THE IMPACT OF REIMBURSEMENT POLICIES AND PRACTICES ON HEALTHCARE TECHNOLOGY INNOVATION

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EXECUTIVE SUMMARY

It is widely accepted that reimbursement policies and practices are important considerations in the research and development (R&D) decisions of potential innovators of healthcare technologies, and the investors who finance them. Experts broadly concurred that reimbursement is one of the factors that determines which products in development eventually make it to market, as well as the level of access to those products and use by care providers and patients. This, in turn, can affect product development and innovation. However, reimbursement is not necessarily among the most important drivers in every circumstance and likely plays different and evolving roles with respect to drugs and devices. Scientific discoveries and perceptions of clinical need may be the most important factors influencing innovation.

It is also widely held that decentralized decision-making, the absence of government-regulated pricing, and lack of restrictions on reimbursement create an environment that is generally conducive to greater R&D expenditure. Without price controls and reimbursement limits, firms are able to invest in drug development with fewer concerns about future market access and reimbursement levels once their product is approved. But, more expenditure on R&D does not necessarily give rise to more innovation that improves consumer welfare (as defined in this project), as more spending in the drug and device development pipeline may not yield products offering value concurrent with the benefits conferred. The appropriate question, therefore, is not how much is spent on R&D (i.e., the enterprise), but how to measure the benefits to patients, payers, and society of the resultant drugs and devices that are brought to market.[1]

Payers account for a large share of the purchases of healthcare technologies.[2] Consequently, the decision by a public program or health plan to subsidize use of a technology (often referred to as a coverage decision) is a critical determinant of expected, and actual, return on investment (ROI) for developers and investors. The level and method of payment selected and any policies or practices defining the circumstances under which the healthcare technology is reimbursed serve as (lesser) determinants. In making these reimbursement decisions, payers make formal and informal evaluations of the value that drugs and devices confer. By doing so, they may establish a market that is more conducive to rational, value-based consumer decisions.

It is thus important to understand how reimbursement affects actual or expected ROI, and by extension, how ROI may impact innovation, as developer and investor assessments of the market viability of a new

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[1] Schaeffer, S., & McCallister, E. (2014, September 1). Paying the piper. *BioCentury*. Retrieved from http://www.biocentury.com/biotech-pharma-news/coverstory/2014-09-01/22nd-biocentury-back-to-school-issue-time-to-try-new-pricing-schemes-a1

[2] An estimated 75-80% of the costs of biopharmaceuticals are borne by payers, according to Kaiser Family Foundation calculations (2008) using National Health Expenditure historical data from the Centers for Medicare and Medicaid Services (https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/index.html?redirect=/NationalHealthExpendData); unfortunately, there is relatively little data available pertaining to insurance cost share for medical devices.

product take into account payers' potential actions (e.g., would it be covered, at what payment level, and with which conditions?). It is also important to identify any potential downstream effects that reimbursement may have on innovation over the long-term, as use of specific reimbursement approaches grows or fades. The objective of this research project was to describe current reimbursement methods and analyze their impacts (if any) on drug and device use and innovation. Our findings incorporate assessments of the effects of reimbursement on innovation based on economic theory, literature reviews, and consultation with experts.

We identified key characteristics of reimbursement methods and selected five of these for closer analysis to determine how they affect factors that contribute to ROI such as pricing, utilization, and provider and patient decision-making. These characteristics were:

- The reimbursement decision-making process: how payers make decisions on which drugs, devices, and other healthcare technologies to make available to patients, at what price, and for whom;
- Product categorization and differentiation: how payers distinguish between the drugs or devices that they cover;
- Method of payment: the terms under which a payer makes reimbursement to a provider;
- Method of defining the payment amount: the methods used to establish the amount the third-party payer will reimburse a provider or supplier furnishing a healthcare technology to a patient, and;
- Patient cost sharing: out-of-pocket costs borne by consumers, net of insurance coverage, when they obtain services or purchase prescription drugs, durable medical equipment (DME), or other health technologies.

Key drivers of the use of different reimbursement methods include state and federal statutes and regulations for public payers such as Medicare and Medicaid; availability of detailed reimbursement information and methodologies for public plans – but generally not private payers – as potential benchmarks; and competition among private payers. Cost containment also appears to be an important factor driving payer choices.

We then assessed whether and, if so, how the aforementioned characteristics of reimbursement methods affect incentives to innovate in drugs and devices in qualitative (direction and relative magnitude of impact) terms. We classify innovations as incremental, substantial, or radical, depending on the significance of the unmet need addressed and the extent of additional benefit (comparative effectiveness) offered relative to existing treatments. Incremental innovations offer small gains in one or both of these areas. Radical innovations address significant unmet needs and provide significant additional benefits, while substantial innovations either address significant unmet needs or provide significant additional benefits – but not both.

The analytical framework that we developed for this purpose posits that reimbursement policies and practices can impact product developers' ROI directly in three ways. The first is by establishing a specific payment level, which in turn affects average sales price. The second is by setting a volume of sales at

that payment level. The third is by influencing seller costs associated with development, manufacture, or sale of a healthcare technology. Our framework also posits that reimbursement policies indirectly influence ROI by establishing different incentives for key actors, including patients/consumers, dispensers, providers, sellers, and payers. In turn, these incentives impact effective sales price, sales volume, and in some cases, sellers' costs of development, manufacturing, and sales. Together these factors determine the revenues and profits to be derived from the product, important determinants of the ROI for the developer and investors.

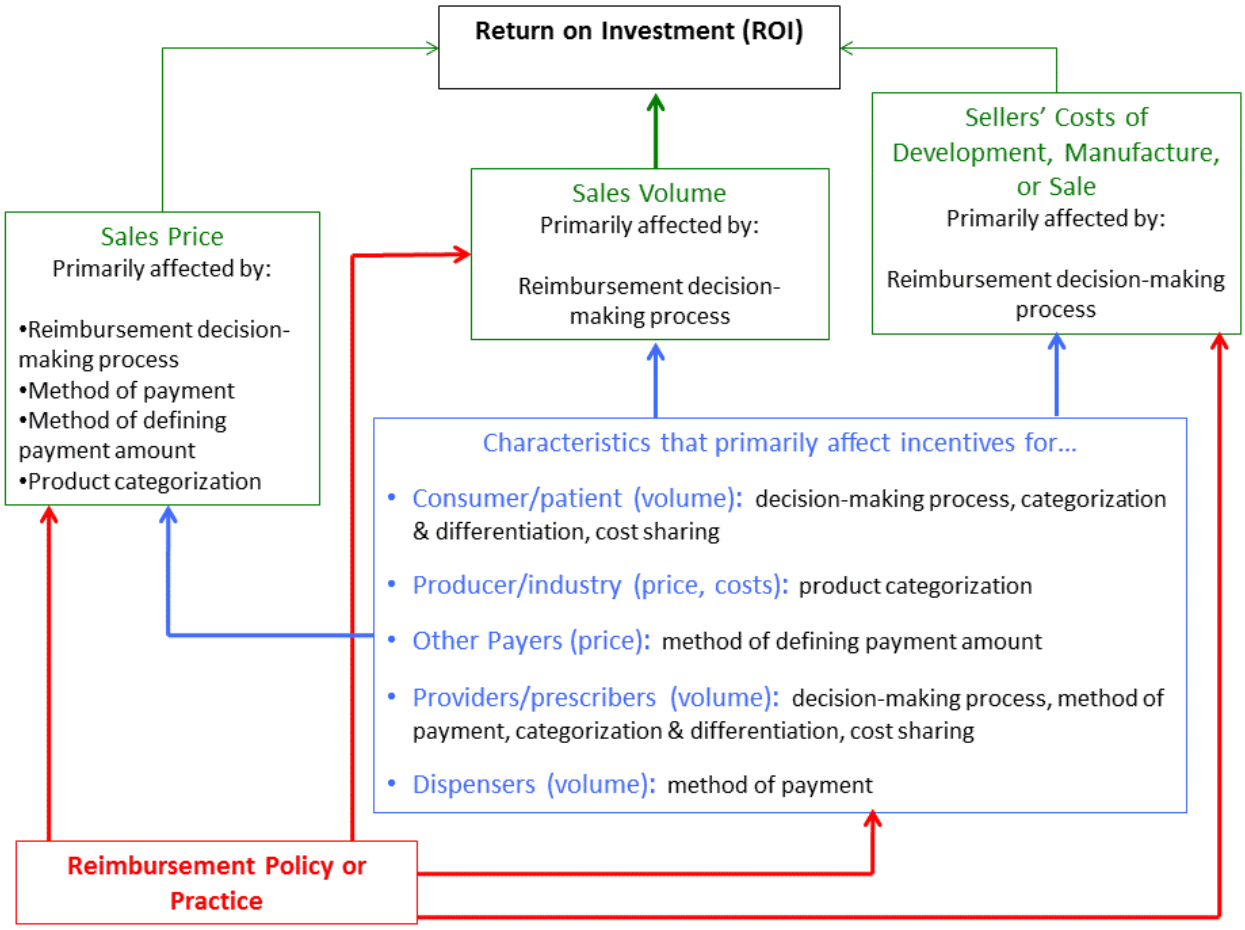
Prospective innovators take into account expectations of the impact of current and anticipated reimbursement policies and practices when deciding to invest in R&D, and in directing investments to particular products. A positive ROI rewards successful innovators and will, in theory, spur the next generation of investment. We assume that larger expected returns on investment provide more incentives to invest in development of novel healthcare technologies, as well as development of new evidence supporting novel uses of existing healthcare technologies.

Figure S1 identifies the primary pathways through which the five aforementioned characteristics of reimbursement policies and practices influence ROI. Although there are direct paths of influence, the connections are not direct in most cases. The distribution systems for healthcare technologies involve many actors and intermediaries whose actions affect ROI for manufacturers, and influence the reimbursement policies and practices used by payers. This complexity makes effects harder to determine and often ambiguous.

Table S1 summarizes our assessments of the direction and magnitude of effects on innovation from each reimbursement characteristic. The primary takeaway is that it remains unclear precisely how reimbursement policies and practices ultimately affect innovation. We found no empirical evidence to directly connect reimbursement policies and practices with the quantity or quality of healthcare technology innovation produced, so our conclusions are frequently drawn from economic theory.

The U.S. retains a pluralist framework with regard to the reimbursement decision-making process – hundreds of payers use their own assessment approaches to reach their judgments, leading to considerable variation. The lack of uniform decision-making weakens the ability of all but the largest payers to motivate developers. The effects of different decision-making *processes* are hard to trace. Theoretically, processes that are transparent and evidence-based will provide the clearest signals to developers and favor development of products that address unmet needs and/or provide added value over existing therapies.

Figure S1: Pathways through which reimbursement characteristics affect ROI



Source: authors' analysis

Table S1: Effects on innovation attributable to reimbursement characteristics

Characteristic	Effects on Incentives to Develop Innovative Products
Reimbursement decision-making process	Effects due to decision-making *processes* are unclear, although specific *components* or *outcomes* of these processes, such as payment, product categorization, and cost sharing, may have more discernable effects (described below). In theory, decision-making processes that are transparent and evidence-based are more likely to foster innovation that enhances consumer welfare by sending clearer signals to developers about the types of products that payers place more value on, and how they assess that value. Timeliness and consistency in decision-making processes may also help by reducing developers' and investors' level of uncertainty about the likelihood of payers reimbursing a new product.
Product categorization or differentiation	Empirical evidence is limited concerning the effects on ROI or innovation from the approaches to product categorization or differentiation used by payers. In theory, approaches that distinguish products based on value are more likely than administrative approaches to promote investment in and development of products that are clinically and cost-effective and address areas of unmet need.
Method of payment	With per-unit payments, effects on innovation largely depend on the method used to determine payment amounts, as discussed in the next panel of this table. With bundled payment, effects on innovation are uncertain. Radical innovations are unlikely to be affected by bundled payments because of the level of benefits they provide and the likelihood that they will be paid as an add-on to the bundle. At the same time, there may be significant disincentives for incremental innovations, unless they are cost-reducing. Effects of bundled payment on substantial innovations, which fall between radical and incremental innovations, are unclear.
Method of defining payment amount	External benchmarking, a process of defining a payment level based on the sales price in the market or markets in which the product is sold, or an estimate of the provider's acquisition cost, is likely to increase ROI and incentives to innovate, compared to other approaches used to define payment amounts. The effects of internal benchmarking, or defining a payment level based on what is paid for comparable covered products for which the payer has already established a payment amount, are largely unclear, but it is most likely that this approach will reduce ROI and incentives to innovate. Value-based approaches are the most promising for yielding effects on ROI that reflect products' benefits relative to their costs (judged from consumer, payer, and/or societal perspective). Effects of lowest possible price strategies are unclear, but this approach may over-incentivize investment in incremental innovations and under-incentivize investment in radical innovations.
Patient cost sharing	Although there is substantial evidence that cost sharing affects utilization, cost sharing seems unlikely to have substantial effects on ROI or incentives to develop or invest in innovative products. Patient demand for innovative products is likely to be relatively inelastic, especially for radical innovations. Coinsurance may lead to greater effects compared to fixed copayments, especially for high-cost products, but it still seems unlikely to have significant effects on innovation. Manufacturers' programs that help patients with their cost sharing further limit potential effects.

Source: authors' analysis

There is limited evidence concerning the effects of different approaches to product categorization and differentiation. Theoretically, evidence-based and value-based approaches offer the potential to have a positive impact on innovation, and interest in value-based insurance designs continues to grow. The unique nature of the U.S. healthcare system, with its multitude of payers and lack of central decision-making, offers challenges for implementation of value-based approaches, such as reaching agreement on what constitutes "value." Our case study of the Premera Blue Cross value-based formulary pilot program highlights some additional challenges, including difficulties in getting access to information needed to assess value and measuring benefits to patients.

While payment methods vary, the fundamental distinction is whether payers compensate providers or suppliers of healthcare technologies on a per-unit basis or as part of a bundled payment for a package of goods and services used for a clinically-defined episode of care. Per-unit payments seem unlikely to favor development of any particular type of innovation, but may also be ineffective at discouraging development of non-innovative products. A shift to bundled payments from per-unit payments may incentivize development of cost-reducing products (from the perspective of the payer), but may discourage incremental innovations.

Payers currently are more likely to rely on external and internal price benchmarking, rather than value-based pricing, to establish payment amounts. Experts consulted for this project also noted that unit costs and budget impact play a role in other policies, such as patient cost sharing and use of utilization management tools (e.g., prior authorization). Theoretically, broader use of value-based or outcomes-based reimbursement would lead to lower returns on products and services offering little value added, higher returns for products with higher value, and greater clarity about where the value-added is uncertain. Our case study of the performance-based risk-sharing agreement for Velcade in the U.K. illustrates some of the administrative and measurement challenges in establishing performance-based payment.

The effects of reimbursement policies and practices on innovation may also be muted by the ability of developers to strategically price their products. Manufacturers' pricing models take into account expectations about lost sales due to higher costs or cost sharing; complex and secretive rebate and discounting mechanisms favor high list prices; and cost sharing offset programs reduce the negative effects on demand when payers apply patient cost sharing. Patient cost sharing does not appear to be an important barrier to innovation at present, at least for substantial or radical innovations. However, with growing levels of patient cost sharing, broader use of coinsurance, and very high list prices for new products, the balance may tip if utilization drops more than manufacturers anticipate or can compensate for with cost-sharing offset programs, or if manufacturers lose pricing power.

INTRODUCTION

There is a long-standing belief that the extent and nature of product reimbursement is a significant factor in the development decisions of potential innovators of healthcare technologies such as drugs, biologics, vaccines, and medical devices, and of the investors who finance them. Analysts posit that payers influence the entry of new products into the market, and their policies have a substantial impact on research and development (R&D) decisions and whether companies choose to advance a technology to market.[3] Experts consulted during this project not only agreed that reimbursement is an important factor in R&D and investment decisions, but also that its influence is growing in importance as the unit costs of many new products exceed the point at which third-party coverage is essential for individual affordability. They also noted that developers approach payers – especially CMS, but also private insurers – during development of new products to try to understand how (or if) a product would be covered, and how payments would be structured.

It is less clear *how* reimbursement affects innovation. In setting out a conceptual model linking reimbursement and innovation, drawing on economic theory and relevant material from the literature, we established that reimbursement policy is one of many influences that affect the expected return on investment (EROI) for developers, investment decisions, and choices about how to direct research and development (R&D) resources (Figure 1).[4] It is not necessarily among the most important drivers in every circumstance and may play different, and evolving, roles with respect to drugs and devices. Other measures, such as the concentration or volume of venture capital directed at specific developers or particular product areas, may be partial proxies for the amount and type of innovation being supported.[5]

In most product markets, sellers set prices in response to perceived demand and willingness to pay by consumers. Two key problems confound healthcare technology markets. One is third-party payment, which makes consumers less sensitive to price. It also has an inflationary effect on both utilization and price. The second problem is that the physicians or health care organizations who act as decision makers on patients' behalf may be insensitive to price at the point of prescribing or dispensing the product. They are also likely to be less sensitive to price than a consumer spending his or her own money. These market distortions can lead to excess consumption, as well as to consumption decisions that are inconsistent with the benefits or value a product offers in relation to available alternatives. For these

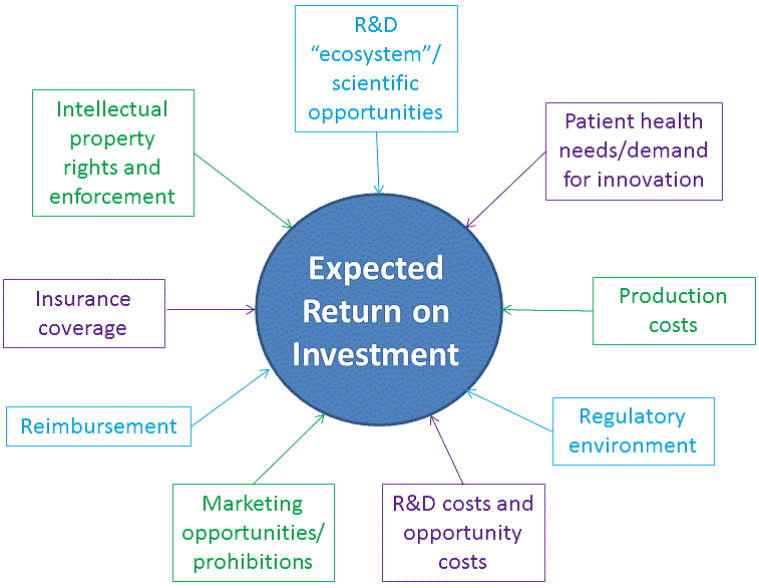
[3] Chambers, J., May, K., & Neumann, P. (2013). Medicare covers the majority of FDA-approved devices and Part B drugs, but restrictions and discrepancies remain. *Health Affairs* 32(6):1109-1115.

[4] Bruen, B., Cohen, J., DiMasi, J., Docteur, E., Dor, A., Lopert, R., …, Shih, C. (2014).*Task 3a deliverables: conceptual model, recommended characteristics for analysis, and analytical framework*. Interim report for the Impact of Reimbursement Policies and Practices on Healthcare Technology Innovation project (Department of Health and Human Services' Contract# HHSP23320095635)

[5] Ackerly, D.C., Valverde, A.M., Diener, L.W., Dossary, K.L., & Schulman, K.A. (2009).Fueling innovation in medical devices (and beyond): Venture capital in health care. *Health Affairs, 28*(1): w68-w75.

reasons, it falls to payers, through reimbursement policies, to offset market distortions by encouraging use of healthcare technologies in cases where the benefits justify the costs.

Figure 1: Determinants of EROI in healthcare technology innovation



Source: authors' analysis

While drug and device expenditures account for a relatively small share of health care expenditures, the absolute amounts are large, and their use can impact other health care costs. Reimbursement strategies and policies directly impact the amount spent on these new technologies, and so it is important to understand their impact on both the allocation of scarce national resources and the incentives that developers and investors have to invest in innovation.

It is also important to understand the incentives that reimbursement policies and practices create, because they can differentiate rewards for products on the basis of assessed value, making them instrumental levers for encouraging valued types of innovation. Conversely, payers may use certain reimbursement policies and practices to limit use of novel technologies that fail to provide health benefits exceeding those offered by existing products (for example, by making them non-preferred products on a formulary). Or, they may set payment levels for these products that make them less expensive than existing products and therefore improve consumer welfare by reducing treatment costs. Experts consulted during this study agreed that reimbursement is one way payers signal what they value to potential innovators. There was a general sense that reimbursement is still a relatively "crude" signal, but it has (still largely untapped) potential to become more nuanced.

RESEARCH OBJECTIVE AND QUESTIONS

The objective of this research project was to describe current reimbursement methodologies and analyze their impacts on drug and device use and innovation, based on economic theory, review of literature, and expert consultation. The following research questions form the basis for this inquiry:

- What are the key characteristics of reimbursement methods and how do they affect pricing, utilization, healthcare spending, and provider and patient decision-making?
- What are the key drivers (statutes, social consensus, cost containment, etc.) of the use of different reimbursement methods? Do different payers have different goals?
- How do the key characteristics of reimbursement methods affect innovation in drugs and devices?

In addition, this research effort examined three specific reimbursement programs identified by experts consulted during this project as not widely used, but worthy of closer examination to see if they have the potential to encourage (or discourage) future innovation. These brief case studies address a final research question:

- What are promising emerging reimbursement strategies to foster useful innovation that improves societal wellbeing?

ORGANIZATION OF THE REPORT

This report describes the findings from our analyses of key reimbursement characteristics and case studies. The methods section that follows describes our approach to the project, including definitions for key terms, development of a conceptual framework and analytic framework, and our approaches to gathering information through reviews of the literature, expert consultations, and studies of specific reimbursement approaches that experts viewed as potential drivers of incentives to innovate. The results section begins with a discussion of our framework, outlining the pathways through which reimbursement may influence innovation. This discussion is followed by a short introduction to five characteristics of reimbursement methods selected for analysis; further detail on these characteristics and factors that contribute to the use of different reimbursement methods is included in Appendix A. The majority of the results section focuses on how reimbursement strategies and policies may impact innovation through financial incentives, pricing, and multiplier effects. The results section includes key findings from our case studies; complete write-ups of each case are included as appendices B-D. The conclusion section highlights important takeaways from our analysis.

METHODS & ANALYTICAL FRAMEWORK

DEFINING KEY TERMS

The project team developed working definitions of key project terms by assessing alternatives, based on definitions in common use in research and policy domains.

REIMBURSEMENT

For the purposes of the study, reimbursement is an umbrella term for the policies and practices that define the terms of coverage and payment for a healthcare technology. More specifically, reimbursement policies or practices encompass the implicit or explicit decisions of a health plan or public program that provides health insurance coverage (e.g., Medicare, Medicaid) – or actors, such as pharmacy benefit managers (PBMs), authorized to act on behalf of the plan or program with respect to healthcare technology decision-making – that:

- Establish whether or not a healthcare technology is a benefit covered by the health plan or public program;
- Define the terms under which a healthcare technology is covered;
- Define the method of payment to the provider, dispenser or supplier of a healthcare technology;
- Set or limit the amount the third-party payer will pay to the provider, dispenser or supplier of a healthcare technology, as well as the terms of any discounts or rebates supplied, or;
- Set or limit any cost-sharing to be incurred by patients using the healthcare technology.

PAYERS

We use the term *payers* to refer to public health coverage programs and private health insurance plans. Payers are distinguished from purchasers in that they do not take possession of a drug or device, but instead compensate those who have purchased health-care technologies used by their beneficiaries or enrollees through the reimbursement policies and practices they adopt. PBMs that operate their own mail-order pharmacy services act as purchasers, as do hospitals and health systems like Kaiser Permanente and the Veterans Health Administration, which integrate the provision of coverage with the provision of care.

Payers in the United States often employ *subsidiaries* to serve as managers of some or all health benefits. Examples include Medicaid managed care plans; Medicare Advantage plans; stand-alone Medicare prescription drug plans (PDPs); and PBMs. PBMs help design and administer drug benefits for public payers, private health plans, and self-insured groups (e.g., employers and organizations). The role of subsidiaries is important to take into account when analyzing the implications of reimbursement practices and policies employed by payers. Importantly, their widespread presence introduces

complications in analyzing the impact of payment methods on outcomes, in that subsidiaries tend to face incentives that differ from those of payers.

Subsidiaries are often well-equipped and motivated to make decisions leading to savings in areas for which they are contractually responsible (e.g., pharmacy benefits), although the extent to which the savings are shared with, or passed on to, payers and consumers varies, depending on factors such as contractual terms and extent of competition among subsidiaries. Furthermore, depending on the terms of their contracts, subsidiaries may not benefit from any savings that accrue on the medical benefit side because of their decisions, and may be less motivated to make decisions that may involve higher up front expenditure but deliver downstream savings. A growing awareness of problems associated with subsidiary incentives have led to the creation of so-called "transparent model" PBMs that purport to pass through to the sponsor all negotiated discounts. These PBMs were estimated to account for 10% of the market in 2013.[6]

INNOVATION

The analytical focus of this study is healthcare technology innovation that enhances consumer welfare. Drawing upon a review of the relevant policy and research literature, we define an innovative healthcare technology as a new product that (a) meets a previously unmet or inadequately met health need and that (b) offers enhanced effectiveness in comparison with existing therapeutic alternatives. We describe a way to classify innovations as incremental, substantial, or radical, depending on the significance of the unmet need addressed and the extent of additional benefit (comparative effectiveness) offered. We further stipulate that healthcare technologies, innovative or not, can be said to enhance consumer welfare when they are offered at a price that is below the maximum price consumers would be willing to pay. In so doing, we take an approach that is consistent with the traditional economic concept of consumer surplus.

Experts consulted during this project noted that the issue of who defines "innovation" is significant, as what is considered to be "innovative" can vary between the payer and the developer, and among payers. For example, one expert noted that payers may not view once-per-day drug dosing as innovative compared to twice-per-day dosing unless health outcomes are better with the single dose, although some payers may view the once-per-day product as innovative if it reduces costs.

Starting from a definition of *innovation* as "(the) development of new drugs or devices or evidence related to drugs or devices that improve consumer welfare," we defined *innovative products* (drugs and devices) as those able to address diseases and conditions for which there is a substantive (i.e., non-trivial) unmet or inadequately met need. We also defined a classification scheme for differentiating innovations in terms of the level and/or type of innovation they represent (Table 1). To arrive at this arrangement, we reviewed and assessed innovation classification schemes currently in use in drug and

[6] Eban, K. (2013, October 23). Painful prescription: Pharmacy benefit managers make out better than their customers. *Fortune*.

device regulation, pricing and reimbursement schemes, and in the academic literature. We designed the scheme to be consistent with our definition of innovation, reflective of the social welfare perspective adopted for this project, and to be useful in distinguishing the impact of various types of reimbursement characteristics and methods/strategies on motivations to innovate.

Table 1: Classification schema for innovative healthcare technologies, with examples

Extent of Comparative Benefit	Gravity of Unmet Need	
	Addresses Lesser Unmet Need	**Addresses Greater Unmet Need**
Negative net health benefit compared to existing alternatives	Not Innovative	Not Innovative
Comparable net health benefit compared to existing alternatives	Not Innovative	Not Innovative
Modest net health benefit compared to existing therapies	Incremental Innovation (Example: dopamine agonists for restless legs syndrome)	Substantial Innovation (Example: tissue plasminogen activator [t-PA] vs. streptokinase for acute MI)
Significant net health benefit compared to existing therapies	Substantial Innovation (Example: Viagra for erectile dysfunction)	Radical Innovation (Example: sofosbuvir vs. interferon for Hepatitis C)

Source: Authors' analysis

We consider a healthcare technology to be a *consumer welfare-enhancing innovation* only if it meets our definition of an innovation and generates *consumer surplus*. A product offers consumer surplus where consumers' willingness to pay exceeds the transaction cost, which we consider synonymous with enhancing social welfare for the purposes of this study.

While our conceptual approach to consumer welfare is consistent with the notion of consumer surplus, it is broader and more nuanced than the standard one-product/one-period framework. Total social surplus is the sum of consumer and producer surplus. Producer surplus (the difference between the effective price obtained by a developer and the marginal cost of producing and distributing the product) cannot be ignored in this case, as it is highly relevant to innovation incentives. As commonly defined, producer surplus will include, in addition to profits, the R&D expenditures that are used to fund development of future products. Maximizing consumer surplus for a new product in a given period leaves no room for current and future R&D. Thus, in a dynamic context, producers must appropriate some of the social surplus created by new products to maintain incentives to continue to innovate.

In practice, the share of social surplus counted as producer surplus can seem low. For example, Philipson and Jena found that producers of HIV/AIDS drugs were able to appropriate only 5% of the social surplus

generated by these products.[7] Expanding on this work, Philipson and Jena examined more than 200 technologies in a cost-effectiveness registry and found that, in the case of the median technology, producers captured only 15% of the social surplus.[8] The modeling did not account for factors such as public funding of R&D and the interpretation of cost-effectiveness analysis in a non-monopoly context that can impact whether there is under- or over-investment in R&D, so further research is needed before such conclusions can be reliably made.

On a conceptual level, however, we do need to account for incentives for future innovation. Thus, we consider consumer surplus for a new product to be the present discounted value of the product's consumer surplus for all periods over its product lifecycle, plus the present discounted value of the share of consumer surplus generated by all future new products whose R&D is funded in part by the producer surplus of the original new product. Additionally, positive social benefits can be generated by the introduction of a new product through effects on pricing and on the economies where R&D and manufacturing are conducted. In general, our notion of social welfare is dependent on the following factors:

- Dynamic innovation (consumer surplus from additional new products developed with funding from a new product's producer surplus);
- General equilibrium effects on demand and pricing (consumer surplus created from competitive pricing within the drug class in both static and dynamic contexts [over time for the class and from the production of new products in newer classes]), and;
- Economic multiplier effects from R&D, manufacturing, and distribution.

The last effect is not unique to investment in this sector, and it may be small in relation to consumer surplus created by the introduction of new products. Thus, our analyses focus on the impacts that reimbursement methods and policies have on the introduction of new innovative products that create positive consumer surplus.

[7] Philipson, T.J., & Jena A.B. (2006). Who benefits from new medical technologies?: estimates of consumer and producer surpluses for HIV/AIDS drugs. *Forum for Health Economics & Policy*, 9(2), ISSN (Online) 1558-9544.

[8] Philipson, T.J., & Jena A.B. (2008). Cost-effectiveness analysis and innovation. *Journal of Health Economics*, 27:1224-1236.

DEVELOPMENT OF AN ANALYTIC FRAMEWORK

We developed a framework with which to explore the link between reimbursement and investment in innovations of various types (incremental, substantial, and radical), as well as products that might be considered to be non-innovative.[9] As a first step, we reviewed academic research and policy-oriented publications to identify relevant models that could be adapted or adopted for this project, or that could inform development of a new framework. We compiled and reviewed existing models that illustrate the mechanisms through which reimbursement methods impact innovation, as well as models that depict closely-related relationships, such as the implications of reimbursement methods on R&D or on pharmaceutical or medical device industry profits.

Our framework follows a conceptual model that depicts the mechanisms of influence by which various characteristics of reimbursement methods may affect drug and device producers' expected return on investment (EROI) and other incentives to innovate. The conceptual model behind this framework established that, although the actual ROI measures the reward (or loss) for innovators and investors once a product reaches the market, an assessment of the EROI informs the decision to invest in the initial development of a healthcare technology. Our model uses EROI as a proxy for incentives to innovate, and assumes that current returns on investment are viewed as indicative of potential future returns.

ANALYSIS OF KEY CHARACTERISTICS OF REIMBURSEMENT METHODS

The project team identified key characteristics of reimbursement methods that are likely to influence innovation, based on theoretical underpinnings or empirical evidence. We developed an illustrative list of reimbursement methods or strategies in current use. Using our analytical framework, we analyzed which characteristics of those methods or strategies stand to impact incentives for innovation, and compiled the results in order to create a taxonomy of characteristics for further analysis.

Following selection of five key reimbursement characteristics in consultation with representatives of ASPE, the project team conducted an in-depth review of these five characteristics to gather empirical evidence pertaining to the impacts of these characteristics on the level and type of innovation in pharmaceuticals and medical devices. The project team scanned the academic research literature using search engines to identify published research, government reports, white papers, and news and trade press included in databases such as MEDLINE/PubMed, EconLit, SCOPUS, Health Policy Reference Center, Pharmaceutical News Index, Google Scholar, and other databases. We identified and reviewed relevant books and policy reports using general Internet search engines and targeted searches of websites for booksellers and industry organizations.

[9] Bruen, B., Cohen, J., DiMasi, J., Docteur, E., Dor, A., Lopert, R., ..., Shih, C. (2014). *Task 3a deliverables: conceptual model, recommended characteristics for analysis, and analytical framework*. Interim report for the Impact of Reimbursement Policies and Practices on Healthcare Technology Innovation project (Department of Health and Human Services' Contract# HHSP23320095635)

EXPERT CONSULTATIONS

The project team identified and consulted with a range of experts to complement our review of the research and other evidence. These experts, listed in Appendix E, included:

- Faculty, researchers, and consultants;
- Representatives of firms engaged in drug and device development;
- Investors specializing in healthcare technologies, and;
- Representatives of commercial payers, PBMs, and government agencies that pay for healthcare technologies.

Consultations occurred via teleconferences and individual telephone calls. The questions for each session varied according to the panel's expertise, but covered topics such as:

- Factors that influence how developers/investors target investments to develop new healthcare technologies, or to find new applications for existing technologies;
- How a product's future market environment, including reimbursement prospects and uncertainty, affects product development or investment decisions;
- Which components or characteristics of reimbursement are most important in influencing how much and what kind of new healthcare technologies are developed;
- How more widespread use of particular reimbursement methods in the United States might change product development or investment decisions;
- Factors that influence payers' reimbursement decisions;
- How payers determine the reimbursement amount for a given healthcare technology;
- Actions by payers that may foster (or inhibit) future drug and device innovation, and;
- How reimbursement policies or practices that are emerging or becoming more widespread might foster or inhibit investment in consumer welfare-enhancing healthcare technologies.

Each session was recorded and transcribed for reference by project staff. Summaries of each meeting were reviewed and approved by the project team and ASPE representatives.

CASE STUDIES

Based on our review of the literature and expert consultations, the project team identified examples of reimbursement methods and programs in private and public markets as candidates for case studies. Candidates included emerging models, as well as older methods that appeared to be gaining interest. ASPE representatives selected three examples for further analysis. These case studies sought to answer the following questions:

- What are the objectives/rationale of the method or program?
- What are the key characteristics of the method or program?
- Is the approach novel or is it a variation of an already established program or method used elsewhere?
- What is the stated or implied theoretical basis of the approach/method?

- How might broader use of the method or program influence innovation in drugs or medical devices?

Using the list of characteristics of reimbursement methods with the greatest potential to impact incentives to innovate, and applying the framework for analyzing how reimbursement affects drug and device innovation that we developed, we qualitatively analyzed the potential impacts of the selected examples on incentives to develop innovations that improve consumer welfare.

We examined three specific examples of reimbursement policies and practices, each identified by experts consulted during this project as not widely used, but worthy of closer examination to see if they have the potential to encourage (or discourage) future innovation: an advance market commitment, a value-based drug formulary, and a performance-based funding arrangement.

RESULTS

Consistent with our conceptual model, the experts consulted in this project cited human curiosity, investment in science/research (public and private), and assessments of clinical need as important factors in fostering initial investment in discoveries, but there was broad agreement that reimbursement is a critical factor in determining which products reach the market. Experts noted that attractive candidates for investment require positive assessments of clinical need and anticipated reimbursement, and that potentially innovative products still may not make it to market if assessments fail to justify the continued investment to develop them. They noted that investors may look for products that offer significant improvements compared to the current standard of care, or are otherwise differentiated from technologies likely to appear in the near term, as this competitive advantage usually translates into more "durable" pricing and stronger reimbursement.

Experts interviewed for this project noted that developers approach CMS, private insurers, and other payers during development of new products to try to understand how (or if) a product would be covered, and how payments would be structured. For drugs, discussions between payers and developers may occur as early as Phase II, to determine the endpoints of interest to payers for later trials. A popular guidebook for device developers puts "payer advocacy" approximately one year prior to expected launch and "conduct[ing] payer education" roughly eight months prior to launch. However, the authors note that timelines vary considerably depending on the type of device, whether it fits under an existing reimbursement code or needs a new one, and other factors.[10]

The experts we interviewed also suggested that reimbursement is growing in importance as the unit costs of new products exceed the point where third-party coverage is

Quotes from experts

My general experience is that when organizations invest in early discovery, it's mostly driven by science… after the product gets further along in its development life cycle and larger and larger investments are needed, that's when people start thinking more about the clinical utility… the value in the marketplace… will physicians want to prescribe it… will payers want to pay for it? But there is a trend… in general to move that marketplace insight earlier in the development process.

[At the last few places I have worked, investment is] primarily driven initially by the clinical need… You are trying to solve that problem up front… and then the second question usually resolves around the business side… the regulatory path, the reimbursement, the market size.

We have a very formal process that we begin very early in product development life cycle, and we have our reimbursement staff across the company very involved in assessing the reimbursement aspects…

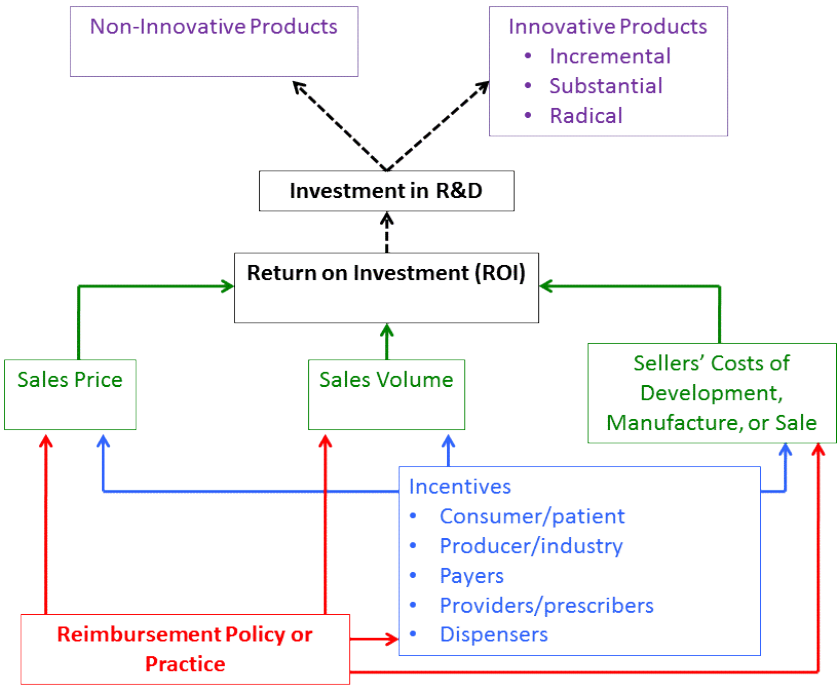
[10] Yock, P., Zenios, S. A., & Brinton, T. J. (2015). *Biodesign: the process of innovating medical technologies*. 2nd Edition. Cambridge University Press.

essential for individual affordability. The broad availability of reimbursement through insurance likely contributes to higher costs for healthcare technologies. New products need reimbursement, but reimbursement leads to new products, which creates the need for more reimbursement. Reimbursement also decreases cost sensitivity for consumers, so manufacturers can charge higher prices.

TRACING THE LINK FROM REIMBURSEMENT TO INNOVATION

The analytical framework that we developed for this project describes a way in which the (prospective) impact on innovation from a particular reimbursement method or strategy can be assessed, in qualitative (direction and relative magnitude of impact), if not quantitative terms. This framework, shown in Figure 2, posits that reimbursement policies and practices can affect product developers' ROI directly in three ways. The first is by establishing a particular payment level, which in turn affects average sales price in line with the share of the prospective market represented by the payer. The second is by setting a volume of sales at that payment level, as may occur in the case of competitive bidding, for example. The third is by influencing seller costs associated with development, manufacture, or sale of a healthcare technology.

Figure 2: Framework for assessing effects on innovation



Source: authors' analysis

Reimbursement policies also indirectly influence ROI by establishing different incentives for key actors, including patients/consumers, dispensers, providers, sellers, and payers. In turn, these incentives affect effective sales price, sales volume, and in some cases, sellers' costs of development, manufacturing, and sales.

While researchers have investigated the links between EROI, ROI, and pharmaceutical industry R&D (see, for example, Scherer[11]), we found no empirical evidence that directly connects ROI with the quantity or quality of healthcare technology innovation. In general, we assume that larger expected returns on investment provide more incentives to invest in development of novel healthcare technologies. We also assume that expectations and time horizons tend to differ between large, established manufacturers and relatively small biotechnology firms and start-ups. The latter have shorter-term horizons; the former have longer-term horizons. Innovators' and investors' expectations and time horizons also vary by therapeutic class. These differences make it very difficult to draw general conclusions about the link(s) between ROI and innovative products. The dashed lines between ROI, investment in R&D, and the various categories of innovation illustrate this uncertainty.

We add a second level of assessment that separates each of the novel products into two groups: those that enhance consumer welfare and those that do not. As noted earlier, we use consumer surplus – the amount by which consumers' willingness to pay exceeds the transaction cost – as the measure of consumer welfare. We do not depict this assessment visually in Figure 2, but it essentially cuts each category of novel products into two parts. For example, a non-innovative product may still enhance consumer welfare by achieving comparable effects at lower cost, and an otherwise-innovative product may fail to enhance consumer welfare if the opportunity costs of its acquisition and diffusion exceed the value of the attained benefits. Similarly, a developer may view as innovative a pacemaker that offers thousands of sophisticated monitoring options, but a payer may view the added complexity as producing uncertainty or risks that may outweigh the benefits of the innovation, because individual physicians can only understand a fraction of the options.

KEY CHARACTERISTICS OF REIMBURSEMENT METHODS

Different characteristics of reimbursement policies and practices serve to define payment levels, volume of service, and seller costs. They also establish different incentives for key actors, which indirectly influence these determinants of ROI. We selected five characteristics of reimbursement policies and practices that appear to be important in explaining the impact of reimbursement policies and practices in motivating and directing innovators' efforts (Table 2).

[11] Scherer, F. M. (2001). The link between gross profitability and pharmaceutical R&D spending. *Health Affairs, 20*(5), 216-220. doi:10.1377/hlthaff.20.5.216

Table 2: Selected characteristics of reimbursement policies and practices

Characteristic	Definition
Reimbursement decision-making process	How payers make decisions on which drugs, devices, and other healthcare technologies to make available, at what cost, and for whom.
Product categorization and differentiation	How payers distinguish the drugs or devices that they cover.
Method of payment	The terms under which a payer makes reimbursement to a provider.
Method of defining the payment amount	The methods used to establish the amount the third-party payer will reimburse a provider or supplier furnishing a healthcare technology to a patient.
Patient cost sharing	Out-of-pocket costs borne by consumers, net of insurance coverage, when they obtain services or purchase prescription drugs, durable medical equipment (DME), or other health technologies

Source: authors' analysis

For most U.S. payers, the REIMBURSEMENT DECISION-MAKING PROCESS involves pharmacy and therapeutics (P&T) committees or other authorized decision-makers who are responsible for evaluating drugs and devices translating the available evidence into decisions for prescribing, availability, and reimbursement of drugs and devices. These decision-makers follow a sequential series of steps, as outlined in Appendix A.[12] Groups of providers, including specialists in the disease, procedure, and/or patient population for which the technology is intended, may evaluate devices used solely in medical practice (i.e., not by patients at home). Payers use these evaluations to make decisions on what products to include in formularies, at what price, and for whom. The decision-making process also encompasses decisions about which tools to use to attempt to affect provider choices/prescribing and manage utilization, such as formulary tier placement (which may affect patient cost sharing), prior authorization, step therapy, and quantity limits. As such, the decision-making process links the four other characteristics noted below.

Payers use a variety of approaches to PRODUCT CATEGORIZATION AND DIFFERENTIATION in the course of deploying their reimbursement practices and policies. They can distinguish between drugs or devices in terms of patent status, route of administration, care setting, price, value, or other attributes. *Administrative* approaches, which may be undertaken without reference to value or evidence, include the following:

1. *Pharmacy versus medical benefit*: All payers make an administrative distinction between drugs or devices subsumed under the pharmacy versus medical benefit. Almost all devices and physician-administered drugs are considered part of a payer's medical benefit; self-administered or outpatient drugs are categorized under the pharmacy benefit.

[12] Wang, Z., Salmon, J.W., & Walton, S. (2004). Cost-effectiveness analysis and the formulary decision-making process. *Journal of Managed Care Pharmacy*, 10(1):48-59.

2. *Substitution*: Payers use different approaches to encourage generic substitution as a cost-containment measure. Over 80% of prescriptions dispensed in the United States are for generics, and much of this is due to payers driving substitution of generic for originator prescriptions.[13] Generic drugs enhance consumer welfare when offered at prices below the maximum price consumers would be willing to pay.

3. *Rebate mechanism*: Almost all payers and manufacturers negotiate rebates in exchange for increased market share; a manufacturer of a particular drug rebates a certain amount to the payer if the payer successfully increases sales of the drug. Payers influence market share by granting a drug preferred status on the formulary. Preferred drugs are in lower patient cost-sharing tiers, while non-preferred drugs are in higher cost-sharing tiers. More competitors in a therapeutic class allows for larger rebates, as competition among products increases payer leverage.

Value-based approaches include product exclusions; value based-insurance design; coverage with evidence development; risk-sharing agreements; and other methods based on evidence or value.

1. *Excluded products*: A few PBMs have removed certain brand products with clinically equivalent alternatives from the formulary entirely. One purpose of exclusions is to extract greater price discounts and rebates. When a payer or PBM delists a drug or device, it rewards the manufacturers of competing products with an increase in market share. Exclusions also cancel out the value of manufacturers' discount cards/coupons from cost-sharing offset programs.

2. *Value-based insurance design (VBID)*: A 2010 review estimated that about one-third of payers have adopted value-based insurance design, wherein they have reduced cost-sharing for a number of "high-value" products and/or services in highly prevalent disease categories and raised cost-sharing for certain "low-value" products and/or services. However, it is not always clear what is "value-based," most adopters only use this design for a very limited number of therapeutic classes, and this still leaves a majority of payers (at least in 2010) who do not use value-based insurance design at all. Value-based formularies, a form of VBID, differentiate groups of drugs based on the disease or condition treated and the therapeutic effect of treatment. We discuss one example, a value-based formulary pilot program run by Premera Blue Cross, later in this report and in Appendix C.

3. *Coverage with evidence development*: Coverage with evidence development (CED) involves coverage of a drug or device with the stipulation that payers and manufacturers collect post-marketing data on the drug or device's real-world safety and effectiveness. Given the possibility of lags between marketing authorization and payer decisions to reimburse, as well as significant uncertainty at launch, payers may be able to foster innovation by shifting more of the clinical

[13] Kleinrock M. (2012). *The use of medicines in the United States: Review of 2011.* IMS Institute for Healthcare Informatics. Parsippany, New Jersey.

evidence gathering to the post-marketing space while providing patients with access to the products being evaluated. To continue to have market access, manufacturers will have to demonstrate that their products confer added benefits.

4. *Risk-sharing arrangements*: Related to CED, "risk-sharing arrangements" (RSAs) between payers and manufacturers have grown in number internationally, although there are more publicized examples overseas than in the U.S. RSAs typically involve measurement of the performance of a technology in a defined patient population over a specified period. They may tie reimbursement for covered products to the measure of clinical outcomes; condition continuation of coverage of a product on meeting specified responses to treatment or absence of disease progression; or tie reimbursement to financial or utilization outcomes.

   There has been limited experience to date in performance-based risk sharing both in the U.S. and other countries. Challenges to broader implementation include high transaction costs; lack of acceptable (e.g., valid, objective) outcome metrics; difficulties in determining treatment effects; and the absence of suitable data capture systems. We examine these issues in the context of a performance-based RSA for Velcade in the United Kingdom later in this report and in Appendix D. Nearly all RSAs have been for drugs, but there was a well-documented United HealthCare (UHC)/Genomic Heath (GH) performance-based RSA for the Oncotype DX diagnostic that began in 2007, and other agreements involving diagnostics/devices have emerged in more recent years.

In the United States, there is currently more use of administrative than value-based approaches.

In the United States, different METHODS OF PAYMENT are employed for drugs and devices used in the care of hospital inpatients; physician-administered drugs and medical devices used in ambulatory care settings; and prescription medicines and medical products prescribed for home use. The same payer may use different payment methods for different plans (e.g., health maintenance organization [HMO], preferred provider organization [PPO], point-of-service [POS]), and employers and other plan sponsors may influence the payment method selected for a particular plan. Different payers also make different reimbursement decisions, even when employing similar methods. The result is a complex system of reimbursement involving many decision-makers and resulting in substantial variation among payers.

While methods vary, there is a fundamental distinction between whether payers compensate providers or suppliers of healthcare technologies on a *per-unit basis* or as part of a *bundled payment* for a package of goods and services used for a clinically-defined episode of care.[14]

- In the case of prescription medicines and durable medical equipment (DME) used in the home setting, per-unit payments are the norm; distinctions lie primarily in how per-unit payment

[14] Both per-unit and bundled payments may be, and increasingly are, subject to retrospective adjustments, withholds and/or bonuses based on meeting of performance targets (so-called pay for performance).

amounts are determined. For DME prescribed for home use, payers are increasingly using competitive bidding for products judged therapeutically equivalent, while other products are reimbursed according to a fee schedule.

- Payers in the United States use bundled payments primarily for care associated with inpatient and outpatient hospital treatment, although some are experimenting with bundled payments for care provided in physicians' offices and clinics.[15]
- In general, bundled payments cover drugs provided in hospitals, and the hospital is not permitted to bill the payer separately unless the drug exceeds a defined threshold cost. Exceptions are often made for products designated as highly innovative and/or high cost, with the result that default unit pricing is applied for those products.
- Similar to drugs, devices and diagnostics used in inpatient and outpatient hospital care are usually bundled, with exceptions for products subject to pass-through payments. Medicare is working to expand the use of bundled payments for devices used in outpatient and ambulatory care settings.[16]
- Drugs administered by physicians in offices or clinics usually are paid on a per-unit basis.
- As a rule, payers compensate pharmacies for each unit sold; however, specific payment levels are negotiated with the pharmacies, and additional rebates or discounts may be negotiated directly with the product manufacturers, such as part of a determination of formulary tier placement.[17]

The use of similar payment methods in many areas by different payers likely reflects the influence of Medicare, which is the largest single payer in the United States, and forged the path in developing technical approaches and tools employed in payment methods. The up-front costs associated with developing new methods can be significant, and private payers would likely face barriers to both investment and deployment of novel methods.

Public and private payers use different guidelines and metrics to DEFINE THE PAYMENT AMOUNT they will reimburse a provider or supplier furnishing a healthcare technology to a patient.[18,19] In the

[15] For example, Medicare tested bundled payments in the outpatient setting in the Medicare Cataract Alternative Payment Demonstration. For further information, see: Painter, M. W., Burns, M.E., & Bailit, M.H. (2012, January). Bundled payment across the U.S. today: Status of implementation and operational findings. *Health Care Incentives Improvement Institute Issue Brief*.

[16] Change is also under way on the ambulatory care front, where a move toward a more comprehensive approach to reimbursement is being discussed because of concerns raised by medical device policy experts about code stacking, a practice in which the payment for a diagnostic test is determined by adding up the costs of the individual component steps.

[17] Formularies are lists of reimbursable drugs or devices, which include provisions for patient cost-sharing as well as coverage conditions. Formulary development is normally informed, in part, by evidence on the safety, effectiveness, and/or cost of drugs and devices.

[18] In the interests of clarity, we exclusively use the term "amount" to refer to how much a payer pays a provider for a healthcare technology. Other terms in common use include payment rate and payment level.

case of bundled payment, payers seek to approximate the cost of drugs and devices used when defining the bundled payment amount. Technological innovations are accounted for either through updates of the bundle or pass-through payments, in the case of technologies considered to be highly innovative, highly costly or both. When payers are reimbursing on a per-unit basis, there are four basic approaches:

- *External benchmarking*, or defining a payment level based on the sales price in the market or markets in which the product is sold, or an estimate of the provider's acquisition cost;
- *Internal benchmarking*, or defining a payment level based on what is paid for comparable, covered products for which the payer has already established a payment amount;
- *Value-based payment*, or defining a payment level based on an assessment of the product's value, such as benefits to the patient, to the payer, or to society as a whole, including cost savings associated with use of the product in place of a therapeutic alternative, and;
- *Lowest possible price payment*, or defining a payment level based on the lowest price that the seller will accept.

External benchmarking is the most widespread approach in prescription drug pricing for publicly financed health programs in the United States and most health systems in the developed world. For example, most public programs in the U.S. benchmark payment levels for prescription drugs using published prices from commercial vendors (e.g., average wholesale price [AWP]) or reported sales prices between manufacturers and purchasers (e.g., average sales price [ASP] or pharmacy invoices). Because Medicare publishes codes and payment rates, its payment levels are visible benchmarks and may influence some payment decisions by other payers.[20,21] Nevertheless, Medicare's method of setting payment levels for diagnostics, based on the average wholesale cost of the steps involved plus a mark-up, is often criticized as being outdated, subject to gaming by laboratories, and not reflective of the products' underlying health benefits.[22,23] Medicaid's drug payment formulas are similarly criticized.[24]

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[19] This discussion focuses on the manner in which the initial payment amount is defined; a secondary question (not addressed here) concerns how the payment amount is updated to reflect new evidence, changes in technology or practice patterns, or other factors.

[20] White, C. (2013). Contrary to cost-shift theory, lower Medicare hospital payment rates for inpatient care lead to lower private payment rates. *Health Affairs*, 32(5):935-943.

[21] Clemens, J., & Gottlieb, J. D. (2013, October). *In the shadow of a giant: Medicare's influence on private physician payments*. NBER Working Paper No. 19503. Cambridge, MA: National Bureau of Economic Research.

[22] Carlson, B. (2010). Seeking a coding solution for molecular tests: managing the estimated 1,700 molecular tests now on the market is impossible without a unique CPT code for each test. What's at stake? The future of personalized medicine. *Biotechnology Healthcare*, 7(4), 16–20.

[23] Gass Kandilov, A. M., Pope, G. C., Kautter, J., & Healy, D. (2012). The national market for Medicare clinical laboratory testing: implications for payment reform. *Medicare & Medicaid Research Review*, 2(2), mmrr.002.02.a04. http://doi.org/10.5600/mmrr.002.02.a04

[24] U.S. Department of Health and Human Services' Office of Inspector General. (2011). *Review of drug costs to pharmacies and their relation to benchmark prices*. A-06-11-00002.

Reimbursement methods and payment rates used by private payers are usually proprietary and confidential. The methods used to compensate pharmacies for drugs provided under the pharmacy benefit programs of private payers in the United States, including Medicare Advantage Plans, most Medicaid managed care plans, and Medicare Part D standalone drug plans, are largely unknown because payers retain proprietary interest in their payment formulas.[25] Only limited details, such as average discounts from AWP based on small samples of employer-based plans, are publicly available.[26] Private payers typically negotiate payment terms directly with hospitals, physicians, and other providers.[27] Because competitive pressures motivate private health plans to minimize costs, it is likely that many private payers employ the lowest possible price approach, in which their payment amount is determined by the degree of leverage they have in a market transaction when facing a particular seller of a healthcare technology.[28]

A relatively smaller number of payers, such as insurers in Germany, the Netherlands, and the Czech Republic, employ a form of internal benchmarking (commonly referred to as "reference pricing" or "therapeutic reference pricing") to define the maximum price they are willing to pay for a product that is a) determined to be comparable to others, and b) where the payer has pre-established a payment amount.[29] Other payers, such as the national health services of the United Kingdom and of Sweden, are experimenting with value-based payment.[30]

Though internal benchmarking is seldom used in the United States, one notable exception is Medicare's functional equivalence and least costly alternative policies. In the early 2000s, Medicare enacted policies for a limited number of drugs and devices where the program would only pay the cost of the least costly drug or device in the case of two or more drugs or devices that were deemed functionally or therapeutically equivalent. A high-profile example was CMS' decision to reduce the payment rate for darbepoetin alfa (Aranesp) by considering it functionally equivalent to epoetin alfa (Procrit).[31] The

[25] Academy of Managed Care Pharmacy. (2013). *AMCP guide to pharmaceutical payment methods*, Version 3.0, executive summary.

[26] Pharmacy Benefit Management Institute. (2013). *2013-2014 Prescription drug benefit cost and plan design report*.

[27] Sorenson, C., Drummond, M., & Burns, L. R. (2013). Evolving reimbursement and pricing policies for devices in Europe and the United States should encourage greater value. *Health Affairs,* 32(4):788-796.

[28] The use of this approach was discussed by experts representing payers who were consulted as part of the research for this project. One expert opined that neither external price benchmarking nor leverage-based pricing offered ideal outcomes, but that appetite for moving to value-based payment was not yet primed in the U.S. context.

[29] This approach is also used by Canada's Patented Medicine Pricing and Review Board, which sets nationally binding price caps for patented medicines sold in Canada. Canadian payers (private plans and provincially-administered public programs) use different approaches to define reimbursement payment levels.

[30] Paris, V. & Belloni, A. (2013). *Value in Pharmaceutical Pricing.* OECD Health Working Paper no. 63. Paris: OECD.

[31] Rubinstein E. (2006). Application of `functional equivalence' to payment for office-administered biopharmaceuticals. *Biotechnol Healthc*;3(6):64-65.

Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) prohibited use of this standard for other drugs, and CMS stopped applying it to Aranesp and Procrit in 2006.[32] In 2008, the U.S. District Court of the District of Columbia held in the case of *Hays v. Leavitt* that the least costly alternative policy for another drug, DuoNeb (albuterol and ipratropium bromide), was not authorized under Medicare's statute.[33] After the U.S. Court of Appeals for the District of Columbia Circuit upheld the District Court's decision, CMS instructed contractors to suspend and remove all least-costly alternative provisions.[34]

PATIENT COST SHARING refers to out-of-pocket costs borne by consumers, net of insurance coverage, when they obtain services or purchase prescription drugs, durable medical equipment (DME), or other health technologies. A cost-sharing approach generally consists of two main elements: The cost-sharing "method" refers to deductibles, fixed copayments, and variable coinsurance.[35] The "level" of cost sharing refers to the overall amount contributed by the beneficiary, such as high deductibles versus low deductibles, or high copayment rates versus low copayment rates. Tiered cost sharing, which is closely linked to the payer's categorization or differentiation, adds an additional dimension.

There is substantial variation in cost sharing among different payers and plan offerings. Commercial plans typically use a mix of deductibles, copayments, and/or coinsurance for medical services, DME, and other devices. Deductibles and coinsurance are the main cost-sharing methods in Medicare's Part A (Hospital Insurance) and Part B (Medical Insurance).[36] There is no annual limit on an individual's cost-sharing liability. Fixed copayments are much more common in Part C (Medicare Advantage; managed care) and Part D (stand-alone Medicare prescription drug plans [PDPs]), which private carriers operate.[37] Under Medicaid, states may require patient cost-sharing for many covered services, but the level is generally limited to "nominal" fixed copayments; a beneficiary's total annual cost-sharing is limited to a

[32] Medicare Payment Advisory Commission (MedPAC). (2010, June). Enhancing Medicare's ability to innovate. *Report to the Congress: Aligning Incentives in Medicare*. Chapter 1.

[33] Hays v. Leavitt, 583 F. Supp. 2d 62, 72 (D.D.C. 2008)

[34] U.S. Department of Health and Human Services' Office of Inspector General. (2012, November). *Least costly alternative policies: impact on prostate cancer drugs covered under Medicare Part B.* (Report #OEI-12-12-00210).

[35] A *deductible* is an amount of healthcare spending that a participant must pay out-of-pocket before the health plan pays for services. A *copayment* is a fixed out-of-pocket amount per service, prescription item, or device. *Coinsurance* is a patient contribution set as a percentage of the price of the service, prescription item, or device.

[36] In 2015, the Part A deductible is $1,260 for each hospitalization and there are copayments for extended stays in hospitals and nursing facilities. Part B has a $147 deductible and most covered services require coinsurance equal to 20% of the Medicare-approved payment amount. There are additional copayments for some services, such as drugs provided with hospital outpatient services.

[37] Part C plans use a mix of deductibles, copayments, and/or coinsurance, depending on the type of service and provider. Copayments are also common in supplemental insurance plans, often called Medi-Gap plans, which private companies offer to beneficiaries enrolled in Parts A/B. These plans may cover services that Medicare does not pay for and make out-of-pocket costs more predictable.

modest percentage of family income; and federal law prohibits cost-sharing for several categories of Medicaid beneficiaries and certain services.[38] Most state Medicaid plans require cost sharing for prescription drugs and DME.[39]

For prescription drugs, most commercial plans use tiered cost sharing with increasing levels on higher tiers; fixed copayments are much more common than percentage coinsurance in these plans.[40,41] Drug-benefit specific deductibles, out-of-pocket limits, or maximum annual benefit limits for drugs are relatively rare in commercial plans.[41] In 2015, roughly 60% of Medicare Part D drug plans have a deductible and nearly all have five cost-sharing tiers: two for generics (preferred/non-preferred), two for brands (preferred/non-preferred), and one for specialty drugs.[42] Although Part D plans use copayments for most tiers, they are increasingly using coinsurance for non-preferred and specialty drugs.

Variations in cost-sharing approaches within the United States, and throughout the world, reflect the diversity of payers. Within the U.S., national, regional (State) and local governments; employers; labor unions; and other organizations make important decisions about the levels and methods of cost-sharing in plans that they either operate directly (self-insured plans) or purchase from insurance companies (fully-insured plans) for their employees, members, citizens, or constituents. Purchasers may have less direct influence over the designs of fully-insured plans offered by commercial carriers, which frequently offer a pre-determined menu of coverage options from which group purchasers select. Commercial carriers also design plans for non-group markets, such as the insurance exchanges established by virtue of the Affordable Care Act. All public and private insurance plans in the U.S. also operate within a web of federal and state government laws and regulations that may influence the range of acceptable cost-sharing levels.

[38] Groups exempt from cost sharing in Medicaid include children under 18; individuals in foster care or for whom adoption or foster care assistance is paid; terminally ill patients receiving hospice care; inpatients in hospitals, nursing homes, and other institutions; and women eligible for breast or cervical cancer treatment. Cost sharing is also prohibited for pregnancy-related services for pregnant women, emergency services, and family planning services and supplies.

[39] Federal regulations issued in 2013 allow state Medicaid programs to use higher cost-sharing levels for non-preferred prescription drugs, including coinsurance of up to 20% of the cost of the drug for individuals with incomes at or above 150% of the federal poverty level (FPL).

[40] Kaiser Family Foundation & Health Research & Educational Trust (HRET). (2014). *Employer health benefits: 2014 annual survey*. Menlo Park, CA: Henry J. Kaiser Family Foundation.

[41] Pharmacy Benefit Management Institute. (2013). *2013-2014 Prescription drug benefit cost and plan design report*.

[42] Hoadley, J., Cubanski, J., Hargrave, E., & Summer, L. (2014, October 10). *Medicare Part D: A first look at plan offerings in 2015*. Washington, DC: Henry J. Kaiser Family Foundation.

HOW REIMBURSEMENT CHARACTERISTICS AFFECT COMPONENTS OF ROI AND INCENTIVES TO INNOVATE

As outlined in the analytic framework (Figure 2, above), reimbursement stands to affect the ROIs for healthcare technologies, and EROIs for products in development, by influencing sales prices, sales volumes, and sellers' costs of development, manufacturing, and sale of these products. Prospective innovators take into account expectations regarding the impact of current and expected future reimbursement policies and practices when deciding to invest in R&D and directing investments to particular therapeutic classes.[43] They have greater incentives to invest in the types of innovations that they expect will produce larger rewards; typically the desired rewards are monetary (i.e., ROI), although some developers and investors may also attach importance to non-monetary rewards (e.g., discovering a cure). Whether and how reimbursement occurs for a product influences its effective price and volume of sales. These factors, in turn, determine the revenues and profits for the product, which are important determinants of the ROI for its innovator and investors. A positive ROI rewards successful innovators and will, in theory, spur the next generation of investment.

Drawing on economic theory, review of literature, and expert consultation, this analysis examined the reimbursement policies and practices described in the previous section, and assessed the direction and general magnitude of their effects on drug and device use and innovation. The findings suggest a number of ways in which characteristics of reimbursement policies and practices can align technology producers' returns with the societal value of the innovations they produce. We discuss the effects of each reimbursement policy and practice separately, below.

THE REIMBURSEMENT DECISION-MAKING PROCESS

Many outcomes of the reimbursement decision-making process have direct implications for sales prices (through payment, rebates), sales volume (through approval or rejection, drug and device-use conditions), and total costs to developers (through requirements for data for clinical and cost effectiveness evaluations). Approaches used in making reimbursement decisions also impact patients and care providers through availability of particular products, as well as payment and cost sharing for drugs and devices, potentially leading to indirect effects on sales volume.

The U.S. retains a pluralist framework with respect to reimbursement decision-making. There are no centralized pricing and reimbursement decisions; instead, hundreds of payers use their own assessment approaches to reach their judgments. Although payers in the United States generally go through a similar set of steps in the decision-making process (see Appendix A), differences in implementation lead to many variations in the interpretation of evidence of clinical and cost-effectiveness for particular products, and ultimately to the decisions on coverage and conditions of reimbursement. Variability in

[43] Scherer, F.M. (2007, June). Pharmaceutical Innovation. *AEI-Brookings Joint Center for Regulatory Studies: Working paper No. 07-13*. Retrieved from http://sacademy.cbv.ns.ca/staff/bdalzell/C1l/Scherer%20Pharmaceutical%20Innovation%20SSRN-id902395-1.pdf

decisions may be appropriate, given that different employers, payers, and consumers may have different preferences and objectives. At the same time, decentralization weakens the effect of decisions made by all but the largest payers, in terms of ability to motivate developers. Experts consulted during this project agreed, noting that although payers individually send signals about where developers should invest, those signals are not coordinated and are not necessarily strong. There also may be a lag between the signal and the industry response. Lags may be due to lack of scientific opportunity, which contribute to waves of innovation when scientific breakthroughs occur, but may also occur when there is significant uncertainty about how a new product would be reimbursed.

Payers also have varying levels of accountability and transparency. Public payers, namely those serving beneficiaries in the non-commercial market, such as Medicare, Medicaid, Veterans Affairs, and Indian Health Service, are generally expected to be more accountable and transparent than private payers. In this respect, payers tend to reveal the general contours of their decision-making processes, though not the specifics. For example, rebates are proprietary, so the public has no way of knowing their magnitude. Payers have generally been hesitant to shed light on the actual evidence base and decision-making process underlying their reimbursement decisions, so current formulary decision-making is mostly a "black box."[44] Even when researchers attempt to pry it open, there are often unique factors that influence each particular coverage decision. Hence, knowing the precise weights attached to factors that figure in reimbursement decisions is difficult, if not impossible. This implies that developers must anticipate different questions of value, depending on which payer (or set of payers) they are most concerned with. It also means that there are less traceable and unambiguous assessments of the direction or magnitude of effects attributable to the decision-making *process* itself, compared to specific features discussed later in this section, such as product categorization, payment, and cost sharing.

During the clinical and/or economic evaluation phases, there may be disconnects between the amount of evidence payers desire and what is available at the time decisions are made. Payers generally prefer to review evidence from randomized clinical trials (RCTs) and other comparative effectiveness research (CER) studies when assessing clinical and cost-effectiveness.[45] Studies have noted that available data are often inadequate or irrelevant to inform decision-making, due to the scarcity of relevant head-to-head comparisons, a perceived lack of credibility with manufacturer-funded studies, and a paucity of available economic information.[46, 47] Comparative economic evidence is often generated post-launch in non-randomized studies; therefore payers often seek other kinds of study designs, including retrospective

[44] Dean, B.B., Ko, K.J., Graff, J.S., Localio, A.R., Wade, R., & Dubois, R.W. (2013). Transparency in evidence evaluation and formulary decision-making. *P&T*, 38(8):465-483.

[45] Wang, Z., Salmon, J.W., & Walton, S. (2004). Cost-effectiveness analysis and the formulary decision-making process. *Journal of Managed Care Pharmacy,* 10(1):48-59.

[46] Schiff, G.D., Galanter, W.L., Duhig, J., Koronkowski, M.J., Lodolce, A.E., Pontikes, P.,… Lambert, B.L. (2012). A prescription for improving drug formulary decision making. *PLoS Medicine,* 9(5):1-7.

[47] Neumann, P., Pei-Jung, L., Greenberg, D., Berger, M., Teutsch, S., Mansley, E.,… Rosen, A. (2006). Do drug formulary policies reflect evidence of value? *AJMC*, 12:30-36.

claims analyses to get needed information.[48] Industry experts and investors interviewed for this project noted that manufacturers are beginning to anticipate payer data requirements before they start phase III studies.

Payers also differ in the ways they approach the establishment of drug and device use conditions. In certain instances, payers may not be able to employ the full array of utilization management tools, including pricing and patient cost-sharing, due to limited treatment options, such as cases involving orphan diseases, or owing to the sensitive nature of the disease, including life-threatening conditions such as cancer or HIV/AIDS. Regulations may prohibit use of certain utilization management tools, such as coverage limits and patient cost-sharing. In these instances, payers have less pricing leverage and may be forced to manage pharmaceutical and device use through instruments such as prior authorization and step therapy.

Ideally, there would be a correlation between preferred formulary placement (with lower patient cost sharing) and greater cost-effectiveness, fewer safety concerns, and/or greater certainty around evidence.[49] However, evidence is mixed on the existence of an association between these factors and preferred formulary placement. Furthermore, it is questionable whether cost-sharing tier placements within formularies actually represent, on balance, evidence-based lists of products that reflect their benefits, relative to costs.[47] This suggests that evidence is either not being gathered, or if it is, it is not always being applied in such a way that formularies reflect added value.[50,51,52] If a reimbursement process rewards non-innovative products with a high ROI, this result muddles incentives for payers to pursue more innovative products.

DESIGNING DECISION-MAKING PROCESSES TO FOSTER INNOVATION

Approaches to reimbursement decision-making force developers to anticipate questions of value in the clinical development pipeline, not simply at or near the point of launch. Industry and investor experts consulted for this study noted that there is a trend to start reimbursement assessments earlier in the development process, mostly during Phase II and Phase III, although approaches vary among and within industries. For example, one expert noted that some companies will not focus scientific research in areas that do not fit within an existing code for reimbursement. Another noted that some companies conduct formal reimbursement assessments very early in the product development life cycle. A third

[48] Orszag, P. (2007). Addressing rising health care costs – a view from the Congressional Budget Office. *NEJM* 357:1885-1887.

[49] Sorenson, C., Drummond, M., & Burns, L. R. (2013). Evolving reimbursement and pricing policies for devices in Europe and the United States should encourage greater value. Health Affairs, 32(4):788-796.

[50] Dean, B.B., Ko, K.J., Graff, J.S., Localio, A.R., Wade, R., & Dubois, R.W. (2013). Transparency in evidence evaluation and formulary decision-making. *P&T*, 38(8):465-483.

[51] Neumann, P.J., & Weinstein, M.C. (2010). Legislating against use of cost-effectiveness information. *New England Journal of Medicine* 363: 1495-1497.

[52] Neumann, P.J., & Greenberg, D. (2009). Is the United States ready for QALYs? *Health Affairs* 28(5): 1366-1371.

panelist noted that some companies, especially small ones, lack the expertise or resources to conduct thorough market assessments. Discussions between developers and payers are usually proprietary, although publicly available information indicates that payers and manufacturers discuss endpoints of importance to the value assessment of a drug or other technology. The discussion among the experts on our panels implied that device developers account for reimbursement earlier in the process than drug developers, but this impression may be due to the (usually) shorter timeline for development of devices.

The discernible impact on incentives to innovate can be substantially affected by the manner in which different reimbursement decision-making processes (by different payers) are transparent, evidence-based, consistent, and timely.[53, 54] Theoretically, it might be expected that transparency in decision-making would lead to a more competitive marketplace and fewer market distortions, which in turn would lead to lower prices for products with less added value, and higher prices for those with more added value. Patients, providers, policymakers, and manufacturers would benefit from having information on *how* different formulary decisions are made, not merely what is on the formulary. Knowing the kind of evidence used to inform formulary decisions could increase clarity with respect to which factors are influential; consistency in understanding how other payers handle comparable situations; and transparency by ensuring those involved in the decision-making process understand what was decided and why.

An evidence-based process means that the rationale for decisions reflects relevant data on safety, efficacy, cost-effectiveness, and budget impact. In theory, decisions that favor novel products aimed at unmet needs, and which provide net benefits relative to existing therapies, should enhance consumer welfare. Reimbursement decisions that fail to reflect the relative added value of a product will be ineffective in establishing incentives for innovations that enhance consumer welfare. If payers do not assess cost-effectiveness and take default "yes" decisions when data are absent, they are likely to be creating incentives to overinvest in R&D. Ideally, lower expected ROIs for products that do not add significant value would lead to less R&D spending on products deemed to be of less value, or that do not address an unmet need.

Expanding data requirements for reimbursement decision-making, before and after product launch, are a clear signal to developers of payers' growing emphasis on better aligning their coverage and payment decisions with outcomes and value. They also directly influence the total costs of development of new products, to the extent that developers must conduct additional studies. Increased data requirements carry some uncertainty for developers, to the extent that negative results may lead to less favorable reimbursement decisions. Positive results, on the other hand, should improve a developer's reimbursement prospects.

[53] Daniels, N., Sabin, J., & Teagarden, J. (2003). An ethical template for pharmacy benefits. *Health Affairs*, 22(1):125-137.

[54] Luce, B., Cohen, R., Hunter, C., Cragin, L., & Johnson, J. (2008, April). *The current evidence-based landscape*. Report prepared for the National Pharmaceutical Council.

It is unclear whether the drug development paradigm is changing in response to increased evidence demands from payers, government policymakers, and consumers. Anecdotal evidence suggests changes may be under way, including the inclusion of active comparators in clinical trials, involvement of stakeholders (e.g., patient representatives, payers, and providers) to help define key Phase IIb and III study design features, incorporation of patient-centered outcome measures, and earlier planning for Phase IV studies. However, we do not have firm evidence that this is indeed happening.

Consistency in decision-making is desirable, although variation is to be expected given the multitude of different payers. Patient access may vary from one payer to another for the same drug or indication, with the result that mixed signals are conveyed to manufacturers regarding the relative value of their product to buyers. Transparency and evidence-based rationales can help to explain these differences and may encourage greater consistency, where appropriate. Developers and investors have a dim view of uncertainty brought about by an opaque decision-making process; they also want to minimize delays in decision making between marketing authorization and formulary placement, which shorten the effective time in which a product has market exclusivity and can garner a higher price and larger market share.[55] We examined one approach that can reduce uncertainty for developers, an advance market commitment, in our case studies (Box 1).

Expert's quote:

Increasingly we are having to think about what sort of information payers are going to demand for the product in order to be able to list it on formulary or provide adequate reimbursement.

Expert's quote:

One thing we're really focused on right now is… achieving broad coverage and reimbursement throughout the world. The bar is getting higher. The evidence level is more significant than it previously was.

Expert's quote:

The more uncertainty there is in the market, the more perceived risk there is, the less investment.

[55] Vernon, J., Goldberg, R., & Golec, J. (2009). Economic evaluation and cost-effectiveness thresholds. Signals to firms and implications for R&D investment and innovation. *Pharmacoeconomics,* 27(10):797-806.

Table 3: How the design of a reimbursement decision-making process may affect the marketplace and innovation

Approach	Impacts on Patients & Providers	Impact on Sellers (Manufacturers)	Impact on Innovation
Transparent	More understanding of the factors that drive decisions.	More understanding of the factors that drive decisions, and the types and amount of evidence required. Potential effects on sales prices if confidential discounts/rebates are exposed.	In theory, sends clearer signals to developers and investors about the types of products that payers (and patients) value. To the extent that payers value innovations, this should encourage more R&D targeted at those types of products.
Evidence-based	More understanding of the evidence in favor of, or against, use of a particular product.	Could increase costs of development, if more or larger studies are required. May add some uncertainty due to the potential for negative results from additional studies, but sellers may gain pricing power if results are positive.	In theory, lower expected ROIs for products that do not add significant value would lead to less R&D spending on products deemed to be of less value, or that do not address an unmet need.
Consistent	Patients and providers may prefer consistency – rather than unexplained variation – across the various formularies that they are faced with.[56]	Less uncertainty in models of expected ROI for new products.	Unlikely to have a differential effect on R&D spending aimed at innovative vs. non-innovative products.
Timely	More timely processes bring new treatments to patients and providers more quickly.	More timely processes get new products in use more quickly (in the case of positive decisions), or leave more time during the market exclusivity period for the developer to get more favorable placement (in the case of negative decisions).	Unlikely to have a differential effect on R&D spending aimed at innovative vs. non-innovative products.

Source: authors' analysis

[56] Landon, B.E., Reschovsky, J.D., & Blumenthal, D. (2004). Physicians' views of formularies: Implications for Medicare drug benefit design. *Health Affairs* 23(1):218-226.

BOX 1 | *HI HEALTHINNOVATIONS*: AN EXAMPLE OF REDUCING UNCERTAINTY WITH ADVANCE MARKET COMMITMENTS

Uncertainty is a driving force behind product development and investment decisions; experts consulted for this project agreed that a greater perceived risk is likely to be a disincentive for investment. One method of reducing uncertainty for developers is an advance market commitment, an agreement between the product developer(s) and potential purchaser(s) that effectively guarantees a market for a proposed product. Although it initially took root in vaccine development, the basic concept is applicable to other circumstances, in which a payer or group of payers seeks to encourage development of a new product that the market does not currently offer through direct investment or some form of prize for successful development.

Believing that meeting an unmet need for hearing aids would produce happier customers, health benefits, and potentially lower health care costs, UnitedHealth Group invested directly in a product and distribution model meant to fill that gap. *hi HealthInnovations*, an Optum business and UnitedHealth Group company, worked with a manufacturing partner to develop and produce hearing aids with a specific set of characteristics, at a price low enough to attract subscribers and to make the overall cost affordable to the payer and to consumers. Initially, *hi HealthInnovations* offered the hearing aids directly to the public and to people enrolled in UnitedHealthcare's Medicare Advantage and Part D plans, and later expanded to UnitedHealthcare's commercial and vision plans, as well as through programs directly to employers and other health plans. Although we could not obtain evidence to directly measure the success of the *hi HealthInnovations* program, it appears to have met its goals of filling an unmet need for hearing aids by bringing to market advanced hearing aids at lower prices, and improving access to hearing care.

Based on the definition of innovation used in this project, the hearing aids offered by *hi HealthInnovation*s might best be deemed incremental innovations. The advance market commitment and new distribution model, rather than the devices, may be the greater innovations, which helped to make hearing aids more affordable and accessible. The specific approach in this case seems most appropriate for similar instances where a payer wants to invest in a relatively low-cost device that does not require extensive testing or regulatory approvals, and the payer has some ability to limit access to the new product. It may be less applicable to devices requiring more extensive testing or regulatory approval or drugs, where the costs of development may be higher or where the payer cannot control access to the new product.

For more on *hi HealthInnovations*, see Appendix B.

PRODUCT CATEGORIZATION AND DIFFERENTIATION

The methods that payers use to categorize and differentiate products can affect innovation by influencing pricing and utilization, creating distortions in the marketplace. Each payer categorizes and differentiates drugs and devices. Different approaches to product categorization or differentiation mostly have an indirect impact on EROI for innovative products, primarily by way of affecting behavioral incentives and market competition. The degree to which product categorization and differentiation is evidence-based is important. Ostensibly, payers establish formularies and categorize/differentiate products on the basis of evidence of clinical efficacy and safety, the existence of treatment alternatives, cost-effectiveness, acquisition cost, budget impact, and state and federal requirements and regulations. As such, these reimbursement decisions are supposed to represent value as a proxy for consumer welfare; i.e., what services, drugs, or devices a payer chooses to include in its medical benefit, or which drugs appear on the formulary (list of covered drugs) tell manufacturers what is of value to payers and consumers.[57,58] Accordingly, prices and formulary parameters reflecting these categorizations may impact development of new products by influencing developers' EROI.

Differentiation can be effective in strengthening incentives to invest in valued innovation, as it may be used to reward more clinically effective or cost-effective products with higher prices or increased market share. Value-based approaches may reflect assessments of added effectiveness or other benefits, but they are only used by a minority of payers in the United States. Most explicitly evidence-based approaches are found in Europe and Australia. For example, France, Germany, and the Netherlands, among other jurisdictions, have established so-called "premium pricing" for drugs and devices considered to be "highly innovative," unlike non-innovative drugs which are subject to reference pricing. Notably, European jurisdictions have generally considered between 10% and 20% of newly approved drugs and devices to be "highly innovative."[59]

Table 4 summarizes the expected impact of numerous approaches to differentiation and categorization on pricing, drug utilization, distortions in the marketplace, and innovation; comments on several of these approaches follow the table. While different approaches taken to product categorization and differentiation may offer varying incentives for future innovation, much remains uncertain because empirical evidence is very limited. According to the experts consulted in the course of this study, many payers in the United States presently lack sufficient incentives, data, and leverage to limit coverage, payment, or utilization of products which offer little or no value added. There are more drugs available

[57] Bouvy, J., & Vogler, S. (2013). *Pricing and Reimbursement Policies: Impacts on Innovation*. Background Paper 8.3. WHO Collaborating Centre for Pharmaceutical Policy and Regulation. Retrieved from http://www.who.int/medicines/areas/priority_medicines/BP8_3_pricing.pdf

[58] Johanesson, M., Jonsson, B., Jonsson, L., Kobelt, G., & Zethraeus, N. (2009, October 1). *Why should economic evaluations of medical innovation have a societal perspective?* OHE Briefing, No 51, Office of Health Economics, London, U.K.

[59] Cohen, J., Faden, L., Predaris, S., & Young, B. (2007). Patient access to pharmaceuticals: An international comparison. *The European Journal of Health Economics,* 8(3):253-266.

on the market in the United States because of fewer restrictions, leading to more utilization and more pharmaceutical spending.[60]

Table 4: Impact of different approaches to product categorization and differentiation on the marketplace and innovation

Approach	Impact on Pricing	Impact on Utilization	Distortions in the Marketplace	Impact on Innovation
Administrative Approaches				
Pharmacy versus medical benefit designation	Market versus administrative pricing	Drugs in medical benefit not subject to formulary; drugs under pharmacy benefit are subject to formulary	Yes - due to administrative price-setting of physician-administered drugs	Negative - due to administrative price-setting of physician-administered drugs
Generic substitution	Downward pressure on prices of drugs in classes with generics, leading to more consumer welfare	More use of generics	No	In theory, more R&D in therapeutic areas without generics
Rebate mechanism	Unknown – savings pass-through is not revealed	Shift to preferred products on formulary	Yes – because preferred formulary placement is not evidence-based	Negative – due to rebates not being a function of value or evidence
Value-based Approaches				
Exclusion lists	Downward pressure on pricing of drugs in classes with excluded products	Shift to included products	Unknown; would depend on whether exclusion lists are evidence-based	In theory, more R&D in therapeutic areas without exclusions
Value-based insurance design (VBID)	Limited, given low numbers of enrollees affected; Theoretically, downward pressure on products with little value added, higher prices for products with higher value	Limited, given low numbers of enrollees affected; Theoretically, less utilization of products with little value added, more utilization for products with higher value	Not likely, except in the case of orphan drugs	In theory, more R&D towards "high-value," "high impact" products (e.g., clinically and cost effective, targeting areas of unmet need)

[60] Cohen, J., Malins, A., & Shahpurwala, Z. (2013). Compared to US practice, evidence-based reviews in Europe appear to lead to lower prices for some drugs. *Health Affairs, 32*(4), 762-770.

Approach	Impact on Pricing	Impact on Utilization	Distortions in the Marketplace	Impact on Innovation
Coverage with evidence development (CED)	Limited, given low numbers of enrollees affected	Limited, given low numbers of enrollees affected	Not likely	In theory, more R&D in clinically and cost-effective treatments, as well as areas of unmet need
Risk-sharing arrangement	Limited, given low numbers of enrollees affected	Limited, given low numbers of enrollees affected	Not likely	In theory, more R&D in clinically and cost-effective treatments, as well as areas of unmet need
Oregon Medicaid's prioritized list of health services	Limited, given low numbers of enrollees	Limited, given low numbers of enrollees affected	Potential spillover effect onto other Medicaid programs	In theory, more R&D in cost-effective treatments
Medicare contractor Palmetto's MolDx program	Limited, given low numbers of enrollees; in theory, diagnostics will increasingly be priced in accordance with benefit provided to patients	Use by Palmetto of diagnostics with proven clinical utility linking diagnostic to health outcomes	Potential spillover to other Medicare contractors	In theory, more R&D towards diagnostics with improved clinical utility

Source: authors' analysis

The choice of pharmacy versus medical benefit designation, generic substitution, and rebate mechanisms are methods widely used by payers, and they are the only approaches that appear to have a direct influence on sales prices. However, these three approaches are not necessarily evidence-based, and not directed at promoting value or innovation. This also implies that they are not conducive to bringing about investment in research targeting unmet needs.

The prevalence of generic or therapeutic substitution may serve as an incentive to steer manufacturers away from incremental innovation and towards substantial or radical innovation, where the likelihood of substitution is much lower. Substitution of either kind may have a significant impact on pharmaceutical product development undertaking and focus. A recent empirical analysis found evidence of a negative relationship between generic penetration and early-stage pharmaceutical R&D activity within therapeutic classes; effects were stronger in classes where one might expect cross-molecular substitution to be relatively high (e.g., anti-infectives, anti-hypertensives, anti-histamines), and not statistically significant where substitution may be relatively low (e.g., neurological disorders).[61] Low

[61] Branstetter, L., Chatterjee, C., & Higgins, M. (2014). *Starving (or fattening) the golden goose? Generic entry and the incentives for early-stage pharmaceutical innovation.* NBER Working Paper Series. Working Paper 20532. Retrieved from http://www.nber.org/papers/w20532

levels of R&D investment may also reflect a variety of other factors, such as lack of scientific or technological opportunities.

Rebates may introduce marketplace distortions or deviations from optimal pricing and utilization, because it is unknown (considered proprietary information) how much of the negotiated rebate is passed on to end-users. Also, preferred products may not be the highest value products, and are not necessarily more cost-effective; the drugs' preferred status is more likely to be a function of negotiating power on the part of payers and manufacturers, than of evidence of value.

Theoretically, VBID could improve resource allocation and encourage development of high-value products that would get preferential treatment with little or no patient cost-sharing. At the same time, it could reduce incentives to invest in innovations to treat orphan diseases. This is because most orphan disease treatments are often not considered cost-effective or good value for money, as manufacturers charge high prices to offset relatively small prospective patient markets. Applications of VBID in the United States have been relatively few in number and narrow in scope, so there is little empirical evidence available to discern the potential impact on innovation from broader use. We looked at one example in our case studies, a pilot program of a value-based drug formulary by Premera Blue Cross (Box 2).

There are many examples of CED implementation in international markets. In the U.S., Medicare has instituted CED programs for more than a dozen devices and a handful of drugs.[62] The idea of only paying for health technologies that work at least as well in real-world settings as they do in clinical trials is intuitively attractive, and a downstream possibility with CED. With conditional access, manufacturers know that there will be some access to their new products upon regulatory approval. Investors anticipating this access will likely continue to invest in the products' development. Alternatively, the use of CED could hinder incentives to innovate, given the fear of an additional post-marketing hurdle. There is anecdotal evidence that manufacturers may think this way.

Risk-sharing arrangements could influence innovation by establishing a pricing model in which payments would be linked to value, as in a pay-for-performance arrangement. Firms would have to incorporate value end-points (demonstrations of innovativeness) in development should this pricing model become more widely used. Additionally, payments would be made over a period of time, during which health benefits are realized and measured. For example, pricing could be set as a flat per-patient price, regardless of the amount of the drug required to achieve the desired outcome, instead of the usual per dosage or per unit amount. The performance-based patient access scheme (PAS) for Velcade in the U.K., which was the focus of our third case study (see Box 3), illustrates the promise and challenges that these programs present.

[62] Centers for Medicare & Medicaid Services. (2015, April 10). *Coverage with evidence development.* Retrieved from http://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/index.html

BOX 2 | PREMERA BLUE CROSS: A VALUE-BASED APPROACH TO PRODUCT CATEGORIZATION & COST SHARING

The value-based insurance design (VBID) concept gained significant attention after its introduction in the early 2000s in the form of a "benefit-based copayment." Multiple experts consulted during this project recommended VBID as a reimbursement strategy worthy of further examination, in part because of its high profile. Although it has generated much interest, applications to date have largely been limited to a few large self-insured health plans, targeting relatively few drug classes or health conditions, and mainly consisting of only cost-sharing reductions for "high value" drugs or conditions, rather than increases for "low-value" ones. Limited evidence from these applications indicates that these programs may improve use of and adherence to medications, but generally do not produce overall savings for health plans, at least not in the short post-implementation periods studied to date.

Premera Blue Cross, a health plan from the northwestern United States and independent licensee of Blue Cross Blue Shield Association, recently piloted a value-based formulary (VBRx) for the drug benefit offered to its own employees. The Premera VBRx is comparatively novel and appears to be the broadest application of the VBID concept in the United States. Evidence from the initial roll-out of the program suggests that it is possible to implement VBID on a broader scale, with a design that may lead to modest savings for the health plan, without negatively affecting adherence to drug therapies for several common health conditions.

Largely based on theory, VBID holds some promise to shift incentives toward development of "high-value" products. However, further evaluation of programs such as Premera's VBRx is needed to determine how broader use may ultimately affect incentives in the marketplace that affect the return on investment for developers of new products, including sales volume, sales prices, and development costs. Longer study periods may help to tease out delayed effects on spending, health outcomes, or other factors. A broader focus on total costs to a health plan is necessary. An assessment of spillover effects is also important; where VBID applies to a particular category of services, such as drugs, but not others, there may be interactions with other reimbursement systems for other services. To date, the evidence base from Premera's VBRx and VBID programs more broadly – at least that available in broadly-accessible public sources – is insufficient to truly understand how broader adoption may affect innovation for healthcare technologies.

For more on Premera's VBRx, see Appendix C.

BOX 3 | NICE (UK): PERFORMANCE-BASED REIMBURSEMENT FOR VELCADE®

In its initial technology appraisal of Velcade® (bortezomib) in 2006, the National Institute for Health and Care Excellence (NICE) in the United Kingdom (UK) found the drug to be comparatively clinically effective, but not cost-effective vis-a-vis the usual standard of care (high dose dexamethasone or HDD). At £31,000 per life year gained and £38,000 per quality adjusted life year (QALY) gained, the estimated incremental cost-effectiveness ratios (ICERs) were substantially higher than the generally accepted ICER threshold in England of £20,000 - £30,000 per QALY.

With the expectation that final guidance from NICE would be unlikely to support the use of Velcade in the UK National Health Service (NHS), the manufacturer (Janssen-Cilag) proposed an arrangement in which the NHS would pay for the drug only for patients in whom a pre-specified response to treatment was demonstrated. A 'payment-by-results' protocol was developed in which treatment response was gauged via a well-accepted tumor marker - an indirect measurement of tumor shrinkage - as a surrogate endpoint. A subsequent reconsideration of the medicine by the NICE appraisal committee, taking into account the impact of the proposed payment-by-results arrangement, gave rise to an anticipated ICER of less than £21,000/QALY, and the drug received a positive recommendation.

Although not the first performance-based funding arrangement implemented in the UK, the *Velcade Patient Access Scheme (PAS)* was the first reimbursement protocol to involve rebates for treatment failure. As the NHS would be required to pay for the drug *only* for those patients who demonstrated an adequate response to treatment, the PAS effectively amounted to both a performance guarantee and a substantial price discount.

At the original price proposed, Velcade did not meet the definition of an innovation that enhances consumer welfare in the UK. The PAS changed the effective price and allowed Velcade to meet the definition of a substantive innovation, albeit with an effect on the manufacturer's expected return-on-investment (EROI). It is unclear whether performance-based RSAs such as the Velcade PAS influence incentives to innovate, in part because of the lack of measured evaluation of this program and because of the challenges of designing and administering an outcome- or performance-based PAS. The vast majority of PAS in the UK since the Velcade example have been financially based arrangements; they are generally considered ways to reduce the price of a new technology to bring it in line with societal "norms" regarding cost-effectiveness.

For more on the NICE PAS for Velcade, see Appendix D.

In the early 1990s, Oregon's Medicaid agency established its "Prioritized List of Health Services" to set priorities for health service expenditure. Prioritization was based on the premise that medical interventions are not of equal value, and therefore a process is needed to decide what will be financed with public resources. Using an explicitly evidence-based decision-making process, the Oregon Health Evidence Review Commission (HERC) maintains the list, which ranks hundreds of condition- treatment pairs in order of clinical effectiveness and cost-effectiveness, and taking into account patient preferences. Treatments that prevent illness, provide maternity and newborn care, and manage chronic diseases are emphasized. As long as the condition being treated is included in the funded region, all associated diagnostic and ancillary services associated with it are assumed to be covered – including prescription drugs and medical devices. Prior to each legislative session, a biennial review and update of the Prioritized List is completed. Modifications are made at other times to issues corrections and include recent advancements in medical technology.

The Oregon approach has received praise for its inclusive and relatively transparent decision-making process, but has encountered resistance from multiple stakeholders. Notably, although Oregon still uses the list, no other state or private payer has since adopted this approach, in part because of the controversy surrounding the explicit use of cost-effectiveness to prioritize services; opposition to the notion of not covering effective treatments because of cost, which draws on concerns about rationing; and the implications for items excluded from coverage.[63]

The Medicare contractor Palmetto designed and implemented the Molecular Diagnostic Services Program (MolDx) as an explicitly evidence-based framework for decision-making on coverage and reimbursement of companion diagnostics. These are diagnostics used to stratify populations into those who will likely benefit, or are at risk of suffering adverse reactions, from a particular therapeutic. In November 2011, Palmetto instituted a payment system that assigns a unique code to molecular diagnostics, and at the same time, Palmetto released a coverage submission checklist for new diagnostics. Under Palmetto's program, applicants must show that the diagnostic test has clinical utility, such as improvement in patient outcomes or changes in physician behavior for the management of the patient. If applicants cannot demonstrate clinical utility, then the tests are not covered. To date, no other Medicare contractor has adopted a similar approach to diagnostic evaluation. However, some Medicare contractors are following Palmetto's decisions for the sake of consistency, as are some private insurers.

[63] Perry, P.A., & Hotze, T. (2011). Oregon's experiment with prioritizing public health care services. *Virtual Mentor (renamed: AMA Journal of Ethics)* 13(4), 241-247.

METHOD OF PAYMENT

The choice of bundled or per-unit payment by third-party payers primarily affects ROI by affecting the price that a manufacturer of a healthcare technology charges purchasers, either directly by affecting manufacturers' pricing decisions, or indirectly by changing incentives for providers or other suppliers to select particular products. When payers use per-unit payments, the effects on the manufacturer's return on investment and incentives to pursue innovative products are largely dependent on the method used to establish the payment level (see "Defining the payment amount," p. 41). Consequently, this section mostly focuses on the question of how a shift toward bundled payments may impact incentives to invest in the development of new healthcare technologies.

Bundled payments incentivize providers or suppliers to reduce their per-bundle cost, thereby increasing demand for products that reduce the cost of goods and services included in the bundle. Economic theory indicates that manufacturers' list prices for these products should rise in response, although there is insufficient evidence to determine the size of the potential effect. Therefore, the shift to bundled payments is likely to have an inflationary effect on the prices of novel products that reduce costs borne by health care providers, regardless of whether those products provide comparative advantage in effectiveness.

> Expert's quote:
>
> Increased use of bundled payment and episode-based care payment… will require a person to think differently in terms of what value do you actually add to this episode of care? Are you [reducing] the cost of care? Are you improving the key metrics that will be measured as part of this episode of care?

Importantly, bundled payments will only have this effect on healthcare technologies that are cost-saving from the *provider* perspective. Providers' demand for these products increases under bundled payments because the incentive for cost minimization shifts from the payer onto the provider. A shift to bundled payments should not affect demand for healthcare technologies that reduce costs borne only by patients or society as a whole, such as technologies that reduce the number of days of recuperation at home and related days of work missed.

Because bundled payments give providers incentives to clamp down on unnecessary or costly health services that cannot be billed on an itemized basis, they also have the potential to distort provider decision-making in favor of lower-cost technologies, even in cases where higher-cost options would be more appropriate or effective. To some extent, quality monitoring systems and focused evaluations can check for unintended effects on outcomes, as was done in the transition to Medicare's prospective payment system for hospital care in the early 1980s.

Where bundled payments are in place, exceptions are often made for products designated as highly innovative and/or high cost, with the result that default unit pricing is applied for those products. For example, Medicare uses "pass through" exceptions for drugs and biologics that have a cost per day in excess of a defined threshold. One expert panelist noted that, at least for products aimed at hospital-based care, the use of pass-through payments and other add-ons to diagnosis related groups (DRGs)

(and similar bundled systems) could help to incentivize innovation where products may not fit into the existing reimbursement bundle, but could potentially reduce total costs of care.

On the other hand, per-unit payment systems reward excessive provision of drugs and devices; a provider, prescriber, or supplier may have many reasons for choosing a particular product, but it is often the case that they benefit financially from the transaction. Therefore, per-unit payment systems can also distort provider decision-making with regard to appropriate utilization of healthcare technologies. Neither bundled payment nor per-unit payment would be expected to distort patient decision-making, except to the extent that they affect cost-sharing arrangements, which we discuss later (see p. 47). Patients are rarely aware of the method of payment used to reimburse the provider.

However, a payer's choice of payment method could affect overall availability and use of products by patients and providers, depending on design of the payment and insurance system. For example, research shows that the initial diffusion of magnetic resonance imaging technology in hospitals was slowed by Medicare's DRG-based reimbursement system.[64] In this case, rather than being driven by the extent of innovation offered by the novel product, the utilization was driven by the up-front outlay of the purchaser, with more costly technologies facing greater barriers in uptake. When identified, such barriers may be addressed on an *ad hoc* basis through payment exceptions and regulatory interventions.

Table 5 summarizes the impact of the use of bundled payments versus per-unit payments on the prices of new healthcare technologies reflecting different levels of innovativeness. All of the described effects are hypothetical, based on an analysis of the incentives created under alternative payment approaches. Furthermore, without adequate information on where new products fall in terms of innovativeness and cost-savings, payers will not respond in ways that correspond with these expectations and markets will function less effectively and predictably.

Table 5: Effects of per-unit and bundled payment methods on pricing of new healthcare technologies

Method of Payment	Novel products that are not innovative		Innovative products		
	Cost-reducing	**Not cost reducing**	**Incremental innovation**	**Substantial innovation**	**Radical innovation**
Per-unit payment	Price-reducing pressure potential	Potential for inflationary pressure on prices	Price-increasing potential	Uncertain effect	Uncertain effect
Bundled payment	Price-increasing pressure possible	Strong price-reducing pressure	Price-reducing pressure	Uncertain effect	Uncertain effect

Source: authors' analysis

[64] Hillman, A., & Schwartz, J.S. (1985, November). The Adoption and Diffusion of MRI and CT in the United States: A Comparative Analysis. *Medical Care* 23(11).

Impact on pricing for products that do not qualify as innovations. Demand for novel products that are not innovative and fail to reduce provider costs should decrease significantly under a bundled payment system, as providers (e.g., hospitals deciding what scanners to buy) face strong financial incentives not to buy and use them. This should result in lower prices, in comparison to an environment characterized by per-unit payment. In the latter case, new products may be awarded a premium, presumed to be better than existing therapeutic alternatives by virtue of their novelty, irrespective of whether improved effectiveness can be demonstrated.[65]

Impact on pricing for less innovative products. In the case of products that offer no or only minimal additional effectiveness over their marketplace competitors (i.e., non-innovations and incremental innovations that payers or prescribers view as largely the same as existing products), bundled payments are likely to pose downward pressure on average prices paid in the market. Buyers in these cases are likely to consider a range of products as suitable for use, and be in a relatively strong negotiating position. This expectation, however, has not been established empirically, and much depends on the extent to which buyers are incentivized to obtain the best possible value for money. For such (incrementally innovative) products, per-unit payment is less likely to exert comparable pressure. The provider or prescriber of the drug or device does not, under this method of payment, share a stake in the payer's incentive to seek value, although this could be mitigated in cases where a payer utilizes a system of reference pricing to define a maximum reimbursement amount.[66]

Impact on pricing for more innovative products. In the case of products that offer more-than-incremental improvement in effectiveness over existing comparators (i.e., substantial or radical innovations), per-unit payments may be more likely to pose indirect pricing pressure by opening the door to negotiations with sellers, which may influence institutional purchasing and formulary management tools. However, the impact on prices is dependent on the degree of leverage that the payer brings to the negotiations. Furthermore, neither bundled payments nor per-unit payments can be seen to have an edge in putting price pressure on sellers of products that represent true "breakthroughs" or radical innovations, as buyers will have limited leverage unless empowered to reject or narrowly constrain coverage on affordability grounds. (This practice is not common in the United States). Per-unit payments may offer more scope to obtain price discounts, to the extent that payers are able to use the "threat" of more (or less) restrictive utilization management as leverage in negotiations with manufacturers or other suppliers.

Broader use of indication pricing, episodic care pricing, or bundled payment would affect patterns of investment. The net prospective impact of a shift toward bundled payments on incentives to innovate with respect to various types of novel products is summarized in Table 6. Overall, it appears likely that

[65] An example would be an extended-release formula of an existing drug released just prior to patent expiry.

[66] In a study that examined prices of anti-hypertensive drugs in Canada, researchers found that (under a pay-per-unit scheme) prices decreased as the number of products of the same family rose, but increased as the number of products in a competitive family increased. See: Benda, M.C., Lu, H., Mallory, C. (2004, May). *An Econometric Estimation of Pricing of Brand-Name Drugs*. Health Canada Working Paper.

shifting toward bundled payments has the potential to increase incentives to innovate in cost-reducing novel products, regardless of their level of innovativeness. Bundled payments should reduce incentives to develop non-innovative products that are not cost-reducing, as well as products representing incremental innovation. This shift is unlikely to have a meaningful impact on incentives for radical innovation, while the effect on investment in substantial innovations is uncertain and dependent on the strength and effectiveness of safeguards put in place to protect such innovations (e.g., pass-through payments, such as those used in Medicare to support hospital use of innovative biologics, drugs and other healthcare technologies).

Table 6: Impact of shift to bundled payments on incentives to invest in the development of innovative healthcare technologies and other novel products

	Novel products that are not innovative		Innovative products		
	Cost-reducing	**Not cost reducing**	**Incremental innovation**	**Substantial innovation**	**Radical innovation**
Shift to bundled payment	Potentially increased incentives to develop new products of this type	Significant disincentives to develop new products of this type	Significant disincentives to innovate, absent targeted regulatory interventions	Uncertain impact	Little likely impact (in that radical innovations are likely to be exempt from bundles)

Source: authors' analysis

Impact on investment in novel products that are not innovative. An attractive feature of the use of bundled payments is the disincentives they create to invest in the development of new products that are neither a) more effective than existing alternatives, nor b) cost saving from a provider perspective. Whereas such products stand a good chance of obtaining a foothold in the healthcare system under a per-unit payment scheme, they are significantly less likely to be adopted and diffused in a scenario where a provider bears responsibility for both excess costs and for maintaining quality of care, potentially in combination with pay-for-performance type incentives. Instead, healthcare technology developers who cannot demonstrate increased effectiveness will need to offer "value" through reduced costs, such as lower unit prices.

As discussed above, bundled payments exert price pressure on products that do not offer substantial additional effectiveness over existing treatments in meeting significant health needs. While this is not necessarily problematic, it could be viewed as undesirable in cases where new additions to a class are sought, as in the case of antibiotics, for example.[67]

[67] To the extent such problems arise and are identified, it may be possible to address them through special regulatory interventions, as is done in the area of orphan drugs, for instance.

Impact on investment in cost-reducing technology. It is often stated that bundled payments, including DRGs and per-capita payments, will provide health plans and providers with incentives to demand new cost-saving technologies, and this demand will spur development of such products.[68] One expert consulted in this project gave an example of how device developers shifted resources to try to find solutions that would reduce or avoid hospital-acquired infections in response to the announcement that Medicare would stop paying for care attributable to these infections, illustrating that firms will target investment to address a need identified by providers and/or payers (e.g., hospitals' desire to reduce costs associated with infections). However, the role of technology in driving cost is complex; a technology that reduces the unit cost of diagnosis or treatment for an individual case may, in fact, increase overall expenditures as the reduced unit costs encourage higher overall utilization.

Furthermore, the alignment of incentives remains a critical issue. Taking steps to reduce silos and encourage full assessment of a product's comparative cost-effectiveness and budget impact could help ensure that bundled payments serve to incentivize development of new healthcare technologies that reduce costs to both payers and consumers. In this regard, we can draw insightful lessons from financer/purchaser models in which the incentive alignment problem is less pronounced, as is the case for closed or integrated systems like Kaiser Permanente and the Veterans Health Administration.[69]

Impact on investment in innovative technologies. Perhaps the greatest uncertainty involves how a move to bundled payments would affect incentives to invest in innovative technologies. It could be argued that the incentives to invest in radical innovations remain unchanged, as such innovations are likely to be exempted from a bundled payment mechanism unless they have limited impact on the cost of the bundle. Additionally, payers are unlikely to restrict access to treatments that radically improve patient outcomes, especially if payment (or regulatory compliance or continued network participation) hinges in part on demonstrated performance. With respect to products that offer modest but meaningful improvement in comparative effectiveness over alternatives, such as substantial innovations, the prospective impact is less clear. A 2014 survey of payers sponsored by the medical device industry found that increasing use of risk-sharing and pay-for-performance payment models stands to shift the traditional paradigm, in which payers act as gatekeepers and providers act as patient advocates in obtaining access to new healthcare technologies, by better aligning payer and provider incentives.[70] However, only four of nine payers interviewed in that survey expressed a view that it would be more difficult for effective yet costly innovations to obtain approval for coverage because of these changes.

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[68] Garber, S., Gates, S. M., Keeler, E. B., Vaiana, M. E., Mulcahy, A. W., Lau, C., & Kellermann, A. L. (2014). *Redirecting Innovation in U.S. Health Care: Options to Decrease Spending and Increase Value*. Santa Monica, CA: RAND Corporation.

[69] An expert from a closed system consulted in panels convened for this study noted that her organization is able to adopt a long-run (10 to 15 year) view of potential benefits and costs of a new healthcare technology being considered for purchase/use that would not make sense for other payers, for example.

[70] Long, G., Mortimer, R., & Sanzenbacher, G. (2014, December). Evolving Provider Payment Models and Patient Access to Innovative Medical Technology. *Journal of Medical Economics.* 17(12); 883-893.

In any case, there are policy interventions that can serve to limit the potential of bundled payments to stifle innovation. These interventions include frequent revisions to the content of each bundle and the use of pass-through exemptions for innovations that meet designated criteria pertaining to effectiveness and/or cost.[71] Bundled payments that come with mandates to measure and report certain quality metrics, possibly with bonuses/penalties tied to those metrics, might also affect incentives to innovate.

Industry and investor panelists felt that wider use of bundled and episode-based payment would require developers to think differently about the "value" added by new technologies: for example, would a product reduce the total cost of care, or improve key outcomes or metrics measured by the payer(s) in conjunction with an episode of care? Although the panelists reached consensus on the importance of value, there was little consensus in the ensuing discussion of how to measure value. While some payers use quality-adjusted life years (QALYs), several panelists noted that this approach is full of challenges, such as incorporating the differing views of stakeholders on what constitutes quality of life (e.g., healthy people vs. those with serious illnesses or disabilities). Others noted that measures could focus on clinical improvements that improved patient health at a reasonable cost without invoking quality of life, but this approach still leaves unanswered questions about what constitutes a "reasonable" cost or even what is an "improvement" in patient health. The lack of consensus or clarity in definitions of these key terms highlights one of the challenges to broader adoption of bundled or episode-based payment mechanisms.

DEFINING THE PAYMENT AMOUNT

The methods used by payers to define payment amounts stand to affect prospective innovators' expected return on investment primarily by influencing sellers' pricing strategies. The method that stands to have most significant impact on consumers is therapeutic reference pricing, a form of internal benchmarking where the payment level is capped at a defined level for all pharmaceuticals judged to be therapeutically equivalent (or similar, in some cases). In this case, patients are required to pay out-of-pocket to cover the difference between the price and the payment amount, which may cause prescribers and patients to favor lower-cost alternatives. Methods that yield higher relative prices may also have an indirect dampening effect on utilization by consumers, particularly where payers tighten eligibility for use due to budget constraints, or pass higher prices on to consumers through cost sharing. However, the evidence base is limited, so most of the linkages between the effects described in this section, expected return on investment (ROI), and various types of innovation remain largely hypothetical and uncertain.

It is an unresolved matter of policy debate which methods yield lower prices. In principle, administered pricing, where prices are set by a policymaker or government regulator and not arrived at through negotiation between buyer and seller, can give rise to prices that are significantly lower than those paid

[71] Scheller-Kreinsen, D., Quentin, W., & Busse, R. (2011, December). DRG-based hospital payment systems and technological innovation in 12 European countries. *Value in Health* 14(8), December 2011: 1166-1172.

by other payers.[72] However, the outcome depends on factors such as the administrator's objectives (which may not be to obtain the lowest possible price); the formulae used to define payment amounts; and the product manufacturer's willingness to forego or delay sales in order to secure or protect a desired price threshold.[73] In the case of negotiated pricing, expert panels convened for this study broadly agreed that the payer's negotiating strength depends both on the number of covered lives represented and the ability to employ formulary and utilization management tools to influence the volume of products used by beneficiaries.[74] Conversely, the product manufacturer's leverage reflects demand for the product by providers and patients, and the extent and strength of competition in the specific market niche the product serves.

With EXTERNAL BENCHMARKING, there is a strong risk that manufacturers' prices will be higher than would be expected in an optimally functioning market. For example, state Medicaid programs usually pay pharmacies based on list prices, but the amounts that manufacturers rebate back to states are based on (much lower) prices for sales to pharmacies and wholesalers, and Medicare pays for physician-administered drugs using a formula based on the average sales price (ASP), plus a 6% mark-up. Both of these approaches establish incentives for manufacturers to charge high list prices, while offering discounts to buyers as competition warrants, because a higher price offers larger margins to dispensing physicians and pharmacies which may, in turn, affect use of particular treatments.[75,76,77] Medicare's fixed 20% coinsurance provides only a weak constraint on pricing because most beneficiaries have supplemental insurance that covers coinsurance and often caps the patient's financial exposure, leading to relative price insensitivity.

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[72] Gellad, W.F., Schneeweiss, S., Brawarsky, P., Lipsitz, S., & Haas, J.S. (2008). What if the Federal Government negotiated pharmaceutical prices for seniors? An Estimate of National Savings. *Journal of General Internal Medicine* 23(9): 1435-1440.

[73] Pharmaceutical manufacturers often delay launch in markets where administered price levels are relatively low when they believe they will have a negative effect on the prices in other markets, due to parallel trade, the practice of external price benchmarking, or both. See OECD. (2008). *Pharmaceutical Pricing and Reimbursement in a Global Market*.

[74] Research has shown that commercial insurance benefited from implementation of Medicare Part D, because the increased number of covered lives represented by insurers gave them more leverage in pharmaceutical price negotiations. As a result, Part D lowered drugs prices for commercially insured patients by 5.8 to 8.5%. (Source: Lakdawalla, D.N., & Yin, W. (2010). Insurers' negotiating leverage and the external effects of Medicare Part D. *Review of Economics and Statistics*.)

[75] Alpert, A., Duggan, M., & Hellerstein, J.K. (2013, August). Perverse reverse price competition: average wholesale prices and Medicaid pharmaceutical spending. National Bureau of Economic Research (NBER) working paper no. 19367.

[76] Jacobson, M., O'Malley, A.J., Earle, C.C., Pakes, J., Gaccione, P., & Newhouse, J.P. (2006). Does reimbursement influence chemotherapy treatment for cancer patients? *Health Affairs* 25(2):437-443.

[77] Danzon P. (2010). Drug pricing and value in oncology. *The Oncologist* 15(Suppl 1):24-31.

External benchmarking also has significant spillover effects in terms of defining global price levels for new healthcare technologies. For example, the widespread practice of external benchmarking in the European Union has resulted in pharmaceutical manufacturers launching new products first in countries that a) allow manufacturers to set their own prices, or b) in countries where relatively high launch prices are common. This enables manufacturers to establish higher prices for their products throughout Europe.[78] Medicaid's mandatory drug rebate program, which requires companies to provide substantial discounts and match the "best price" given to non-governmental payers, has been similarly criticized for reducing discounts to commercial payers.[79,80,81]

Higher prices tend to lead to relatively high *payment* levels under external benchmarking, with market shares awarded to products on the basis of novelty alone, as opposed to value or relative effectiveness. This occurs because sellers are adept at using techniques to obtain inflated market prices, such as strategic sequencing of market launch and requiring confidentiality with respect to rebates. These inflated prices are then subject to benchmarking by other payers. An example cited by experts consulted for this project was the proton pump inhibitor (PPI) Prilosec, and its successor, Nexium. The manufacturer of Prilosec (omeprazole) introduced Nexium (esomeprazole) after Prilosec's patent expired, while simultaneously taking steps to delay introduction of generic version of Prilosec to the market. Through this launch, the manufacturer was able to establish a high sales price and market share in the United States for the follow-on product, even though Nexium offered minimal, if any, added benefits over Prilosec.[82]

LOWEST POSSIBLE PRICE STRATEGIES seem likely to produce spillover effects for payers who pay based on external benchmarking. In the case of pharmaceutical manufacturers, a common strategy for sellers is establishment of a narrow range of acceptable public prices on a global basis and having confidential negotiations with purchasers over rebates or discounts. In practice, this likely means that payment levels reflect market leverage and negotiating capacity rather than willingness and ability to pay for products that offer a given set of benefits.

Lowest possible price methods may encourage over-investment in products that offer little or no added value. For such products, there is often less uncertainty about the potential market for the new product, because of observable payment amounts for close competitors and other factors, such as a clear

[78] OECD. (2008). *Pharmaceutical Pricing and Reimbursement in a Global Market*.

[79] Congressional Budget Office. (1996). *How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry*.

[80] Morton, F.S. (1997). The strategic response by pharmaceutical firms to the Medicaid most- favored-customer rules. *The Rand Journal of Economics, 28*(2), 269-290. doi:10.2307/2555805

[81] Academy of Managed Care Pharmacy. (2009). *Where we stand: the best price requirement of the Medicaid rebate program.*

[82] Kesselheim, A.S., Fischer, M.A., & Avorn, J. (2006). Extensions of Intellectual Property Rights and Delayed Adoption of Generic Drugs: Effects on Medicaid Spending. *Health Affairs* 25(6):1637-1647.

placement within the existing code sets used to determine payment amounts in inpatient, outpatient, and other provider settings.

In cases where payers have little or no leverage, such as with highly innovative products for which there are no therapeutic alternatives (and where payers are not empowered to reject coverage on non-clinical grounds), the lowest possible price payment method is equivalent to external price benchmarking. Prices are set at a common public price with no confidential discounts or rebates granted. By using market leverage to pay the lowest possible amount for a product, payers risk fostering incentives to under-invest in radical innovation and cost-saving technology if developers or investors fear that these technologies will be undervalued.

By contrast, there is evidence that using INTERNAL BENCHMARKING (also called therapeutic reference pricing) to establish payment levels can influence manufacturers to reduce the sales price of less innovative products. In Germany, manufacturers were, until recently, free to establish prices for pharmaceutical products sold in the country; however, social insurers' payment levels for new products were limited to the price of products judged to be therapeutically equivalent, including off-patent products and their generic equivalents. Patients were required to pay out-of-pocket for any additional cost for higher priced products. In many cases, after a product was assigned to a therapeutic reference group, its manufacturer lowered the sales price to avoid risking reduction in the product's market share, due to comparatively high cost-sharing.[83] Based on these observations, internal benchmarking will tend to result in lower payment levels for products that offer little to no added value in terms of enhanced effectiveness or cost savings associated with use. EROI for such products will be lower in an environment where many payers, or a few payers representing significant market share, are using internal benchmarking to establish payment levels.

Danzon and Ketcham have argued that reference pricing would "likely have a more negative effect on prices of on-patent products because of the more competitive U.S. generic market, and on research and development and the future supply of new drugs, because of the much larger U.S. share of global pharmaceutical sales," if systematically applied in the United States.[84]

In theory, VALUE-BASED METHODS of determining payment amounts should decrease payment amounts (at least the payer's share) for novel products that are not innovative or cost-reducing, while potentially increasing payment amounts for innovative products, commensurate with the level of additional benefit. Value-based pricing also provides the greatest potential to increase incentives to invest in substantial and radical innovations. In principal, value-based methods that define payment based on an assessment of benefits offered, whether in terms of added effectiveness or improved cost-

[83] Paris, V., & Docteur, E. (2008, October). *Pharmaceutical Pricing and Reimbursement Policy in Germany.* OECD Working Paper no. 39. OECD: Paris.

[84] Danzon, P., & Ketcham, J. (2004). Reference pricing of pharmaceuticals for Medicare: Evidence from Germany, the Netherlands, and New Zealand. *Frontiers in Health Policy Research. Volume 7,* 1 – 54. David M. Cutler and Alan M. Garber, editors.

effectiveness, could yield the highest prices for radical innovations as a reward for furnishing new benefits. Manufacturers may themselves price radical innovations at a level that reflects the benefits offered.[85] However, existing applications of VBID are relatively few and generally narrow in scope, providing insufficient empirical evidence to identify effects on ROI and/or innovation (see Box 2 and Appendix C).

With internal benchmarking and value-based pricing, any premium awarded reflects an assessment of added effectiveness or other benefits to society, the patient, or the payer. For example, the Arkansas State Employee Benefits Division used a reference pricing system for Nexium, which limited the reimbursement payment level for esomeprazole to the amount it paid for generic omeprazole ($.90 in 2005). This approach accrued savings of $7.2 million over the subsequent 43 months, in comparison with PPI costs of health insurance plans that were not using reference pricing.[86] Internal benchmarking and value-based pricing are less likely to have spillover effects, although the pricing decisions that result from use of such methods may be referenced via external benchmarking approaches.

Value-based pricing provides potential to increase incentives to invest in substantial and radical innovations. Payment methods that define the amount paid based on an assessment of benefit offered are not widely used for a number of reasons, including technical challenges and the perceived risk of adopting an approach that could result in higher payments, particularly for products offering substantial benefits. However, some experts have noted that these value-based methods may reduce market distortions in supply and demand for healthcare goods and services. Danzon and colleagues analyzed alternative arrangements for establishing pharmaceutical payments in countries with universal insurance coverage, which distorts the market and constrains the ability to attain maximum static (short-term) and dynamic (long-term) efficiency:[87]

> *..if each payer unilaterally sets an incremental cost effectiveness ratio (ICER) threshold based on its citizens' willingness to pay for health; manufacturers price to that ICER threshold; and payers limit reimbursement to patients for whom a drug is cost-effective at that price and ICER, then the resulting price levels and use within each country and price differentials across countries are roughly consistent with second best static and dynamic efficiency.*

[85] Rankin, P.J., Bell, G.K., & Wilsdon, T. (2003). Global Pricing Strategies for Pharmaceutical Product Launches. *Pharmaceutical Pricing Compendium—A Practical Guide to the Pricing and Reimbursement of Medicines*. Chapter 2. Charles River and Associates, Urch Publishing.

[86] Johnson, J.T., Neil, K.K., & Davis, D.A. (2011). Five-year examination of utilization and drug cost outcomes associated with benefit design changes including reference pricing for proton pump inhibitors in a state employee health plan. *Journal of Managed Care Pharm.* 17(3):200-212.

[87] Danzon, P., Towse, A.K., & Mestre-Ferrandiz, J. (2012, December). *Value-Based Differential Pricing: Efficient Prices for Drugs in a Global Context.* NBER Working Paper No. 18593.

Skeptics of value-based payment raise concerns about the limitations of explicit thresholds or anchor points for value, and point out that existence of such measures would lead to pricing that gravitates toward the threshold from levels both above and below. At present, only a handful of payers are pursuing value-based strategies to define payment levels, although there is some experimentation in the United States with value-based insurance design (in which benefits, rather than payments, are defined according to an assessment of relative value).[88] Sophisticated approaches, such as performance-based risk-sharing arrangements, may allow for greater experimentation with such approaches in the future. Table 7 summarizes the relationships between methods of defining payment amounts, expected ROI, and incentives to research and develop innovative products.

Table 7: Impact of method used to define reimbursement amount on expected return on investment in healthcare technologies

	Novel products that are not innovative		Innovative products		
	Cost-reducing	**Not cost-reducing**	**Incremental innovation**	**Substantial innovation**	**Radical innovation**
External bench-marking	Likely to increase ROI (& incentives to invest), compared with other approaches	Likely to increase ROI (& incentives to invest), compared with other approaches	Likely to increase ROI (& incentives to invest), compared with other approaches	Likely to increase ROI (& incentives to invest), compared with other approaches	Likely to increase ROI (& incentives to invest), compared with other approaches
Internal bench-marking	Impact unclear	Likely to reduce ROI (& incentives to invest), compared with other approaches.	Likely to reduce ROI (& incentives to invest), compared with other approaches	Impact unclear	Impact unclear
Value-based payment	Likely to increase ROI (& incentives to invest), compared with other approaches	Likely to reduce ROI (& incentives to invest), compared with other approaches.	Most promising approach for yielding ROI that is equivalent to value (as judged from consumer, payer and/or social perspective)		
Lowest possible price payment	Likely to reduce ROI (& incentives to invest), compared with other approaches.	Impact unclear	Uncertain. There is significant risk that this payment method will over-incentivize investment in incremental innovations and under-incentivize investment in radical innovations.		

Source: authors' analysis

[88] University of Michigan Center for Value-Based Insurance Design. (2014). *The evidence for V-BID: Validating an intuitive concept.* Brief. Retrieved from http://vbidcenter.org/wp-content/uploads/2014/10/The-Evidence-for-V-BID-Validating-intuitive-concept-Brief-Feb2014.pdf

PATIENT COST SHARING

Different levels and methods of cost sharing primarily change incentives for consumers to use services and products. Despite the relative wealth of studies concerning effects on consumers, there are scant evidence-based research or evaluation studies that make the subsequent linkages to ROI or future innovations. Nevertheless, certain conjectures can be made from an understanding of cost-sharing features, such as how changes in consumer demand or payer leverage might translate into changes in sales prices and/or sales volumes, which are key components of ROI/EROI.

EFFECTS OF INCREASING/DECREASING COST-SHARING LEVELS

Economic theory predicts that increasing cost sharing (or adding it where there is none) leads to lower demand for products and services because the patient faces more of the cost of care. Empirical literature indicates that adding or increasing cost sharing for prescription drugs typically reduces utilization, including appropriate use, and may lead to higher costs for other services.[89,90,91] One literature review identified a broad range of estimates of the elasticity of demand for medical services with respect to cost sharing, including estimates of -0.1 to -0.6 for prescription drugs.[92] Another review found that increased cost sharing is associated with lower rates of drug utilization and poorer adherence to ongoing treatments in a wide range of therapeutic areas; generally, a 10% increase in cost sharing results in a 2% to 6% decrease in prescription drug spending, regardless of the cost-sharing method.[93]

Responses to changes in cost-sharing levels vary widely, depending on factors such as the underlying medical conditions and/or socioeconomic status of users. In one study, doubling the cost sharing amount resulted in a 23% decline in use of anti-diabetic drugs, compared with declines of 10% for hypertension drugs and 8% for antidepressants.[94] A study of statin use among Medicare beneficiaries found that increasing out-of-pocket costs from $200 to $240 reduced the rate of adherent beneficiaries

[89] Newhouse, J. P. (1993). *Free for all? Lessons from the Rand health insurance experiment*. Cambridge, MA: Harvard University Press.

[90] Swartz, K. (2010). *Cost-sharing: Effects on spending and outcomes.* (Research Synthesis Report No. 20). Princeton, NJ: Robert Wood Johnson Foundation.

[91] Eaddy, M.T., Cook, C.L., O'Day, K., Burch, S.P., & Cantrell, C.R. (2012). How patient cost-sharing trends affect adherence and outcomes: A literature review. *Pharmacy and Therapeutics*. 37(1):45-55.

[92] Liu, S., & Chollet, D. (2006). *Price and income elasticity of the demand for health insurance and health care services: A critical review of the literature.* (Final Report, ASPE/HHS Contract No. 233-02-0086). Washington, D.C.: Mathematica Policy Research, Inc.

[93] Goldman, D. P., Joyce, G. F., & Zhang, Y. (2007). Prescription drug cost sharing associations with medication and medical utilization and spending and health. *JAMA, 298*(1), 61-69.

[94] Goldman D.P., Joyce G.F., Escarce J.J., Pace, J.E., Solomon, M.D., Laouri, M.,… , Teutsch, S.M. (2004). Pharmacy benefits and the use of drugs by the chronically ill. *JAMA, 291*(19), 2344-2350.

from 67% to 56%.[95] Conversely, eliminating cost sharing for medications prescribed following myocardial infarction increased adherence and decreased patient spending without increasing overall health costs.[96] The effects of cost sharing on utilization are relatively strong among low-income populations, who are more price sensitive.[97,98,99,100,101] However, even among low-income patients, responses may differ across drug classes.[102]

Economic theory suggests that increases in utilization, which result from increases in consumer demand, imply increased pricing power for sellers, and generally exert upward pressure on prices. Put together, these effects suggest sellers' expected revenues increase as cost sharing falls. Except in cases where cost offset programs are used (see Box 4), the manufacturers' total costs of development, manufacture, or sale of a healthcare technology are not affected by patient cost sharing. This implies that ROI also increases as the overall level of cost sharing declines. Although increased ROI creates opportunities for firms to increase investment in R&D, prior research suggests that cost sharing may not produce a differential impact for R&D focused on development of innovative products, compared to novel but non-innovative products.[103]

[95] Karaca-Mandic, P., Swenson, T., Abraham, J. M., & Kane, R. L. (2012). Association of Medicare Part D medication out-of-pocket costs with utilization of statin medications. *Health Services Research, 48*(4), 1311-1333.

[96] Choudhry, N. K., Avorn, J., Glynn, R. J., Antman, E. M., Schneeweiss, S., Toscano, M., . . . Shrank, W. H. (2011). Full coverage for preventive medications after myocardial infarction. *N Engl J Med, 365*(22), 2088-2097. doi:10.1056/NEJMsa1107913

[97] Ku, L., & Wachino, V. (2005). *The effect of increased cost-sharing in Medicaid: A summary of research findings.* Washington, D.C.: Center on Budget and Policy Priorities.

[98] Hartung, D. M., Carlson, M. J., Kraemer, D. F., Haxby, D. G., Ketchum, K. L., & Greenlick, M. R. (2008). Impact of a Medicaid copayment policy on prescription drug and health services utilization in a fee-for-service Medicaid population. *Medical Care, 46*(6), 565-572.

[99] Wallace, N. T., McConnell, K. J., Gallia, C. A., & Smith, J. A. (2008). How effective are copayments in reducing expenditures for low-income adult Medicaid beneficiaries? Experience from the Oregon health plan. *Health Services Research, 43*(2), 515-530.

[100] Subramanian, S. (2011). Impact of Medicaid copayments on patients with cancer: Lessons for Medicaid expansion under health reform. *Medical Care, 49*(9), 842-847.

[101] Lurk, J. T., DeJong, D. J., Woods, T. M., Knell, M. E., & Carroll, C. A. (2004). Effects of changes in patient cost sharing and drug sample policies on prescription drug costs and utilization in a safety-net-provider setting. *American Journal of Health-System Pharmacy, 61*(3), 267-272.

[102] Blais, L., Couture, J., Rahme, E., & LeLorier, J. (2003). Impact of a cost sharing drug insurance plan on drug utilization among individuals receiving social assistance. *Health Policy (Amsterdam, Netherlands), 64*(2), 163-172.

[103] Grossman, V. (2013). *Do cost-sharing and entry deregulation curb pharmaceutical innovation?* Journal of Health Economics 32, 881– 894.

BOX 4 | COST-SHARING OFFSET PROGRAMS

Drug manufacturers have responded to recent growth of cost-sharing levels by introducing *cost-sharing offset programs*, which alter financial incentives for insured patients by subsidizing their out-of-pocket costs through coupons, rebates, or direct reimbursements. According to industry sources, cost-offset programs are rapidly growing the United States, with 561 such programs covering 708 brand-name drugs identified in early 2014, a 34% increase compared to mid-2012.[i] These programs appear to engender opposition from third-party payers when they affect choices between competing products on different cost-sharing tiers, such as between a preferred brand-name drug and a non-preferred brand-name drug.[ii] Experts consulted during this project noted that in such cases, the manufacturer's discount to the consumer undermines the cost-sharing structure (which tends to favor products that are less expensive for the payer) and negatively affects the power of payers in negotiations with manufacturers. Moreover, the manufacturer only offers the discount for patients who request and qualify for assistance, and not for every sale covered by the payer (as is likely to be the case with agreements that affect tier placement). Third-party payers may view cost offset programs more favorably when they apply to products that are clinically effective and save money elsewhere in the system, or where they apply to high-cost products for which payers would likely require high levels of cost sharing anyway. In these cases, the offset programs become an indirect way of capturing discounts from manufacturers.

Notes:

i. Zitter Health Insights. (2014, March). *Co-pay offset monitor*. As described in: Fein, A. (2014). *A new reality check on co-pay offset programs*. Retrieved from http://www.drugchannels.net/ 2014/03/co-pay-offset-programs-are-blooming-in.html

ii. Visante, Inc. (2011, November). *How copay coupons could raise prescription drug costs by $32 billion over the next decade*. Prepared for the Pharmaceutical Care Management Association.

Conversely, increased cost sharing reduces utilization and confers less pricing power for sellers, pushing revenues and ROI downward. Recent growth in Part D and commercial plans with four or more tiers reflects efforts by plans to pass on at least part of the high costs of certain drugs to insured patients. For example, plans have been largely unable to negotiate formulary rebates and price discounts for biologics, in part because these products cannot be replicated precisely and, until 2015, no biosimilar products had been approved by the FDA. These products frequently end up on the highest cost-sharing tiers, which frequently use coinsurance of 25%-40% or more of the cost of the drug.[104,105,106]

Industry and investor experts consulted in this study noted that increased cost-sharing levels is a universal problem, with little room left for inflating costs to the patient, especially among the highest cost/highest use patients. One posited that effects may differ between technologies that produce effects the patient can feel (e.g., reduced pain), versus therapies aimed more at prevention where the benefits are less obvious/immediate.

Although existing research focuses primarily on drug classes and not specific drugs, the variation in effects observed across different classes suggests that cost sharing (of any type) may have smaller effects on use and pricing of innovative products, especially substantial or radical innovations as defined in this project. By definition, these products confer greater benefits to patients in comparison with existing therapeutic alternatives, or they address a more significant previously unmet or inadequately met health need, so demand for them is potentially more inelastic. Any effects on utilization are also likely to be smaller for products that target more severe conditions, compared to those for less severe or asymptomatic conditions, regardless of whether the product is determined to be innovative or not.

Differential cost sharing offers the potential to reward more valuable innovations over less valuable innovations, to the extent that cost sharing is higher for products offering lower consumer welfare enhancement and lower for products offering more consumer welfare enhancements. Experts we interviewed noted the possibility of value-based reimbursement with lower copays for more "value" – although this led to a discussion among several panelists of the pros and cons of QALYs and other ways of measuring value, which highlighted that defining what constitutes value is a challenge and often controversial. In the cases offered as examples by panelists, the payer defines and determines what "value" is, but the process is not always transparent to outside observers.

There is also no evidence that assessments of value from a consumer or societal perspective are the basis for most formulary placement decisions that determine cost sharing levels. Plans typically apply lower cost-sharing amounts to incentivize use of preferred (often less expensive) services, such as

[104] Kaiser Family Foundation & Health Research & Educational Trust (HRET). (2014). *Employer Health Benefits: 2014 Annual Survey*. Menlo Park, CA: Henry J. Kaiser Family Foundation.

[105] Pharmacy Benefit Management Institute. (2013). *2013-2014 Prescription Drug Benefit Cost and Plan Design Report*.

[106] Hoadley, J., Cubanski, J., Hargrave, E., & Summer, L. (2014, October 10). *Medicare Part D: A first look at plan offerings in 2015.* Washington, DC: Henry J. Kaiser Family Foundation.

primary care physicians instead of emergency rooms for non-emergent care, or preferred products, such as generic drugs. Higher cost-sharing levels usually apply to non-preferred products and services. For example, most commercial plans require higher cost sharing for services and devices from non-network providers (and may not cover such services at all). A more recent trend is that commercial, Part C, and Part D plans are beginning to use tiered cost sharing to distinguish between preferred and non-preferred providers *within* their networks.

COPAYMENTS VS. COINSURANCE

Coinsurance may have greater effects on utilization, even when configured to achieve the same cost-sharing levels as fixed copayments. Theoretical models suggest that copayments lead to better adherence with prescription drug regimens than variable coinsurance, by reducing patient uncertainty with regard to out-of-pocket payments. Based on a national sample of privately-insured patients using drugs for diabetes, adherence declined by 23% following a large increase in coinsurance, but adherence only fell by 9% after a comparable increase in fixed copayments.[107,108]

Even relatively low coinsurance rates may create a financial burden for users of expensive non-preferred and specialty drugs. To some extent, maximum out-of-pocket provisions alleviate this burden, but not until consumers pay substantial sums out-of-pocket (usually several thousand dollars). Very high cost-sharing levels may reduce the ROI for manufacturers of high-cost and specialty drugs, as the cost sharing weakens demand and reduces sales.[109,110] These products may not meet the definition of consumer welfare-enhancing innovations used in this project, although they frequently target serious and chronic conditions.

The greatest potential effects from cost sharing may occur where coinsurance (cost sharing applied as a proportion of the price, rather than a fixed amount) applies to high-cost, yet innovative products. However, neither copayments nor coinsurance seems likely to have significant effects on innovation. One reason is that manufacturers are in a relatively strong position to establish initial prices for their products in the United States, and they frequently employ sophisticated pricing models that enable them to account for anticipated cost sharing. Manufacturers' cost-sharing offset programs also may mitigate effects, and the willingness of drug makers to participate in these programs on a relatively large scale suggests they are willing to accept lower rates of return on a per-unit basis for certain transactions,

[107] Dor, A., & Encinosa, W. (2010). How does cost-sharing affect drug purchases? Insurance regimes in the private market for prescription drugs. *Journal of Economic Management and Strategy,* 19(4).

[108] Dor, A., & Encinosa, W. (2004). *Does cost sharing affect compliance?: The case of prescription drugs.* NBER Working Paper no. 10738.

[109] Goldman, D. P., Joyce, G. F., & Zhang, Y. (2007). Prescription drug cost sharing associations with medication and medical utilization and spending and health. *JAMA, 298*(1), 61-69.

[110] Goldman D.P., Joyce G.F., Escarce J.J., Pace, J.E., Solomon, M.D., Laouri, M.,… , Teutsch, S.M. (2004). Pharmacy benefits and the use of drugs by the chronically ill. *JAMA, 291*(19), 2344-2350.

in exchange for maintaining higher list prices for other transactions and greater sales volume to bolster ROI.

DEDUCTIBLES & COVERAGE LIMITS

With deductibles, consumers pay the full, approved amount for any services or products to which the deductible applies, until their out-of-pocket costs reach the deductible limit. Theory posits that deductibles will discourage unnecessary use of services, because they expose consumers to the full prices of these items. Empirical studies indicate that, in practice, increasing deductibles likely decreases use of unnecessary or inappropriate services *and* desirable and appropriate services, such as preventive care, until the consumer reaches the deductible limit.[111,112] Studies also suggest that use of prescription drugs decreases where prescription drugs are subject to the deductible, but effects may be tempered for more severe conditions.[113,114] These findings suggest possible reductions in utilization of drugs and devices that patients pay for directly. Deductibles are unlikely to affect use when the cost of the drug or device is part of an inclusive rate.

It is unclear whether deductibles affect selling prices. They may incentivize manufacturers to set higher prices to push patients past the deductible limit more quickly. There is no evidence suggesting that any potential effect would differ between non-innovative and innovative products, although innovative products are more likely to command higher prices generally (with or without deductibles) due to higher demand. Considering these potential effects, deductibles seem unlikely to have significant effects on the ROI/EROI for innovative products relative to non-innovative products, or incentives for development of innovative products.

Coverage limits, where insurance stops paying after a patient incurs total health care costs exceeding an annual or lifetime threshold, are relatively rare. Patients face the full cost of drugs and services above the limit, but people reaching the limits are likely to have serious chronic or acute conditions and little incentive to cease treatment. Coverage limits are unlikely to affect developers' decisions about pricing or whether to invest in potentially innovative healthcare technologies, as the limits are rare and tend to be quite high, relative to the cost of any single healthcare technology.

Table 8 summarizes the effects described in this section.

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[111] Dixon, A., Greene, J., & Hibbard, J. (2008). Do consumer-directed health plans drive change in enrollees' health care behavior? *Health Affairs (Project Hope), 27*(4), 1120-1131.

[112] Gupta, N., & Polsky, D. (2012). High deductible health plans: Does cost sharing stimulate increased consumer sophistication? *Health Expectations*. doi:10.1111/hex.12031

[113] Greene, J., Hibbard, J., Murray, J. F., Teutsch, S. M., & Berger, M. L. (2008). The impact of consumer-directed health plans on prescription drug use. *Health Affairs, 27*(4), 1111-1119. doi:10.1377/hlthaff.27.4.1111

[114] Reiss, S. K., Ross-Degnan, D., Zhang, F., Soumerai, S. B., Zaslavsky, A. M., & Wharam, J. F. (2011). Effect of switching to a high-deductible health plan on use of chronic medications. *Health Services Research, 46*(5), 1382-1401. doi:10.1111/j.1475-6773.2011.01252.x

Table 8: Effects of cost-sharing approaches on ROI and incentives to invest in development of healthcare technologies

	Novel products that are not innovative		Innovative products		
	Cost-reducing	**Not cost-reducing**	**Incremental innovation**	**Substantial innovation**	**Radical innovation**
Increase cost-sharing level	• Likely to decrease use • Some price-reducing pressure, particularly for products that are not cost-reducing • Should reduce ROI and incentives to invest		• Likely to decrease use • Some price-reducing pressure • Effects may be smaller for substantial and radical innovations if demand for those products is relatively inelastic • Unlikely to have substantial effects on ROI or incentives to invest in innovative products		
Decrease cost-sharing level	• Likely to increase use • Some price-increasing incentive • Should increase ROI • Unlikely to have differential effects on incentives for innovative vs. non-innovative products unless reductions are only for innovative products				
Coinsurance (vs. copayment)	• Likely to have larger effects on use than copayments, especially for high-cost products • Potential for price-reducing pressure, particularly for high-cost products • Price and use impact may be offset by manufacturer cost-offset programs • Net effects on ROI are unclear • Although effects may be greater than with copayments, coinsurance is still unlikely to have significant effects on incentives to invest in innovative products as long as manufacturers are able to set higher prices for these products to counteract the effects of lost sales due to cost sharing, or use cost sharing offset programs to help patients afford the out-of-pocket costs and reduce the volume of lost sales				
Deductible	• May affect use, particularly for high-cost products • Effects on sales prices and ROI are unclear, but probably small • No clear expected effects on incentives to invest		• Effects on use, pricing, or ROI are unclear, but probably smaller than for non-innovative products or incremental innovations. • Unlikely to have significant effects on incentives to invest		
Coverage limit	• Unlikely to affect use, pricing, or ROI for individual products • No expected effects on incentives to invest in either innovative or non-innovative products (based on current prevalence and size of limits)				

Source: authors' analysis

CONCLUSIONS

Although it is widely accepted that the extent and nature of product reimbursement is a significant factor in the development decisions of potential developers of novel healthcare technologies and the investors who finance them, there is only limited empirical evidence of connections between reimbursement and innovation per se. Analysts posit that payment policies influence the diffusion of new products, and as a result have a substantial impact on R&D decisions and whether companies choose to advance a technology to market.[115] Experts consulted during this project agreed that reimbursement is an important factor in R&D and investment decisions; that it is a critical factor in determining which products in development are brought to the market; and that its influence appears to be growing in importance. However, several experts questioned whether reimbursement policies and practices can truly steer developers and investors toward innovative products. Reimbursement is just one of many factors that may influence developers' ability to innovate. Scientific opportunities are very important – a developer cannot produce a breakthrough product if the science is not there. A focused push by government or private organizations for new products in a particular area, such as an orphan disease, may also carry significant weight. For example, the Orphan Drug Act of 1983 and the FDA's 2014 guidance to industry on expedited programs for serious conditions reflect government efforts to encourage innovation.[116] Patient groups are also developing patient registries to generate data about their diseases, and pressuring developers to focus on unmet needs.

The question of how payers can foster innovation in healthcare technologies that improve consumer welfare could also be taken to imply that payer policies are *ipso facto* discouraging or impeding it. However we did not find evidence that this is likely to be the case. On the contrary, experts consulted on this project suggested that very few substantial or radical innovations are held back; generally, it was hypothesized that payers are willing to pay more for these types of products (e.g., one panelist described payers as willing to reward developers for "going into a whole new therapeutic area, and doing something quite special"). If this is the case, the questions then become: are incremental innovations being held back; if so, which ones; and, if they really are of value, how do we move them forward in development and get payers to recognize their value? Although by definition substantial and radical innovations offer greater advances relative to existing standards of care, a series of incremental innovations can add up to significant therapeutic progress.

Our research indicates that reimbursement policies and practices affect key components of ROI for developers and investors, such as prices and sales volumes, and change incentives for many other actors in the marketplace that indirectly influence ROI. However it remains unclear precisely how these impacts ultimately affect innovation. There is a dearth of empirical evidence pertinent to the links

[115] Chambers, J., May, K., & Neumann, P. (2013). Medicare covers the majority of FDA-approved devices and Part B drugs, but restrictions and discrepancies remain. *Health Affairs* 32(6):1109-1115.

[116] U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). (2014, May). *Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics*. OMB Control No. 0910-0765.

between reimbursement and ROI for developers (or investors). It is difficult, if not impossible, to measure and control for all potential variables in an experimental setting. In addition, many characteristics, such as bundled payments, are relatively new phenomena in the U.S. and therefore do not offer much documented experience or outcomes. Long timelines for development also muddy the effects (at least the ability to track them), particularly for drugs, biologics, and vaccines. We found no empirical evidence to directly connect reimbursement policies and practices with the quantity or quality of healthcare technology innovation.

Our analytic framework, shown in Figure 2 on page 12, illustrates the connections between reimbursement policies and practices, and ROI for developers (and investors). Although there are direct paths of influence, including impacts on manufacturers' selling prices and/or sales volume, or the costs associated with the development, manufacture, or sale of their products, the connections are not direct in most cases. The distribution systems for healthcare technologies involve many actors. The actions of providers, wholesalers, PBMs, and other intermediaries affect ROI for manufacturers, as they often receive a portion of the reimbursement. These intermediaries can also influence the reimbursement policies and practices used by payers; for example, healthcare providers make many decisions on behalf of patients and thereby influence product uptake. Intermediaries also may have different views from patients or third-party payers in terms of what constitutes value, or even the level of innovation (incremental, substantial, or radical) offered by a particular product. This complexity makes effects harder to determine and often ambiguous. In addition, the complexity of the U.S. healthcare system, diversity of approaches to reimbursement around the world, and the global nature of the drug and device industries create potential for unintended impacts from reimbursement policies and practices.

The *hi HealthInnovations* advance market commitment (AMC) case study illustrates the potential effectiveness of establishing a direct link between reimbursement and a desired innovation. In this case, UnitedHealth Group filled an unmet need for hearing aids among its patients and the broader population by partnering directly with a manufacturer. The result was a set of devices with features the payer valued at price points that enabled more patients to afford the technology. The hearing aids developed in this case were relatively low-cost devices that did not require extensive testing. Broader applications of the AMC concept may be limited because of the greater development demands for more complex devices or drugs, and lack of ability for a single payer to control access to these types of products.

Because the connection between reimbursement and innovation is usually not as straightforward as in the *hi HealthInnovations* case, this research project examined how five characteristics of reimbursement policies and practices may impact developers' ROI and incentives to innovate: the reimbursement decision-making process; approaches to product categorization and differentiation; method of payment; methods of defining payment amounts; and patient cost sharing. The U.S. retains a pluralist framework with regard to the reimbursement decision-making process – hundreds of payers use their own assessment approaches to reach their judgments, leading to considerable variation. While variation may be appropriate for the different populations they serve, the lack of uniform decision-making weakens the ability of all but the largest payers to motivate developers to develop innovative products. The effects of different decision-making *processes* are hard to trace. Theoretically, processes that are

transparent and evidence-based will provide the clearest signals to developers and favor development of products that address unmet needs and/or provide added value over existing therapies.

There is limited evidence concerning the effects of different approaches to product categorization and differentiation. Value-based approaches may reflect assessments of added effectiveness or other benefits, but a minority of payers in the United States uses them. There is optimism about the promise of value-based methods to align incentives for developers with the interests of patients, providers, and payers, but there are also many challenges to overcome. For example, although the experts interviewed in this project reached near consensus on the importance of accounting for value, there was little consensus in the ensuing discussions of how to measure value, what constitutes a "reasonable" cost, or even what is an "improvement" in patient health. The lack of consensus or clarity in definitions of these key terms highlights one of the challenges to broader adoption of value-based approaches. Different payers are likely to have varying definitions of innovation and value. Determinations of value may be case-specific.

The case study of the Premera Blue Cross value-based formulary pilot program highlights some additional challenges for value-based approaches. For example, even with a systematic approach to measuring value, payers may lack access to data, research evidence, or other information necessary to determine who should receive treatment and in what circumstances. Limited availability of evidence may prevent optimal placement of drugs or other treatments. Quantifying the return for payers is also challenging.

Whereas the reimbursement decision-making process sets the parameters for availability, prescribing, and reimbursement of drugs and devices, and methods of product categorization and differentiation help to distinguish among products, the next two characteristics – the method of payment and methods of defining payment amounts – determine the structure and size of payments for new technologies. While payment methods vary, the fundamental distinction is whether payers compensate providers or suppliers of healthcare technologies on a per-unit basis or as part of a bundled payment for a package of goods and services used for a clinically-defined episode of care. Per-unit payments seem unlikely to favor development of any particular type of innovation, but may also be ineffective at discouraging development of non-innovative products. A shift to bundled payments from per-unit payments may incentivize development of cost-reducing products (from the perspective of the payer), but may discourage incremental innovations.

Theoretically, broader use of value-based or outcomes-based reimbursement would lead to lower returns on products and services offering little value added, higher returns for products with higher value, and greater clarity about where the value-added is uncertain. This could potentially increase incentives to invest in R&D aimed at products more likely to be deemed substantial or radical innovations, or at least it could stimulate investment in the identification of biomarkers that could be used as proxies for the clinical outcomes of interest in outcomes-based reimbursement.

The case study of the performance-based risk-sharing agreement for Velcade in the U.K. illustrates some of the challenges in establishing performance-based payment. (Performance-based payment is closely

related to value-based or outcomes-based reimbursement, and involves use of a specific outcome target that is considered a way of attaining value-for-money.) For the manufacturer, there is the uncertainty about whether the drug will perform as expected, whether the outcomes achieved in a highly controlled clinical trial environment can be replicated in every day clinical practice.[117] It also highlights the practical challenges, such as the identification of a clearly defined, objective metric of treatment effect (performance) that is either a direct measure of clinical outcome (such as survival or cure) or a well-accepted surrogate endpoint that closely corresponds to or reliably predicts the desired treatment effect and is unaffected by other treatments. For payers, there is also a burden of measuring and monitoring patient progress, and there may be the challenging prospect of having to withdraw coverage of a drug either entirely, or in individual patients, depending on the nature of the risk-sharing agreement. The vast majority of patient access schemes (PAS) in the U.K. subsequent to Velcade have been financially-based arrangements, which are perceived as being simpler to administer than the outcome- or performance-based PAS.[118]

The effects of reimbursement on innovation may also be muted by the ability of developers to strategically price their products. Manufacturers' pricing models take into account expectations about lost sales due to higher costs or cost sharing; complex and secretive rebate and discounting mechanisms favor high list prices; and cost sharing offset programs reduce the negative effects on demand when payers apply patient cost sharing. Patient cost sharing does not appear to be an important barrier to innovation at present, at least for substantial or radical innovations. However, with growing levels of patient cost sharing, broader use of coinsurance, and very high list prices for new products, the balance may tip if utilization drops more than manufacturers anticipate or can compensate for with cost-sharing offset programs, or if manufacturers lose pricing power.

SUGGESTIONS FOR FUTURE RESEARCH

The direction and magnitude of effects on innovation resulting from most of the reimbursement characteristics and three specific cases examined in this project remain unknown or uncertain, in part because many of the effects reimbursement may have on innovation are indirect. Because there is no centralized entity in the United States that establishes standards for defining what constitutes value or that promotes investment in particular innovations, researchers focusing on the U.S. context are left with a selection of initiatives from the private sector and public demonstration projects.

In-depth case studies that look at specific approaches to reimbursement may help to reduce some of the uncertainty about how reimbursement acts to incentivize or deter development of products that are

[117] Towse, A., & Garrison, L.P. Jr. (2010). Can't get no satisfaction? Will pay for performance help? Toward an economic framework for understanding performance-based risk-sharing agreements for innovative medical products. *Pharmacoeconomics* 28(2):93–102.

[118] National Institute for Health and Care Excellence. (2015). Patient Access Scheme Liaison Unit (PASLU) List of technologies with approved Patient Access Schemes. Retrieved from http://www.nice.org.uk/About/What-we-do/Patient-access-schemes-liaison-unit/List-of-technologies-with-approved-Patient-Access-Schemes

more likely to meet the definition of innovation used in this project. A well-designed and extensive case study approach is the most likely to provide insights into all aspects of innovation, given the relative scarcity of empirical evidence in the published literature. The expert panels we convened for this project provided a rich level of insight into the diverse beliefs about the relationship between reimbursement and innovation.

One example of a broader case study could be an extension of the value-based insurance design (VBID) case study to include more payers. Premera is one of several private payers and employers that have launched VBID initiatives, and the Medicare Advantage Value-Based Insurance Design Model announced by CMS in September 2015 should provide additional opportunities. A comparison of the different designs could provide insights into the differences and similarities between these programs, particularly in terms of decisions concerning coverage and payment for drugs and devices. Indication-based pricing is another concept that has recently garnered interest, for example as a way to link prices of oncology drugs to their benefits.[119] Indication-specific pricing is not yet being applied in the U.S., but a case study could examine emerging models, such as the American Society of Clinical Oncology's conceptual framework to assess the value of cancer treatment options, or the Memorial Sloane Kettering Cancer Center's DrugAbacus (http://www.drugabacus.org/).[120]

There are several initiatives from the CMS Innovation Center announced or underway that may serve as opportunities to evaluate how drug and device developers respond to bundled payments and other reimbursement approaches focused more specifically on payment methods. These include the Health Care Payment Learning and Action Network, and episode-based payment initiatives such as the Bundled Payments for Care Improvements (BPCI) and the Comprehensive Care for Joint Replacement Model.

Ultimately, the impact of reimbursement on innovation hinges on the decision-making processes of drug and device developers. A potential research study might involve a well-designed questionnaire of senior R&D decision-makers about how their discovery and clinical development programs would differ under various hypothetical reimbursement policies and programs, assuming they become universal or at least widespread, and how they think that their target product profiles (TPPs) would be affected under these scenarios. The questionnaire might be coupled with in-depth individual interviews of at least a subset of survey respondents. The scenarios for this study could be derived from the case studies described above. The willingness of R&D leaders to participate in such an analysis is uncertain. However, such a study could offer a peek into the "black box" of decision-making within organizations engaged in drug and device development.

Future research could also focus on implementation barriers related to use of comparative effectiveness research findings. As noted in our assessment of Premera Blue Cross' value-based formulary, several

[119] Bach, P.B. (2014). Indication-specific pricing for cancer drugs. *JAMA* 312(16):1629-1630.

[120] Schnipper, L. E., Davidson, N. E., Wollins, D. S., Tyne, C., Blayney, D. W., Blum, D.,… , Schilsky, R.L. (2015). American society of clinical oncology statement: A conceptual framework to assess the value of cancer treatment options. *Journal of Clinical Oncology*, doi:10.1200/JCO.2015.61.6706

people involved in that program's roll-out were concerned by how often requests for economic data from manufacturers were unmet, and it is resource-intensive for individual payers to assess the available information. The Patient-Centered Outcomes Research Institute (PCORI) and other federal programs are generating more comparative effectiveness evidence, and more private sector entities are allocating resources towards comparative effectiveness. But, whether this is having or will have an effect on prescribing patterns, and whether it is having or will have an effect on product development remains to be seen.

APPENDIX A: A STANDARD REIMBURSEMENT DECISION-MAKING PROCESS

The approach to reimbursement decision-making is how payers make decisions on which drugs, devices, and other healthcare technologies to make available to patients, at what price, and for whom. The following steps are illustrative of a typical decision-making process by a P&T Committee or other decision-making body.

1. *Clinical evaluation*. Typically, payers will review FDA documents providing details of efficacy and safety of new molecules or biologics; they may also review the published literature and clinical trial reports. Where comparative effectiveness evidence is available, this may also be considered provided the comparisons are relevant and reflect current treatment patterns. Devices are evaluated using a similar set of measures, although industry experts consulted during this project noted that CMS coverage decisions are crucial for devices because other payers frequently follow those decisions. Committee members typically seek to address the following questions:
    a. Is there compelling evidence of a need to add this drug to the formulary, or to cover the device?
    b. What is the quality of the evidence submitted for approval (and comparative evidence, if available)?
    c. Does the new product address an unmet or inadequately met need?[121]

2. *Coverage of the drug or device under the medical or pharmacy benefit*. This administrative decision has numerous implications for drug and device reimbursement, as payers may use different methods of payment; different methods to establish the amounts that they will pay for a product; or different patient cost sharing depending on the designated benefit package (we discuss all of these characteristics in more detail later in this Appendix).

3. *Potential for misuse*. The committee examines the possibility for expansion of indications, which could include supplemental approvals as well as off-label uses of new drugs, and inappropriate use of devices. Accordingly, the payer may tag new drugs and devices with prior authorization or other utilization controls.

4. *Economic evaluation*. The committee may assess a new drug or device's total cost to the payer and cost-effectiveness relative to existing treatment alternatives. In this context, the committee asks whether the additional costs of the drug or device are justified by the additional benefits expected. Industry and investor panelists viewed the increasing focus of payers/providers on cost and health care economics as a key development, making bottom-line impact assessments increasingly important. They noted that the expanding evidence requirements for new products

[121] Wang, Z., Salmon, J.W., & Walton, S. (2004). Cost-effectiveness analysis and the formulary decision-making process. *Journal of Managed Care Pharmacy.* 10(1):48-59.

in the U.S. and the rest of the world complicate the process of bringing technologies to market and add cost and uncertainty to the process.

5. *Approval or rejection by the committee*. The committee makes the binary choice whether to cover a drug or device.

6. *Development of drug and device-use conditions*. For covered items, the committee establishes conditions of reimbursement, such as patient cost-sharing, prior authorization, quantity limits, and step therapy requirements. Rebates are often a key driver of the development of drug-use conditions. Payers negotiate rebates from manufacturers in exchange for their ability to move market share. In this context, payers assign preferred status, such as lower patient cost-sharing or fewer conditions of reimbursement, to products on the formulary in exchange for rebates. For most payers, pricing information is confidential, but it is known that pricing decisions are made during this phase of formulary management.

7. *Drug and device-use monitoring and follow-up review*. The committee reviews drug and device claims and utilization data, in addition to medical claims where appropriate.

APPENDIX B: HI HEALTHINNOVATIONS CASE STUDY

BACKGROUND

The advance market commitment (AMC) concept gained traction in the early 2000s as a potential means to encourage the development of new vaccines and treatments for neglected diseases.[122,123,124] The rationale was that diseases such as malaria and tuberculosis primarily affect developing countries, which limits the commercial value of products targeting those diseases.[123] By guaranteeing a market, or removing at least some of the uncertainty about the size of the market, and therefore the projected revenues, these commitments theoretically encourage more firms to invest in development of the desired product(s). Observers note that the incentives for manufacturers may vary depending on the structure of the agreement, such as "winner-take-all" or "multiple winners" approaches; front-loaded or back-loaded financial incentives; and guarantees of quantity or guarantee of price only.[122] Others raise concerns that particular setups may require contributors to guarantee to pay for potentially medically inferior products.[125] "Bounties" or awards may be other, similar approaches to encourage development of such products by providing a financial reward for production of a particular drug or device.

There are differences between the initial AMC concept and the *hi HealthInnovations* hearing aid model, but both concepts are, at their core, formal agreements by a payer or other organization to guarantee a vendor (or vendors) a viable market for a product viewed as desirable by payers, or, more broadly, by society. Through an agreement with IntriCon Corporation, a developer and manufacturer of body-worn medical and hearing devices, *hi HealthInnovations* established a line of custom hearing aids with features it deemed necessary, at a price point that expanded the hearing aid market to many new consumers. This case is an example of direct investment by a third-party payer to develop a device tailored to its specifications, with a goal of improving health outcomes and reducing costs.

Experts consulted for this project noted that greater sharing with developers of information on what items and services are being used and at what cost to payers would likely lead to new innovations developed to reduce those costs, and target improvements on the most costly issues within particular patient groups. However, commercial payers in the United States operate in a competitive business environment, where it is unlikely for open sharing of cost information to take place. Current efforts to expand all-payer databases and develop new tools to analyze "big data" sources, such as electronic

[122] Berndt, E. R., & Hurvitz, J. A. (2005). Vaccine advance-purchase agreements for low-income countries: Practical issues. *Health Affairs, 24*(3), 653-665. doi:10.1377/hlthaff.24.3.653

[123] Berndt, E. R., Glennerster, R., Kremer, M. R., Lee, J., Levine, R., Weizsäcker, G., & Williams, H. (2007). Advance market commitments for vaccines against neglected diseases: Estimating costs and effectiveness. *Health Economics, 16*(5), 491-511. doi:10.1002/hec.1176

[124] Levine, R., Kremer, M. R., & Albright, A. (2005). *Making markets for vaccines: Ideas to action.* Center for Global Development, Advance Market Commitment Working Group.

[125] Sonderholm, J. (2010). A theoretical flaw in the advance market commitment idea. *Journal of Medical Ethics, 36*(6), 339-343. doi:10.1136/jme.2009.033092

medical records, may make efforts to identify payers' unmet needs more feasible in the future. In the absence of such data sharing, developers are more reliant on payers and consumers to send signals about the types of products they value. An advance market commitment clearly indicates a desire for a particular innovation.

OBJECTIVES/RATIONALE OF *HI HEALTHINNOVATIONS*

Lisa Tseng, MD, CEO of *hi HealthInnovations*, offered several reasons for the development of the hearing aid devices and related benefit program(s). One objective was to respond to a significant unmet need, both among UnitedHealthcare health plan participants and the general U.S. population.[126] The prevalence of hearing loss increases by age, with more than 40 percent of people age 60 or older in the U.S. having loss in at least one ear, per World Health Organization criteria.[127] The National Institute on Deafness and Other Communication Disorders (NIDCD), part of the National Institutes of Health (NIH), estimates that about 25 percent of the population between the ages of 65 to 74 and 50 percent of the population aged 75 and older have disabling hearing loss. The NIDCD also estimates that just 30 percent of adults ages 70 and older who could benefit from hearing aids, and only 16 percent of adults from ages 20 to 69 who could also benefit, have ever used them.[128] Studies indicate that hearing loss leads to lower workforce productivity and social isolation, and is associated with higher rates of depression and cognitive decline, as well as other mental health concerns.[129] Researchers have also observed a relationship between hearing loss and increased risk of falls.[130]

Additional objectives for *hi HealthInnovations* were to improve access to hearing care and reduce the price of hearing aids for all consumers and for people enrolled in the UnitedHealthcare's commercial, Medicare Advantage, and stand-alone Medicare prescription drug plans (PDPs). Along with affordable health insurance and prescription drugs, Dr. Tseng noted that affordable hearing aids are one of the most frequently-requested services among health care consumers.[126] One reason is cost: health insurance coverage for hearing aids is often limited, and costs for these devices can be high. Media reports cite average out-of-pocket costs to consumers ranging from $1,000 to $4,000, and pricing for

[126] Tseng, L. (2015, March 26). *Personal communication*.

[127] Lin, F.R., Niparko, J.K., & Ferrucci L. (2011). Hearing loss prevalence in the United States. *Archives of Internal Medicine, 171*(20), 1851-1853. doi:10.1001/archinternmed.2011.506

[128] National Institute on Deafness and Other Communication Disorders (NIDCD). (April 20, 2015). Quick statistics. Retrieved from http://www.nidcd.nih.gov/health/statistics/Pages/quick.aspx

[129] Lin, F. R., Yaffe, K., Xia, J., Xue, Q.L., Harris, T.B., Purchase-Helzner, E.,… , Simonsick, E.M. (2013). Hearing loss and cognitive decline in older adults. *JAMA Internal Medicine, 173*(4), 293-299. Retrieved from http://dx.doi.org/10.1001/jamainternmed.2013.1868

[130] Lin, F. R., & Ferrucci, L. (2012). Hearing loss and falls among older adults in the United States. *Archives of Internal Medicine, 172*(4), 369-371. Retrieved from http://dx.doi.org/10.1001/archinternmed.2011.728

specific hearing aids may be much higher.[131,132] Pricing can also be confusing, with some prices including bundled services such as fitting, adjustment, and follow-up care, and other prices reflecting just the purchase of the device itself. The traditional Medicare fee-for-service Medical Insurance program (Part B) does not cover routine hearing exams, hearing aids, or exams for fitting hearing aids; coverage of hearing aids is excluded by statute. Some Medicare Advantage (Part C) managed care plans cover them. Hearing aids and related care are covered services in Medicaid.

In addition to making hearing aids more affordable and accessible, *hi HealthInnovations* wanted to offer a line of products that gave consumers the benefit of advanced technologies, offering high-quality sound and customizable settings for individual users, while avoiding "unnecessary" features.[133] The company wanted the hearing aids to be easy to use, particularly for older consumers and technophobes; another objective was delivery of the hearing aids in a consumer-friendly manner.

KEY CHARACTERISTICS OF *HI HEALTHINNOVATIONS*

In 2011, *hi HealthInnovations* reached an agreement with IntriCon to develop and manufacture a set of lower-cost hearing aids, using behind-the-ear and new (at the time) in-the-canal technologies. All of the new hearing aids are "air conduction devices," which are Class I medical devices and exempt from the Food and Drug Administration's (FDA) 510(k) submission process.[134] Theoretically, such technologies require fewer resources and time to develop because they do not need to demonstrate substantial equivalence to an approved device, or go through a full scientific and regulatory review process.

By working with its own hearing health professionals and primary care providers in UnitedHealthcare's national networks to offer hearing testing, *hi HealthInnovations* was able to program and dispense hearing aids custom-tailored to people via a direct-to-consumer distribution channel, removing distribution intermediaries that may drive up costs. Moreover, in contrast to traditional hearing aids where support was often available only from the original local supplier, UnitedHealthcare's size made it possible to support the devices nationwide through its care provider network or *hi HealthInnovations* staff, including in-person, over-the-phone, or online.

UnitedHealthcare announced the new hearing aid program in October 2011, during the open enrollment period for Medicare Advantage plans. The hearing aids were fully covered or offered with a low co-payment to consumers in those plans, depending on the plan chosen by the consumer. It was not long before the hearing aid discount was available to people enrolled in UnitedHealthcare's commercial plans as a fully covered or low co-payment benefit. At the time, it was a unique offering among major U.S.

[131] Andrews, M. (2012, Apr 9). Unlike most insurers, UnitedHealthcare is offering big discounts on hearing aids. *The Washington Post*.

[132] Robertson, K. (2013, Jun 7). UnitedHealthcare now one of few insurers offering hearing aid benefit. *Sacramento Business Journal*.

[133] Tseng, L. (2015, March 26). *Personal communication.*

[134] IntriCon Corporation. (2015). Form 10-K annual report filed 3/6/15 for the period ending 12/31/14. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-15-290

Medicare and commercial payers. While other insurers provided some coverage for hearing aids, this program stood out with its direct-to-consumer sales model and low out-of-pocket costs. The high level of observed demand led *hi HealthInnovations* to expand its offerings to non-UnitedHealthcare consumers and to develop "turn-key" programs, which enabled employers to directly adopt the discount program, while enabling other health plans to also participate.

The *hi HealthInnovations* program offered relatively low out-of-pocket costs for hearing aids, compared to traditional distribution channels. The *hi HealthInnovations* website listed retail prices of $799-$999 for these products in late April, while Medicare Advantage plan participants can access the devices for cost-sharing amounts ranging from no cost to $450 per aid.

In addition to offering a selection of hearing aids for purchase online from *hi HealthInnovations*, the program initially included an online hearing test. The intent of the online test was to increase access to hearing care by enabling consumers to test their hearing at home. The test results provided information necessary for the company to customize hearing gain levels on new hearing aids before shipping them to customers. The online test was removed from the market shortly after launch due to regulatory issues, discussed later in this report. *hi HealthInnovations* now provides hearing tests through a staff of audiologists and hearing health professionals, and a network of contracted care providers; prospective customers may also use hearing test results from their own care providers. *hi HealthInnovations* staff noted that the company recently earned a U.S. patent for a hearing test kit that is available to health care professionals for $179, compared to other in-office tests that retail for more than $1,000. Many UnitedHealthcare network care providers can access the kit at no cost.

HOW MIGHT BROADER USE OF PROGRAMS SUCH AS *HI HEALTHINNOVATIONS* INFLUENCE INNOVATION IN DRUGS OR MEDICAL DEVICES?

Dr. Tseng noted that achieving cost-effectiveness in developing the hearing benefit and the associated testing and follow-up care was a significant hurdle in developing the hearing aid program. In part, it was initially developed for individuals subscribed to UnitedHealthcare's Medicare Advantage plans, and the benefit needed to be affordable for those plans under their existing reimbursement levels.

Innovation, as defined for this research project, is a function of the extent to which a drug or device addresses a disease or condition for which there is a substantive (i.e., non-trivial) unmet or inadequately met need, and whether, and to what extent, the new product offers clinically meaningful benefits compared to existing treatments. By this definition, the *hi HealthInnovations* hearing aids produced by IntriCon may be "incremental" or even "substantial" innovations; they target a potentially significant unmet need that can improve consumers' quality of life and may help to reduce medical and behavioral health expenditures. IntriCon asserts that the new hearing aids offer improved benefits over existing technologies at comparable price points, such as better clarity and greater ability to filter out

background noise.[135] If so, they may offer increased net health benefit compared to existing, similarly-priced aids. The aids also appear to be consumer welfare-enhancing, by being offered at a price that more patients are willing to pay. Payers and consumers often cite the high cost of hearing aids sold through traditional channels as a significant barrier to broader adoption, so the lower cost of IntriCon's devices factors into their value-add assessments.

The conceptual model for this research project establishes expected return-on-investment (EROI) as a proxy for incentives to innovate and posits that current returns on investment are viewed as indicative of potential future returns. Our framework for analysis notes that reimbursement policies and practices can affect EROI (or ROI) directly by establishing a particular payment level, which in turn affects average sales price; by setting a volume of sales at that payment level; and/or by influencing the seller's costs associated with development, manufacture, or sale of a healthcare technology. Reimbursement policies also stand to indirectly influence EROI/ROI by establishing different incentives for key actors, including patients/consumers, dispensers, care providers, sellers, and payers. These incentives, in turn, affect effective price, volume and, in some cases, seller costs.

The agreement between IntriCon and *hi HealthInnovations* is proprietary, so details are not publicly available. IntriCon's investor documents suggest that the agreement required a sizable ramp-up of production to cover an anticipated surge in demand following the program's launch and to meet ongoing demand thereafter, with negotiated sales prices for those products.[135] By pre-negotiating rates with the developer, *hi HealthInnovations* provided consumers with a hearing aid benefit with little or no out-of-pocket costs, at a much lower cost to the payer (UnitedHealthcare) than hearing aids in the traditional channel. This type of arrangement would have directly affected IntriCon's EROI by establishing a sales price and offering the company assurance that a large number of potential customers would gain access to its hearing devices and be able to afford them, virtually assuring a substantial increase in sales. United Health Group does not disclose business unit-specific results, but Dr. Tseng said that "large numbers" of consumers have taken up the benefit.[136]

IntriCon developed the hearing aids at the request of *hi HealthInnovations*, spurring innovation with a promise that sales would follow. Direct investment by payers or other organizations in the development of a potential technology is not a guarantee of successful innovation. Developers may face numerous hurdles during research and development or commercialization, such as scientific challenges, regulatory delays or failures, and unexpected economic costs that reduce the economic value of the new product, relative to any clinical benefits. However, the risks of these adverse events are almost certainly lower for Class I devices such as the hearing aids in this case.

Even if an innovative product is successfully developed and brought to market, the payer and developer may not achieve the desired benefits/returns envisioned in the initial agreement. Depending on the structure of the agreement, the returns may also fluctuate due to market conditions that are hard to

[135] IntriCon Corporation. (2012). Form 10-K annual report filed 3/14/12 for the period ending 12/31/11. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-12-440

[136] Tseng, L. (2015, March 26). *Personal communication.*

predict. Adverse selection is a potential concern for payers with a unique offering in the market, as they may attract disproportionate numbers of people who want and need the new product. Although selection may be a minor concern with a hearing device, it could be significant with technologies targeting expensive treatments or sicker patient groups. Another risk is that competing developers may bring a superior – more innovative – product to market. For the payer, the agreement may lock them into using the inferior product. For the developer, the competition may reduce the potential market for the product developed under the advanced market commitment. In its 2015 annual report for investors, IntriCon noted that several of the firm's competitors "offer more standardized and less technologically advanced products at lower prices," and that competition negatively affected the firm's sales and margins.[137]

Sales of the innovative product may represent a large share of the developer's revenues. Although it is an established company, IntriCon's most recent annual report notes that the firm depends on five customers for about 57 percent of its net sales; the largest customer accounts for almost two-thirds of that amount.[137] Although IntriCon does not disclose that *hi HealthInnovations* is one of those top five customers, it is an important one. Net sales in IntriCon's hearing health business increased by 13.2 percent in calendar year 2012, the first full year of the *hi HealthInnovations* program.[138] Net sales fell by 17.1 percent in 2013, which IntriCon primarily attributed to reduced purchases by *hi HealthInnovations* and weak hearing device sales in conventional channels.[139] Net sales rebounded in 2014, growing by 16.3 percent, because of strong sales to *hi HealthInnovations* and conventional channels.[137]

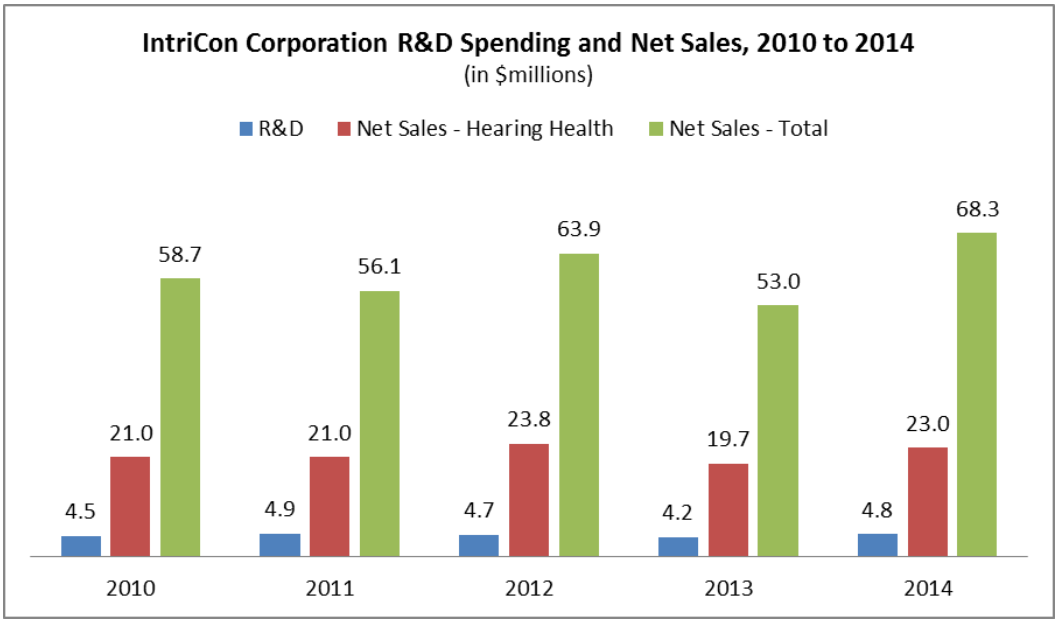
By removing at least some of the uncertainty about the size of the market, and therefore the projected revenues, an advance market commitment theoretically encourages firms to invest in development of the desired product(s). It is not clear how the agreement with *hi HealthInnovations* affected IntriCon's level of investment in efforts to develop new products. IntriCon's filings for investors state that the company conducts research and development (R&D) activities primarily to improve existing products and proprietary technology, including technologies in the *hi HealthInnovations* devices, to spur long-term revenues and margin growth.[137] The manufacturer reported R&D expenditures of $4.9 million in 2011, $4.5 million in 2012, $4.2 million in 2013, and $4.8 million in 2014.[137,138,139] These amounts represent between 7 and 8 percent of total net sales over this period (Figure B1). The variation in the ratio of R&D spending to total net sales does not align with trends in total sales, using either the same year's sales or sales in the preceding year. While it is reasonable to assume that the additional revenues from *hi HealthInnovations* bolstered recent R&D budgets, IntriCon attributed the drop in R&D spending in 2013 primarily to receipt of tax credits and global restructuring – not lower sales.

[137] IntriCon Corporation. (2015). Form 10-K annual report filed 3/6/15 for the period ending 12/31/14. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-15-290

[138] IntriCon Corporation. (2013). Form 10-K annual report filed 3/13/13 for the period ending 12/31/12. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-13-348

[139] IntriCon Corporation. (2014). Form 10-K annual report filed 3/12/14 for the period ending 12/31/13. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-14-317

Figure B1



Source: IntriCon Corporation 2012; 2013; 2014; 2015[140,141,142,143]

As noted, the incentives for manufacturers may vary depending on the structure of the agreement. An approach similar to the design of *hi HealthInnovations*, which appears to be primarily a guarantee of price only with some assurances about quantity, may work best in circumstances where a payer desires a particular product and maintains control over access to that technology once it reaches the market. *hi HealthInnovations* is the sole source for the specific hearing aids it contracted with IntriCon to produce. This winner-take-all approach assured IntriCon of significant sales volume up front, while *hi HealthInnovations* paid discounted rates. As such, this arrangement was beneficial to the payer (UnitedHealth Group) and the developer (IntriCon). However, the arrangement carries risk for IntriCon because it does not guarantee a minimum amount of purchases from *hi HealthInnovations*, those purchases can cease at any time, and it limits the company's ability to sell hearing aids or accessories to another health insurer or directly to consumers.[141] The risk to *hi HealthInnovations* appears to be low, at least with regard to the agreement for the hearing aids, given the characteristics of the agreement disclosed by IntriCon. The primary risk to *hi HealthInnovations* appears to be underutilization of the

[140] IntriCon Corporation. (2012). Form 10-K annual report filed 3/14/12 for the period ending 12/31/11. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-12-440

[141] IntriCon Corporation. (2013). Form 10-K annual report filed 3/13/13 for the period ending 12/31/12. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-13-348

[142] IntriCon Corporation. (2014). Form 10-K annual report filed 3/12/14 for the period ending 12/31/13. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-14-317

[143] IntriCon Corporation. (2015). Form 10-K annual report filed 3/6/15 for the period ending 12/31/14. Retrieved from http://investorrelations.intricon.com/secfiling.cfm?filingID=897101-15-290

benefit or increased competition in the "value" hearing health market, which would reduce return on the investment in setting up the program.

Market competition and regulatory challenges are other potential hurdles that may affect the volume of sales, either directly or by changing incentives for prescribers and consumers. Shortly after launch, *hi HealthInnovations* faced opposition from hearing care providers. The American Academy of Audiology and the Academy of Doctors of Audiology voiced concerns about the lack of intervention by professional audiologists, the validity of the online hearing test and representation of the devices as a "cure" for hearing loss.[144,145] These and other organizations representing audiologists and hearing instrument (aid) specialists argued that direct-to-consumer sales violated state dispensing laws and practices.[145] Other hearing-related organizations, such as the Hearing Loss Association of America which represents consumers, were more supportive of *hi HealthInnovations* as a way to expand access to hearing health care and hearing aids.[146]

Responding to complaints, the FDA investigated the online hearing test and determined that it was a medical device, and it had not received FDA approval prior to marketing. *hi HealthInnovations* was ordered to cease marketing the online test.[147] The FDA's decision did not prohibit marketing and sales of the hearing aids, only the online hearing test developed by *hi HealthInnovations*. However, this decision likely contributed to the drop-off in IntriCon's hearing health sales by reducing consumers' access to testing that was necessary before obtaining the new devices. *hi HealthInnovations* eventually developed a new hearing test kit for use by primary care physicians, nurse practitioners, physician assistants, and other licensed medical professionals.

Although the initial opposition to this new model by hearing health provider groups focused on consumer protection, it also reflects a common reaction when the established providers of a drug, device, or related service see a new product or business model as a threat to their own businesses. Opposition by provider organizations seems to have waned over time; several of the aforementioned

[144] Walden, T., & Vircks, B. (2011, October 31). *Letter to Lisa Tseng, CEO of hi HealthInnovations, from the American Academy of Audiology and the Academy of Doctors of Audiology.*

[145] American Academy of Audiology. (2012). Academy efforts with regard to the UnitedHealthcare/hi HealthInnovations direct-to-consumer hearing aid benefit and online hearing test. Retrieved from http://www.audiology.org/advocacy/academy-efforts-regard-united-healthcarehi-healthinnovations-direct-consumer-hearing-aid

[146] Battat, B. (2012, April 2). Message to audiologists, hearing aid specialists, hearing aid manufacturers. HLAA updates. Retrieved from http://www.hearingloss.org/content/message-audiologists-hearing-aid-specialists-hearing-aid-manufacturers

[147] Silverman, S. D. (2012, March 28). *Letter to Lisa Tseng, CEO of hi HealthInnovations.* Silver Spring, MD: Food and Drug Administration.

organizations sent a joint statement to care providers in August 2012 about how to work with programs such as *hi HealthInnovations*.[148]

The *hi HealthInnovations* approach, led by a single company, may be best suited to fostering innovation in Class I medical devices. In contrast, this approach may not be as well suited to drugs. If a payer invested directly in the development of a new drug product, it would not be possible for the payer, or a subsidiary, to be the exclusive supplier of the drug. A large private payer might be able to get a significant price concession, but use of external benchmarking or administrative pricing schemes by other payers may limit the extent of discounts. For example, Medicaid's "Best Price" provision requires manufacturers to sell drugs to Medicaid at the lowest price offered to commercial payers, in most cases. The private payer would therefore invest in a product that would benefit other payers and society more broadly – including those that did not invest in the product. It is unlikely that this model is feasible for a lone commercial payer to use to promote innovation of a new drug. Similarly, a larger coalition would almost certainly be necessary to drive development of Class II or Class III devices that require more extensive testing and regulatory approvals, which would generally increase research and development costs. Other conditions would also need to be present, such as well-defined endpoints for measuring benefits, and data and infrastructure to do so.[149]

Coalitions of multiple payers, social organizations, or governments may still find the AMC approach feasible for development of products that produce social gains, as illustrated by the GAVI Alliance (formerly, the Global Alliance for Vaccines and Immunization) and its Pneumococcal Vaccine Advance Market Commitment Program for vaccines in developing countries. Research on a pilot program suggests that this model accelerated the roll out of new vaccines to developing countries.[150] Critics of the GAVI program argue that programs that expand use of existing vaccines targeting more common diseases, rather than development of new ones for less common conditions may save more lives for less money, or that traditional discount purchasing mechanisms such UNICEF may be less expensive.[151] However, the AMC approach appears to work well as a mechanism for bringing specific advances to market, relatively quickly.

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[148] American Academy of Audiology, Academy of Doctors of Audiology, & American Speech-Language-Hearing Association. (2012, August 17). *Dear colleague letter*. Retrieved from http://audiology-web.s3.amazonaws.com/migrated/20120817_HearingHealthParadigmShift_letter_to_members.pdf_53a17b4ca667d2.77577871.pdf

[149] Neumann, P. J., Chambers, J. D., Simon, F., & Meckley, L. M. (2011). Risk-sharing arrangements that link payment for drugs to health outcomes are proving hard to implement. *Health Affairs.* 30(12), 2329-2337.

[150] Snyder, C. M., Begor, W., & Berndt, E. R. (2011). Economic perspectives on the advance market commitment for pneumococcal vaccines. *Health Affairs.* 30(8), 1508-1517. doi: 10.1377/hlthaff.2011.0403

[151] Scudellari, M. (2011). Are advance market commitments for drugs a real advance?. *Nature medicine*, *17*(2), 139-139.

CONCLUSION

In sum, the *hi HealthInnovations* hearing aid program is a case in which a payer observed a significant unmet need among its subscribers and the general population. Believing that meeting that unmet need would produce happier customers, health benefits, and potentially lower health care costs, UnitedHealth Group invested directly in a product and distribution model meant to fill that gap. Based on the definition of innovation used in this project, the hearing aids offered by *hi HealthInnovations* might best be deemed incremental innovations. The advance market commitment and new distribution model, rather than the devices, may be the greater innovations, which helped to make hearing aids more affordable and accessible. The specific approach in this case seems most appropriate for similar instances where a payer wants to invest in a relatively low-cost Class I device and has some ability to limit access to the new product. A broader coalition would likely be necessary for the model to work as a tool for encouraging investment in drug products or more complex devices.

APPENDIX C: PREMERA VALUE-BASED FORMULARY CASE STUDY

BACKGROUND

Originally termed the "benefit-based copay," the intent of VBID is to align patients' out-of-pocket costs with the expected clinical benefits of products or services, relative to costs.[152,153] With VBID, patients who are expected to gain the greatest benefit from a product or service pay lower out-of-pocket costs than patients expected to achieve more modest or minimal gains. Economic theory posits that insurance coverage encourages greater consumption of health care products and services by reducing patients' out-of-pocket costs. One of the arguments in favor of cost sharing is that it may reduce overconsumption by incentivizing patients to avoid "low-value" services – that is, where the total costs outweigh the clinical or health benefits. However, patients generally do not have the time, aptitude, access to resources, or motivation to accurately weigh the benefits and costs to themselves, much less from an insurer's or societal perspective. Consequently, patients tend to reduce use of all types of care when cost sharing is applied, not just "low-value" services. By reducing cost-sharing levels for "better" or "more effective" care, and raising cost-sharing levels for less effective care, VBID theoretically steers consumers towards these options and leads to more appropriate use and better outcomes.[152]

One rationale for VBID is to increase patient adherence to beneficial medications and potentially achieve savings (or at least cost neutrality) through reductions in the use of high-cost services such as emergency room visits and hospitalizations. As documented in other reports from this project, many studies indicate that lower cost-sharing levels are associated with more use of medications and services and better adherence to continuing therapies, while increases in cost sharing are associated with reductions in use and adherence, even for "high-value" care.[154]

In theory, cost sharing in a VBID program should vary according to individual circumstances.[155] Economic theory also suggests that, for a given level of value, cost sharing generally should be lower if demand is

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[152] Chernew, M. E., Rosen, A. B., & Fendrick, A. M. (2007). Value-based insurance design. *Health Affairs*, 26(2), w195-w203. Retrieved from http://content.healthaffairs.org/content/26/2/w195.abstract

[153] Fendrick, A. M., Smith, D. G., Chernew, M. E., & Shah, S. N. (2001). A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *American Journal of Managed Care, 7*(9), 861-861-867.

[154] Bruen, B., Cohen, J., DiMasi, J., Docteur, E., Dor, A., Lopert, R., ..., Shih, C. (2014). *Task 3b deliverable: The impact of selected characteristics of reimbursement policies on incentives to invest in the development of innovative healthcare technologies.* Interim report for the Impact of Reimbursement Policies and Practices on Healthcare Technology Innovation project (Department of Health and Human Services' Contract # HHSP23320095635)

[155] Fendrick, A. M., Smith, D. G., Chernew, M. E., & Shah, S. N. (2001). A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *American Journal of Managed Care, 7*(9), 861-861-867.

inelastic, such as for chemotherapy, and higher where it is more elastic.[156] Observers have noted in the past that a cost sharing system with such a significant degree of complexity may not be practical on a broad scale because of the high costs of setting up and maintaining the necessary administrative systems; the paucity of information from which to assess value; and the difficulties of real-time communication of clinical information and cost-sharing amounts between payers, care providers, and consumers.[157] These concerns still appear to be valid, although they may lessen as electronic record systems and data sharing become more common.

Given these challenges, there are two typical approaches to VBID in practice. One approach reduces cost sharing for products and services determined to have greater clinical value irrespective of individual patient characteristics. For example, Pitney Bowes, a large U.S.-based employer, moved asthma inhalers, beta blockers, and statins to its lowest cost tier in 2001. The second approach targets patients with particular diagnoses, offering reduced cost sharing for specific services deemed likely to offer more value. The city of Asheville, NC, and the University of Michigan used this approach in their VBID offerings, specifically targeting employees with diabetes. Aetna operated a program that combined elements of VBID (free or reduced cost sharing) and disease management for post-myocardial infarction patients. Early adopters typically only reduced cost-sharing levels for products and services deemed more valuable, and did not raise cost-sharing levels for other products to compensate.[158]

Regardless of the particular approach, VBID requires a clearly-defined, formal system of assessing value – in terms of benefits relative to costs – to determine the appropriate copayment level.[156] The perspective of the benefit designer, which may be a third-party payer and/or plan sponsor, is critical because that point of view will be a strong determinant of the definition of "value." Although the definition could incorporate social equity or other concerns, the interests of a third-party payer may not align with a societal perspective.

RATIONALE AND OBJECTIVES FOR PREMERA'S VBRX

Discussing the rollout of VBRx at a 2013 conference, Prof. Louis Garrison, a health economist from the University of Washington and member of the Premera Value Assessment Committee, noted that health plans and their sponsors face rapidly rising drug benefit costs, with so-called "specialty drugs" a major driver of growth.[159] He noted that "typical" responses by plan sponsors include changing benefit designs

[156] Fendrick, A. M., Smith, D. G., Chernew, M. E., & Shah, S. N. (2001). A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *American Journal of Managed Care, 7*(9), 861-861-867.

[157] Chernew, M. E., Rosen, A. B., & Fendrick, A. M. (2007). Value-based insurance design. *Health Affairs*, 26(2), w195-w203. Retrieved from http://content.healthaffairs.org/content/26/2/w195.abstract

[158] Choudhry, N. K., Rosenthal, M. B., & Milstein, A. (2010). Assessing the evidence for value-based insurance design. *Health Affairs, 29*(11), 1988-1994. doi:10.1377/hlthaff.2009.0324

[159] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our version?* San Antonio, TX.

to increase patients' cost-sharing amounts and/or shift to consumer-driven models with high deductibles or health savings accounts (HSAs). These changes put the onus on members to be more responsible for their own health care utilization; payers may also put in place patient education, disease management, or other programs focusing on primary or secondary prevention to support these efforts. Prof. Garrison also noted that traditional pharmacy benefit designs use formularies based on the type of drug, such as single source or multiple source, preferred or non-preferred.[160] "Value" in this context tended to be limited to the assessment of net unit costs.

The Premera VBRx program seeks to separate high value drugs from low value ones. A stated objective is to develop a formulary based on incremental comparative effectiveness, where "value" incorporates assessments of both clinical value and cost.[160] Some of the guiding principles were:

- The design should be evidence-based, following the guidance of a decision-making committee made up of internal and external experts;
- The process should be transparent, and take into account input from practicing physicians and other providers, and;
- It should explicitly incorporate health economic data.[160]

CHARACTERISTICS OF THE PREMERA VBRX PROGRAM

Two committees formally evaluate each drug to determine coverage and placement on the Premera VBRx. The first is the Pharmacy and Therapeutics (P&T) Committee, which consists of seven physicians, three pharmacists, a pharmacy benefit manager, and a lay member – none of whom may be Premera associates.[160] The P&T Committee examines the clinical benefit of products, including efficacy and safety. The detailed clinical review includes synthesis of evidence from multiple sources, peer review of the evidence, and presentation of findings during a formal P&T Committee review. Although the P&T Committee may consider cost in cases where there are multiple therapies deemed to have comparable clinical benefit, no formal economic evaluation occurs at this point.[161]

The second committee is the Value Assessment Committee (VAC), which determines a drug's value and tier placement. The VAC includes four economists, two practicing clinicians, a bioethicist, and one member of the public.[161] The diversity of the membership reflects the fact that the VAC considers the quality of evidence for comparative effectiveness; effects on other medical costs and quality of life/productivity; and societal values including patient preferences, equity, and end of life care.

[160] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our Version?* San Antonio, TX.

[161] Sullivan, S. D., Yeung, K., Vogeler, C., Ramsey, S. D., Wong, E., Murphy, C. O., . . . Watkins, J. B. (2015). Design, implementation, and first-year outcomes of a value-based drug formulary. *Journal of Managed Care & Specialty Pharmacy: JMCP, 21*(4), 269-269-275.

The VAC assessments rely on "credible" sources of data and results from cost-effectiveness analyses, such as manufacturers' models; published economic studies and systematic reviews (e.g., Cochrane reviews); data from the Cost Effectiveness Analysis Registry compiled by the Center for the Evaluation of Value and Risk in Health (CEVR) at Tufts Medical Center; and reviews from assessment organizations in other countries, including the National Institute for Health and Care Excellence (NICE) in the United Kingdom and the Canadian Agency for Drugs and Technologies in Health (CADTH).[162] To prepare for the VAC meetings, reviewers examine the evidence; develop specifications for cost-effectiveness model(s); build, run, and test model(s) for sensitivity to different assumptions; and then synthesize the evidence into a monograph for peer review and presentation to the VAC.[163] Premera developed assessments for drugs in the 25 highest-volume drug classes used by its members, representing approximately 75% of drug utilization in the plan.[162] Drugs in classes that were not assessed received a tier assignment based on their placement in the standard formulary used in Premera's other drug plans.[162]

The Premera VBRx strays somewhat from the ideal VBID structure in that the amount of cost sharing does not explicitly account for the value of the specific service for a particular patient. The latter would be difficult and resource intensive to implement and maintain, as it would require tailored assessments of value. Instead, the VBRx benefit has four tiers, based on each drug's incremental cost effectiveness ratio (ICER), which is measured as cost per quality-adjusted life year (QALY) of the drug generally, not for a specific patient. Premera created the thresholds for each tier, shown in Table C1, based on thresholds used internationally and cost-sharing arrangements of U.S. commercial plans.[162] The "standard" QALY thresholds are not absolute, and some products may be placed on a "preventive list." Drugs for rare conditions ("ultra-orphan" drugs) are subject to different, more liberal "special case" thresholds (Table C1). Even after this assessment, a product's placement on the VBRx may still depend on extenuating clinical or societal circumstances.

[162] Sullivan, S. D., Yeung, K., Vogeler, C., Ramsey, S. D., Wong, E., Murphy, C. O., . . . Watkins, J. B. (2015). Design, implementation, and first-year outcomes of a value-based drug formulary. *Journal of Managed Care & Specialty Pharmacy: JMCP, 21*(4), 269-269-275.

[163] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our Version?* San Antonio, TX.

Table C1

Tier	Standard Thresholds	Special Case Thresholds
Preventive tier	-- not applicable --	-- not applicable --
Tier 1: Highly cost-effective	<$10,000 per QALY	<$50,000 per QALY
Tier 2: cost-effective	$10,000 to $50,000 per QALY	$50,000 to $150,000 per QALY
Tier 3: somewhat cost-effective	$50,000 to $150,000 per QALY	>$150,000 per QALY
Tier 4: minimally cost-effective	>$150,000 per QALY or insufficient evidence to determine cost-effectiveness	Insufficient evidence to determine cost-effectiveness

Source: Sullivan et al., 2015[164]

Table C2

Tier	Co-payment
Preventive	$0
Tier 1	$20
Tier 2	$40
Tier 3	$65
Tier 4	$100

Source: Sullivan et al., 2015[164]

The VBRx copayments vary by tier (Table C2). Products designated for the preventive tier have no cost sharing. Products on the other tiers have fixed cost sharing amounts that increase on each successive tier – that is, as the assessed cost-effectiveness of a product decreases, the out-of-pocket cost to the consumer increases.

For Premera, the VBRx program enabled an initial cost shift to members without affecting adherence in high value drug classes in the first year following implementation.[165] The plan's pharmacy payments dropped by about 3% per member per month (PMPM) compared to payments in the prior year.[164] Compared to simulated PMPM amounts based on historical trends, which were intended to model a counterfactual where the VBRx had not been implemented, the estimated savings were about 11 percent PMPM.[164]

The impact on member and overall health plan costs has not been determined and is unclear.[164] Consumers experienced a range of effects under the VBRx. Overall, group members saw their out-of-pocket costs increase by 12 percent for all medications, but patient with diabetes, hypertension, and dyslipidemia experienced lower overall increases across all of their medications (5%, 8%, and 2%, respectively).[164] However, the plan increased cost-sharing levels simultaneous to the launch of the VBRx,

[164] Sullivan, S. D., Yeung, K., Vogeler, C., Ramsey, S. D., Wong, E., Murphy, C. O., . . . Watkins, J. B. (2015). Design, implementation, and first-year outcomes of a value-based drug formulary. *Journal of Managed Care & Specialty Pharmacy: JMCP, 21*(4), 269-269-275.

[165] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our Version?* San Antonio, TX.

which contributed to a cost shift: high-utilizers experienced both co-payment decreases and increases, while low-utilizers generally paid higher out-of-pocket costs.[166]

Subscribers' responses to the cost shift varied, with some shifting to lower-cost drugs, and some paying the higher costs and continuing on original medications.[166] Skipping medications, cutting tablets, or other strategies to reduce out-of-pocket costs were purportedly rare.[166] Overall use and adherence increased among hypertension patients; effects for other groups were not statistically significant.[166] Although Premera intended to convey the value of products through variation in copayment levels, participants in focus groups convened by the organization were generally unaware or lacked understanding regarding the VBRx.[167] Members of the Premera VAC and others involved in the development of the VBRx characterized these focus group participants as "positive" toward the use of evidence and efforts to hold down costs and encourage consumers to take more responsibility for their own health, but noted that they also wanted to know who determined the value of drugs.[166,167]

HOW MIGHT BROADER USE OF PROGRAMS LIKE VBRX INFLUENCE INNOVATION IN DRUGS OR MEDICAL DEVICES?

VBID is a concept with significant traction among state and federal policymakers, who appear to view it as conceptually appealing even though implementation has been limited to date. Many stakeholders have voiced support for VBID, and Section 2713(a) of the Affordable Care Act explicitly encourages development of guidelines for VBID programs. There has been some controversy about the attention given to VBID, in part due to the limited evidence available for assessment of the potential effects on clinical outcomes, other benefits, and costs from the perspective of patients, third-party payers, and plan sponsors.[168]

Despite its high profile, uptake of VBID has been slow among payers and plan sponsors. To date, most efforts in the U.S. have been limited in scope compared to the Premera VBRx program. Most payers apply VBID programs to a very small number of therapeutic classes. One effort that was broader in scope was a value-based formulary called RxImpact developed by Humana, where drugs were placed into one of four groups based on the insurer's assessment of the ability of a drug to avoid more serious medical events (e.g., hospitalizations) and the length of time before its use might affect total medical expenditures for the plan. The cost-sharing structure did not vary for different patients, but instead the

[166] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our Version?* San Antonio, TX.

[167] Sullivan, S. D., Yeung, K., Vogeler, C., Ramsey, S. D., Wong, E., Murphy, C. O., . . . Watkins, J. B. (2015). Design, implementation, and first-year outcomes of a value-based drug formulary. *Journal of Managed Care & Specialty Pharmacy: JMCP, 21*(4), 269-269-275.

[168] Choudhry, N. K., Rosenthal, M. B., & Milstein, A. (2010). Assessing the evidence for value-based insurance design. *Health Affairs, 29*(11), 1988-1994. doi:10.1377/hlthaff.2009.0324

plan paid a fixed allowance per prescription depending on the group the drug was in, and the patient paid any difference between the allowance and the drug's retail cost.[169]

Chernew and colleagues (2007) list a number of challenges and concerns that may dissuade payers and plan sponsors from broader adoption of programs like VBRx, including:

- Cost of implementation;
- Cost of increased use of drugs relative to potential benefits;
- Lack of access to data/information necessary to determine appropriate cost-sharing levels;
- Lack of sufficiently detailed data/research evidence for all groups and/or conditions;
- Human resources and ethics concerns (e.g., "favoring" certain people with lower cost sharing);
- HIPAA/privacy concerns with high levels of information about specific patients changing hands to administer the program;
- Legal barriers (e.g., government program restrictions on financial incentives for patients);
- Concerns about affecting incentives for patients to use products with lower total costs to the payer or system (such as generic drugs) if cost sharing is also reduced for products with higher total costs, and;
- Possibility of adverse selection, if a benefit viewed as particularly generous for people with a particular condition attracts those people to the employer/health plan. [170]

From the perspective of a third-party payer, plan sponsor, or self-insured organization – all groups for which total costs of care are most relevant – higher levels of churn/turnover among plan participants may discourage use of VBID if they believe they will incur higher total costs for drug benefits without capturing the future benefits, such as better health outcomes and cost savings.[171] Payers with less participant turnover, such as Medicare or the Veterans' Administration, may have longer investment horizons. Experts consulted for this study noted that private payers may also be taking longer perspectives than may have assumed in the past.[172]

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[169] Lewis, C. (2007). Will value-based pharmacy design take off? *National managed care outlook*. HealthLeaders-Interstudy.

[170] Chernew, M. E., Rosen, A. B., & Fendrick, A. M. (2007). Value-based insurance design. *Health Affairs*, 26(2), w195-w203. Retrieved from http://content.healthaffairs.org/content/26/2/w195.abstract

[171] Choudhry, N. K., Rosenthal, M. B., & Milstein, A. (2010). Assessing the evidence for value-based insurance design. *Health Affairs, 29*(11), 1988-1994. doi:10.1377/hlthaff.2009.0324

[172] These experts offered several reasons why plans may be taking on longer investment horizons: (1) they may have lower levels of expected turnover of plan participants, related to people holding onto jobs longer both during and immediately following the recent recession; (2) consolidation in the marketplace has led to larger health plans and increased the likelihood that people will remain in a plan operated by the insurer, even if they change jobs, and; (3) many insurers participate in multiple markets, including employer-based, Marketplace exchanges (individual), and Medicare Advantage, so they may cover the same person at multiple points during his/her lifetime, even if there are gaps in coverage.

Studies indicate that VBID initiatives are associated with modest increases in adherence to targeted therapies, although effects on costs and clinical outcomes are less clear.[173] Consequently, for payers, drug spending tends to increase, while effects on non-medication spending and total spending are unclear. For example, Blue Cross, Blue Shield of North Carolina attempted a VBID plan in 2008, which eliminated copayments for generic medications and lowered copays for brand-name drugs; though patient adherence improved and hospital admissions decreased, there were no changes in emergency department use or in health expenditures and early experience was not cost-neutral.[174] A recent review of empirical evidence from VBID programs found that the plans that achieved the best patient adherence were those that targeted high-risk patient subgroups (for whom cost is a significant barrier), had more generous reductions in out of pocket costs, offered wellness programs, and were only available for medication ordered by mail.[175]

Quantifying the return for payers from VBID is challenging. Overall, for the patient and payer combined, evidence suggests that drug spending may increase without a significant change in non-medication or total spending.[176] However, observers have noted that changes in adherence attributed to VBID programs tend to be modest, the evidence base is small, and the methods often not very rigorous.[177] Some observers have suggested that VBID plans may not achieve savings because patients in commercial plans tend to be less price sensitive, and the high-cost events that these programs may seek to avoid, such as emergency room visits and hospital stays, are relatively rare – so it is harder to offset the extra costs from lower copayments.[178]

PBMs have sometimes expressed doubts about VBID, with some viewing it as a higher cost method to improve adherence than other strategies.[177] A 2007 Health Leaders-Interstudy report quoted Bob Craig, an executive from Medco Health Solutions, saying that, with regard to VBID, "[e]mployers want to know the [return on investment] as well as the time required for the healthcare payment on the

[173] University of Michigan Center for Value-Based Insurance Design. (2014). *The evidence for V-BID: Validating an intuitive concept.* (Brief).

[174] Maciejewski, M. L., Wansink, D., Lindquist, J. H., Parker, J. C., & Farley, J. F. (2014). Value-based insurance design program in North Carolina increased medication adherence but was not cost neutral. *Health Affairs, 33*(2), 300-308. doi:10.1377/hlthaff.2013.0260

[175] Choudhry, N. K., Fischer, M. A., Smith, B. F., Brill, G., Girdish, C., Matlin, O. S., . . . Shrank, W. H. (2014). Five features of value-based insurance design plans were associated with higher rates of medication adherence. *Health Affairs, 33*(3), 493-501. doi:10.1377/hlthaff.2013.0060

[176] Yeung, K. (2014). Design, implementation, and first-year results of a value-based formulary. *ISPOR 19th Annual International Meeting,* Montreal, Quebec, Canada.

[177] Fairman, K. A., & Curtiss, F. R. (2011). What do we really know about VBID? Quality of the evidence and ethical considerations for health plan sponsors. *Journal of Managed Care Pharmacy : JMCP, 17*(2), 156-174. doi:2011(17)2: 156-174

[178] Melnick, S. J., & Motheral, B. R. (2010). Is "value-based" value wasted? Examining value-based insurance designs through the lens of cost-effectiveness. *Journal of Managed Care Pharmacy* 16(2), 130-133.

investment."[179] Mr. Craig noted that how an employer or other plan sponsor or designer views VBID for a particular set of patients may depend on the quality of the available evidence used to inform decisions about "value," the investment horizon of the employer or payer, and the underlying benefit philosophy and expectations.[179] He added that "[VBID] may prove to be less well suited for employers with younger workforces or higher turnover."[179] Some of the experts consulted for this project echoed these sentiments.

Both patients and health care providers must buy into the VBID concept.[180] VBID raises difficult questions that require value judgments. Who decides what constitutes "value" for a particular plan is clearly important and potentially controversial. Some may disagree about which evidence is best or conclusions based on that evidence – for example, the controversy over the U.S. Preventive Task Force's recommendations concerning breast cancer screening highlight that major differences of opinion are likely to remain even in cases where decisions are evidence-based. Concerns about value judgments, and the challenges of obtaining patient and provider buy-in, are likely to be magnified in the context of specialty drugs.[181] A systematic review of the literature on specialty drug therapies for rheumatoid arthritis, multiple sclerosis, and breast cancer concluded that these therapies offered significant potential benefits for patients, but achieving the best outcomes and most cost-effective use required identifying the most effective product(s) and the most appropriate patients within each category.[182] Other research indicates that specialty drugs may confer somewhat greater benefits than traditional drugs, but at higher costs and with considerable variation in costs per QALY.[183]

For programs like Premera's VBRx to succeed on a broader scale, plans and plan sponsors will require access to data and empirical evidence about clinical benefits and costs, both monetary and non-monetary. One potential limitation is that limited availability of evidence from cost-effectiveness assessments may prevent optimal placement of drugs.[184] Some developers such as Novartis, BMS, Amgen, Lilly, and Sanofi-Aventis reportedly adapted European models for use in the U.S. context or

[179] Lewis, C. (2007). *Will value-based pharmacy design take off? National managed care outlook*. HealthLeaders-Interstudy.

[180] Fendrick, A. M., Smith, D. G., Chernew, M. E., & Shah, S. N. (2001). A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *American Journal of Managed Care, 7*(9), 861-861-867.

[181] Fendrick, A. M., Buxbaum, J., & Westrich, K. (2014). *Supporting consumer access to specialty medications through value-based insurance design.* Washington, DC: National Pharmaceutical Council.

[182] Zalesak, M., Greenbaum, J. S., Cohen, J. T., Kokkotos, F., Lustig, A., Neumann, P. J., . . . Dubois, R. W. (2014). The value of specialty pharmaceuticals - A systematic review. *Journal of Managed Care Pharmacy, 20*(6)

[183] Chambers, J. D., Thorat, T., Pyo, J., Chenoweth, M., & Neumann, P. J. (2014). Despite high costs, specialty drugs may offer value for money comparable to that of traditional drugs. *Health Affairs*, 33(10), 1751-1760

[184] Yeung, K. (2014). Design, implementation, and first-year results of a value-based formulary. *ISPOR 19th Annual International Meeting,* Montreal, Quebec, Canada.

otherwise cooperated with the Premera VAC.[185] However, the authors of a recent article describing the program's roll-out and early results were "concerned by the frequency with which [the VAC's] requests for economic data [from manufacturers] were either denied or ignored," some of which may have been attributable to manufacturers' perceptions about the legality of sharing this information.[186]

The willingness of manufacturers to assist in value-based assessment processes may depend on the extent to which they view the processes as transparent, fair, and, ultimately, beneficial in terms of placement of at least some of their most important products. Given the general sentiments expressed in studies of existing VBID programs that more and better data are needed, expansion of VBID programs would likely lead to more pressures on developers to collect and share data. In theory, more data requires more studies and higher costs of product development and/or sale, potentially reducing developers' expected return on investment (EROI). However, experts consulted during this study noted that payers worldwide are already demanding more and better data for decision-making, so it is not clear whether more use of VBID would dramatically increase costs of new drug and device development for manufacturers relative to current trends. Current trends also may already reflect a growing emphasis on value in other reimbursement approaches, not just VBID. Theoretically, if more plans explicitly incorporate value into their assessments that determine availability of products and cost sharing for patients, developers and manufacturers would be incentivized to invest in products that they believe payers will view as innovative (i.e., meeting more significant unmet needs and/or providing greater net health benefits relative to existing treatments) and potentially consumer-welfare enhancing.

In lieu of manufacturer participation in assessment processes, plans will need to develop expertise and capacity internally to conduct value assessments, as Premera did, but that will likely raise administrative costs for the payer. The Premera experience suggests that local champions at the plan, accompanied by health economists and others who will provide expertise, are important for creation and sustainability of a VBID program.

VBID explicitly implicates changes in out-of-pocket payments for patients, but it is less clear that formal assessments of value would lead to changes in sales prices for manufacturers/developers. Rebates and other discounts negotiated between payers and manufacturers or other sellers are almost always kept secret, and the Premera VBRx program is no exception. In theory, value-based methods of determining payment amounts should decrease payment amounts (at least the payer's share) for novel products that are not innovative or cost-reducing, while increasing payment amounts for innovative products, commensurate with the level of additional benefit. The VBRx uses cost-effectiveness thresholds to determine tier placement, but with the caveat that a product's placement on the VBRx may still depend

[185] Garrison, L. (2013). Are the Europeans doing a better job evaluating drugs than US P&T committees? The gap between CER and HTA. *AMCP Foundation Symposium: Transplanting European Health Technology Assessment (HTA) to America? What's wrong with our Version?* San Antonio, TX.

[186] Sullivan, S. D., Yeung, K., Vogeler, C., Ramsey, S. D., Wong, E., Murphy, C. O., ..., Watkins, J. B. (2015). Design, implementation, and first-year outcomes of a value-based drug formulary. *Journal of Managed Care & Specialty Pharmacy: JMCP, 21*(4), 269-269-275.

on extenuating clinical or societal circumstances. Therefore, it is unclear how closely Premera's concept of value aligns with the definition of innovation used in this project, which is a function of the extent to which a drug or device addresses a disease or condition for which there is a substantive (i.e., non-trivial) unmet or inadequately met need, and whether, and to what extent, the new product offers clinically meaningful benefits compared to existing treatments.

Theoretically, broader use of VBID and value-based formularies also would lead to less utilization of products and services with little value added, and more utilization for products with higher value. Assuming payments and utilization change in this manner, VBID may potentially increase incentives to invest in R&D aimed at products that are more likely to be deemed as substantial and radical innovations. The modest effects on utilization in the few VBID programs assessed to date do not suggest major changes in health plans' negotiating power compared to manufacturers solely because of VBID, but the existing evidence is insufficient to draw any definitive conclusions about broader applications.

CONCLUSION

Further evaluation of programs such as Premera's VBRx is needed to determine how broader use may ultimately affect incentives in the marketplace that affect the return on investment for developers of new products, including sales volume, sales prices, and development costs. Longer study periods may help to tease out delayed effects on spending, health outcomes, or other factors. A broader focus on total costs to a health plan is necessary. An assessment of spillover effects is also important; where VBID applies to a particular category of services, such as drugs, but not others, there may be interactions with other reimbursement systems for other services.[187] To date, the evidence base from Premera's VBRx and VBID programs more broadly – at least that available in broadly-accessible public sources – is insufficient to truly understand how broader adoption may affect innovation for healthcare technologies.

[187] Fendrick, A. M., Smith, D. G., Chernew, M. E., & Shah, S. N. (2001). A benefit-based copay for prescription drugs: Patient contribution based on total benefits, not drug acquisition cost. *American Journal of Managed Care, 7*(9), 861-861-867.

APPENDIX D: NICE (UK) PERFORMANCE-BASED REIMBURSEMENT FOR VELCADE®

BACKGROUND - NICE AND ITS ROLE

The National Institute for Health and Care Excellence (NICE) was established in 1999 as the National Institute for Clinical Excellence, a special health authority with the explicit objectives of reducing variation in the availability and quality of treatments and care in the UK National Health Service (NHS), promoting the diffusion and uptake of new technologies, setting quality standards, and improving efficiency.[188] In 2005 NICE was merged with the Health Development Agency, the development of public health guidance was added to its remit, and its name changed to the National Institute for Health and Clinical Excellence.

Since January of that year the NHS in England and Wales has been legally obliged to provide funding for those medicines and treatments recommended by NICE, within three months of the release of the relevant NICE Guidance.[189] This was, at least in part, the result of an effort to address well-publicized "postcode lottery" anomalies in which certain less-common treatments were funded in some parts of the UK but not in others, due to local decision-making and fundholding within the NHS.[189]

Subsequently, in April 2013 NICE was established in primary legislation, becoming a Non-Departmental Public Body (NDPB) accountable to the Department of Health, but operationally independent of government. At that time the name was changed again, to the National Institute for Health and Care Excellence, reflecting the acquisition of additional responsibility for developing guidance and quality standards in social care.[190]

Today NICE's role involves developing and promulgating guidance in four areas:

- the use of health technologies within the NHS (such as the use of new and existing medicines, treatments and procedures);
- clinical practice (guidance on the appropriate treatment and care of people with specific diseases and conditions);
- guidance for public sector workers on health promotion and ill-health avoidance; and
- guidance for social care services and users.

NICE appraisals of medicines and other health technologies are based primarily on assessments of comparative clinical effectiveness and cost–effectiveness in various circumstances. Importantly, while

[188] Chalkidou K, Tunis S, Lopert R, Rochaix L et al. Comparative Effectiveness Research and Evidence-Based Health Policy: Experience from Four Countries. *Milbank Quarterly*. 2009;87(2):339–67.

[189] Sorenson C, Drummond M, Kanavos P, McGuire A (2008). *National Institute for Health and Clinical Excellence (NICE): How does it work and what are the implications for the US?* (Washington: National Pharmaceutical Council, 2008).

[190] National Institute for Health and Care Excellence (2013). *NICE Charter*. Retrieved from http://www.nice.org.uk/Media/Default/About/Who-we-are/NICE_Charter.pdf

the NICE Board sets the organization's strategic priorities and policies, NICE guidance and other recommendations are made by independent committees.

The status of NICE guidance is reinforced in the NHS Constitution, which states that patients have the right to any drugs and treatments recommended by NICE for use in the NHS, if the physician responsible for the patient's care considers them to be clinically appropriate.[191]

NICE'S APPRAISAL OF VELCADE (BORTEZOMIB)

Bortezomib is an anti-neoplastic agent belonging to a novel class of drugs known as proteasome inhibitors. In 2005 bortezomib held UK marketing authorization as monotherapy *for the treatment of progressive multiple myeloma in patients who have received at least one prior therapy, and who have undergone, or are unsuitable for, bone marrow transplantation.*

NICE's appraisal was based largely on evidence from the APEX (Assessment of Proteasome Inhibition for Extending Remissions) trial, at that time the largest published randomized controlled trial of the treatment of relapsed multiple myeloma. The trial compared response rate, time to disease progression and overall survival in patients treated with bortezomib with those treated with high dose dexamethasone (HDD), the standard of care at the time for patients who had relapsed following initial treatment for multiple myeloma.[192] Patients in the bortezomib arm experienced statistically significant improvements in time to disease progression and overall survival, and the NICE APPraisal Committee concluded that bortezomib monotherapy was more clinically effective than HDD monotherapy for the treatment of relapsed multiple myeloma.[193]

Bortezomib was not found to be comparatively cost effective however; for patients at first relapse, the ICER for bortezomib over HDD was estimated at £31,000 per life year gained, or £38,000 per QALY.[193,194,195] The ICER threshold in England is generally in the range of £20,000 - £30,000,[196] unless certain 'end-of-life criteria' apply.[197,198,199]

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[191] National Institute for Health and Care Excellence (2013). *NICE Charter*. Retrieved from www.nice.org.uk/Media/Default/About/Who-we-are/NICE_Charter.pdf

[192] Richardson PG et al (2005). Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. *N Engl J Med* 352(24):2487-98.

[193] National Institute for Health and Clinical Excellence (2006). *Final Appraisal Determination Bortezomib Monotherapy for Relapsed Multiple Myeloma.* Retrieved from http://www.nice.org.uk/guidance/ta129/resources/final-appraisal-determination-bortezomib-monotherapy-for-relapsed-multiple-myeloma3 (accessed May 05, 2015).

[194] Where treatment was limited to patients at second relapse or third relapse, the ICERs increased to £77,000 and £107,000 per life year gained, respectively.

[195] Ferrario, A., & Kanavos, P. (2015). Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden. *Social Science & Medicine*; 124: 39–47

As noted in the Task 3a report, we define a healthcare technology to be a consumer welfare-enhancing innovation if it meets our criteria for innovation *and* generates consumer surplus.[200] NICE's appraisal committee concluded that despite evidence that bortezomib was more clinically effective than HDD, the opportunity costs of its acquisition and diffusion would exceed the anticipated value of the projected incremental benefits of treatment. Thus in this circumstances bortezomib would not meet the definition of a consumer welfare-enhancing innovation.

THE MANUFACTURER'S RESPONSE – A RISK SHARING PROPOSAL

Wishing to avoid a negative recommendation by NICE, Janssen-Cilag put forward a proposal to the UK Department of Health (DoH) for a novel, performance-based, risk-sharing arrangement (referred to as a Patient Access Scheme or PAS). The proposal included a provision for treatment cessation in patients failing to achieve a pre-defined response (based on measuring serum levels of M-protein, a tumor marker indicative of tumor shrinkage and an accepted surrogate measure of disease progression), and reimbursement to the NHS for cases of treatment failure. For each patient failing to achieve sufficient tumor shrinkage as measured by a reduction in serum M protein of 50% or more, Janssen-Cilag agreed to provide the NHS with a refund equal to the cost of that patient's treatment, or the same amount of the drug for another patient, at no charge to the NHS.[195,201]

Following the DoH's in-principle acceptance of the risk-sharing arrangement, the drug was reanalyzed by NICE. After analyzing various new economic considerations brought about by the risk-sharing arrangements, the anticipated ICER was calculated to be £20,700 and the medicine was recommended for use within the NHS.[201]

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[196] National Institute for Health and Clinical Excellence (2004). *Guide to the methods of technology appraisal*. Retrieved from http://www.nice.org.uk/page.aspx?o=201974

[197] NICE's 'reference case' states that all QALYs are deemed to be of equal social value, regardless of to whom they accrue or the context in which they are enjoyed. However in January 2009, NICE issued supplementary advice effectively allowing a higher acceptable ICER when appraising life-extending, end-of-life treatments. See (NICE, 2009a) and (NICE, 2009b):

[198] National Institute for Health and Clinical Excellence (2009a). *Appraising Life-extending, End of Life Treatments* (London: NICE, 2009)

[199] National Institute for Health and Clinical Excellence (2009b). *End of Life Treatments: Summary Response to Consultation* (London: NICE, 2009)

[200] Bruen, B., Cohen, J., DiMasi, J., Docteur, E., Dor, A., Lopert, R., …, Shih, C. (2014). *Task 3a deliverables: Conceptual Model, Recommended Characteristics for Analysis, and Analytical Framework.* Interim Report for the Impact of Reimbursement Policies and Practices on Healthcare Technology Innovation project (Department of Health & Human Services' Contract# HHSP23320095635).

[201] National Institute for Health and Clinical Excellence (2007). *Final Appraisal Determination Bortezomib Monotherapy for Relapsed Multiple Myeloma*. Retrieved from http://www.nice.org.uk/guidance/ta129/resources/bortezomib-monotherapy-for-relapsed-multiple-myeloma-final-appraisal-determination3 (accessed May 05, 2015)

The final guidance issued by NICE specified that:

Bortezomib monotherapy is recommended as an option for the treatment of progressive multiple myeloma in people who are at first relapse having received one prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation, under the following circumstances:

- *the response to bortezomib is measured using serum M protein after a maximum of four cycles of treatment, and treatment is continued only in people who have a complete or partial response (that is, reduction in serum M protein of 50% or more or, where serum M protein is not measurable, an appropriate alternative biochemical measure of response) and*
- *the manufacturer rebates the full cost of bortezomib for people who, after a maximum of four cycles of treatment, have less than a partial response (as defined above).*

DISCUSSION

Risk-sharing arrangements (RSAs) in healthcare between payers and manufacturers are not new. Purely financial RSAs, under which rebates are paid or prices reduced where utilization or expenditure exceed pre-determined thresholds,[202] have been part of the reimbursement landscape in a number of countries for some time.[203,204] More recent, however, is the advent of the performance-based RSA, where payment is contingent on the benefit of a technology being monitored in individual patients within a specified population over a pre-determined period (reflecting actual clinical use), and with the price paid, or amount of reimbursement based on the demonstration of a pre-specified response to treatment.

In the UK, PAS are negotiated within the framework of the general voluntary agreement between the DoH and the pharmaceutical industry, known as the Pharmaceutical Price Regulation Scheme (PPRS). The PPRS underwent substantial reform in 2009, following an evaluation by the Office of Fair Trading (OFT) that recommended replacing existing profit and price controls with a more value-based approach to pricing.[205] As a result of the OFT report, the new PPRS defined a clear typology of PASs in the UK, consisting of two main types: financially based schemes and outcome-based schemes. In the first case, the company does not alter the list price of the medicine but offers discounts or rebates linked to

[202] These may, for example, represent the anticipated size of the population with a particular disease or condition, or in which a drug is thought to be acceptably cost effective.

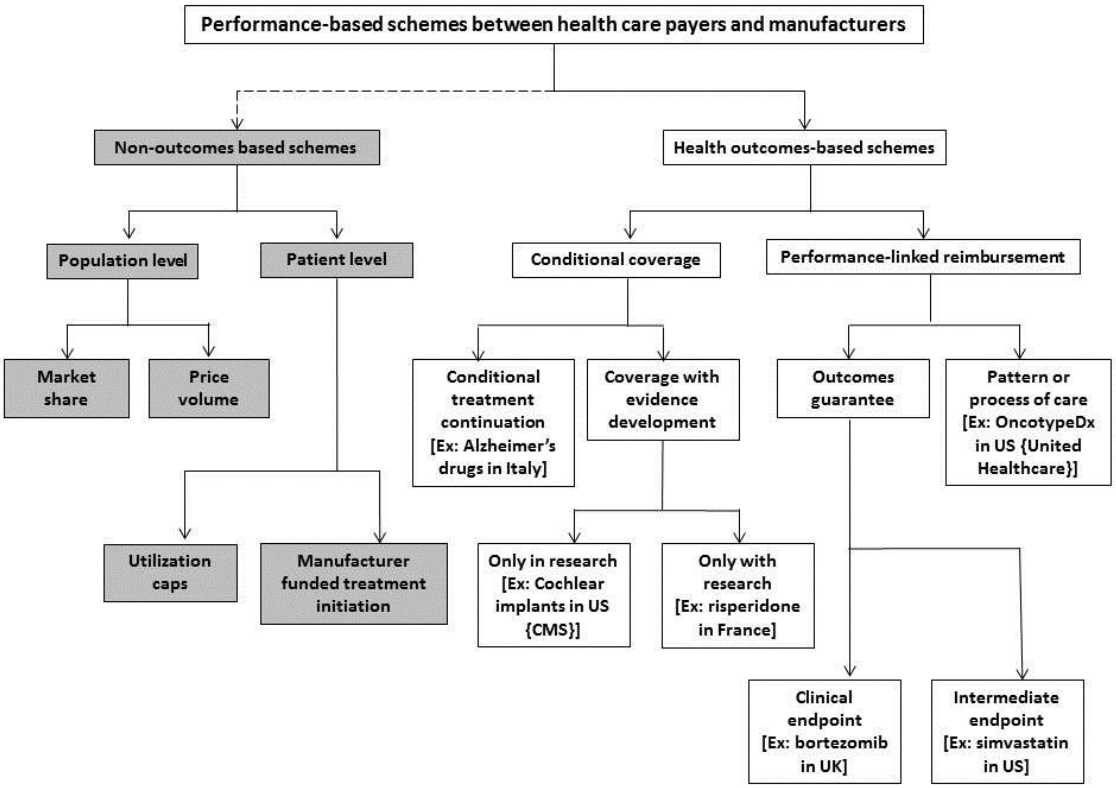
[203] Adamski, J., Godman, B., Ofierska-Sujkowska, G., Boguslawa, O., Herholz, H., Wendykowska, K., …, Gustafsson, L.L. (2010). Risk sharing arrangements for pharmaceuticals: potential considerations and recommendations for European payers. *BMC Health Services Research*;10:153.

[204] Neumann, P.J., Chambers, J.D., Simon, F., & Meckley, L.M. (2011). Risk-sharing arrangements that link payment for drugs to health outcomes are proving hard to implement. *Health Affairs* ;30(12):2329-37.

[205] Office of Fair Trading (2007). *The Pharmaceutical Price Regulation Scheme: An OFT market study.* Retrieved from http://webarchive.nationalarchives.gov.uk/20140402142426/http://www.oft.gov.uk/shared_oft /reports/comp_policy/oft885.pdf

several variables, such as the number of patients treated, or the response of these patients to the treatment. In the second case, the outcome-based schemes have four different subtypes: proven value, price increase, expected value rebate, and risk sharing.[206] Figure D1 illustrates that typology.

Figure D1: Typology of Performance-based Patient Access Schemes in the UK



Source: Carlson et al (2010)[207]

The Velcade PAS was not the first arrangement to involve *performance-based* risk-sharing in the UK (see Figure D2). In 2002 an agreement was reached to facilitate access to a number of multiple sclerosis (MS) medications within the NHS, subject to data collection to support prior estimates of cost-effectiveness. Uncertainty about the long-term cost-effectiveness of beta interferons (Avonex, Betaferon, Rebif) and

[206] The Association of the British Pharmaceutical Industry, Department of Health, et al. *The Pharmaceutical Price Regulation Scheme, 2009*. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/207462/dh_098498.pdf

[207] Carlson, J.J., Sullivan, S.D., Garrison, L.P., Neumann, P.J., & Veenstra, D.L. (2010). Linking payment to health outcomes: A taxonomy and examination of performance-based reimbursement schemes between healthcare payers and manufacturers. *Health Policy*; 96(3): 179-190

glatiramer (Copaxone) for MS had led NICE to recommend against their use in the NHS.[208] Under an arrangement reached with the manufacturers, the DoH agreed to allow the prescribing of these drugs according to the Association of British Neurologists' 2001 guidelines, conditional on the development of a 10-year monitoring study that would collect data on the progression of disease in treated patients. If any product failed to show benefits consistent with projections made at the outset of the arrangement, the subsequent price to the NHS would be reduced to restore cost effectiveness to a benchmark of £36,000 per quality adjusted life year (QALY) evaluated over a 20-year horizon.[209] Aspects of the design of the arrangement were subsequently criticized, including the time horizon, choice of outcome measure, and use of historical controls. Concerns were also expressed about data governance issues, and the costs and effort involved in data collection.[208,210,211,212]

[208] Sudlow, C.L., & Counsell, C.E. (2003). Problems with UK government's risk sharing scheme for assessing drugs for multiple sclerosis. *BMJ*; 326(7385):388–92.

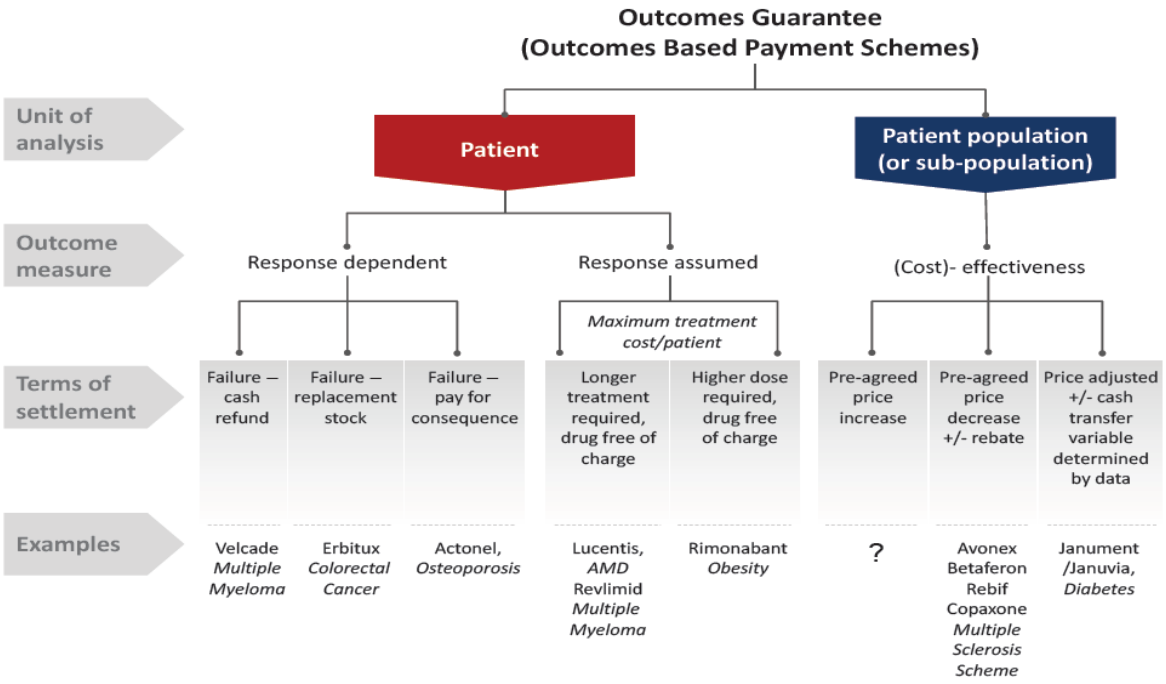
[209] Boggild, M., Palace, J., Barton, P., Ben-Shlomo, Y., Bregenzer, T., Dobson, C., & Gray, R. (2009). Multiple sclerosis risk sharing scheme: two year results of clinical cohort study with historical comparator. *BMJ*; 339 :b4677.

[210] Warlow, C. (2003). Not such a bright idea: the UK risk sharing scheme for beta interferon and glatiramer acetate in multiple sclerosis. *Pract Neurol;* 3:194-5.

[211] Ebers, G. C. (2010). Commentary: Outcome measures were flawed. *BMJ*; 340 :c2693.

[212] Raftery, J. (2010). Multiple sclerosis risk sharing scheme: A costly failure. *BMJ*; 340 :c1672.

Figure D2: Different types of performance-based reimbursement



Source: Coulton et al, 2010[213]

The Velcade PAS was however, the first to involve a manufacturer rebate for treatment failure. Because the NHS would pay for the drug *only* for those patients who demonstrated an adequate response to treatment, the PAS effectively amounted to both a performance guarantee and a substantial price discount.[214,215] However, unlike a simple discount arrangement or price-volume agreement, the manufacturer has a strong incentive to maximize the number of patients who respond, not merely the number treated or the quantity of drug sold.[214] The result is potentially positive for all stakeholders; the manufacturer gains market access and maintains its list price, the latter being extremely valuable as many countries reference their prices against those in the UK;[216] patients gain access to a therapy that might otherwise not be subsidized, and may also benefit from more active, protocol-driven follow-up; and the payer benefits from reduced budgetary risk, albeit with the added effort and cost of establishing

[213] Coulton, L., Annemans, L., Javier, J., Brown, R., & Keskinaslan, A. (2010). *Risk-sharing Schemes Worldwide: A Landscape Analysis of Health Outcomes-based Reimbursement Agreements.* United BioSource Corporation. Retrieved from http://www.ispor.org/research_pdfs/35/pdffiles/PHP15.pdf

[214] Garber, A.M., & McClellan, M.B. (2007). Satisfaction guaranteed—"payment by results" for biologic agents. *N Engl J Med*;357(16):1575–7.

[215] Neumann, P.J., Chambers, J.D., Simon, F., & Meckley, L.M. (2011). Risk-sharing arrangements that link payment for drugs to health outcomes are proving hard to implement. *Health Aff* ;30(12):2329-37.

[216] Ruggeri, K., & Nolte, E. (2013). *Pharmaceutical pricing: The use of external reference pricing*. Rand Corporation. Retrieved from http://www.rand.org/pubs/research_reports/RR240.html

and maintaining a suitable patient tracking system—a burden which can, depending on the nature of the performance metric, prove to be quite substantial.[215]

While to date there has been no formal evaluation of the Velcade PAS, both the MS and Velcade examples highlight the practical challenges of performance-based or "payment by results" reimbursement schemes. To be workable there should be a clearly defined, objective metric of treatment effect (performance) that is either a direct measure of clinical outcome (such as survival or cure) or a well-accepted surrogate endpoint that closely corresponds to or reliably predicts the desired treatment effect and is unaffected by other treatments. The clinical outcome measure should not be confounded by patient characteristics or the use of concomitant treatments that would obscure the effect of the index therapy, unless these issues can be adjusted for in an analysis. The availability of a validated and reliable well-accepted surrogate outcome, such as the serum M-protein level in the Velcade PAS, was a clear advantage, and limiting the arrangement to second-line treatment—patients in whom prior treatment had failed—reduced the likelihood that the results would be contaminated by other treatments.[217]

Nevertheless Neumann et al (2011) found that performance-based risk-sharing arrangements for pharmaceuticals are "appealing in theory but hard in practice."[218] For the manufacturer there is the uncertainty about whether the drug will perform adequately, and whether the outcomes achieved in a highly controlled clinical trial environment can be replicated in real-life settings.[219] For payers there is burden of measuring and monitoring patient progress, and there may also be the challenging prospect of having to withdraw coverage of a drug either entirely, or in individual patients, depending on the nature of the RSA. Although the PAS has become an integral part of the UK pharmaceutical environment, since the Velcade example the vast majority have been financially based arrangements. These are perceived as being far simpler to administer than the outcome- or performance-based PAS.[220] There are currently 40 drugs with 55 approved PAS in place in the UK;[221] of these the Velcade PAS is the only current performance-based scheme.[220]

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[217] Garber, A.M., & McClellan, M.B. (2007). Satisfaction guaranteed—"payment by results" for biologic agents. *N Engl J Med*;357(16):1575–7.

[218] Neumann, P.J., Chambers, J.D., Simon, F., & Meckley, L.M. (2011). Risk-sharing arrangements that link payment for drugs to health outcomes are proving hard to implement. *Health Aff* ;30(12):2329-37.

[219] Towse, A., & Garrison, L.P. Jr. (2010) Can't get no satisfaction? Will pay for performance help? Toward an economic framework for understanding performance-based risk-sharing agreements for innovative medical products. *Pharmacoeconomics*; 28(2):93–102.

[220] National Institute for Health and Care Excellence (2015). *Patient Access Scheme Liaison Unit (PASLU) List of technologies with approved Patient Access Schemes.* Retrieved from http://www.nice.org.uk/About/What-we-do/Patient-access-schemes-liaison-unit/List-of-technologies-with-approved-Patient-Access-Schemes

[221] Several drugs have multiple PAS, each applying to a different indication.

HOW MIGHT BROADER USE OF ARRANGEMENTS SUCH AS THE VELCADE PAS INFLUENCE INNOVATION IN DRUGS OR MEDICAL DEVICES?

Whether performance-based RSAs such as the Velcade PAS influence incentives to innovate remains unclear. Velcade was demonstrated to offer a clinical benefit over existing treatment options for multiple myeloma, but at a net cost deemed to represent inadequate value for money relative to the expected health gains. By this definition, at the original price proposed, Velcade did not meet the definition of an innovation that enhances consumer welfare in the United Kingdom. By modifying the *effective* price, and by inference, the cost effectiveness of the drug, the PAS modified this calculus, allowing Velcade to meet the definition of a substantive innovation, albeit with an effect on the manufacturer's expected return-on-investment (EROI). While the PAS likely reduced the EROI relative to unrestricted coverage, the EROI would almost certainly be better with the PAS than with a negative recommendation from NICE. The PAS also enabled the manufacturer to maintain its list price for the drug in the UK, a country from which prices are referenced all around (and beyond) Europe, thereby helping to preserve EROI on sales made elsewhere.

The conceptual model presented in this research project cast EROI as a proxy for incentive to innovate and posited that current returns on investment are viewed as indicative of potential future returns. Our analysis has shown that reimbursement policies and practices can affect EROI (or ROI) directly by establishing a particular payment level, which in turn affects average sales price; by setting a volume of sales at that payment level; and by influencing the seller's costs associated with development, manufacture, or sale of a healthcare technology. Moreover, as noted previously, reimbursement policies can also influence EROI/ROI indirectly by establishing different incentives for the various stakeholders which can, in turn, impact effective price, volume and, in some cases, seller costs.

A Velcade PAS-style scheme is effectively a value-based method of determining an overall payment amount that averts payer costs for novel products that are not innovative, while increasing payment amounts for innovative products, commensurate with the level of additional benefit.

Theoretically, broader use of outcomes-based reimbursement would lead to lower returns on products and services offering little value added, higher returns for products with higher value, and greater clarity where value-added is uncertain—albeit at the cost (and risk) of implementing the outcomes-based reimbursement scheme. This could potentially increase incentives to invest in R&D aimed at products more likely to be deemed substantial or radical innovations—at the very least it may stimulate investment in the identification and validation of biomarkers that could be tendered as proxies for the clinical outcomes of interest when outcomes-based reimbursement is under consideration.

In light of the lack of measured evaluation of experience to date, coupled with the previously identified challenges in effective implementation of outcomes-based arrangements, the Velcade case provides insufficient evidence from which to draw definitive conclusions about the impact of the approach on incentives to innovate.

CONCLUSION

The Velcade PAS in the UK was the first reimbursement protocol implemented in the UK to involve rebates for treatment failure. NICE's appraisal committee concluded that the opportunity costs of acquisition and diffusion would exceed the anticipated value of the projected incremental benefits of treatment. The PAS, a performance-based, risk-sharing arrangement, included a provision for treatment cessation in patients failing to achieve a pre-defined response, and reimbursement to the NHS for cases of treatment failure. At the original price proposed, Velcade did not meet the definition of an innovation that enhances consumer welfare in the UK. The PAS changed the effective price and allowed Velcade to meet the definition of a substantive innovation, albeit with an effect on the manufacturer's expected return-on-investment (EROI). It is unclear whether performance-based RSAs such as the Velcade PAS influence incentives to innovate, in part because of the lack of measured evaluation of this program and because of the challenges of designing and administering an outcome- or performance-based PAS. The vast majority of PAS in the UK since the Velcade example have been financially based arrangements.

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