer innovation considered above are pure information goods; there is typically no new physical product that the payer can sell as a result of the knowledge gained from observational studies of patient health records, for example.<sup>178</sup> 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.<sup>179</sup> More fundamentally, the excludability at the center of intellectual property is not a viable option for some types of payer innovations discussed above.<sup>180</sup>

<sup>176</sup> As a formal matter, anyone may file a 'citizen petition' asking FDA to take regulatory action, but the citizens that submit such petitions are mostly drug companies. Michael A. Carrier & Daryl Wander, *Citizen Petitions: An Empirical Study*, 34 CARDOZO L. REV. 249 (2012).

<sup>177</sup> See *supra* part I.C.1; cf. Eisenberg, *supra* note 92.

<sup>178</sup> The patent on the relevant drug—and the higher prices it enables—provide a different incentive, discussed below at *infra* note 186 and accompanying text.

<sup>179</sup> 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. See 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.

<sup>180</sup> 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 healthcare quality initiatives).

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 caregivers before they can put it to use in a clinical setting. Caregivers in turn 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.<sup>181</sup> 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 precision medicine information are likely unavailable, unenforceable, and impractical. Judicial limitations on what sorts of inventions constitute patentable subject matter have cast considerable doubt on the patent eligibility of algorithms for selecting medical treatments for patients.<sup>182</sup> Standard patent law rules about prior art prevent patenting 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, on sale, and likely disclosed in published literature and prior patents.<sup>183</sup> 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;<sup>184</sup> second, medical practitioners performing medical activities have a statutory

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<sup>181</sup> 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.

<sup>182</sup> 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) (analysing *Prometheus* in the context of medical algorithms); Rebecca S. Eisenberg, *Diagnostics Need Not Apply*, 21 B.U.J. SCI. & TECH. L. 256 (2015).

<sup>183</sup> Sections 102 and 103 require that inventions must be new and non-obvious, 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 (2012).

<sup>184</sup> See Kapczynski & Syed, *supra* note 180, at 1938–40 (describing the difficulty in enforcing healthcare 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.*

exemption from patent infringement remedies;<sup>185</sup> 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 Vioxx.<sup>186</sup> 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 toward more scrutiny of the clinical benefits of patented treatments.

#### D. Privacy of Health Information

Privacy laws, principally the Health Insurance Portability and Accountability Act of 1996 (HIPAA),<sup>187</sup> present a challenging obstacle to the use of patient health information for research purposes.<sup>188</sup>

HIPAA aimed to facilitate the flow of information for healthcare and administrative purposes (such as claims processing), while protecting patient privacy by restricting uses and disclosure for other purposes.<sup>189</sup> The Department of Health and Human Services has elaborated upon these general statutory provisions in detailed rules, including a Privacy Rule.<sup>190</sup> The Privacy Rule sets limits on disclosure and use of ‘protected health information’ by ‘covered entities’<sup>191</sup> and their ‘business associates’.<sup>192</sup> ‘Protected

<sup>185</sup> Under 35 U.S.C. § 287(c), medical practitioners and related healthcare 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 (2012).

<sup>186</sup> Barbara Martinez et al., *Merck Pulls Vioxx Off Market After Link to Heart Problems*, WALL STREET JOURNAL (Oct. 1, 2004) <http://www.wsj.com/articles/SB109654671320932405> (accessed Oct. 28, 2016).

<sup>187</sup> Pub. L. No. 104-191, 100 Stat. 2548 (hereinafter HIPAA).

<sup>188</sup> Others have argued that privacy protections are strikingly inadequate to actually safeguard patient privacy in the age of electronic medical records and Big Data. See eg Sharona Hoffman, *Electronic Health Records and Research: Privacy Versus Scientific Priorities*, 10 AM. J. BIOETHICS 19 (2010); Sharona Hoffman & Andy Podgurski, *In Sickness, Health, and Cyberspace: Protecting the Security of Electronic Private Health Information*, 48 B.C. L. REV. 331 (2007). Since we focus here on the role of payer innovation, we describe privacy rules as challenges for that innovation. Better solutions that maintain or increase privacy while still facilitating innovation may or may not 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*, 23 MICH. TELECOMM. & TECH. L. REV. 1 (2016). We do not here take a position on how best to balance privacy and innovation when they are strictly opposed.

<sup>189</sup> 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).

<sup>190</sup> 45 C.F.R. Parts 160, 164 (2012).

<sup>191</sup> ‘Covered entities’ is defined at 45 C.F.R. § 160.103 to include a health plan, a healthcare clearinghouse, or a healthcare provider who transmits any health information in electronic form. 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 C.F.R. §§ 160.103, 164.500(b) (2012).

<sup>192</sup> 45 C.F.R. § 160.103. 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



health information’ includes both medical and billing records.<sup>193</sup> The baseline rule under HIPAA is that all use or disclosure of protected health information is prohibited unless it is specifically allowed.<sup>194</sup> 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.<sup>195</sup>

Complicating the picture, different kinds of health information are subject to different rules. The Privacy Rule itself provides additional protection for psychotherapy notes<sup>196</sup> and allows other more stringent privacy protections under various state laws.<sup>197</sup> Some state statutes, for example, provide additional protections against disclosure of information related to HIV status and treatment.<sup>198</sup> Other federal statutes provide additional protection for genetic information<sup>199</sup> and substance abuse treatment records.<sup>200</sup> This uneven landscape of privacy restrictions, varying by state, by condition, and by information type, further complicates the challenge of assembling broad, comprehensive, longitudinal health records.

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 may enable normally prohibited uses.

### 1. Normally permitted uses

The wording of the Privacy Rule creates considerable confusion about when the study of healthcare records to improve future patient care is allowable. The Privacy Rule permits a covered entity to use or disclose protected health information ‘for treatment,

aggregation . . . management, administrative, accreditation, or financial services’. 45 C.F.R. § 160.103 (emphasis added) (2012).

<sup>193</sup> 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’. ‘Health information’ is defined broadly. *Id.* (2012).

<sup>194</sup> 45 C.F.R. §§ 164.502 (2012).

<sup>195</sup> 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) (2012).

<sup>196</sup> 45 C.F.R. § 164.508(a)(2) (prohibiting disclosure without specific written authorization) (2012).

<sup>197</sup> 45 C.F.R. § 160.203(b); 42 U.S.C. § 1320d-2(c)(2) (2012).

<sup>198</sup> For example, New York Public Health Law § 2783 (2012).

<sup>199</sup> Genetic Information Nondiscrimination Act, Pub. L. No. 110-233, 122 Stat. 881 (2008). The protections of GINA are particularly notable because of the importance of genetic information to precision medicine researchers. GINA prohibits discrimination in health insurance coverage based on an individual’s genetic information. *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).

<sup>200</sup> 42 U.S.C. § 290dd-2(a) creates additional limits for the disclosure of substance abuse-related records. Less protective state laws are preempted, but more protective state laws are not. 42 C.F.R. § 2.20 (2012). For a helpful overview, see Timothy S. Jost, *Appendix B: Constraints on Sharing Mental Health and Substance-Use Treatment Information Imposed by Federal and State Medical Records Privacy Laws* in INSTITUTE OF MEDICINE (US) COMMITTEE ON CROSSING THE QUALITY CHASM: ADAPTATION TO MENTAL HEALTH AND ADDICTIVE DISORDERS, HEALTH CARE FOR MENTAL & SUBSTANCE-USE CONDITIONS (2006).

payment or health care operations.’<sup>201</sup> Although this explicitly includes ‘quality assessment and improvement activities, including outcomes evaluation and development of clinical guidelines’, such activities may not have the primary purpose of ‘obtaining [] generalizable knowledge’.<sup>202</sup> These provisions are tough to reconcile, since it would seem irresponsible to develop clinical guidelines on the basis of anything short of generalizable knowledge.<sup>203</sup> At 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’.<sup>204</sup> The 21st Century Cures Act requires the creation of a working group to study the creation of a full research exemption for the use of protected health information.<sup>205</sup>

*De-identified data.* De-identified data are not covered at all by the Privacy Rule, which applies only to ‘individually identifiable health information’.<sup>206</sup> Although advances in information technology have made it increasingly easy to re-identify individuals on the basis of limited information,<sup>207</sup> the Privacy Rule nonetheless provides a safe harbor that qualifies data as de-identified if seventeen pieces of identifying information are removed.<sup>208</sup> De-identifying data is a key way to navigate HIPAA restrictions even for government entities.<sup>209</sup>

However, de-identification brings its own problems. The list of impermissible identifiers includes information that may be relevant to researchers, such as dates, ages,

<sup>201</sup> 45 C.F.R. § 164.506(a). Information used should be ‘the minimum necessary’. 164.502(b) (2012).

<sup>202</sup> 45 C.F.R. § 164.501 (2012).

<sup>203</sup> 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 HIPAA Privacy Rule: Unrealized Patient Autonomy and Burdensome Government Regulation*, 49 S.D. L. REV. 447, 450–55 (2004) (discussing the applicability of HIPAA restrictions to research).

<sup>204</sup> ‘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 (2012).

<sup>205</sup> 21st Century Cures Act, Pub. L. 114–255 (2016), §2063.

<sup>206</sup> 45 C.F.R. § 164.514(a) (2012).

<sup>207</sup> 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](http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2076397); (accessed Oct. 28, 2016) 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).

<sup>208</sup> 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 re-identify 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) (2012).

<sup>209</sup> When California’s individual health 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. 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> (accessed Oct. 28, 2016).

and biometric identifiers; excluding this information limits the value of the data.<sup>210</sup> Moreover, retention of identifiers may be necessary to link data from different sources and over time.<sup>211</sup> 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.<sup>212</sup> Removing identifying information hinders this aggregation. There are technological ways to partially avoid this problem, but they can be complex and typically require some form of centralized infrastructure.<sup>213</sup>

*Limited data sets.* The Privacy Rule allows 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’.<sup>214</sup> A limited data set may include slightly more identifying information.<sup>215</sup> However, 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.<sup>216</sup>

*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.<sup>217</sup> This allows disclosures to FDA for post-marketing safety monitoring under the Sentinel Initiative.<sup>218</sup> Another provision permits disclosure to sponsors of FDA-approved products for postmarketing surveillance and adverse-event reporting.<sup>219</sup> This particularly provision may have been inartfully drafted; while it 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 use in comparative effectiveness research.<sup>220</sup>

<sup>210</sup> 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 203, at 230–33.

<sup>211</sup> *Id.* at 177–179.

<sup>212</sup> See LOIS M. BUJOLD, *BROTHERS IN ARMS* (1989) (elaborating the potential consequences of access to uniquely identified biomedical information and samples).

<sup>213</sup> See Ioana Danciu et al., *Secondary Use of Clinical Data: The Vanderbilt Approach*, 52 J. BIOMED. INFORM. 28, 30 (2014) (describing de-identification techniques).

<sup>214</sup> 45 C.F.R. § 164.514(e) (2012).

<sup>215</sup> *Id.* § 164.514(e)(2). 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.*

<sup>216</sup> 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. 45 C.F.R. § 164.514(e)(4)(ii) (2012).

<sup>217</sup> 45 C.F.R. § 164.512(b)(i) (2012).

<sup>218</sup> 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](http://www.mini-sentinel.org/work_products/About_Us/HIPAA_and_CommonRuleCompliance_in_the_Mini-SentinelPilot.pdf) (accessed Oct. 28, 2016).

<sup>219</sup> 45 C.F.R. § 164.514(b)(iii) (2012).

<sup>220</sup> 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).

The foregoing limitations<sup>221</sup> 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.

## 2. Authorization and waivers

In addition to normally permitted uses, the Privacy Rule allows otherwise prohibited uses and disclosures in two circumstances. First, individual patients may authorize the use of their protected health information for any purpose, including research.<sup>222</sup> However, the requirements for a valid authorization are exacting and limit possibilities for unplanned future research.<sup>223</sup> In addition to these practical challenges, a requirement of getting individual authorizations presents a different and less tractable problem for research use. There may be significant medical differences between patients who are willing to authorize the use of their information and those who are not.<sup>224</sup> Relying on individual authorizations could thus bias the results of observational studies, making them less informative than they could be.

Second, an Institutional Review Board or a Privacy Board<sup>225</sup> may also waive the authorization requirement for individual research studies that meet strict specified criteria.<sup>226</sup> This can mitigate the serious problem of selection 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.<sup>227</sup> 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.<sup>228</sup>

Despite these obstacles and gaps in incentives, some payers are already making notable efforts to advance the use of payer data for medical innovation. We suggest at least three reasons why this is so. First, as we noted above, for innovation related to costly patent-protected treatment, high costs give payers 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

<sup>221</sup> For other, narrower permitted uses, see 45 C.F.R. § 164.512(i)(1)(ii)-(iii) (2012).

<sup>222</sup> 45 C.F.R. § 164.508 (2012).

<sup>223</sup> Authorizations must describe the information and the request's purpose, identify the recipients or users, and specify an expiration date (which may be 'none' for research). 45 C.F.R. § 164.508(c). The authorization must also follow numerous procedural requirements. *Id.* (2012).

<sup>224</sup> IOM Beyond HIPAA, *supra* note 203, 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.

<sup>225</sup> 45 C.F.R. § 164.512(i)(1)(i)(A), (B) (2012). 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 paper. For overviews of each, see NATIONAL INSTITUTES OF HEALTH, INSTITUTIONAL REVIEW BOARDS AND THE HIPAA PRIVACY RULE, <http://privacyruleandresearch.nih.gov/irbandprivacyrule.asp> (2004) (accessed Oct. 28, 2016), and NATIONAL INSTITUTES OF HEALTH, PRIVACY BOARDS AND THE HIPAA PRIVACY RULE, [http://privacyruleandresearch.nih.gov/privacy.boards.hipaa\\_privacy\\_rule.asp](http://privacyruleandresearch.nih.gov/privacy.boards.hipaa_privacy_rule.asp) (2004) (accessed Oct. 28, 2016), respectively.

<sup>226</sup> These criteria include findings of no more than a minimal risk to privacy of individuals and that the research could not practically be conducted without the waiver and without access to and use of the protected health information, among others. 45 C.F.R. § 164.512(i)(2) (2012).

<sup>227</sup> IOM Beyond HIPAA, *supra* note 203, at 223.

<sup>228</sup> *Id.* at 169–170, 221–227.

partnering with payers and helping them to overcome obstacles and to kickstart their own research. In the next part, we explore some of these initiatives and consider additional mechanisms to encourage payer innovation.

### III. ASSISTANCE FROM GOVERNMENT INITIATIVES

Although the challenges and obstacles to payer innovation are substantial, a number of federal legislative and regulatory initiatives are facilitating the use of health records in research. These efforts include providing incentives to promote the adoption and use of interoperable health records by caregivers and hospitals, creating a network of data sources for public health monitoring of postmarket drug safety issues, and sponsoring research initiatives in the areas of comparative effectiveness studies and precision medicine.

#### A. Electronic Health Records

The federal government has been actively promoting the use of EHRs for well over a decade in the hope of reducing medical errors, reducing costs, and improving the quality of care.<sup>229</sup> Policymakers have also touted the potential for research use of EHRs as part of a ‘learning healthcare system’ in which caregivers continuously adapt their treatment choices in light of ever-expanding knowledge about healthcare outcomes.<sup>230</sup>

The healthcare industry has been extraordinarily slow to adopt information technology, lagging far behind the rest of the economy.<sup>231</sup> For a variety of reasons, paper records and hard copies dominated health records well into the first decade of the 21st century.<sup>232</sup> President George W. Bush called for computerizing health records in his 2004 State of the Union address,<sup>233</sup> 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.<sup>234</sup> But progress remained slow.

Federal incentives to make use of EHRs were strengthened considerably in the Obama administration,<sup>235</sup> largely as a result of the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH Act), passed as part of the

<sup>229</sup> 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/> (accessed Oct. 28, 2016).

<sup>230</sup> *Id.* at 145–160.

<sup>231</sup> 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* 1 (Jan. 2006), <http://www.biomedcentral.com/1472-6947/6/1>; (accessed Oct. 28, 2016) Gerard F. Anderson et al., *Health Care Spending and Use of Information Technology in OECD Countries*, 25 *HEALTH AFF.* 819–831 (2006).

<sup>232</sup> INSTITUTE OF MEDICINE. *CROSSING THE QUALITY CHASM: A NEW HEALTH SYSTEM FOR THE 21ST CENTURY* (2001) [IOM QUALITY CHASM].

<sup>233</sup> GEORGE W. BUSH, *STATE OF THE UNION ADDRESS* (2004), <http://georgewbush-whitehouse.archives.gov/news/releases/2004/01/20040120-7.html> (accessed Oct. 28, 2016).

<sup>234</sup> David J. Brailer, *Interview: Guiding the Health Information Technology Agenda*, 29 *HEALTH AFF.* 586–595, 588 (2010).

<sup>235</sup> *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).

American Recovery and Reinvestment Act of 2009.<sup>236</sup> The HITECH Act 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.<sup>237</sup> The legislation also established committees to make recommendations to the ONC regarding health information technology standards and the creation of a nationwide health information technology infrastructure.<sup>238</sup> 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’, disseminate best practices, and allow for the exchange and use of information in compliance with standards.<sup>239</sup> And it provided \$30 billion for incentive payments through Medicare and Medicaid to reward the adoption and ‘meaningful use’ of EHRs by providers and hospitals.<sup>240</sup> 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,<sup>241</sup> although this has hardly been an unqualified success story.<sup>242</sup> 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’.<sup>243</sup>

<sup>236</sup> American Recovery and Reinvestment Act, Pub. L. No. 111-5, 123 Stat. 115 (Feb. 17, 2009) (ARRA), Div. A, Title XIII, Div. B, Title IV [HITECH Act].

<sup>237</sup> ARRA § 3001.

<sup>238</sup> ARRA Div. A Tit. I.; §§ 3002–03.

<sup>239</sup> ARRA § 3012.

<sup>240</sup> ARRA §§ 4101, 4102. See Department of Health & Human Services, Centers for Medicare and Medicaid Services, 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).

<sup>241</sup> 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 Chun-Ju 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 (National Bureau of Economic Research, NBER Working Paper No. 20553, Oct. 2014), <http://www.nber.org/papers/w20553> (accessed Oct. 28, 2016) (finding that HITECH incentives only modestly increased rate of adoption of EHRs by hospitals).

<sup>242</sup> A comparison of survey results in 2012 and 2015 by Accenture shows 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> (accessed Oct. 28, 2016). For a narrative account of the impact of electronic medical records on providers and hospitals, see WACHTER, *supra* note 150.

<sup>243</sup> 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>; (accessed Oct. 28, 2016) Office of the National Coordinator for Health Information Technology, *Connecting Health and Care for the*

HITECH-driven adoption of EHRs offers considerable potential benefits for research users. EHRs provide richer and more complete information than claims data, and are much easier to aggregate for use as research data than the paper records used by providers in the past. Although lack of interoperability is an ongoing problem,<sup>244</sup> 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.<sup>245</sup> 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.<sup>246</sup> For research purposes, it may be possible to achieve considerable benefits without nationwide interoperability by using the records of a single large provider.<sup>247</sup> 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) billing purposes.<sup>248</sup>

### *B. Regulatory Use of Networked Data for Observational Studies*

Payer innovators also stand to benefit from the infrastructure and technology developed to support the FDA Sentinel System, a legislatively mandated network of data sources and tools for postmarket monitoring of the safety of FDA-approved products. This initiative arose from a series of studies that convened a wide range of experts and stakeholders to come up with ideas for improving drug safety.

A series of high-profile drug safety cases (including the Vioxx episode)<sup>249</sup> 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.<sup>250</sup> The GAO Report was highly critical of FDA's system of postmarket surveillance, noting that it was underfunded<sup>251</sup> and relied too heavily on an unreliable system of adverse event reporting.<sup>252</sup> 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

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*Nation: A Shared Nationwide Interoperability Roadmap* (Draft Version 1.0 Ap. 2015) (hereinafter *Interoperability Roadmap*), <https://www.healthit.gov/sites/default/files/ONC10yearInteroperabilityConceptPaper.pdf> (accessed Dec. 15, 2016).

<sup>244</sup> See *supra* part I.D.

<sup>245</sup> *Interoperability Roadmap*, *supra* note 243, at 13.

<sup>246</sup> *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').

<sup>247</sup> The Kaiser Permanente study of the effects of Vioxx, for example, was limited to the records of one large, integrated provider.

<sup>248</sup> WACHTER, *supra* note 150, 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').

<sup>249</sup> 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]

<sup>250</sup> U.S. GOV'T ACCOUNTABILITY OFFICE, REPORT TO REQUESTERS: DRUG SAFETY, IMPROVEMENTS NEEDED IN FDA'S POSTMARKET DECISION-MAKING AND OVERSIGHT PROCESS (2006).

<sup>251</sup> *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).

<sup>252</sup> *Id.* at 24–25.

expanding FDA's authority to require drug sponsors to conduct postmarket studies, such as clinical trials or observational studies'.<sup>253</sup>

Around the same time, FDA and the Department of Health and Human Services asked the Institute of Medicine (IOM) to convene experts to assess the US drug safety system and to make recommendations to improve risk assessment, surveillance, and the safe use of drugs.<sup>254</sup> The IOM 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'.<sup>255</sup>

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 payers as the institutions with stewardship of those records.

Congress responded by passing the Food and Drug Administration Amendments Act of 2007 (FDAAA 2007),<sup>256</sup> a complex piece of legislation that gave FDA significant new authorities to oversee the safety of drugs after approval.<sup>257</sup> This legislation marked a 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 companies<sup>258</sup> toward new sources of data and expertise.<sup>259</sup> 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'.<sup>260</sup> Once

<sup>253</sup> *Id.* at 36.

<sup>254</sup> IOM COMM. ON THE ASSESSMENT OF THE US DRUG SAFETY SYSTEM, THE FUTURE OF DRUG SAFETY: PROMOTING AND PROTECTING THE HEALTH OF THE PUBLIC, 2–3 (2007).

<sup>255</sup> *Id.* at 7–8.

<sup>256</sup> Pub. L. No. 110-85, 121 Stat. 823 (codified as amended in scattered sections of 21 U.S.C.).

<sup>257</sup> Particularly notable are new authorities to require a drug sponsor to conduct post-approval 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 (2012).

<sup>258</sup> 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 (2012).

<sup>259</sup> 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).

<sup>260</sup> 21 U.S.C. § 355(k)(3) (2012).



these methods were developed, it directed FDA to ‘establish and maintain procedures for risk identification and analysis based on electronic health data’.<sup>261</sup>

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 institutions, and authorizes FDA to enter into contracts with public and private entities to achieve these goals.<sup>262</sup> 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 worked with payers and others 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 50 healthcare organizations and academic institutions.<sup>263</sup>

Mini-Sentinel has already facilitated innovative analysis of information using payer data. In 2010, FDA launched a study of the risk of intussusception<sup>264</sup> in infants receiving rotavirus vaccines after ambiguous postmarketing studies conducted by the vaccine sponsors.<sup>265</sup> FDA used Mini-Sentinel to access payer information from Aetna, Healthcore, and Humana relating to over 1.3 million vaccine administrations.<sup>266</sup> Researchers found a small but significant increase in intussusception, enough to require labeling changes for the vaccines.<sup>267</sup> 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 primarily 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.<sup>268</sup>

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.<sup>269</sup> The statute explicitly calls for the

<sup>261</sup> 21 U.S.C. § 355(k)(3)(C)(i) (2012).

<sup>262</sup> 21 U.S.C. § 355(k)(3)(C)(v) (2012).

<sup>263</sup> 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](http://healthaffairs.org/healthpolicybriefs/brief.pdfs/healthpolicybrief_139.pdf) (accessed Oct. 28, 2016).

<sup>264</sup> Intussusception is a serious medical condition in which part of the intestine folds into another section of the intestine.

<sup>265</sup> 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> (accessed Oct. 28, 2016).

<sup>266</sup> W. Katherine Yih et al., *Intussusception Risk after Rotavirus Vaccination in U.S. Infants*, 370 *NEW ENGL. J. MED.* 503 (2014).

<sup>267</sup> *Id.*

<sup>268</sup> *Id.* at 4.

<sup>269</sup> FDA officials have announced plans to make the technical Sentinel infrastructure—though not the data themselves—available to other users in the future who may wish to set up similar systems as part of a national data infrastructure. Janet Woodcock, *Another Important Step in FDA’s Journey Towards Enhanced Safety Through Full-Scale ‘Active Surveillance’*, *FDA VOICE* (Dec. 30, 2014),

development and validation of new analytical methods.<sup>270</sup> 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. It identifies obstacles (such as data quality and interoperability and privacy) and challenges participants to develop strategies to overcome them.<sup>271</sup> 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.

### C. 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.

#### 1. 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 non-profit, non-governmental research institute with an initial appropriation from Congress and subsequent funding from a new fee on health insurers until it sunsets in 2019.<sup>272</sup>

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

The PCORI provisions of the ACA specifically target the same technical difficulties that payers would confront in their own comparative effectiveness research,<sup>273</sup> 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

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<http://blogs.fda.gov/fdavoiced/index.php/2014/12/another-important-step-in-fdas-journey-towards-enhanced-safety-through-full-scale-active-surveillance/> (accessed Oct. 28, 2016).

<sup>270</sup> 21 U.S.C. § 355(k)(3)(B) (2012).

<sup>271</sup> Health Affairs Sentinel Brief, *supra* note 263, at 4.

<sup>272</sup> The choice to set up an organization outside the existing science agencies is interesting, and may reflect 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, which in turn is a part of the Department of Health and Human Services. The 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 HEALTH AFF. 1777, 1777–82 (2010).

<sup>273</sup> 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) (2012).

18 patient-group-based networks, which will generate interoperable data sets to support multinet network studies. 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 left PCORI with an ambiguous statutory limit on performing cost-effectiveness research.<sup>274</sup> It reflects concerns by some opponents of comparative effectiveness research that the establishment of PCORI 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 provision broadly to prohibit consideration of cost-effectiveness in PCORI-funded research.<sup>275</sup> PCORI apparently agrees.<sup>276</sup> 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 ....’<sup>277</sup>

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.

<sup>274</sup> The relevant section reads, ‘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 adjusted life year (or such a similar measure) as a threshold to determine coverage, reimbursement, or incentive programs under title XVIIIACA § 1182, codified at 42 U.S.C. § 1320e-1(e).’

<sup>275</sup> See eg Henry A. Glick et al., *Comparative Effectiveness and Cost-Effectiveness Analyses Frequently Agree on Value*, 34 HEALTH AFF. 805, 805 (2015) (‘Provisions of the ACA prohibit the use of a cost-effectiveness analysis threshold and quality-adjusted life-years (QALYs) in PCORI comparative effectiveness studies, which has been understood as a prohibition on support for PCORI’s conducting conventional cost-effectiveness analyses.’); but see Nicholas Bagley, *Who Says PCORI Can’t Do Cost-Effectiveness?*, <http://theincidentaleconomist.com/wordpress/who-says-pcori-cant-do-cost-effectiveness/> (accessed 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).

<sup>276</sup> PCORI, *What is PCORI’s Official Position on Cost-effectiveness Analysis*, <https://help.pcori.org/hc/en-us/articles/213716587-What-is-PCORI-s-official-policy-on-cost-effectiveness-analysis-> (accessed July 24, 2016) (‘Applications will be considered nonresponsive if the proposed research [c]onducts a formal cost-effectiveness analysis [or] [d]irectly compares the costs of care between two or more alternative approaches to providing care’).

<sup>277</sup> ACA § 6301(a), codified at 42 U.S.C. § 1320e (j)(1)(A).

## 2. Precision 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 precision medicine research. We focus on two NIH initiatives: the Precision 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 precision medicine forward through public–private partnerships, including work with drug companies on cancer genomics.<sup>278</sup> 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.<sup>279</sup> The President called for an initial \$215 million in funding to drive this research.<sup>280</sup> 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.<sup>281</sup>

Another NIH-funded 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.<sup>282</sup>

The eMERGE Network aims to combine information from EHRs 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.<sup>283</sup> 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.<sup>284</sup> eMERGE's sponsor, the National Human Genome Research Institute, has a long history of sponsoring research on ethical and legal issues associated with human genome research and incorporating best practices into research.<sup>285</sup>

<sup>278</sup> See Francis S. Collins & Harold Varmus, *A New Initiative on Precision Medicine*, 372 *NEW ENG. J. MED.* 793, 793 (2015); National Institute of Health, *Near-Term Goals*, <http://nihprod.cit.nih.gov/precisionmedicine/goals.htm> (accessed Oct. 13, 2015).

<sup>279</sup> See eg Robert Pear, *Uncle Sam Wants You—Or at Least Your Genetic and Lifestyle Information*, *NEW YORK TIMES* (July 23, 2016), <http://www.nytimes.com/2016/07/24/us/politics/precision-medicine-initiative-volunteers.html> (accessed Oct. 28, 2016) (describing the cohort's planned progress).

<sup>280</sup> 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> (accessed Dec. 15, 2016).

<sup>281</sup> Collins & Varmus, *supra* note 278.

<sup>282</sup> eMERGE Network, <https://emerge.mc.vanderbilt.edu/> (accessed 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).

<sup>283</sup> eMERGE Network, *About eMERGE*, <https://emerge.mc.vanderbilt.edu/about-emerge/> (accessed Feb. 24, 2016).

<sup>284</sup> See Laura M. Beskow et al., *Model Consent Language* (2009) [http://www.ninds.nih.gov/research/clinical\\_research/application\\_process/eMerge\\_model\\_language.pdf](http://www.ninds.nih.gov/research/clinical_research/application_process/eMerge_model_language.pdf) (accessed Oct. 28, 2016).

<sup>285</sup> 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).

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 beyond 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.<sup>286</sup> The eMERGE 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.<sup>287</sup> 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.

#### D. The HITECH Act and amendments to the Privacy Rule

Although HIPAA privacy regulations create challenges for payer innovation, recent legislative activity has made some of those challenges slightly easier to overcome. The HITECH Act largely fortified the privacy protections of HIPAA, including applying its provisions to a broader set of entities,<sup>288</sup> requiring notification to individuals of breaches,<sup>289</sup> and strengthening enforcement provisions.<sup>290</sup> It also imposed a new statutory requirement for individual authorization for the sale of protected health information,<sup>291</sup> subject to certain exceptions, including an exception for sale for research purposes for a price that 'reflects the cost of preparation and transmittal of the data.'<sup>292</sup>

However, in the course of amending the Privacy Rule to comply with the HITECH Act requirements,<sup>293</sup> HHS made a number of changes and interpretations to facilitate authorizations for use of health records in research.<sup>294</sup> HHS clarified that the receipt of grant funding to perform a research study that involves provision of protected health

<sup>286</sup> See PheKB, <https://phekb.org/> (accessed Feb. 24, 2016).

<sup>287</sup> 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*, 22 J. AM. MED. INFORM. ASSOC. 1072–80 (2015) (implementing similar system to collect data in Chicago).

<sup>288</sup> HITECH Act, *supra* note 236, §§ 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).

<sup>289</sup> HITECH Act, *supra* note 236, § 13402 (requiring notification to individuals of breaches).

<sup>290</sup> HITECH Act, *supra* note 236, § 13410.

<sup>291</sup> *Id.* § 13405(d)(1).

<sup>292</sup> *Id.* § 13405(d)(2)(B). Other exceptions include sales for public health activities, treatment, healthcare 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).

<sup>293</sup> DEP'T OF HEALTH & HUMAN SERVICES, 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 RULES, 78 Fed. Reg. 5566 (Jan. 25, 2013) [2013 HIPAA Modifications].

<sup>294</sup> 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 41, 525–528 (Summer 2013).

information is not considered a sale of protected health information.<sup>295</sup> 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,<sup>296</sup> and modified its interpretation of the Privacy Rule to permit use of a single authorization form for multiple future studies.<sup>297</sup> These changes minimize bureaucratic costs by allowing a single authorization to cover multiple studies, and even to include future health information.

Overall, HIPAA still creates substantial legal barriers to innovation by payers.<sup>298</sup> In addition to direct legal restrictions, privacy rules may 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.

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: MOVING FORWARD

Demand-side innovation by healthcare payers has tremendous potential to improve healthcare quality and to lower its costs. Payers have access to health data on millions of patients, giving them the opportunity to develop new information about drug toxicity, comparative effectiveness, precision medicine, and to perform other forms of innovation. Just as important, payers have substantially different incentives than the product-developing innovators that more typically benefit from the standard tools of innovation policy such as intellectual property. 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 those 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 healthcare 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 EHRs, engagement of stakeholders in building research networks, and modest changes to privacy rules are helping to make new research initiatives possible.

<sup>295</sup> See 2013 HIPAA Modifications, *supra* note 293, 78 Fed. Reg. 5606.

<sup>296</sup> 45 C.F.R. § 164.508(b)(3) (2012).

<sup>297</sup> The new interpretation is explained at 2013 HIPAA Modifications, *supra* note 293, 78 Fed. Reg. 5611–13.

<sup>298</sup> See Tovino, *supra* note 203, at 450 (describing HIPAA's restrictions on research as 'onerous').

While we applaud these efforts, there is more to be done to take advantage of the incentives and capabilities of payers as innovators. Continued support of technological enablers for payer innovation is key. HIPAA's privacy protections can also be streamlined to ease the use of data in innovative medical research. Perhaps most important, though, payer innovation needs improved pathways to implementation. Payers can share innovative information with physicians, and can create incentives to try to align the actions of physicians with that information. But payers have limited access to FDA, a central arbiter of what technology gets used and how. FDA determinations go a long way in influencing how physicians and patients use drugs or other treatments, and payer information about comparative effectiveness, toxicity, and precision medicine could aid those determinations. Unfortunately, as described in our opening examples of OTC antihistamines and Vioxx toxicity, FDA has been resistant to using information proffered by payers in the past. Congress in 2007 enacted FDAAA and invited FDA to receive input from non-traditional sources including observational studies. FDA has taken steps in that direction, partnering with payers to develop the Sentinel system—but FDA has made limited use of that system to date. Healthcare payers—both private and public—could work with FDA to use this resource more broadly to use healthcare data to improve regulatory decisions that are inadequately informed by premarket clinical trials. In a larger sense, healthcare payers should have an explicit and ongoing seat at the table when discussing the development and evaluation of health technology, both new and old. Meanwhile, scholars of innovation law and policy may find a fruitful, if largely unnoticed, target of study in demand-side innovation.

#### ACKNOWLEDGEMENTS

For helpful comments and conversations, we thank Kevin Haynes, Lucy Hodder, Andrea Leeb, Oskar Liivak, Michael Madison, Nina Mendelson, Robert Moses, Lisa Larrimore Ouellette, Jeanne Ryer, Jordan VanLare, and participants at the Northwestern University Conference on the Law-STEM Alliance as a Catalyst for Innovation, the Intellectual Property Scholars' Conference at DePaul University, the University of Michigan Law School Legal Theory Workshop, the University of Michigan Law School Student Scholars Workshop, and the Health Law Professors Conference at Boston University. Cassandra Simmons provided excellent research assistance. All errors are our own.