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How Big Business is Re-Defining Illness and Health: Fabrication of a Block Buster Drug Market

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ABSTRACT

SHORT: Using diabetes as an example, we consider how the pharmaceutical industry has commandeered authoritative medical knowledge, and state-sponsored oversight institutions, to recast the condition such that it builds and protects a blockbuster drug market.

LONG: While generally assumed that evolving medical concepts reflect the latest scientific knowledge, health care is a highly lucrative economic sector, and may be best understood in terms of strategic market manipulations. Using diabetes as an example, we argue that the pharmaceutical industry commandeers authoritative medical knowledge, and influences state-sponsored oversight institutions, to recast the condition in ways that build and protect the market it serves. The industry has produced information and promoted its interpretation in ways that have resulted in important revisions in how the condition is understood and addressed, paving the way for blockbuster drugs. By converting "risk" into a pathology requiring pharmaceutical management, and changing professional standards for who is tested, how they are tested and how tests are interpreted, industry affiliates, facilitated by sympathetic professional and regulatory bodies, have fabricated a diabetes "epidemic" and treatment standards that require heavy use of pharmaceuticals. Despite weak or contrary evidence of the benefit of maintaining tight glucose control, and substantial indication that the pharmaceuticals used toward this end may be harmful, polypharmacy is now common place even for those with only mildly elevated glucose levels. We note that such data and regulatory manipulations are the everyday business practices of this industry which are likely being applied to many other illnesses and conditions. We call for considering the real public health costs of tolerating this pervasive and multi-faceted industry distortion of the facts, and allowing their influence over the agencies intended to provide checks and balances to industry aspirations.

Although health care is one of the largest sectors of the U.S. economy, accounting for nearly 20% of GDP, emerging healthcare innovations and developments are largely presumed to be free from the influence of market interests—grounded in sound scientific principles and governed by regulatory oversight. We will argue instead, that health innovations, particularly those that produce unprecedented corporate profits, may be better understood in terms of the manufacture and manipulation of medical "facts" by the pharmaceutical industry toward building and sustaining lucrative healthcare markets. I will focus on the U.S. in this paper, but want to note that these practices impact health markets worldwide.

The first obligation of pharmaceutical corporations is of course, to pursue profits for their shareholders. This they accomplish not by curing illness, but by creating and sustaining markets. That health care corporations seek to make profit is not in itself problematic. However when clinical standards are systematically manipulated to facilitate the goals of industry (Greene 2007), public health is jeopardized. We are concerned that industry-driven "facts" now dominate the imaginations and actions of health researchers, regulators, clinicians and patients, leading them to embrace and adhere to market-serving definitions of illness and health.

One particularly effective strategy for expanding health markets has been to shift the health care agenda from managing disease to managing "risk" for future disease (Kreiner and Hunt 2014), opening the almost limitless growth potential of "preventative pharmacology" (Dumit 2012). Today medications are widely prescribed to otherwise healthy people for only slightly elevated cholesterol, blood pressure, and glucose, purportedly to reduce risk for serious conditions such as heart disease and stroke. This has resulted in a massive expansion of the pharmaceutical markets in the U.S., with nearly 55% of American adults currently taking

prescription medications, and pharmaceutical profits are skyrocketing (Kirzinger, Wu, and Brodie 2016; Cory et al. 2010)

A Diabetes Epidemic?

Here, we turn our attention to diabetes as an example, to consider how "facts" have been produced and manipulated in order to accomplish such massive market expansion. In this new world of equating risk with pathology, diabetes and pre-diabetes diagnoses have grown at an alarming rate, nearly doubling globally in the past thirty years (WHO 2016), and affecting more than one in three American adults (CDC 2016). As this epidemic has unfolded, the market for diabetes drugs has expanded radically. There are currently 14 classes of drugs approved for treating type 2 diabetes in the U.S., which include some of the most frequently prescribed and highest-grossing medications currently on the market (Express Scripts Lab 2016; Pharmacist's Letter/Prescriber's Letter 2017).

How is it, one might wonder, that a non-communicable disease could so rapidly come to affect such a large number of people? Can changes in life expectancy, diet and lifestyle alone account for this dramatic increase? A more proximate set of causes would seem to be regular changes in clinical standards for diabetes screening, diagnosis, and management, which have had the net effect of systematically expanding the market for diabetes medications.

The Conflation of Science and Marketing

In recent years, clinical guidelines and standards of care, that identify specific numeric diagnostic criteria and treatment goals, have come to dominate clinical medicine, (Timmermans and Berg 2003), reinforced by the growth of requirements for institutional oversight and quality monitoring. The authority of practice guidelines is rooted in their being evidence-based,

reflecting careful review of scientific evidence for ideal clinical practice (Hunt et al. 2017). However, a matter of great concern is that the "evidence" underlying guideline recommendations may not be scientifically neutral, but instead is under heavy influence of the pharmaceutical industry. The industry funds the majority of clinical trials research and controls nearly all data published on clinical trials (Matheson 2017; Padamsee 2011). The industry has great influence over how data are produced, interpreted and disseminated. Marketing objectives can be integrated into every stage of research, from research design to dissemination; in order to highlight a product's characteristics, differentiate it from other products, and convince payers of its cost-effectiveness. (See Bernard 2015).

While industry-sponsored research may be scientifically sound, the market-mandate introduces bias toward producing "facts" that are market-enhancing, while suppressing those that may disrupt a product's market. Indeed, critics have pointed out many questionable practices in clinical trials, such as strategic manipulation of study design, targeted data mining, disguising study sponsorship with university-based research contracts, and ghost-authoring to hide industry authorship and create the illusion of multiple studies (Brody 2007; Dumit 2012; Elliott 2010; Timmermans and Oh 2010).

Let us next consider the evolution of diabetes management practice guidelines provides a clear illustration of how marketing strategies may directly impact definitions of illness and health.

Building an Ever-Expanding Market

The American Diabetes Association (ADA), was founded by the Eli-Lily pharmaceutical corporation –the patent holders for the first insulin used to treat diabetes—and the ADA continues to have heavy involvement of pharmaceutical industry affiliates on its experts panels

and among its major donors (Striker 1947). For decades the ADA has published clinical practice guidelines for diabetes diagnosis and management. These guidelines are highly influential: they are widely read by clinicians and incorporated into most institutional oversight and quality monitoring systems. Periodic revisions to these guidelines have consistently resulted in radical expansion of the market for diabetes therapy. In the interest of time, I will only briefly note here that these revisions have systematically expanded the population targeted for screening, simplified testing, and lowered numeric cut-points for diagnosis and treatment goals. Taken together, these changes have resulted in a radical increase in the number of people targeted for pharmaceutical management of their glucose levels.

Next we consider some developments in treatment recommendations that occurred simultaneous to changes in these diagnostic criteria and treatment goals.

Down a Slippery Slope: Revising Treatment Recommendations

For decades, diabetes treatment recommendations had emphasized "lifestyle changes"—diet and exercise—as central to diabetes management, citing increasing evidence that weight management could have a significant impact on blood glucose and other bio-indicators. This all began to change in the mid-90s, when the Diabetes Control and Complications Trial (DCCT) (Diabetes Control and Complications Trial Research Group 1996), reported that maintaining tight glucose control through aggressive use of medications reduced diabetes complications in type 1diabetes patients. This finding was soon extended to the much larger group of type 2 diabetics, and using pharmaceuticals to tightly control glucose was quickly taken up in

guidelines as the appropriate objective for all diabetes patients. At the same time, lifestyle changes were spoken of skeptically, if at all in subsequent guidelines.

We don't have time to review the details, but let me summarize what has happened since. A number of large follow-up studies were undertaken, seeking to document the value of expanding use of pharmaceuticals for type 2 diabetes, as well as for preventing diabetes in so-called "prediabetics." Each of these studies did not support expanding the pharmaceutical markets to these groups, and instead raised concerns of worsening hypoglycemia and increases in serious side effects, and increased mortality. (ACCORD Study Group 2011; Heller and The ADVANCE Collaborative Group 2009; Cooper-DeHoff et al. 2010; Zoungas et al. 2010; Knowler et al. 2002, Montori and Fernandez-Balsells 2009).

While the findings of these various studies as first reported would not support expanding the use of pharmaceuticals for preventing and managing the diabetes "epidemic," the data have been analyzed, re-analyzed, followed-up and reinterpreted in ways that support aggressive medication use.

Across time in the ADA diabetes management guidelines there has been a striking intensification in the sense of urgency ascribed to reaching goal numbers, as though having a test reading above the population norm is itself a pathology, requiring immediate and aggressive pharmaceutical intervention. The ADA Standards of Care now include elaborate pharmaceutical recommendations in the form of medication treatment algorithms. Currently these call for medications to be started at the time of diagnosis, with additional drugs added every three months if the goal glycemic level is not reached. Patients thus are routinely prescribed three anti-diabetic medications within six months of diagnosis. The net result is that polypharmacy is now

the norm in diabetes management, even for mildly elevated glucose (Hunt, Kreiner, and Brody 2012).

Blurring the Boundary between Commercial and Public Interests

Thus, despite weak and contradictory evidence for the value of expanding diabetes diagnosis and for the aggressive use of pharmaceuticals in managing mild cases, the "facts" have been spun in ways that continually expand and stabilize the highly lucrative market for diabetes drugs. This raises the question of whether there may be institutional biases that facilitate building and protecting such markets.

Critics argue that the pharmaceutical industry uses its wealth to influence institutions that should be providing checks and balances, establishing unprecedented control over its own regulatory environment (Abraham and Ballinger 2012, Angell 2004). Concerns have been raised about the independence, quality, and trustworthiness of professional societies such as the ADA, noting large numbers of pharmaceutical industry affiliated individuals sit on guideline-setting panels which rely on questionable evidence or even "expert opinion" (Choudhry, Stelfox, and Detsky 2002; Graham et al. 2011; Neuman et al. 2011; Sox 2017).

Even if there is bias at the ADA, one might expect that if these drugs are truly dangerous, the government drug regulators, like the U.S. Food and Drug Administration (FDA), would not permit them to be used. Unfortunately, there appears to be a pro-industry bias at the FDA as well. The pharmaceutical industry has been particularly successful in wielding political pressure over the FDA (Angell 2004; Brody 2007). There is a preponderance of industry-affiliated experts on FDA advisory committees (Pham-Kanter 2014; Lurie et al. 2006), and long-time director of the FDA Center for Drug Evaluation and Research, Janet Woodcock, has made it clear she is

working to position the FDA to act as a partner to the drug industry rather than an adversarial regulator (Kaplan 2016). It is interesting to note that approval of some of the most profitable diabetes drugs align neatly with the market-expanding changes in diagnostic and management criteria.

Indeed, the FDA has clearly been reluctant to respond to mounting evidence of serious health concerns associated with some diabetes medications. For example, despite strong evidence that Actos and Avandia (TZDs) cause congestive heart failure, they have been relabeled with stern warnings, but have not been removed from the market (Davis and Abraham 2011). Similarly, Invokana, a drug expected to quickly reach blockbuster status, had been associated with very serious health effects prior to its release. Still, the FDA went forward with an expedited approval, then two years later began adding warnings to the drug's label amid mounting evidence of it causing ketoacidosis, bone loss, and kidney damage. The drug remains on the market today, and the FDA has left further evaluation of these and other problems to a five-year post-market review (McElrath 2016; FDA 2016)—in effect using the general public as clinical trial subjects.

Beyond the impact of conflicts of interest in the composition of panels and review boards, be reminded of the industry influence over producing and interpreting the very data on which guideline panels and regulators base their recommendations. Thus the heavy influence of the industry permeates all levels of the processes the public trusts to provide checks and balances in setting clinical goals, and assessing the benefits and harms of the emerging pharmaceuticals designed to help reach them.

Conclusion

We have argued that the massive growth in the population targeted for pharmaceutical diabetes management is the result of a concerted and highly successful effort by the pharmaceutical industry to control and construct the "facts" in ways that extend and secure mass markets for emerging drugs. Broadening screening, amending testing standards, extending diagnostic criteria, and engendering a sense of urgency that requires aggressive use of pharmaceuticals—all of these strategies operate together, paving the road to blockbuster drug sales.

While our analysis has focused only on diabetes, it is important to consider that these are the everyday business strategies of a highly successful industry, that have assuredly been applied to all kinds of conditions—hypertension, cancers, hyperlipidemia, depression, thyroid disorders—wherever money can be made. In large part, strategies to expand and protect markets recast clinical knowledge in ways that require extensive and permanent use of prescription medications. When commercial interests dominate not only the production and interpretation of scientific "facts" as well as the regulatory processes determining how health and illness are defined and managed, we are all at risk.

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