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Rethinking value in health innovation: *from mystifications towards prescriptions*

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ABSTRACT

Debates over value in health innovation in the U.S. and Europe have become increasingly dominated by “value-based pricing”. We examine this prevailing narrative and its weaknesses and then present an alternative framework for rethinking value in health. Drawing on scholarship from the political economy of innovation, we argue that value in health must be considered in terms of both value creation as a collective process amongst public and private actors, as well as value extraction that occurs due to financialization. In building this alternative framework, we pose three questions that present areas for further research and public policy change.

KEYWORDS

Value-based pricing; public value; health economics

JEL CLASSIFICATIONS

I18; H40; L16; O3

Policy Highlights

- Prices of drugs should be better aligned to the actual risk sharing between public and private actors, rather than myths around value created by a narrow set of actors.
- Policy can be used to steer public purpose missions in health – not only to de-risk private costs.
- Markets are outcomes of public and private investments, hence health innovation policy should be seen not as “regulating” or intervening but as actively co-shaping markets.

1. Introduction

In response to an intensifying debate in the summer of 2015 over Gilead Science’s price for new curative medicines for hepatitis C – launched in the United States at over \$80,000 – the company’s senior executive Gregg Alton responded, “price is the wrong discussion”. Instead, he argued, “value should be the subject.”¹ In Alton’s narrative of value, Gilead’s medicines are curing patients of an infectious disease at a far higher rate than prior medicines and averting the downstream expenses of liver transplants and hospitalizations incurred by health systems from untreated disease progression. In his view, the price reflected the value of the therapies for patients and health systems. Alton is not alone; this conception of value has gained wider

currency in U.S. and European policy debates over pricing and access to new technologies for health (Bach and Pearson 2015; Gregson et al. 2005).

Scholarship on value in health has tended to be dominated by cost-benefit analysis, in which value is quantified and represented by comparing the prices and clinical benefits of competing health technologies for a given disease (that is, value-based pricing). In this paper we question the concept of “value” that has been accepted in the health sector in Europe and the U.S. and propose an alternative framework that builds on perspectives from the political economy of innovation and pragmatic philosophies of public value to build a wider and more dynamic account of value (Bozeman 2007; Mazzucato 2016b). We focus on health innovation, defining innovation as changes that allow higher-quality products at competitive cost to emerge and be diffused (Lazonick and Mazzucato 2013). Within the innovation process, we differentiate between the sources and directions of *value creation* at different stages in the value chain (including diffusion), and the links with particular mechanisms of *value extraction*. Our account addresses several of the main problems with searching for value solely through the cost-benefit lens, with escalating drug prices and the recurring conundrum of “me-too” drugs being two symptoms of prevailing narratives of value.

Rather than defining value in terms of the comparative cost-benefit ratios of competing therapies, we locate value in three fundamental questions related to the innovation process: (1) CREATION: How does value creation happen across multiple stages and actors (that is, division of innovative labor) (Arora and Gambardella 1994)?; (2) DIRECTION: What are the different directions that health innovation can take (Stirling 2007; Abraham 2010); (3) REWARDS: How are the risks and rewards of innovation shared and distributed (Mazzucato 2013; Mazzucato, 2016a)? We bring these three questions together to build a different notion of *value* in which value is viewed as a product of strategic deliberation and collective investment between multiple actors – where both the rate and direction of value creation is contestable rather than seen as determined by “market forces”. In this context, we view markets in health as outcomes of the investments between public, private and third sector organisations, so that policy is not about “fixing market failures”, but involves actively shaping and co-creating value and innovation.

Recognizing that directionality is not an inevitable outcome left to markets, but a contestable question amongst multiple actors, we take a normative view on how directions can be set through “missions” that can meet societal needs, such as healthy aging, antibiotic resistance, obesity and diabetes, cancer, and epidemic prevention (Mazzucato 2018). We also examine the role of the public sector in making the necessary risk-taking investments to pursue those directions along with the private sector and governing the distribution of risks and rewards to ensure sustainable and equitable outcomes. Our aim is to provoke a discussion that broadens our understanding of value in health innovation and enables new public policy directions.

We begin in section two by documenting the narratives used to discuss value in health economics and the assumptions upon which these narratives are based. In section three, we demystify these assumptions by pointing out the key pitfalls of these prevailing narratives. To build an alternative view of value, we build on different political economic perspectives in section four to pose the key questions and possibilities for reimagining value. We conclude with some directions for further inquiry and policy entrepreneurship.

2. Narratives of pricing and value in health innovation: costs of R&D and “value-based pricing”

In bringing new products to health systems, large, incumbent pharmaceutical companies have increasingly begun to make arguments of “value-based pricing” to governments and health systems.² The pharmaceutical industry had traditionally opposed public assessments of the value of new therapies, viewing them as a form of government pricing regulation (Scannell 2016). Instead, the industry has argued its prices were based on the “costs of research and development”, with patented protected monopoly pricing viewed as necessary to pay for the lengthy and failure-ridden process involved in successfully bringing a therapy to market (DiMasi et al. 1991, 2016). The industry-supported Tufts Center for Drug Development has produced periodic studies illustrating the escalating costs of research and development, arriving at a figure of US\$2.6 billion per newly approved molecule in 2015 (DiMasi 2003, 2016). However, the Tufts figures have been criticized on numerous grounds, such as the lack of transparency about what is counted as part of a company’s research and development costs as well as the inclusion of “opportunity costs” (via cost of capital) accounting for nearly half of the estimated totals (Light and Warburton 2011; Avorn 2015).³ As the evidence behind this view has faced mounting criticism and prices appear to be uncoupling from research and development investments made by companies (for reasons we discuss in the following section), the industry has turned to a new narrative to justify the prices of new medicines: value.

More than a decade ago, health industry consultants described this shift towards a “value-based pricing strategy” as follows: “in essence, the fundamental pricing question has shifted from ‘what price do we need to charge to cover our costs and make a good return?’ to ‘given market perceptions of value, which products can we profitability produce?’” (Gregson et al. 2005). One way of understanding the “market perceptions of value” is to set prices that fall within the thresholds signaled by health systems. However, with health systems facing significant budgetary pressures with highly priced products (such as new cancer, cholesterol, and hepatitis C medicines) that might also benefit larger populations (not just for rare diseases), manufacturers are also turning to a second method of valuing therapeutic innovation: quantifying the “prevention value” of new medicines.

This value-based pricing narrative of value has gained traction among multiple stakeholders in U.S. and Europe. In the United States, for example, pharmaceutical lobbying group PhRMA has developed “The Value Collaborative” as a new research and marketing campaign to demonstrate “the value of innovation”, purported to be developed by the industry on whose behalf they lobby. Policy-makers in Europe are exploring ways to refine value assessment already used in pricing negotiations with companies while a new U.S. organization ICER (Institute for Clinical and Economic Review) is working to help health systems there adopt similar approaches (Bach and Pearson 2015; Claxton et al. 2008). Physicians, patient groups, and public health agencies also use this version of the value narrative to engage in debates over resource allocation and treatment access (Rein et al. 2015; Van Nuys et al. 2015). However, this road carries perils that have yet to be fully elaborated – a task to which we turn in the following section.

The prevailing value narrative for health innovation can be summed up as “higher prices represent the value of health improvements.” This narrative relies on an alluring logic: that

“consumers” are willing to pay more for better health outcomes, and that this payment will direct innovation toward producing more “high-value” therapies. In the case of health, however, the consumers are *not* individual patients. Because the prices of patent-protected medicines are multiples above the median wages of individuals, the responsibility to “value” new medicines falls on the ultimate buyers: public health systems (Reinhardt 2015).

From the perspective of health system leaders facing rising health care costs and budgetary pressures, deliberations about the realization of “value” have come increasingly to the foreground over the past two decades (Claxton et al. 2008; Gregson et al. 2005). From the perspective of manufacturers aiming to grow profits, public deliberations about value are said to reveal the preferences of health systems, thereby enabling companies to set prices and investments accordingly. Drawing on the relatively young field of health economics, this value is quantified and evaluated largely based on two metrics: cost-effectiveness and prevention. Before identifying the pitfalls of using this mode of assessment to represent value, we describe these two metrics in turn.

2.1 Cost-effectiveness as value

To assess whether and how much to pay for new health technologies, health systems have increasingly used what is called cost-effectiveness research in health economics – with manufacturers in turn aiming to set their prices in alignment with these assessments. Such research involves comparing the costs and benefits of two therapies, such as a new therapy against a competing standard of care, to see whether the benefits (if any) can be generated under a certain monetary level called the “value threshold”. This research links prices of new technologies to units of health improvements called “quality-adjusted life years” (QALYs), with health systems *being willing to pay for medicines that generate an additional QALY for patients under the upward limits of the value threshold*.

For example, the United Kingdom’s National Institutes for Clinical Excellence (NICE) has set a threshold of £30,000 per QALY as what the NHS is willing to pay for new technologies (McCabe, Claxton, and Culyer 2008). In other words, the NHS believes it creates an additional quality life year in the English population for each £30,000 it spends on a given new technology. In theory, “cost-effectiveness” – as pegged to QALYs – is a measure of opportunity costs and cost efficiency for health systems, with the notion that new health technologies must offer greater benefits than the programs and technologies that are displaced by funding the new technology (Badano, Junghans, and Johns 2017). This measure is supposed to provide health systems with confidence that they are getting value for money, while also providing an incentive for the pharmaceutical industry to bring new drugs to market that demonstrate health improvement over existing options.

2.2 Prevention as value

In this orientation to value, health technologies are priced not only based on their cost-effectiveness compared to existing options, but also based on the health savings and economic benefits that early treatment may bring society. With therapeutic innovation that can modify the trajectory of pathology (for example, lipid-lowering agents that can prevent heart attacks, or hepatitis C antivirals that can prevent liver cirrhosis) if taken early in a disease course, manufacturers argue that innovation saves health systems

downstream costs that might otherwise be incurred while also creating spillover effects in the overall economy (Dumit 2012; Maldonado Castañeda 2016).

Such a view can be found in the marketing materials produced by the industry. A fact sheet produced by PhRMA claims that, “every additional dollar spent on medicines or adherent patients with congestive heart failure, high blood pressure, diabetes and high cholesterol generated \$3 to \$10 in savings on emergency room visits and in patient hospitalizations” and that “a 10 percent decrease in the cancer death rate is worth roughly \$4.4 trillion in economic value to current and future generations” (Zirkelbach 2015). PhRMA argues that paying for high priced medicines today creates future-oriented value for society. Health economic studies quantify this prevention value by measuring two quantities at the level of populations: the total amount of health savings that early treatment yields to health systems, and the total economic value of overall health improvements that this early treatment creates. As health systems and the public weigh drug prices, companies argue that this “value as prevention” should bear into resource allocation.

3. Value as value-based pricing? Demystifying the prevailing narrative

Taken together, cost-effectiveness and prevention value research is used to represent the value of health innovation in debates over pricing and drug development. Methodologically, these approaches are fraught with vexing questions, such as what monetary value to impute to a QALY (Knapp and Mangalore 2011; Neumann and Cohen 2014; Nord, Daniels, and Kamlet 2009). This paper does not delve into the methodological pitfalls of value-based pricing, but rather unpacks the *conceptual underpinnings* of the narrative of value in which a confounding logic – *the higher the price, the higher the value of the medicine* – seemingly becomes normalized. In other words, if people are willing to pay a high price, then the therapy must be valuable. Such a logic is exemplary of Neoclassical economics whereby it is price that determines value not vice versa, as it was in Classical economic theory (Mazzucato 2018). By taking a static conception of value based largely on cost-benefit analyses – divorced from the structural conditions of production – in which the price of comparative clinical improvements is deemed commensurate with value, the prevailing narrative fails to consider the dynamic nature by which value is created and distributed in the health innovation process. Before pointing towards alternative directions, the next section unpacks four key problems with value-based pricing that challenge the very underpinnings of the conventional wisdom on value in health innovation.

3.1. Problem #1: monopoly and demand inelasticity means prices are ‘what society can bear’⁴

The value-based pricing narrative misses the most basic economic reason for higher prices for new health technologies: publicly granted monopoly protections for manufacturers combined with rigid demand elasticity for medicines. New medicines are covered by patents. Therefore, operating as monopolists in a given therapeutic area, manufacturers can set prices unrestrained by competition. With many goods, the elasticity of demand would be a constraint based on simple supply and demand logics:

the higher the price, the lower the demand for the monopolists' product. Of course, the elasticity of demand for medicines is quite different: people's health is at stake. This rigidity of demand elasticity means that public and private insurers often bear high prices in order to meet their obligations to patients and their livelihoods. Rather than reflecting value, higher prices are a manifestation of "what society can bear" in the face of monopoly power.

Under this configuration, manufacturers are not merely accruing a share of the total social value created through health innovation; they are accumulating sizeable rents, or unearned income, through the period of patent protections. This basic feature – of monopoly combined with demand inelasticity – is a major reason why the pharmaceutical industry has the highest profit margins of any sector, surpassing even the energy and banking sectors. Our concern here is less with the existence of rent, but what happens with this accumulation.⁵ As we describe in problem #4, rather than being reinvested in innovation and value creation, a significant share of this rent is directed towards shareholder extraction in the form of stock repurchases.

3.2 Problem #2: the structure of financial market expectations leads to spiraling drug prices that distort value-based assessments

The monopoly dimension of health innovation is grafted onto a second dimension: the financial environments in which these monopolists operate. Large publicly traded

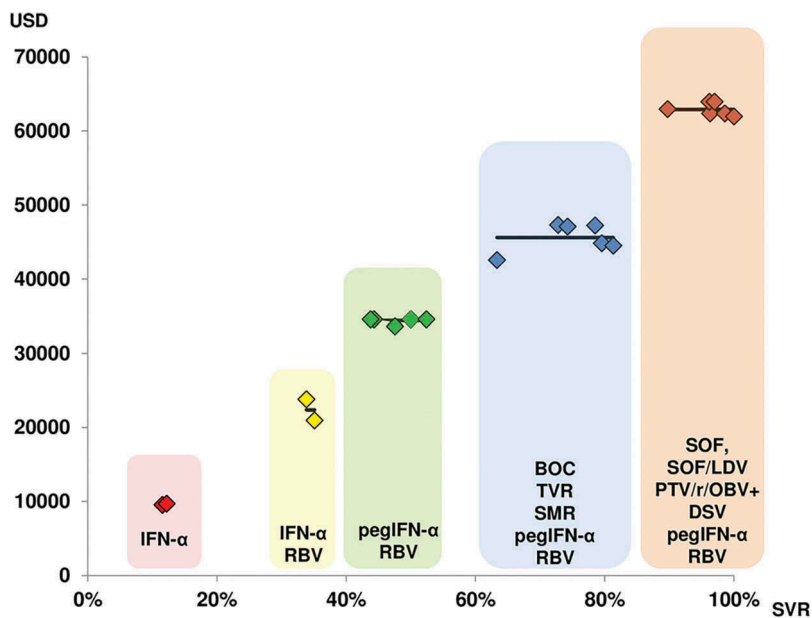


Figure 1. Price increases for each generation of hepatitis C therapies.

Caption: each generation of improved therapies, indicated by increases in sustained virologic response (SVR, from left to right along x-axis), has been coupled to increases in prices. Medicines with increasing prices and budgetary consequences can still appear cost-effective in such comparisons. This pricing data is specifically from the Swiss case, but is similar across U.S. and European contexts. Source: Vernaz et al. (2016).

biopharmaceutical companies are valued on stock markets that are not based on their profits, but on the anticipation of *growth* in profits over time. This expectation of near-term and continual growth, signaled through share price, has become the core metric by which shareholders evaluate a company's performance (Birch 2016). Because growth through new product development in health innovation takes many years, companies turn to another vehicle to generate growth: price increases, both on an annualized basis for already approved drugs and also in bringing new therapies to market (Glabau 2016). Higher prices for new therapies (compared to the standard of care that may be replaced) signal, for example, the potential for earnings growth – thereby serving as a driver for a company's share price.

This creates an escalator phenomenon for drug prices, with each price setting the floor for the next price. When such prices exist for drugs with small potential patient populations, health systems can often plan for increases in health spending. But when such prices apply to drugs with large numbers of potential beneficiaries, health systems face a much steeper challenge in coping with the escalation in expenses. Take the example of hepatitis C, for which each new generation of treatments since the 1980s has involved a significant price leap (see Figure 1 from the previous generation (Vernaz et al. 2016). Even though the latest curative therapies had “value-based prices”, the large numbers of patients meant that health systems had to choose to either allocate significant new spending for the medicines or restrict access to treatment

As one group of cancer doctors put it, this mode of assessment “allows a BMW to look like a bargain when the only other car on the lot is a Ferrari” (Bach, Giralt, and Saltz 2017). A price for a new health technology may be deemed to be cost-effective compared to a prior option, but the price of the prior option may already have been quite high. In analyzing cancer drugs, health policy scholar Peter Bach (2015) observed: “expensive drugs can still seem deceptively cost-effective, because of the long upward spiral we have seen in the prices of cancer treatments”. In this context, rather than reflecting value as conceived of in the conventional narrative, prices are instead artifacts of financial market expectations that are used to maximize short-term growth.

This focus on near-term growth means that health systems are supposed to “buy health now” in return for savings in the future. Yet this logic suffers from a serious limitation: these “savings” are a mirage. As the doctor and epidemiologist most credited for advancing preventative medicine Geoffrey Rose (2008) has noted, using clinical interventions to prevent disease cannot be defended on purely economic grounds. Rose pointed out that the longer one lives, the more treatments one tends to require. In the instance of highly priced medicines, states would inevitably need to spend this money on other areas of social and health concern; furthermore, the large-scale costs of using these breakthrough medicines in the present (unlike more affordable medicines like vaccines) could in many cases dwarf any future savings (see Van Nuys et al. 2015 as an example from hepatitis C). The main grounds on which to use medicines to prevent disease then is a humanitarian one – more life with less disease; yet this humanitarian benefit is threatened by an adoption of “value-based assessments” that do not consider rising prices over time and their impact on access to treatment.

3.3 Problem #3: value-based pricing does not account for the role of an entrepreneurial state in value creation

A third major problem is the failure to see innovation as a cumulative and collective outcome, in which value creation occurs through multiple actors taking risks for the sake of uncertain rewards. In this context, health innovation requires long-term risk-taking – and a major source of this patient capital comes not from manufacturers (which operate in short-term-oriented stock markets), but from investments by an *entrepreneurial state* (Mazzucato 2013). The existing value narrative renders these investments largely invisible, or merely as public goods to be taken for granted in the innovation process. In the US, however, public investment from the National Institutes of Health (NIH) amounted to \$804 billion between 1934 and 2015 (Lazonick and Mazzucato 2013). Although public investment is often depicted only as an input to “basic science”, the NIH has gone beyond early-stage science to directly fund the research tools that create new markets for later private investment (such as the emergence of the biotechnology sector in the 1980s), as well as provide direct funding to start-ups through the Small Business Innovation Research (SBIR) program at their riskiest stages of development (Keller and Block 2013; Stevens et al. 2011).

In many major therapeutic advances, an entrepreneurial state has made vital contributions over many decades and taken risks across the innovation chain, from basic and “translational” science to clinical trials (Mazzucato 2013). For example, an investigation by Cleary et al. (2018) showed that NIH financed research was associated with *every one of the 210 drugs approved by the FDA between 2010–2016*, collectively accounting for >200,000 years of grant funding totaling more than \$100 billion. Other studies have illustrated the contribution of public investment to an array of breakthrough therapies (Angell 2004; Goozner 2005; Sampat and Lichtenberg 2011).

Because these investments are not considered in the conventional value narrative, the sources of value *creation* are not considered in the innovation process. For example, the NIH does not take a stake in the start-ups that it funds, and it typically earns a low level of royalties given the extent of its investments. Other US government agencies that invest in health innovation, such as the Veterans Affairs, are even more poorly positioned (Flier 2016). The UK government, one of the world’s leading funders of biomedical research, also suffers from a similar posture (Dzintars et al. 2017). Furthermore, price negotiations between manufacturers and public payers do not reflect the investments made by the public – creating the phenomenon of the public “paying twice”: both for pivotal research as well as for high-priced medicines.

3.4 Problem #4: value-based pricing masks significant value extraction and financialization

In addition to lacking a theory of value creation, the existing narrative also fails to account for the *value extraction* that occurs in the innovation process for new health technologies. The biopharmaceutical industry has long argued that monopoly rent, enabled through patents, is necessary to finance further value creation.⁶ However, evidence from the pharmaceutical sector over the past decade runs counter to this claim. Rather than reinvest accumulated capital into further innovation, companies are

increasingly turning to financial maneuvers to boost share price. One of the most common such maneuvers is the share buyback, in which companies buy back their own shares to boost the value of the remaining ones to shareholders in equity markets (Lazonick et al. 2016). From 2005 to 2014, for example, the 19 pharmaceutical companies in the S&P 500 Index spent \$226 billion repurchasing their own shares, equivalent to 51 percent of their combined research and development expenditures over this period.⁷ Thus, significant shares of monopoly rent from the sector have gone towards shareholders in the form of buybacks in the name of “maximizing shareholder value.”

However, the theory of maximizing shareholder value is ultimately a strategy of value extraction that lacks a theory of value creation (Lazonick 2015). The dominant aim of executives of publicly traded biopharmaceutical companies is to generate accumulation for shareholders within near-term time horizons. Any investments that may put this aim at risk – such as long-term and early-stage scientific research – are to be eschewed, with surplus capital instead directed to shareholders who are held in legal and neo-classical economic theory to be the sole claimants on any “residual earnings” (Stout 2013). Unlike managers, workers and contractors, shareholders are held to be the only actors that take risks in the innovation process without certainty of return (such as a salary or contractual payment).

And yet shareholders of large pharmaceutical companies seldom risk significant capital in the innovation process; rather, they trade on stock price to generate capital gains (Lazonick 2015; Stout 2013). For these companies, accumulated sales from high-priced drugs are the primary source of risk capital, which is spent primarily on late-stage clinical trials, acquisitions, and share buybacks. In this way, value-based pricing can be observed as a way of normalizing significant amounts of value extraction in which rewards are accrued to the financial actors (that is, shareholders of large pharmaceutical companies) that have taken the least risks in the innovation process.

In sum, the current narrative on value has significant limitations. Value is confined to a measure of cost-benefit utility that obscures the influence of monopoly, financial markets, and value extraction in the innovation process, and renders pivotal sources of value creation – such as the state – invisible. In a critique of this narrative, biotech venture capitalist Jack Scannell stated simply: “value-based pricing evolved as a way of charging customers more” (Scannell 2016). Through the methodologies of quantifying cost-effectiveness and prevention value, however, value-based pricing has become a powerful narrative catering to the financial interests of shareholders while appearing to align with the vital goals of health systems.

4. Directions, divisions of labor, and distributions of risks and rewards: towards a framework of public value

A different account of value must thus go beyond a narrowing assessment of cost-benefit analysis of individual drugs. Such an evaluation requires, in the first instance, a departure from the market failure theory that dominates economic thinking, in which the role of the state is seen as merely addressing different types of market failures such as those that arise from negative externalities (such as regulating pollution), positive externalities (for example, those arising from public goods like clean air or basic science), or information asymmetries (such as those that prevent small firms from receiving the loans they require).

However, this perspective ignores how markets are actually outcomes of different investments, including those of the entrepreneurial state (described above), which have often gone beyond fixing positive and negative externalities, actively co-shaping and co-creating markets (Mazzucato 2016a). To relate this viewpoint to the area of health, it is necessary to reimagine such deliberations beyond value-based pricing and develop a theory of *public value*.

As Bozeman and Sarewitz (2005) have described, conventional market failure theory in neoclassical economics has come at the cost of considering whether, even in cases of market successes, there has been a failure to meet some essential public values. In contrast to market failure theory, *public failures* are situations where “neither the market nor the public sector provides goods and services required to achieve core public values” (Bozeman 2007).⁸ In contrast to the market failure model, Bozeman 2007 argues, “a public failure approach changes the discussion of public policy by making government (and public values) something other than a residual category or an issue of technical efficiency in pricing structures”.

As we have highlighted here, public organizations have long played pivotal roles beyond fixing markets. The investments in research and development, protection of knowledge property, and government payments for medicines that now create markets and enable private capital investments means that the value of health innovation is fundamentally shaped by an array of choices in which the public plays a market-shaping role (Mazzucato 2017). Yet these public roles are often rendered invisible, with the deliberations necessary for making choices about public value left to private actors.

It is necessary to go beyond the failure narrative where public deliberations are primarily in response to some absence, problem, or social crisis. To do this, we draw on insights from the political economy of innovation to consider a new way of thinking about value in terms collective value *creation*. From this vantage point, the central areas of deliberation and strategy for health innovation involve the *directions* for possible trajectories of innovation, the *divisions* of labor between public and private actors in the innovation process, and the *distribution* of risks and rewards of innovation. In considering these questions, cost-benefit tools used by governments to make and implement decisions are simply insufficient, as the core aims of the innovation process for health – such as genuine therapeutic advances and access to these advances – hang in the balance. Rather than reducing these aims (and the overall discussion on value) to a price mechanism that does not capture the social nature of health innovation, consideration of these questions can open previously closed pathways for health and innovation.

4.1 Directions: meeting unmet patient and public health needs

A critical determinant of value creation in innovation is understanding that innovation not only has a rate (or pace), but also a direction, in which new products, markets, and services are used to address *societal challenges* (Mazzucato 2016a, 2017). Throughout history, public-sector organizations have played a pivotal role in shaping these directions for innovation; techno-economic paradigms did not emerge spontaneously from market forces. Mass production and the IT revolution are two examples where governments made direct investments in technologies and then formulated bold policies that allowed these

technologies to be fully deployed throughout the economy. In the alternative view, where public investments are viewed merely as fixing market failures (such as basic research), market forces are believed to efficiently direct the economy to a path of growth and development. Yet, as Dosi (1982) argued, markets are “blind”, with the direction of change provided by markets often creating suboptimal outcomes from a societal point of view.

In the domain of health, the key question is what is the purpose of innovation in health? A common-sense answer would be: *to address unmet health needs for patients and populations, from rare diseases to public health threats*. However, the market failure view has not been useful for guiding investments to achieve these objectives. Even as public investment has enabled the creation of entirely new socio-technical paradigms, such as genomic science and biotechnology, the terrain of product development, pricing, and access have been largely left for private industry to dictate. This division of labor has had three consequences.

First, as Gary Pisano (2006) described in *Science Business*, many of the promises of biotechnology have not been fully translated into clinical advances. As Pisano demonstrated through an analysis of the history of the sector, the short-term-oriented venture and equity market financing for biotechnology has been ill-equipped to deliver the long-term, patient financing needed for the risk-laden and failure-ridden nature of scientific and clinical research (Pisano 2006). In other words, because finance itself is not neutral, the sources of finance affect the directions of what is financed (Mazzucato and Semieniuk 2017).

Second, in the absence of directionality in public policy, industry players have more readily captured regulatory pathways to meet near-term financial targets through the proliferation of me-too drugs and incremental advances – this is part of the “pharmaceuticalization” of health (Abraham 2010). By contrast, setting directions through purpose-led missions (detailed in the next section) would involve addressing unmet areas of patient and public health need in need of radical innovation, from diseases of aging and cognition, to curative cancer therapies, to infectious diseases (such as antibiotics, vaccines for epidemic viruses).

Third, even in cases where therapeutic advances have been made (in many cases with public investment enabling the technological breakthroughs underpinning therapeutic advances), monopoly pricing (now disguised in the value-based discourse) has undermined the realization of optimal patient and public health outcomes – a crucial directional outcome of interest from innovation for health.

On the other hand, understanding directionality as a dimension of value in health innovation can embolden public sector organizations and foster more symbiotic interactions between public and private actors to tackle societal health challenges. As Stirling has documented, directions can be deliberative outcomes of the state, together with other stakeholders, and can help define “what ‘winning’ even means” (Stirling 2009, 2).⁹ In the space of health, winning may not simply be more drugs, but new kinds of therapeutic, diagnostic, and surgical interventions, as well as the realization of public health targets.

4.2 Divisions of innovative labor: value creation as a dynamic, collective process

Another fundamental question related to value in health innovation is: What is the division of innovative labor that will best produce the desired outcomes? As described in Gambardella (1995) and Arora and Gambardella (1994), innovation occurs through a

division of labor among the state, business, and intermediary organizations. A critical question is how to structure this division of labor across an innovation process in ways that make use of the expertise of each type of actor, but also create opportunities for learning and serendipity that may only occur through overlapping roles. Arora et al. (2015) used a large array of scientific publishing data to argue that the increasing specialization of labor (with large corporations taking on only the final stages of product development or patenting) may be harming the technical capabilities of innovation systems.¹⁰

The conventional narrative on value assumes a public sector that provides basic goods and then “gets out of the way” of private actors, with innovation an outcome of risk-hungry capitalists. In this formulation, the exchange between manufacturers and public health systems is a cost-benefit calculation in which government spending on a new therapy is weighed against the status-quo alternative (which may be spending on an older standard of care, or no action). Public action, such as downstream investments in clinical trials or fair drug pricing contracts for therapies of public health importance, is eschewed because it “crowds out” the incentives for risk-taking pharmaceutical companies.

Such a picture, in which the public sector operates in a hermetically sealed stage of an innovation process, is at historical odds with how new advances have unfolded in health (and other domains). Instead, innovation is the result of *dynamic* interactions between public and private actors in what is a *cumulative, collective, and uncertain* process (Lazonick and Mazzucato 2013). In this process, rather than crowding out private actors, public investment has served to “crowd in” private investment; through long-term risk-taking at technical frontiers – in other words, the public sector has actively created and shaped markets by creating new opportunities for investment.

Given this crowding-in dynamic, with private finance often *following* public investments, a first step is to acknowledge this very dynamic (which is often ignored or obscured). A second step is to ensure that such policies have steady funding streams and not undermined by problematic schemes. A third step is to reward high-risk public investments. Large pharmaceutical companies often lobby for tax policies that diminish the capabilities of high-risk public investments. Alongside pushing for tax inversions, one example of such a policy is the “patent box”, in which companies seek to reduce taxes on profits from patents. Rather than focusing on increasing profits, policy-makers should focus on strategies that lead to greater investment along the innovation chain from *both* public and private actors. Many of these indirect policies have only increased profits of pharmaceutical companies, without affecting their investment patterns. In other words, while public investment can crowd in private finance, this configuration can only be sustained if the interactions between the public and private are structured in strategic and durable ways – a point to which we turn next.

4.3 Distributed: sharing risks and rewards in innovation

Because innovation is a process in which multiple actors take risks for the sake of uncertain rewards, an analysis of value must also assess the distribution of these risks and rewards across the process (Lazonick and Mazzucato 2013); in other words, who takes the risks, and who receives the rewards? This distributive outcome has two critical consequences for the realization of value in innovation. The first is the realization of directional possibilities for patients and public health. When rewards are skewed to a

small group of actors, such as shareholders of large companies, the value of therapeutic advances can be diminished (that is, access restrictions due to high prices) and radical directions for innovation may be displaced by more risk-averse, incremental routes to ensure near-term accumulation for those actors. Put simply, maximizing shareholder value can come to dominate the aim of innovation, rather than maximizing patient and public health value.

The second consequence relates to the first: the very sustainability of the innovation system to generate value is threatened without an equitable distribution of risks and rewards. For example, public health systems face the regular crises of providing access to treatment while balancing opportunity costs in other vital areas of health and social spending (Reinhardt 2015). Furthermore, public investment in risk-taking science and technological change can be jeopardized in a system where the companies that benefit from this risk-taking regularly exercise tax avoidance strategies, while public sector organizations retain few tools to gain a direct return on the investments in laboratories and businesses (Pollack 2014). For example, one study estimated that by domiciling assets (that is, applying patents to approved medicines) in their favored tax haven of Ireland, US pharmaceutical companies have paid a tax rate of only six percent on over \$100 billion in profits over the past decade (Houlder, Boland, and Politi 2014). This avoidance threatens the very tax base that funds the scientific research upon which further innovation depends.

Alternatively, innovation systems in which risks and rewards are shared can produce *sustainable* investments across the process in ways that realize the technical and public health directions necessary to meet societal challenges. As part of such an innovation system, a critical question is how the public gets rewarded for value it has *co-created*, and how long-termism and deployment of new technologies are effectively rewarded. Such a distribution of risks and rewards will, in turn, depend on a shift in both the organizational and policy configurations towards innovation as well as the prevailing narrative of value underpinning them.

5. Conclusion: new pathways for value in health innovation

In this paper, we have argued that notions of value in health innovation can be reimagined by asking three pivotal questions, each of which are promising areas for research and can, if taken together, provide new horizons for public policy. First, what are the directions for innovation that can fulfill societal needs related to health? Second, what is the optimal division of innovative labor and sets of dynamic interactions that will lead to better product development outcomes? Finally, how can risks and rewards be distributed in a way that sustains the value creation process in health? Ultimately, because value creation is a collective process, discussions about directions of innovation and distributions of rewards must also be the subject of proactive public deliberation.

To build a new approach to value in health, the policy process cannot be relegated as residual to innovation and fixing market failures, and assessments of value cannot be reduced to value-based pricing. Rather than “value-based pricing” rewarding each incremental advance with significant increases in pricing (with prices in many cases outpacing the extent of therapeutic advance), value can be re-framed in terms of public health value, where directions of innovation are aimed at societal health needs. Rather

than disproportionately rewarding end-stage value-extraction by manufacturers and their shareholders, value can also be re-imagined in terms of *value creation*, which brings to the forefront the long-term public leadership required for innovation. Such a consideration of value as “public value” should encourage a radical re-thinking of health innovation as currently conceived, with attempts to both reform the dominant shareholder model while also experimenting with paradigm-shifting strategies.

How can this be achieved? First, governments can take major steps by shaping mission-oriented directions for health innovation (Mazzucato 2018). While governments have made precision medicine and personalized medicine based on genetic advances a major focus of new mission-oriented strategies in a bid to create new commercial opportunities while improving health, they have yet to build the bold strategies required across an array of population-level health challenges (Collins and Varmus 2015). Rather than leaving directions to be shaped by commercial interests alone, public organizations should take an active role in deliberating on potential directions. In other words, given that the public actively co-creates value, what is created should itself be up for public debate. Across many industrialized countries, aging and dementia-related diseases and cancers present major public health threats. Globally, epidemic disease and growing anti-biotic resistance loom as challenges that require proactive public investments (Gates 2015; Lowy and Collins 2016). Shaping these directions as purpose-led missions to address major health challenges can create entirely new technological horizons and attract an array of patient investments from public and private actors, while also addressing crucial health needs for patients.

Second, alternative ways of organizing and incentivizing innovative labor can spur this kind of mission-oriented value creation. Rather than enabling financial markets to incentivize the production of more me-too or high-priced drugs, governments can actively coordinate mission-oriented R&D projects and portfolios through de-centralized networks of public and private partners. Financing for such an approach would combine grants, milestone prizes, and contracts, with rewards focusing on health benefits rather than patentability (Quigley 2017). For example, prizes could allow the exchange of financial rewards for licensing of a new technology to a generic producer, thereby bringing the price of new technologies closer to the costs of production rather than those expected by shareholders in financial markets (Love and Hubbard 2009). The example of product development partnerships such as the Drugs for Neglected Diseases Initiative (DnDi), as well as innovative government agencies such as DARPA and BARDA, are examples of such models that can be tested for wider areas of critical unmet health needs (DnDi 2013). In these cases, the ultimate access to innovations – and the pricing of these innovations – is aligned in a way that reflects the proportionate upstream investments of the state (as observed in the US military and its development and procurement strategies). Such a division of labor would reflect a mission-oriented view of innovation, in which the value chain of drug development would be linked up to the realization of the missions defined through public deliberation. While missions may be set in a relatively top down way, policy instruments should be chosen to foster bottom up exploration for creative experimentation in the innovative process.

Third, new strategies for governing the distribution of risks and rewards can encourage value creation, long-termism, and the diffusion and deployment of new technologies while preventing the kind of rent-seeking and extraction that threatens health innovation and public health. For example, methods for the public to gain a greater return on their

investment could include earning royalties from companies in which public funding played a major role, with these funds used for financing future innovation (innovation funds, for example) (Mazzucato 2013). Another strategy would be for the public to retain a “golden share” of patents developed with public funding, with patents governed to be weak and narrow (rather than strong and broad) to spur greater use and innovation (Mazzoleni and Nelson 1998). Rather than paying for escalating prices, public health systems should pay prices that reflect both public contributions as well as the impacts of new therapies on public budgets, with the price of new drugs linked to the possibility of universal access for health systems and patients (Institute for Clinical and Review 2015). Another major shift would be to change the rules of the game in shareholder-driven, financial-market-based economies so that companies are accountable to multiple stakeholders, including patients and health systems, rather than only shareholders (Lazonick 2014). Such rule changes (such as limiting buybacks) would direct profits generated through collective investment to be *reinvested* to benefit the public, rather than hoarded or “financialized”, as observed through the cash stockpiles and share buybacks deployed by large pharmaceutical companies.

Each of these three areas provide horizons upon which to search for policy options and innovation models that focus on value less in terms of cost-benefit analysis alone and more in terms of the directions, dynamic divisions of labor, and distribution of risks and rewards for innovation. Mystifications over value, on the other hand, can lead to a situation where static assessments come to normalize high prices and incentivize incremental advances over therapeutic breakthroughs. If value should indeed be the subject of discussion, as Gilead’s Alton argues, a wider deliberation on value (how it is created and how the creative process can be directed at achieving public value) is required, not one based on the illusory assumptions underlying value-based pricing. Tackling the challenges faced by patients and populations in coming years will hang on whether we can bring this view of value to fruition.

Notes

1. See Paul and Langreth (2015).
2. Newer biotechnology companies are also concerned with arguments over “value-based pricing” as well, but in a different way than the large incumbent firms. With few exceptions (such as Genentech), these biotechnology companies are reliant on external capital markets (venture and equity markets), where questions of value have less to do with setting specific prices for approved products (as most of their valuation comes from products still in development stages), but with the capability to attract financing (and valuation) on the basis of potential “value-based pricing” in the future. This value-based pricing strategy is thus critical for maintaining valuations, particularly when biotech companies are looking to launch an IPO or to be bought by larger pharmaceutical companies. While focusing primarily on the value-based pricing strategies and narratives advanced by large pharmaceutical companies, we make reference to implications for the biotechnology sector at relevant points in the paper. Further analysis of biotechnology companies would involve a more extensive elaboration of the kinds of financing necessary for early stage and translational research.
3. Opportunity cost in this situation refers to the gains that investors could make through other investment strategies (such as the stock market) versus making capital allocations towards research. Critics point out that these studies include inflated opportunity costs of greater than 9%, thereby leading to larger estimates for research and development (see Light and Warburton 2011).

4. Our description of problem #1 is adapted text from Mazzucato (2018).
5. See Mazzucato (2018), Zeller (2008), and Birch (2017) for more in-depth discussions on the concept of rent and its evolution in economic thinking as well as its function within science and biomedicine.
6. From this vantage, patents have been understood to facilitate scientific development, in which inventions receive monopoly rights for a specific period of time, only after which the public can gain full access (that is, generic licensing) to the knowledge protected by the patent (Grabowski 2002). As Biagoli (2006) has pointed out, patents technically govern a legal exchange between the consumers and the investors of patent-protected products, with these transactions conceptualized in the law as a “bargain” or “fair exchange”: investors’ right to recuperate costs of research and development in exchange for customers’ access to the inventor’s product.
7. Comprising 4.14 percent of the sample of all companies in the index, pharmaceutical companies accounted for 7.38 percent of all buybacks, indicating the disproportionate extent to which this sector has engaged in extractive strategies. See Lazonick et al (2016).
8. Bozeman and Sarewitz (2005) describe several criteria for identifying public failures that are relevant to health and the political economy of innovation we have described, such as imperfect monopoly (monopoly pricing prevents access and is not used to re-invest in innovation), benefit hoarding (see the levels of buybacks and cash hoarding in the industry), and threats to fundamental human subsistence (health and life is at stake).
9. Stirling (2009, 2): “The more demanding the innovation challenges like poverty, ill health or environmental damage, the greater becomes the importance of effective policy. This is not a question of ‘picking winners’ – an uncertainty-shrouded dilemma which is anyhow equally shared between public, private, and third sectors. Instead, it is about engaging widely across society, in order to build the most fruitful conditions for deciding what ‘winning’ even means.”
10. Arora et al.’s (2015) findings relate to Pisano’s research into the biotechnology sector’s lack of productivity, in which he described why a dis-integrated model of innovation (with each organization doing its own part of a process) would fail to solve the kind of complex, non-modular problems in biomedicine – in Pisano’s (2006) view, long-term collaborations and integrated organizations would instead be required to confront uncertainty.

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