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Exploring the Formation of Digital Therapeutics

Margaret Martin

Abstract

Purpose: This critical ethnographic study explores regulatory, social, and commercial spheres of behavioral health innovation in the United States through the lens of a burgeoning employment sector: digital therapeutics. By examining ways that digital therapeutics are being defined and operationalized in connection with shifting policies to evaluate digital health, this study draws on collected data to examine evolving conceptions of evidence, access, and public benefit happening in the name of health innovation.

Background: Pursuant to the 2016 passage of the 21st Century Cures Act, The U.S. Food and Drug Administration is actively revamping its evaluation frameworks for digital health products. Policies to appropriately regulate software as a medical device (SaMD) are in development to review whole company characteristics rather than individual product efficacy, address the iterative nature of software product development cycles, and empower commercial actors to provide their own effectiveness analytics for post-market assessment purposes.

Methods: A qualitative approach was used drawing on multiple data sources for this project. These sources included: collected documents (n=25), in-depth individual interviews with stakeholders working on or with knowledge of digital therapeutic products across professional areas including engineering, clinical science, regulatory science, executive leadership, academia, and financial services (n=41), and ethnographic observations (n=75 hours) taking place at two digital therapeutic conferences, technology sector worksites, interview locations, and an FDA

workshop. Data were transcribed, thematically coded, and analyzed using a qualitative software program, Dedoose.

Results: Digital therapeutics are being defined and operationalized in connection with the digitization of behavioral health. This shift entails a connected commercialization of behavioral science interventions. In an environment where standards to guide product development are unclear, regulatory expertise is heightened as an asset for which companies compete. The FDA's evolving regulatory schema advantages commercial actors with more resources, which may impact the types of organizations from which innovative and FDA approved digital health products originate.

Digital therapeutics advance conceptions of health that center the optimization of individual selfhood through processes that seek to "purify" interventions. These "purified" interventions, often digitized therapeutic encounters, eliminate interference and variation by human actors in the name of improving biomedical intervention standards. Commercial promises to increase digital access to care ignore varying ways that access is invoked through product creation, including the possibility that digital therapeutics may hinder in-person access to therapeutic relationships and contribute to stratifying occupational dynamics with implications for health equity.

Conclusion: This study highlights ways that scientific evidence is being reshaped in the commercialization of behavioral health, in addition to the co-production of digitization and commercialization as stratifying processes. Findings shed light on the need to assess evidence production within emergent health technology production more closely. Ethical guidelines to define and center equity should be incorporated into digital health implementation strategies and are of considerable importance to the domains of regulatory and translational science.

Table of Contents

List of Figures

Chapter 1: Methods

Introduction

In November 2017, the New York Times released a news article entitled "First Digital Pill Approved to Worries about Big Brother." The piece garnered 152 comments and was widely circulated, pointing to ethical questions associated with MyCite, an ingestible sensor produced by a company called Proteus Digital Health, used to track medication compliance in people living with Schizophrenia and Bipolar I disorder (Belluck, 2017; Proteus Digital Health Website, 2017). Recently approved for sale by the U.S. Food and Drug Administration (FDA), it was deemed safe enough to market, but the jury was out as to whether it was effective. A few months later, in May 2018, another New York Times article featured a start-up company named Pear Therapeutics in a piece discussing ReSet™, the newly approved digital therapy used to treat opioid use addiction through cognitive behavioral programs delivered on your iPhone. The article prominently featured the company's MD/venture capitalist founder, Corey Mann, and mentioned the $500 million fundraise, to date (Singer, 2018).

Digital therapeutics, as they were called in the news, popped up in public news outlets in 2017 as the next important wave of health technology innovations, leveraging artificial intelligence and occupying a middle ground between pharmaceutical drugs and medical devices. Ostensibly more rigorously validated than general digital health products, many of their makers were partnering with traditional pharmaceutical firms to develop novel addenda and substitutes for existing therapies. Their hype dovetailed with both a flurry of venture capital dollars into artificial intelligence for health care (a figure estimated at $4 billion during the 2019 year alone) as well as congressional approval for the 21st Century Cures Act, a public law designed to expedite availability of novel drugs and devices (Landi, 2019; H.R.34, 114th Cong., 2016.)

As President Barack Obama left office, both fiscal and regulatory incentives were set to create a new market for novel healthcare gadgets. Remarkable in light of the polarized political climate of the time, the 21st Century Cures Act was shepherded in with ubiquitous bi-partisan support on November 16, 2016 and included urgent language to allocate $6.2 Billion in funding to expedite "21st century cures" to patients (Lupkin, 2016; Mendoza, 2017).

Following an influx of funding from public and private sources after passage of the 21st Century Cures Act, federal agencies like the United States Food and Drug Administration (FDA) which benefitted from the boost in dollars, still had to figure out how to actually allocate the funds. Tasked with the job of revitalizing their approach to evaluating digital health, FDA's Center for Radiologic and Digital Health went to work crafting early risk-based guidance, hiring artificial intelligence experts, and seeking public input (Kesselheim and Hwang, 2016). Largely built with hardware devices in mind, neither their timelines for approving digital health products, nor their expertise in algorithmic evaluation was concurrent with 21st century software capabilities (Gottlieb, 2017). It was time for them to revamp their frameworks and the looming question was how to do this while assuring the safety and efficacy of the products they were tasked with reviewing.

Currently, FDA has no specific framework for evaluating digital therapeutics as differentiated from other types of digital health technologies, but policies to appropriately regulate the more general product area termed "software as a medical device (SaMD), are in development (FDA Precertification Pilot Program, 2017; Wechsler; 2017). FDA's goals are to envision a regulatory pathway that lifts barriers to market for SaMD devices—serving as an incentive for technological innovation— while protecting the public from risks. The current method for categorizing low-risk SaMD leaves significant grey area among products, including

many classified as “digital therapeutics” which do not fit squarely within a specific risk category as determined by FDA. These loopholes leave considerable space for companies developing novel products to shape the regulatory environment overseeing them.

This dissertation was foregrounded by almost two years of work within a startup company environment attempting to build a caregiver navigation app. The work experience was a dramatic shift for me personally; prior to joining this startup group, I had worked as a public health nurse solely in community settings. Acknowledging the frustration that often accompanies community-level work, I was motivated by the exuberance of this startup group to create a product that would make resources more accessible to patients. Its partnership with a notable healthcare institution seemed to elevate the group’s credibility in my mind, and to some degree, I drank the startup Kool-aid. I was eager to contribute to a rising tide of innovations aimed at improving health, and also deeply curious about the nature of work within “tech” environments. Our company was building an application to assist caregivers of people living with chronic disease and my mandate was both to work with patients through our application, as well as to set up pilot programs within health institutions to trial the product.

What commenced in my job change was a dizzying 18 months working out of a venture capitalist’s garage in Palo Alto, where the boss of the show hosted midday poker tournaments from a glass room with floor-to-ceiling curtains in the middle of our office space. We were a congenial bunch of 12 that grew to 29, walking to lunch together most days, always finding time to ham it up over HipChat. In truth I was usually about 30 seconds behind the joke punchlines, if I caught them at all, and spent the first several days completely bewildered both by how to send a GIF as well as by the sheer magnitude of them coming across our group chat window. I was trying hard to get used to what it felt like to sit and stand in front of a computer screen all day

long matching the friendly, easygoing demeanor of my colleagues. And I was in the midst of packaging my clinical experience into a systematic approach for working with people, one that involved x and y axes, inputs and outputs. Our founder asked me to prioritize the development of our "caregiver journey," to map on a timeline all the experiences someone would go through both in living with a chronic disease, as well as in caring for a person living with chronic disease. Once we had this information perfectly arranged, we would map service offerings onto these experiences, and define the things that our team of assistants would do to be helpful to customers of our service.

With candor, I recall our user-experience expert emphasizing how crucial the development of these services were, joking that, "No one is going to pay us to call them and say, 'Hey, I'm thinking about you!'" While we all laughed in agreement, I was the only employee who had previously worked with patients and felt embarrassed by remembering the number of times I had done just that very thing as a nurse. In my experience working with families caring for someone nearing the end of life, the simple statement had seemed at times to be the only thing I could offer, in addition to being an honest thing to say. Nevertheless, I recognized that this environment was different from healthcare settings I had worked in previously, and that our service was something people would need to find valuable enough to pay for -- so I kept my past employment blunders to myself and deferred to our user-experience expert, whom I trusted knew way more about marketable services than I did.

As time wore on, it became clear that our start-up group was missing some special, crucial ingredient. Despite our CEO's myriad conference appearances and pitches, despite the notable venture capital firms who'd come to meet with us, no one was willing to commit capital. Investors were concerned about our services' lack of "scalability," which made good sense at the

time since at that point our services were largely oriented around filing insurance claims and following up on outstanding or equivocal medical bills – tasks so far from standardizable that even as we completed them, we couldn't explain how we had done so. Our successes seemed like random strokes of luck – getting the right call center employee on the phone, catching the right claims representative after a good lunch. We didn't have a specific enough focus, and the pilot projects we had sourced with academic medical centers were taking too long to get up and running. What's more, the conversations between our clinical partners and the investment personnel always seemed to reveal something of an impasse, or at least the extent to which no one understood the other person's language. Our investors, early ex-Facebook billionaires, had gamed our position in the Apple App Store, prompting a bounty of videogame-playing teenagers to download our application and send in gratuitous photos of their genitalia. All the while, the real number of meaningful users on our service were few.

These predicaments were as anxiety-provoking for our founders as they were fascinating to me. I wasn't sitting in the hotseat with our clinical partners or our investors, so in most ways I bore no real consequence for the potential outcomes of this trouble, and was rather enjoying the bird's eye view inside the ring. After a year and a half of these shenanigans, I was presented with the opportunity to start a Ph.D. where I could gain the skills to study these dynamics. I jumped ship. The company closed down a few months later, unable to raise the next round of financing it needed to grow and keep the lights on. Most of my former colleagues found positions at other start-ups, a couple left for medical school, and our founder took a break from working, recasting his twitter profile to be less about health care and more about the Boston Red Sox, at least for a short while, following the company's close.

Fast-forwarding to 2020, several digital health companies that started at the same time as our group are now sitting on the precipice of an initial public offering, or company acquisition. The circumstances we encountered then were chalked up to the destinies of most start-ups: the wrong smattering of people, a product too early for the market. It was the nascent days of digital health.

* * *

This project, while the extension of a pilot study I conducted in 2016-2017 on stakeholder collaboration in digital health, is also the product of my own sense-making about what is happening at the border between technology companies and health care organizations. Findings from my earlier research pointed to a blurring of professional roles across institutions, and to an increasingly fluid employment environment where employees switch jobs frequently, and leverage discourses from both established health care institutions as well as technology firms in order to bolster start-up company legitimacy.

Considering digital therapeutics was a way, in keeping with the call to "follow the money," to study healthcare industry formation. Even the notion that there are discrete industries for healthcare (notwithstanding controversy about referring to healthcare as an industry in and of itself) is a somewhat new phenomenon. Traditionally these industries are considered pharmaceutical, medical device, and biotechnology (Grundy, 2018). More recently, "digital health" might be added to the group, particularly in light of software advances in the last decade (Sharon, 2016). Nevertheless, I chose digital therapeutics as a "category" because it presented the most pressing regulatory "blurriness." The area exhibited sufficient cohesiveness (e.g. industry conferences, visible companies, an established non-profit trade group) to render it

visible enough for examination despite its invisibility as a defined category with attending regulatory framing by FDA. As I plowed further into the empirical literature on digital health technology, I also became more curious about the widespread assumption that digital access solves problems, or, put a different way, that framing "access" as a basic health problem appropriately characterizes the issues at stake.

In crafting this project, I was especially interested in how people work together in the name of innovation, and for whom this collaboration matters. Health care innovation – the environments in which it is taking place, the resources allocated to its promise, the mission-specific glue affiliating its proponents across institutions – is redefining the way we think about care problems within and across health systems. Studying digital therapeutics, a nascent area of digital health, was an opportunity to examine how early industry activity takes place across regulatory, commercial, ethical, and social arenas in the name of advancing 21st century cures. I chose to focus on the creation rather than uptake of these inventions as a way to examine how sociocultural elements of a burgeoning workforce become built into physical "things," and how stakeholders work together in absence of regulatory guidance to bring them into existence. While my data are specific to digital therapeutic product creation, they speak to larger trends across other new labor arenas and beckon further qualitative analysis on the ethical and social dimensions of technology production more generally.

Review of the Literature

Digital health product development, including the social processes and federal policies that inform which types of products and product models are built and deployed within health systems, is understudied. To date, there is no research on technology production practices for health, and quantitative methods routinely employed in health services research are poorly suited

for characterizing sociocultural aspects of organizational activity in emergent and novel situations. Research on existing digital products for human health tends to focus on clinical contexts, stressing the advances that machine learning can make in efficiency, quality, and safety (Faggella, 2018 and Jiang et al., 2017).

The study of digital health production – how product prototypes originate, how resources are allocated to build them, the motivations of their crafting, and the social, cultural, and financial arrangements girding their creation – is virtually non-existent both because of the perceived difficulty of obtaining entrée to private company employees, as well as a current focus on implementation science that shapes the public fundability of research proposals. The qualitative expertise necessary for analyzing these arrangements is scarce within many health research institutions. Further, the pace in which technology propels advances and new research-worthy social phenomena is hard to match with federally-supported grants requiring long timelines for funding through to dissemination of results. Nevertheless, there is growing interest in examining these topics from the standpoint of resource allocation and the equitable provision of care. Calls for work that can investigate the "datafication of health" have begun to surface both in social science arenas, as well as in clinical care contexts where the public interest is at stake (Ruckenstein, et al., 2017; Milstein, 2020).

This research engages questions crossing several areas of scholarship including bioethics, biomedicalization, and science and technology studies. A common thread knitting the areas together, one that became more evident with the hindsight of data gathered for this project, is the notion of health equity. If digital therapeutic products are better appreciated as originating from a complex set of social arrangements, it is possible to identify and examine upstream aspects of their structural development that impact care provision.

As empirical work, this project aims to fill a gap in public knowledge about how digital products for health are originating, and what sorts of processes underlie their creation. Significant aspects of my research deal with the policy context in which digital therapeutics are being built, and how regulatory and commercial activities take place in tandem. In order to provide some background that contextualizes the policy environment, I will provide a brief history leading up to the passage of the 21st Century Cures Act and then discuss the connected areas of scholarship to which this research contributes.

A Brief Digital Health Policy History

While "health IT" and "med tech" are terms that have been around for several decades to describe the industry spaces supporting technology development for health care, the advent of the smart phone ushered "digital health" into vernacular language. The United States' Food and Drug Administration (FDA) defines digital health as an umbrella term that, "includes categories such as mobile health (mhealth), health information technology (IT), wearable devices, telehealth, and precision medicine (U.S. Food and Drug Administration, 2017a)." What is distinctive about these technologies in comparison to the health tech of yore is that they: 1) often include a significant software component, if not existing solely as a software technology 2) are often designed for patient use rather than health systems and 3) do not confine use to the boundaries of the clinic setting. Additionally, a very blurry regulatory landscape has developed in response to these technological evolutions. Where once a medical device was something either embedded in the body or not, distinct from a pharmaceutical drug, and/or existed as a clear hardware product with a specific use-case, pharmacologic products now contain ingestible sensors and software that resides in the body, while also monitoring it. The FDA has stretched to

develop regulatory processes capable of assessing risk and efficacy alongside rapidly evolving technological capabilities.

Alongside the formation of a new industry space, and outside the FDA clearinghouse, health institutions have shifted to computerized health records during the last decade. The newly amassed "big data" contained within electronic health records (EHRs) has transformed health system problems into challenges mirroring those found in other industries striving to optimize the efficient flow of information from one place to another. The piece of legislation that enabled this shift was passed in 2009, the Health Information Technology for Economic and Clinical Health (HITECH) Act. Since then, two other policy pieces, the Precision Medicine Initiative (PMI), and The 21st Century Cures Act have also been enacted, and each has influenced the development of Digital Health as a field.

The HITECH Act

The piece of health care legislation responsible for bringing about the "big data revolution" in health care is the Health Information Technology for Economic and Clinical Health (HITECH) act of 2009. This piece of federal legislation was signed into law as part of Obama's stimulus package in the wake of the 2007 economic recession (H.R.1, 111th Cong., 2009). The bill, part of the American Recovery and Reinvestment Act, allocated approximately $19 billion to be given to health systems in order to incent health systems to make a final transition from paper to electronic health records (Centers for Disease Control and Prevention, 2017). The act "provid[ed] HHS with the authority to establish programs to improve health care quality, safety, and efficiency through the promotion of health IT, including electronic health records and private and secure electronic health information exchange (U.S. Government, 2017)." Apart from any analysis regarding the effectiveness of this piece of legislation eight

years later, the technology intended to solve for a trifecta of quality, safety, and efficiency. The transition from paper to software meant that throughout the U.S., a giant sea of structured medical information was amassing, a data source which promised new knowledge about treating patients and curing disease– aims also leveraged by the Precision Medicine Initiative and its prioritization of individualized care.

While efficiency has ostensibly increased by having more organized and accessible patient information stored in computers, this machine-enabled management of health information has been fraught with interoperability issues. A surge of structured and institutionalized medical data accumulation within health institutions ensued, enabled by software packages that were not universally implemented and compatible across practice and institutional domains. Meanwhile, a separate ocean of personal health data has formed outside of the clinical domain, enabled by consumer technology advances in the form of mobile-based applications, trackers, and self-monitoring devices for consumer health. Much of these data are housed within private technology companies that have built the machines to collect it. Little is known about the practices and policies within these institutions, a gap which has informed digital health evaluation research on the trustworthiness of the information they collect (Sbaffi & Rowley, 2017). Several questions arising from new practices pertaining to the meeting points between digital health and the provisioning of health care are: Where is the line between health and illness, between clinical information and personal health information and who gets to decide? How are clinicians supposed to respond to patient-generated data? What responsibility do private companies bear for the reliability of the data their technologies gather? Each of these questions, and many more, are further implicated in the aims of the Precision Medicine Initiative.

The Precision Medicine Initiative

In 2015, President Obama called for the PMI to "enable a new era of medicine through research, technology, and policies that empower patients, researchers, and providers to work together toward development of individualized care" (Precision Medicine Initiative, 2015). On the National Institutes of Health (NIH) website, the Precision Medicine Initiative describes its goal as one in which treatments can be personally tailored to individuals on the basis of their own unique set of genomic characteristics (National Institutes of Health, 2018). Pharmacogenomics, as it is characterized, promises to impact care across a wide range of conditions including diabetes, cardiac disease, and cancer (Pereira, 2011; Dawed, 2016; Rodriguez-Antona & Taron, 2015). To date, many progressive health systems are in the midst of figuring out how to implement pharmacogenomics information into models of care, as well as genomics education for clinicians in training, all in in keeping with the mission of the Precision Medicine Initiative (Carabello et al., 2017; Flowers et al., 2019).

In addition to pharmacogenomics goals, in conjunction with PMI, the National Institutes of Health spearheaded the All of Us research program as an effort to gather personal health data from 1,000,000 or more people in order to develop better tailored treatments, earmarking approximately $55 Million to further its goals. In October 2017, a video series was released describing the potential benefits of research enabled by data from electronic health records (National institutes of Health, 2016). The All of Us campaign is described as a collaborative effort between industry and academic partners across the United States, working together to usher in the best, most innovative treatments. The program presents a platform for researchers and an intention to leverage the best technologies for human health, working across institutional lines in order to do so (Bresnick, 2017).

Whereas the HITECH act made big data gathering possible within health care environments, the Precision Medicine Initiative extends its goals in aspiring to use this health data to improve treatment outcomes. While it is clear through the PMI's mission statement that a new era of technology-enabled health care is on the horizon – bolstered by academic, health system, government, and industry alignment – the practices of various collaborating industry partners building the "platforms" for digitized information remain basically opaque. These production practices – specifically for medical device creation – have been encouraged by a final piece of digital health production legislation, the 21st Century Cures Act, passed in December 2016.

The 21st Century Cures Act

The 21st Century Cures Act, which has both pharmaceutical and medical device stipulations, has helped usher forward a restructuring of the FDA's safety and efficacy evaluation processes, de-emphasizing pre-market approval and focusing heavily on post-market assessment using real-world data. One of the most significant aspects of the bill with regard to digital health production is that it exempts many forms of software from FDA approval, including software for clinical decision support, electronic health record, administrative, and lifestyle purposes (H.R.34, 114th Cong., 2016). Since December 2016, the FDA has been in the midst of restructuring its approach to evaluating digital health technologies in order to better clarify guidelines for developers. In the summer of 2017, the Centers for Devices and Radiologic Health (CDRH), the FDA unit charged with overseeing digital health technology, published a Digital Health Innovation Action Plan in order to 1) Clarify the new act's guidelines for designating software as a medical device and 2) Launch a precertification pilot with 9 companies in order to draft new digital health technology oversight. The pilot was conceived in part to move the FDA away from

reviewing medical device products on a case-by-case basis, and move the agency toward streamlining products through an approval process based on the extent to which a company is known as having a "culture of quality and excellence" (U.S. Food and Drug Administration, 2017b). As Bakul Patel was quoted during a public webinar on the precertification pilot, "The goal for having…a culture of quality and organization excellence is to have an ability to get a software as medical device to market faster." He continued: "Traditional implementation of the premarket requirements may impede or delay patient access to critical evolutions of software technology, particularly those presenting a lower risk to patients" (U.S. Food and Drug Administration, 2017c).

Analysis of the Bill: Repercussions for Digital Health Labor Space

Federal initiatives like Obama's 2016 National Artificial Intelligence Research and Development Strategic Plan aim to create legislative pathways for boosting the economy and keeping pace with international technology innovation. It follows that, not only does a bill like the 21st Century Cures Act signal a change in regulatory stance that seeks to quicken the FDA approval process for new technology products, but, equally important, it is favorable to the labor sectors developing it. Just as the passage of the HITECH bill in 2009 benefitted the companies developing meaningful use software as part of an economic stimulus package pushing technology into health systems, the 21st Century Cures Act also incents companies through a language of patient access.

The first way companies experience a heightened incentive is through a streamlined, faster, and less burdensome regulatory pathway to market. This helps make an entrepreneur's opportunity to develop health technology more equivalent in risk to that of other industries without strong regulatory oversight, particularly among new software products that will be

exempt from FDA jurisdiction. Second, among digital health technologies that are still subject to FDA approval due to a higher health risk classification, there is more complete information as to how these technologies will be evaluated by the FDA and what the timeline for evaluation looks like, thus lessening the risk from an investment perspective. Third, with the FDA's newly initiated precertification pilot, it will be companies rather than individual products that are subject to evaluation according to whether and how they demonstrate the "culture of quality and organizational excellence (U.S. Food and Drug Administration, 2017c)." The nine companies taking part in the pilot project are a mix of public, private, and non-profit corporations including Apple, Google's Verily, Roche, and Tidepool (U.S. Food and Drug Administration, 2017b). This shift to a company rather than product focus will orient other burgeoning digital health groups to whatever legitimacy standards are being set. While it is too early to know how and in what ways these legislative and concurrent programming changes will affect the nature of digital health work, in considering new device legislation in relationship to the pharmaceutical industry and concurrent legislative levers, there are many corollaries.

Similarities with Drug Development Pathway

Certain provisions of the 21st Century Cures Act mimic legislative pieces already in place for drug development, namely the designation of a "Breakthrough Device" pathway for innovative pharmaceutical therapies (H.R. 34 111th Cong., 2009). According to the bill, an extension of the previous Expedited Review Pathway, the FDA has agreed to create a program to streamline the development and review of technologies considered to present novel treatment or diagnosis of debilitating conditions and diseases where no alternatives exist, or when having the technology available is in the best interest of the patient (Kesselheim & Hwang, 2016). This pathway already exists on the pharmaceutical side and is designed for drug therapies such as

ones developed in accordance with the Orphan Drug Act of the 1980's. The provision decreases the time it takes devices and/or drugs to get into the market (H.R. 34, 111th Cong., 2016; Letourneau et al., 2016; Cortez, et. al, 2017). On the pharmaceutical side, however, Orphan Drug classification also entails a monopoly pricing mechanism such that drugs with this designation are not only allowed to come into the market more quickly, but are also promised 8 years of competition-free sales as other comparable drugs are prohibited from entering the market during that time. Of note, in 2017 34% of newly approved drugs were Orphan Drugs (Challener, 2018). While there has been no discussion of a monopoly pricing mechanism for breakthrough medical devices, with drug and device categories becoming so blurred and needing such similar legislation to ensure safety and efficacy, it is possible that a pricing mechanism like this could come to pass in the future which would further incent the area for developers and investors alike. Venture capital funding mechanisms have evolved in response to the Orphan Drug Act because of the profit opportunity present in regulated pricing (Beier, 2017; Stack et al., 2016).

Connections with Digital Health

Thus, within the present-day landscape of digital health, significant software components of many technologies and the heightened risk profile of others are blurring the lines between drug and device categories, calling for new regulation needs (e.g. Pear Therapeutics and Proteus Digital Health). In doing so, the FDA is taking steps to become more collaborative with industry in its standard-setting practices and in late 2017 formed a group of "Entrepreneurs in Residence, (EIRs)" appointed technology experts to help define the architecture for how the FDA will approach digital health oversight moving forward (U.S. Food and Drug Administration, 2017b). Previously the public has grown accustomed to seeing progressive venture capital firms and other start-up accelerators host EIRs in an effort to incubate profitable projects onsite, providing

resources and guidance to fledgling developers. The FDA is replicating this learning approach in an effort to build a relevant and timely regulatory process that will reward approved companies with faster pathways to market.

The structure of the legislation and resulting changes signals a federal position supporting the need to get medical device technology out to the market more quickly. This is in keeping with the legislation's placement within a stimulus package designed to bolster the economy. In effect, it supports the perceived economic benefit to these labor spaces above the protective mechanisms that have been in place to prevent products from being sold until they are deemed safe and effective.

Proponents of the overhaul cite patient need as a primary driver. Opponents perceive a danger in bringing more products into the market without safety assurance processes (Brown et al., 2016). The real risk to patients is currently undetermined and the FDA is faced with creating new risk-classification classes for technologies that do not fit squarely within any existing class designations. The timing of the passage of the 21st Century Cures Act is significant because, dovetailing with the era of Precision Medicine, it has helped create a larger opportunity for digital health products to come into existence. In this era of incentivized developer opportunity and forthcoming medical device market-entrants, we have little understanding of digital health production practices themselves. Increasing public knowledge in this area is important not just for individual patient safety, but also for advancing a more nuanced conversation about resource allocation, the integrity of scientific evidence, and potential underlying mechanisms for the commercial determinants of health.

Datafication, Public Health, and Biomedicalization

There is a widely implicit assumption within the evaluation literature on Artificial Intelligence projects for health/care that the positive impact of digital health technology to patients, providers, and health systems is imminently forthcoming. For several years, a mounting discourse has named health/care issues as "adaptability and interoperability problems," positioning digitized health care as an "unlocking" agent in the puzzle (Black, et. al, 2011; Wachter, 2015; McCann, 2017). This techno-optimistic attitude reveals the promissory aspect of technological enterprise, namely, that problems may have already been defined in a way to show technological answers as the solutions (Alam, 2016). This logic encourages attention toward tweaking existing, imperfect machines rather than defining health problems in ways that allow for non-technical solutions.

As stated by Kuziemsky, et al. (2017), "there is a shortcoming of empirical research on "contextual factors" in health information technology development. Social aspects of technology development, such as those that are the focus of this project, are examples of contextual factors. In defining characteristics of "human-centered design" and "sociotechnical" design processes, the goals of these activities are described as understanding the relationships between technology, the users of the technology, and the social context of the technology use. "Technology," however, is often not considered as itself socially constructed – it is treated as neutral territory in juxtaposition to other social phenomena (Kuziemsky et al., 2017: 2).

Empirical literature within the realm of participatory design for digital health tends to describe production processes by a) naming members of the decision-making team -- usually a combination of clinicians, technology designers, and end-users [sometimes clinicians and sometimes patients]), b) naming a software development methodology such as "iterative" or

"Agile" design and c) describing the frequency of the design team's meeting schedule (Agile Design Manifesto, 2018; Tang, et al., 2018, Pollack et al., 2017). In most cases the design process usually begins with a functional prototype that has been incubated elsewhere, about which there is no mention. Notable exceptions to this construct are arrangements where the developers hold academic appointments within institutions and are founders of the technology, hold equity interest in the technology, and/or are among its employees or paid consultants. This design structure has been prevalent in the creation of digital translations of in-person or paper-and-pencil interventions/tools (e.g. Matthews et al., 2016; and Chen et al., 2016), and is prominent in the social arrangements of stakeholders involved in building digital therapeutics.

Within critical social science literature on digital health practices, attention has been given to digital health discourses as a form of practice emphasizing the "customer empowerment" language used by companies to market their technologies, even in the midst of ambivalent customer experiences in using them (Schull, 2017; Sharon, 2017; Ruckenstein and Schull; 2017). Within this genre of scholarship, empirical work has focused on non-human elements of digital health culture, namely the growing literature on algorithms and dangers associated with the interpretive power of health data. Algorithmic investigations have focused on cases where their decision-making replaces human autonomy (Gillespie, 2014 in Ruckenstein and Schull; 2017), where they are programmed to reproduce social difference (Hogle 2016 in Ruckenstein and Schull, 2017) as well as gendered assumptions (Eveleth, 2014; Lupon, 2015). Further scholarship in this area uses a language of "imaginaries" to describe production practices centered on building electronic nudging mechanisms to encourage behavior change, "reducing uncertainty over which day-to-day activities to pursue" (Berg, 2017: 6 and Schull, 2016 in Ruckenstein and Schull, 2017: 269.) In connection to emerging scholarship on the datafication of

health, these investigations look at digital health practices associated with marketing discourses, as well as algorithmic implications for human action (Prainsack, 2020; Recht et al., 2020). These critical lenses speak to a consideration of data as inherently non-neutral and connect with a public health ethics that is concerned with equity in development and dissemination activities.

In public health ethics, the concept of "relational personhood" is central to social justice and equity concerns (Sherwin, 1998; Jennings, 2017; Prainsack, 2017; Cole, 2020). This focus on personhood as bound up in relationships is a move away from historic considerations of individual actions as a function of personal independence, autonomy, and strategic rationality and stems from feminist scholarship on care practices (Butler, 1990; Benner, 1994; MacKenzie and Stoljar, 2000; MacKenzie, 2010; Wardrope, 2015; Prainsack, 2017). Notions of relational personhood underpin normative decision-making for social goods such as medical information commons and public biobanks, as well as the re-envisioning of consent practices in medical contexts (Koenig and Gates-William, 1995; Manson and O'Neill, 2007; Foster, 2008; Dickenson, 2013; Prainsack, 2017; Cole, 2020). Relational personhood also has implications for this project, and the way that patients/consumers are being considered by companies developing digital therapeutic products. "Championing the 'We' in 'Me'" seems to run counterintuitive to the era of personalized medicine in which digital therapeutics are situated; it challenges the idea that individuals are organized for empowerment and improvement by the latest healthcare gadgets for self-tracking and diagnosing wellness. Nevertheless, insofar as this research contributes to a public health interest, work on relational personhood and relational aspects of care practices asks, "what is in the common good?" and "how can it be achieved?" This directly connects to questions of access and equity at the core of this project's motivations to better understand technology development logics. Emergent scholarship in this area has used a

justification framework (Boltanski and Thevenot, 2006) to consider a plurality of ways that "the common good" is conceptualized by technology companies such as Google, Microsoft, and Apple (Sharon, 2016; Sharon, 2018). This research considers the common good in examining how problem formation and resource allocation coalesce to make digital therapeutic innovations possible. While distinct from Sharon's examinations of the common good within the activities and discourses of large corporations, this project examines early start-up company activity that is subject to and benefits from many of the same capital arrangements that have fueled these types of corporations during infancy.

Finally, this work contributes to other scholarship in the realm of biomedicalization (Clarke, et al., 2003), including better understanding the types of human, financial, and cultural capital (Shim, 2010) going into digital therapeutics as one example of technoscientific development in action. Previous work has considered how and in what ways value is constituted by digital health company activity (Alam, 2016) and how health information is financialized (Blacker, 2014), however regulatory aspects of the area are largely unexamined by scholars, particularly in connection with company formation. In this dissertation, I pull from the broader Science and Technology Studies literature to consider ways that regulatory and commercial activities are being co-produced, privileging certain types of knowledge production over others (Ostrom and Ostrom, 1977; Latour, 1990; Jasanoff, 2004, Chapter 1; Kristensen and Ruckenstein, 2018).

Overview

In the chapters that follow, I explore the development of digital therapeutics as a subset of the digital health commercial enterprise in connection with its regulatory framework, and situate this work in San Francisco, where many companies are physically present and where my in-person interviews took place across two years of fieldwork. In Chapter 1, "Methods and Reflections," I describe the overall structure and iterative approach to this ethnographic project and reflect on the contributions of contextual data present at interview sites, made more explicit by my experiences providing patient care in the same urban environment. I reflect on the place and appropriateness of ethnographic research, discuss data analysis procedures, as well as challenges and limitations of the work. In Chapter 2, "The Regulatory Morass," I explore the interpretation of the 21st Century Cures Act as it applies to Software as a Medical Device (SaMD), and what I name the "iterative conundrum" of how regulation is forming to vet products that are ephemeral in nature. Chapter 2 discusses the logics of regulation presented by employees of digital therapeutics companies working in quality management capacities, as well as their interpretation of FDA's mandate to build "cultures of quality and organizational excellence." In this chapter, I explore a challenge named salient by several people across professional roles, that of melding clinical and technical approaches to vetting quality, and the larger cultural divide these companies are faced with in managing employees from traditional healthcare environments as well as technology sector engineering firms. The chapter concludes by using Richard Matland's conflict-ambiguity model to characterize implicit institutional effects of the 21st Century Cures Act and competing digital therapeutic start-up behaviors.

Chapter 3, "Defining Digital Therapeutics" explores what it means to be a "digital therapeutic," where the term originated and for what reasons, and how it is being operationalized

among people working in connection with the development of these products. I examine the way an industry trade organization positions the term and discuss a salient position threaded through interview data: that digital therapeutics are evidence-based interventions based on individual diagnostic approaches to behavioral medicine. Chapter 3 discusses digital therapeutics' promise to remove therapeutic benefit from entanglement with human relations and resituate it within standardized software protocols that minimize the effects of "bad (human) actors." I situate this movement within bioethics literature on relational personhood. The chapter considers participants' perspectives on defining digital therapeutics as mechanistic interventions divisible by objective and quantifiable parts, lending transparency and trustworthiness to their deployment. Chapter 3 presents a critique of the co-mingling of codes in my interview data, that codes for "defining digital therapeutics," were frequently overlaid with codes for "descriptions of behavioral science/medicine." Using case examples, I show how participant descriptions of digital therapeutics speak to a movement of behavioral science out of academic labs and into company settings over the last 5-7 years by way of the "digital" promise. The leveraging of certain types of data production were connected with this shift, particularly methods and evidence that demonstrate positive health outcomes of the digital therapeutic product. This chapter connects a drive for positive outcomes to the commercial enterprise, and to new logics that locate disease responsibility with the end user of the technology – the consumer, or the patient. In this relocation of responsibility—or, in this empowerment of the technology user – the company benefits based on the effectiveness of their engagement metrics, and the value of the personal data they design their product to collect.

Chapter 3 zooms out to consider the logics of a phenomenon called "blitzscaling," a term coined by entrepreneur Reid Hoffman to describe a set of recommended practices for start-ups

interested in rapidly growing and outpacing their competition. In considering the definitional hallmarks of digital therapeutics as an aspiring industry, I center their drive to obtain positive clinical evidence within this context as a necessary ingredient for company success. I show through interview data how time pressures and the bracketed role of the researcher within start-up environments contribute to this aim, propelling company legitimacy and growth through increased credibility. Lastly, I elaborate on the significance of "digital therapeutics" defined as the translation of behavioral medicine to the digital realm.

Chapter 4, "Problematizing Access," turns to questions of equity as they apply to the development of digital therapeutics. By outlining the varying ways that concepts of access surfaced in my interview, media, and document data, the chapter troubles traditional notions about technology's benevolent promise to extend access by removing geographic boundaries to intervention. The chapter addresses ways that participants called upon notions of access to further company mission statements, particularly in connection to extending the pharmaceutical company sales model and concepts of "population health" in relationship to patients as consumers. The chapter goes on to address access as something leveraged in participant notions of safeguarding health, both by using digital therapeutics as substitutes for highly regulated and monitored pharmaceutical drugs like psychotropic prescriptions, as well as for their benefit in treating addiction. In the case of addiction, I use the way that access appears in my interview data to show how digital therapeutic companies frame disease as biologically based and behaviorally perpetuated, omitting possible social determinants as a cause.

Chapter 4 echoes some of the preliminary themes touched upon in Chapters 2 and 3 by addressing the shifting locus of scientific evidence – that with access to improved standards of expertise, digital therapeutic companies present their products as superior treatment alternatives

to what is currently available, if anything. Examining access in this study shows ways that "caring" and "curing" are differentiated by digital innovations in therapeutic benefit that center on systems-based approaches to diagnosis. Lastly, the chapter touches on ideas of "access to what" and "access for whom" in briefly outlining a culture of persistent fundraising efforts where company founders are usually in the midst of striving to access more capital. In this environment, despite their potential access to large sums of capital, the perceived scarcity of resources acts as a barrier to candor about company status and activities. The chapter ends with reflections on the "digital divide," discussing ways that the ubiquity of digital access may be shifting the value of human therapeutic resources, despite interview data touting the increased quality of a standardized digital therapeutic option. I complete the chapter with reflections about access in conducting research on this topic and present it as a frame for future studies that center health equity.

The dissertation concludes by circling back to the beginning to revisit the 21st Century Cures Act as lawmakers call for public input in the formulation of a Cures 2.0 bill emphasizing digital cures (Martin, forthcoming). I conclude by considering the COVID-19 pandemic that broke out at the final writing of this dissertation, forcing widespread regulatory approval of many digital forms of care. Particularly given central findings from this study on the shift toward commercial evidence production, I argue that framing "access" in its plurality may present a helpful framing for future studies involving health equity.

Chapter 1: Methods

This research is the result of ethnographic fieldwork taking place between August 2018-December 2019. During the course of the project, I drew on policy documents, industry conference materials, news media articles, and interviews to analyze the development, history and dissemination of the term "digital therapeutic." I knew from having worked at a now defunct start-up that technology products come and go quickly along with the companies that make them. Taking the ephemeral nature of these phenomena into consideration, I was less interested in any one product or company, and more interested in the arrangements giving rise to them. I was also interested in how the motivation to define "digital therapeutics" as a real thing dovetailed with regulatory efforts happening concurrently, and in what ways, if at all, these activities were "extending access" to therapy.

During the 16 months of fieldwork, I conducted 75 hours of observation: in specific areas of San Francisco where I met interview participants (namely in the mid-market neighborhood) (n=12 hours), at two multi-day digital therapeutics industry conferences (n=50 hours), at one FDA virtual public workshop (n=8 hours) and informally at two technology company worksites (n=5 hours). During the industry conferences, I conducted 18 informal interviews with attendees which were developed into field notes and considered alongside formal interview data.

In addition to observational data, I conducted 41 in-depth semi-structured interviews with individuals working as part of or with knowledge of digital therapeutics production including professionals across clinical, sales, finance, executive leadership, regulatory, academic, and engineering roles. These interviews were meant to tease out individual perspectives on how digital therapeutics is being defined, is evolving, how evaluation and safety is considered, and

what notions of health they are making. The interview guide utilized during these conversations is attached as part of the Appendix. Lastly, I triangulated (Creswell, 2013; Tracy, 2010; Bloor, 2001) observational and interview data with documents collected during the course of the research including policy guidance, salient news articles, industry reports, and thought leadership on aligned areas including digital health, artificial intelligence, innovation, inequity, and trends across the technology sector. These documents helped situate my interview data in a larger public conversation about technology sector development, regulatory logics, and health technology practices. News articles popping up over the course of the research helped corroborate or refine questions I had in following up with interview participants, particularly in relationship to digital therapeutics' connection with pharmaceutical firms. Specific source data, sampling, and recruitment strategies are further explicated in the Approach that follows.

Approach

The three types of data utilized for this study: 1) Collected Documents, 2) In-depth Individual Interviews, and 3) Ethnographic Observations are depicted below.

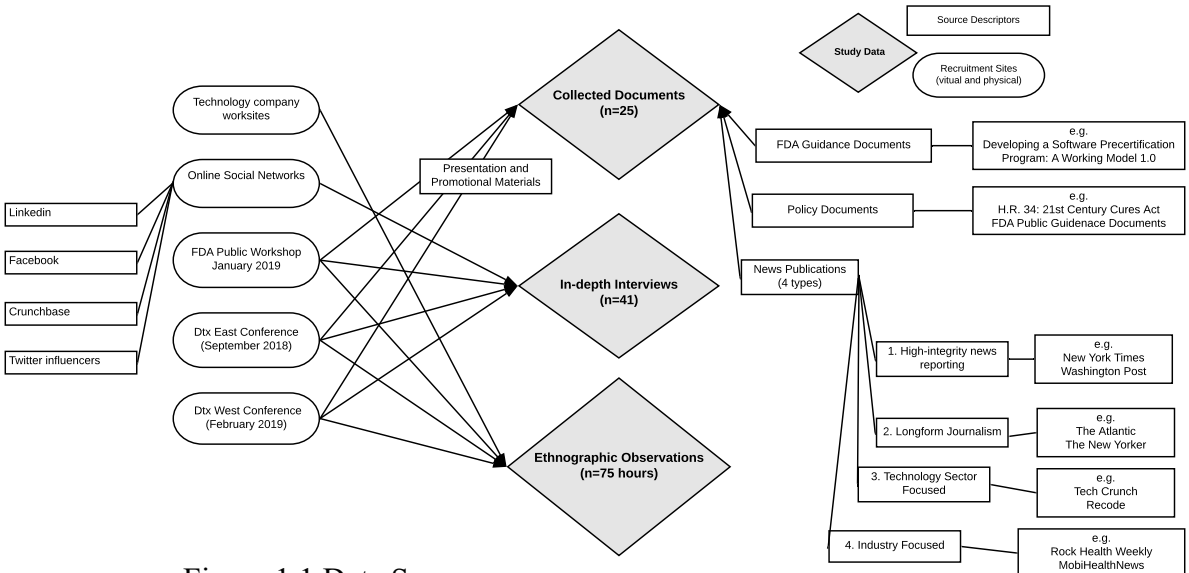

Figure 1.1 Data Sources

Collected Documents (n=25) included relevant text-based data including policy documents, digital therapeutics conference materials, and news media articles.

In-Depth semi-structured individual interviews (n=41) were conducted across clinical, sales, finance, executive leadership, regulatory, academic, and engineering roles. Follow-up interviews were conducted (n=7) following particularly rich accounts of stakeholder experiences.

Ethnographic Observations (n=75 hours) were conducted in-person at Digital Therapeutics conferences in September 2018 and February 2019 (n=50 hours), at interview locations (n=12 hours), at two technology company worksites (n=5 hours), and at one FDA virtual workshop (n=8 hours). Informal interviews (n=18) with conference attendees at both digital therapeutics were included in this observational data, as they were not recorded but incorporated into field notes from memory and audio-memos.

Collected Documents

Written accounts, particularly FDA's evolving development guidelines and organizational perspectives, comprise materials that are part of social functioning within and across institutional settings. They provide rich sources for interpretive analysis. Documents are invaluable in ethnographic work as part of a triangulation scheme to achieve convergence and corroboration of other source data. They may contain data that can no longer be observed, provide details that interview participants have forgotten, and/or can track change and development over time (Bowen, 2009). They may also reveal differences in formal and informal understandings about "how things work" within organizations.

Documents collected for this study included those that 1) provided a perspective on what "digital therapeutics" means, including its origin, history, and dissemination as a term 2) provided information about regulatory formation, funding, or evaluation of SaMD products 3)

provided media accounts of digital therapeutic company activities. Documents were used to examine the emergence of digital therapeutics as an industry, as well as to extend observational and interview data in analyzing convergences and discrepancies in public information and ways that stakeholders collaborate (Marshall, 1996).

A range of documents as outlined in Figure 1 was collected for this study in order to enable a thorough understanding of how "digital therapeutics" is being operationalized, and how regulatory formation is taking place for these products. The source and method of access for each document was detailed in field notes and all documents were uploaded into data analysis software.

Document Collection: Search Strategy

A purposive sampling of written documents was collected through systematic procedures pertaining to four types of text data: i) Policy Documents ii) FDA Public Guidance iii) Digital Therapeutics Conference Materials iv) News Media Articles.

i) Policy Documents

The 21st Century Cures Act was screened for portions of the Act dealing with SaMD translatable to digital therapeutic products. These sections were uploaded into data analysis software for inclusion. The FDA Center for Devices and Radiologic Health's website was scanned for all published guidelines related to SaMD classification and the Digital Health Precertification Program from 2015-December 2019. These documents were screened for relevance to 1) stakeholder involvement and 2) regulatory framework development. Any applicable documents, or portions of documents were uploaded for inclusion. When applicable, field notes were also taken on collected documents and included for analysis. All documents were uploaded into data analysis software.

ii) FDA guidance documents

FDA Guidance Documents were screened for inclusion based on their detail of works in progress dealing with 1) SaMD evaluation 2) Cultures of Quality and Organizational Excellence 3) the Software Precertification Program 4) newly approved or cleared products that could be considered as a digital therapeutic 5) stakeholder collaboration.

iii) Digital Therapeutics Conference Materials

Digital Therapeutic Conference Materials including panel slides and from the Digital Therapeutics 2018/2019 conference events were screened for inclusion. All conference materials from these multi-day events was screened for inclusion based on relevance to 1) stakeholder involvement and 2) regulatory framework development. Of related materials, those selected for inclusion were only those with the most information-rich substance.

iv) News Media Articles

I tested different search strings by evaluating the first three pages of search results on GoogleScholar searching for terms “digital therapeutics” and “Software as a Medical Device.” Many newspapers now offer readers the opportunity to respond to particular articles by posting comments on-line; I captured this content by going to the original source of the article, searching for and downloading readers' comments. I utilized the Lexis Nexis database available free to University of California San Francisco affiliates to search for full articles appearing in the publication categories outlined in figure 1. These categories were purposively selected to cover a range of publication genres.

In-Depth Individual Interviews

In-depth semi-structured individual interviews were conducted with a range of digital therapeutics stakeholders including employees, investors, clinicians, academic researchers, and

regulatory personnel (n=41). Individual interviews are an important data source for ethnographic research, helping to clarify, extend, and "thicken" observational data with accounts of individual experiences told in the research participant's own words. Repeat interviews were conducted as necessary to reach data saturation with regard to emergent themes with participants who provided particularly rich accounts of stakeholder collaboration, or where clarification of concepts was necessary.

Sampling and Eligibility

Individuals recruited for this research were adults (>18 years of age) currently working for or in connection with a digital therapeutics company, the FDA, an organization that sets standards for digital therapeutics product development, an academic medical institution, or an investment firm (institutional and/or strategic) currently investing in, or considering investing in digital therapeutic products. These types of personnel were well-represented at Digital Therapeutics conferences, the primary physical recruitment sites for the study.

Recruitment Procedures

Participants were recruited across various professional roles, including but not limited to: Data science, software engineering, research, clinical/medical affairs, regulatory operations, quality assurance, sales, and investing. Twenty-six of the 41 individual interviews conducted were recruited at the Digital Therapeutics Conference in September 2018 and February 2019 and arrangements were made for interviewing during the weeks that followed the conference events. Previous participants from my pilot study also assisted with participant recruitment, facilitating entrée to current employees of digital therapeutics companies who would have been difficult to reach through random sampling or impersonal recruitment strategies (Sadler, 2010). The number of interview participants for this study was based on publicly available evidence that there are at

least 30 identifiable digital therapeutics companies to date, 18 of which are based in or have significant operations located in the San Francisco Bay Area or Los Angeles, CA. Utilizing the February 2019 conference event and FDA public workshop, introductions made by previous research participants, and a purposive sample of additional employees identified through publicly available social media information on Linkedin, Crunchbase, and Facebook, an additional 15 individuals were recruited. Individuals from at least one third of the 30 identifiable companies, in addition to investment personnel participated. Flexibility was allowed for additional referred enrollees (n=4).

Interview Procedures

Interviews addressed individual experiences considering safety and efficacy in day-to-day work responsibilities, as well as participant descriptions of company approaches to the same. Using a semi-structured interview guide with open-ended questions (see Appendix), participants were asked to describe experiences working with others, solving problems, making decisions, considering regulatory guidelines, and the technology tools used on a day-to-day basis to facilitate these activities. Interviews were conducted in-person, by video-conference, or telephone at places of the participants' choosing. They lasted approximately 60 minutes. Interviews were audio recorded for verbatim transcription, de-identified, and uploaded into data analysis software. Following completion of data analysis, audiofiles were destroyed.

Ethnographic Observations

Conducting observations at conferences and start-up company worksites provided insight into how regulatory discourse is developed and shared across companies in spaces where individuals gather to network and speak about the sector, as well as how employees work together in actual practice at company worksites. Direct observation of digital therapeutics

stakeholder interactions provided access to the ways in which individuals collaborate across institutional settings to form consensus, and identify shared problems and motivations. Targeted observations included: instances of consensus and disagreement among stakeholders, the process of defining problems that aim to be solved by digital therapeutics, and how individuals utilize software tools in their everyday work. At the Digital Therapeutics Conference event in September 2018, for example, there was considerable disagreement about the appropriateness of using Randomized Controlled Trials to demonstrate product effectiveness. Examining this site of disagreement enhanced understanding of the values and implicit understandings about priorities and constraints among/between companies and regulatory agents, particularly with regard to the commercial presence of pharmaceutical firms.

Conducting observations at the interview locations provided insight into one urban environment, San Francisco, in which many digital therapeutic products are being developed. It further linked company activity in this area to the technology sector, as the presence of other technology firms was evident at the interview locations by the tenure of the customer base. It also situated digital therapeutics within the city environment of San Francisco in which very apparent social distress often flanked the outside of our meeting locations and seemed to be normalized amidst the hustle and bustle of an otherwise vibrant urban core.

Sampling and Eligibility

Two conference events, one FDA public workshop, and a company setting were purposively selected for this research. Based on rigorous web searches, the conference events constituted 100% of the public events held specific to digital therapeutics and/or the development of its regulatory process during the 2018-2019 data collection timeframe. The varied nature of the public events – two formally sponsored by digital therapeutics companies

and the third hosted by the FDA – provided opportunities for comparison of perspectives within and across settings as well as comparison of group dynamics and culture. Did it feel stiff and formal here? Did people seem to know one another? How were people dressed? What did they talk about to each other?

As for the companies selected for conducting observations, one larger (>100 employees), one smaller (< 50 employees) was intended to enable comparison of differences in company structure and motivations based on growth stage. Because I was unable to garner formal permission to conduct observations at digital therapeutics company locations, I conducted informal observations at adjacent technology firms where I had a social or professional contact. Observations conducted at the technology company (>100 employees) in October 2018 provided information as to the original motivations and use-cases for building open source software tools that have been taken up by digital therapeutics software engineers in product development.

Procedures

At conference events, I observed panel presentations and group discussions, as well as informal conversations between presentations during each of the two-day events. At the FDA event, I participated in workshop panels virtually with other virtual attendants. In meeting with interview participants, I would usually arrive early to mid-market meeting places, or remain at the location following the interview in order to gather a thicker account of activities taking place in the respective location. At technology company locations, I observed social dynamics and the arrangement of office configurations. I recorded audio-files of my observations during and immediately following field activities which also contained information from informal conversations with individuals. I drafted memos from these activities that I subjected to analysis alongside formal interview transcripts.

Ethical approval for this research was obtained in August 2018 through the University of California, San Francisco's Institutional Review Board and specific permission to conduct observations at industry conferences was granted by conference organizers in exchange for producing a report on the conference which was disseminated to conference attendees following both public events. Reflections on this exchange with industry conference organizers are included as part of my research findings in Chapter 4, "Problematizing Access."

Data Analysis

Data analysis for this study was iterative and commenced with data collection. The analyzed text for this study included all transcripts from field notes, interviews, and collected documents. All transcripts were checked for accuracy alongside audio-files, de-identified, and stored in a password protected, encrypted electronic format. Using interpretive methods, analysis was a circular rather than linear process. Writing notes or memos helped in this initial phase of exploring the database. I first read through a complete interview text, field note and/or document, and noted overarching themes, analytic puzzles, and any contradictions between data sources related to the way "digital therapeutics" was being discussed, or the way a regulatory concept was being conceived. Iteratively reviewing all data, I searched for contrasting cases, instances where some sort of breakdown or conflict occurred, and discrepancies between discourse (such as that at industry public events) and practice within companies. Instances of breakdown and silences in the data were particularly valuable to study as they revealed implicit assumptions about normal practices that were otherwise invisible and taken for granted.

Using data analysis software, I assigned preliminary codes, which involved aggregating the text into smaller categories of information where detailed descriptions of concepts were identified. For example, a document described a justification for not requiring a clinical trial for

digital therapeutic devices, and that section of text was categorized under codes: EVIDENCE PRODUCTION, RANDOMIZED CONTROLLED TRIALS, and RATIONALE. These preliminary codes were shaped, refined, compared, and extended as I moved through more of the transcript data. I examined situations where there were multiple codes for one section of text, and considered the constellation of codes that surfaced concurrently in the data. I also considered absences in the data that these constellations brought to light, and from this method was able to develop most of the entirety of Chapter 4, "Beyond Access" which was made possible by tracing the ways that the word "access" surfaced throughout transcript text. A coding schema was developed from the first half of the interview data as a way to capture preliminary emerging themes. This schema evolved with time and with the addition of interview, document, and memo data and is included in the Appendix.

Interpretive Research

Many criticisms of post-positivist research persist despite several decades of consensus among philosophers of science and sociologists that they have been put to rest by the post-modern turn (Popper, 1959; Kuhn, 1970; Clarke, 2003; Denzin and Lincoln, 1994; Gubrium and Holstein, 2002). In many ways, acknowledging a person's subjectivity as a researcher continues to open up their work to criticism (Schuessier, 2015) that may be otherwise prevented by presenting the research as taking place within objective and value-free framing (Giddings, 2006; Smythe 2005). Despite the continued privileging of positivist empirical traditions within public discourse, interpretive ethnographic analysis is well-suited for explicating nuance, range, subjectivity, and multiplicity in producing data – for producing "truth**s** with a 'little t'"(Creswell, 2013; Schwartz-Shea and Yanow, 2012;). For this project, the chosen methods present one way to consider implications of social arrangements forming across multiple arenas. Situational

mapping aided in the analysis, both as a visual way "into the data," as well as a way to explicate and then examine what kinds of non-human elements (e.g. virtual networks, software platforms) were important to them (Dreyfus, 1991; Bowker and Starr, 1999; Bowker, et al., 2010; Clarke, 2003; 2005).

This project identifies and describes emergent aspects of group culture. (Geertz, 1975; Fisher et al., 2006). My sorting of groups took place initially at a professional level in conceiving of a recruitment strategy to aptly represent the roles of people working to develop digital therapeutic products. As mentioned, these areas included: engineering, sales, clinical support, executive leadership, finance, academic, and regulatory roles. Nevertheless, these roles do not always capture the social dimensions of specific work arrangements and for that reason, it is significant to note that the project also took place against a professional backdrop of the technology sector in San Francisco

Interpretive research is no exception to any other form of empirical work where methodological choices the researcher makes influence the results they produce (Silberzahn et al., 2018). Ethnographic analysis, in particulary, is characterized as immersive. It is useful for revealing everyday practices, and discrepancies between policy and practice, that may be lost in other types of empirical examination. Preliminary data from a pilot study revealed that the creation of digital therapeutics as an industry, as well as its regulatory framework, took place across both physical and virtual sites of production. Thus, this study was comprehensively immersive across virtual sites such as Zoom calls and participatory webinars, as well as physical sites such as conference events, company workplaces, and the mid-market meeting places convenient for many interview participants working in downtown San Francisco.

Challenges and Limitations

This descriptive, exploratory study identifies ways that the burgeoning field of digital therapeutics is being defined, and ways that collaboration is taking place across physical and virtual arenas in its formation during the period of 2018-2020. While the findings cannot be used in empirical hypothesis testing, results from this research contribute to public knowledge regarding stakeholder collaboration in the formation of both a new industry as well as its regulatory considerations. Entrée is usually challenging in this type of research; however the collaborative nature of this critical period in both industry and regulatory formation enabled ready access to interview participants.

Findings from this research may inform upstream activities such as the incorporation of new regulatory considerations for SaMD at the organizational or federal level, as well as the development of ethical frameworks to guide health technology development and implementation within health systems. This study aims to elucidate some of the place-based aspects of an urban environment in which digital therapeutic production practices are occurring. As such, it brings to light the need for structural competencies within commercial environments building novel health interventions, and ways that the forms of "access" a product intervenes on need to be better explicated in product claims and development motivations. This study generates new questions that can be empirically tested in quantitative studies, and clarifies areas demanding further qualitative analysis in order to ensure the adequate and appropriate crafting of policy.

Chapter 2: The Regulatory Morass

"No regulator in the world could keep
pace with the volume of software being
created."

-Bakul Patel
FDA Director of Digital Health

The 21st Century Cures Act passed with bi-partisan congressional support in an environment overshadowed by the United States election of President Donald Trump in November 2016 (H.R.34, 114th Cong., 2016). Patient safety lobbyists, including Senator Elizabeth Warren, had been starkly opposed to its passage in the first place, warning that the proposed legislation was a cover for pharmaceutical company profit-making at the expense of legitimate patient benefit (Warren, Smith and Murray 2019; Lupkin, 2016; Mendoza, 2017). Nevertheless, in connection with the election of President Trump, the Act was rumored to have been a crucial guard against possible future actions to defund public agencies. Accordingly, it allocated money to FDA with very broad guidelines for intended use, and FDA would spend the next several years spending it in figuring out how to properly revamp its evaluation framework for digital health products.

The process of revamping FDA's evaluation procedures has been a very public and collaborative one including the creation of a pilot project involving 9 companies, a group of FDA "Entrepreneurs in Residence," the shift to whole company rather than individual product assessment, and the promise to interfere as little as possible with the entrance of products into the market but for vetting their safety (FDA Website, 2017; Cortez, 2019; Schwartz, 2017; Ropes and Gray, 2016). In keeping with this promise, a risk-based schema was created to assess safety, while effectiveness testing moved to post-market activities, at least for low-risk medical devices

(FDA Proposed Evaluation Framework, 2019). FDA's activities within the Center for Digital and Radiologic Health are centered on crafting best practices for evaluating software – moving away from an old model that was designed to vet the development of hardware products.

While FDA has been busy issuing draft guidance for public commentary to be eventually utilized by manufacturers, an active ecosystem of digital health enthusiasts in the Bay Area across industry, academic, and health care settings has formed to provide input to the federal agency's initial iterations. A group named ADviCE sprung up as a collaboration among prevailing medical centers and industry partners to outline implementation stipulations for medical device developers.

During this project, my recruitment process led me to the posh surroundings of UCSF's Mission Bay campus, and to my own academic institution's situation at the epicenter of this new frontier of medical innovation. Closely nestled in the same building as UCSF's Center for Digital Health Innovation at 1700 Owens Street in San Francisco were two life sciences investment firms, several biotech start-ups and at least one digital therapeutics company that I could name at the time. I didn't know what to make of this co-mingling quite yet, but the arrangements certainly shrunk the physical space between labs and companies and spoke to an aim of my research – to better understand the collaborative nature of this moment.

In this chapter, I situate the 21st Century Cures Act and aligned FDA changes with the burgeoning segment of digital therapeutics. I discuss the uniqueness of software as a health product, and the attending issues this uniqueness brings to bear for evaluation practices to regulate its safety and effectiveness. I name existing regulatory practices as taking place within a decentralized "regulatory ecosystem," formed through loose collaboratives of academic, industry, and agency partners. I discuss findings from my data that illustrate how the growth of

startup companies, their "professionalization," is dependent on the negotiation between clinical and technical occupations within these work environments. Quality plays a centralizing role in this process which advantages larger company actors over smaller ones, and speaks to ways that the 21st Century Cures Act – while appealing to notions of innovative cures – benefits commercial actors.

The 21st Century Cures Act

The 21st Century Cures Act includes a wide-ranging criteria for oncology, pharmacotherapy, and medical device innovation, aiming to usher in novel cures to patients without sacrificing safety. As applicable to the development of digital therapeutics, its stipulations positioned medical device manufacturers as beneficiaries of less stringent and meddlesome regulatory forces (Public Law 114-255, 206; Martin, forthcoming 2020). This act is not the first public law purporting to help patients by bolstering commercial enterprise, nor was it passed without opposition from a plethora of patient safety lobbyists at the time (Lupkin, 2016; Mendoza, 2017). Regulatory formation to bolster innovation was an important part of the 1983 Orphan Drug Act, the 2009 HITECH Act, as well as the 2015 Precision Medicine Initiative. In each case, regulation deeply incentivized development of novel cures/technology where they were deemed to be needed, thereby creating increased labor activity in these domains, as well as increased interest on behalf of private investment entities privy to new opportunities (Reaves, 2003; Aspinall and Hamermesh, 2007; Wellman-Labadie and Zhao, 2010; Kesselheim et al., 2011; Halamka and Tripathi, 2017).

Coupled with increased enthusiasm for funding translational medicine within academic medical centers, new programs for advancing discoveries with clinical impact have popped up over the last decade, bringing the so-called "academic lab" closer to the commercial venture

(UCSF Catalyst Program Website, 2019). Throughout my research, but especially at industry conferences, there was widespread acceptance across professional domains that this commercial engine was "simply the way to things get done." While I had no expectation that commercial enterprise would be criticized at an industry conference, I was disappointed in speaking with folks who fund these technologies that there wasn't a more academic conversation happening about funding arrangements and shareholder benefit. It seemed to me a digital therapeutic product should be considered as distinct from other forms of digital innovations and may necessitate different kinds of capital formation because of its intended public use as a human therapy. Aside from potentially being reviewed by FDA, however, there is no regulatory body for monitoring the activity of these products in the marketplace, nor are there regulatory protections in place to ensure that public benefit is considered in their initial formation.

Currently, FDA reviews digital therapeutics just as they review other Software as a Medical Device (SaMD) products: according to a risk-based schema. They are therefore invisible within any formal FDA guidance documents and do not contain their own standards or metrics for evaluation. Despite this fact, the director of FDA's Center for Radiologic and Digital Health (CRDH), Bakul Patel, has participated as a speaker at numerous Digital Therapeutic conference events over the last 4 years, as well as investment conferences for digital health more generally, signaling agency awareness and monitoring of varying digital health "things." FDA's most significant move in connection to these swirling worlds of venture capital dollars, start-up gadgets, and health systems is its current plan to evaluate companies rather than products for quality.

Pursuant to the passage of the 21st Century Cures Act, in 2017, FDA's appointed Commissioner, Scott Gottlieb, also a partner at the world's largest venture capital firm, New Enterprise Associates, issued a public statement to:

> "Empower Consumers and Advance Digital Healthcare… Historically, healthcare has been slow to implement disruptive technology tools that have transformed other areas of commerce and daily life. One factor that's been cited, among many, is the regulation that accompanies medical products. But momentum toward a digital future in healthcare is advancing. Not all of these tools are subject to FDA regulation. For the devices we are asked to evaluate, we know that our policies must continue to empower consumers and facilitate innovation" (Gottlieb, 2017).

Accordingly, FDA developed a schema for examining Software as Medical Device (SaMD) products, whereby low-risk products, including those intended to augment clinical decision-making, will not be pursuant to ongoing evaluation. Rather, companies are audited, whereby those exhibiting "cultures of quality and organizational excellence" (CQOE), defined according to seven "excellence principles" receive expedited product approval. In 2017, FDA started a pilot program of 9 companies of varying sizes, age, and organizational structure to help determine key performance metrics for use in defining CQOE. (U.S. Food and Drug Administration, 2017).

FDA's changes since 2017 have attracted considerable attention from device manufacturers, researchers, policy, and business audiences with different concerns. At the dawn of the 21st Century Cures Act's passage into public law, scholars expressed apprehension that the Act would create an environment with sub-standard product evaluation, with effectiveness testing moved to the realm of post-market surveillance (Kessleheim and Hwang, 2017; Kinney, 2018; Orlando, and Rosoff, 2018; Uzdavines, 2017). Investment audiences, as evidenced by the

surge in business consultancy-produced white papers on the topic, were aware of potential business opportunities that could result from a relaxing of regulatory activity (Chatterjee, et al., 2018 and "21st Century Cures," 2017). Six firm representatives interviewed in connection with this ethnography expressed that their company was "looking for a regulatory person," acknowledging that what was going on at FDA was new and important, and also that the acquisition of regulatory expertise may result in a competitive advantage against other firms. As one CEO mentioned to me, describing his recent experience hiring a new senior executive,

> "That was how she [senior executive] sold her last company, by ensuring that industry measures were being met. When she asked us, 'What industry metrics are you being measured up against?' we were basically like, 'We don't know.' So right now she's investigating what those metrics are. If you end up finding out the things that people use, I'd be extremely grateful to hear back."

Harkening to others' descriptions of digital therapeutics as "the wild west," this quote highlights the commercial value that an understanding of "industry metrics" brings to a company, particularly when actors are competing with poorly defined regulatory information. In an environment where regulatory bodies have not yet codified their evaluation procedures to vet these products and where commercial actors do not fully understand the rules of the game, regulatory expertise is heightened as a desirable commodity to capture within a private firm setting. It becomes a competitive point among firms. Having it may position company actors at an advantage to collaborate with FDA in rule formation, and ultimately to compete against other firms for market share. So, backing up a bit, why was it necessary for FDA to create this regulatory vacuum in the first place?

Software is a Different Beast

FDA's stated motivation for changing its procedures was the fact that many medical devices currently look much different than they did a decade ago. The term "Software as a Medical Device" has come into common parlance, signifying realities of the virtual world such as electronic health records, smart-phone mediated prescriptions, and the interface for hardware products like glucometers and defibrillator machines. Developing software products is different from developing hardware products. In the world of hardware, design cycles are time-consuming because engineers have to translate their concepts to the physical world. Once they are produced, they cannot be cheaply altered. For this reason, hardware manufacturers usually apply upfront time perfecting designs before building a working prototype to submit for review. With software development, on the other hand, a working prototype is developed through lines of computer coding almost instantaneously. The working code contains a wide range of possibilities for how it may be altered. Because of this development ease, there is no wait time for a prototype and software developers can continue to tweak the software product without incurring additional incremental costs .

FDA's procedures for validating medical devices have been traditionally based on hardware development cycles. The agency was accustomed to reviewing tangible products, examining the different pieces, and approving, step-by-step, each iteration of a device. Advances in software development technology have rendered much of this evaluation paradigm obsolete. Given the numerous iterations and tweaks made when creating SaMD, prior to the current changes underway, FDA was struggling to use its hardware evaluation paradigm for review of not only a very different type of device, but also a very different type pf design process. This poor attempt to retrofit an outdated framework to 21st century technology was only exacerbated

by the fact that prior to the new funding from 21st Century Cures, FDA lacked appropriate engineering resources to update its review process. Thus the problem was twofold: The agency tasked with regulating safety and efficacy did not have appropriate procedures for evaluating some of the most novel products submitted for approval, and it did not have the expertise within the organization to guide necessary changes to create them. Thus, the 21st Century Cures Act was passed with a political tagline about addressing patient need while implicitly satisfying a commercial driver — one for regulation to keep up with advances in technology. One of the first challenges to this understanding was posed to me by several engineers and regulatory personnel I spoke with: What does it mean to regulate something that is under constant iteration?

The Iterative Conundrum

I arrived to the coffee shop in downtown San Francisco just a few minutes before my scheduled 9:00 am meeting with Chris, the engineer I had been corresponding with by email. Scanning the café, only a couple of others were present inside. Scattered on concrete outside were several individuals wrapped in blankets, one of whom appeared to be reading out loud from a tattered novel, as a frenzy of morning workers in ear buds deliberately avoided him, briskly making their way to what I imagined were office locations in the sky. Upon realizing that one of the others in the coffee shop matched the description I'd received by email, I walked over to the couch where he was sitting to confirm that the person typing was Chris. He looked up from his computer, smiled and verified that he was in fact himself, and said that he would be ready in just a few minutes after finishing something up. "Great, take your time," I replied, sitting down next to him and setting up for the interview while he pushed keys for a few more minutes.

As I waited for Chris to finish up, the man in a blanket outside looked up from the book and came in approaching the register, exchanging some inaudible words with one of the baristas,

who then exchanged some inaudible words with the other barista, who handed the blanketed man a croissant and coffee. As he was exiting the café, he started singing, which turned both my and Chris' attention toward the door, then toward each other. I muttered something along the lines of, "that was nice that they gave him some food, I hope he's ok, Chris agreeing with, "it's just so bad here," the "it" seeming to mean "homeless people," and both of us taking a deep breath. I suggested we start the interview, missing the opportunity to ask questions about what Chris thought of the blanketed situation. Chris was eager to jump in and with seeming relief, launched off by letting me know he was a lead engineer at a start-up working in "stealth mode." I had heard this term before and knew it was one that connoted a strategy for temporary secretiveness to avoid mimicry of competitors (Wertz, 2019).

Chris came into his work in digital therapeutics with a diverse background in real estate and business and was the first technical employee I had spoken with to explain how, in developing software, it was crucial to fail. "If you create an environment where you're not able to fail then you're not able to accelerate your development," he said. He went on to discuss the specific pressures on him and his team to experiment quickly, detailing ways that this was ultimately the smartest approach to claiming a place in the market.

The notion of "failing fast, failing often" was a trope I'd encountered previously in connection with start-up ideology. It stems from Agile Development principles espousing active collaboration, response to change, working software over documentation, and efficiency over burdensome documentation protocols (Manifesto for Agile Software Development, 2001). Implicit in this methodology is a race against time. In start-up environments, it dictates a lean process of rapidly evolving product prototypes and self-organized teams. It contrasts with the idea that product design should be perfected before product construction. In building much of the

software infrastructure that runs our digital world, this methodology has served engineers well. When executed appropriately, it lends teams an edge against their competitors. Nevertheless, as an approach to building digital therapeutics, it presents a challenge for engineers who need to craft safety and effectiveness, and account for these concepts in an environment that disparages documentation. Chris' explanation dovetailed with that of the VP of Regulatory Science at a leading digital therapeutics company who explained:

> "Here's an example of the challenging case: You have the software engineers whose motto is, "fail fast, fail often." But on the device side, or for any sort of regulated product, failure is not great. If you fail ... Like Facebook can push out a feature, or Instagram can push out a feature, and the patient population they could get pissed off and not want to use the product anymore, and that's it. But if we push out a feature to our patients that upsets them, you get them into mood disorders, which are adverse events. There's a big difference in paradigm there. Basically in an ideal scenario, the quality management system would be able to seamlessly and in a least burdensome way, try to adapt software development practices in a way that is still highly rigorous but produces documented outputs. But in reality, that's something our industry is still trying to solve. Look, let's be honest, a lot of software development companies that are really good, they don't document anything. They don't document a thing. And so asking a product manager who's used to using a [software tool] to pause before deployment and do a design review with a bunch of people…that comes across as very burdensome for that product and engineering team. …That's the challenge that digital therapeutics companies face. How do we blend a traditionally linear burdensome,

heavily documented process into an equally rigorous but less documented software developing process?"

This participant's explanation demonstrates several important points. First, the modus operandi for software developers, coming from non-clinical work environments where speed and deployment of engineering features takes priority, stands in tension with the safety considerations of patients who will be using the engineering product as a clinical intervention. Second, the modus operandi of software developers within a company's product team also stand in tension with employee functions at the same company who are tasked with vetting quality and regulatory appropriateness. "How do you reconcile those tensions?" I asked this same participant at the time, referring to the differences in priority between a quality management group and a product development group at a single firm. "Well, if I knew how to do that, I'd be a multi-billionaire," he replied smiling, acknowledging the difficulty of the task. In the hasty environment that digital therapeutics employees are working, there are few discrete guidelines for leading these types of "negotiations," if they can even be termed something so formal.

Work decisions described to me were often charged with an air of urgency, where in many or most cases, the speed of building took priority over cross-team discussion about documentation or validation needs. In instances where a more thorough risk-analysis may have been warranted, when I asked questions like, "How do you know, at any given time along the product development journey, what the right thing is?" I was told that it, "usually comes down to a gut feeling between a group of people, where the people whose input weighs heaviest are the product managers, me [the CTO], and other technical leads."

Despite regulatory employees' described need for quality management systems that provide documentation without slowing down product development progress, the mechanics for

how this becomes possible within a company setting remained opaque. While the regulatory function within a company may be tasked with the highest degree of responsibility for patient safety, if a central aspect of iterative design is the eschewing of documentation, it presents an even deeper challenge for outside regulators like FDA, who have limited visibility into the process through which a working prototype came into existence, or any algorithmic information contained therein. Currently FDA does not review the source code for any of its submissions. In guidance documents dated November 2019, FDA mentions,

> "To date, FDA has cleared or approved several AI/ML [Artificial intelligent/Machine Learning]-based SaMD. Typically, these have only included algorithms that are 'locked' prior to marketing, where algorithmic changes likely require FDA premarket review for changes beyond the original market authorization. However, not all AI/ML-based SaMD are locked; some algorithms can adapt over time…the power of these lies in the ability to continuously learn, where the adaptation of change is realized after the SaMD is distributed for use." (FDA Website Proposed Regulatory Framework for AI/ML SaMD, 2019).

FDA's discussion paper further describes how product approval will exist on a continuum of locked to unlocked in relationship to how much risk the device poses to patients. Of course, regulators must understand and appropriately label the category of risk that a product poses, which is also complicated when predicting everything that the product may "continuously learn" to do over time (Hwang, Kesselheim, & Vokinger, 2019).

To date, FDA's approach, while still in its infancy, does not reflect revisions following public input. In a flow diagram explaining "Good Machine Learning Practices," FDA makes mention of a second type of model evaluation in addition to performance: clinical validation

(FDA Website Proposed Regulatory Framework For AI/ML SaMD, 2019, p. 8). The distinction bears mentioning in relationship to a larger conversation about quality that seemed to weave itself problematically through my interviews. Although I spoke with several employees whose job function entailed "quality assurance," the type of quality this merited was largely one of a technical nature. In FDA's flowchart, clinical validation is separated from performance evaluation, but the two concepts seemed intertwined, or at least difficult to tease apart, in speaking with digital therapeutic employees. Given the infinite tweaking that is part of software iteration, it is challenging to identify when or at what point performance modifications justify clinical evaluation. The same VP of regulatory science explained:

> It's fairly qualitative, there is FDA guidance, for instance, on what constitutes a politically significant software modification, but it is a crapshoot. It's just up to the discretion of the manufacturer to determine what's important or not. We always do a clinical analysis to determine whether a change in the software is going to lead to any changes in safety and efficacy that we should be aware of. …but the therapeutic content is really entrenched in the actual text audios, videos that are delivered in that product. You could imagine that changing the wording of, for example, there's a module on risky behaviors and there's a module on the underlying basis of addiction and so if, for example, you're just changing texts, that sounds pretty innocuous. "Like, oh, we're just changing some texts." And for some other products that are software driven, that'd be fine if the main mechanism of action wasn't cognitive behavioral therapy. But in this case, the text is part of the therapy, and so we are very careful. We do a deep clinical analysis to see if we

> change that text, are people going to react negatively to it? Is it going to drive behavioral change in the same way that the old text was?

As this participant laid out, determining what constitutes a significant software change – one that warrants FDA submission – is far from a measured science. It is a qualitative process, relying on individual judgement and manufacturing discretion, as well as the company's own crafted procedures for performing "deep clinical analyses." The subjectivity of these activities contrasts with the idea of therapeutics being objectively "effective" or easily tweaked on the fly for personalization. At the least, it begs questioning as to what kind of meaningful tweak can be made on the fly, given the complicated nature of determining what the stakes are and what types of product modifications may be needed. It also begs questioning as to what kinds of professional expertise are needed to sufficiently vet products, and whether and how companies are operationalizing an awareness of these needs. The word this participant used is "embedded." The company's therapy is embedded in text that is embedded in audio and video clips, that themselves are embedded in a smart phone device. No wonder it becomes hard to tease out the changes or to define what, exactly the "there" inside of there really is; the very notion of transparency is conflated by how the technology is designed.

The Regulatory Ecosystem

It seems significant to mention that while 55% of FDA's funding is allocated by the federal budget, 45% of it accrues through user fees. Digital therapeutic submissions to FDA for authorization, whether through the 510k clearance pathway or de novo route, range in cost from approximately $10,000 to $100,000 (FDA Medical Device User Fee Amendments, 2020). Data is not currently available as to whether current FDA changes have increased the number of submissions, but this outcome is probable, particularly in the long run. Prior to changes

implemented as part of the 21st Century Cures Act, scholars were already bringing attention to the growing problematic of FDA's reliance on user fees stating, "In a different political climate, adequate public funding in place of user fees would allow the FDA to continue its current performance levels while adding further confidence that the public remains the primary client of the FDA" (Darron, Avorn, and Kessleheim, 2017). While concerning with regard to commercial influence of regulatory practices, FDA's growing reliance on user fees also contains varying implications for its commercial actors, since higher fees indirectly advantage larger firms that can more easily weather their price tag. This bias is also implicit in the CQOE framework, since satisfying FDA dashboard requirements for "excellence," requires building unique infrastructure that is cost-additive.

The advent of the Cures Act has ushered in a new era where the public persona of FDA'S Center for Radiologic and Digital Health appears to be very friendly and collaborative. This center within the agency must strike an awkward balance. On the one hand, it must interact closely with companies in order to learn about the most novel products being presented to them to ensure that agency review procedures are appropriate for 21st century advances in technology. On the other hand, the Center must maintain impartiality as the arbiter of safety and efficacy. Concurrent with striking this balance, Bakul Patel has joined the University of California San Francisco (UCSF)-initiated Accelerated Digital Clinical Ecosystem (ADviCE), a multi-stakeholder collaboration, "helping to ensure that digital health software tools can enter into use quickly, safely, and effectively." Members of the collaboration include other employees of FDA in addition to digital health center faculty from several academic medical centers, and individuals working at organizations such as Apple, Johnson and Johnson, and BlueCross BlueShield. As the collaboration's website states,

> "FDA ADviCE is not a regulatory or compliance entity, but rather a voluntary organization that assists in effective collaboration between the healthcare marketplace and [FDA] Pre-Certified companies… ADviCE may help set expectations and implicit standards for innovators and investors developing Digital Health Software Tools, as well as for healthcare systems seeking to adopt them in practice" (Initiatives of ADviCE, 2019).

While not a regulatory body, this alliance functions as its own type of clearinghouse for quality: providing "best practices" documentation for implementing digital health in clinical environments, a model for gathering real-world performance data, and a set of quasi-standardized questions for health systems to ask of vendors prior to commercial engagement (ADviCE Website, 2019). These functions are aimed at creating transparency and reducing friction between health systems and vendors, are proposed as informal "rules of engagement." As disclosed in the website text, the collaboration is entirely voluntary and works by setting expectations and developing implicit standards for commercial developers. It is enabled by a diverse group of influential participants across their respective organizations and sectors.

As the ADviCE collaborative suggests, my interviews among individuals with connection to digital therapeutics are situated in a regulatory environment that includes more than simply FDA as a clearinghouse. In FDA's attempt to situate themselves in a learning position to keep pace with technology advances, some of the most pressing work for safety and efficacy has shifted to health system administrators charged with implementation science—how to implement digital health tools within health institutions safely and effectively. In this sense, FDA is one actor within a regulatory ecosystem – to pull from ADviCE's title – an informal smattering of alliances with connection to a common goal of implementing digital health tools within health

systems. While the ecosystem extends beyond digital therapeutics, the landscape helps reveal aspects of this particular cultural moment in connection to health where there is somewhat of a regulatory vacuum for what the safety and effectiveness standards should be.

I expected to sense ubiquitous enthusiasm for digital health implementation among industry partners I interviewed, and it was certainly palpable at the industry conferences I attended. I was surprised, however, to learn that FDA's 23rd commissioner was a partner at a venture capital firm, and also surprised by the fervor of academic and health system actors I interviewed who acknowledged the myriad of regulatory predicaments connected to development and implementation of digital therapeutics, while also remaining solid in the position that their production was needed and would be beneficial. One reason for this may be that among health system participants in the decision-making ecosystem, all are acting in an environment of privatized care provisioning where technology promises cost-effective solutions in the long run.

Cultures of Quality

An expressed part of FDA's revamping includes the establishment of indicators for CQOE among institutions. In its draft appraisal documents dated April 2019, the agency lays out five categories in which to prove organizational excellence: patient safety, product quality, clinical responsibility, cybersecurity responsibility, and proactive culture. While the key performance indicators for each excellence category are currently outstanding, the four common validating perspectives for each respective excellence area (patient safety, product quality, clinical responsibility, cybersecurity responsibility, and proactive culture) include 1) organizational resources 2) customer voice 3) learning and growth and 4) process (FDA Website Developing a Software Precertification Model, 2019). For each excellence area, companies will

need to demonstrate ways in which the four perspectives are being satisfied in their software development process. These categories stand to bear on organizational staffing requirements, as well as job function, and probably even organizational size. Thus, the process of building clinical competency within a product organization, such that a company is able to perform "deep clinical analyses" may really entail a staffing overhaul for many organizations currently lacking that expertise. In this sense, "building a culture of quality" likely aligns with the professionalization practices of young companies after receiving a large round of funding. It may only be at this point that company founders can afford to hire more seasoned expertise for growing the organization into a more mature institution. It also means, as alluded to early in this chapter, that large firms already possessing these resources, or subsidiaries of larger corporations enabled by these resources, will not only be at a significant advantage, but may be the only organizations with sufficient bandwidth to bring products to the market.

Professionalization

While most of my interview participants were only vaguely familiar with the CQOE concepts, many individuals I interviewed were intimately acquainted with the challenges of professionalization. These challenges often had more to do with "clashes of culture" in building out the clinical arm of an organization than they did with pains pertaining to growth-related change. A Chief Technology Officer (CTO) I spoke with reflected:

> "It came to mind for me when you asked what was one of the biggest challenges. I think one of the biggest challenges in this space – I'm going to say the biggest challenge in this space, not from a <company> standpoint, but for digital therapeutics period, is having a very capable group of technologists and clinical scientists, who can understand each other's perspectives, and factor in clinical

> evidence of therapy into the products at the same time that you're factoring in the common knowledge and commonplace user experience type things. There are people who have been working in technology for a very long time, and have been building apps and software, and have learned from common mistakes and things like this. Companies like Google, Facebook, and all those spend literally tens of billions of dollars in advancing their products. There's a ton of expertise on that side, just like there's a ton of expertise from people who have been practicing medicine for 25 years, and are psychiatrists working in a certain space, and they know from talking to patients, and from doing this time and time again what will work, what will not work. The blend of those two into creating a product is, I think, the biggest challenge, or the biggest opportunity as well…We have a new scientist who comes from a purely clinical standpoint, and we're like, 'Ultimately no one's going to want to read that text [generated by the new scientist for product users]. It sounds like it's from a doctor, or like a warning label type of speech, versus something that's more friendly.' So, people definitely come across that gap. Ultimately everyone has to realize that our end product is software as a medical treatment. And people who come from all the different perspectives there have to understand that all of those things are a component."

The challenges of melding clinical and technical perspectives were often mentioned in my interviews, as they are in the paradigm quote here. In lay terms, a purely "clinical" perspective is defined in two ways: first as "relating to the observation and treatment of actual patients rather than theoretical or laboratory studies" and second as "efficient and unemotional; coldly detached" (Dictionary.com, 2020). The CTO seems to leverage the latter interpretation of

the term, implying that clinical language wouldn't be as engaging for an end-user as friendlier, more easy-going words would be. The first definition of "clinical," however, is one that centers the patient rather than the research lab and implies a specific kind of evidence. In this interpretation, "clinical" means evidence relevant to human patients rather than hypothetical or controlled settings. "Technical," in lay terms, is defined as: 1)"related to a particular subject, art, or craft," 2) "involving or concerned with applied industrial sciences" and 3) according to a strict application of the rules. "Technical," in these definitions implies specificity of components, commercialization, and compliance.

Taking the participant's description, the entanglement of these words as descriptors for different ways of knowing reveals company perspectives on both the use-value of institutional knowledge in considering patients as users of products, as well as a clash in ideas about the worthiness of institutional knowledge more generally. Healthcare expertise is limited, in this participant's view. It can contribute to a component of the product, but wouldn't necessarily inform how the company designs the interactive features of it, nor does it overshadow what can be learned from a patient by collecting and analyzing their product data. But more than a difference in clinical and technical perspectives, this engineer brings attention to a cultural divide between employees coming from very different professional worlds. The cultural rift hangs on a comparison between clinical expertise and consumer expertise, or "the common knowledge and commonplace user experience type of things" that result in more friendliness, a strategy that boosts product engagement. He describes the new scientist's text as lacking in this type of approach, and an overall rift between people who have worked on consumer products and understand how to craft something that people will want to use, versus people who come from a clinical background and sound stiff and inhuman in their interactions, cautioning against a

"warning label type of speech." Consumer engagement knowledge in this context operates by eliminating a sense of danger or hierarchy between the knowledge holders (software developers) and the patients using the product, hopefully translating into increased use. The goal, by this engineer's measure, is to make the product as approachable as possible. Doctor-patient interactions, on the other hand, marked by the implicit inequality of a doctor's professional expertise and a patient's naiveté, may effectively push patients away from the digital realm, working against a company's goal of user acquisition and retention.

Perhaps not ironically, start-up offices I visited reflected this same cultural ethos of "flat and friendly." Evidenced by large open office environments and many self-designed job titles aimed at eradicating structural hierarchy among employees, modern work spaces with tall windows and catered lunch all seemed to exude the same tacit belief that hipness begets company success. The fun, informal nature of these work places differs from that of most clinical settings where patient privacy is prioritized, and where the potential severity of life-threatening illness mixes with low-budget, sterile design aesthetics. While far from advocating for more hospital-like work spaces, research shows that the open office – supposedly an enabler of transparency, congeniality, and collaboration – actually inhibits employee productivity and in-person interactions (Bernstein and Turban, 2018; Bernstein and Warber, 2019; McGregor, 2018).

As it turns out, employees prefer privacy in pursuing their daily work activities; in an ever-noisy open office, this can mean a room of headphone-clad young adults, socially isolated yet sitting among others attempting concentration. This distinction between appearance and reality is significant in relation to the process of developing software products for health. Despite a friendly and approachable interface, the source code of a product's intervention – as well as its capabilities and previous iterations – are invisible to consumers, patients, regulators, and non-

technical employees. The product's insides, its code lines and branches, form a technological infrastructure that is inherently non-transparent. While its invisibility may not be as troubling to the user of a product as might be a negative in-person interaction with a care provider, it makes the risks of use nearly impossible to measure. In conversation with the senior official of an international non-profit body that authors medical device standards for uptake by FDA and other regulators, we spoke about the challenges of defining quality in this context. He mused:

> When you say a digital therapeutic, how do you know that the code you're getting or what they're playing is really what it is? How does one know that it isn't full of bugs or contain more nefarious code that may do some bad things? How do you know that it's actually doing something, or what is the strength of it? One of the things that I like to talk about when we talk to people about this is, what's the difference between a digital therapeutic game and a game that somebody's 16-year- old nephew or niece is creating in the basement? Not a whole lot, because it all looks the same. How do you know that, or the doctor, or the patients, or the insurance companies, how can they be assured that what the doctor prescribed and you downloaded from the iStore is "Evelyn" from <digital therapeutic company> and not something that looks like "Evelyn?".

The regulator went on to describe how the central concepts girding pharmaceutical development, notions of identity, purity, strength, and quality, will likely be utilized in the development of a framework to evaluate digital therapeutics. "The outcome of course will be different, and how we manage that, and how we define and/or describe, and then test, verify it will be different, but the ideas are really the same."

Opaque and Productive

"Many legislative compromises depend on language sufficiently ambiguous that diverse actors can interpret the same act in different ways. This is a natural and inevitable result of the working of political process." –(Matland, 1995, p. 158.)

Within policy implementation literature, Richard Matland's oft-cited 1995 conflict-ambiguity model is still used to help explain how policy is passed in differing circumstances (Matland, 1995). In situations where there is low conflict among stakeholders and a high degree of goal ambiguity, implementation is theorized to take on an experimental nature, where the process is governed largely by contextual factors. While there were policy opponents of the 21st Century Cures Act, the passage of the public law was a swift and unanimous effort in congress, signaling a low degree of formal conflict. And while the law is written to minimize apparent goal ambiguity by stating a basic objective of expediting cures to patients, its consequences are more nuanced and far reaching than this language states. Implications of the Act extend to FDA's development of software-appropriate evaluation frameworks, whole-company appraisal, and a new reliance on real world evidence to affirm product claims. Moreover, FDA's development of new regulatory pathways for SaMD has taken a collaborative tone as evidenced by the agency's pilot program and evolving guidance documents open to public input, signaling an experimental implementation period.

One speculated outcome of the Act's passage is that large, established firms will have considerably more influence in getting medical device products approved. Small firms may not have resources to house a "Quality Management System" within their organization, or the means to outsource this function to a third party. This may, in turn, translate to FDA adoption of more corporatized guidelines, particularly as the FDA's designated pilot organizations work with FDA to refine key performance indicators. Extending from this, heightened cost of entry may mean

that true innovation – the kind the 21st Century Cures Act purported to incentivize – is hampered since competitive firms will use existing technological infrastructure to build products that are marketable quickly. This same logic underpins a commercial justification for increasing public funding for FDA. In the climate where only large corporations are the commercial players who can pay to have their products reviewed, it stands to reason that they will have an outsized influence on the type of innovation that happens in this product category. Increasing FDA's funding so that it is less reliant on user fees would mean a more equal playing field for commercial actors in addition to preserving the public's interest as the heart of FDA's mission to safeguard safety and efficacy.

While the 21st Century Cures Act keeps patients front and center in its language, one of the most direct results of its passage pertains to advantages bestowed to certain private industry actors creating new technologies for health. If the originally crafted legislation had named digital health companies as its explicit beneficiaries, it might have been more hotly contested in congress as a veil for corporate interests. By keeping patients front and center, lawmakers were able to pass the Act easily – leaving considerably more ambiguous regulatory terrain to be negotiated between FDA and private firms, and among health system administrators in the name of implementation science.

Similar to crafting policy that appeals unequivocally to patients, digital therapeutic mission statements promise unparalleled health improvements, marrying the path to market success with therapeutic benefit. The mechanisms for achieving these improvements are opaque and their market presence does not contain substantive regulatory oversight. More research is needed to better explicate public risks associated with the differences between product marketing

claims and product capabilities, and the consequences of shifting regulatory activities to loosely networked ecosystems with varied priorities beyond the public interest.

Central Themes

Findings from this chapter demonstrate a troubling quagmire of commercial and regulatory practices, digital therapeutics situated at their nexus. This chapter engages with several "big picture" ideas brought forth by my findings. Central to these themes are questions about transparency, quality, and the discrepancy between behavior and discourse. The chapter begins by describing the advent of the 21st Century Cures Act, and ways that its legislation has filtered into changes the FDA is making to revamp evaluation frameworks for SaMD products. It then goes on to examine the difficulty of regulating products that are essentially ephemeral in nature, and the advantages that beget certain firms in making this regulatory shift. The next chapter elaborates on these findings, particularly those relating to the regulatory vacuum of the present moment, by discussing ways that the term "digital therapeutics" was defined for me in interviews, and the "translational" moment that it marked for behavioral science.

Chapter 3: Defining Digital Therapeutics

"In order to get income,
you've got to show outcomes!"

-Anand Iyer, PhD MBA
Chief Strategy Officer, Welldoc

I spent much of late August 2018 through May 2019 running across San Francisco to interview start-up employees, hovering over email to catch people by phone or, if luck would have it, for a coffee. Arriving to the midmarket neighborhood of well-appointed buildings with sleek exteriors and street level coffee shops, I enjoyed learning about the hustle and predicaments of eager digital therapeutics company employees over the last year, despite some bracketed skepticism about the area more generally. My desire to study the emergence of these products started in late 2016 when I began to hear the term "digital therapeutics" in connection with the latest wave of digital health gadgets. The term peppered a wide variety of news publications and industry reports, pointing to a new incarnation of "datafied" health interventions, one stretched across traditional pharmaceutical firms and other more robust technology companies. Early on in crafting this project, after learning about the first FDA approved digital therapeutic that Dr Oz hosted part of his show to discuss, but before I had a firm idea of what about this area was research worthy, I realized that digital therapeutics were being talked about in varying ways. Part of what I hoped to clarify though this project was how digital therapeutics came into being, as a term, and why. I hoped to gain a better understanding of how the term was being put to work – not just how people assigned a definition for it, but what kinds of health imaginings it may be offering to the world.

Over the course of 2018-2019, I spoke with many people working on the development of these products – digital therapeutics company employees, regulators, academics, clinicians, and investors with working knowledge of the area. What follows is an account of how my conversations with them, my document analyses, and observations from field sites triangulated to suggest a productive quality in the breadth of the term, one that was connected to a field's migration from academic labs to private company settings, helped along by specific types of evidence production.

In this chapter, I investigate ways in which my data show how digital therapeutics are being defined as something other than existing things – both situated outside of digital health as well as pharmaceutical development – whose effectiveness rely on proprietary knowledge. I show through my data ways in which the highly targeted and individualized nature of these interventions confers with notions of health that aim to de-center human relationships as constitutive of the therapeutic encounter. Digital therapeutics were presented and defined as therapeutic interventions superior in nature for their freedom from the messiness of human interactions. As I came to learn, these products were an extension of the field of behavioral health. Their development demonstrated the movement of behavioral health out of psychology labs and into startup company environments, with attending commercialization. The process of commercialization was aided by an incentivized drive for positive health outcomes shaping evidence production and points to the need for closer examination of these products' scientific integrity.

What's in a Name

In conducting this research, I formally set out to explain how the term "digital therapeutics" is being defined and operationalized by people working in connection with its

development. In order to accomplish this task, I tracked media coverage of "Digital Therapeutics" in salient news publications, reviewed trade organization and industry reports mentioning the term, and I analyzed my own interview and fieldnotes data. In virtually all of the interviews I asked people to define the term, and where they first heard it used. In response, I received a myriad of explanations. Digital Therapeutics were described to me as medical interventions different from in-person medical interventions, as therapeutics separate from pharmaceutical therapies, as software instead of hardware, and as a subset of technology interventions among other digital health products. They were described to me as something that only a small handful of people could really understand at this point and they were consistently characterized as "evolving."

Several members of executive leadership at different companies mentioned that while they couldn't remember where it had first been used, they "may have been guilty of coming up with [the term] ourselves," while several other interview participants noted digital therapeutics as having first been coined by Omada Health, a leading digital therapeutics firm founded in 2014 that has attracted approximately $200 million in venture capital funding (Crunchbase, 2020). Omada was the front runner in translating an in-person protocol to a digital format, creating a software product from the Centers for Disease Control's (CDC) lifestyle guidelines for diabetes prevention. In a 2017 interview with an Omada engineer I spoke with during the pilot project that foregrounded this research, he hesitantly mentioned the term when I asked him to explain what they were building, "I think the official name of what we do is 'digital therapeutics,' but specifically right now we focus on helping people who are at risk for diabetes hopefully avoid getting full blown diabetes."

Two company founders I spoke with mentioned a Harvard Business Review article published in November 2016 entitled, "Simple digital technologies can reduce healthcare costs," that first named digital therapeutics as an area. In the article, digital therapeutics were defined as "technology-based solutions that have a clinical impact on disease comparable to that of a drug" (Fogel and Kvedar, 2016). The article launched off by recommending:

> "Businesses that are serious about reducing health care costs — and improving the health and well-being of their employees — should take a serious look at digital therapeutics, which have the potential to provide effective, low-cost ways to prevent and treat chronic diseases and their consequences."

Within the second paragraph of the article there was a disclosure statement mentioning one of the author's positions in advising "several companies involved in the digital therapeutic space." (Fogel and Kvedar, 2016).

The numerous descriptions I received about where the term "digital therapeutics" came from and what it meant – existing as a preventative solution for patients, a cost-saving agent for health systems, an investment opportunity for financiers – reflected different actors' positions in relationship to the product. I also realized that over half of my interview participants, particularly those I spoke with later in 2019 during my interview process, referenced the Digital Therapeutics Alliance (DTA) in defining the "space."

DTA, as I immediately learned at the first digital therapeutics conference I attended in Fall 2018, is a subscription-based non-profit trade group comprised of 37 digital therapeutics companies (DTA Website, 2020). Annual membership dues follow a tiered model based on annual global company revenue. The lowest price tag is $3,000 for an academic institution with $75,000 for a pharmaceutical firm on the upper end of the spectrum (DTA Website, Annual

Membership Dues, 2020). DTA was founded by a previous employee of Voluntis, a European pharmaceutical company. A representative from DTA explained to me that the group formed following conversations among attendees at the 35th annual J.P. Morgan Healthcare Conference in January 2017. These conversations conferred the need for a centralized non-profit group to differentiate digital therapeutics from other types of wellness software, thereby advancing their reputation as clinically rigorous. In a formal interview with the same person, she told me:

> "What I've respected most about all the companies I've worked with so far is that everyone really wants to be on board with ensuring that these products are being developed in a way that will support patient care and improve clinical outcomes across the board due to the strong foundation they all have and being able to prove that they are doing what they say they're doing."

In explaining DTA's specific role, she went on:

> "We are not a certification body or accreditation body. Nor are we an official standard setting body and nor do I want to be. But I do want to start to point to the standards that people are using across Asia, Europe and the US and all these other places. There are internationally recognized standards that we can all adhere to. And that I think gives more applicability also to a product developed in the US that launches in Europe. If they are all still achieving these internationally recognized standards, you're not replicating efforts and you're not confusing different regulatory agencies or payers on either side of the regulatory jurisdictions or along the spectrum of them."

This participant's description of DTA's role echoed the explanation of the ADviCE collaborative's role in helping advance implicit standards for digital therapeutics

companies to work from, as discussed in Chapter 2. Similar to ADviCE, work was being taken up by this entity in the absence of "industry metrics" as established by a more global regulatory body. Despite stating that that she didn't want DTA to take on a formal standard setting role, advancing global standards being utilized in other places would help member companies to establish legitimacy and position their products for uptake in other markets. DTA is a trade organization; its membership comprises digital therapeutics companies paying to participate in the collaborative. It therefore benefits both these companies as well as DTA to advance legitimizing frameworks for them. In doing so, DTA gains recognition as an entity advancing their credibility, as well as the collective commercial interest, while remaining impartial to any one company over another. At the San Jose Digital Therapeutics Conference, a presenting venture capitalist referenced DTA several times on stage in discussing the extent to which his investment calculus, a "highly qualitative process," relied on trusted sources who knew more about the products than he did.

Text on DTA's website defining digital therapeutics has been consistent over the two years that data collection took place for this project. The website includes the following explanation:

> "Digital therapeutics (DTx) deliver evidence-based therapeutic interventions to patients that are driven by high quality software programs to prevent, manage, or treat a medical disorder or disease. They are used independently or in concert with medications, devices, or other therapies to optimize patient care and health outcomes. DTx products incorporate advanced technology best practices relating to design, clinical validation, usability, and data security. They are validated by

> regulatory bodies as required to support product claims regarding risk, efficacy, and intended use. Digital therapeutics empower patients, healthcare providers, and payers with intelligent and accessible tools for addressing a wide range of conditions through high quality, safe, and effective data-driven interventions."
>
> -DTA Alliance Homepage (April 2020)

The website text demonstrates a sentiment that was shared with me in interviews, one that offers digital therapeutics as evidence-based interventions. At face value, this seems like an obvious observation since all biomedical treatments can be considered interventions on disease. Nevertheless, it signals the idea that some digital health products are not evidence-based, or that being evidence-based is some kind of unique and special differentiator. It also implies an individual-level diagnostic approach to health where problems are identified and intervened upon at the level of the body, rather than through structural or systems-based approaches. The DTA's mission statement leverages the logics of optimization and empowerment – concepts that were present in many of my conversations with digital therapeutics company employees, ones that were reinforced by the FDA commissioner's statement in revamping the regulatory framework for digital health products outlined in Chapter 2. "Evidence-based" was also a frequent tagline present at the industry conferences I attended for fieldwork. Given the frequency with which it came up as a differentiator (e.g. digital therapeutics are "evidence-based" solutions), it seemed important to unpack what kind of evidence these products were relying on and advancing.

Evidence-Based

In the time that I attended two conference events for fieldwork and interview recruitment, the name of these events changed from "Digital Medicine and Digital Therapeutics," to simply "Digital Therapeutics," reflecting both a desired shift away from traditional medicine as well as

the title's appropriateness for conference attendees and sponsors, mostly digital therapeutics company employees. In keeping with the shift away from medicine, individuals I interviewed expressed a desire for digital therapeutics to go beyond medicine, as was evident in the promise of these products to not only treat disease, but to collect more types of observable behavioral information more quickly that has ever been possible. Through making good on this task, the promise of a faster intervention looms at the forefront of digital therapeutics, and in the background there is a unanimous sense that the therapies themselves will be improvable because of the observability of the intervention in real time. As one former nurse and Chief Operating Officer of a digital therapeutics company explained to me:

> "Some of the advantages are we can collect, of course, a lot of data. We can use that data on the fly to adjust programs. We can make sure that everybody's getting the protocol as designed. Even if it's customized for them, I'm not dependent on a therapist or a doctor or a nurse or provider to do it right. When you do other studies, especially around behavioral [health], you have two wildcards in the mix: You have the patient and you have the person delivering it and how they respond. The nice thing about doing research, especially, on technology-delivered protocols, is that everyone's getting the same protocol. Even if there's customization for the individual, you can really start to see what's effective and what's not, not based on how good the therapist is at delivering and adjusting, but on the protocol, itself. That's really exciting to us."

An engineer I spoke with said of traditional mental health therapy,

> "Yes, so a lot of these [interactions with patients] are face to face and so they're ephemeral. Whereas when we're creating something in a quality management

system that's gonna get reproduced infinitely, it releases that kind of technique, and makes it observable to arsenalize. …it will be a good way of disseminating knowledge… People treat therapy as a black box: you enter, you exit and that's that. And so even breaking it down, I consider it as an engineer. I have my breakdowns and my systems so we can model it and optimize it, right? That's what I do. So breaking it down into those components, I can say, "How do we accomplish the same thing?" The means by which we accomplish it will be different, right? The means are not human, the means are going to be an app. But what are these effects? How do we establish a sense of duty? How do we establish a sense of authority? How do we establish a sense of personalization?"

What is evident from the quotes of these two interview participants, ones highly representative of many folks I spoke with, is that by both accounts, descriptions for what constitutes successful therapy are dependent upon elements of human therapy that can be separated from human relations, teased out, adjusted, and improved. For the Nurse COO, creating a digital therapeutic product was a way to eliminate human interference with protocols in order to more accurately assess how the therapy was working. In this sense, she wasn't dependent on a reliable clinician in order to be able to deliver the therapy, thereby liberating the intervention from the level of human activity, democratizing it for use without the need for a doctor or nurse. Harkening also to the bifurcation between clinical and technical understandings of quality and the institutional arrangements these differentiations spoke to in Chapter 2, the COO here alludes to the idea that the technology frees the intervention from interference by healthcare – from provider relations altogether.

In the case of the Engineer, the technology offered new ways of understanding human therapy in terms of its individualized parts that could be observed and tested. By his description, digital therapeutics lent transparency to therapy, making observable that which otherwise normally takes place within the privacy of an in-person patient encounter. In both cases, we receive the perspective that by taking a medical intervention outside human encounters and situating it in the encounter with a technology product, new research possibilities are created. The standardized and observable ways the therapy is being delivered enable these research capacities, as well as the therapy's reproducability and potential for wider dissemination.

From these accounts, digital therapeutics present a sense of therapy, even in its previous in-person incarnation, as a deliverable set of interventions that stand separate – though not impervious to – the humans working with them. In this narrative, what counts as therapy is not some messy amalgamation of protocols and human interactions, but a purified set of deliverables that stand only to be improved upon with time. To be therapeutic, then, is to be both free from humans, but also superior to them, and identifiable as a discrete set of observable components that can be dismantled, reconstructed, and delivered by something – human or machine agnostic.

The mechanistic definitions of digital therapeutics that came through in my interview encounters spoke to particular understandings of therapeutic concepts as objective and quantifiable scientific processes. They revealed logics of empowerment and optimization put forth by the DTA's definition of digital therapeutics where there was an optimistically moral aspect of liberating these products from their dependence on delivery by "good actors," or adequately human therapists. With app-based therapy, the patient is empowered to seek out the intervention on their own, especially, as another participant described to me, "because there is way less stigma in working with an app than there is in working with a human." App-based

therapy, then, appeals to a world where human stigmatization is not something to be socially addressed, but rather, a problem to be gotten around by eliminating the human encounter altogether. Evidence, in this sense, aims at building things to bypass people and their messiness.

The Nurse COO states that their products can "be tweaked on the fly," implying a state of constant iteration to better tailor the intervention to the patient. The precision of this treatment, consistent with the hype of personalized medicine, presents a picture of not only highly individualized care, but of highly individualized patients. It contrasts with ideas of relational personhood as advanced by Barbara Prainsack and others (Prainsack, 2017; MacKenzie, 2010), where the very idea of a self is understood as an evolving mesh of human relations.

According to my data, the idea of being "therapeutic" according to this nurse and engineer is made meaningful not because of its immediate care outcome for the patient – in fact, any rendering of this sort is largely absent from their descriptions – but instead because of the future potential that patient data presents to the companies developing the product. In both cases, the potential for a refined protocol rests at the heart of their conceptions of benefit. The engineer's specific interest in how their technology can mimic human success in establishing duty, authority, and personalization points to a specific understanding of the human role in establishing compliance during therapeutic encounters more generally. Both descriptions make highly instrumental use of the patient and contrast with notions of healing as an activity constituted through relationships (Benner, 1994; Malone, 2003).

The Migration of Behavioral Science

Despite the difficulty in defining digital therapeutics in practice and with specificity, within my interview data, codes for "defining digital therapeutics" overlapped with codes for "behavioral science" as well as "time." What emerged in my interviews, unique from news

media coverage, white paper analysis, or DTA reports was that whenever someone began to define what digital therapeutics were, they also began talking about the "translation of behavioral medicine" to the digital realm. At the same time that a confluence of definitions was presented to me, people building digital therapeutics were fervent in their discussions with me about the necessity to strive for at least equivalent clinical outcomes as in-person interventions, when there was an in-person analog (or predicate, to use FDA language). In some cases, digital therapeutics were being built as part of or in extension to a pharmaceutical product, and borrowing expertise from clinical and technical domains. One ubiquitous answer I received amidst all of what digital therapeutics were in relationship to other things, and amidst many references to the DTA as a credible and centralizing industry source, was that somehow this term was inseparable from moving behavioral health out of the in-person sphere and into an on-phone format.

Maybe it should not have surprised me that these products were being described as the translation of behavioral health to the digital realm. As one psychologist casually explained to me in conversation, "behavioral health is just euphemistic for mental health. There's less stigma in calling it behavioral health, and most digital therapeutics, even if they're designed for a physical disease, are aiming to impact the behavioral components of it." There again, the concept of stigma came up in my data. This time it was not in connection with the benefits of digital therapy to work around stigma – but in the benefit of calling mental health by a different name (behavioral health) to avoid it. Nevertheless, I was actually surprised by the consistency of the notion that digital therapeutics represented some type of field movement for behavioral health. I hadn't planned on tracing any of these products from bench to bedside, and yet in interviews with people across professional roles and institutions, I began to hear stories about the way that behavioral health – not only as a set of intended interventions, but also its related expertise and

tools – was moving out of academic labs and into company settings. The following vignette, including the participant's quotes, stands out as a paradigm case illustrating this finding.

November 2018

Claire and I met in downtown San Francisco. I was running to get there. The location was a corner café on Market Street and while the interior was posh and modernly decorated – you could see it from the outside -- to get inside I passed two people asking for change and one man urinating on the sidewalk, appearing to have an auditory hallucination. As usual, as it seemed, no one was paying him much attention aside from working hard to avoid contact while passing by. I found a seat and Claire arrived momentarily with her suitcase as she was headed to a Behavioral Science conference directly following our meeting. We jumped into talking – she was the VP of Research for a digital therapeutics company, had spent the last decade toggling between industry and academia. I asked her how she would define digital therapeutics and she told me:

> "Well, it's probably more relevant for me to tell you how I got into this. Yeah so, how I got into this? Well, I actually got into it through academia. I was a faculty member in the department of psychiatry at an academic medical school for 5 years, and during my time there as a faculty member, I was exposed to several early ... not necessarily early stage, just kind of the early folks out there doing this kind of work, building various digital health products and solutions. So at that point I wasn't really aware that this field existed. And yet this was back in 2013, 2014 when we started having meetings with these types of companies. …But in terms of how I got started it was exposure to these really interesting companies that were just sort of showing up to us in our department of psychiatry. Like, they were showing up and saying, "hey, we either wanna do research with you or we want your time as a consultant."

You know, "we wanna partner with you in some way." And this happened both internally at <academic medical center> because they started an innovation hub to cultivate ideas from the faculty there, and then also externally. So I saw a lot of activity happening around this like, 2013, 2014. And I think at that time something kind of clicked in my head where I thought, 'this isn't going away, this is an industry now that's growing.' And I started seeing how funding was changing around this. Grant funding was really bad around that time and these small companies, that are venture backed companies, were helping to fund some of the research. I saw how it could be mutually beneficial for the investigators on the academic side. So all of this was really interesting to me. I think my attention was always also peaked because ... psychology, or evidence-based psychology, has never had an industry like this. And I'm an interventionist so I'm in behavioral medicine and I create brief or regular length interventions for various medical populations and in various care delivery models. So, I was really interested in where this industry was going. I also had the experience. They needed a psychologist or psychiatrist or somebody who's an expert in mental health or the healthcare system, because a lot of them didn't have that person on their team, or that type of a person, or that discipline on the team. And so I just saw a huge opportunity for the field of psychology and wanted to jump on board. I was like, the train is taking off whether we're on it or not and like, better for us to be on it."

I was curious and asked Claire how her research was different then than it is now.

"Well, just in terms of the research aims, they were totally different. … the start up rules for venture backed companies, if they're gonna become credible in a

> healthcare setting or adopted in a healthcare setting, whether or not you go the FDA route, you've gotta show outcomes. You have to show positive outcomes… the number one goal of these companies is to have a randomized control trial, a very fixed randomized control trial, to show outcomes, to show benefits. That are meaningful, like commercially relevant. Commercially relevant to the company, and then you know, also meaningful to the healthcare stakeholders."

In this memo, Claire lays out a brief history of how, at her previous medical center, behavioral science began to shift outside of the health care setting and into the commercial world by virtue of individuals working at venture backed companies. She describes this history as one that surprised her – an industry for psychology that formed a field in its own right, one that she hadn't known about, that was new. This movement was nested around the concept of "innovation" – a hub that had been created within her own institution, but then also a heightened commercial presence within her department of Psychiatry as a result of the attention to innovation. Claire went on to describe how this shift was taking place at the same time that the predominant academic funding mechanism – grant money – was drying up, making hard money alternatives for research funding particularly appealing, especially, as she notes, because she understood how these kinds of partnerships could benefit the academic researcher.

In the early 2010's, innovation hubs began to pop up within academic medical centers. They tended to be called "Centers for Digital Health," or "Centers for Clinical Innovation," and came a couple years after the passage of the 2009 High Tech Act, with discretionary budgets to seed new products and programs, usually involving technological interventions. In connection with observing these developments within her own institution, Claire made note of the time pressure she experienced, likening her decision to work for a company doing behavioral health to

that of jumping aboard a moving train. Her urgent description reflects the shifting landscape of the time – moving the expertise of psychology labs from academic institutions to privatized venture capital-backed company environments interested in leveraging the science for commercial value. This shift was made possible by not only the advances in software technology, but also by the increased standardization of psychological protocols delivered by therapists and now translatable to machine-enabled services.

Between the years 2010 – 2015, other health care related standardization procedures were well underway at a federal level. During this time, the United States government incentivized medical systems to adopt electronic health records as part of the American Recovery and Reinvestment Act, an economic stimulus bill aimed at pulling the national economy out of recession. As a result, the burgeoning sector of digital health began to grow as entrepreneurs took on investment dollars to tackle the problem of organizing health care. This tactic, an ostensible win-win, was intended to help patients by improving care, while at the same time creating jobs within the technology sector (Pattani, 2016). One of the iconic organizational veterans of this movement was Practice Fusion, a company that offered free cloud-based Electronic Health Record (EHR) systems to individual medical practitioners. In 2019, after the company had been acquired by another EHR company giant, Allscripts, it was subpoenaed for alleged Health Insurance Portability and Accountability Act of 1996 (HIPAA, Public Law 104-191) and anti-kickback violations. By this time, the company founder, Ryan Howard, had already left to co-found a behavioral health company, iBeat, described as the "heart-monitoring smartwatch that [could] save your life" (Feit, 2018).

Claire's personal account of psychology moving out of the academic lab and into company environments is nested within a broader shift toward standardization. In attempting to

trace this movement, it is difficult to discern whether the technology created the drive for standardization, or whether the drive to contain and understand health problems via standardization created the need for technology. Both were connected to a legislated attempt to lift economic recession, and both were and are connected to the commercial promise of turning psychological interventions into profit-making companies. This movement is shrouded in a language of impact and patient access, as I heard time and time again from the people I interviewed. Commercial success was intertwined with product success. A drive for positive outcomes, as I began to find out, was the fuel propelling these activities along the same road.

A Drive for Positive Outcomes

Claire described a specific type of research desired by digital therapeutic companies: the Randomized Controlled Trial (RCT). She positioned this type of research design as the gold standard, the surefire way to prove effectiveness in an environment where the purpose of research is to generate proof that the product works. Nothing about this seemed particularly surprising. The Randomized Controlled Trial is regarded as the Gold Standard within academic institutions, and is taught that way in Research Methods courses within the academy – the best of quantifiable research approaches, and often the most likely study design to be funded by public institutions. I remember very clearly during my research training, a venerated research nurse displaying a pyramid of quantitative research methods from weakest to strongest with RCTs occupying a cherished position on top. By Claire's description, the presence of bench scientists in advisory board positions for these companies, individuals with considerable clout in shaping company directions whose careers have largely been defined by conducting RCT-centric research, had a lot to do with this trend in digital therapeutics.

For digital therapeutics, or any technology product, health problems must be defined in such a way that the product can present a viable, clinically validated solution for them. To present disease as something that shows up in individual bodies with roots in psychosocial, cultural, institutional, and environmental circumstances is to present something that an app on your cell phone has little ability to impact. To instead define disease in terms of behavioral components means that a person can take some basic responsibility for the disease, and improve their situation through acts of individual autonomy and agency. Because the individual is at the helm, there is a locatable end user for the technology, a consumer or institutional actor who can be billed for the technology's use. By leveraging the use of RCTs, building things that are "generalizable" to a population, the technology can be reproduced for wider use and consumption. In this way, we see that the methods used to chart a product's effectiveness – methods that have been adapted from academic research settings as standard quantifiable and objective science, are well aligned with commercial mechanisms for large scale profit-making.

Research for Success

"Scalability" is the mode of potential that attracts venture-backed funding for companies. By "scaling" a product, companies grow massively through deploying duplicates of their technology to many, many users. Because of the facility of doing this so quickly and cheaply with software, as described in Chapter 2, a new era of venture capital backed entities has emerged with larger-than-ever money valuations. These companies, in anticipating such wide up-take, are able to leverage the bets of investors, take on funding in larger amounts, and stand by multi-million (or even billion) dollar valuations. The original founder of LinkedIn, Reid Hoffman, describes this process in a book called "Blitzscaling."

Hoffman explains how the financial success of large technology companies like Facebook and Google is due to the organizational prioritization of speed over efficiency in times of uncertainty. In his book trailer, he notes, "The world is changing faster and faster, and the only way to thrive is to accept the inevitability of change. If you are willing to accept the risks when others aren't, and learn how to navigate those risks responsibly, you'll be able to move faster than your competition, and race to the future."

While I found no references to "Blitzscaling" in my interviews, I include the reference here because of the sentiment among many entrepreneurs I spoke with that, as a digital health CEO once said to me, "there is still a Facebook-like opportunity out there in healthcare." Aside from referencing Facebook for its ability to produce and capture revenue in a new or different way, or for impacting the way millions of people spend time on the internet, I understood this reference in a most basic way to mean that healthcare represented a problem in the world that people could make a lot of money solving. He presented a sense of health care as a "thing" that could be fixed like cracking the code to a lock, similar to the therapeutic dreams of the nurse and engineer I spoke with describing excitement for the potential of their products. Many of my interviews described how scientific methods borrowed from academic research institutions were making their way to company settings in service of producing the clinical evidence needed to garner credibility and profit. In addition to the "start-up rules" that Claire described, she talked to me about how working at a start-up differed from working at an academic medical center:

> "Of course I was at a startup that had a very young group of employees. Like, they were very, very young. So you know, they were much less formal. They were more able to just like, send emails with gifs and emoticons, lots of exclamation points, and things like that. And just put meetings on your calendar.

I'm used to controlling my own calendar, at least in academia I was. Like I lost time and ... just how friendly and nonchalant it was was really interesting to me. There are good and bad things about that. So that was one of the major shifts like, right away, that I noticed. When I was in academia, it was very fast paced work. Very, very fast paced, like I saw patients, I taught in training, I had research, dealt with corrective issues, things like that. It was very fast paced in a specific way. Long, long, long hours, for sure. And then startup was very fast paced too, but in a totally different way. And certainly not as long of hours as I put in when I was at [academic medical institution]. But it's fast paced in a sense that there's just multiple streams of work going on all at one time. And you have this sense of, of course urgency, but then of also catching people and the other teams to make sure you know what they're doing because everyone's moving so fast and it's hard to backtrack."

Another psychologist, Ann, who was working as a consultant to digital therapeutics groups went on to say:

"I was the first PhD and I really helped them. I think they didn't initially understand maybe exactly what I could contribute, but then I was very capable of just carving out like little bits and pieces of research without really bothering people tremendously or costing a whole lot of money. So I think they were pleased that I was able to work within the parameters of the resources that they had…I was producing data that they could take to customers or investors, they can talk to clients and say,"this is what we're seeing." And, and they could use it for product iterations and innovations…I was coming from experimental

> psychology, like randomized control trials, very vigorous and counterbalance. But I realized that in this real-world clinical setting, you need to do the research differently and oftentimes you don't have the luxury of large samples and you need to produce data sets in a shorter period of time. So what I tried to do was create rigor, but on a smaller scale."…Science is a little bit prejudiced towards some of the methods, more of the qualitative or the smaller scale studies where it's a combination of qualitative and quantitative methods. And so one of the hurdles that I'm running into now is where, you know, people I think, you know, everyone's in awe of stem cells or AI or something that they don't understand. Like, oh, that must be difficult. But I think people don't always recognize that behavior or behavioral science is a science too… I regularly have clients that will invest lots of money in the technology and then nothing, or very little in the validation. They will validate in the lab and made sure that the technology works and that the App works, but they don't validate it with end users… You want to improve population health or health outcomes. So that has human being and behavior written all over it. But human, you know, behavioral scientists are rarely part of the discussion."

In the first quote, academic research is contrasted with start-up research in terms of the control the researcher had, the time pressures, the autonomy, and her sense of research as moving from being the center of attention to being one of many priorities within a company. In Ann's case, she describes how she changed the work that she did to create results within a shorter timeframe – manufacturing credible research by altering the size of her sample, scaling down the scope of her work in order for the company to scale up. Competition among firms, demands from

investors, and the need to attract investment dollars may dictate the need for faster results, positioning the research as a credibility marker for attracting more value to the product. These activities harken back to the sense of urgency driving a pursuit of positive outcomes evident in other interview excerpts, and the value placed on attaining them in order to generate revenue.

Ann's description is also a fairly differentiated understanding of the goal of evidence production as compared to the nurse and engineer from earlier in the chapter. Here, rather than leveraging the patient in order to refine a research protocol for reproducibility, the researcher describes her frustration with clients for not using behavioral science to prove the effectiveness of the product with the patients/consumers for whom it is intended. For her, behavioral science is a type of knowing "with human being written all over it," casting its methods into the realm of the qualitative. While we don't have a description of what rigor means in this context aside from it being something she was aiming to create on a smaller scale, we do receive an opinion that behavioral science of this "human" form intending to validate product effectiveness with patients, is frequently left out of the company equation. This connected with the description of research detailed to me by a Clinical Director at another firm describing the importance of testing their diabetes software on the intended audience, elderly people:

> "It was really surprising these young engineers, they're in their 20s and they were just so surprised that people didn't understand scrolling...in our app, there wasn't a very obvious indication that a person should scroll and so people were stuck on that screen going like, 'I don't know what to do next.' There's not enough information here, but these 70-year-old people, they didn't know they were supposed to scroll. Then in a human factors study, for the delete button we had put D-E-L because that's pretty common. So we were testing this with people with

> diabetes and even though “DEL” was pretty common for “delete” on an insulin pump, people were hesitant to touch it because they thought it might mean “deliver.” They weren't ready to deliver their insulin, they were still kind of calculating their dose. So we didn't even think about that, that they might think “DEL” meant deliver versus the delete. In that case, we quickly put a back-arrow as the icon for “delete,” and then people knew what it meant, there was no ambiguity. That's why it's so important to test in the intended audience. If your audience is 60 or 70 years old, you need to test in that audience so you can get what their perspectives and perceptions and health beliefs are to see if they can use your health app.”

While this anecdote very clearly lays out a case for rigorous product testing before market deployment from the perspective of patient safety, the research director doesn’t mention that the point of testing with the intended audience is to prevent something really bad from happening to the patient. In this case, the focus is on the product and its capabilities, and the way that the patient’s behavior aligns with whether and how the product can be taken up for use.

Speaking with a recent psychology PhD graduate who had been hired to clinically validate products at Digital Therapeutics company in San Francisco, he reflected,

> “So, if I were working at my old job in a medical center doing research, it would take a long time to get a research project started and funded and running. But here we can just quickly test whether things are working or not. So for me, that's really exciting because I like things that are faster paced. And testing that we're just interested in and not have to rely on funding to do that. So that's a really cool aspect of it…Throughout graduate school my mentor started doing anxiety

> disorder treatment research, but that wasn't as fundable. So he ended up developing another line of research combing anxiety with smoking cessation, helping people who have anxiety quit smoking. And that way it's interesting because you still get to work with people who are anxious and you get to work on anxiety, but you're also adding in this other component. Which I guess he has an interest in, but I felt burnt out by the idea of having to research things based on what's fundable."

I followed up by asking why anxiety research wasn't fundable, and he replied:

> "I think it is if you are doing more genetic-based work or studying biological models of anxiety. But, the type of work that I'm interested in is basically how can we help people get access to anxiety treatments and make sure that they're effective for different groups of people. And that is fundable through some sources, but less commonly funded. There are some resources for implementation research, but most of those are within VA [Veteran's Administration] settings. Maybe it's just harder to come by than other types of basic science or biomedical studies of anxiety."

In this participant's view, the question of joining a start-up was, similar to others' marked by funding considerations. Different from Ann, his expertise in behavioral science on anxiety was readily taken up by the start-up group, and working on something "tweakable" presented a fun new challenge in a faster-paced, dynamic setting. Here, he found an alignment with his interest in "access" to that of the mission statement of the start-up firm wanting to increase dissemination of the digital intervention. His description of constraints as to what was fundable in the academic environment align with the biomedical bias that Ann discussed in light of her

clients' unwillingness to invest in clinical product validation. Contrary to Ann, however, his skills and interest in "access" aligned with a company objective in disseminating digital interventions, so his experience of translating behavioral science found a more natural fit in the commercial setting. This notion of increasing "access" points to an important area for unpacking, one at the center of Chapter 4.

Discussion

This chapter focuses on the breadth of activities the term "digital therapeutic" was invoked to mean during the time that I conducted research from 2018-2019. Through my analysis, I describe its multiple commercial roots, both in its purported imagining by attendees at an investment bank-sponsored healthcare conference, as well as in the traveling of expertise from behavioral psychology labs to start-up environments. Through my interview experiences, I came to learn that digital therapeutics were connected to ideas about how behavioral science, traditionally a psychological domain of interventional science, was becoming something else within its translation to a digital sphere.

Previous investigations of translational science in the bioeconomy (Birch, 2017; Birch 2020) describe data as something produced in a lab that then gets transported to commercial settings in a process of turning datasets into valuable assets. This leads to a lab's ability to rent its data to commercial entities, trading the dataset's value for revenue to support the maintenance of research activities (Pinel, 2020). What emerged in my research, however, was not such a clean transaction to be traced in the leveraging of scientific interventions. In the case of digital therapeutics, what I observed was not only the shifting of whole human capital – researchers with their attending skills, knowledge, and methods – from academic science to commercial

domains, but the more fluid and enmeshed reshaping of evidence production that was occurring as a result of it.

Participants described processes of research "scaling down" in order for the company to "scale up," and of crafting research agendas within companies to prove positive outcomes quickly, or to orient their methods to product-related questions. In this highly dynamic, very networked sphere, workers moved between jobs frequently, and research methods were massaged to appeal to their intended audience, whether investors, internal company colleagues, or health system clients. Some participants were drawn to the start-up environment because of the excitement of being part of the future, as Claire described the train that was moving whether or not she was aboard. Others, however, were motivated by the experience of academic burnout and funding constraints, ultimately looking to start-up employment as a place where creative experimentation was possible, encouraged, and compensated.

While I did not conduct a thorough analysis of company product evidence as part of this project, the scientific integrity of evidence that supports pharmaceutical product development has been and continues to be deeply interrogated by scholars (Moynihan et al., 2019). Findings from this chapter speak to similarly aligned concerns in connection with digital therapeutics, in so far as they are defined by the digital translation of behavioral science and its attending commercialization.

Chapter 4: Problematizing Access

"Abstaining from care is something
that worries me a lot about this space."

-Senior Software Engineer

Across organizations developing digital health technologies, there is a widely-held, implicit view that technological interventions facilitate patient access to services and that this increased access is of public benefit. Digital therapeutics are expressly defined as interventions that have come to be through the process of commercializing behavioral health interventions. As the previous chapter demonstrates, producing positive health outcomes and disseminating products to more people aligns with commercial logics and constitute core definitional features of digital therapeutics. The mission-worthy task of increasing their access, as was ubiquitously explained to me, lies at the heart of digital therapeutic company taglines. Concepts of access, however, also lie the heart of equity: who has access to the various forms of capital needed to build technological interventions, who has access the jobs these influxes in capital create, who has access to the potential benefits of the product outcomes, and who is absolved from their potential harms.

Despite a seeming ubiquity to the "do-good" marketing language of technology company discourse, critical data and technology scholars have exposed many problems behind this ostensive technological benevolence (Benjamin, 2019; Alam, 2016). Behind the veil of company mission statements espousing the inherent societal benefit of technological advances, there are often conflicting and conflating representations of public benefit inherent in company activities (Sharon, 2018). Further, the activities constitutive of building technologies belie stratifying processes at work (Benjamin, 2019; Costanza-Chock, 2020). In the technoscientific realm, this is

especially true. As such, this chapter contributes to critical scholarship on translational science by tracing the ways that "access" surfaced throughout my data. Conducting this exercise was a path into considering ways that stratifying forces were invoked within my interviews, and spoke to differing notions of what health equity means in the context of digitizing behavioral health.

Throughout interviews in connection with this project, tracing "access" was a way of getting to grips with how the promises of increased access might be overshadowing other types of access falling outside the purview of public benefit. This chapter aims to address the nuance and range with which access showed up in the project. I begin by discussing the different kinds of access constituted by my data, and then turn to a discussion of "access to what" and "access for whom" as extensions of the analysis. My hope is that considering the data in this light may lead to new avenues for normative intervention, and shed light on how organizing activities within novel occupational environments confer structural arrangements with downstream implications.

Commercial Promises

The most ubiquitous notion of digital therapeutics celebrates these products as containing the potential to increase patient access to health care services in a digital form as a helpful alternative to in-person interventions. My data show participants' views about how this aims to improve the quality of care standards, as well as facilitate care when a shortage of providers renders it unavailable. These ideas of "access" came up most commonly in reference to the problem of provider shortages in rural areas, or in areas without significant healthcare infrastructure, positioning digital therapeutics as a way of navigating around geographical barriers to care. The Digital therapeutics Alliance (DTA), notes in its Industry Foundations Report the potential for these products to achieve global reach:

> "As a class, digital therapeutics have vast potential to establish a significant global presence given their ability to: Deliver high quality, evidence-based therapies to underserved and under-diagnosed populations. Make effective, patient-centered treatments accessible and scalable at relatively low units of cost. Support healthcare teams in countries with varying degrees of health care infrastructure. Transform how patients and populations manage medical conditions and engage in their healthcare." (DTA Industry Foundations, 2018, 11)

This explanation for what digital therapeutics can do fits squarely with the promissory explanation of digital technologies more generally – that through their accessibility by smart phone, the need for person-mediated service is eliminated. Nevertheless, as this excerpt shows, the fact that the products have global potential is couched in language extolling their benefits as a scalable product to establish "global presence," again coupling the notion of commercial success with widespread adoption without mention of how the presence of these alternatives impacts existing care models.

What kind of access

Makers of digital therapeutics fairly ubiquitously mentioned the premise that digital therapeutics will benefit patients by extending access to care. Across professional roles, individuals mentioned that digital therapeutics would lessen a dependency on geographical proximity to providers, helping to solve the shortage of medical care staff. In addition to this explanation, discussions of "access" also focused on: extending the pharmaceutical sales model, safeguarding public health, and standardizing professional expertise.

Extending the pharmaceutical sales model

At both industry conferences I attended, the presence of the pharmaceutical sales industry hung heavy in the background of many panel discussions and presentations. Several digital therapeutics companies, including at least one with significant funding, aim to develop digital therapies that will enter the healthcare system through existing pharmaceutical development and sales channels such that a digital therapeutic would be vetted by the FDA and priced in much the same way as a traditional pill. This path, one that seems well-established among health systems, has taken the appearance of digital therapeutics start-ups formally partnering with pharmaceutical companies, or taking on significant investment from them. In this way, digital therapeutics start-ups can work collaboratively with a more seasoned organization that has the experience of moving products through FDA's approval process and into vetted sales and distribution channels within health systems. As one Chief Commercial Officer described to me,

> "So what we have to do at this point is take our pilot trials, which showed efficacy in depression, and do large scale federal trials that could lead to FDA giving us a label for promotion, make marketing claims, and those kind of things. Just like drugs do. I mean, if a drug looks good in pilot trials, the drug company works with FDA to get the drug approved. And then there's a label given to the drug that frames how a sales representative has to interact with the physician in terms of promoting that drug. In terms of what it can do, what side effects might be. So that'll be the same for our software. It'll come with a FDA cleared label. And then sales reps will begin to promote the product based on its benefits because of the exceptional technology platform, which creates the efficacy that's needed. And the fact that we're already aligned with a major payer, you'd expect that we'd have

> decent coverage right out the gates. And then we'd be able to get the word out pretty easily because we have the relationship with a major pharmaceutical company like _____. And we think that paves the way for success. For us, success looks like this: the patient goes to the doctor's office, and the doctor goes to treat depression, the doctor diagnoses the patient as having symptoms of depression, and then makes the determination on what the treatment course is going to be. Maybe they don't want to put him on drugs for one reason or another, and they suggest to the patient that if they have a smart phone, they can try an application to help them overcome their symptoms. If the patient agrees, they go ahead and prescribe it, and then the payer would cover it, and the patient would get better. That's what we aim to do, and that's what we're working on doing."

In this description, the Chief Commercial Officer lays out the ways their company intends to mimic the drug development process – both by following the same procedures that the drug developers follow, as well as by having a partnership with a pharmaceutical firm. Gaining FDA approval, according to this participant, is connected with being able to access appropriate marketing claims. His description of the promotional process positions their product as superior because of its technology platform, "creating the efficiency that's needed," and enables their digital therapeutic to serve as an alternative to pharmaceutical products, eschewing the need for pharmaceutical intervention provided the patient has a Smart phone and willingness to engage with their program.

In a conversation with the Chief Operating Officer of another digital therapeutics firm, I received a differentiated account of this mission statement:

> "One of my concerns, to be perfectly honest, is at our core mission. Of course we want to make more money. We're a startup. We have some investors, that kind of stuff. Our mission is really to use technology to expand access to evidence-based healthcare. But if everything has to go down a true pharma route, maybe you have to get approval, distribute it only through a prescription, that kind of stuff, we're not expanding access. We're limiting access."

I interrupted by asking the participant to say a little more about that.

> "Yeah. I know, I'm a little contrarian here. I think it's why <company> will continue to have a population health arm and a digital therapeutic arm. The digital therapeutic arm that wants to be prescribed by a physician, that should be really rigorous. That should probably have FDA or some other group, maybe, in the long run that approves this, that looks at your science, that looks at your technology, that looks at your ... Everyone should be looking at IT security and privacy. I'm surprised at how many are not. Those should be rigorous like any other medical treatment. Although, people tend to say it's a very pharma-specific route because there's more money in the pharma route. But, to me, it might be a little bit closer to other types of therapy, like physical therapy, behavioral therapy, and some of those kinds of things. I'm not totally sold on the idea that everything belongs in the full pharma model. … To me, a therapeutic doesn't have to be a drug. I felt [at the conference] like there was alignment to say, "This is definitely aimed at going down a pharmaceutical route." I think that's smart.

> Pharmaceuticals know how to distribute things through healthcare. They have in's. They have processes in place. You don't have to reinvent the wheel. They have fail cues. They know how to communicate with docs. I think there's validity there, and I don't think it's a bad idea. I think, sometimes, though we don't give enough credit to the other options."

In this example, the participant sets up a situation where access is constrained by human relationships, by the existing health system, and by market forces shaping the availability of pharmaceutical products. The digital therapeutic must be prescribed by a medical provider, therefore a patient must have some kind of relationship with a provider in order to get it. The participant's perspective was that because of the costs involved in developing a digital therapeutic along the traditional drug development route, the product would likely become expensive and limited in accessibility – only people with access to health care services, and a health care provider would be able to get it. She contrasts this access with the type of access a consumer has to dowloadable smart-phone applications, naming those kinds of health applications as ones that fall into the bucket of "population health."

In medical research contexts, "population health" refers to the care and management of large numbers of individuals, particularly within a given geographical or clinical context (Kindig, 2015). In this interview excerpt, the participant seems to craft a definition of population health that rests on consumer access to smart-phone applications. The distinction in her company's "digital therapy" and "population health"arms is one based on the time and resources available for the development of either application. If not everything "belongs in the pharma model" involving time-intensive development cycles and FDA approval, then the other options are to build digital therapy applications that could become available in a way more reminiscent

of other non-pharmaceutical therapies like physical or behavioral therapy. These alternate paths may not be as lucrative for a company as developing a drug, but they also may not be as costly to bring to market.

According to this participant, patient access to therapy does not stand to be dramatically altered by the advent of digital therapeutics. At least, the relative difference to patients is not mentioned, but for the potential to gain an additional treatment option through their medical provider. Even in the case of therapeutics that would be disseminated through a population health arm, their distribution would be dependent on existing health care infrastructure such as the kind that enables a patient to access physical therapy following an injury.

Safeguarding Health

Another way that "access" surfaced in my interview and document data was in relationship to safeguarding concepts of public health. The initial digital therapeutic to gain FDA approval, Abilify MyCite, demonstrated ways that the basic promises of digital therapeutics – unfettered access to the patient – while bioethically fraught, could pose a form of protection to society. Negative critiques of MyCite hinge on the inappropriateness of trialing novel forms of patient monitoring on a vulnerable (and potentially paranoid) patient population. This technology is designed to increase medication adherence and control the negative symptoms associated with schizophrenia and Bipolar I disorder. These diseases are strongly correlated with social circumstances of homelessness, poverty, and behavior that may be considered dangerous to society at large. Thus, the development of a technology to encourage their control is something that could be considered desirable by health care workers and law enforcement. Similarly, companies are developing digital therapeutics to serve as a substitute for problematic pharmaceutical therapies like opioids and psychotropic meds that may be heavily regulated and

pose institutional challenges to prescribe. Digital Therapeutics, then, may increase provider access to legal ways of controlling unruly patient populations. This came through subtly in my interview data, and was described through a language of empowering caregivers working with elderly senior populations, as one former digital therapeutics CEO described:

> "…But, you can't put enough objects, enough different things to do, in any one community to be able to reach any one individual. So we think about digital therapeutics in a very pointed definition. A digital therapeutic replaces a med. Customers, providers of longterm care were using <product> as a digital therapy instead of medications. Specifically psychotropic drugs. My thinking was this simple. A clinician goes to identify that for Mrs. Jones she can administer this psychotropic drug, why shouldn't she also in that EHR, have an indicator, have a prescription for digital therapy and be able to prescribe <product>. All of that should be and could be tracked. I was recruited to run <digital therapeutic company> in a bit of a turnaround. I saw more and more firsthand this anecdotal demonstration on probably eight or so customers that did their own studies. Again, I stress I wouldn't call it "research," but they did their own studies to demonstrate not only the impact they had on the individuals with cognitive challenges, but the impact that this also had on caregivers, and families, and socialization. If you think about it, now I'm a caregiver and I didn't just put somebody to sleep in their bed. I also got them engaged in something that's of interest. As a caregiver, there's a great sense of value that now I have, that I did something fundamentally different and fundamentally better."

In this particular example, the participant is referencing longterm care facilities, places where the use of some psychotropic drugs to control patients has been outlawed among dementia patients because of their abuse as "medical restraints" (Human Rights Watch, 2018; Stockwell, 2018). One particular example I am familiar with from my hospice work is the use of Haldol. Haldol, a commonly prescribed psychotropic drug used to treat symptoms of agitation and nausea at the end of life, is commonly discouraged by facility administrators from being ordered for patients in order to avoid the possibility of misuse – or accusations of misuse. For this reason, the staff at long-term care facilities are more limited in what they have on hand to soothe elderly patients. Meanwhile, they often lack the necessary staffing for continued human-human interaction, something that has been shown to reduce symptoms of agitation in elderly patients living with dementia. Thus, the design of a digital intervention to occupy these patients could be of great interest. While described in light of the personal satisfaction it would bring caregivers, access to digital interventions like this reduces the burden of continuously responding to the needs of agitated patients, and it could potentially replace the need for hiring additional staff.

In a different but aligned example, some of the latest digital therapeutic products have been designed with the opioid epidemic in mind. In these cases, a sense of safeguarding public health is also invoked as the technology is leveraged for application to an epidemic rooted in social, structural determinants. Different from the situation with elderly patients, the opioid epidemic is geographically linked to rural, economically depressed areas of the United States where job opportunities are limited and where poverty is a basic reality for many citizens (Rigg, Monnat and Chavaz, 2016; Rigg and Monnat, 2018). By designing a digital tool to intervene on behavioral issues, the makers of the technologies propose increased control of a patient population that have traditionally been hard to reach. In a press release from January 2019, a

pharmaceutical company, Novartis, now partnered with pear Therapeutics, a Digital Therapeutics start-up, stated in reference to their intervention ReSet ™:

> "'Addiction is a chronic and relapsing disease that requires constant support, monitoring and access to treatment,' said Corey McCann, M.D., Ph.D, President and CEO of Pear Therapeutics. 'We believe prescription digital therapeutics can transform the way clinicians treat addiction by providing a way for patients to access treatment when and where it's needed. reSET-O has been clinically proven to increase the likelihood that a patient will remain in treatment, while also providing a way for patients to access treatment anytime, anywhere, under clinician supervision.'" …High attrition and relapse rates represent a significant obstacle to providing care to patients with OUD [Opioid Use Disorder]. Therefore, it is important to retain patients in treatment. Retention in treatment is a well-established indicator of successful treatment outcomes for OUD patients. The study data demonstrate that reSET-O significantly improved OUD patient retention rates in outpatient treatment." (Novartis Website, 2019)

In this situation, addiction is framed as a disease that persists because of patients' lack of access to appropriate forms of treatment – and appropriate forms of treatment, the improvement that digital therapeutics can make, are framed as those that provide a constant veil of surveillance. The promise of the digital therapeutic is that providing a behaviorally based, continuously present treatment option to providers will enable them to maintain better control over their patients, solving issues of patient attrition. Behavioral components of addiction are thus identified and prioritized in connection with the explanation of a disease as biologically based and behaviorally perpetuated.

Improved Medical Standards

While my data revealed how access connected to ideas about safeguarding health – protecting it, controlling it, and granting medical providers increased ways of intervening on it – access also came up in connection with the provisioning of health care expertise. As discussed in Chapters 2 and 3 in connection with technical quality and the migration of expertise, interview participants described digital therapeutics as a way to improve medical standards. An academic researcher focused on addiction research reflected:

> "Basically centers that provide treatment for addiction, many of them it, if you look at the employees who they employ, at the educational backgrounds of who they employ, it looks very different from other health conditions. And what I mean by that is the proportion of people with master's level training is very low. And so there's a lot of folks without clinical credentials providing care at those agencies, which tends to go along with not having been exposed to training in psychosocial treatment or therapies that have been shown to have evidence. And <evidence based> therapies are the ones that are incorporated into digital treatments for addiction, like digitized cognitive behavioral therapy, community reinforcement therapy, or contingency management. Some of these things have been tested in research. They're effective. They are providing a way for people to be able to access what works without the human there."

Here the participant describes how, within the context of addiction treatment, part of the problem associated with ineffective treatment is that the people working in treatment facilities do not have appropriate training. With the advent of digital therapeutics, patients have access to an improved standard of care without having to rely on the credentials of a human provider. This

perspective was echoed and elaborated on in an engineer's explanation of disease and digital therapeutic benefit:

> "Part of why people are sick is because they avoid doing things that affect their health that are unpleasant. And so we're trying to overcome that. So giving them a reason to is going to be hard but identifying a reason they already have is a little bit more doable. And when you're talking to someone maybe they can do that, we could do that same kind of question and answer kind of thing or what I really love to do is demonstrate other patients going through that process of discovering why they want to do something. You can identify with that patient, even if you don't have the same reason, recognizing that, "Okay yeah there's something I care about." It's different than what that patient cared about, but I could identify my own reason for wanting to do this. And you don't need a person to be able to do that."

I asked:

> "And so then you build what you learn into the interaction that the person's having with the program?"

Participant:

> "Yes, exactly…It could be video, it could be some kind of interactive video. Like when we're using technology we have all of these tools that are available to us to think about what could work and trying it and then of these ideas, what works the best? Do that enough, and you're able to segment populations to see what techniques match with different segments, you could even present those as options like, "Would you rather watch a video? Would you rather hear an audio?

> Would you rather see a diagram? Would you rather read?" And this is what I mean by having that variety of content and data is how we're going to create the best overall solution for our heterogeneous model."

This conversation with a senior software engineer shows the varied sense of access that creators of digital therapeutics are advancing. First, he describes advancing access to early identification – that enabling patients to name their reasons for being healthy is a key driver, then he connects that with providing access to connection – to the experience of other patients going through similar travails. Next he discusses the digital format as advancing access to different options for engaging patients, personalizing their intervention to different people through various media – videos, audio programs, diagrams, or something to read.

Access to What

Access was invoked in my data in reference to patient access, to provider access and the many forms this may take: patient access to data, patient access to care, provider access to the patient, provider access to treatment options. Little mentioned in interviews, but mentioned in large ways throughout more public conversations is the notion of privatized company access. The digital therapeutic company (or the pharmaceutical company, as the case may be), is the third party that has access not only to patient information, but also to expertise and capital. None of my interview participants talked about the value inherent in housing these assets, but several participants mentioned the lengths their companies go to in securing them. My data spoke to notions of competition and scarcity in light of seeking financial capital. This was evident in the number of interviews with participants who mentioned that their company was working in stealth

mode, as well as in the justifications of engineers for their decision making. Take this quote from a data engineering manager:

> "The way that our team tries to approach things is we use something for as long as possible until it gets really painful (laughing), like for a small company where the resources are limited, that's a really effective philosophy so that you don't end up over-engineering and adopting things that they might not need just yet. So, the old software that we had had been around for at least a few years, and for the most part was working, it kind of grew organically, but over time it just became really slow, so we worked on improving that part of it by adopting some other technology and then after we addressed that issue it became more apparent that it was harder for the data scientists and data analysts to work with their data effectively using the software that we had written. It was very much written from the perspective of an engineer trying to move data through the system – like it was written in a particular programming language that was just all code for the most part. That code was orchestrated using <proprietary software>, but that's not something that data scientists could use. It's not a tool that they're very familiar with. For the most part, the data analysts—sorry, the data scientists – are familiar with Python because Python has a lot of reusable software packages for performing analysis and performing statistics and working the data. So the data scientists were already familiar with those tools and actually, some of them were already exploring using <New software> and another similar tool. So, when we saw that, it was kind of this indicator that there was something missing in our system and it was making it harder for, essentially for our customers, to get what

> they needed. We [engineers] provided some things – we provided the raw data, but we didn't provide as much of the infrastructure for working with that data as we hoped we could [emphasis theirs]. …Our product manager, who is also a data scientist, was the one pushing for us to explore available options. So we started looking into <New Software> and <Another New Software> and dug more into the problems we had that could be solved by those tools. So that's basically how we eventually ended up settling on <New Software>.

Here the data manager shows how not only engineering constraints, but also the priorities of the product manager and data scientist drove decision making and narrowed the types of tools that were up for consideration such that they, or their customers, could get the information they needed faster.

Participants with a technical role in a digital therapeutics company, when asked "what is the biggest priority for you right now?," commonly mentioned the security of data, because, as one Chief Technology Officer said to me, "There is just a massive amount of room for damage if we screw it up." The "massive amount of room" speaks to the dissemination capacity with software, where features and programs are deployed to all of the users, or some portion of them, on a company's digital platform. Hiring practices supported this priority, as many of the senior level technical professionals I spoke with had professional backgrounds working on software systems to secure financial data; they had been recruited specifically for this expertise.

Keeping an individual's health data secure for these companies also means that the company preserves their access to the data. Because of the nascence of these companies, conversations about what they intend to do with the data in the future tended to beget somewhat unformulated explanations. While the capacity to leverage patient data is central to these

technologies, the full capabilities of them are largely unknown. There was a widespread sentiment among most executive level leaders I spoke with that part of the novelty of digital therapeutics was first in the capability of the technology to collect more and different information on patients than has ever before been possible, particularly information of a behavioral nature. Second, there was a strong sentiment that respective digital therapeutics companies housed the unique, "systems-based" thinking to learn from this accessible data, to make data-driven recommendations to patients who were suffering from inadequate and siloed treatment approaches within the traditional biomedical paradigm. As one CEO described:

> "It's crazy to me that it has taken so long for us to actually get to this place. I'm not kidding, we have people that have been sick for twenty-five years and they go through a sixteen-week protocol and they are symptom free and their kidneys that were failing are back to one-hundred percent, their blood work is back, their insulin is reduced, their daily sixty milligrams of prednisone is gone, their drugs went from twenty-one to seven. …When it comes to our bodies, traditionally we've looked at it like a game of whack-a-mole. Like every symptom pops up and we just hammer it down, but we don't actually figure out what in the system that's fundamentally signaling in the first place."

In response I commented:

> "What you are describing sounds like a diagnostic approach. Why hasn't the healthcare system taken that up as their approach?"
>
> CEO:
>
> "Exactly. That's just how we see ourselves. We call ourselves traditional therapeutic but of course we have a diagnostic approach, right? We're essentially

> applying a business model optimizing for scanning, or something like that, to the human body. By looking at a single person in our computer system, we're debunking our health. A lot of times people talk about organs like, "oh we need your appendix" or "we really don't need your gall bladder" or whatever... but we don't look at it from a symptoms approach. We look at it isolated like, "Oh we can take out the appendix and people are fine." But we don't actually know, two years later, when they have a big issue, if that's actually because the system processes are no longer aligned. I think that's the kind of approach that we are fostering. To actually look at how are all these systems are interrelated and if you establish that, you can help your system by doing something in a completely different compartment. Maybe that's actually the way to understand our body processes better."

This participant describes with verve how collecting and analyzing a patient's behavioral data then enables a novel, systems-based approach to diagnosis and cure, something radically differentiated from existing biomedical care models. In speaking with them, I had to stave off some amount of skepticism that they were not guilty of at least a modicum of magical thinking; the effectiveness of the company's technology described seemed almost too good to be true. As I found myself gawking at what seemed like the absurdity of some product success stories, I remembered the time I had been struck by the same sense of outlandishness as a start-up employee. Speaking with executive leadership, particularly those in the throes of fundraising efforts, often felt akin to being an audience member at a product marketing campaign.

Accessing capital is usually always a near-term goal for start-up companies pursuing venture capital backed financing. For this reason, access to accurate information about how

thoroughly effective, or vetted a product is, can be challenging to obtain. Short of working as part of a company in the midst of courting potential investors, talking with employees is typically the only road to learning about the internal activities within a firm. And a start-up CEO's pitch is often the same explanation as a response detailing their company's challenges, the product's effectiveness, and/or the potential of a company's technology to do something beyond what it can presently perform. In keeping, some data from this study speak as much to my participants' palpable exuberance for technology to impact care, as they do to their applied knowledge of effective marketing.

Access for Whom

I did not receive many nuanced explanations of how relocating diagnostic or care activities to software modalities and data servers in the cloud actually made it easier to access by individuals for whom access is an existing issue. The rural populations of patients suffering from provider shortage may also be suffering from a lack of broadband access, as a recent article detailed that up to 40 million Americans do not have highspeed internet (Poon, 2020), and approximately 20% are without a smartphone (Pew Research Center Mobile Fact Sheet, 2019). This truth changes the manner in which we think about patient access as a care barrier– the dependencies may shift from geographic challenges to sociocultural and technological ones, at least in the global north, but they may not mitigate the number of challenges.

Descriptions within my interview data speak to ways in which care is conceptually distilled to systems-based interventions through a language of increased access; it also speaks to ways in which access itself may not be increased, but rather altered by the creation of digital therapeutics. As medical providers become less involved in mediating the provision of intervention-based digital care, care may at the same time take on a more consumer-based

appearance where patients access interventions at home. This seems particularly true in creating the "population based" health applications mentioned by my interview participants whose acquisition and use may be mediated by downloading applications from a central repository such as the Apple corporation's iTunes store. Accessibility in this case then, means considering social, cultural, and economic considerations that impact this modality's likely use as a tool in connection with health.

In a May 2019 New York Times article entitled, "Human Contact is Now a Luxury Good," the authors describe a low-income senior living in San Francisco being monitored by an avatar on a digital tablet, Sox. The article describes the latest permutation of the "digital divide:"

> Life for anyone but the very rich — the physical experience of learning, living and dying — is increasingly mediated by screens. Not only are screens themselves cheap to make, but they also make things cheaper. Any place that can fit a screen in (classrooms, hospitals, airports, restaurants) can cut costs. And any activity that can happen on a screen becomes cheaper. The texture of life, the tactile experience, is becoming smooth glass. The rich do not live like this. The rich have grown afraid of screens. They want their children to play with blocks, and tech-free private schools are booming. Humans are more expensive, and rich people are willing and able to pay for them. Conspicuous human interaction — living without a phone for a day, quitting social networks and not answering email — has become a status symbol. All of this has led to a curious new reality: Human contact is becoming a luxury good. As more screens appear in the lives of the poor, screens are disappearing from the lives of the rich. The richer you are, the more you spend to be offscreen. Milton Pedraza, the chief executive of

> the Luxury Institute, advises companies on how the wealthiest want to live and spend, and what he has found is that the wealthy want to spend on anything human. 'What we are seeing now is the luxurification of human engagement,' Mr. Pedraza said (Bowles, 2019).

While hinting towards a bit of a puff piece in the stark dichotomy drawn between "rich" and "poor," the article speaks to new ways that life is being organized along class lines as a result of technology's cheap substitution effect. Typically, the term "digital divide" is invoked to compare technologically dense areas of the world to places (such as parts of the United States mentioned previously in this chapter) where access to technology is lacking. This piece points to a different emerging trend, however, that as access to screens becomes more ubiquitous, its detrimental effects – about which we are still learning – also become stratified along class lines.

If we consider digital therapeutics in this regard, particularly those interventions with mental health applications striving to (and celebrating) the elimination of the human therapist, it is possible to see how the divide between care bound in relationships as opposed to curing through intervention also stands to widen. My interview data speak to myriad ways that this human elimination is a good thing – eradicating the risk of bad therapists and providing patients with access to improved standards, to an intervention that has been proven effective, designed to cure. The silences of the data – and perhaps simply the limitations of it given that this research did not include patient interviews – speak to all the things we do not know about what happens when you reduce care to non-human interventions entirely.

Place-Based Reflections

Doing this project in the Bay Area meant confronting multiple urban realities in the midst of interviewing a tiny sliver of the tech sector workforce. Woven as they are into small aspects of

my participant interviews, the context for meeting people in the mid-market neighborhood was one of convenience – it was the place most commonly suggested by participants as near to their office location, a spot where they wouldn't lose extra time going. It was also a place where having coffee on shiny street corners was flanked by a noticeable degree of human suffering. Thinking through the encounters with interview participants meant bracketing questions like, "What am I/are we doing right now in light of these folks who are asking for food and money?" Listening to the promises of digital therapeutics in the comfort of clean clothes and the understanding that I had a place to sleep that felt safe, was something much easier to do over Zoom or by phone than out in the world. When these conversations happened in the middle of San Francisco's downtown, they were starkly positioned alongside a raw and visceral sense of scarcity unparalleled by the form of scarcity conjured in my interviews by company founders competing for venture capital dollars. Could anyone care about these products if they didn't have supportive relationships, a home, or money for a meal? Does producing these products help to create any of these necessities for people who might need them? While those thoughts often ran through my mind and may have been running through the mind of my participants during interviews, answers to them obviously fall with a resounding, "No." Neither studying this segment of labor activity, nor participating in it would be possible without some basic supports in place. It is my earnest hope that studying this area, while unhelpful in providing immediate relief to any pressing issues of inequity, helps bring to light ways in which future work can get at some of its upstream determinants.

Analyzing memo data showed, in a felt sense, how goals of self-empowerment and betterment as advanced by digital therapeutics products may push against work centering a social responsibility to care about those living in different ways within the same geographical

boundaries of a city. For one thing, the frenzied and consuming pace of start-up culture described to me, "trying to learn things as quickly as possible, failing fast, racing to the future" (Composite of interview and Blitzscaling quotes, 2019), does not leave human bandwidth for considering much else. Moreover, concepts of health as bound up in the individual optimizing logics of technology products contrast with the idea of relational personhood put forth earlier in Chapter 3 (Prainsack, 2018). While previous work has highlighted this problematic in light of the personalized medicine movement, I am unaware of ways that it has been applied to technoscientific arrangements more generally, or to digital health production specifically. My well-being as linked to that of the blanketed man from my interview with Claire is unaccounted for in the context of a digital therapeutic encounter. Neither, on the other hand, would the digital therapeutic encounter provide new possibilities to the blanketed man for accessing human relationships, shelter, or food. In a basic way, individual interventions do not get at the social and structural arrangements that give rise to varying depictions of health, nor can they offer much to public health when those arrangements are not present.

Although tangential to the research aims of this ethnography, differing ways that "access" was constituted by my data show, at a minimum, the need for more nuanced investigations of what actors are talking about when they invoke the word. Framing access in its pluralist forms may be a new way to get at considerations of health equity in studying tech sector development. At a minimum, this framing shows a thread that runs through my data and points to the necessity for closer investigations of ways that inequity is situated in the context of digital therapeutic production and the places it takes place.

Discussion

At a friend-of-a-friend's birthday party, I found myself speaking with a venture capitalist who makes financial investments focused exclusively on Type I Diabetes. She was interested in trying to bolster the interest of her colleagues in digital therapeutics as all of their financial stakes were currently rooted in traditional pharmaceutical development. I listened to her share a little bit about her work, and she returned the focus to me, excited for the completion of my research so that I may impart to her the clear front runners of the area. Not too long after this meeting, a physician crafting statewide policy for opioid prescribing approached me with similar enthusiasm, noting that digital alternatives to in-person therapies were "crucial" for the feasibility of substance abuse treatment.

Perhaps these two occurrences should not have surprised me, but they did. Over the course of the research, I was struck by how often people I spoke with assumed that I was studying digital therapeutics in order to advance their implementation. Non-technically trained people, including the women referenced here (neither of whom lived in the Bay Area or were a part of my immediate social web) referenced technology as an obvious answer to structural-level care problems, the cost-effective solution to issues ranging from provider shortage to patient attrition. While I was actually studying digital therapeutics because of my original skepticism and curiosity about how an industry could advance in the absence of clear regulatory guidance, what seemed to evolve throughout the course of research was my own position as an outlier among popular sentiment that digital therapeutics were a necessary, inevitable future in care.

During the course of this fieldwork, I wrestled with the ethical question of how, if at all, the research I was performing would impact digital therapeutics formation. Perhaps giving attention to this burgeoning area as a legitimate research topic lent legitimacy to it. The phrase,

"all press is good press" came to mind, pointing to the possibility that nearly any attention, and particularly academic attention, given to research phenomena helps codify them as "real things." At times I found myself acting as a spokesperson for digital therapeutics; it was a hard position to avoid as someone studying their production. To some degree it was incumbent on me to form an opinion about the activities I was examining. When research participants emailed asking for lists of characteristics of current digital therapeutic companies, information I had readily at hand, I willingly provided it to them both in the spirit of sharing, as well as in gratitude for the time they had given to interview. I weighed the trade-off and did not find it any more troubling than the one I made with conference organizers where, in exchange for free admission to both digital therapeutics conferences, I produced summary reports of the events to conference attendees. Striving to maintain a partiality to the public interest, I saw no serious problem with this agreement since the summaries became part of my dissertation data in contribution towards a publicly disseminated dissertation.

Conclusion

"Digital therapeutic makers see
opportunity as pandemic prompts
FDA to ease rules."

-Medtech news headline
April 24, 2020

In December 2019, Congresspeople called for public input in the creation of Cures 2.0, a bill designed to foster unachieved aims of the 21st Century Cures Act with a specific focus on digital health (Martin, forthcoming; Degette and Upton, 2019). By March 2020, The United States of America had declared a state of national emergency concerning the COVID-19 disease outbreak. People living in San Francisco (but for its homeless residents) were ordered to shelter-in-place following containment measures to curb the spread of the pandemic. Schools closed, many individuals became unemployed, and much of the city's tech workforce scrambled in a shift to work-from-home. In response to the pandemic, the Centers for Medicare and Medicaid and private insurers loosened restrictions on reimbursement for telemedicine, prompting health system attorneys to finalize contracts with digital health vendors, ushering in an era of ubiquitous remote care for many types of clinical visits. Rock Health, a prominent digital health incubator sent out its regular newsletter on March 23rd, 2020 entitling it, "Telemedicine's tipping point" (Rock Health, 2020).

As for my dissertation writing that was suddenly taking place more slowly and entirely from home, it seemed slightly ill-fated that writing and analysis should come to an end in March 2020, right when such salient precedents were being set both for workplace norms and digital health regulatory schema. What would this mean for the digitization of behavioral health? In the midst of it all, on March 26, 2020 one of the digital therapeutic company frontrunners, Pear

Therapeutics, obtained FDA authorization for a new product, SOMRYST, to treat insomnia. It was the first product approval to take place as part of FDA's initial Software Precertification Pilot Program, and in reading the press release I wondered if its dovetail with COVID-19 had been serendipitously engineered to profit from the forthcoming sleeplessness of newly unemployed people. In any case, as with all research on novel and evolving phenomena, the findings from my work mark a specific point in time – two years in time – which seemed to quickly recede against the backdrop of a global public health crisis. I've tried to do service in elucidating the overall climate in which this research took place, including some of the situational aspects of San Francisco's urban environment and its attending specificities.

Between August 2018 and March 2020, public conversations about widening wealth inequality in the United States were taking center stage in news publications (Chetty et al., 2017; United Nations Report, 2020; Ingraham, 2020; Zucman, 2019; Badger and Quely, 2019). San Francisco was often positioned as the brunt of a joke about the impossibility of life in a place with $3690/month average rent for a 1-bedroom apartment, scorning out-of-touch elites who transformed city corners into tech-sector luxury bus stations while pushing long-time residents to the margins (Brinklow, 2020). Following the COVID-19 outbreak, storefronts boarded up in San Francisco and panicked social media posts pleaded for unused personal protective equipment. The virtual anxiety pulsing through Zoom conference software and social media platforms seemed to speak to the precarity of economic and social models, rather than to people's generosity in observing shelter-in-place orders. A robust ecosystem wouldn't be this fragile, and yet, its un-sustainability is something that scholars have highlighted for years (Wilkinson and Pickett, 2011; Deaton, 2013; Jennings, 2013).

While this dissertation is not an urban ethnography of health innovation in San Francisco, health tech sector environments and prevailing concerns with fundraising do contrast with the very apparent precarity lining many city areas. A double-edged analysis of these worlds would advance understandings of who and how certain communities benefit at the expense of others, a concern for both scientists and policymakers interested in the appropriate crafting of structural interventions.

Overview of Findings

Defining Digital Therapeutics

In this project, I set out to investigate the trajectories of digital therapeutics industry formation in tandem with its regulatory development in San Francisco. My findings present ways in which digital therapeutics are being defined and operationalized in proximity to the commercialization of behavioral science. This is abetted by shifts in evidence production prioritizing the attainment of positive health outcomes. The formation of digital therapeutics confers new types of occupational arrangements in both clinical and technical domains, and brings to light ways that quality is differentiated along clinical and technical lines.

Regulation

A central finding of this research is that in the current environment where there are not clear regulatory standards for digital therapeutics products, regulatory guidance is effectively outsourced to an ecosystem of "implicit standards" as advanced by collaboratives such as the ADviCE group and the Digital Therapeutics Alliance. In connection to this finding, my data also show how in the absence of regulatory oversight, regulatory expertise becomes an asset for firms, advantaging actors with more resources. Current commercial actors who can capture regulatory expertise within their specific company position themselves to collaborate with FDA

in defining the rules for other players, thereby helping to shape the regulatory landscape according to their interests. Given new regulatory frameworks aiming to evaluate whole companies rather than individual products for "Cultures of Quality and Organizational Excellence," the opportunity to positively interact with FDA in an initial authorization process would be beneficial for future rapport and potential designation as an excellent organization.

Selfhood

Findings from this project demonstrate particular conceptions of health advanced by digital therapeutics companies as centering on optimizable, behavioral processes that increase individual access to higher care standards. This research highlights the role of behavioral science in furthering individualized ideas about health, and the position that commercial entities occupy in their service as expertise migrates from academic labs to commercial domains. For developers, health is constructed as the sum of divisible parts that, when faulty, present a problem that digital therapeutic solutions can intervene upon for profit. Ideas of health as advanced by digital therapeutic companies center on notions of selfhood that are constructed outside of relationships, where disease burden is placed in the hands of the consumer to fix, should they be empowered enough to do so. These digital interventions further reassign responsibility to patients/consumers for their health, distancing solutions from traditional healthcare, and choosing against possibilities for structural intervention, linking people to the enterprises that house their personal health data through individual empowerment logics. These notions of health diverge from relational aspects of health and wellness, privileging traditionally Eurocentric ideas about autonomy, ownership, and individualism as enacted through self-care.

Evidence

In the process of "empowering" individuals, expertise is relocated to the digital therapeutic product. This relocation of expertise aims to "purify" interventions in heightening standards of care and in the process, "liberate" patients from dependence on bad medical actors. In building these products, researchers with expertise in behavioral science shape the research agenda to fit within condensed timeframes and produce outcomes that align with commercial success. This finding contains implications for studying the commercial determinants of health, particularly in light of the fact that many firms produce their own research, in addition to generating and submitting their own analytics to FDA in fulfillment of post-market assessment analysis.

Access

Finally, my data speak to conflicting ideas about what "access" means in relationship to digital therapeutics, where the idea that they increase patients' entrée to services oversimplifies the tangle of meanings that access assumes in consideration of these products. Teasing out the discrepancies between company mission statements and commercial activities using access as a frame may be a way to empirically examine how commercial activities influence some of the structural arrangements that have health equity concerns at their core.

Discussion

A question I consistently asked myself during this research was: what is being produced alongside the making of digital therapeutic products in the name of health innovation? My interviews speak to commercialization as constitutive of innovation for behavioral health, and they speak to an occupational reorganizing that occurs in the midst of these activities, in order to craft and advance products serving as interventions. My findings also speak to a co-mingling of

commercial and regulatory activities, particularly during a period where the nature of regulation is in flux as a response to the iterative nature of software. FDA's focus, aside from expediting the time to market for products, is to prevent one-off adverse events. In this climate, there is virtually no entity tasked with evaluating a) the integrity of evidence that is proving these product claims b) the equitable distribution of resources fueling the creation of these products or c) any promise for the product to produce public benefit in the form of a social good. As such, the types of trade-offs made within our current framework for vetting safety and effectiveness deserve more attention, particularly in light of who benefits from them, and at whose expense.

As an industry, digital therapeutics is very visible to the public – company founders have worked with conference organizers to make sure it is a defined area within the digital health landscape, it has a non-profit trade group advocating for its heightened presence as well as lobbying for its furthered uptake in the context of COVID-19 (Brodwin and Robbins, 2020). Pharmaceutical firms have begun partnering with its frontrunners to build companion products and/or act as a strategic investment entity. The public has read about digital therapeutics in the New York Times and the Harvard Business Review, or seen them presented on Dr Oz. Despite these different forms of public presence, this cadre of products – as representative of digitized behavioral health interventions – remains invisible from the perspective of regulatory oversight. This duality of public-facing presence and regulatory non-presence works to the advantage of product manufacturers since it presents opportunities to collaborate with FDA in defining the area and setting precedents for ways that future products will be vetted.

Emergent scholarship on assetization has named innovation as a problem in and of itself – that innovation and financialization are inextricably bound up in the research strategies of monopolistic giants (Google, Apple, Facebook, Amazon) whose company agendas flow from the

exploitation of our digitized personal data (Birch, Chiapetta, Artyushina, 2020). While none of these companies have come out with a digital therapeutic product as of yet, the strategies of digital therapeutics companies fall squarely within this problematic. Some of the normative recommendations the authors make may also extend to digital therapeutics as considerations for policies centering social responsibility.

Recommendations

Based on findings from this research, I propose several recommendations in connection with the formation of digital therapeutics across regulatory, health system, and research domains.

Regulatory Science

- Digital therapeutics' formal recognition by FDA: FDA should recognize Digital therapeutics as a distinct product category within the Center for Radiologic and Digital Health. This product category should use a capabilities approach to establish guidelines for vetting submissions according to stated, implied, current, and future diagnostic as well as therapeutic benefits.
- Product Claims in grey areas: FDA should establish a work group with appropriate expertise to review SaMD low-risk devices that contain both diagnostic and therapeutic benefits as part of individual product claims.
- Post-market assessment activities: FDA should establish third parties with descriptive metrics for assessing the integrity of post-market assessment data presented by companies producing SaMD.
- Assessment of commercial evidence production: The U.S. Offices of Research Integrity and Government Accountability should include the assessment of digital research/ digital evidence production in its 2020/2021 priority agenda.

Health Systems

- Incorporating ethical guidance into implementation science. Biomedical health centers should incorporate ethical guidance into evolving digital health implementation strategies. Such guidance may incorporate a full assessment of the health issue a digital intervention is aimed at solving including its non-technical solution alternatives. It should include equity assessments for how and in what ways varying patient populations served by the health system will benefit, thereby creating opportunities to fill gaps with alternate forms of care/support as needed.
- Bolstering structural competency training: Education about "commercial determinants of health" should be incorporated into structural competency training for health professionals. While the structural determinants of health disparities have been largely incorporated into physician training models in medical school curricula, this is not the case for all allied health professions, particularly those existing on the "front lines" of care. Information pertaining to commercial determinants of health should be incorporated into structural competency training, and structural competency training should be incorporated into required the coursework for allied health professionals in areas including nursing, occupational, physical, and speech therapy, and medical social work.

Future Research

As alluded to in Chapter 4, this research points to "access" in its plurality as a helpful concept for framing research on technoscientific development and its stratifying effects. In crafting future research on health innovation, attention should be given to specific ways in which evidence production is shifting alongside commercialization in moving behavioral health interventions into products. Specific questions to consider are: What are the epistemological

foundations of the effectiveness testing for these products? Who are the beta testers for a product and how were they recruited? For whom is a product intended and how has it been "taken up" by consumers/patients/users?

Empirical examination of health innovation funding arrangements is also an area deserving of more attention by researchers. Beyond the financing of individual health startups in comparison to startups of other industries, dollars flowing into product formation should be weighed against financial support for other types of health improvements within geographies.

A Final Word

Studying the formation of digital therapeutics presents a case study in how technological innovation is reshaping the nature of evidence production, therapeutic standards, and human interaction for behavioral health. This domain is virtually unregulated and deserves attention for the sake of public health, evidence integrity, and future promises of equity.

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Appendix

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
INDIVIDUAL INTERVIEW GUIDE

1. What is a digital therapeutic?
    a. If participant mentions more than one, or conflicting definitions: How have you heard it being used and by whom?

2. Where did you first learn about Digital Therapeutics?
    a. Where did Digital Therapeutics originate?

3. How did you come to work in [current job role/organization]?

4. How would you characterize your organization's culture?
    a. Can you tell me a brief story about your company that reveals the culture of your company?

5. What do you do to enable the quality of the product you're working on?
        i. Can you tell me the story of how you made a product decision about quality?
        ii. If there was any conflict, how did it play out?
    b. What are the key performance indicators you are using for your product?
        i. Can you tell me the story of how you came to choose these?

6. What are your job responsibilities?
    a. How do you think about regulation in the context of your job responsibilities?
    b. Can you talk with me about some of the things you do related to ethics and innovation?

7. Can you tell me anything about "Cultures of Quality and Organizational Excellence?"

8. Have you heard of post-market assessment?
    a. What are your thoughts about what post-market assessment markers should look like for this product/for digital therapeutics products in general?

9. Can you please describe for a me one kind of typical day?
    a. If none, talk to me about how you spent your time on a couple of the days of last week?
    b. Who do you work with on a day-to-day basis?
    c. How is your company structured (e.g. teams)
    d. How do you work with other people in your company?
        i. Can you tell me the story of how a recent decision was made within your company?

ii. Once the decision was made, where did the decision get documented?
    1. What software tools supported this process?
    2. How do company employees learn about decisions that are made if they do not include them?
        a. (e.g. are there software tools that are used to document this?)

e. What policies exist within your company?
f. What tools (software or otherwise, do you use on a day-to-day basis?)

<u>Generalized interview questions to ask of all participants:</u>

1. What does optimal health look like for you?
2. How would you describe digital therapeutics to someone who didn't know what it was?

<u>Differentiated interview questions by professional area:</u>

1. Question for investment management
    a. What do you look for in a digital therapeutics company as a potential investment?

2. Question for clinical affairs, engineering
    a. How do you know your product is working for patients?

3. Question for Sales/Business Development, executive leadership
    a. What is the most important thing for your company's success?
        i. How does this thing get measured?

4. Question for regulatory affairs, executive leadership
    a. How do you incorporate FDA guidelines for digital health into your company's decisions? (Can you tell me a story about this)?

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