Health Informatics

Sharon Wulfovich
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Digital Health Entrepreneurship

Springer

Health Informatics

This series is directed to healthcare professionals leading the transformation of healthcare by using information and knowledge. For over 20 years, Health Informatics has offered a broad range of titles: some address specific professions such as nursing, medicine, and health administration; others cover special areas of practice such as trauma and radiology; still other books in the series focus on interdisciplinary issues, such as the computer based patient record, electronic health records, and networked healthcare systems. Editors and authors, eminent experts in their fields, offer their accounts of innovations in health informatics. Increasingly, these accounts go beyond hardware and software to address the role of information in influencing the transformation of healthcare delivery systems around the world. The series also increasingly focuses on the users of the information and systems: the organizational, behavioral, and societal changes that accompany the diffusion of information technology in health services environments.

Developments in healthcare delivery are constant; in recent years, bioinformatics has emerged as a new field in health informatics to support emerging and ongoing developments in molecular biology. At the same time, further evolution of the field of health informatics is reflected in the introduction of concepts at the macro or health systems delivery level with major national initiatives related to electronic health records (EHR), data standards, and public health informatics.

These changes will continue to shape health services in the twenty-first century. By making full and creative use of the technology to tame data and to transform information, Health Informatics will foster the development and use of new knowledge in healthcare.

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Digital Health Entrepreneurship

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Preface

Digital health, the use of information and communications technologies to exchange medical information to diagnose and treat disease and improve care processes and decision making, has exploded in the past few years. Examples are electronic medical records, remote sensing devices, telemedicine, artificial intelligence and machine learning.

Digital health entrepreneurs, those who pursue opportunity under conditions of uncertainty with the goal of creating healthcare stakeholder value through the deployment of digital health innovation, are at the forefront of creating these new platforms and models.

However, there are still significant barriers to the design, development, testing, deployment and post-deployment surveillance of digital health technologies and products. This book is for those interested in closing the gaps by outlining the many stops along the digital health innovation roadmap, including:

- Stage 1: Industry and market analysis
- Stage 2: Opportunity identification and assessment
- Stage 3: Crafting a solution and demonstrating technical, commercial and clinical validation and verification
- Stage 4: Deployment
- Stage 5: Dissemination and implantation, promoting the diffusion of innovation across the various customer segments such that it becomes the standard of care
- Stage 6: Marketing and post-market surveillance
- Stage 7: Continuous quality improvement and product development

We would like to acknowledge and thank the many authors, each a practicing domain expert, for their contributions and expertise.

We hope these lessons learned in the trenches of digital health innovation and entrepreneurship help you prevent mistakes and alert you to the landmines.

Good luck in your new digital health venture!

Denver, CO, USA — Arlen Meyers
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Chapter 1
Introduction to Digital Health Entrepreneurship

Sharon Wulfovich and Arlen Meyers

Overview and Importance of Digital Health Entrepreneurship

Digital health entrepreneurship is the pursuit of opportunity under conditions of uncertainty with the goal of creating user defined value through the deployment of digital health innovations. It is the pursuit of information and communication technologies (including telemedicine, wearables, mobile health and data analytics) to transform the medical field with the goal of improving patient outcomes, increasing quality of health care, improving the health professional experience and reducing costs. Using this quadruple aim framework, we will discuss how digital health entrepreneurship has the potential and opportunity to greatly improve the U.S. health care system.

In terms of improving patient outcomes, there is always room for improvement. Digital health technologies have the potential to not only measure patient outcomes in in more diverse and complete ways but also simultaneously improve patient outcomes. There are many current examples that illustrate this potential including multiple studies on the impact of telehealth on chronic conditions. For example, multiple studies have shown that telehealth can improve outcomes in patients with congestive heart failure [1–4]. A systematic review that analyzed 14 randomized controlled trials with a total of 4264 patients found that remote monitoring systems decreased hospital readmission rates by 21% and all-cause mortality by 20% [5]. This provides evidence for the use of telehealth on improving patient outcomes. Additional

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telemonitoring technology and other telehealth technologies need to be created, accepted and used in order to continue improving patient outcomes.

There are many factors that influence the quality of health care. The growing physician shortage greatly impacts access and as a result the current and future quality of health care. According to the 2018 report by the Association of American Medical Colleges (AAMC), there may be a shortage of up to 120,000 physicians in the United States by 2030 [6]. Digital health entrepreneurship has the potential to lower the effect of this shortage on health care. For example, the application My GI Health (My Total Health) (https://mygi.health) is a digital health platform that systematically compiles patient reported gastrointestinal symptom data and turns it into a report for the physician to read before seeing the patient. This allows the clinic visit to become more focused on addressing the problem versus collecting patient information [7]. A cross-sectional study compared the identification of risk factors by the My GI Health algorithm to those of physicians and found that the algorithm was able to identify a greater quantity of risk factors [8]. This shows that there can be great value in using digital health platforms and checklists. It could reduce the time needed for each patient and allow physicians to focus on doctor-patient communication while seeing more patients in a given day. This idea could be scaled to many specialties and used to maximize and improve doctor-patient communication and interactions, increasing the quality of care provided.

Similarly, the growing physician shortage results in an increased burden on all health professionals. Health professionals are overworked and have a high rate of burn out. Digital health entrepreneurship has the potential to improve the health professional experience. The application discussed above, My GI Health (My Total Health), can not only increase the quality of care but also greatly improve the health professional experience. In reducing the amount of time that health professional collect data from patients specifically data that could be accurately and efficiently be located by applications, health professionals can reduce the time needed for each patient. This could allow health professionals to feel less overworked and focus on providing quality care. This is just one example of how new digital health technology could greatly improve the health professional experience.

Healthcare costs are continuing to rise—in 2016 U.S. healthcare expenditures made up 18% of the total GDP or $3.4 trillion [9]. According to the National Health Expenditure Data from the U.S. Centers for Medicare and Medicaid Services (CMS), healthcare spending is projected to increase at an average rate of 5.5% per year (2017–2026), reaching a projected $5.7 trillion by 2026 [10]. Digital health could help lower these increasing costs. For example, the Veterans Health Administration (VHA) initiated a national home telehealth program entitled “Care Coordination/Home Telehealth” (CCHT) [11]. vThis program used health informatics, telehealth, and disease management technologies to allow veterans with chronic conditions to live at home and delay the need for long-term residential care [11]. The data collected over a four year period from 17,025 participants demonstrated a 25% decrease in total bed days of care and a 19% decrease in total hospital admissions [11]. The continued growth of this program (over 380,000 enrolled veterans)

has resulted in significant financial savings with an average yearly saving ranging from $1238 to $1999 per patient in 2011 [12]. This impact is continuing to grow and illustrates the potential of digital health in lowering health care costs while continuing to provide quality care.

This quadruple aim does not fully illustrate the benefits and importance of digital health entrepreneurship. Digital health entrepreneurship provides other benefits to healthcare industry and population health including bringing new perspectives, empowering individuals, increasing use of preventative medicine, and increasing access to care. Digital health entrepreneurs are not just healthcare providers, cooperation with non-healthcare related is highly common (and sometimes even needed). The increase in communication and collaboration between a diversity of disciplines brings new perspectives and solutions. Digital health empowers individuals with the rise of the do-it-yourself applications and devices. Individuals can now take greater control over their health, by using applications that are convenient and accurate to control or track the progression of an illnesses or simply monitor health. Additionally, these devices may even have an innovative new approach to treatment. It is through these applications and devices, that digital health plays an increasing role in preventative medicine. It can help detect and intervene promptly as well as be used as a tool to improve health. Lastly, digital health is also enabling an increase in access to healthcare for rural and remote communities. Communities where hospitals or clinics are not conveniently accessible can now use telemedicine to get access to care more conveniently.

Recent Trends

Recent trends in digital health entrepreneurship highlight the growing acceptance of digital health as well as areas of improvement. They include:

1. **Stable levels of investment and new investment vehicles**—Investors are becoming more confident in the digital health sector, Quarter 1 of 2018, marked the largest Quarter 1 for digital health with $1.62 Billion invested in 77 digital health deals [13].
2. **Technologies are being applied to medicine**—Social media, blockchain, artificial intelligence, internet of things
3. **Policy and regulatory changes**—Regulations and policies are being changed to hamper or adapt to the dissemination and implementation of digital health innovation. For example, the FDA recently issued the Digital Health Innovation Action Plan [14] and the 21st Century Cures Act (Cures Act) [15]. These improved policies allow products to get to patients in a more efficient and timely manner.
4. **Large companies are getting involved**—Apple, Amazon, Google, Facebook, Microsoft

5. **More health IT education**—Education programs are offering more degrees and interdisciplinary courses in digital health entrepreneurship and data science [16]. These programs are being offered both at undergraduate and graduate levels.
6. **Academic medical centers, innovation centers, accelerators, incubators and generators are increasingly emphasizing digital health development and implementation**
7. **The rise of physician entrepreneurs**—Physicians are becoming more involved in early stage start-ups and many medical students are forgoing residency for startup involvement [16].
8. **Digital health clinical trials**—Entrepreneurs are starting to collect evidence of the effectiveness and necessity of their products and services [16, 17]
9. **Increased medical and non-medical collaboration**—Entrepreneurs in the healthcare field are bringing non-healthcare related entrepreneurs to help. Additionally, the complexity of the healthcare industry creates the need for team members with healthcare experience. The vast amount of regulations including HIPAA, FCC, FTC and FDA create many barriers to success. Additionally, the intricate healthcare delivery system contains reimbursement models coupled with various stakeholders. This makes it very challenging to create a functional, compliant and profitable product and especially challenging if there is not a team member with relevant healthcare related experience. The fact that medical and non-medical entrepreneurs are starting to work together has enabled an evolution of regional digital health ecosystems.
10. **Increased comfort in using digital health technologies**—Patients, healthcare providers and individuals are becoming more comfortable using digital health technologies as part of their daily practice.

Barriers and Possible Solutions

Although digital health entrepreneurship has picked up in the past couple of years and continues to grow at a high rate. There are many barriers that digital health entrepreneurship faces. Here are some highlights and possible solutions:

1. **Physicians as entrepreneurs**—There are many persistent barriers for physicians to become entrepreneurs including: lack of an entrepreneurial mindset; lack of courage to persist with an entrepreneurial venture; lack of knowledge (intellectual property, business development, funding, recruiting team members, FDA clearance etc.); poor innovation culture; lack of recognition; anti-entrepreneurial culture of education and training; high opportunity costs and risk management [18].
   Possible Solutions: developing social support and mentorship networks, increasing early-on education about entrepreneurship and innovation

2. **Targeting multiple stakeholders**—the healthcare industry is constantly dependent and intertwined with multiple stakeholders (patients, providers, payers, partners etc.). Therefore, it is very challenging to simple target one stakeholder without making sure that the other stakeholders also see value for the given product or service.
   Possible Solutions: create fully integrated solutions that fulfill the needs of multiple stakeholders; understand every stakeholders point of view
3. **Security and privacy**—Privacy and security are very important concerns for the healthcare industry. A recent national survey, the eighth Annual Industry Pulse Survey from Change Healthcare and HealthCare Executive Group, found that for about half of the organizations surveyed, privacy and security concerns were the leading factor on why adoption of these technologies was not more extensive [19].
   Possible Solutions: make it a priority, lots of trials
4. **Risk adverse nature of the health industry**—In order to ensure quality patient care, the health industry is naturally very risk adverse. This results in a lot of oversight and the hurdles that come with it. Entrepreneurs need to worry about satisfying the FDA, FCC, HIPPA, FTC etc.
   Possible Solutions: Consider the risks early on in product development; clinical trials and evidence go a long way
5. **Successful implementation into clinical practice**—Healthcare providers may not have all the information that they require to know whether to recommend or use a given digital health technology in a given scenario.
   Possible Solution: Communication with healthcare providers on the scenarios when to recommend or use a given digital health technology, create better knowledge exchange programs

The New Era of Medicine

We are entering the new digital era of medicine where telemedicine, virtual reality, robotics, smart phones, and other technological advancements are slowly becoming part of regular healthcare practices. Digital health technology offers a way to change many of the current issues that the U.S. healthcare system faces. However, there is an urgent need for entrepreneurs, both in the healthcare field and non-related fields, to challenge the status quo, work together and forge ahead. As discussed, digital health entrepreneurship has many benefits. It has the potential to transform the medical field by improving patient outcomes, increasing quality of health care and reducing costs (specifically long-term costs).

This book provides an overview of a large variety of topics ranging from artificial intelligence to regulatory affairs in digital health with the aim of helping digital health technologists, entrepreneurs, health care providers, investors, service providers and other stakeholders transform the healthcare system.

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Chapter 2
Real Challenge in Digital Health Entrepreneurship: Changing the Human Behavior

Mehmet Kazgan

Technology Adoption

If someone were to tell you, when Apple launched the iPhone, that you would be using that phone to call a driver or book a room in someone's house, and you would pay using the very same phone, you would've listed 100 different issues with this process. Yet, today, the iPhone or similar products are at the center of many of our daily tasks.

So what has changed? In short, human behavior has changed to adopt new technologies. It is incredible to watch the rate at which technology accelerates. Software development models have changed drastically, as everything now happens in the "cloud." We do not have old servers that need modems or loud dial up tones to connect to the internet. We also, in time, learned to adapt faster. A 5-year-old child likely knows 10 times more than we knew when we were that age. Human behavior is using the foundational brain power to quickly adapt to the technological shift.

Healthcare Side of Things

Healthcare is not following the same rate of adoption. Changing human behavior in the healthcare sector now has multiple layers, patient behavior, and clinician behavior controlled with heavy regulatory processes. Spending time in the healthcare community, it becomes clear it is not about sales but it is about convincing a series of stakeholders that your solution offers value for patient care and physician experience which should translate into outcome-based value. Hospital systems and big

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institutions have excruciatingly painful procurement processes. They typically require the solution to provide:

1. Better quality of life to the patients
2. Time savings to clinicians
3. Security and privacy around data
4. Business value and ROI fits into the care model
5. Easy implementation with almost no cost to the entity
6. Scalability
7. Integration ability into different applications and reporting systems
8. Ability to measure outcomes

However, this applies to any healthcare entity to increase interest in your solution. It starts with relationship management. Solutions need to attract enough of an audience in the healthcare system to be able to entertain your concept, your solution.

Innovation Programs

Innovation programs are one of the easiest paths of entry for startups today. However, it comes with its challenges. Now, as an entrepreneur with the best idea, you need to face the first layer of contact in healthcare institutions, which is usually classified as "Innovation Program". These days it is an overrated term in any technology space, just like "disruptive" and "entrepreneurial".

Innovation teams in health institutions are tasked with exploring and discovering solutions out there which might not be mature enough to could handle their internal challenges. If done right, innovation and discovery models are great time and money investments.

Innovation programs sometimes act like typical accelerator programs. Startup accelerators might be a very good startup route for just conceptual types of businesses. Accelerator programs invest a small amount of money and get non-diluted shares to attract promising startups. Their investment model usually is based on 10% of the startups who might exit or value bigger. Programs like this also attract vendors and advisors who are passionate about the startup community, new ideas and partnerships. If targeted right, accelerator programs offer partnerships and pilots within hospital systems which might be a great way to develop, improve and validate the product.

In some cases, accelerator program entities partner with healthcare systems, raise non-profit based funds to fund the program to find solutions for the challenges. Whether it is a startup accelerator program or it is an innovation program, the path is the same: It starts with identification of the problem. All hospital systems have multiple layers of challenges from patient intake process to discharge during the care continuum.

Problem identification It is very easy to identify problems in healthcare models and systems. If you start to explore the quality processes in departments, you will find handful of challenges.

Solution matching Once the problems are listed, innovation programs plan to either form their own innovation teams to tackle these problems to find the right fit or partner with the accelerator programs either with equity or fee-based partnership.

Impact to stakeholders Once the solution is matched, the innovation teams start to discover the impact of the solution to stakeholders in care model such as patients, care teams, disease prevention models and population health management. This is an important step as there will be cases where innovation programs will start looking into very similar startup concepts within the same cohort.

Product readiness Another layer of filtering a set of companies is to monitor the product readiness (i.e., if the startup phase is concept, development or ready to launch.) Sometimes having a ready-to-go product is not a good option as application might not be flexible enough to customize the solution to care team's needs.

Clinicians live in their electronic medical records systems throughout the day, which are very limited, and must-have tools for billing and tracking patient care. In recent years, EMR systems have come a long way; however, statistics today still tell us, clinicians are not fans of EMR systems. Today's EMR systems' history starts with a billing mechanism for clinics. EMR systems now act like decision support tools and ecosystems are now available within EMR systems. Meaning, EMR companies create Play stores for themselves where vendors can build solutions within the EMR system ecosystem. The advantage is because the marketplace platform is built within the ecosystem and has been through the approval process, it has been vetted and verified and becomes immediately available to any customer who is paying for the EMR. The downside is that the vendor has to pay 20–25% of the revenues to the EMR company. This is actually a win-win solution as the vendor can access any client within that ecosystem. In fact, EMR companies market these solutions to their subscribers as "add-ons" so that they can charge additional fees.

Scalability The solution that is offered through the innovation program should be scalable within the healthcare organization so that the ROI will be higher.

Privacy and security One of the nightmares of healthcare startups is the process to become compliant with HIPAA and other regulatory processes. Even for the healthcare facility to be credentialed with payors and specifically subspecialties also are big challenges. If there is not a great framework around how the data is handled, companies cannot even make it to the procurement step and get dropped. Privacy and security are very important for healthcare. Therefore, institutions have teams for Technology Risk Office Management. Not only should these teams be up-to-date

with what is going on with data breaches, latest security threats, but also they need to create and manage security reviews for any product implemented. For healthcare startups this is a nightmare because a simple sales cycle can turn into a 1–2 year timeframe as the security and privacy reviews could take months. If I were to give one piece of advice to digital healthcare startups, I would tell them to make sure their platform has a plan for HIPAA coverage. Otherwise, they will face a direct rejection later in the engagement game.

EMR Integration Challenges

Lots of startup pitch decks in healthcare have a common slide with similar content: barriers to entry- EMR integration challenges. In order to provide patient-oriented solution and increase patient satisfaction, companies try to build transactional platforms to communicate patient data in and out electronic medical records systems. Small clinics prefer to have light versions of EMR systems, which are relatively cheap compared to larger ones like Epic, All Scripts and similar. Even Epic lately announced that they are coming with a light version of EMR to be able to target small clinics. One way or another, talking to a highly regulated system, working on a software platform that interacts with EMR is a big challenge for any company. Because of this problem, many ex-EMR employees have been building middleware applications to create communication layers for vendors and hospital systems. Not only do they provide integration solutions, they also handle the project management part of the implementation. That way they open doors to install and engage an agent of theirs with client institution. Bigger healthcare systems tend to stay away from agents that reside within their backend systems for variety of reasons, security concerns being the biggest. We all know that patient data, or Protected Health Information (PHI), is vital for continuity of care. It gets even more complicated when patients have multiple levels and segments of data stored within different clinics. Imagine patients with lab reports, MRI's, other condition reports, and historical records for each clinic. Today, blockchain technology is another route the innovators are taking. Just like revolutionizing the bank and finance transactions, blockchain startups have started to build transactional based data verification systems which can be securely shared among relevant parties.

Hype of Blockchain and AI

Personalization of EMR systems has been around for a while. Blockchain startups has been looking for ways to create a transactional system for personal health data that can be verified by users to validate and share. Like majority of technology

followers, I would still be skeptical about Blockchain for healthcare. For many, it is already happening, and I definitely do not want to miss that train. Now missing that train might be a relative term when it comes to technology, as we always miss one of those trains because of the way that technology has branched out over the past 10 years. As a technology veteran myself, I am having hard time following what is the latest with the tech trends. There are so many updates, integrations, add-ons, plugins, apps, cloud infrastructure services, open source tools and how all these things are related to each other within their own context. For example: Imagine a healthcare technology platform that uses Blockchain methodology, AI to provide decision support to doctors where they can make more informed decisions, and these workflows could be stored and run using Docker containers, really simple file system-based models. Even now, virtual servers and application servers are operating in Docker containers and PC operating systems are almost dead. You probably see lots of laptops with "Chromebook" text on it. Interestingly enough, Citrix, which is a widely used platform for internal applications, is enabling everything to be processed somewhere in a server farm. All of these processes take place behind the scenes, that way we do not need to invest in computers and hard drives, which have become obsolete or old within months.

Today, custom computers and PC's are alive because of the gaming industry, which is already dominated by Sony, Microsoft, Nintendo. That industry, like any other, has also changed the user behavior by offering something easier, better, and more convenient. That is the key of user adoption and engagement, even within healthcare. The user for healthcare could apply to a variety of people: the patient, clinician, practice admins or healthcare executives.

Blockchain and AI already have started to make their way in to the healthcare setup. Personalized EMR with blockchain in healthcare is already getting lots of venture dollars, despite the risk. Everyone is now familiar with how things can be valued within a year or so if the right investment is made. Blockchain is getting there in many areas, and healthcare is being one. Blockchain might be a more secure method than the traditional protected health information data storage. What makes it even more interesting is that this model is a great lead to make patient data available to anyone once the patient gives a consent and approves a transaction when requested. Like every technology, there are early adopters and risk-free users. It is the healthcare norm, for startups, that all the institutions are risk free users and let someone take the lead first before the tools becomes problematic.

For AI, health industry is a gold mine, because there is a lot of dynamic data points changing and correlating with drugs, treatment models, demographics, gene sequences, etc. Once the correct methodology is followed to collect, map and index data, AI can learn and output faster. Just like any other area of technology, AI within healthcare is also progressing fast, however regulatory processes also affect AI. Today, the FDA is trying to figure out ways to clarify the grey zones related to digital health and decision support. These factors have made data a gold mine for healthcare.

EMR Integration Challenges and Hitting the Wall

Currently, bi-directional data flow with EMRs is the biggest challenge. Once the clinics and institutions establish the infrastructure and it get running, they do not want to affect their internal workflows and processes with another risky integration, and understandably so. Any digital health vendor that is trying to sell a product to a healthcare facility, needs to first pass the clinical reviews by the clinicians, and only then they move to the next step with Privacy and Security teams within IT. Many of the digital health startups fail because of this step. It is the viscous circle of validation, especially if the product requires the EMR integration for validation step that might take months. This problem arises from the innovation model of the institutions. Unfortunately, EMR companies will not help much because they do not want to do anything else that might require extra support for the product that they are already making revenues on through subscriptions. At the end of the day, EMR companies are responsible to provide full support for their product.

Government entities and non-profits have tried for years to solve this integration program by creating a common form of secure messaging framework for these types of integrations, like HL7 and FIHR. It is a completely different world out there with these messaging frameworks and the ones who are brave enough play the role of the middleware and provide integration services to vendors and health institutions. These are one of the most successful startups as it is a huge demand and there are not many of them. Usually, ex-integration engineers from the big EMR companies leave their companies and start the middleware services company to basically create the API layer which talks to the institutions EMR bi-directionally. By getting this load off of the startups' shoulders, they let startups worry about their external services and products. That way this process challenge creates new business areas and opportunities to other middleware companies. Usually, the ones who can partner early in the game with these companies can become successful as they hire the people who can handle one of the most challenging tasks in this realm.

EMR integration works in the following stages:

1. Identifying the discrete data specs that will flow into the EMR backend services
2. Building the API layer to consume calls in and out to the EMR backend services
3. Identify security and privacy vulnerabilities and resolve all of them
4. Build a secure tunnel between vendor data services and institutions' services
5. Configure EMR backend data parsing and posting processes
6. Configure the EMR front-end to provide the interface and taste of data for clinicians

Each step above requires internal resources to be allocated including the budgets. Usually, bigger healthcare institutions might come up around $500,000 internal implementation cost code. As anyone can see, in order to justify that dollar amount, every clinician or stakeholder for this shared decision-making process will be

working hard to find any weaknesses and pitfalls, and if you are not ready, opportunity is lost, especially in this challenging and competitive arena.

Typical EMR integration would require the following resources to be able to deliver this project:

- Integration Team (HL7 or FIHR Engineers): 150 h
- Information Security and Data Security Team: 30 h
- Privacy and Security Team (Legal): 20 h
- Networking Team (VPN, ETL): 30 h
- Database Administration Team: 50 h
- Configuration Analysts: 10 h
- Help Desk & IT Support: 10 h

These are the typical minimum number of hours required for an average EMR integration project. The rough part is to get this budget approved to be able to move forward for business validation as the validation process would be as follows:

1. Clinical Validation
2. Technology Validation
3. Business Validation

Supposedly, the business case and validation are the up-front sales to get #1 and #2 started.

Internet of Things

Data and accessibility are two big terms in technology today. The point is to make one more significant, and the other easier and faster. This builds the value proposition for healthcare. Fortunately, today these benefits can be offered with IoT devices. As there are more products coming to the market, accessibility is getting easier naturally. There are companies raising millions of dollars by just providing common API services to provide these devices' data to users, platforms.

A critical point just like in any statistical research, is marrying one data point to another to create more meaningful patterns. In other words, adding biometric device data to any condition and observing data across time can lead to many critical decision points that might change the healthcare system. The FDA has been trying to find ways to regulate this as it expands.

The benefits of IoT are not only limited to these. Constant reporting and monitoring without any human interaction, especially in ambulatory models can make differences between life and death. Imagine a patient experiencing heart failure, and data is already triggering a paramedic call and pushing HR data to the ambulance as well as the hospital Emergency Department. We are slowly getting there with healthcare, as long as the model is framed properly with data security and privacy and build security measures to monitor updates, should make it a faster process.

One other perspective in this space is the medical diagnostics and costs. Today, medical diagnostics is a big slice of the cake considering the medical bills in hospitals. There is no argument that the constant and frequent data connection will provide lots of cost savings. From the patient compliance angle, clinicians can monitor anything from functionality to vitals. Accuracy of the data collection is improving everyday with revolutionary designs. Once the validation end points are also added to the data collection, such as physical or virtual assessments data becomes more significant.

Improvements in this area should help with one of the biggest challenges: security and privacy. Even though, lots of guidelines are shared and being implemented, the lack of data security protocols can cause lots of security issues. Having more end points as part of this process such as patients, clinicians and payors, data sharing is essential for any of these stakeholders. However, each entity can protect and guard entry points and exit points from their side. In this triangle, the weakest point is the end-user, the patient.

As individuals, we are as informed as we can be on our rights, however, with so much going on with data around us, social networking, financing and many other distractions, data security and privacy is getting harder to track and guard. Institutions have guidelines and guarded version control systems. With teams overseeing these processes with legal, IT, security and clinical perspective, it is much safer to have control of any healthcare data.

Another big challenge with IoT is the integration between many devices. Each device today can collect different types of data. A fitness watch can track functionality, a glucometer can detect blood sugar levels, a HR monitor can somewhat accurately track HR data. For a diabetes patient with cardiovascular disease, it is essential to have all data points to be able to have a better understanding of what is going on with each condition. Adding the handful medication to the mix and the complications, problems can get even more sophisticated.

Today, many clinicians think the collected data from IoT devices are not either accurate enough or data are not significant enough to make informed decisions. Moving forward, it is obvious that the accuracy of the IoT devices will increase, data would get validated with outcomes, AI will take over to process data quicker and more intelligently. That is the pattern as we see it.

User Engagement

As the technology gets smarter, we need to find ways to make users more engaged with the product. Investors for startups question the user engagement and retention heavily. Customer experience becomes a serious task for any technology company who is providing continuous services to their users via mobile platforms or applications. Obviously, clinicians and providers as customers for digital health question the very same thing. Despite most people thinking healthcare is more challenging than any other industry when it comes to user engagement, it actually might be an

advantage as it is related to human lives and conditions. Typically, one would expect that patients would be engaged to their digital health tools more than any other standard user profile, because non-compliance would make their life worse. However, human behavior tends to get distracted from regular patterns and required tasks easily, even though it could have negative impacts on their lives. It is about a choice they make. Smoking would be a very good example. How many of the smokers you know that it is not healthy for them to smoke, but they still do for various reasons? With the same token, digital health startups need to convince their users, whether they are providers or patients, to be engaged to the tools they offer to be able to present value and ROI. That itself, is the biggest challenge of all. We all are looking for answers in fact, not to provide the best product, but to be able to adapt human behavior to benefit our own health.

Chapter 3
Driving Outcomes-Digital Health Business Models

Jeffrey M. Nathanson

Healthcare-A Complex System

The U.S. healthcare system is broken. Year after year, healthcare costs in the United States have increased while our health outcomes are worse than most industrialized nations on the planet. We spend close to $4 trillion annually, surpassing $10,000 per person in 2016, accounting for over 17.8% of our National Gross Domestic Product (GDP). In 2017, another 6% cost increase was recorded [1].

Employers originally provided healthcare to attract and retain employees-enhancing their productivity and health as a benefit for their families. As a result, the consumers of healthcare services did not fully pay for it. Without cost considerations, consumers used their health services. Concurrently, providers of health services were able to sell them at reasonable margins. We have now reached a tipping point. Cost increases are no longer sustainable for consumers, employers, payers, providers or healthcare delivery systems [2].

The cost containment imperative has been well recognized by all engaged healthcare players for the last several years including state and federal government. The National Academy of Sciences, Institute of Medicine in 2012 recommended adopting new efficiency measures and information technologies to reduce costs by upwards to one third [3]. A few years earlier the Institute for Healthcare Improvement developed and promoted the ***"triple aim"-high patient satisfaction, quality; improved health outcomes and reduced costs*** as an assessment tool to measure the value of new health interventions [4].

Electronic Health Records (EHRs) previously funded by the 2009 HITECH Act were a parallel attempt to improve health delivery efficiency and lower costs. Actual use, though, added new physician administrative burdens and dramatically decreased

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provider satisfaction. Physicians now are retiring at a rapid pace. The greying provider workforce, private practice consolidation throughout the industry and decreased patient interaction while using these electronic tools has revealed ***a fourth required aim in addition to the other three-the quadruple aim- provider satisfaction.***

With shrinking profit margins, employers are no longer willing to support increasing employee health plan costs. Just less than half of our population is covered under employer sponsored health insurance, and this percentage is declining. More employers are considering providing employees fixed yearly health stipends to allow them to purchase their own benefit packages. Consumers, whether part of an employee health plan or an individual purchased plan are challenged with greater responsibility for their health and payment for any cost increases. For the first time, consumers, the users of health services, are responsible and increasingly engaged with how they use health services as they become patients.

Study after study has determined, regardless of whether the costs are insurance premiums, copayments, deductibles for employer or direct consumer purchased health plans or self-pay, consumers are shouldering increased costs. All varieties of "health system" components are shifting this increased healthcare cost burden and the responsibility for health to the patient [2, 5, 6]. It has been difficult to gain the benefit of behavioral economics when someone else pays for the costs of healthcare, like employers or insurance companies. A change to the payment formula is needed. Is opportunity hiding?

Most healthcare experts acknowledge unhealthy behaviors are healthcare cost drivers for upwards to 80% of all healthcare costs from a variety of chronic medical conditions like diabetes, hypertension, cardiovascular disease and the impact of smoking. Considering the variety of healthcare service components requiring increased participation from consumers, the patients are key targets for increased engagement. A key question remains, are consumers willing to pay for the value of maintaining their health? Are they willing to have a more active role in maintaining healthy behaviors as the data points to greater costs for unhealthy behaviors?

Entrenched healthcare market incumbents have no incentive to disrupt the system. They are well aware of the market requirements for cost reduction. Without incentives, though, these current "system" members have no reason to help "decrease the cost curve." Will a passionate digital health entrepreneur find a solution that delivers the desired ***quadruple aim***?

This is a unique time for healthcare solutions. Market indicators point to an increased need for new approaches that deliver the ***quadruple aim***. Digital interventions have clearly impacted other industries, through cost reductions, productivity enhancements and efficiency improvements. Mobile phones, texting, facetiming, social media and online gaming have all seen significant ubiquitous adoption and engagement. We have seen the incredible profitability and consumer engagement online retail has developed with consumer goods and now medical and pharmaceutical supplies. It is clear similar gains can be made in healthcare.

These same processes and systems might positively impact the delivery of healthcare services in a sustainable fashion. Digital entrepreneurs have significant

opportunities to intervene with demonstrable cost efficiency, high consumer satisfaction; improved quality and improved health outcomes by continuing to do what they do now, in addition to more data analysis informing decisions.

Healthcare Is Ripe for Disruption. It Is Hard, Not Impossible. Yet, Where Do We Start?

This is a unique time for entrepreneurs and their startups. The process for developing new opportunities has never been more sophisticated, outcome driven or methodological. This directly aligns with the requirements for healthcare in adopting new products.

Generally, the costs for starting a business have decreased, aided by digital products and systems. With more and more startups now, there is increased competition for financing and market share. Speed to market and lower customer acquisition costs are all key elements for startup competitive advantage. There are now tested tools and systems to better target the "pain" of potential customers and determine if a proposed solution has traction. There are new methodologies to assess customer personas and analyze the specific sub tasks and processes needing improvement within a system like healthcare. If we use the National Academy of Sciences study as a benchmark there is a close to a trillion dollars of wasted expenditures in healthcare. Will we ever see the Amazon, or Uber of Healthcare disrupt the delivery of health? Will the business combination of Amazon, Berkshire Hathaway and J.P. Morgan, focused on transforming healthcare for their employees using their relentless focus on consumer experience, create new solutions for the greater market? To be sure, whoever enters the digital health marketplace will use many of the tools and processes highlighted below.

Gaining Marketplace Insight

Steve Blank and Eric Ries introduced a new standard process for bringing entrepreneurial opportunities to market [7–10]. First, they recognized startups were not miniature enterprises. Their shared experience and insight as serial entrepreneurs revealed startups were not really, yet in business. They recognized from their own startup failure and success experience, that most-startups didn't always have a clear understanding of true market needs or wants before they spent all of their investment funds. Startups, they recognized, were in fact unique search organizations seeking a repeatable and scalable business model. They began to work with Alexander Osterwalder on a single page business model template. See Fig. 3.1, below.

They urged entrepreneurs and eventually investors to forget business plans. They realized that business plans made assumptions about customers that were not correct. Instead they recognized, tested and demonstrated a methodology that

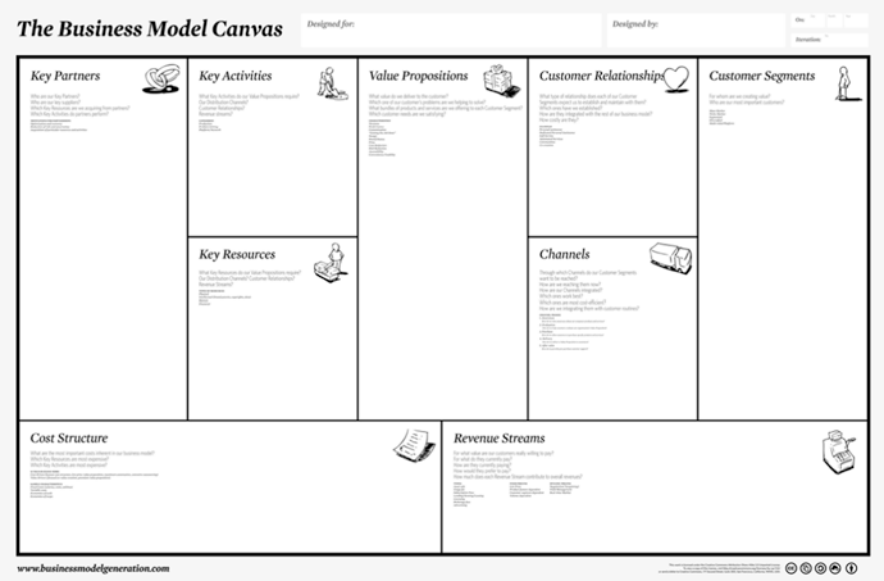

Fig. 3.1 The business model canvas. Creative Commons Attribution-Share Alike 3.0 Unported License. To view a copy of this license, visit http://creativecommons.org/licenses/by-sa/3.0/ or send a letter to Creative Commons, 171 Second Street, Suite 300, San Francisco, California, 94105, USA

increases speed to market focusing on delivering paying customers. They coined the term "lean startup" methodology with shortened, iterative product development cycles.

Their goal was to quickly discover and determine market insights regarding the "pain" a prospective customer experiences, first through customer discovery and then a process called customer development. The processes enhanced an entrepreneur's recognition and determination of the (customer's) market pain, the depth of the pain and their willingness to resolve the pain through a purchased or created solution. The methodology includes a design process, hypothesizing a solution, testing the hypotheses, iterating toward the development of an initial product offering and quantifiably testing the startup solution with prospective customers. The process focused on iterative product releases validated through data driven learning continuously improving the product/solution offering.

Their process demonstrated finding market interest was best done through a minimum viable product (MVP) a far more agile and effective iterative approach than building a costly prototype to beta test a product. It is a way to fail fast and learn. They urged entrepreneurs to "get out of the building" to speak to prospective customers. Their efforts focused on finding "**product/market fit**" [9]. Entrepreneurs and investors have grown to see product/market fit as the match between the customer's needs and the solution the entrepreneur's company is providing.

- Product/market fit is the sought-after prize for early stage startups. When there is alignment with customer needs and your solution, customers are so eager to have your product or service, they jump at the chance to open their wallets wide to use what you've developed.
- Product/market fit is the thing entrepreneurs work so very hard to identify *after* they have created their venture, developed a hypothesis and have begun to "get out of the building" to test their proposed solution with real customers.
- Product/market fit is the magic for digital health startups as well, like Omada, Propeller Health, Cirrus MD, My Strength, My Rounding, Burst IQ, Concert Health and Apostrophe Health are beginning to realize.

Blank and Ries shared the Lean Startup Methodology through multiple distribution channels-universities, federal agencies, venture and angel investors, and business accelerators. Steve Blank developed *iCorps* in 2011 with funding from the U.S. National Science Foundation (NSF) to train scientists and engineers in how to commercialize their discoveries? Their process now is a dominant method for starting and building a company and has spawned a cottage industry of lean startup books, workshops and websites.

Gaining product/market fit testing within the digital health industry is really no different. There are additional elements determining fit in addition to the standard consumer requirements. There is a universal dependency on mobile devices like mobile phones either flip (feature) phones or smartphones or tablets. There are heightened expectation levels for product features including user interfaces or the quality of user experience, the UI/UX. Healthcare purchase decisions also, have additional elements for purchase and adoption-does it work and is it HIPAA compliant? Does it get the job done, particularly in clinical settings? Does it deliver the ***quadruple aim*** and can the company deliver those results and document validated outcomes?

We are experiencing the next wave of electronic health records use. We are collecting better and better data to help inform health decisions. We are even seeing the international collection of standards for health outcome metrics. The International Consortium for Health Outcome Measurements, (ICHOM), has created a set of care standards for various conditions and the expected data driven outcomes that matter to patients. All the while they promote tracking the costs per institution required to achieve those expected outcomes. The leaders and founders are the Harvard Business School, Boston Consulting Group and the Karolinska Institutet. They formed after the publishing of Michael Porter's Book that outlined the argument for using health outcomes data to redefine the nature of competition in health care [11]. Might we see the compensation formula change to one that compensates for value instead of volume?

Digital health provides a key enhancement for the increased focus on data collection and data analysis. Huge challenges persist with health data liquidity and the interoperability of health data systems. We are still challenged to secure data and ensure it is tied to a specific identity.

As the digital health market matures there are twinkles of bright shining stars delivering solutions. There is an increased need to go further, to understand the key elements needed to seize more substantial entrepreneurial opportunity in healthcare.

The insights from Blank and Ries added to a product development process that evolved around Stanford University. In the early 1990s a new company IDEO, was formed by a group of designers and product development professionals bringing a key ingredient to many new products developed in Silicon Valley. Design thinking was created, focused on the needs of the customer. A new process for rapid product development and a new cottage industry was created, filled with whiteboards, individual brainstorming, sticky pads, dot voting and filling out templated "artifacts".

With their early success, the IDEO founders brought the idea of a customer centered design training institute to Stanford University. The non-degree oriented Stanford d. School was formed. Customer insight gained from customer interviews informed the customer centered "design thinking" practiced in the new design efforts of IDEO the Stanford d. School and their minions.

New systems for product development propagated within the Silicon Valley area surrounding the Stanford campus. One of the area spin-out corporate unicorns was Google. The founders, Larry Page and Sergey Brin fostered the development of additional internal design and product development processes, they called them design sprints. Their goal was to build and test prototypes for a product in just five days. They too wanted to fail quickly. They focused on small teams challenged to rapidly progress from problem to tested solution using a proven repeatable step by step process. They cleared participating staff schedules for an entire week to determine how customers react to a product design prior to the investment of time and expense for a completed product.

Testing the process within various Google divisions, Jake Knapp of Google Ventures wrote a step by step cookbook for these sprints [12]. Over the five days in the sprint process each day has a unique focus on one of five key steps **Map, Sketch, Decide, Prototype** and **Test**.

Customer Development

Accurately determining customer pain proved to be challenging though. Sometimes the customers true pain was elusive to the assessment process. How could an entrepreneur ensure they learned candidly from prospective customers their truthful feelings about a product hypothesis or MVP? This became known as the "mom test"-recognizing a mother would often tell you what you wanted to hear rather than a candid, truthful review of your product idea? [13]

Understanding the customer assessment process became a passion for Tony Ulwick, the key product manager for the IBM PC Jr. a computer system-developed and launched with great market acclaim only to be ultimately deemed a market failure, as it missed solving the markets' key needs. Ulwick created the "job to be done" theory to decrease the customer's reporting bias in describing their pain [14].

Together with Professor Clayton Christensen, Ulwick postulated innovation was borne on understanding the "job to be done" methodology to discover ways to improve systems and processes. Ulwick hypothesized the assessment of the "job to be done" would uncover key insight within a market segment. Without this prospective, customer interviews he postulated, were little more than hopeful wandering with unsystematic inquiry that may occasionally turn up interesting tidbits of information but rarely uncover the best ideas or an exhaustive set of opportunities for growth. To aid the process, he developed an outcome driven innovation process.

Ulwick developed a simple system called "job mapping" breaking down the tasks the customer wants completed into a series of discrete process steps. The process provided a complete view of the constraints or points of friction a customer might want help in overcoming.

With this process and the insight gained, entrepreneurs can assess the features and benefits most significant and helpful to the customer. Ulwick's process provides a comprehensive framework with identified metrics customer themselves use to measure success in executing a task. *This approach would be most appropriate to map the jobs to be done in certain healthcare processes and condition management settings.*

Business Model Innovation

As mentioned above, concurrent and connected with Blank and Ries's efforts with Lean Startup methodology, Alexander Osterwalder [15] is credited with leading a team effort to invent, describe, design, challenge and pivot a business model through the Business Model Canvas. Osterwalder and his team recognized that a business model could be described in a single page broken into nine components (see Fig. 3.1, www.businessmodelgeneration.com).

Ash Maurya, another entrepreneur and author in pursuit of even greater speed in product development, created another enhanced, yet compatible methodology for raising the odds for success-the Lean Startup [16].

Through insight from his predecessors in Lean Startup methodology and customer development processes, Maurya determined that Osterwalder's Business Model Canvas might be more appropriate for the enterprise than the startup. Following Ulwick and Christiansen, he determined that to better understand the customer value creation process, an entrepreneur must better understand customer problems. He developed a modified process to map those problems.

Maurya created a new template to change the emphasis of the business model canvas to include the segments of problem, solution and unfair advantage (see Fig. 3.2).

These same processes and methodologies can significantly aid a digital health entrepreneur in finding opportunities within the Health marketplace. We have indications of where opportunity may reside in terms of cost reduction strategies. Recent studies have found that the costs for major procedures continue to escalate.

Fig. 3.2 Lean canvas. To view a copy of this license, visit http://creativecommons.org/licenses/by-sa/3.0/ or send a letter to Creative Commons, 171 Second Street, Suite 300, San Francisco, California, 94105, USA

The key medical specialties with the highest out-of-pocket cost estimates for patients, include: Orthopedics Plastic Surgery, Urology and Neurology all of which are above the $1,000 average across all specialties in 2017. These represent problems. Are there business opportunities present in delivering care through digital means that will cut the cost of delivering care into these segments? To be sure.

Throughout the country and around the world there are robust biomedical innovation networks and trade association groups in which an entrepreneur can gain insight on the healthcare industry actors and their relationships. Although the networks exist, the decision makers, the influencers are not always available to make a connection. As an entrepreneur searches for opportunity and product market fit there are several rabbit holes one might fall into as one searches.

Healthcare-A Complex Adaptive System

Understanding the Healthcare (Health) marketplace landscape is difficult, though not impossible. Healthcare is a complex adaptive system (CAS). With its unique properties, it generates wicked problems like childhood obesity, toxic stress, the

need for integrated mental health, data liquidity, affordable housing and other social determinants. Government has tried to understand the system and solve some of the wicked problems. We have learned though, it is complicated. Government sets policy though will not, by itself, solve these wicked problems. Large industry may recognize these opportunities, but will they disrupt themselves? Will they strive for lower costs while attempting to maintain profit? Research institutions will not bring solutions to these problems to market. A new perspective is required. This is a unique time for entrepreneurs.

For an entrepreneur seeking opportunity within the system, understanding the complex system of health is required. What are the components of the complex adaptive system? What are the wicked problems? How are these wicked problems generated?

Complex Adaptive Systems (CAS) are dynamic and non-linear. There are a wide variety of elements in the system. There are independent agents each with their own goals and behaviors. These behaviors are likely to change, evolve and conflict. One agent's action, process or function can change the context for the others. The agents respond in unpredictable ways, either innovative, creative or in error. They are part of a living system. The whole is not the sum of the parts. A key trait is they lack a single system point of control. There is no single actor in charge. The individual components are not always linked in a system. Sometimes, the components are self-organizing into a collection of individual strands of value generation delivering health with the constraints of the rest of the system. The CAS of healthcare as a result is unpredictable. Throughout the CAS, various segments create value throughout the created supply chain. Yet, each of the components are usually dependent on health and cost outcomes based on other individual component performances rather than operating as an integrated whole.

As a result, wicked problems arise and are entrenched in complex adaptive systems. A problem doesn't achieve wicked status just because it's large or really difficult though. Building a skyscraper is a huge and complicated problem. Deriving the field equations for Einstein's Theory of General Relativity is extraordinarily hard to do. But neither of these problems are wicked problems. "Wickedness" is not merely a matter of degree of difficulty. First outlined by two University of California, Berkeley professors in 1973, wicked problems elude description and defy solution [17]. Wicked problems can be in healthcare, water, food, energy and many other systems [18]. Wicked problems stem from numerous causes, spread in every direction and tend to become entangled with other wicked problems. What's worse, conventional approaches usually just make things worse. They can be a societal scourge, such as poverty, or a seemingly more specific problem, like health data liquidity or Alzheimer's disease.

Discovering Opportunity Within Wicked Problems

How would an entrepreneur start? Where would you begin to address this unique need for disruption of an entire huge health system while gaining a defensible market opportunity? Entrepreneurs have the potential to turn wicked problems into great opportunities. yet, it often takes process, methodology and focus.

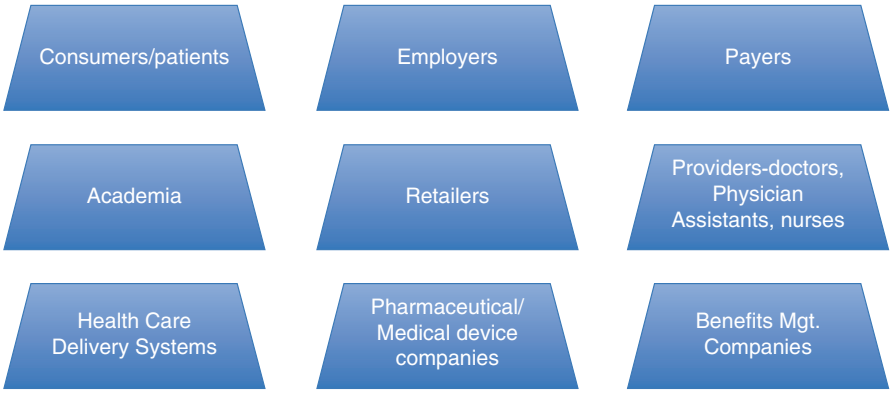

Fig. 3.3 Mapping health

Gaining insight on the components by mapping the complex adaptive system and the wicked problems are key steps in the process. How would an entrepreneur whiteboard map the system? What are the associations between actors? What are the constellation of actors and their various interactions? What are the various enablers or inhibitors for each of the segments? Where are the various points of greatest pain or friction that customers wish to resolve?

While mapping the healthcare CAS, the entrepreneur must identify the key stakeholders (see Fig. 3.3). Who are the customers experiencing the pain and how will they pay for the solution? Are there feedback loops that influence the actors? Once the CAS components are mapped, there are specific tools, and processes, and powerful communities needed to turn the world's wicked problems into the world's biggest opportunities for impact and ROI. A systems approach to solutions is necessary.

Mapping Wicked Problems

To discover hidden market opportunities, entrepreneurs would be well served to map any wicked problems that have spun out from the larger complex system. Andrew Nelson and Jeff Leitner have developed a problem mapping process called Innovation Dynamics to identify the various components of difficult to solve problems [19]. They also start with mapping the Actors. Their process includes the assessment of the following components and functions.

Actors—people, groups, and institutions that play a role in the problem.

History—collection of stories people tell—true and untrue—about why a problem exists or persists.

Future—collection of possible outcomes for the problem, will evolve or resolve, likely and unlikely.

Limits—formal rules and physical constraints that influence a problem.

Configuration—sets of categories or labels people use to make sense of a problem.

Parthood—the role a problem plays as a part of other problems.

Start with the Problem

If we compare the various highlighted processes, wicked problems will most likely be more difficult to analyze and map than individual jobs to be done. They tend to require a systematic approach to finding a path to solution, ROI and impact-delivering the *quadruple aim*.

Tom Higley another successful serial entrepreneur and angel investor founded 10.10.10. The organization is built on the premise that entrepreneurs can change the world for the better by focusing exclusively on turning wicked problems into entrepreneurial opportunities.

Higley addresses the problem of the time, talent and capital that goes to waste pursuing surprisingly mundane businesses and business models even as substantial problems that represent enormous market opportunity are systematically ignored. To be effective, Higley argues that startup founders and teams need to gain deeper understanding of the requirements for solutions and potential value creation they might develop and control. With his team, Higley developed a 10 day program for 10 recruited and vetted serial entrepreneurs, to unpack 10 wicked problems in a vertical segment by developing market based solutions.

Higley advises startup founders begin with a problem they care about. He suggests entrepreneurs start with a customer they care about with a problem they care about. Higley recently tweeted all customers have problems, all problems have solutions. Yet, not all solutions have problems, and not all problems have customers (Higley 2017) [20–22]. This may become a mantra for digital health entrepreneurs.

Finding market based opportunities in wicked problems requires tighter focus on understanding the components and influencers within the problem to be solved. This requires a higher-level macro analysis of the "job to be done". Both Higley and Maurya point out entrepreneurs too often fall in love with their solution [23]. The processes they have developed challenge entrepreneurs to start, with a specific problem or wicked problem in mind [24, 25].

Higley describes wicked problems as doors guarding a treasure with both monetary benefit and social impact. Higley posted the challenge and opportunity to love the wicked problem or love the customer experiencing it [26].

If as Higley suggests, wicked problems are the doors, then how does an entrepreneur get hold of the right key? How does an entrepreneur choose a door behind which tremendous opportunity may be found and then create, develop, find, or buy the key—perhaps the dynamite—that will open the lock? How do they ensure they take advantage of what lies behind? [20].

The life of a startup entrepreneur is difficult. It is a lifestyle of pioneers, not of settlers. Startup entrepreneurs usually don't follow easy, existing paths. They think

differently. When you are a startup entrepreneur in a market segment emanating from a complex adaptive system, the doors of market opportunity are more tightly protected with significant fortifications. For the digital health entrepreneur, these protections include long sales cycles and validated health outcomes or process improvements required for positive purchase decisions. Entrepreneurs trying to find opportunity within complex adaptive systems often find more adversity, more hurdles, more rejection, slower time to full adoption as well as product market fit.

Startup entrepreneurship is not for everyone. It requires deep introspection to ensure one has what it takes to be successful. Higley and 10.10.10 focus their ten-day program and beyond on a process they call Founder Due Diligence and Founder/Opportunity fit [27].

Higley suggests when an entrepreneur puts her heart into a new venture she is making an investment. Just like a financial investor she needs tools to help her make good decisions. **Unlike financial investors, most entrepreneurs only get to choose a few doors they'd like to open during their career—so picking the right door (and key) matters. A lot.**

At each phase, an entrepreneur explores and gathers information to decide where to invest more time and energy in an opportunity, and what to leave aside. 10.10.10 presents this diligence or decision-process as a critical tool for deciding whether to invest in an opportunity. They believe there are large risks if you enter too early and if you realize too late the opportunity wasn't actually aligned with your passion or there was a hidden deal breaker. Until you are fully engaged, most startup entrepreneurs pursue multiple opportunities in tandem for far too long resulting in waffling or being spread too thin.

Higley, and his 10.10.10 team are focused on *tackling the world's wicked problems through public education and engagement that inspires entrepreneurs to action.* 10.10.10 envisions a world where impact entrepreneurs and their ventures are a ubiquitous and indispensable force for good solving wicked problems. The 10.10.10 programs help experienced entrepreneurs discover the best and biggest opportunities for new impact-driven businesses that tackle wicked problems in health, water, infrastructure, education and beyond. They work with existing entrepreneurial ecosystems to enhance their focus on targeted wicked problems for participating entrepreneurs (Prospective CEOs) in a community of domain experts (Validators), surrounding them with a temporary startup team (Ninjas), and leading them through a set of design sprints all the while delivering on their "founder due diligence" process to identify a viable business concept and arrive at "founder/opportunity fit" [27, 28].

The Bowtie

10.10.10 uses a bowtie image to represent its role in founder startup activities [29, 30] (see Fig. 3.4). The knot in the bowtie represents that moment when a new venture is created. 10.10.10 developed a founder due diligence and founder

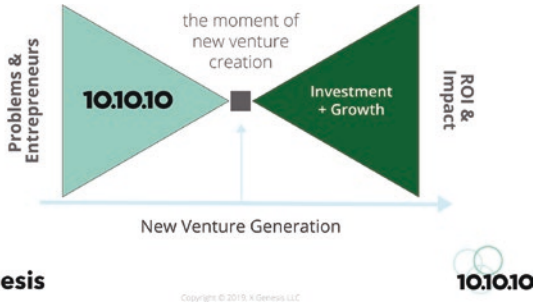

Fig. 3.4 The startup bowtie. By Thomas K. Higley, CEO of 10.10.10 and X Genesis

opportunity fit process that might be understood as living on the left side of the bowtie. Most other startup resources highlighted here and those of entrepreneur networks, accelerators, angel, seed, and VC resources are all focused on the right side.

The Founder Due Diligence and Founder Opportunity Fit tools developed by X Genesis for the 10.10.10 programs utilize customized design sprints to aid entrepreneurs in recognizing and generating companies that discover opportunities hidden within wicked problems. Their process aids entrepreneurs map complex adaptive systems and the wicked problems that are developed within them. As the other startup design processes have matured and developed, 10.10.10's tools integrate with, and focus the previously highlighted design sprint methodologies combined in a unique way (see Fig. 3.5).

Listen, Learn, Leverage, Launch

With their focus on wicked problems, the first phase of the 10.10.10 process is understanding the problems [31]. With guidance from knowledgeable domain experts (Validators), insights and opportunities are identified. This first step involves careful **LISTEN**ing and exploration of the problems, system, and stakeholders. This is followed by a phase of interactive **LEARN**ing and collaboration during which potential solutions are generated and tested. The entrepreneur develops a business concept that **LEVERAGE**s sources of "unfair advantage" in the form of technology, intellectual property, changes to policy or regulation, discoveries, trends, and networks. Next the focus shifts toward the team, go-to-market strategy, capital requirements, and investors. Only after these elements have been carefully traversed and linked together is a new venture **LAUNCH**ed.

Together these four phases comprise a founder due-diligence and opportunity generation process that begins with wicked problems and ends with the creation of a new venture. You may notice from Fig. 3.6 below at the end of that funnel 10.10.10 expects to inspire prospective CEOs in the process with a new understanding about how to turn a wicked problem into a "validated venture."

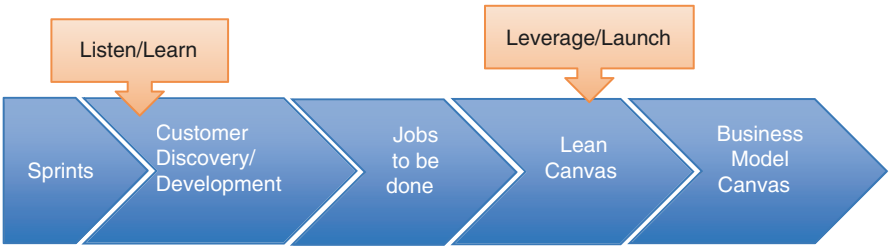

Fig. 3.5 10.10.10 opportunity generation process

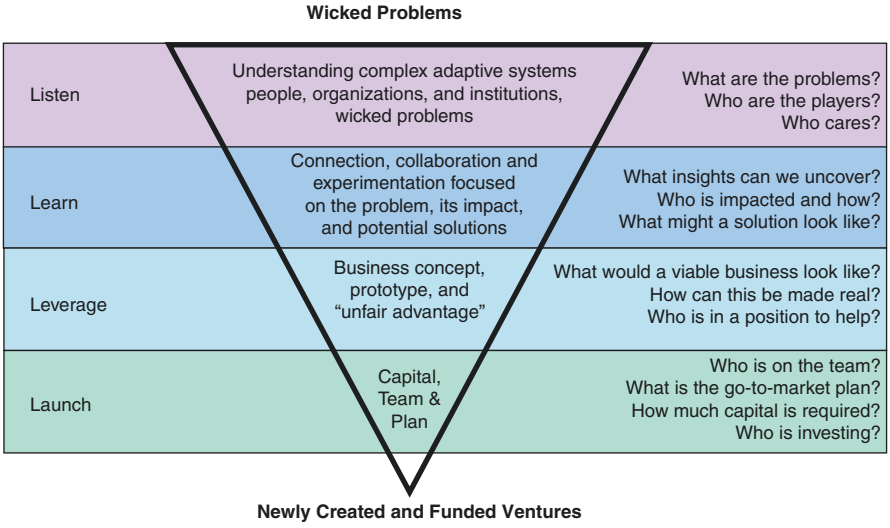

Fig. 3.6 The X Genesis Listen, Learn, Leverage, Launch funnel. By Thomas K. Higley, CEO of 10.10.10 and X Genesis

Unpacking the Funnel

Each phase in the 10.10.10 Listen, Learn, Leverage and Launch process outlined above is explored and broken down further into several additional process steps during a 10-day program. Each step supports those that come after it, and utilizes the outputs of those that come before. Taken together, they constitute the Why, Who, How and What of a startup, and offer a complete process for new venture generation.

- A proprietary **Problem-Solution Sprint** is designed and held to help Prospective CEOs decide what opportunity and solution they want to pursue. The primary deliverable from the problem-solution sprint is a **viable solution concept** based on an identified real customer problem. This sprint includes frequent interaction with Validators, stakeholder, customer interviews, and rapid ideation exercises.
- The **Springboard Sprint** helps Prospective CEOs decide what business they want to build. The primary focus is a **viable business concept** built around a novel solution. Initially the entrepreneurs generate and vet potential product offerings, business models and pricing models, as well as understand potential sources of unfair advantage and gather support from the 10.10.10 community and her own networks. The sprint includes fast and frequent use of the Lean canvas, continued interactions with Validators, and analysis of risk and the competitive landscape.
- The **Product Sprint** is designed to help Prospective CEOs decide what product should be built. The primary deliverable of the product sprint is a **mockup or prototype** that demonstrates the product concept and can act as the starting point for future product iterations. The Prospective CEO's goal is to choose a clear product direction based on previous learnings and to make it as real as possible within a short period of time. The sprint includes a series of ideation and direction-setting exercises to develop a basic user experience flow, as well as tools for user testing [32].

From Product/Market to Founder/Opportunity

Throughout the 10.10.10 program Founder Opportunity Fit is emphasized as significantly as product/market fit. This is the match between the founder, and a particular opportunity that may become their next new venture. Unless there is passion for your customer and their problem you may have difficulty in overcoming the steps to successfully launch a solution to a wicked problem. 10.10.10 has had several Prospective CEOs develop wonderful market based products only to recognize the Founder Opportunity Fit was not there.

Founder Opportunity Fit is similar to the focus area, thesis or "theme" that helps an angel or venture investor make decisions. The most successful investors exclude opportunities (even those that may otherwise be viable) that are inconsistent with the investors' investment thesis, passion and values.

Too many of the world's capable entrepreneurs start ventures without understanding Founder Opportunity Fit (or the lack thereof). The result may be the loss of months or years of time, capital and focus. When you invest your life in one thing, you are missing out on other opportunities, and any one of those things might be a better fit for you.

From the four 10.10.10 programs focused on health so far, several new companies are leading the charge in challenging wicked problems and gaining market traction. Some examples include

Burst IQ (Health 2015) BurstIQ, focused on patient health data security. They are now one of the leading enterprise-level block chain healthcare data companies. They have raised a significant amount of early stage capital and they are generating revenue. They were recently selected by Red Herring Magazine as one of the Top 100 North America Award recognized as one of the most exciting and innovative private technology companies.

Apostrophe Health (Health 2015): Focused on making health more manageable and easier to navigate. Apostrophe Health's SaSS platform is live with 1,800 members (school employees on the eastern plains of Colorado), and they're making a difference. They provide health concierge services for the employees of self-insured employers, improving health outcomes and reducing costs.

Concert Health (Health 2016): Integrating behavioral health care by helping physicians integrate screening, therapy, and psychiatric consultations into their practice and adopt Medicare's new Collaborative Care Management (CoCM) program in two Arizona Primary Care Groups, they are ramping up to launch with a 50 physician group in Southern California. In addition to raising a pre-seed round this winter, they were also recently published in MGMA (Medical Group Management Association) Connections magazine and delivered an address at American Nephrology Nursing Associations annual conference.

Recalibrate Solutions (Health 2017): Recalibrate Solutions is a medical-device company currently raising seed-stage capital to develop a rapid, disposable, low-cost, test to identify and monitor toxic stress, and the efficacy of intervention-therapies. They are in the midst of raising seed round of financing.

These highlighted design processes have been helpful for entrepreneurs tackling wicked problems and are potential models for digital health entrepreneurs. Each step aids the founding entrepreneur in the development of their insight into the "pain" of their prospective customer and the requirements of the users of their proposed products. Each step validates with data, the requirements for a customer to buy their solution. Each step allows them to test, fail fast and iterate on the learnings they have received in the previous steps along the way. Whether you are trying to solve a customer's pain in a process improvement or if you are trying to solve the wicked problem of health data liquidity and interoperability, using the processes identified in this chapter will aid in your founder due diligence.

If investment in an entrepreneurial segment is an indication of opportunity, digital health continues to acquire funding at record pace for a new market segment. Year over year investment funding continues to increase. This funding growth shows a maturing market and stability. Investors continue to see value created and product adoption.

The most successful digital health market leaders are built on evidence-based product validation. The current market leaders demonstrated key validation milestones. One leader, Omada Health, has 10 peer-reviewed studies demonstrating their product efficacy. They also demonstrated to the U.S. Centers for Disease

Control how their virtual program could deliver the diabetes prevention program cost effectively with higher outcomes. The company showed how their program was delivered digitally, privately and securely. They also showed how the long-standing program could be scaled cost effectively.

There are many new entrants in the field. We have seen the entry of Apple, Google, Salesforce and Microsoft. We are still waiting to learn more about the earthshaking Amazon, Berkshire Hathaway, JP Morgan initiative. The announcement of their new CEO Atul Gawande, the famous physician, author and healthcare thought leader has captured headlines. We expect that despite their size and product development expertise they will all use similar variations of the design methodologies to bring their products to market. Yet, will they truly disrupt healthcare? Or, is this a great time a passionate aligned entrepreneur?

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Chapter 4
Innovating with Health System Partners: Value Propositions and Business Models

Susan L. Moore

Health Care Innovation and Digital Health Opportunity

In 2001, as part of its historic in-depth analysis of health care in the United States, the National Academy of Medicine (NAM) found that information technology (IT) had the potential to promote the provision of health care that achieved the six key aims of being safe, effective, patient-centered, timely, efficient, and equitable [1]. In its report, the committee noted the potential for health IT to play a critical role in the transformation of the health system. Over the decade and a half since, technological advances in health care and otherwise have occurred at an extraordinary pace, resulting in a "digital revolution" as new, previously unimagined systems and solutions have come into being, together with the ability to capture near-unfathomable volumes of data that promise hidden answers to all of health care's problems [2].

A clear trend has emerged over the last few years with regard to the use of existing and emerging digital health technologies to identify and implement novel solutions, augmented by a perceived need for collaboration among industry partners, technology developers, health care leaders, clinicians, patients, community members, and public health practitioners. The passage of the 21st Century Cures Act reflected additional interest in this direction at the federal level by providing $4.8 billion to the National Institutes of Health over 10 years, dedicated to multiple initiatives that drive innovation in digital health [3]. Increasingly, these technologies are miniaturized and mobilized, taking advantage of ever-increasing computing power contained in smaller and smaller devices [4]. The pace of global market growth in mobile digital health alone clearly demonstrates the extensive landscape

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of opportunity in this sector, with a 47.6% compound annual growth rate and a projected market value of up to $59 billion by 2020 [5].

In 2015, the *New England Journal of Medicine* (NEJM) Group announced a new resource, NEJM Catalyst, targeted toward clinical decision makers and health care leaders who seek to drive transformative change in health care through innovation [6]. In a business context, the concept of innovation represents not only the new idea itself, but the application of the new idea as a solution to an existing problem or unmet need [7]. Considered from this perspective, innovation encompasses a range of activities designed to discover, develop, and improve solutions, processes, operations, functions, and outcomes. As a result, it seems only natural that the health care industry, with its commitment to continually improving aspects of health care such as quality, value, delivery, and overall population health, would be a welcoming environment for innovation, even disruptive innovation.

In a recent survey of health care leaders, Catalyst reported that hospitals and health systems, health care information technology (IT), and primary care were identified as the top three areas most in need of innovation [8]. Moreover, respondents overwhelmingly felt that not only was innovation essential to improve health care, but that the principal drivers of innovative change would come from outside health care organizations [8]. Health care executives, administrators, and clinicians all believed that crucial change for hospitals and delivery systems overall and in health IT in particular would come from focused startups rather than internal experts or existing organizations, which is good news for digital health entrepreneurs.

However, despite identified need and express willingness to innovate, health care is a complex adaptive system [9–11]. Such systems are non-linear, dynamic, and inherently chaotic, exhibiting emergent behaviors and unanticipated consequences [10]. As a result, innovation in one area of health care can cause unexpected problems in other areas. In *The Digital Doctor*, Robert Wachter describes in detail how a series of perfectly logical, automated, error-checked steps within a state-of-the-art computerized prescription order-and-dispensing system resulted in a 16-year-old patient being given an overdose of medication that was *39 times higher* than what he should have gotten [12]. Awareness of such risk leads to notable reluctance among health system stakeholders when it comes to adopting unproven solutions.

Resistance to change is also a factor that affects innovation adoption, driven in part by the complex adaptive system, but also by innovation fatigue among end users [13]. A 2016 study in the Annals of Internal Medicine found that for each hour health care providers spent providing direct clinical care to patients, they spent an additional 2–3 hours performing administrative work—the majority of it due to required interactions with electronic health records and similar systems [14]. No matter how impressive the technology, it's perhaps quite understandable why providers might be reluctant to further burden themselves without good reason. In short, without substantial evidence of impact and worth, innovative digital health solutions may never be adopted at all.

Making the Case for Digital Health Solutions: The Value Proposition

One way for digital health entrepreneurs to distinguish themselves and their products from the mass of competitors, promote adoption, and increase their chances of establishing advantageous relationships with health system partners is to develop a strong *value proposition*.

A value proposition is a clear, concise statement that convincingly articulates why a customer should purchase a particular product. A digital health company or product can have more than one value proposition, depending on how many different market sectors or unique customers are being targeted. At its core, the value proposition describes **what the product does** to solve a problem or meet a need, for **whom**, and **what benefit** can be expected as a result. An effective value proposition should address the following key elements [15]:

- Relevance
- Quantified value
- Unique differentiation

Relevance refers to the product's appropriateness and ability to meet the customer's needs or solve a problem that the customer has. Quantified value refers to the specific benefits that the product can provide to the customer. Finally, unique differentiation refers to the set of identifiable factors that enable a product to stand out from other similar products in the market in ways that make the product well-suited for the customer (the product's **fit**).

The Value Proposition Canvas, created by Alexander Osterwalder, is a diagram and visual tool set that digital health entrepreneurs can use to define and refine their products and offerings, understand and describe their customer and target market, and identify ways to achieve fit (Fig. 4.1) [16].

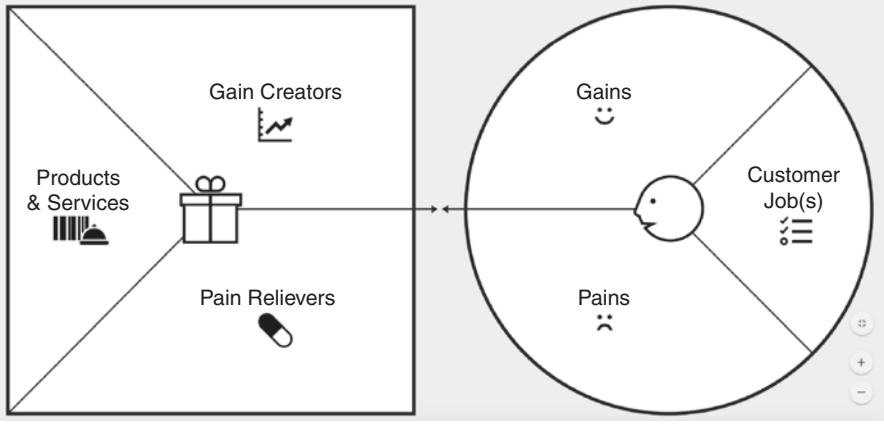

Fig. 4.1 The Value Proposition Canvas (©Strategyzer AG)

On the left side of the Value Proposition Canvas is the Value Map (the square box). The Value Map is where the user defines the features and characteristics of their innovative, entrepreneurial solution. The more specific the definition, the better; vague and nebulous descriptions won't help promote clarity or understanding either for the entrepreneur or the customer. At the same time, it's best to keep things short and sweet, because the more detailed the explanation required, the less likely the customer is to be successfully engaged by what the entrepreneur is trying to do.

The three sections of the Value Map are:

- **Products and Services:** This section is where the user identifies the specific items or things that their solution is, does, and provides to the customer. The list created in this sector of the map comprises the central elements of a value proposition.
- **Gain Creators:** This section should be used to identify the ways in which a digital health solution can provide or create value for the client.
- **Pain Relievers:** This section should be used to match the needs that a customer has to the particular aspects of the digital health solution that will solve the customer's problems for them.

Both gain creators and pain relievers should ideally be written in such a way as to describe not only the *what*, but the *how.* The ideal statement should be explanatory, but succinct, with no more than one short sentence per gain creator or pain reliever.

The right side of the Value Proposition Canvas contains the Customer Segment Profile circle. The sections of this circle can be used to quantify and describe a customer in a detailed, structured fashion. This allows the entrepreneur to simplify the customer down to core components which comprise the central nature of a business relationship: namely, what does the customer do in their work (the customer's **jobs**), what needs or problems does the customer have (the customer's **pains**), and what precise advantages the entrepreneur's solution can provide (the customer's **gains**).

Rather than trying to use the circle to create a single profile that represents all things to all customers, separate profiles should be created for each customer market segment. This allows the capture of unique elements that might be different from one customer to another, which in turn helps identify a specific value proposition for each.

In order to craft a good value proposition, therefore, digital health entrepreneurs first need to understand their customers' profile characteristics and their overall target market. This includes the things that their customers need to do and the problems or the difficulties that their customers currently have which could be solved by a digital health product.

Understanding the Health Care Market

The health care market represents a significant opportunity for digital health business investment. National health expenditures in 2016 amounted to $3.3 trillion and accounted for 17.9% of total national gross domestic product [17]. Within those expenditures, hospital care accounted for 32%, physician and clinical services

accounted for 20%, and prescription drugs accounted for a 10% share. Health care spending is expected to continue growth at a rapid pace, and is projected to increase overall by almost 75% to $5.7 trillion over a mere ten years [18]. As of March 2018, hospitals and health delivery systems in the United States accounted for $991 billion in market share, which alone represents a full 5% of national gross domestic product ($19.4 trillion, 2017) [19, 20].

According to the American Hospital Association, there are currently 5534 hospitals in the United States, including 4840 community hospitals, 209 federal government hospitals, 397 non-federal psychiatric hospitals, and 88 other hospital types including prison hospitals, long term care facilities, and school infirmaries [19]. Among community hospitals, the vast majority (n = 2849) are not-for-profit and non-governmental, with an additional 956 nonprofit hospitals supported by state and local government. The remaining 1035 community hospitals are classified as for-profit or investor owned. Geographically, 62% of community hospitals are located in cities and other metropolitan localities, with the remaining 38% located in rural areas.

Hospitals don't always operate as independent entities—in fact, just the opposite. Two-thirds (68%, n = 3321) of community hospitals are classified as members of health delivery systems, and 35% (n = 1689) are members of health care networks [19]. Health delivery systems are each owned or managed by a central organization. A system can be structured as multiple hospitals in association or as diversified, integrated delivery systems that include a single hospital combined with three or more other integrated health service organizations, such as primary care clinics, that represent at least 25% of the overall business makeup. In contrast, health care networks represent multiple organizations in collaboration to deliver coordinated services to their region. Membership in one does not preclude membership in the other, as an organization can be a member of both a system and a network.

When it comes to meeting health care needs and providing benefits to hospital, health system and practice partners, it's important to recall that the actual decision-making customer is not the organization itself, but one or more of the people within it. There are over 13 million people in the United States health care workforce in 2018, of whom just under one million (n = 968,743) are physicians [21]. According to the American Medical Association's Physician Practice Benchmark Survey, most physicians (68%) work in group practices, whether single-specialty (43%) or multi-specialty groups (25%), as opposed to other practice types, and under ten percent of health care providers are directly employed by hospitals [22]. Only 17% of physicians work in solo practices, and fewer than half of physicians (47%) own their own businesses.

Examples of hospital, health system, and health care practice influencers, key stakeholders and decision makers include:

- **C-suite executives.** Among the roles filled by these personnel are chief executive officer, chief financial officer, chief operating officer, and chief information or technology officer. These individuals hold high-level responsibility for organizational and operational performance, and often have the final say over budgets, discretionary spending, and other financial matters.

- **Health care administrators.** These personnel include various management and leadership roles, such as innovation managers, practice managers, and team leads.
- **Health care providers.** Providers include physicians, nurses, and advanced practice providers such as nurse practitioners and physician assistants [23, 24]. As targeted end users who often serve in leadership roles, providers often have particularly strong influence on digital health product decisions.
- **IT professionals.** Database and application administrators, security specialists, and technical support managers all have the potential to influence purchasing decisions for products that need to be integrated into existing information system architectures.
- **Patients and caregivers.** In addition to making purchasing decisions as consumers, patients and caregivers often serve in advisory capacities for hospitals, health systems, and practices, and provide their insight and expertise accordingly.

Hospital, Health Delivery System, and Health Care Practice Pains and Gains

As part of creating an entrepreneurial profile for targeted health care customers, it is essential to appreciate the work that potential health care clients are trying to do, the challenges that they are experiencing, and the sectors of the market that hold the greatest possibility of benefit. Digital health products and solutions that align with health care market needs are significantly more likely to be adopted. In short, what matters to the potential client must also matter to a digital health entrepreneur. While a comprehensive review of all current health care needs is beyond the scope of this chapter, several key concerns are presented below.

A Commonwealth Fund survey of 33 innovation centers affiliated with health care delivery systems across the United States found that nearly 90% of respondents were focused on care coordination, disease-specific outcomes, and access issues [25]. Additional areas of emphasis included patient engagement (84%), population health (77%), and clinical decision support (74%). These spheres of opportunity are closely aligned with critical needs identified by health system leaders [26, 27]. Such pains include but are not limited to providing value-based care, particularly in a rapidly-changing legislative environment with the potential to exert major impact on industry payment models and reimbursement approaches; providing care that is more patient-centered, consumer-focused, and personalized; and improving health outcomes and care management at the population level in addition to the individual level. Each of these broad topics can be further segmented, for instance into an interest in predictive analytics for chronic condition management or a desire to improve care across the continuum by addressing the social determinants of health. Being aware of these and other health care trends in developing and promoting solutions that are responsive to the market will contribute to entrepreneurial success.

In addition, while there is broad consensus that digital health holds great promise for addressing health care's critical pains, the context for implementing such solutions also matters. Over 98% of hospitals have implemented certified electronic health record (EHR) technology, manufactured by only 10 health IT developers and vendors [28]. More vendor diversity exists in the office-based ambulatory care practice market, where 684 developers supply solutions to over 350,000 providers who participate in federal EHR incentive programs, but the majority of the market share (60%) is still divided among just 5 vendor companies, with Epic alone supplying 30% of the market [29]. This is an important consideration when making a case for a digital health product, as solutions that interface easily with existing clinical information systems have lower barriers to adoption than solutions which need complex programming to achieve integration into the health care setting. Entrepreneurs who are familiar with clinical information system communications protocols and standards such as those curated by Health Level Seven (HL7) International will have an advantage over their competition [30]. HL7 is a standards-developing organization for health information exchange and management, accredited by the American National Standards Institute (ANSI).

Another consideration of critical importance for digital health entrepreneurs looking to establish client relationships with hospitals, health systems, and health care practice partners is the Health Insurance Portability and Accountability Act (HIPAA). HIPAA governs both health information privacy and the security of health information stored and exchanged in electronic form. The penalties for breaching HIPAA can be severe, from a minimum of $100 to $50,000 per violation up to annual maximums of $25,000 to $1.5 million [31]. As of 2013, business associates, such as digital health vendors, are legally held to the same HIPAA standards and subject to the same potential penalties as the health system partners that they work with, which makes information security, data storage, and data governance for digital health solutions even more important.

Finally, digital health entrepreneurs should consider whether or not their product is required to be approved by the U.S. Food and Drug Administration (FDA), which oversees authorization and regulation for medical drugs, devices vaccines, and certain digital health products [32]. Prior to introducing a digital health solution into the health care workflow, client stakeholders will want to know about its FDA approval status.

From Innovation to Infrastructure: Why Business Models Matter

Understanding the customer profile, creating a value map, and crafting a superior value proposition are only part of the path toward digital health innovation success. At the same time that the entrepreneur is working to learn and understand the potential customer, the customer is likewise evaluating the entrepreneur. Moreover, the

strength of the value proposition and fit of the digital health product is necessary but often not sufficient for the potential client to make a purchase decision. The customer also needs to have confidence in the viability and stability of the company as well, including considerations such as the costs of continuance (e.g., technical support, licensing and maintenance fees, and upgrade fees) and vendor stability. After all, no matter how good a product may be, it can quickly become a futile investment if the business which provides it undergoes a collapse.

Developing a well-crafted **business model** is a fundamental process that entrepreneurs can use to demonstrate the viability and sustainability of their digital health products and solutions. A business model is a structured description of a company's plan for profit, and includes such aspects as the core customer base, essential infrastructure to support business operations, income sources and financial planning, and how the company's products or solutions can provide a return from the market. A good business model can serve as the basis for a detailed business plan. It can be used to inform strategic planning, as a roadmap for business development, and as a tool to guide response to customers' questions and concerns. Examples of questions that customers might ask when assessing a digital health product and company for potential fit which could be answered with the aid of a detailed business model include:

- What impact does the product have on existing workflows?
- Does the product require technical integration, or is it a stand-alone solution?
- How is training conducted, how long does it take, and how much does it cost?
- What personnel are required for product implementation and use?
- How is the product deployed? Are there access control, device management, security, and upgrade considerations that need to be cooperatively managed?
- What does available product inventory look like? What are the lead times for ordering, development, and delivery?
- What surety exists that the company will still be around in five years?

As with the value proposition, Alexander Osterwalder and Yves Pigneur have created a visual tool for business model development: the Business Model Canvas (Fig. 4.2) [33]. The Business Model Canvas encompasses nine foundational sections that can be assembled as building blocks to construct a comprehensive whole. Value propositions and customer segment profiles comprise two of the nine business model sections, described further below.

1. **Key Partners.** This section is used to identify business relationships that are essential to or which strategically influence the function and performance of a company, such as suppliers, collaborators, and competitors.
2. **Key Activities.** These encompass the tasks and actions that must take place in order for the business to operate properly.
3. **Key Resources.** These are the assets necessary to support business operations. These resources not only include tangible things like supplies and equipment, but also include personnel resources, intellectual property, and operating cash (financial resources).

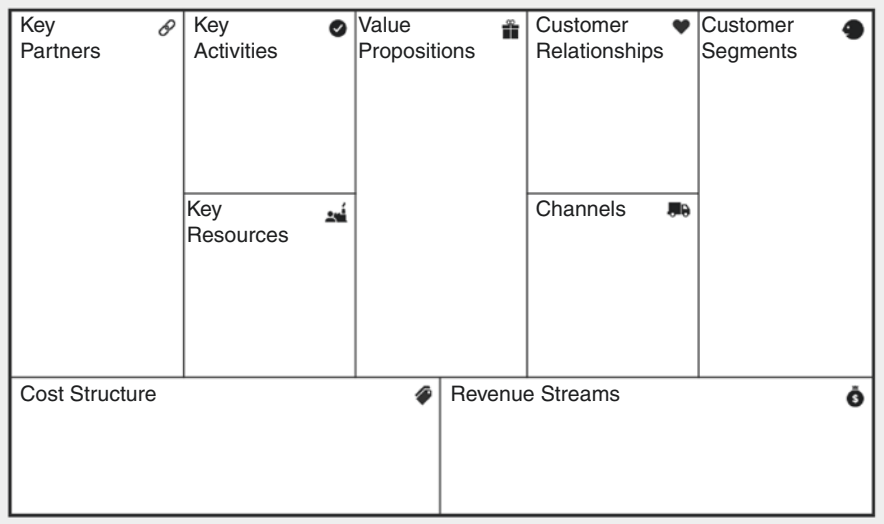

Fig. 4.2 The Business Model Canvas (©Strategyzer AG)

4. **Value Propositions.** As described previously, a value proposition is a clear statement of why a customer should purchase a product, which includes a summary of what specific benefits the product provides and how the product meets customer needs.
5. **Customer Relationships.** These comprise the various types of relationships that can be established between the company and the customers identified in segment profiles. In addition to relatively straightforward provider-client associations, these can also refer to collaborative or co-creation relationships, support relationships, and referral relationships, among others.
6. **Channels.** Channels refer to the points and mechanisms for a company to use when communicating and engaging with customers. Channels can be used for disseminating information, distributing products, sales to support and everything in between.
7. **Customer Segments.** As discussed earlier, customer segments (or customer profiles) are structured descriptions of customer types and groups to be targeted and served by a company, based on their needs, the specific value the company's product can provide, and the goodness of fit between the company and the customer.
8. **Cost Structure.** This section is designed to include all of the costs associated with business operations. Production costs, office space and supply costs, personnel costs such as salaries and benefits, and materials costs are some of the more common elements to include in a detailed cost structure.
9. **Revenue Streams.** Sometimes described as lines of business, revenue streams refer to all the various sources of financial support attributable to a company through its products, services, and investments. Product purchase prices, licensing

or service fees, and advertising income are all examples of revenue streams. A company's net revenue comes from one or more streams after all costs have been accounted for.

Once a business model has been drafted, it's important to test its underlying premise and subsequent fit for the intended market – and not just once, but on a regular basis. Conducting a SWOT analysis can provide great insight into whether a business is poised for success or must adapt to survive. As an acronym, SWOT stands for:

- **Strengths.** These are the elements of a business, solution, or strategy that position a company to address pains, provide value, and outperform its competitors. Examples of strengths might include the uniqueness of a product or established relationships with key clients that help secure market advantage.
- **Weaknesses.** The inverse of strengths, these are the vulnerabilities that place a company at risk. Lack of financial capital is but one example of a significant weakness.
- **Opportunities.** These represent prospects that can be leveraged to improve aspects of business success such as company performance or market share. For example, changes in health insurance reimbursement models for preventive care might create business opportunity for digital health entrepreneurs whose solutions address care coordination or population health management.
- **Threats.** The inverse of opportunities, threats signify challenges or pressures that could strain company resources or decrease market share. For example, the same changes in payment models that might benefit companies with population health products could reduce the client base for companies that focus on high-end fee-for-service solutions.

As the digital health business environment continues to develop, the savvy entrepreneur will reexamine their assumptions on a regular basis to ensure that they are able to pivot in response to market pressures and that they haven't been unexpectedly outmaneuvered by their competitors. Developing value propositions and business models are not one-off activities that can be completed and set aside after checking the appropriate box on the entrepreneurial success to-do list.

Final Thoughts

The field of digital health is highly competitive and rapidly evolving. New legislation continues to change the health care market, and new and emerging technologies constantly reshape the landscape of the possible. Health care stakeholders are inundated by multiple competing responsibilities which must be achieved within the constraints of complex systems and are subjected to a constant barrage of sales pitches in an exploding market. Understanding these customer needs and challenges is essential. Digital health entrepreneurs can position themselves for success through

effective use of tools and strategies such as value propositions and business models to make their case for innovation.

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Chapter 5
Overcoming the Barriers to Dissemination and Implementation

Alan S. Young

The Age of the Electronic Medical Record

The rapid adoption of electronic medical records (EMRs) was catalyzed by government mandate and financial incentives to encourage healthcare practitioners, clinics, hospitals and systems to effectively transition the documentation within the electronic medical record from paper-based, manual processes to electronic and digital platforms. The rise of several electronic health record software companies eventually gave way to a handful of significant players who maintained dominance of the market for several years. While the survival of Epic, Cerner, Allscripts, Meditech and athenahealth promotes healthy competition, the implications on interoperability and data sharing are profoundly impactful. Today, the tight control each software vendor has maintained with their clients has limited the ability to share data in a meaningful way to find solutions to complex population health problems or gather relevant case studies for rare diseases. However, this tight control and corporate competition likely helped drive the adoption and utility of electronic medical records among the front-line users such as physicians and nurses. Despite the view that EMRs are costly, burdensome to physicians and interfere with the doctor-patient relationship, wide spread adoption is continuing.[1] Epic Corporation

[1] https://www.mercatus.org/system/files/graboyes-electronic-health-records-mr-mercatus-v1.pdf

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was founded by the daughter of a physician who ultimately recognized the gross inefficiencies of hand-written medical charts and the inadequate use of historical charts to help patients.[2] As more and more entrepreneurs joined the race to create the ultimate electronic medical record, the adoption of the digital age in healthcare had begun.

Physicians who enjoyed creating detailed medical records for each patient encounter were a rare breed in comparison to those physicians who managed to capture the bare minimum amount of information in illegible notes. With the added pressure of productivity metrics such as RVU compensation or maximizing surgical caseloads, the volume of patient data was exceeding the ability of any individual to review and interpret on a regular basis. The added challenge was the variety of formats, hand-writing, abbreviations and clinical jargon that existed between different practice groups. Depending on your medical training in residency, fellowship and even medical school, the expectations for clinical documentation were not consistent across geographies. The concept of typing clinical notes or using a computer word processing software to capture this information was generally regarded as a distant dream that might happen in several decades. Leading healthcare organizations made initial investments to create their own proprietary medical record system or enlisted the help of these digital health entrepreneurs who offered a solution that could be used out of the box. Organizations like Kaiser Permanente chose a product from Epic[3] while other systems like Geisinger chose an alternate product from Cerner Corporation for population health.[4] During this time, there was no clear mandate to use electronic health records or penalties by way of government reimbursement to encourage wide adoption. The first movers who boldly took the risk by investing in the software soon faced the challenging task of achieving widespread stakeholder adoption and engagement.

Physicians are trained from an early age to excel at acquiring large volumes of scientific data and applying this information in a systematic way to help cure disease or alleviate suffering. The Hippocratic oath is usually taken at the end of medical school before a physician or surgeon embarks on another rigorous path of learning through an apprenticeship model. The focus on core sciences leaves physicians with very little bandwidth to explore other academic pursuits, such as music, literature or computer programming. Fast forward to the early years of electronic medical records and you have a population of extremely intelligent over achievers all able to perform procedures or deliver a differential diagnosis, but with limited computer or word processing skills. The newly introduced expectation of using computers during the practice of medicine was no doubt a challenging experience for many physicians young and old. Like any attempts at changing human behavior, there was a spectrum of responses ranging from angry rejection to joyful acceptance. Rebellion, outrage, burnout, cynicism and other emotional extremes could

[2] https://www.epic.com/about

[3] https://ehrintelligence.com/news/10-biggest-epic-ehr-implementations-in-united-states

[4] https://www.healthcarefinancenews.com/news/geisinger-taps-cerner-population-health

have impeded the progress of the software implementations, but it is more likely that physicians responded with cautious or reluctant acceptance. To those who viewed the problems facing the healthcare industry with an astute perspective, the transition to an electronic health record was inevitable, so why fight the change? The proposed benefits of more efficient workflows, greater patient satisfaction and access to information previously unavailable convinced many physicians to take on the challenge and struggle through a clunky implementation project at the mercy of the IT department. The results were mixed as some organizations reported immediate benefits from using the software while others struggled to regain productivity, profitability and physician buy-in.

The surge in electronic medical record implementations followed closely behind the introduction of the HITECH Act and Meaningful Use.[5] For the first time, the U.S. government was in support of widespread adoption of some form of electronic medical records and used a combination of legislation, policy, incentive payments and reimbursement penalties to accelerate adoption of a software solution for paper and hand-written medical records. The specific reasons why physicians started to finally embrace the effort to move away from paper-based records could have been one of many, but it is safe to assume that financial incentives coupled with financial penalties for non-compliance were strong motivators for behavioral change. If clinical providers were salaried employees of larger health systems, the decision to adopt an electronic medical record was usually made without any of their input or agreement. This perceived oversight or lack of collaboration served as the basis for many physicians and clinicians from fully engaging in the adoption and integration process. There are several well documented examples of electronic medical record implementation failures across the U.S. In one example, the medical group affiliated with a large hospital in California felt neglected when they were not included in the decision to purchase a specific software product. When it came time for the IT implementation, the physician group remained detached. By the time the system went live, the physicians reacted by refusing to use the system and instead reverted to manual paper-based documentation processes while providing care. The hospital leadership eventually succumbed to the demands of the medical group and had to convert the current electronic medical record to another vendor solution that the physicians preferred. There have been many organizations that have also switched between software vendors such as Epic and Cerner due to early struggles following implementation impacting operations or financial performance or because of merger and acquisition activity.[6] The notion that consolidation and standardization leads to cost savings and greater efficiency is carried over from the success of large health systems such as Kaiser, Intermountain and Geisinger who used similar approaches to manage hospital and ambulatory operations. Independent physicians and free-standing community hospitals tended to delay spending to implement a new electronic health record and preferred to watch and learn as others went down the path

[5] https://www.cdc.gov/ehrmeaningfuluse/introduction.html

[6] https://ehrintelligence.com/news/ballad-health-swaps-cerner-ehr-for-epic-ehr-replacement

towards the EMR first. Even then, sometimes the capital requirements to meet the demands of Meaningful Use or other legislation forced physicians or smaller hospitals to seek assistance in the form of an acquisition partner who would then invest to implement the needed technology.

The key lessons learned from observing the gradual adoption of electronic medical records over the past decade are as follows:

1. Adoption takes time—the complexity of healthcare systems and the personal nature of medicine make it unlikely that drastic changes will spread quickly and decisively
2. Healthcare stakeholders need incentives to drive change—Meaningful Use incentives and penalties created an irresistible pull for many organizations who viewed financial success as a critical part of their mission
3. There isn't a single magic bullet solution—the variation across software solutions and no single dominant player indicates that different organizations and patient populations require customized or localized solutions to meet their needs
4. Alignment from the executive office to the front lines will accelerate overall engagement but doesn't necessarily guarantee rapid adoption—stakeholder alignment is a pre-requisite for project success, but implementation plans still need to be systematic and dedicate enough time and resources to key components of the process such as change management and training

The Age of Big Data

The steady but persistent adoption of electronic medical records (EMRs) created growing databases of structured and unstructured clinical, financial and operational data. The promise of data-driven insights derived from the volume of collected information was one of the reasons EMR adoption gained momentum. Research studies benefitted from the easily accessible and categorized clinical charts compared to the previous experience of trying to collect and coordinate huge piles of paper charts with incomplete information in many cases. Revenue cycle departments gained access to more accurate and complete patient encounter records and clinical documentation to align with claims submissions and medical necessity reviews. The rising number of clinics, physicians and hospitals adopting EMR systems contributed to the data explosion that many organizations were not prepared to take advantage of. Those that did were able to apply business intelligence to the data and create clinical decision support tools, revenue cycle integrity practices and patient experience metrics as examples of successful implementation of analytics.

Having a repository of discrete data captured in the EMR gave physicians and other users the confidence they needed to accept the insights derived from any algorithms or analytics applied to the data sets. Reliability and reproducibility of data is a key factor in the eventual adoption and successful implementation of any dash-

boards or performance metrics used to support change. The use of evidence-based protocols and primary research sources have traditionally been used to convince stakeholders that a more proven methodology or process can be used instead of the current state. Even more powerful is the dissemination of peer-reviewed literature produced by authors that maintain some relationship with their colleagues in a selected sub-specialty or discipline in healthcare. Once the data has been blessed, it makes it easier to scale solutions to impact a larger number of stakeholders. The next hurdle to overcome is the wide range of applications that can be leveraged to manipulate data and to find the right solution for the problem at hand.

Scaling a concept to impact the greatest number of stakeholders is the dream of many entrepreneurs who have overcome adversity to achieve eventual success. Historically, the path to achieving this goal was well understood within the healthcare industry. New entrants into the healthcare space slowly developed their product or solution and gradually gained enough visibility to capture sufficient market share. The rise of new digital health companies continues to help push the envelop as to what is feasible for conservative, budget-conscious executives. However, many of the most promising start-up companies are facing cultural and logistical challenges that consume their time and resources. One approach to do is bring talented, like-minded high performing individuals to serve as champions for the adoption or change management process. A digital health startup may have the potential to solve very challenging and complex problems, but without advocates and champions across the various layers in a hospital or healthcare setting, the barriers to success are discouraging. A foundation of quality data is almost a prerequisite since many stakeholders evaluate novel ideas through objective measures and apply the same scrutiny previously reserved for research articles or journal publications. Merging reliable and reproducible data with strong champions across the organization has shown to accelerate the spread of entrepreneurial endeavors.

Big data by itself is not enough to win over all the relevant stakeholders to drive implementation of new ideas. The real value of the data comes from the insights or predictive models that can be derived from the aggregate information. It is important that gradual education and sharing of new ideas take place before any radical changes are introduced. Sometimes the culture and supporting infrastructure are not in a mature enough state to maintain the growth and development of new ideas. A carefully thought-out approach combined with effective execution of the strategic plan that includes big data as a component will likely be better positioned for success than forcing stakeholders to accept a new workflow without their early buy-in. The big ideas or "moonshots" tend to generate a lot of publicity, but it is the smaller, less glamorous projects that focus on solving relevant and practical problems that can generate positive early results when successful.[7] Learning from the challenges of adopting big data for practical applications in healthcare provides another exam-

[7] http://fortune.com/2018/03/19/big-data-digital-health-tech/

ple of how to slowly disseminate a fundamental change in behavior and workflows through the introduction of a new decision-making tool.

The key lessons learned from the rise of data repositories because of wide-spread electronic medical record implementation and usage over the past decade are as follow:

1. You can't engage downstream stakeholders and users without high quality, robust and accurate data to build credibility and eliminate one of the most common reasons for poor adoption and failed implementation of data tools
2. After establishing the data source is reliable and relative free of significant errors, the continued use of analytic tools is determined in large part by the driving force between the key performance indicators (KPIs). Be cautious of KPIs focused too heavily on financial or technical goals over clinical or quality ones.
3. Regular review and realignment of organizational goals and outside trends is needed to keep the performance targets of the data analytics consistent with the strategic objectives year after year.
4. The ability to scale and handle the exponential increase in data volume requires significant computing power and storage capabilities. A cloud migration strategy to integrate the data warehouse and the software applications needs to be carefully executed to avoid significant performance issues that could erode confidence in the data itself.

The Age of Value-Based Care

The increasing costs of delivering healthcare in the United States prompted the previous administration to enact several pieces of legislation that mandated the slow but inevitable migration of care delivery from fee for service to value-based care (VBC) models. Although the recent change in party leadership has threatened to undo several key features of the Affordable Care Act (ACA), otherwise referred to as Obamacare, the bipartisan support of value-based care initiatives reflects the stark reality that without significant intervention, the cost of healthcare in this country will outpace any attempts by politicians to control it.[8] The challenge lies in the incentives currently offered to healthcare organizations and physicians to generate revenue sometimes at the expense of the tax payers and the administrative expenses generated by health insurance companies and other non-essential parties that feed off the wasted dollars consumed and show no impact on health or outcomes. Value-based care is a noble aim and despite enormous effort and almost universal acknowledgement of the unsustainable course the healthcare system is on, the adoption of new policies, standards of care and well-intended technology have barely begun to make any change to the cost structure of the U.S. population.

[8] https://healthpayerintelligence.com/news/value-based-care-key-to-bipartisan-healthcare-system-reform

Measuring the true impact of new healthcare policy at either the federal or state level down to the individual patient in a rural town requires the appropriate definition of what is the desired goal. There is no shortage of opinions around what the most important attributes are in our health system. Are we trying to extend the average life expectancy for all U.S. males and females? Do we want to lower the average per capita cost of delivering care? Is the elimination of certain chronic diseases or cancers an indication of how superior our healthcare system is compared to the rest of the world? A recent research article released by the World Health Organization (WHO) placed the United States at number 37 for overall health system performance. The Organization for Economic Cooperation and Development (OECD) in 2017 pointed out that the United States spends the most of any developed nation on healthcare but does not achieve better health outcomes for life expectancy at birth, infant mortality, management of asthma or diabetes or heart attack mortality.[9] How is this discrepancy explained between the amount of resources spent on healthcare in the U.S. (According to CMS, in 2016 17.9% of GDP was spent on healthcare which equals $3.3 trillion or $10,348 per person)[10] compared to measurements of performance? There is simply no easy answer but the move towards value-based care is an attempt to stop the bleeding before costs create a national budget crisis.

The single largest insurer in this country is expected to run out of funds needed to maintain Medicare, Medicaid and a whole host of other healthcare programs that millions of Americans depend on. A recent report released in June 2018 from key government program trustees revealed that Medicare will run out of money 3 years sooner than expected in 2026.[11] With this knowledge and the prospect of a failed system to care for the country's most vulnerable, there has been modest engagement across all levels of healthcare leadership to bend the cost curve and prolong the life of Medicare and other similar programs. While it is unlikely that solo or group practitioners will dramatically alter their current way of practicing medicine to save Medicare, larger organizations like Kaiser Permanente have strong leadership in place to implement value-based care programs that can impact the population on a grander scale. The recent increase in merger and acquisition activity across healthcare has folded many physician practices into health systems which move quickly to integrate new partners. Some view this activity as precautionary to prevent increased competition in a time of declining margins and reimbursements. Financial pressure on federal, state and local governments also put strain on the private nonprofit health systems who care for a large percentage of the Medicare and Medicaid populations. The outcome of this stress produces long-lasting changes to workflows designed to lower the cost of caring for patient populations who do not generate profitable reimbursement.

[9] http://www.oecd.org/health/health-systems/health-at-a-glance-19991312.htm

[10] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/NationalHealthAccountsHistorical.html

[11] https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/ReportsTrustFunds/Downloads/TR2018.pdf

Successful organizations have been able to adopt value-based care initiatives through internal projects or by bringing in outside expertise and leveraging recent wins. If there is no previous momentum around making the transition away from a fee-for-service model, the journey can be a long and arduous one. Early adopters of value-based care discovered that it was a difficult task to suddenly ask healthcare stakeholders to change the way they had been practicing medicine for decades if not generations. Physician champions or leaders were put in the middle of tense conversations between executives and clinicians. Even though the reasoning behind value-based care made sense, the reality was that financial contracts and incentives did not reward a more holistic approach to delivering cost-effective and outcomes-based care. Furthermore, some clinical departments lacked the project management experience to drive systematic process improvement with governance and change management. The result of these circumstances led to very slow incremental changes that did not significantly bend the cost curve or cause widespread behavioral change across clinical areas. Even today, many organizations still compensate physicians based on volume or RVUs and maximize financial returns without much thought given to better outcomes and lowering the cost of care burden. The success of some health systems to make significant progress in achieving the objectives of value-based care demonstrate that there is not a single uniform path to reach this goal. Rather, it is a pain-staking, complex journey that requires engagement and support from all areas of healthcare sharing the same goal of fixing a broken system for the benefit of the patients.

Value-based care resulted in a gradual movement that is still in the process of transforming the healthcare industry today. The focus on uncontrolled and unsustainable rising costs coupled with the misaligned incentives for hospital, doctors and executives led to legislative attempts to course-correct one of the most expensive and personal industries in the country. Some of the key drivers behind the expansion of value-based care include:

1. Financial and budget constraints at the level of federal, state and local government
2. Poor performance of the U.S. healthcare system when compared to the rest of the developed world and adjusting for average GDP expenditure per person
3. Shift towards quality performance and outcomes-based incentives for providers and payers
4. Consumerism in healthcare with changing population demographics and consumption patterns

The Age of Digital Health

The proliferation of digital health companies, applications and devices in healthcare has changed the way we think about innovation in medicine. The exponential growth in high speed internet service and wireless fidelity (Wi-Fi) access along with the

ubiquitous nature of smart devices such as the iPhone, iPad and Apple Watch has created the foundation necessary for digital solutions to impact industries and business processes.[12] Some of the most profound examples of how a digital technology company has completed transformed the industry it evolved within include ride-sharing companies like Uber and Lyft, accommodation rental platforms like Airbnb, media and entertainment offerings like Netflix and Hulu and food delivery services like Postmates and Grubhub. The unifying theme of all these digital technology titans is the dramatic way they have transformed how normal business is conducted and the new standard that customers expect, while decimating competition that failed to adapt to the new norms of operating in a digital age. Healthcare has remained more resistant to dramatic industry disruption thanks in large part to the layers of regulation, compliance and regard for human safety. However, the demand is growing for digital health solutions and companies disrupting normal operating workflows to meet the consumer demand of growing populations of patients such as millennials and future generations of savvy buyers. The ideas of convenience, crowd-sourcing and virtual care have already created niche industries where patients can receive a telehealth consultation, order prescriptions and pay for services without leaving the comfort of their own home or other popular destinations. However, there are still significant challenges for these companies to enter the mainstream of healthcare delivery and convince established leaders to adopt digital health and accept the risks with any innovation. Digital health faces challenges to achieve widespread adoption and practical integration into the current healthcare landscape and infrastructure.

Healthcare providers are seeing a widening generational gap between themselves and their patients. A large segment of physicians, nurses and executives are considered traditionalists, baby-boomers or generation X. As the population ages, people born in generation Y, generation Z and the millennials are finding themselves in need of various healthcare services. Consumer behavior and expectations have shifted dramatically and in a short time coinciding with the proliferation of smart devices, internet access and technology applications. Instant communication and convenience are prevalent in multiple industries such as retail shopping, banking, dining and leisure travel. The ability to order food, make reservations, pay bills and communicate via text or emojis from a mobile device is transforming how companies engage their customers. Although healthcare is more than just a collection of simple transactions of goods and services, the growing sentiment among generation Z and millennials is to make healthcare as convenient and accessible as other necessities in life.[13] This dichotomy that exists between providers and patients has contributed to the slower adoption of digital health solutions and for many new entrants into the industry, caused their eventual demise. The demand for digital health solutions continues to grow, but the current supply of validated, compliant and evidence-based applications is limited and not enough to meet expectations. The result is a

[12] https://www.ft.com/content/1efb95ba-d852-11e6-944b-e7eb37a6aa8e

[13] http://blogs.deloitte.com/centerforhealthsolutions/bboomers-millennials-gen-z/

misalignment of priorities and a lack of empathy for each group's point of view. The acceptance of change and adoption of new care delivery models beginning with selected medical specialties or patient populations is starting to penetrate years of complacency and the reluctance to break from the traditional practice of medicine.

A major obstacle for digital health adoption is the ability of front-line staff and providers to become efficient users of a new technology or application. This challenge mirrors the difficulties faced by electronic medical record companies as they attempted to train thousands of providers to put down the pen and pad while turning to a computer keyboard regardless of their word processing or typing abilities. Frustration can be a long-term symptom of poorly integrated digital health solutions if the proper training, change management and elbow support is not in place. This frustration can easily turn to rejection of the solution or technology despite the positive benefits it may be able to demonstrate with continued usage. Careful planning and strategic mapping of key activities and milestones to engage stakeholders early is one approach to avoid poor adoption. Realistic expectations around how much training can be deployed and absorbed in relation to the group's baseline technical abilities can reduce friction when productivity and workflows do not return to baseline as quickly as planned. Applications can't be bolted on to existing tools without ensuring that workflows will be maintained and integration is achievable in a reasonable time frame. A one size fits all approach does not apply when you have a diverse and sophisticated work force that is accustomed to functioning at a high level at all times and understands the sensitivity of change when a patient's health is potentially at stake. Achieving the desired level of competency for a digital health tool requires a thoughtful and well-executed strategic plan that addresses the unique needs of the core users and bolsters their confidence with steady progression to a desired proficiency.

Another determining factor for digital health dissemination is the credibility and reproducibility of the underlying programming and data characteristics. During the rise of big data and analytics, physicians were quick to discredit algorithms or analyses that they did not fully understand or have visibility around the details. Some stakeholders can feel threatened when a new technology offers insights that seem to be generated from a non-medical or non-scientific formula. Despite the rigorous demands of computer engineering and data science programs that serve as the foundation for digital health solutions, medical professionals are slow to accept that a new idea originating from outside the industry can improve the current standard of care. A collaboration between clinicians and engineers or programmers in the form of a digital hackathon can create synergy and a deeper appreciation for each discipline. Transparency and sharing knowledge assist to drive support for digital health in organizations where multi-disciplinary teams work together to solve complex problems. This culture tends to be more receptive to outside contributors and can readily implement new technologies that have already been considered or discussed internally. When health organizations review data consistently and apply analytical tools to help mine for insights, it fosters an environment that values evidence-based

approaches to clinical problems. This may result in higher standards for achieving recognition but is valuable to help identify quality initiatives that are sustainable and grounded in fundamental objective data to drive physician adoption.

Digital health implementation efforts also need to consider governance structure, data protection and cybersecurity along with current value-based care requirements. The volume of innovation and technology solutions can be overwhelming, and many organizations rely on the leadership of a Chief Information, Chief Innovation or Chief Intelligence Officer to help evaluate multiple options. Not all organizations have identified this leadership role and instead depend on seasoned executives who may not have the requisite background to fully evaluate the feasibility and applicability of new emerging technologies. The recent string of healthcare cybersecurity incidents has resulted in the loss of millions of personal health records containing sensitive information and increased scrutiny by organizations to identify their own vulnerabilities. New threats can distract leadership from considering substantial investments in unproven areas and instead increase their ongoing budgets for data security measures or infrastructure upgrades. Taking a conservative approach and being fiscally responsible is a comfortable approach for veteran hospital leadership, but this cultural preference makes it challenging for innovative digital health opportunities to gain traction and broad support. When an organization has achieved a robust data security infrastructure and has a forward-thinking governance and leadership in place, advancing projects in digital health is more achievable.

The challenges facing entrepreneurs in the digital health space can be daunting and may stifle creative ideas that require perseverance and patience to succeed in the healthcare industry. History suggests that the emergence of innovation in healthcare takes several years to reach a significant level of dissemination and adoption. The gradual implementation of electronic medical records was incentivized by government programs like the original Meaningful Use and HITECH Act that motivated physicians and healthcare organizations to invest in technology and change workflows. The rise of big data and analytics depended on high quality and reproducible data sets that withstood the scrutiny of skeptical physicians and other end users of the information. Slowly, stakeholders became comfortable with the tools and objectives of big data and started to see the benefits of continued adoption of analytics. The eventual realization of healthcare leaders that a volume driven or fee-for-service industry is unsustainable led to the introduction of more regulation by government to curb costs and shift to value-based care. The implementation of various quality reporting programs provided a combination of incentive payments or penalty avoidance along with the expected improvement to health outcomes. The overarching theme behind general adoption of new processes or solutions in healthcare is the alignment of not only incentives, but also the identification of what is most important to various stakeholders. Motivating people to change certain behaviors that pertain to an individual's health or personal values is a complicated and often time-consuming process. The momentum behind digital technologies across other industries may proceed at a break-neck speed, but in healthcare we are seeing a gradual

adoption with pockets of hyper-activity depending on the specific demand or availability of a digital health innovation.[14]

Summary

The future of digital health is going to introduce even greater change to the healthcare industry in the form of artificial intelligence, blockchain, wearable devices, virtual care and other technologies that will be applied to medicine in unique ways. One of the greatest barriers to adoption and knowledge sharing is the resistance of patients, providers and administrators to the unknown and untested. Scientific evidence has long been the gold standard against which new research and medical therapy is evaluated. However, the application of artificial intelligence in the form of computational decision making and cognitive learning using deep neural networks can greatly accelerate the time to bring novel ideas and therapies to the forefront. The expectations and needs of each generation has shifted towards a more on-demand and convenience focused life-style where it is normal to have access to almost all aspects of a person's preferences through a smart device connected to the internet. Healthcare is facing the challenge of adapting to the needs of a younger patient population and an aging workforce that bring differing views on how to best deliver effective, compassionate and cost-effective care through current technology.

[14] https://rockhealth.com/reports/digital-health-consumer-adoption-2015/

Chapter 6
Financing Your Digital Health Venture

Peter Adams

There has never been a better time to be raising capital for a digital health startup with the number and size of digital health deals increasing every year. The $100 million+ funding club continues to increase as companies grow and mature. Many digital health Digital Health companies are growing to become Unicorns worth $1 billion or more. Driven by an active M&Amergers and acquisitions environment, companies are able to raise capital, grow fast and provide liquidity for their investors. At the same time, with more and more digital health companies getting funded, it is getting harder to stand out from the crowd and digital health startups will have to show a strong awareness of activity in their space and present a clear differentiation from the rest. Understanding the early stage funding environment is a critical step towards success, and yet the process and language of venture capital are unfamiliar to many. In this chapter we'll cover some of the main points that lead to successful early stage digital health funding including the stages of funding and milestones, sources of funding, capital strategy, exit strategy, valuation and term sheets.

Sources of Funding for Digital Health Startups

Digital health startups are well poised to raise the funding they need for growth because of an active investor community in this space, great acquisition/exit environment and an industry that is hungry for innovation. We will review some of the most popular sources of capital for digital health companies at every stage of their growth.

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The earliest stage digital health startups still typically operate in bootstrap mode, raising money from friends, family and founders. While working towards development of a prototype or MVP (Minimum Viable Product) startup founders often keep their day jobs to pay the bills and work on their startup at nights or weekends. Additional cash resources may come from savings, credit cards or HELOC (Home Equity Line of Credit) from their bank. While the startup company itself will not qualify for funding, the founders themselves may have access to capital through these sources.

There is a caveat to using debt as an early stage funding source for the company. Angel and Venture Capital investors typically want their investments to go towards growing the company and will rarely allow founders to pay themselves back for the debt they may have incurred either from themselves or friends and relatives. An amortization schedule of 12–48 months is typically acceptable, so early debt investors should be prepared to be patient. Additionally, many founders are asked to convert their debt into equity, so it will be a long path to liquidity which should be considered before going down that path.

SBA (Small Business Administration) loan guarantees are another way for early stage companies to borrow money for their startup. The SBA effectively provides a loan guarantee to a local bank whose risk is significantly mitigated because of that. Many banks will still want to see your company as being close to positive cash flow before they will make the loan however, so that they know you will have the ability to pay off the loan. In addition to the caveat made earlier about investors not wanting to repay early debt, you should also be aware that SBA loans come with personal guarantee requirements, so you are personally on the hook in case of failure of the company and default. This additional risk to founders personally may make sense if they are the only owner of the company, but can be unfairly burdensome when stock is sold and others own the company and benefit from the use of the capital, but without their own personal risk.

Grants are a common source of early stage funding for digital health companies. SBIR (Small Business Innovation Research) grants are quite common. These grants range from $150,000 to over $1 million for different phases of research. The purpose of the grants is to outsource federal research and development expenses to companies with a strong likelihood of commercializing the technology. SBIR grants are issued through federal agencies such as the department of Health and Human Services, National Institute of Health, the National Science Foundation and others. STTR (Small business Technology TransfeR) grants provide funding for technology transfer from research institutions and can be a good source of early funding for projects coming out of U.S. research institutions.

The main things you need to do in order to be successful with grants is to become familiar with the granting agencies and develop relationships. Grant applications from parties unknown to the agencies are rarely granted. Additionally, grants work according to a strict calendar, so start early and get your ducks in a row. Finally, letters of support are crucial for success, so think through your reference strategy carefully.

In addition to federal grants you should also be looking at local economic development grants closer to home. These grants often require “matching funds”, meaning that you need to match the grant dollars with dollars from other sources including

revenue, investment or other grants. Some companies with strong grant strategies can create a domino effect when one grant is offered, two or three others may become activated.

Crowdfunding for either equity or "rewards" can work with some digital health companies, especially if the technology centers around some consumer oriented product such as wearables or fitness trackers. Rewards crowdfunding can be more effective in gauging consumer interest in a product than in actually raising capital. Being able to point to greater than expected consumer adoption is a great traction point that companies can use in their angel or venture capital pitch later on. The lure of crowdfunding can be great because it looks so easy from the outside. Be aware that it can cost tens of thousands of dollars to put together a crowdfunding campaign. Successful campaigns involve investors you already have in your network vs. investors who are registered on a platform. Additionally, if you are raising capital from an equity crowdfunding platform you should be aware of the dangers of taking on non-accredited investors or even large numbers of accredited investors. Both of those can be a red flag to VCs, many of whom will not want to join a capitalization table with so many other people. If you do use equity crowdfunding of any kind, be sure to have all the investors put their money into a Single Purpose Vehicle, an LLC that is a holding company for their investment, so that only one entity will show up on your capitalization table.

Accelerators can also be a source of funding for digital health startups. There are "horizontal" accelerators like TechStars that focus across technology in multiple industries. Other accelerators like Rock Health, Startup Health, Blueprint Health, Healthbox, TMCx, New York Digital Health Accelerator and many more are "vertically" oriented and focus just on digital health and/or healthcare oriented companies. Accelerators often contribute $25,000–$125,000 to their participants, usually from an accelerator fund, and also host a "demo day" for participants to pitch to the community of angel and VC investors for more capital.

Angel investors will typically look at a digital health startup when it is at the MVP or prototype stage. Angels will typically see their money used for putting finishing touches on technology and getting your company into some pilot projects with healthcare providers, or test your marketing channel strategies. When angels invest as individuals the typical investment range is between $25,000 and $100,000 per investor. When angels invest in groups, the typical range is $500,000–$1 million.

Many people confuse angel investors with the friends and family investors who invest early in the company. Angels think a lot more like venture capitalists than they do like your friends and family. While friends and family will invest primarily in you, the angels are investing primarily to make a profit. They will want to see a clear path to exit which provides them with at least ten times their money in return, with the possibility of up to one hundred times returned.

Angel investors present themselves in several ways, but one big distinction is that some angels are lone-eagles who invest on their own and others invest through angel groups. There are hundreds of angel groups across the U.S. Canada, Europe and Asia. You can find many of them on the Angel Capital Association website (www.angelcapitalassociation.org). The benefit of working through an angel group is that

groups typically do their due diligence once all together and help angels make decisions to invest with having the entrepreneur go through "Groundhog Day" (as in the movie with Bill Murray) and having to go through diligence over and over for each investor. Additionally, many angel groups syndicate with other angel groups, so if you make the right connections, you can get your company funded by the collaboration of many groups investing together. Syndication is basically the process of one or more investors investing together on the same deal terms.

Family Offices are another source of capital. These act almost as a super-angel, doing their own due diligence and investing separately or through groups or syndicates. Family Offices have millions to invest, but often have only a small portion of their assets allocated for startup investments.

Venture capital is an option once you're well into revenue. Seed stage VCs may look at your deal in a pre-revenue stage, but getting to Series A, which is the first round of institutional venture capital, typically takes revenue in the $1 million–$2 million per year range. Series A investments can range anywhere from $3 million to $10 million dollars today.

You should begin developing relationships with venture capital funds up to a year or more before you actually need the money. VC is a relationship based transaction and they want to know you for a while and see how your company performs against its goals. If you meet with a VC and let them know your expected milestones for the next six months, it's a good strategy to over perform and come back six months later to show how you are able to execute. This extended relationship is actually a part of many VCs due diligence strategies. By watching your performance over time, they can get an idea of how well you'll execute once they have invested.

Corporate Venture Capital (CVC) has become a powerful player in the venture capital world and now accounts for over 25% of all venture capital investments. There is a particularly high amount of CVC action in the digital health space as institutions and healthcare companies are looking towards venture capital investments to keep their fingers on the pulse of the industry and to tap into new technologies. There is a saying that "M&A is the new R&D". This means that while research and development expenditures from major companies has been on the decline for many years, CVCs are investing in early stage companies to help fill their pipeline for mergers and acquisitions. It is easier, cheaper and faster for companies to bring on new products and revenue by acquiring companies rather than developing new technologies in house.

Keep in mind that working with CVCs is a two edged sword. On the one hand, having a "strategic" investor can provide you with faster growth, if your investors become customers, and on the other hand there can be a problem with "signaling" if they are on your cap table (a table showing all investors in your company) and they choose not to acquire you. When other companies are going through due diligence when looking to make an acquisition offer for your company, they will be wondering what the CVC knew after having sat on your board of directors for years and having decided not to acquire you. There may be perfectly good reasons why they did not choose to buy, but regardless it sends a signal to others that there may be something wrong with your company.

ICO or Initial Coin Offerings are a new way for digital health companies to raise money, especially if their technology is in some way blockchain enabled. There have been many successful ICOs and the average ICO last year was about $44 million. There are many strategies for raising money using an ICO and the SEC (Securities Exchange Commission) is developing more transparent guidelines about whether "tokens" which are sold in the ICO are securities. There is too much detail to go into here, but if you think this could be a good source of funding, do your research first!

Other sources of funding include factoring (accounts receivable finance), purchase order lending, other asset backed lending, revenue sharing (for companies with positive cash flow), and asking your customers to become investors—both by buying your product or service, and also by making a direct debt or equity investment in your company.

You may want to think about all of these funding choices as a suite of tools to serve your capital needs. You do not need to choose just one type or another. You can mix and match the most effective sources for capital for your stage of business and capital use needs.

A Tranching strategy is a good way to minimize your dilution as you raise capital. Regardless of the source of capital that you choose, you will want to think carefully about your capital tranching strategy. Tranching is basically the process of breaking up your total capital needs into phases. By raising only as much as you need to reach your next major milestones (and a little extra buffer since it will likely take you longer than you thought), you can minimize your dilution and make it easier to raise each round.

Most startup capital raises are enough to fund 12–24 months of runway. But it's not just about the amount of time you need to fund, you also need to be aware of the milestones you need to hit. For example, if you are raising a seed round which you hope will take you to a Series A venture capital round, then you should make sure that your raise will be sufficient for you to build your sales up to $1 million or more in annual revenue run rate.

Valuing Your Digital Health Startup

While valuing a pre-revenue startup may seem difficult or near impossible to many, this is something that is done every day and there are good tools to get you to a valuation number that will be satisfactory for both investors and entrepreneurs.

The first thing to realize when you're valuing your company is that the goal is not to come up with a number like $3,257,456.67. There is no process to get to a number that exact, and even if you could, negotiations for early stage equity are typically done more in round numbers. In fact, our goal is to come up with a satisfactory "negotiation range" in which there will be a fair deal for both founders and investors.

Many people think that you can't value early stage pre-revenue companies and that instead of doing a "priced round" in which the valuation is clearly negotiated

and investors invest in stock in the company, some people think that you can escape valuation by using "convertible debt" (a note payable that has a provision for conversion to equity at a set time or when a qualifying funding round occurs.) Just using a convertible note does not get you out of having to value the company. One of the main terms of the convertible note is the "valuation cap" or the value above which the conversion price will not go. So, if the valuation cap on a convertible note is $3.5 million, then the investor is likely to end up converting to stock at a later date at the $3.5 million price. So, obviously, if you use a convertible note, you still need to go through the valuation exercise to determine the valuation cap. The simple formula for calculating the valuation cap and better understanding the difference between the company valuation cap and the company valuation is shown below. (Hint: they are the same.)

Valuation Cap = Equity Valuation

Valuation and negotiation in the venture capital world is not like it is in other types of commerce where the buyer wants the lowest price and the seller wants the highest price. In VC the best deal is the one that is most fair for both parties. If the price is too low, then there will not be enough dry powder equity available for future rounds of investment. If the price is too high then there is a risk of a "down round" where the share price in the next round is lower than the previous round, resulting in significant dilution for the founders.

The process of finding the negotiation range involves using multiple valuation methods. Think of this as an uncertainty reduction exercise in which your job is to start with great uncertainty and then, by applying several valuation methodologies, reducing uncertainty down to where you have a reasonable negotiating range.

The methodologies that you use are rarely satisfactory for coming up with a valuation on their own. Each has its own challenges and imperfections, but when used together, it actually works. Think of these as five drunks in an alley who can barely stand up on their own, but who, when working together manage to stand up. That's why we use multiple models. Another reason for using multiple models is that we are tackling the question of valuation from multiple viewpoints. It would not make sense to do five different DCF (Discounted Future Cash Flow) models, because they would all use the same inputs and would likely reproduce the outputs of each other. In our case we will recommend models that use DCF, models that use risk adjustment, models that are finance based, and models that are based on comps, much like a real-estate appraisal. By attacking the question of valuation from multiple angles, we get a fairly comprehensive view of what creates value in a startup company.

Here are a few samples of valuation methodologies at work. We don't have enough space to do them all, but these should give you a good idea of how you can get a good valuation even if the company is not in revenues yet. Note one benefit of using models like this is that when you are negotiating your deal you have supporting data to support your arguments. Investors and founders can negotiate on the assumptions vs. the Big Number all by itself.

The Venture Capital Method

The venture capital method comes to a valuation number by working from the exit and backing into a valuation number. This is a DCF (Discounted Future Cash Flow) method because we're going to model what a likely exit scenario is and then apply a venture capital discount to that to determine the value of the company today.

You can see in Table 6.1 that the Exit Year, Revenue at Year Five, Price to Revenues Ratio and the Exit Valuation are all working together to create the number from which we are going to be deriving our present day valuation. If the revenues are $10 million at year 5 and the standard exit valuation is 5 times top line revenues, then the exit valuation in our model is 5 times $10 million, or $50 million. Now we apply our discount rate of 60% IRR (Internal Rate of Return—IRR is effectively an interest rate that compounds over five years. One dollar invested at 60% IRR will yield about $10 dollars in 5 years). The discount multiple is based on the lack of liquidity for the investment, lack of control (since angel/vc investors are typically minority shareholders), and the extraordinary risk in investing in tech startups.

While coming up with the year five revenues in your proforma financial projections can be difficult, and researching the common price to revenues ratios can be difficult, doing the math for this method is easy. What number times ten equals our exit valuation? The number is $5 million. That is our post-money valuation (the valuation of the company including the investors capital contribution). Now we subtract our investment of $1 million and come up with the pre-money valuation of $4 million. You should always use the pre-money valuation when talking to investors.

You will note that the Venture Capital Method only works on deals that have one round of funding. Other models will allow you to model valuations after Series A, Series B, etc. and will help you to calculate cumulative dilution for both founders and investors.

Dilution is not as bad as most entrepreneurs and investors think. If you mistakenly believe that owning 1,000,000 shares of founder stock and selling 25% of the company means that you have 750,000 shares after the transaction, then you would be justified in being worried about dilution. Instead, the founders will always have 1,000,000 shares of stock, and selling 25% of the company means that they are issuing 333,333 new shares of stock. Since 1,000,000 is 75% of 1,333,333 the founders keep their stock and dilution is not as bad as they thought. Additionally, any further

Table 6.1 Venture capital valuation method

Investment amount	$1,000,000
Exit year (estimated)	Year 5
Revenue at year 5 (proforma)	$10,000,000
Price to revenues ratio for exits	5
Exit valuation	$50,000,000
Discount rate	60%
Discount multiple	10×
Post money valuation	$5,000,000
Pre-money valuation	$4,000,000

rounds equally dilute first round investors and founders, so the dilution effect is shared. The average angel investment round in the U.S. is about 23.5%, but the investment range can vary widely from deal to deal.

The Scorecard Method

The scorecard method works like a real-estate appraisal. To do a real estate appraisal, the appraiser researches recent comparable transactions in the neighborhood. The appraiser then adjusts the prices up or down compared to the target house based on factors such as total square footage, number of bedrooms, number of bathrooms, granite countertops, etc. The scorecard method works much the same way. We start by researching the average startup value, then adjust the valuation up or down based on the key factors that impact startup valuation such as Team, Opportunity Size, Product, etc.

To use the Scorecard method shown in Table 6.2, you first need to research the average valuation for seed rounds in your industry. Last year the average was about $3.65 million nationwide. You can find this information from a variety of sources including the HALO Report, Crunchbase, Pitchbook or CB Insights among others.

The Value Drivers and Weighting stay the same for every valuation. Team, for example, is always 30% of the value. It should be surprising to anyone that this is the most important driver.

The actual valuation exercise is in the Score column. If all of the rows were set to 100%, then the company would be average in all ways and the multiplier would be 1.0 and the valuation would then be $3.5 million (or whatever you used for your average for digital health startups). But companies are not all alike and this is where we score them. For the Team driver, 100% looks like three developers and a dog. If they have more people, then they would go up to 150% and even higher for a big team. It's not just about quantity of course but getting a lot of people to quit their day job to join your team is a significant validator of the quality of your company and demonstration of traction. On the other hand if you had only

Table 6.2 Scorecard valuation method

Average company valuation			$3,500,000
Value drivers	Weight	Score (0–400%)	Weight × Score
Team	30%	200%	.60
Opportunity size	25%	200%	.50
Product/technology	15%	100%	.15
Competitive environment	10%	125%	.13
Marketing/sales partnerships	10%	200%	.20
Need for additional investment	5%	50%	−.03
Other factors	5%	150%	.08
			1.625
Scorecard adjusted valuation			**$4,875,000**

two people, then the score might be 50–75%. If you had a CEO with multiple $100 million exits under their belt, and a full team of highly qualified individuals, with all of the main areas covered (finance, strategy, marketing, technology, etc.) then it might get to 400%. Once you have entered all the scores, then you would multiply the score by the weighting and add it all up to get your valuation multiplier which you would apply to your baseline valuation to get your final valuation.

The Scorecard method is a good way to help you get through negotiation, but it takes a lot of experience and comparisons to other teams before you can do this one well. It does have a lot of subjectivity to it, but when used along with the other methods, it is quite valuable.

One last word on valuation. Now that you have an idea about how to calculate the valuation of a company, you should also know that the valuation of the company is not necessarily the same as the price for that company. One of the first digital health companies I ever invested in had a price that was easily $1 million less than the valuation that I got when I ran these models. I told the CEO that I had come up with a higher valuation and he told me that he knew the value was $4 million, but he was pricing it at $3 million because he had two pilots launching in 3 months and he needed the capital quickly to make sure that all the development work was done in time for the pilots. Indeed he raised the round in just a few weeks and the two pilots launched successfully and on time. The company is now worth more than $54 million and continues to grow very quickly. If he had priced it at the value of the company, it would have taken a few months and the opportunity window for the pilots would have closed.

Exit Strategies

Digital health startups are getting funded fairly easily today in part because there is such a robust M&A market for digital health companies. Established companies are buying up digital health companies for a variety of reasons and they are paying higher and higher multiples for them. Having a strong exit strategy is almost a necessity for raising capital today.

Just being a good digital health company is not enough to grab the interest of investors and then ultimately acquirers—you need to have a well-articulated exit strategy to maximize the value of your company. We've created the Exit Strategy Canvas to help you work through the exit value proposition and timing so that you can present the strongest story to your investors. Many investors will not admit it, but the exit strategy is the number one filter for whether they jump into a deal or not. It should be no surprise that having a well thought out strategy for returning the investor's money would be helpful in getting them to write a check.

Many people struggle to state their exit strategy and will resort to generalizations like "we're going to shoot for M&A or IPO". This is NOT a strategy and will do little to engage your investors. The six sections of the Exit Strategy Canvas will help you to find the elements of a strategy which can then be used to create your exit story.

Industry Vectors is the first segment to complete. A good CEO is also a good Futurist and should have a deep knowledge of his or her industry and the vectors that are impacting the future of the industry. Vectors could include "rising cost of healthcare", "problems with uninsured people," "changes in regulations", "competing technologies", "rapid growth of IoT", "blockchain", "DNA sequencing", etc. Another way to look at the Industry Vectors is to watch what the incumbents are doing and where their pain points are. What pain points now will be even bigger for them in the next three to 5 years. If you build your strategy by thinking about what the potential acquirers need rather than just the customer's needs, then you are a step ahead of your competition.

Values are the next thing to consider. If your goal is to be acquired, this is a relationship similar to getting married and you should make sure you understand the values of your organization and to find ways to ensure that your potential acquirers share those values. A significant amount of M&A transactions fail and a failure to match values is one of the biggest causes.

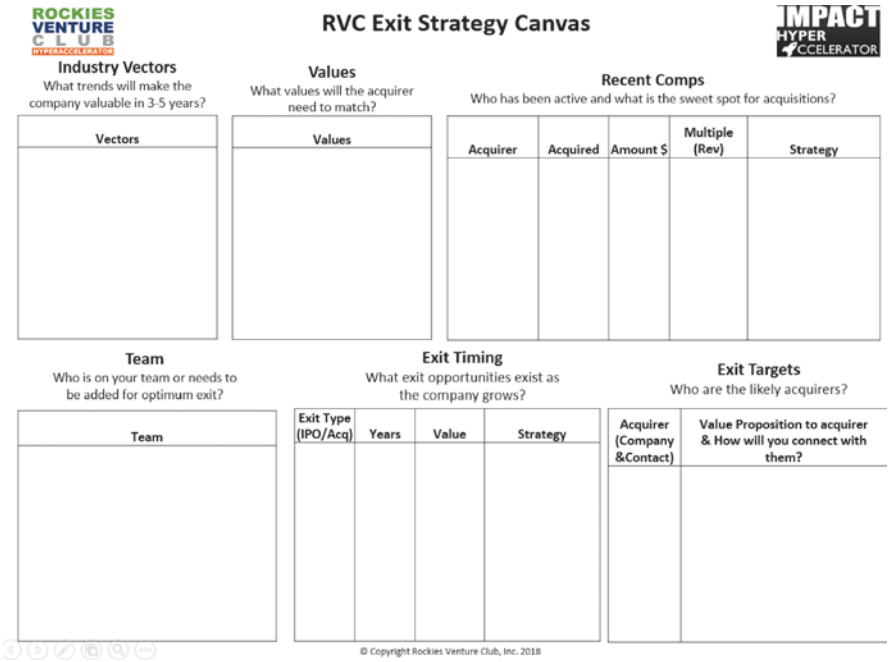
Recent Comparable Transactions are your next section to complete. Here you will report your research on acquisitions, showing who the acquiring company was, who got acquired, what the dollar amount of the transaction was, what the sales price was as a multiple of revenues and a summary of the acquisition strategy. Collecting this information tells you several important things. First, you learn about where the sweet spot is for acquisitions. You will find some outliers and digital health has certainly had a good number of unicorns (private companies valued at $1 billion or more) which are typically outliers. You will find that companies like yours will mostly be acquired within a certain zone like $100 million–$150 million. This helps you to develop your strategy and populate your proforma financial projections you give to investors. If, for example, you find that companies like yours are being bought for five times revenues and average $100 million, then you know that your target revenue run rate to have an optimal exit should be around $20 million.

The second thing you learn in this space is what the revenue multipliers have been. If you create a value oriented strategic plan, you may be able to sell at the higher end of the multiples you find. If you just build a company that focuses on customers but not the acquirer, then you may end up with lower multiples. I call this principle the "second customer" principle, meaning that you need to simultaneously build your company to serve the first customer who buys your digital health product, and also to provide maximum value to your "second customer" who buys your company. These value propositions are not the same and should be considered simultaneously in any important strategic decision.

You will find that it is difficult to locate much of this information. If you have incomplete information on some transactions, that is ok. Go ahead and use them to fill out the table. Some information is better than none at all. You can find some of this information in the SEC EDGAR database online, or at Pitchbook, CBInsights, Crunchbase and other data sources (Table 6.3).

Your Team is the next section. The team is NOT the same team you might have on a pitch deck slide. You should identify the gaps in your team that need to be filled to achieve an optimal exit. These people may be consultants or advisors, or they

Table 6.3 Exit strategy canvas



may be full time on your staff. Examples include lawyers, accountants, investment bankers, CEOs with exit experience, etc. By identifying and engaging these individuals now, you can use them to build your exit strategy as well as to execute on it.

Exit timing is one of the most important issues to consider because you never know when an acquirer might come knocking on your door. You should be thinking about your value proposition to acquirers and how that changes over time. Early on in your startup, the value may be for the technology, patents or employees (an "acquihire" is an acquisition just to get your team). You should be thinking about that value proposition as it evolves to include customers, distribution channels, cash flow, new technology or other competitive advantages. It's a good idea to always know what your company is worth, so when an offer does come along, you know if it's a fair one or not.

Exit Targets is the final segment to complete. You will want to identify who are the likely acquirers of your company. You should identify not only the company that will do the acquiring, but the people inside the company who will lead the decision making process. This is different for all companies, so you may need to do some research. In some cases it comes from the CEO or CFO, others have strategy departments, M&A groups, corporate development teams, or product managers.

Once you have identified the people you need to know, it's time to do some research. Get on LinkedIn and connect to them. Join the LinkedIn groups that they are members of. Find out what conferences and trade shows they attend. Read their blogs and find out how they think. Write your own blogs and send them to your contacts. Be

a thought leader in your industry and get known for that. M&A is much like venture capital because it is a people oriented business. Corporate Development teams like to get to know you six or twelve months before they consider making an offer, so starting the relationships early on in your company life-cycle is a really good idea.

Once you have completed the Exit Strategy Canvas, you can use it to help make decisions, make a better story for your pitch deck and to drive alignment between your team members, board members and investors. One investor I know asks to have a review of the exit strategy at every board meeting. It does not need to take a lot of time, but it ensures that everyone is still on the same page for this important piece of your company's strategy.

Remember, exit strategy is the number one filter that investors have for making investments, so having a well-researched exit strategy is your best strategy for raising capital for your business.

There are many other factors for you to consider in your fundraising strategy including putting together a killer pitch deck and presentation style, building a team, developing a prototype or MVP of your product, getting your legal house in order, preparing for due diligence so it goes smoothly, refining your strategic execution plan, validating your customer value proposition, writing up a draft term sheet so you're always ready to close on an investor meeting and much, much more. We have covered some of the more complex topics here that apply especially to digital health startups and there is a wealth of resources that serve the needs of all startups that I would encourage you to become familiar with.

Funding your startup is hard—good luck!

Chapter 7
The Role of Artificial Intelligence in Digital Health

Anthony Chang

> *"Healthcare is an information industry that continues to think that it is a biological industry."*
> Laurence McMahon at the AAHC Thought Leadership Institute meeting, August, 2016

Artificial Intelligence: Basic Concepts

Intelligence can be defined as the ability to learn or understand or to deal with new situations or to apply knowledge or skills to manipulate one's environment. These definitions have interesting implications for artificial intelligence. Perhaps the best definition of artificial intelligence is the one conjured by the American cognitive scientist Marvin Minsky: the science of making machines do things that would require intelligence if done by man (woman).

Artificial intelligence can be categorized as weak vs. strong: weak (or specific, narrow) AI pertains to AI technologies that are capable of performing specific tasks (like playing chess or *Jeopardy!*) and strong (or broad, general) AI, also called artificial general intelligence (or AGI), relates to machines that are capable of performing intellectual tasks that involve human elements of senses and reason. The public perception of artificial intelligence, however, continues to be that of the menacing robots that threaten mankind (such as HAL in *2001: A Space Odyssey* or the Terminator). Recently, this perception is modified to that of the more sophisticated and complex artificial intelligence-inspired but humanoid robots seen in the movies *Her* (2013) and *Ex Machina* (2015).

Machine learning (and its specific domain deep learning) are not synonymous with artificial intelligence but are rather types of AI methodology. AI, however, does overlap with data science and data mining as well as big data. Other AI methodologies

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can include cognitive computing and natural language processing. Cognitive computing (as exemplified by IBM's Watson cognitive computing platform) can involve a myriad of AI tools that simulates human thinking processes while natural language processing involves connecting human language with computer programmed understanding.

A Brief History of Artificial Intelligence and Its Role in Medicine

It is the British mathematician and computer scientist Alan Turing, however, who would be considered the absolute progenitor of artificial intelligence with his pioneering works that included his theory of computation and his work on computing machines [1, 2]. His most valuable contribution was his deciphering of the German Enigma machine during the second World War at Bletchley Park using machine intelligence (portrayed in the film *The Imitation Game*). The eponymous Turing Test is a test of machine AI's ability to pass as a human.

In 1956, mathematicians and scientists gathered at the seminal Dartmouth Conference and it is the proposal for this august gathering that the term "artificial intelligence" was coined by the Stanford computer scientist John McCarthy. This summer conference and its discussions is widely thought to be the birth of AI as an interdisciplinary field.

Following this early epoch of machine intelligence, two AI "winters" in the 1970s and then subsequently in the following decade occurred due to concomitant lofty expectations and suboptimal realities, resulting in an overall disappointing outlook on AI. Main shortcomings include the lack of a theory-to-use coupling as well as the inadequate integration of the existing AI techniques into workflows to achieve user support.

Initial efforts in artificial intelligence and its application in medicine began in the 1960s and focused mainly on diagnosis and therapy. Among the best known early works on AI in medicine was the Stanford physician and biomedical informatician Edward Shortliffe's innovative heuristic programming project MYCIN. This pioneering work was a rule-based expert system (written in the Lisp programming language) that had if-then rules; these rules yielded certainty values that mimicked a human's expertise (such as recommended selection of antibiotics for various infectious diseases) [3]. The knowledge from a human expert was entered into a knowledge base, which in turn was connected to an inference engine. The non-expert user then queries a user interface that was coupled to the inference engine. The advice was then given to the user via this user interface.

The Current Era of Artificial Intelligence and Its Impact on Medicine

The data mining and machine learning focus in the 1990s then slowly revived the field of AI and this era was best symbolized by IBM's supercomputer Deep Blue, which defeated the reigning world chess champion Gary Kasparov in 1997. Another IBM supercomputer, Watson (named after its first CEO Thomas Watson), with access to over 200 million pages of content and developed in IBM's DeepQA (question and answer) project, easily defeated the human champions Ken Jennings and Brad Rutter on February 14, 2011, on the game show *Jeopardy!*. In a similarly dominant fashion, the AlphaGo program of DeepMind easily defeated the human Go champion Lee Sedol in March 2016, thus heralding a new era of AI with deep learning.

The recent advent of an AI "trinity" that consists of: (1) the increasingly large volumes of available data that requires new computational methodologies (or simply "Big Data"), (2) the escalating capability of computational power (with faster, cheaper, and more powerful parallel processing that defied Moore's Law) and cloud computing (with nearly infinite storage), and (3) the emergence of machine and deep learning with its variants have together promulgated this new dawn of AI.

Algorithms. The advent of complex and efficient algorithms (sets of steps to accomplish certain tasks) that are available for not only calculations and data processing but also automated reasoning has advanced the capabilities of machine intelligence. Examples of complex algorithms that are in current use include Pixar's coloring of 3D characters in virtual space (rendering algorithm) and NASA's operations of the solar panels on the international space station (optimization algorithm).

Big Data. Data have escalated in a myriad of ways to the point that traditional data processing applications are no longer adequate. The four "V"s of big data often discussed are: (1) volume (over 40 zettabytes, or the equivalent of 40 trillion gigabytes, are expected to be in existence by 2020 with internet of things accelerating this growth), (2) variety (videos, wearable technology, tweets, and structured vs. unstructured types of data can create a digital chaos), (3) velocity (speed data is accessed such as with streaming data and over 20 billion network connections by the end of this year), and (4) veracity (uncertainty of data is not only costly but leads to inaccurate conclusions). Additional "V"s in big data include: value, visualization, and variability.

Cognitive Computing. Cognitive computing uses machine learning, pattern recognition, and natural language processing (NLP) as well as other AI tools to mimic the human brain and its self-learning capability. The IBM supercomputer Watson with its victory in the game show *Jeopardy!* against human champions in 2011 heralded the era of cognitive computing with its potent NLP and knowledge

representation and reasoning capabilities along with machine learning [4]. The supercomputer can scan 40 million documents in 15 s.

There is sometimes understandable confusion between AI and cognitive computing. While AI does not intentionally mimic human thought processes, cognitive computing with its origin in cognitive science, does attempt to simulate the human problem-solving process in a computerized model via AI tools such as machine learning, neural networks, and natural language processing as well as sentiment analysis and contextual awareness. While the present day virtual assistants are pre-programmed collection of responses, a cognitive system can yield a more thoughtful "human" response in the near future.

Machine Learning. Machine learning is an increasingly popular sub-discipline of AI and focuses on big data. In machine learning, a computer uses algorithms to find patterns in data. The sophisticated algorithms are used to interpret data (from a "training set") with the use of classifiers (features or attributes that are used to classify the subjects in a process called feature extraction) in order to make predictions (from an initial "test set" first followed by new datasets).

In other words, the features are predictor variables with labeled outcomes. In short, the four steps of machine learning are: data pre-processing, feature extraction, machine learning algorithm, and predictive model as the last step (see Fig. 7.1).

Machine learning is usually categorized into three types of learning:

First, supervised learning take raw data and use an algorithm to predict the outcome based on a prior training set of data that are labeled. These supervised learning methodologies lead to classification and regression. Classification leads to categorization of output variables whereas regression leads to numerical representation of output variables.

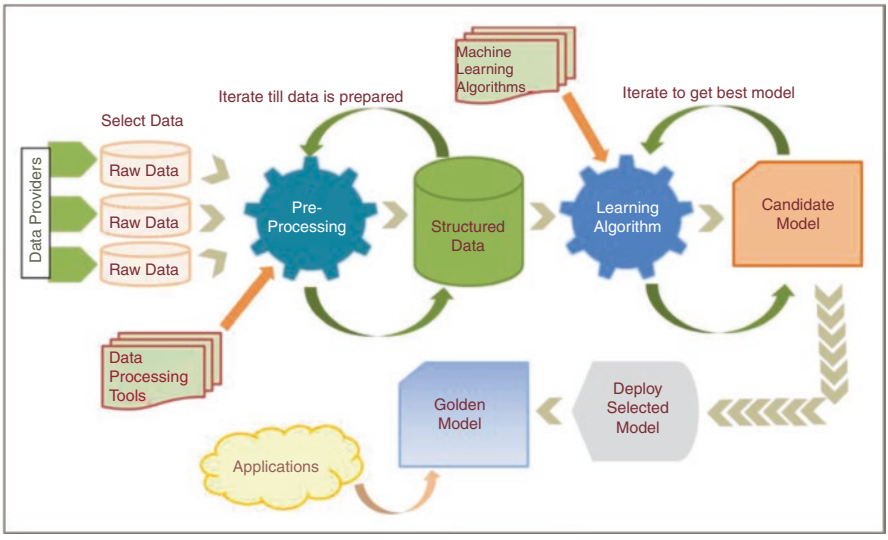

Fig. 7.1 Machine learning (From imarticus.org/ 079/07/17 blog)

These supervised learning methodologies include: support vector machines (SVM), naive Bayesian classifiers, *k*-nearest neighbor (*k*-NN), linear and logistic regression, and decision trees methods (like random forest).

Second, unsupervised learning take unlabeled data and use algorithms to predict patterns or groupings in the raw data set. These unsupervised learning methodologies lead to clustering or association. Other questions unsupervised learning can answer include segmentation and dimension reduction.

Recent hybrid techniques such as semi-supervised learning can be used with less labeled data than that required for supervised learning. These methodologies can therefore be trained on a mixture of labeled and unlabeled data. The introduction of unlabeled data may reduce human bias and improve accuracy of the final model.

In addition to the aforementioned supervised and unsupervised learning, a third type of learning is reinforcement learning. In this type of learning, the model finds the optimal method to achieve the most desirable outcome analogous to humans attempting to attain the highest score in a game (see Fig. 7.1). In other words, there is a positive and negative feedback to the solution of the algorithm so reinforcement learning is well suited for decision process. Reinforcement learning is the methodology that AlphaGo utilized in its defeat of the human Go champion and may be an asset for biomedicine as it is designed to make decisions in an uncertain environment.

There are several limitations with machine learning. A common issue with machine learning resides in its "black box" characteristic- for those who are not data scientists, it is difficult to understand the data science in the machine learning process (see Fig. 7.1) [5]. Some of the higher prediction accuracy machine learning methodologies (deep learning, random forest, support vector machines, etc.) have the least explainability whereas others (Bayesian belief nets, decision tress) have more explainability (but lower prediction accuracy). There is an ongoing effort to elevate explainability in the form of "explainable AI or XAI") while maintaining (or even increasing) prediction accuracy with a new suite of techniques.

Deep Learning

In 2012, the team from University of Toronto used a deep learning algorithm with 650,000 neurons and five convolutional layers to reduce the error rate in half during a computer vision challenge [6]. Andrew Ng of Stanford and Google and others synthesized huge neural networks by increasing the number of layers and neurons to enable large data sets to be trained to promulgate deep learning [7–9].

Whereas traditional machine learning flow has feature extraction followed by machine learning algorithm that leads to output, deep learning flow involves an artificial neural network that can combine feature extraction with the classification as one step.

Machine learning, compared to deep learning, is relatively easy to train and test but its performance is dependent upon its features and is limited even with increasing

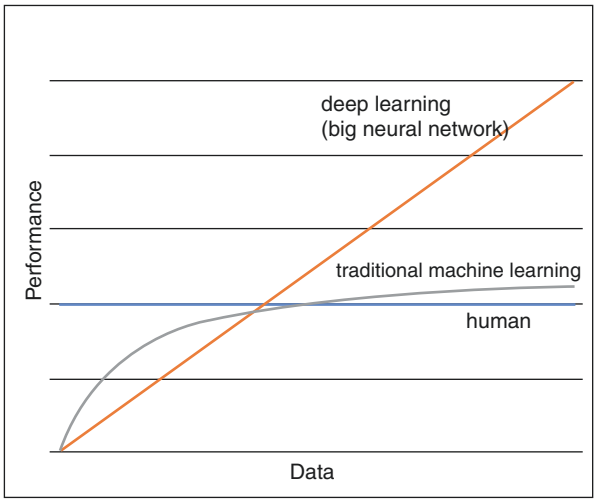

Fig. 7.2 Machine vs. deep learning (Kevin Dewalt's blog titled Deep learning matters for one simple reason in blog.Prolog.io)

volume of data (see Fig. 7.2). On the other hand, while deep learning can learn high-level features representation, it does require large amounts of data for training ("big data") and can be expensive from a computation usage perspective. In addition, deep learning are more difficult to comprehend as the algorithms are largely self-directed.

Current Concepts of Artificial Intelligence in Medicine

Doctors and Machines

How Doctors Think. In Jerome Groopman's How Doctors Think [10], he aptly described several deficiencies in the way physicians think. One such mechanism is confirmation bias, which is the tendency for physicians to search for information that confirms one's preexisting hypothesis. In Sherlock Holme's parlance: "It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts." Another example of cognitive error is the availability heuristic or an intellectual shortcut that relies on immediate recall when evaluating a situation. The myriad of human biases and heuristics can potentially be neutralized with an AI-supported strategy in decision-making process.

Comparing Doctors and Data Scientists. Daniel Kahneman, the Nobel Prize-winning psychologist noted for his work on decision making, described System 1 vs. System 2 thinking (fast and experiential vs. slow and analytical, respectively) [11]. This dichotomy conveniently delineates some of the key differences between clinicians (prone to System 1 thinking) and data scientists (with their affinity for System 2 thinking).

For example, physicians often rely on a fast intuition-based "System I" thinking that is based on experience and accumulated judgment. Data scientists, on the other

hand, more frequently approach problems with slower and more logical progressive thinking that is rationality-based "System 2" thinking.

Similarly, the partnership between the inspector Sherlock Holmes and Dr. Watson describes their two predominantly different systems or "brains" for investigative work: the former (system 2) is more logical and objective (albeit cognitively more costly) while the latter (system 1) is more emotional and subjective (faster but with inherent biases and fallacies). Medicine ideally should perhaps incorporate both types of thinking and individualize decisions based on how much of either type is appropriate. This strategy will minimize the pitfalls in diagnosis and treatment due to inherent heuristics and biases in clinicians [12].

Healthcare Data and Databases

The Conundrum of Healthcare Data. The current imbroglio in health care data is highlighted by an escalating volume of unstructured, heterogeneous medical data with little embedded predictive analytics or machine learning (see Fig. 7.3) [13, 14].

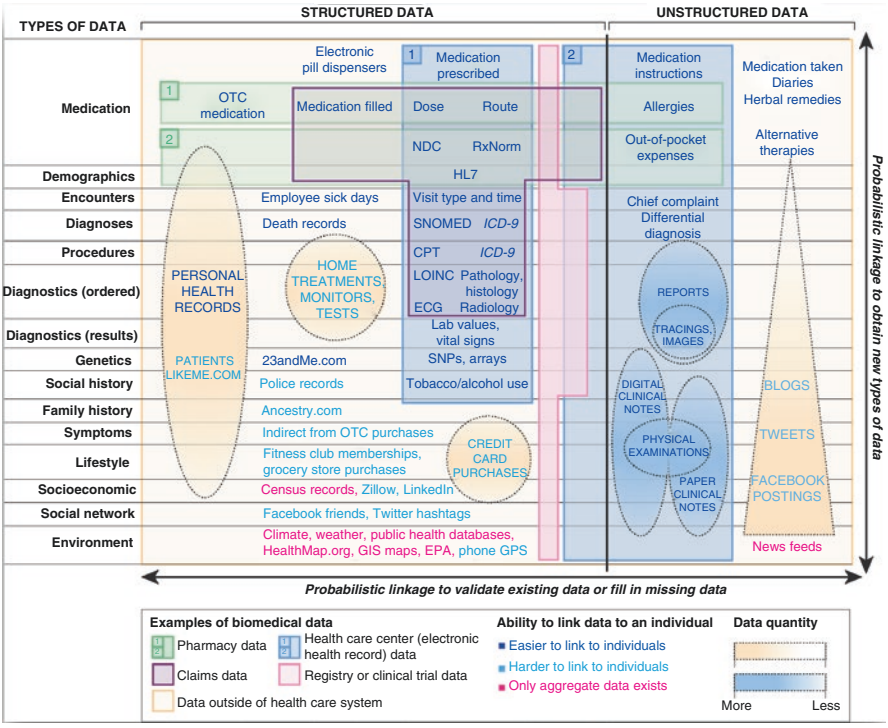

Fig. 7.3 Healthcare data (Enrico Coeira, author)

The complex portfolio of health care data includes not only electronic medical records (patient encounters, vital signs, laboratory results, prescriptions, etc.) but also advanced imaging studies (such as MRI, CT scans, and echocardiograms and angiograms) [15]. In addition, it is estimated that about 80% of health care data is unstructured [16]. Lastly, current estimate of health care data volume is above 150 exabytes in volume and escalating rapidly [17].

Despite the large volume, variety, and velocity of big data in biomedicine, there is little dividend in the form of information from this health care big data [18, 19]. Yet, there are opportunities for utilizing health care big data to reduce costs: high-cost patients, readmissions, triage, decompensation, adverse events, and treatment optimization [20].

This situation will soon be far more complex and daunting with the advent of data "tsunamis": genomic data (as a result of the high throughput next generation sequencing) [21] and physiologic data (from home monitoring and wearable physiologic devices) [22].

Artificial Intelligence in Digital Medicine

The Perfect Storm. The physicians are facing the perfect storm: exponentially increasing medical knowledge, more patients with higher degree of complexity of chronic diseases with increasingly more data, and high level of stress and burnout from the mounting burdens of EHR and workload.

There is a myriad of reasons that physicians in any subspecialty could benefit from incorporation of AI into their practices. First, the amount of medical knowledge is exponentially increasing and doubling at a rate of a few months, and yet physicians do not have enough time to read and maintain their knowledge capacity. AI can be a useful knowledge "partner". Second, AI can help organize and facilitate the care of chronic diseases in many of the patients especially as they have more relevant data from disparate sources such as genomic sequencing and wearable technology. Lastly, physicians have currently a high rate of stress and many are facing or having had burnout from their careers. The use of AI can mitigate the EHR burden and simplify their workload.

Digital Medicine. Digital medicine and health herald the era of technological advances such as apps, wearable technology and remote monitoring, telemedicine and communication tools, and other diagnostic devices to affect a more optimal quality of care as well as a more timely response to any situation. An essential part of digital medicine and wearable devices is the data mining of the incoming data for anomaly detection, prediction, and diagnosis/decision making [23]. The data mining process for wearable data (see Fig. 7.4) includes a feature extraction/selection process for modeling/learning to yield detection, prediction, and decision

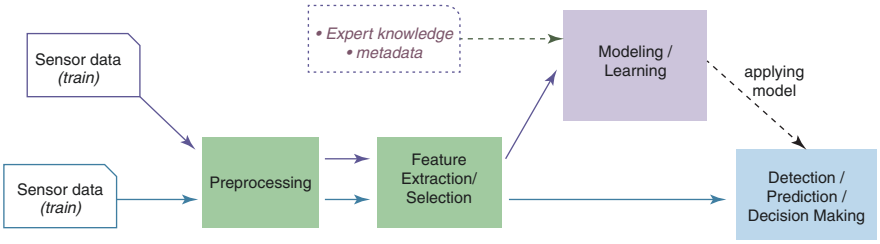

Fig. 7.4 Machine learning for wearable data (Figure 3 in Banaee H et al. Data Mining for Wearable Sensors in Health Monitoring Systems: A Review of Recent Trends and Challenges. Sensors 2013; 13(12): 17472–17500)

making for the clinician. Expert knowledge and metadata can influence modeling and learning.

The advent of wearable devices and sensors to continuously track physiologic parameters can provide an overall patient care strategy that will improve outcome and lower healthcare costs in cardiac patients with heart failure [24]. This new paradigm of cardiovascular disease management can also improve the physician-patient relationship. Machine learning algorithms have also been applied to large-scale wearable sensor data in neurological disorders such as Parkinson's disease to significantly improve both clinical diagnosis and management [25]. This sensor-based, quantitative, objective, and easy-to-use system for assessing Parkinson's disease has potential to replace traditional qualitative and subjective ratings by human interpretation.

AI Strategy. The overarching theme in digital health and medicine in the use of AI is orchestrating, storing, and interpreting the huge amounts of data derived from the devices to facilitate acute and chronic disease diagnosis and management via AI-enabled acquisition and interpretation of data. This strategy will both increase the ability to proactively intervene when appropriate as well as decrease the burden on both the patient and the caretakers when the decisions are relatively straightforward.

Published Works. There is a paucity of reports in digital medicine and AI that clearly demonstrates not only proof of concept in applying AI to an app or device but also clinical benefit. As a matter of fact, a recent editorial in *Lancet* cautions the use of AI in digital medicine and strongly recommends a continual evaluation of digital health interventions for both clinical effectiveness and economic impact [26].

A more positive review by Fogel discussed how AI in digital medicine can improve not only basic health screening and prevention as well as medication adherence but also the human-to-human experience of healthcare [27]. Another review in this domain focused on the concept of a medical internet of things (mIoT) in digital healthcare that is imbued with AI-related tools [28]. In order to reduce overall costs

for both prevention and management of chronic diseases, devices are needed to execute this strategy: to monitor health biometrics, to auto-administer therapies, and to track real-time health data during therapy. Along with these devices, mobile applications for access to medical records as well as tools for telemedicine and telehealth for this new paradigm of medical IoT. All of these devices and equipment will need an AI-centric strategy for data integration and interpretation for delivering optimal healthcare advice and direction.

While chronic diseases such as diabetes care can benefit greatly from a coordinated and efficient strategy, use of technology including AI remains fragmented at present due to a myriad of issues: lack of supportive policy and regulation, unsustainable reimbursement, inefficient business models, and concerns regarding data security and privacy [29].

Future Applications. In the near future, embedded AI (eAI) and machine learning algorithms evolve toward the internet of everything (IoE) and will bring together people, process, data, and things; this strategy will allow the accrued data be streamlined and organized in the cloud proactively in an overall paradigm of personalized precision medicine. As these devices become more intelligent, increasingly higher levels of sophistication in decision support can also be part of both (1) preventive medicine (such as retinal images for retinopathy screening or skin lesions for melanoma detection) as well as (2) chronic disease care management (such as diabetes, hypertension, or heart failure).

An overall strategy for preliminary and continual evaluation of AI applications in digital medicine is needed as the barrier to entry may continue to be low for some apps and devices. This evaluation process will need insight from not only organizations such as the AMA or the FDA, but perhaps also by an international consortium of multidisciplinary experts. Finally, attention needs to be directed towards the cybersecurity of these intelligent devices to mitigate the risk of data breaches and therefore intentional harm to patients and caretakers.

In conclusion, the future of artificial intelligence in digital medicine is extremely propitious with a myriad of advanced AI techniques such as deep reinforcement learning, one-shot learning, and capsule network that will need to be in synergy with clinicians to allow data to be an enabler of new knowledge and intelligence in biomedicine and healthcare. All healthcare data will need to be liberated and shared without any obstacles so that AI can be ubiquitous and invisible in the future health care arena and discover new knowledge from all sources of data and information. In addition, there needs to be an interface between clinicians with data and computer scientists with analytics to assure a data-to-information continuum and eventually a knowledge-to-intelligence transfer. Finally, we need to promulgate a human-machine synergy via a clinician-data scientist collaboration without hubris to push future healthcare and medicine to the highest echelon.

With AI in medicine and healthcare, it is not man versus machine, but man *and* machine.

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Chapter 8
Applying Blockchain and Artificial Intelligence to Digital Health

Dragos Ilinca

A Blockchain Primer

A blockchain is a decentralized, distributed and tamper-proof cryptographic database most suitable for storing transaction information. It is maintained by multiple parties in a distributed fashion. Each record is timestamped, encrypted and linked to previous records.

Records are immutable, can only be added, never removed. Once added, a record can't be changed. Adding a record can only be done through a mechanism called consensus, where most or all parties maintaining the blockchain have to agree to adding it.

Since all records are cryptographically linked to previous records, if a party tries to manipulate previous records or maliciously add a new record, that action will break the overall consistency of the database and is easily detectable.

This makes blockchains valuable in trust-less environments. In such environments it is not necessary to trust that third parties will not be malicious in order to agree on using a shared database. The blockchain encryption, cryptographic linking of records and consensus mechanisms ensure that all data stays consistent and parties can't alter it.

The blockchain network is made up of individual nodes. A node stores the blockchain data and validates transactions through consensus with other network nodes. For this storage and computing work, a node can be compensated within the network through different incentive mechanisms. All this can only work by using a few key ideas, such as strong encryption, immutability, decentralized consensus and baked-in incentives together to provide a self-regulating system.

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Encryption

When storing healthcare data, the owner of the data being stored can encrypt the data or transaction with a cryptographic key, making sure that only the intended recipient of the data can decrypt and access its contents. This is equivalent to digitally signing the transaction, which ensures both data privacy and can prove that the message originated with the party that encrypted it.

Immutability

A blockchain literally means "a chain of blocks". The blockchain data structure is constructed by time stamping a record, linking it to the previous records and the encrypting it. A group of records is called a block and multiple blocks are chained together into a "blockchain". The immutable nature of the blockchain makes it suitable for storing any kind of data where provenance, accuracy and auditability are critical, such as in healthcare, finance, supply chains and more.

Decentralized Consensus

A blockchain's power comes from it being decentralized. Encryption and immutability are the foundations of the blockchain being tamper-proof. However, it's decentralized consensus that enforces it. A blockchain where all nodes are run by a single entity or organization can be altered by that organization, since all it takes is the blockchain nodes agreeing on approving the transaction.

However, when multiple parties with differing incentives have to agree on what constitutes a valid transaction through decentralized consensus, the consistency of the blockchain is much more difficult to compromise. In this case, the most effective model is having a large number of entities running very few nodes each, so that it's highly unlikely for over 50% of the nodes to maliciously agree on compromising the blockchain data.

Baked-In Incentives

A blockchain, at a high level, transforms networks into markets. A participant in the network has to perform some work as part of the network, such as storing data and validating transactions. As a reward for that work, the node receives some kind of benefit in proportion to the work performed. The more work performed, the higher the benefit.

In the original Bitcoin paper [1], Satoshi Nakamoto described this benefit as a coin or token called Bitcoin, which can be used as virtual currency. However, the reward doesn't have to be virtual currency. In healthcare, for example, we can assume some pool of anonymized data can be stored on a blockchain for research purposes. The nodes performing the most work could be rewarded with access to more data for data mining or analytics instead of being awarded a coin. There are many ways to incentivize nodes but making sure the incentive structure aligns the participant with the larger goal of the network is critical to having a successful blockchain network.

Smart Contracts

A Smart Contract [2] is a self-executing piece of code that runs on top of a blockchain. This piece of code can run any computation conceivable, since the virtual machine it runs on is Turing complete. A blockchain with smart contract capabilities becomes a decentralized computer working with tamper-proof data, which is very powerful.

A smart contract can codify actual legal contracts and since they're automated, they can remove the middleman in a multitude of processes. For example, a smart contract can codify the provisions of a payer-provider contract and automate the process of claims processing and payments. Another smart contract can request patient consent for data sharing and once that's given, it can unlock access to patient data, all in an automated fashion.

If blockchains provide secure, tamper-proof decentralized data storage, smart contracts allow blockchains to become much more useful by automating processes.

Identifying Opportunities for Blockchain in Healthcare

When to Use a Blockchain

According to consulting company Deloitte [3], there's a simple checklist that an organization should consult before embarking on a blockchain project.

- Multiple parties generate transactions that change a central repository of data
- These parties have to trust that whatever transaction is added is valid
- Intermediaries are not trusted as arbiters of truth, or it is very inefficient to use intermediaries
- High security and privacy are critical to the system

These conditions make healthcare a prime candidate for using blockchain systems in a variety of use cases.

Most healthcare data has to be shared in one form or another with other parties, whether between providers and patients, provider to provider, providers and payers, payers and pharmaceutical companies and more.

Data integrity is critical, as bad or inconsistent data can put patients' lives at risk. Since healthcare data is very sensitive and private, the system has to be very secure and the number of parties touching the data has be minimized. The fewer middlemen, the better.

Other blockchain benefits for healthcare organizations include:

- Compliance-friendliness: since a blockchain is immutable and very easy to audit, using it makes compliance reporting easier, faster and more cost-effective
- Fault-tolerance: by definition, a blockchain is made up of multiple network nodes that replicate the data stored. Since a blockchain is encrypted, it's very difficult to hack a node and hold an organization's data hostage through a ransomware attack. If a node does get compromised, it can easily be kicked out of the network and since data is replicated across multiple nodes, the organization can continue to operate without downtime as they investigate the issue.

Healthcare Use Cases

Electronic Medical Records

The vast majority of healthcare organizations in the US have implemented some kind of electronic medical records system in the past 10 years. However, most EMR systems make it difficult to share data with other systems or with patients. Many EMR systems are also do not store data in a secure enough manner.

According to Protenus [4], a company tracking data breaches in healthcare, in 2017 "there were 477 incidents reported to HHS, the media, or other sources. Interestingly, 74% of all incidents were either the result of insiders (176 incidents) or hacking (178 incidents)." During Q1 and Q2 of 2018 alone, there were close to 3.5 million patient records compromised [5].

When a patient tries to access her healthcare data, she's faced with a daunting task. The data is trapped within disparate systems and is not easily exportable. Some EMR vendors make it exceedingly difficult to get data out of their systems, even charging patients for access to their records.

A blockchain solution could store all of the patient's medical records in a single place to avoid duplication, while putting the patient in charge of managing access and consent. The data would travel with the patient everywhere and different third parties would access it by requesting consent from the patient. The data would always be complete and up to date, since it would be stored in a shared ledger and managed by the patient.

The MedRec [6] project in conjunction with Beth Israel Deaconess Medical Center have piloted just such a system. "MedRec doesn't store health records or require a change in practice. It stores a signature of the record on a blockchain and

notifies the patient, who is ultimately in control of where that record can travel. The signature assures that an unaltered copy of the record is obtained. It also shifts the locus of control from the institution to the patient, and in return both burdens and enables the patient to take charge of management.", according to John Halamka, MD, CIO of Beth Israel Deaconess Medical Center [7].

Health Information Exchanges

Imagine a patient that is diagnosed with something like diabetes. They will be sent to a lab to get blood work done. They will be sent to a specialist to begin treatment. They might be sent to a nutritionist as well. Since diabetes is associated with a number of comorbidities, the patient might then be sent to a suite of specialists for further investigations. While managing their disease, the patient might use consumer or medical grade apps and wearable devices to record HbA1c, insulin levels, their weight, etc.

This process requires that data is shared between a large number of parties and updated accordingly. Currently, that process relies on all these systems being interoperable, which isn't the case. Health Information Exchanges solve some of these problems by routing information from one party to another, but this is also quite error prone and duplicates a lot of data in the process. If a party sends the wrong information or forgets to send information at all, the issue is difficult to diagnose or track easily.

A nationwide, blockchain based information exchange holds the promise of solving all the aforementioned issues. The information exchange could either store the information within a network of local or state exchanges and provide third party access to pieces of data based on access permission levels, need and timing. Another option is for the blockchain based exchange to only keep track of record locations, access roles and consent mechanisms, while the data itself is stored off-chain within current EMR systems.

Both approaches would provide a smarter solution that would be specifically tasked with proactively managing data flow instead of being a passive data router. For example, smart contracts that are medical protocol aware could automatically send a lab requisition order and notify a specialist with a consult request once a certain patient diagnostic has been established, all the while keeping the patient informed of the next step they need to take.

Clinical Admin and Backend

Current practice management and hospital information management systems have to work with many external stakeholders—patients, clinicians, payers, admin staff to name just a few. This makes current hospital processes more cumbersome than they need to be.

A blockchain based solution could integrate with current systems, while keeping a pool of relevant data shared and managed by smart contracts.

For example, once a patient has been discharged, smart contracts can execute and notify and schedule the patient for follow-up, while sending the patient reminders. A very large number of medical errors happen after the patient has been discharged and follow-up and transfer aren't properly managed.

Claims documents can be compiled and sent to the payer based on the EMR information related to the care and procedure types that the patient has received, as well as the requirements of the payer contract.

Additional smart contracts could automatically gather and mine all necessary information for compliance purposes, while notifying relevant parties when a potential compliance breach is happening.

All these systems rely on the premise that the data shared or provided has to be trustworthy, either to the payer, patient or compliance authority. A blockchain system ensures data and process integrity through its immutable nature and smart contract automation.

Pharma

Of all healthcare stakeholders, the pharmaceutical industry looks most ripe for improvement by implementing blockchain technology within their infrastructure. The combination of third-party patient data required, consent tracking, strict adherence to clinical trial protocols, huge costs of running clinical trials as well as a complex and highly sensitive supply chain make blockchain a prime candidate to improving a pharmaceutical company's operations.

Research and Development

Most pharmaceutical research initiatives rely on having access to wide-ranging population-level medical data. This approach allows Pharma companies to observe and detect wide ranging patterns in medical treatment and drug effects. However, getting access to this type of data poses privacy, data ownership, consent and data integrity concerns.

A shared, blockchain-based system that's managed by patients would provide the means to accelerate drug development, reduce costs while preserving data privacy and rewarding all participants and stakeholders.

The system could work as follows:

- The patients would store their records on a blockchain based system.
- Patients could choose to either make de-identified data available for free, or subject to some sort of compensation mechanism

- Participating companies would have access to huge swaths of census-level, de-identified data to analyze.
- Consent would be automatically tracked on the blockchain for each data item that's used
- The patients providing the data would be compensated in proportion to how their data is used, either through a flat fee or by being issued a stake in the new drug that's being developed.

Such a system would incentivize more patients to share their data, since they're both compensated and they can see and trust that their data is used appropriately.

Another, related issue concerns the management and reporting of clinical trials. "[…] the COMPare project, which monitors clinical trials, found only nine out of 67 studies it has so far looked at had reported their results accurately, while 60 reported on outcomes they were not looking for, according to their original protocol" [8].

A blockchain solution maintained by a national authority could require the tracking of proposed outcomes and protocols against the ultimate results reported as well as ensuring that the original protocol is being accurately followed.

A more interesting use case is, however, running adaptive clinical trials. The trial could start with a proposed outcome and protocol and would record patient progress at each step of the protocol. Based on certain conditions encoded in smart contracts, such as side effects or magnitude of the drug response, certain cohorts of patients could be routed to a different adaptive track of the clinical trial, which is personalized to the patient cohort characteristics.

Supply Chain and Counterfeit Drugs

Pharmaceutical production relies on a complex supply chain of producers and distributors. Many compounds used within drug development are either highly regulated or proprietary and have to be managed with caution. While in transit, certain compounds have to be kept within a very specific temperature range and any deviation makes that compound batch unsuitable for further use.

In order to run such a sensitive supply chain, all parties have to share information in a timely and secure manner and be able to quickly identify any deviations from the required process. This is one of the best environments for deploying a blockchain based solution.

Starting with the producers, a batch can be scanned and logged onto a blockchain at every checkpoint within the system, all they way to the pharmacy shelf. This provides near real-time information of the status of all products flowing through the supply chain.

If, for example, a bad batch is detected, the blockchain system makes it easy to track the bad batch to its manufacturer. If a certain temperature-sensitive container deviates from its acceptable temperature range, a smart contract can be automatically triggered, notifying both the manufacturer and the pharma company that the

batch has been compromised and can't be used anymore. This is logged on the blockchain, preventing the company from using it anyway.

Last but not least, a significant percentage of drugs on the market are counterfeit, especially in developing countries [9]. A genuine container could provide a QR code that, when scanned, can show the buyer the full supply chain checkpoint flow that has been logged on a blockchain, thus proving its authenticity.

Insurance, Claims, Payments

Insurance companies are highly reliant on accurate third-party data in order to function. They need provider claim data for calculating payments. They require patient population data to assess risk profiles for covered entities and to incentivize patients to manage their health better. And they need treatment effectiveness information to understand what treatments and procedures they should cover.

Acquiring and managing this data poses both security and operational issues. The insurance company Anthem, for example, had their IT systems hacked and as a result, sensitive data for over 78 million patients was compromised [10].

We can easily imagine a better system that keeps patient data secure, incentivizes the patients to lower their health risk factors as well as running a more efficient claims process.

A provider organization could, through a blockchain system and smart contracts, automatically gather the relevant claims documentation as required by the provider-payer contract. Once sent, that data would be checked against the payer's claims and payments process. Payments would then be automatically made through smart contracts.

On the patient side, an insurance company could provide the member with health & wellness management apps that log information on the blockchain to ensure accuracy and prevent insurance fraud. Members that lower their risk factors would be incentivized by reductions in their premiums, deductibles or copays.

IoT and Precision Medicine

IoT (Internet of Things) and IoMT (Internet of Medical Things) technologies hold the promise of revolutionizing precision and remote medicine. One can easily imagine a whole suite of sensor-enabled, wearable or smart devices that track vitals and biomarkers or remotely administer drugs and remotely report on the effect.

However, deploying such a network of devices poses security, privacy, management and analysis problems.

These devices generate large amounts of data that require significant resources for analysis. Sharing this data with multiple third parties can drive down the cost of

management and analysis, but raises privacy concerns. Here too, using a blockchain based system can alleviate some of these issues.

Recording and synthesizing IoT data through a blockchain would allow multiple third parties to collaborate in both mining the data and co-ordinating in order to help the patient with disease management and remote care. The blockchain would ensure data integrity and consistency, since all parties would use the same up-to-date information.

Mining the sensor data could be done while preserving patient privacy since it could be anonymized and access would be logged. The end patient would provide express consent for the use of their data. By layering an incentive model on top of the blockchain system, all the stakeholders (patients, IoT manufacturers, providers, payers, machine learning companies) would share in the benefits in proportion to the value they bring to the network. Projects such as IOTA and ModelChain are already experimenting with this model and are already working with corporate and provider organizations on running pilots [11].

Blockchain Tools

As we have seen, the healthcare industry is ripe for disruption through blockchain and associated technologies. Since a blockchain protocol has to be highly secure, scalable, fast and feature-rich (identity, consensus, storage, smart contracts, deployment and monitoring tools), the best way to start is by adopting an existing protocol that's already proven. Luckily, the blockchain community is one of the most open software communities out there so the vast majority of the tools and even the blockchains themselves are open source and pretty well documented. Below are a few of the best candidates for healthcare use.

Ethereum

The Ethereum project was the first blockchain protocol to implement smart contract capabilities. It has been around since 2014 and is the largest active blockchain protocol in the world. Currently, there are over 17,000 active nodes in the networks. The Ethereum developer community is estimated at over 250,000 developers. Of the top 800 cryptocurrency tokens by market capitalization, 87% are based on Ethereum.

All this makes Ethereum one of the best choices in terms of security, scale, toolsets and developer pool available. However, Ethereum is not a fast protocol and it faces scalability issues. There are numerous projects aimed at making Ethereum faster so that it can process a greater number of transactions per second [12].

Hyperledger

The Hyperledger project is maintained by The Linux Foundation and is the premier solution for enterprise blockchain projects. The project is steered by hundreds of members, including companies such as IBM, Airbus, Change Healthcare, SAP, Aetna or Kaiser Permanente. Hyperledger has been used for large scale supply chain tracking projects in production. Its main benefit is its modularity: most components can be swapped out in order to create a customized solution that maps to the business use case. Hyperledger is mainly used for running private blockchains, where only pre-approved members can act as nodes on the network.

Healthcare-Specific Blockchain Projects

MedRec

MedRec is a blockchain project out of MIT in collaboration with Beth Israel Deaconess Medical Center. It is described as follows: *"MedRec applies novel, blockchain smart contracts to create a decentralized content-management system for your healthcare data, across providers. The MedRec authentication log governs medical record access, while providing means for audit-ability and data sharing. A modular design integrates with providers' existing, local data storage solutions, enabling interoperability and making our system convenient and adaptable"* [6].

MedRec provides the benefits of a general-purpose blockchain while being already setup to tackle the quirks and intricacies of healthcare interoperability. However, it is a new, unproven project that's only undergone a few pilot projects.

SimplyVital Health

SimplyVital Health is a blockchain project that combines a HIPAA compliant blockchain infrastructure with value-based care and care-coordination workflows. As with MedRec, it is a new, early stage project that has a promising vision but has yet to prove its value, scalability and cost-effectiveness.

Artificial Intelligence

Artificial intelligence is intelligence demonstrated by machines. The definition of artificial intelligence is very fluid—as machine capabilities progress, tasks that were considered "intelligent" in the past keep being removed from the definition of AI. Peter Norvig, one of the top figures in the field, defines AI as "the study of

agents that receive percepts from the environment and perform actions. Each such agent implements a function that maps percept sequences to actions, and we cover different ways to represent these functions, such as reactive agents, real-time planners, and decision-theoretic systems. We explain the role of learning as extending the reach of the designer into unknown environments, and we show how that role constrains agent design, favoring explicit knowledge representation and reasoning. We treat robotics and vision not as independently defined problems, but as occurring in the service of achieving goals. We stress the importance of the task environment in determining the appropriate agent design" [13].

This broad field encompasses everything from statistical methods, such as machine learning, to robotics. In the sections below, we will use AI and machine learning interchangeably, since right now machine learning and deep learning are delivering the greatest innovations within the field.

AI Applied to Healthcare

Artificial intelligence has a rich history in healthcare. One of the first useful expert systems, for example, was MYCIN. Developed at Stanford in the early 1970s, it used artificial intelligence to identify bacteria that was causing severe infections [14].

The large and varied amounts of data created within the healthcare ecosystem (medical records, genomic data, clinical trials and drug development data, imaging, operational and financial data) make it one of the prime candidates for developing and deploying AI systems.

Challenges

The new AI boom is fueled by very powerful and inexpensive GPUs as well as massive amounts of available data. The outstanding progress in image and speech recognition, natural language processing, text understanding and reinforcement learning can mostly be attributed to these factors. In healthcare, however, some of these benefits have not translated directly into AI progress.

Current challenges include:

- **Privacy**—most data in healthcare is locked up in silos and can't easily be used for model training because of privacy and consent issues.
- **Lack of large scale, high quality data sets**—while there is significantly more data available in healthcare today than a decade ago, it still doesn't approach the level of availability in other domains, such as natural language processing.
- **High dimensionality**—healthcare data is very complex. Hundreds or thousands of variables might contribute to a certain outcome. AI models run into the tens of millions of parameters.

- **High sensitivity and specificity required**—For many use cases, especially related to diagnosis or natural language understanding, the AI models require a high accuracy for them to be useful.

In spite of these challenges, many projects have made significant inroads into creating and deploying AI in healthcare. By combining AI with other cutting edge technologies, such as blockchains, most of these challenges can be overcome.

A Few Use Cases

Clinical Assistants

According to a study published in the American Journal of Medicine, "Physician burnout increased significantly, from 45.5% to 54.4%. Parallel studies of all US workers during the same period showed no changes" [15].

One of the issues cited is that doctors spend more time in their EMR systems than with patients [16].

This is a great opportunity for using AI to decrease the time doctors spend filling out forms in their EMR. The significant progress made by companies such as Google and Amazon in voice recognition and natural language understanding points to this technology being almost ready to be deployed in healthcare. One can imagine one of these digital assistants recording the conversation between the doctor and patient, understanding the key topics and terminology, filling in the right information in the EMR and completing a set of automated follow-up steps, such as sending out a lab requisition order.

Diagnosis

Due to the increasing power of convolutional neural networks (CNNs) in image recognition, there are a whole suite of products available that process imaging data in order to provide diagnosis help to imaging specialists. These products do not aim to provide an automated diagnosis, but instead provide a second opinion to the radiologist. Such systems are already extensively used in mammography [17].

IBM Watson is also making inroads into diagnosing a whole suite of cancers, but with mixed results to far.

Pharmacogenomics and Drug Discovery

As pharmaceutical companies are facing increasing costs required for drug development, they have begun to investigate the potential of genomics for drug discovery.

Deep learning techniques, specifically, have shown great promise in computational drug discovery, through "ubiquity and broad applicability to a wide range of challenges in the field, including quantitative structure activity relationship, virtual screening, protein structure prediction, quantum chemistry, materials design, and property prediction" [18, 19].

One key result that uses state of the art deep learning techniques, for example, is predicting chromatin accessibility. The model, using convolutional long short-term memory networks, a type of deep neural network, has shown that the "method gains high-quality fixed-length features from variable-length sequences and consistently outperforms baseline methods" [20].

These techniques have only been around for a few years and yet they've already shown a very high potential.

Robotics

The combination of powerful, miniature, cheap hardware and sensors, and advances in computer vision have made robotic surgeries a reality. These robotic surgical assistant systems, such as da Vinci, help promote minimally invasive surgery, leading to decreased blood loss, smaller incisions, decreased hospital stay and use of pain medication [21].

More interestingly, patient perception is much more positive than the actual results. "In a 1000-patient survey reported by Patel and colleagues, 20 patients chose RALP based upon a perceived decreased morbidity (54%), potential improved outcomes (37%), decreased blood loss (57%) and less postoperative pain (31%)" [21, 22].

These results pave the way to making surgical robots more autonomous as AI techniques such as reinforcement learning improve [23].

Insurance

The health insurance industry generates large amounts of data that are well suited to analysis and application of machine learning techniques. Insurance companies can use AI systems throughout their revenue cycle management [24], such as:

- Identifying denial patterns
- Predicting denials
- Detecting fraud and preventing abuse
- Understanding where the company overpays

Another large opportunity is in using AI to better understand the make-up of their member population in terms of risk profiles and to predict the likelihood of disease.

Algorithms and Techniques

Healthcare is a complex field where solving the more useful and interesting problems through AI requires a combination of techniques and models working together. Below, we will provide a short guide to existing algorithms and their potential uses in healthcare.

Classification and Regression

A classification problem deals with mapping an input to a label, such as "is this photo of a cat". A regression problem, on the other hand, deals with mapping an input to a quantity. For example, "predict the sale price of this house".

Common uses in healthcare:

- Classifying patients into different risk buckets
- Suggesting diagnoses
- Recommending treatment plans
- Building chase lists for chronic disease management
- etc.

Common algorithms: Linear regression, logistic regression, Multivariate Adaptive Regression Splines (MARS), Support Vector Machines (SVM), some deep neural networks, Classification and Regression Tree (CART).

Instance-Based Learning

This class of algorithms classifies a new problem instance by computing the similarities between the new instance and other instances seen during training.

Common uses in healthcare:

- Second opinion diagnosis tools [25]
- Knowledge extraction in the process of knowledge discovery from databases [25]
- Healthcare fraud detection [26]
- Patient and case similarity

Common algorithms: K-nearest neighbours, Learning Vector Quantization, Self-Organizing Map.

Clustering Algorithms

Clustering relates to detecting and using inherent structures in the data in order to organize it into buckets of most commonality. For example, on PET scans, clustering can tell the difference between types of tissues in three dimensions.

Application in healthcare:

- Clustering has been used in genome annotation by building groups of genes with related expression patterns
- Using genetic data to infer population structures
- Analyzing patterns of antibiotic resistance
- Patients like mine and population health management

Common algorithms: k-Means, k-Medians, Hierarchical clustering, EM clustering.

Deep Learning

Inspired by biological neural networks, deep artificial neural networks comprise a huge class of algorithms used for detecting patterns mostly used for regression and classification problem. This class of algorithms has delivered the largest number of recent advances in machine learning.

An artificial neural network is comprised of nodes connected through edges. These edges usually contain weights, which are real numbers. The function of the nodes is to compute an output based on the inputs into the node, the edge weights. The network "learns" by adjusting the weights based on the result of the previous prediction.

Deep neural networks refers to artificial neural networks with multiple connected layers of neurons.

While artificial neural networks have been around since 1943 [27] only recently has running large networks become possible computationally.

Deep neural network architectures vary significantly, leading to their wide applicability to classes of problems:

- Convolutional Neural Networks (CNN)—used mainly for image recognition, CNNs have achieved greater than human accuracy in detecting traffic signs.
- Recurrent Neural Networks (RNN)—including long short-term memory networks, represent state of the art models in dealing with sequences, such as text, audio, video and time series
- Auto-encoders—this type of network learns to compress input data into a more computationally efficient short code and then un-compress the code into something very similar to the input data
- Generative Adversarial Networks (GAN)—this class of generative models is useful in generating new data that's almost indistinguishable from input data. Mostly used for generating completely new image data that resembles the original input images, GANs could be re-purposed to generate other types of data.

Common applications in healthcare [28]:

- Diagnosing tumors in X-Rays and MRIs through CNNs, tissue classification, cell clustering, hemorrhage detection [29–33]
- Generating candidate molecules in the drug discovery process through generative models [34–36]

- Compound-protein interaction, DNA methylation [37, 38]
- Predicting hospital re-admission rates [39]
- Speech recognition and natural language understanding assisting doctors in note taking and transcription as well as patient coaching [40]
- Risk prediction
- Workflow monitoring and procedure compliance
- Automated coding based on encounter notes and annual chart reviews.
- Intelligent remote patient monitoring through video analysis—based on patient posture, facial expressions, etc. [41]
- Detecting human activity using mobile sensors [42]
- Infections disease epidemics [43]

Dimensionality Reduction Algorithms

This set of techniques aims at reducing the number of variables under consideration when building a model. Similar to clustering, these algorithms use structure inherent in the data to summarize it or describe it using less information. Since healthcare data is vast with hundreds of potential variables affecting an outcome, reducing data dimensionality is key to making machine learning models computationally approachable.

Applications in healthcare:

- Automated diagnosis or cardiac health using ECG [44]
- Analysis of 4D computed tomography [45]
- Early diagnosis of Alzheimer's [46]

Common algorithms: Principal Component Analysis (PCA), Principal Component Regression (PCR), Linear Discriminant Analysis (LDA).

Conclusions

While both blockchain technology and the new resurgence of AI hold great promise for revolutionizing healthcare, it's still early days. Healthcare is a complicated industry with many stakeholders whose incentives are at odds. Whether these technologies can be implemented at scale while delivering both better patient outcomes and providing more value to stakeholders remains to be seen.

Data must be broken out of silos and shared while keeping it secure and private. It must then be labeled and annotated correctly if it's to be useful in AI. High quality data is the cornerstone of reaching high accuracy models and it is surprisingly difficult to find. Entrepreneurs must consider making large up-front investments in acquiring or creating clean data and in incentivizing data holders correctly. This is where a blockchain solution can help. Entrepreneurs must also establish tight feed-

back loops with clinical experts in the field to tune their products quickly and to deliver on the burden of proof through pilots.

Entrepreneurs who can build good technology and navigate this space have a higher likelihood of getting adoption for their products.

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Chapter 9
Protecting Your Digital Health Intellectual Property: Fundamentals of Intellectual Property and How It Applies to Software, Hardware and Business Processes

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Why Intellectual Property Matters to the Digital Health Entrepreneur

The primary focus of many entrepreneurs when setting out on a new business venture is often research and development, team formation, funding, and burn rate. Intellectual property (IP) issues and concerns can often take a back seat to these considerations. This is a mistake, as IP is often the most valuable asset of a digital health startup.

Protecting your IP rights can be critical to building a successful business and establishing a market presence. However, many entrepreneurs fail to recognize valuable IP opportunities and thus fail to protect them. Patents and trade secrets can help protect competitive advantages gained by an inventive device for example, while trademarks and servicemarks present your brand to the public and distinguish it from everyone else's. Having an effective IP strategy and obtaining protection for key IP assets early can provide a competitive edge and can help attract investors.

This chapter aims to give the digital health entrepreneur an introduction to IP, will help entrepreneurs identify protectable IP, provide information regarding what protections are available for the various forms of IP, and provide some considerations to allow them to begin to devise an IP strategy that advances their business goals. This chapter is not intended to be all-encompassing, and does not provide guidance on all possible IP issues. Entrepreneurs with IP-related questions would be well-advised to consult an attorney.

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Types of IP

The term 'intellectual property' often brings to mind a patent. While patents can and should form a part of a digital health startup's IP strategy, other forms of protection, including copyright, trademarks and servicemarks, trade secrets, and contracts, also exist and must be considered. Each of these forms of IP protection is discussed below.

Patents

There are two types of U.S. patents that the digital health entrepreneur should be aware of: utility patents and design patents. Utility patents are what most people think of when they imagine a patent. They are available to protect inventions such as traditional medical devices, digital health wearable devices, software (*see* section "Critical Patent Issues for Software-Based Inventions" for further discussion), and some business methods. Design patents offer protection for the ornamental design of a functional item, allowing the patent holder to prevent others from copying the look and feel of their patented product.

Both U.S. utility and design patents offer the patent holder the right to exclude others from making or using the patented invention, offering the patented invention for sale, selling the patented invention in the U.S., and importing the patented invention into the U.S. throughout the term of a patent. A utility patent can be maintained for up to 20 years from the date the patent application was filed. A design patent is valid for 15 years from the date the patent is granted.

Utility Patents

In the U.S., non-provisional utility patent applications are examined and patents are granted by the United States Patent and Trademark Office (USPTO) on behalf of the U.S. government. Codified in Title 35 of the United States Code (*i.e.*, 35 U.S.C.), section 101 of 35 U.S.C. provides that "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof" is patentable, provided that the described product or process meets certain requirements (*see* section "Critical Patent Issues for Software-Based Inventions" for further discussion of patent-eligible subject matter). Two basic requirements must be met in order for a patent to be granted: the claimed product or process must be novel, and it must be non-obvious.

In order to meet the novelty requirement, the invention must be new. That is, it cannot be the same (*i.e.,* identical) as a product or process previously described in the prior art (*e.g.*, printed publications, published patent applications, issued patents or other publications), in public use, on sale, "or otherwise available to the public" before

a patent application describing the product or process was filed.[1] In short, to be new an invention cannot have been in the public domain prior to filing a patent application directed to it. Having a firm grasp of the non-patent and patent literature in one's field and related fields can help determine whether or not the same invention has been previously described or was publicly available. In some instances, a prior art search performed and/or reviewed by a patent attorney can provide guidance on whether a product or process is likely to obtain patent protection in view of the prior art.

To satisfy the non-obvious requirement, a product or process, as a whole, as of its earliest filing date, cannot have been obvious to "a person having ordinary skill in the art."[2] This requirement essentially determines whether or not the claimed invention represents an inventive advancement over what was previously known and not simply an example of taking the next logical step. Determining what may be considered "obvious" by the USPTO poses a significant challenge to entrepreneurs. While inventors want to know whether they will likely be able to obtain a patent, this can be difficult to predict.

In order to help avoid a rejection by the USPTO on the grounds of obviousness, it can again be beneficial to have knowledge of the literature and patent landscapes in one's filed and related fields. Perhaps the claimed product or process includes one or more elements not disclosed in the prior art, or the elements of the claimed product or process are arranged in a unique manner resulting in a new or improved function. These differences can be highlighted in a patent application to help demonstrate non-obviousness.

Whether hardware, software, or a business method, if a product or process is both novel and non-obvious, it may be patentable.

For hardware such as wearable devices, the path to a granted patent is perhaps the most clear. If no one has described or made an identical device available to the public, and the parts of two or more known devices could not have been obviously combined to form the claimed device, a patent is likely to be granted. Where patentability issues arise most often for digital health entrepreneurs is in the areas of software and business methods.

That the USPTO grants patents for software-related inventions remains controversial in many circles. However, provided the claimed invention meets novelty, non-obviousness, and patentability requirements (*see* section "Critical Patent Issues for Software-Based Inventions"), it is possible to patent certain software-related inventions. This can provide a valuable asset to a startup.

Historically, business methods were not patentable. However, in 1998 the Federal Circuit rejected the "business method exception" in its decision in *State Street Bank v. Signature Financial Group*, in which the court upheld a patent to a "hub and spoke" automated data processing system that employed a series of calculations to transfer assets among a pool of mutual funds.[3] More recent case law has made

[1] 35 U.S.C. § 102(a).

[2] 35 U.S.C. § 103.

[3] State Street Bank & Trust Co. v. Signature Financial Group, 149 F.3d 1368 (Fed. Cir. 1998).

business method patents difficult to obtain. Following the Supreme Court's decision in *Alice Corp. v. CLS Bank International*,[4] most business method claims reviewed by the U.S. Court of Appeals for the Federal Circuit, the appellate court for all patent issues in the U.S., have been found invalid for merely reciting an abstract idea, and thus not directed to patent-eligible subject matter (*see* section "Critical Patent Issues for Software-Based Inventions" for further discussion of patent-eligible subject matter and business methods).

Critical Patent Issues for Software-Based Inventions

The practices and policies surrounding software-related patents have changed rapidly in recent years, leaving many uncertain about the role these types of patents will have in our modern economy. For example, at least one appellate judge believes these changes have "sounded the death knell for software patents."[5] While that viewpoint has not been adopted by the courts or the patent office, the exact criteria for distinguishing the good inventions from the bad continue to evolve. Notwithstanding the uncertainty created by those changes, the outlines of a safe harbor for software-based inventions have begun to emerge and will remain important to software-based inventions as this area of the law continues to change in the coming years. Accordingly, digital health companies relying on software-based inventions would be well-advised to consult a patent attorney who is familiar with this rapidly evolving area of the law.

As noted above, 35 U.S.C. § 101 defines patent-eligible subject matter, using relatively broad language to describe the types of inventions that are eligible for patent protection. Despite that broad language, the U.S. Supreme Court has interpreted Section 101 to exclude certain types of inventions from patent protection, specifically inventions that cover "laws of nature, physical phenomena, and abstract ideas."[6] For software-based inventions, the "abstract idea" exception is applied most frequently. However, the "laws of nature" and "physical phenomena" exceptions have been applied to invalidate patent claims in the life sciences relating to, for example, medical diagnostic techniques and genetic sequences.[7]

The Supreme Court's interpretations of Section 101 created a new, two-step test for determining whether a patent is even eligible for patent protection—creating a new hurdle to clear in addition to the requirements for novelty and non-obviousness. Under that test for patent eligibility, often referred to as the "*Alice*" test, courts and patent examiners are to (1) determine whether the patent claim is "directed to" an

[4] Alice Corp v. CLS Bank International, 134 S. Ct. 2347 (2014).

[5] Intellectual Ventures I v. Symantec, 838 F.3d 1307, 1325(Fed. Cir. 2016) (Mayer, J., concurring).

[6] *Bilski*, 593 U.S. at 601.

[7] *See, e.g., Mayo v. Prometheus*, 566 U.S. 66 (2012); *Association for Molecular Pathology v. Myriad Genetics, Inc*., 569 U.S. 576 (2013); *Ariosa Diagnostics, Inc. v. Sequenom, Inc*., 788 F.3d 1371 (Fed. Cir. 2015).

"abstract idea"[8] and (2) determine whether the claim—either through individual limitations or as a whole—includes something "significantly more" than the abstract idea.[9] But what does that really mean? The Supreme Court was clear that implementing an abstract idea using conventional computing components is not enough for a patent, but the Court did not explain what sort of technical requirements are sufficient.[10] In addition, the Court expressly declined to clarify "the precise contours of the 'abstract ideas' category," deliberately leaving that term ambiguously undefined.[11] As a result, lower courts and the USPTO have been forced to wrestle with these complex issues without meaningful guidance from the Supreme Court.

Since that decision, the Federal Circuit has wrestled with Section 101 on many occasions. The Federal Circuit has upheld inventions as patent eligible only a few times, with several of those decisions relating to software-based patents. Unsurprisingly, the Federal Circuit has struggled to apply the Supreme Court's vague, two-step analysis. While many issues remain unsettled, a few trends have begun to emerge. Of particular note is the emergence of a "safe harbor" for patents that claim a "technical improvement."

For example, in *Enfish LLC v. Microsoft Corp*., the Federal Circuit held that a software-based invention was patent eligible, because those claims were focused on a particular "improvement in computer capabilities."[12] Specifically, in that case the patent claimed a new way of storing information in a computer—using a "self-referential table" that improved the way that the computer operated (*e.g.*, storing and retrieving data from the memory). For that reason, the court held that those claims are not directed to an "abstract idea" but instead to a patent-eligible improvement. Other cases have followed *Enfish* and have upheld patent claims that provide improvements to computers and other technologies. (*e.g.*, *Thales Visionix Inc. v. U.S*., and *Visual Memory LLC v. NVIDIA Corp*.[13]). Despite the Federal Circuit's attempts to provide clarity to the Section 101 analysis, the boundaries of this safe harbor remain unclear. In particular, the Federal Circuit did not define what it meant by "technological improvement" or even "technology."

What about business methods? Those types of inventions have fared especially poorly under *Alice*, and the Federal Circuit has yet to hold that a business method patent provides a technical improvement. Nevertheless, the USPTO has provided some guidance on how business methods can become patent eligible. As part of its "Subject Matter Eligibility Examples," the USPTO provides an example of an improvement to the banking practice of verifying a customer's identity, along with claims that it deems would be patent eligible and claims that it deems would be

[8] Or any other judicial exception to Section 101. But since most Section 101 issues for software-related claims are for "abstract ideas," we focus on that particular judicial exception here.

[9] *Alice*, 134 S.Ct. at 2360.

[10] *Id*. at 2354-55.

[11] *Id*. at 2357.

[12] *Id.* at 1335-36.

[13] 867 F.3d 1253 (Fed. Cir. 2017).

patent ineligible.[14] The difference? Claims that recite specific interactive steps taken by an ATM and the customer's mobile device make the cut, because those claims recite a non-conventional and non-generic way to ensure that the customer's identity is verified in a secure manner that is more than the conventional verification process employed by an ATM alone. In contrast, the exemplary claims that fail the Section 101 analysis contained the same core concept but used more generic language that did not require either the ATMs or the customer's mobile device. In other words, claims that recite a non-conventional use of technology (in this example, ATMs and cell phones) are patent eligible, even if the ultimate goal of the claim is a new business method.

In the end, the safe harbor approach may not be the only pathway to patent eligibility, and other doctrines and approaches may develop as the Federal Circuit attempts to provide further clarity. Nevertheless, at this moment, patents that can quickly tie their claims to a technical improvement are the ones most likely to survive a Section 101 challenge. It is also important to note that many—including a few Federal Circuit judges and a former director of the USPTO—have spoken in favor of changes to the patent eligibility requirements, such as legislative amendments to Section 101. For example, in a recent concurring opinion, Judge Lourie of the Federal Circuit expressly called for "[r]esolution of patent-eligibility issues" by "higher intervention, hopefully with ideas reflective of the best thinking that can be brought to bear on the subject."[15] In addition, several industry organizations have drafted specific legislative amendments to address this issue. Thus, the coming months may continue to provide important changes that will affect how software-based inventions and business methods are protected in the U.S.

Design Patents

An often overlooked form of IP protection, design patents provide protection for the visual ornamental characteristics embodied in, or applied to, an article of manufacture. A design patent may relate to the shape or configuration of an article, to the surface ornamentation applied to the article, or a combination of these. In order to be patentable, the shape, configuration, and/or surface ornamentation must be unique (novel), and non-obvious. Importantly, the design patent protects the way something looks, and not the way it functions, which is the domain of the utility patent.

Relevant to the digital health entrepreneur, the shape and look of products such as wearable devices (*e.g.*, a smartwatch), as well as the look of graphical user interfaces (GUIs) may be protected by design patents. As an article of manufacture, the shape of a wearable device may be protected by a design patent. However, as the

[14] Subject Matter Eligibility Examples: Business Methods, Example 35, USPTO (Dec. 15, 2016).

[15] *Berkheimer v. HP Inc.*, Case No. 2017-1437 (Fed. Cir. May 31, 2018) (denying petition for review en banc) (Lourie, J., concurring).

GUI itself is not an article of manufacture, the GUI is only protectable by design patent when placed on a computer or mobile device display, as it is then associated with an article of manufacture (*i.e.*, the computer or mobile device display).

Design patents offer numerous benefits, and should be considered by entrepreneurs when developing an IP strategy. Benefits include a shorter time to grant (as few as 6–9 months) and lower cost than utility patents and the ability to protect new designs for known products. Further, if a new product is both functionally unique and also has a unique design and visual presentation, it may be possible to get a utility patent covering the novel function as well as a design patent to cover the product's unique design.

Copyright

Governed by the federal Copyright Act of 1976, U.S. copyright laws protect against the unauthorized copying of a "work of authorship." "Works of authorship" encompasses a wide range of types of works, and can include software code, digital information and databases. Registering a copyright or placing a copyright notice on a work is not necessary in order for the work to be protected by the copyright laws, although doing so provides the copyright holder with several advantages. These include enabling the copyright holder to sue infringers in federal court, establishing a public record of the copyright holder's ownership, allowing for the collection of statutory damages and attorney's fees in infringement actions if registration is made within 3 months of publication of the work, and providing for the prevention of importation of infringing copies of a work.

In order to qualify for copyright protection, a work of authorship must be original (although the amount of originality included in the work may be minimal), must be the product of a minimal amount of creativity, and must be fixed in a tangible medium of expression (*i.e.*, stored on some medium in which the work can be perceived, reproduced, or otherwise communicated). The term of copyright protection for an original work of authorship is ordinarily for the duration of the author's life, plus 70 years. The term of protection for works made for hire (where a third party was hired to create the work) is the shorter of 95 years from the first date of publication, or 120 years from the date of creation. Generally, the creator or author of a work is the owner of all copyright interests in the work. In a work made for hire, the "author" of the work is not the individual who created the work, but is rather the entity which hired the creators of the work. Examples of a work made for hire include a work prepared by an employee within the scope of their employment, or a work specially ordered or commissioned for use within a specific set of circumstances.

The protection provided by a copyright can vary. With respect to software code, copyright prohibits others from copying the actual code, but does not preclude others from copying the functionality of the code. This remains the domain of the utility patent. Because of the ease by which a similar functionality can be obtained

using a different code, the ability for copyright protection to protect software applications is limited. While a copyright cannot prevent copying of a software application's functionality, it can prevent direct copying by others.

In instances where a database is original in its selection, coordination, and arrangement, the database may be protected by copyright. Although databases may be protected under U.S. copyright law, the underlying data is not automatically granted protection; protection is only available for the unique selection, coordination, and arrangement of the data. As much of the value of digital health products is derived from datasets, the relatively weak protection for databases by copyright is a significant concern. Fortunately, this concern can often be minimized through the use of contracts, as noted below.

Trademarks and Servicemarks

Trademarks are signs, designs or expressions that identify and distinguish the source of goods from one company from the goods of others. Servicemarks similarly function to identify and distinguish the services one company provides from the services provided by others. In the U.S., trademark rights arise from the actual use of the mark in commerce. The very first time a product is sold or a service performed under a brand name (*i.e.*, trademark), common law trademark rights have been created. Common law trademark rights are governed by state law and are limited to those geographical areas in which the mark is used. Trademarks may be filed at the state level, often with the Secretary of State's office, and may, in some states, be admissible as evidence of the validity of the registration of the trademark, the registrant's ownership of the trademark, and the registrant's exclusive right to use the trademark in that state in connection with the goods or services specified in the certificate.

Federal registration of a trademark provides protection for a trademark throughout the U.S., and provides constructive notice of the validity and ownership of the trademark. Like patents, trademark and servicemark applications are examined and marks are granted by the USPTO. Governed by Title 15 of the United States Code (15 U.S.C., also called the Trademark Act or Lanham Act), federal trademark law exists alongside state laws. In order to qualify for federal trademark registration, goods bearing the mark must be sold in interstate commerce, or there must be a real intent to use the trademark in interstate commerce. Federal trademark registration offers several benefits. For instance, the mark is protected in all 50 states; the trademark owner might be able to recover profits, damages, and costs for infringement, as well as attorney's fees in infringement actions; the mark attains 'incontestable' status after 5 years of registration; the trademark owner may sue in federal court; and the trademark owner may block the importation of goods bearing an infringing mark. As federal registration carries significant benefits, it is almost always advisable to federally register marks with the USPTO.

Things capable of being registered as a trademark include words, phrases, symbols, logos, colors, sounds, and combinations of these, such as a combination of words and a logo. Many times, companies will trademark more than one item, or several variations of an item. Together, these trademarks form the basis for a brand, which can have tremendous value to a company in the market.

Selection of strong trademarks and/or servicemarks can add significant value to a startup by distinguishing the company from others. Marks vary in strength, often depending on where they fall along a spectrum of distinctiveness. From most distinctive to least, this spectrum includes fanciful marks, arbitrary marks, suggestive marks, descriptive marks, and generic marks.

Fanciful marks are considered to be the strongest type of mark, and include those marks which have been created for the sole purpose of functioning as a trademark or servicemark. The mark has no other outside meaning (*e.g.*, Xerox®). Arbitrary marks have a common meaning, but the meaning has no relation to the goods or services being offered or sold (*e.g.*, Apple® for computers). Suggestive marks suggest to a consumer a quality or characteristic of the goods or services being offered (*e.g.*, Microsoft®, suggestive of software for microcomputers). Although suggestive marks can be difficult to distinguish from descriptive marks, a suggestive mark requires some imagination, thought, or perception to reach a conclusion as to the nature of the goods. Descriptive marks require no such imagination, thought, or perception, and merely describe the services or goods on which the mark is used. Since a descriptive mark does not serve to identify the source of the goods or service, a descriptive mark is not immediately protectable. In order for a descriptive mark to be protectable as a trademark, it must "become distinctive" by achieving secondary meaning. Secondary meaning is achieved once it can be shown that consumers recognize a mark as indicating the source of the goods or services, despite the mark simply describing the goods or services. Generic "marks" are those devices that merely name a product (*e.g.*, smartphone). Generic marks are incapable of functioning as a trademark.

While descriptive marks are often selected by startups and entrepreneurs, focusing some time and energy on selecting a strong fanciful or arbitrary mark can pay dividends down the road. Mark selection should include checking to see whether the same or a similar mark has been registered (running a search on the USPTO database) or used elsewhere (running a search using an internet search engine), and whether the ".com" (or other) domain name is available. An experienced trademark attorney can assist with developing a comprehensive search and interpreting the results in a meaningful way.

Trade Secrets

Until recently, trade secret law was predominantly protected under state law. Recently, most states (except New York, North Carolina, and Massachusetts) adopted a version of the Uniform Trade Secrets Act (UTSA) to help unify the law

relating to this form of IP protection. The UTSA defines a 'trade secret' as "information, including a formula, pattern, compilation, program device, method, technique, or process" that is economically valuable and not generally known to or readily acquired by others by "proper means," and is the subject of efforts to maintain the information secret.[16]

A trade secret is therefore a secret, something that is not known by others. Trade secret protection can be utilized to protect anything capable of being kept secret such as a product under development (until a patent application is filed), or a proprietary database or software code that will not be published or otherwise made publicly available. Note that one cannot protect a single item under both copyright/patent and trade secret, as copyrighted and patented technology is made available to the public. Trade secret protection may not be suitable if the economically valuable information is subject to publication, readily reverse-engineered from a legally-obtained product, or developed independently by another company.

Provided that reasonable efforts are continuously made to keep information a secret, a trade secret may be maintained indefinitely. However, as soon as the trade secret becomes publicly available, trade secret protection ceases to exist. Efforts made to maintain information as a trade secret should be outlined in a trade secret policy, and may include restricting access to the information (*e.g.*, locking a prototype away and limiting access to certain individuals; restricting access to computers maintaining the information, such as code, and/or via computer or network security), limiting the number of people who know of and have access to the information, having appropriate non-disclosure agreements and/or employment agreements in place, and marking any secret information as such.

A startup may keep some aspects of its technology as a trade secret, while pursuing patent protection around others. For example, patent protection may be sought for a wearable sensor while a particular software application (*e.g.*, a machine learning algorithm) is kept as a trade secret.

Contracts

Contracts can play a key role in obtaining and/or maintaining IP rights. Typically in the form of a license, an enforceable contract can prohibit users from extracting or otherwise using data from the database for uses other than those intended by the owner. A license can also be used by a startup to obtain technology from a third party. Entrepreneurs must ensure that any contract entered into with another party—whether with a licensor, a licensee, an employee, a consultant, or a contractor—sufficiently addresses IP issues to meet the needs of the startup. IP ownership is an essential consideration at all stages of a product life cycle. Entrepreneurs must secure all rights necessary to enable their business to continue to develop its

[16] Uniform Trade Secret Act § 1.4.

product. This can mean securing ownership of all new technology developed for the startup or in cooperation with the startup, or obtaining the right to use pre-existing IP being used in the development of the startups product.

Contracts can also play a key role in preventing unwanted or premature disclosure of sensitive information. For example, confidentiality or non-disclosure agreements with contractors and consultants can help prevent these third parties from disclosing the information to others, or using this information in later work with others. While many consultants and contractors are accustomed to such agreements, many investors are wary of non-disclosure agreements, and may balk if presented with one. It is important to know where potential investors stand on this issue before getting in the room. Having early IP protections in place, such a provisional patent application or a trademark application can help alleviate an entrepreneur's worries.

Developing a Holistic IP Strategy

When considering intellectual property protection, perhaps the most important thing an emerging company can do is conduct a critical analysis of its path to the marketplace as well as its development product(s) and assess what forms of IP may, or may not, be worthy of pursuing. Obtaining meaningful IP protection can be expensive, after all, and it does not make sense for a startup, with a limited budget, to be wasteful of precious funds. Additionally, investors often require a company to develop a comprehensive IP strategy before they will invest any money, so development of this type of strategy will not only help a startup obtain funds, but will also ensure that those funds are wisely spent.

Timing

There is no hard-and-fast rule that dictates when to start developing an IP strategy, timing can vary depending on the IP asset to be protected, the type of technology in question, and the desired form of IP protection. That said, developing a comprehensive strategy early in the life of the company is always best. It is good practice to think about IP when *first* creating an asset that warrants protection. Doing so will ensure that a plan for the protection of an IP asset is in place right away, before protection can be overlooked.

Unfortunately, as noted above, this rarely happens. Most individuals involved in startup companies tend to focus on the development of their technology, sometimes to the exclusion of everything else. It is axiomatic that fully developed technology is essential for the survival of a startup company. However, the creation of fully developed technology is typically not, by itself, sufficient to get that technology to the marketplace. A company must take steps to bring that technology to the marketplace. There are numerous forms of IP protection available, each of which will help

protect the company's assets. It is therefore crucial to think comprehensively about IP early, to protect what needs to be protected and to ensure that a critical form of protection is not overlooked.

Developing a Comprehensive Plan

How does one develop a comprehensive IP plan? Simply put, by considering the forms of IP protection described above, and matching them with the company's IP assets. When doing so, you should consider all of the company's IP assets at once, as a whole. Distinguish those IP assets that warrant immediate protection from those that can wait, identify those assets that do not reasonably require protection, and budget accordingly. A word of caution: even though the word "budget" is in the preceding sentence, when undertaking this exercise, try to do so without considering money or costs at all. It is far more useful to identify what must be protected and gain a realistic view of what it will cost to do so, than it will be to begin mentally bargaining with yourself about what can and cannot be protected based on the available funds in a bank account. Understanding what it will cost to protect the company's IP assets can help you set fundraising goals, which will impress investors. Investors regularly look for an honest assessment of the company's projected IP costs, and this exercise will help you give them that.

A useful first step is to identify the company's "core" technology, the technology that will serve as the building blocks for the company's technological development for years to come, and protect that first. This is typically easy for a startup, as the technology is nascent and still under development, making everything core technology. It probably goes without saying, but just in case: *core technology is worth spending the money to protect*. If a competitor gets its hands on unprotected core technology, it can copy it, recreate it, and freely practice it without recourse. Nonexistent or inadequate protection of core technology can also scare off investors, which may impede the company's development.

Second, separate those IP assets that are transient, or that may be updated regularly (*e.g.*, software, apps, etc.), from those that are static, or will exist for long periods of time (*e.g.*, hardware, diagnostic devices, etc.). This will help the company identify the type of IP protection to pursue for an asset. As noted below, patent protection can take several years to obtain, whereas copyright takes only a few months. It does not make sense for a company to pursue patent protection for a transient asset, especially when other forms of IP protection are available. For example, a software program that will be updated regularly is not a good candidate for patent protection. By the time a patent issues on version 1.0 of the software, the company could be utilizing version 3.0. Copyright makes much more sense for this type of transient asset, as it can be obtained quickly and inexpensively.

Then, prioritize. You've already identified your core technology as requiring immediate protection, so make it a priority. Other IP assets may be secondary to the success of the company, or still under development. Protection of those assets can

likely wait until they are closer to reaching the market. Finally, some items may technically qualify as IP assets, but may not warrant protection at all (*e.g.*, marketing pamphlets, photographs, etc.). Rank each item in terms of importance, review the considerations set out below, and then begin by obtaining protection for item number one, then two, etc.

Copyright Considerations

Copyright protection can be obtained quickly and inexpensively. On average, the US Copyright Office examines and grants copyright requests 7–9 months after submission. The cost to obtain copyright protection is low—a standard application, submitted electronically, is presently less than US $100. In the US, copyright protection can last for a period of 95 years or more, making the term of protection very good for the price.

Given the low cost and quick return, it is useful to consider protecting every copyrightable item immediately upon its creation. Copyright is a great way to protect transient forms of IP assets, but should also be considered for IP assets that will exist for a long time, such as software. In many instances copyright protection for software assets can be obtained in addition to patent protection. It is best to consult with an IP attorney before doing so.

Trademark Considerations

Obtaining trademark protection takes slightly longer than copyright, but is still relatively quick and inexpensive. The official fees for filing a trademark application electronically with the US Patent and Trademark Office are currently US $400 or less. On average, the Office examines and grants trademark applications 6–12 months after filing. Trademark protection exists initially for a period of 10 years, but can be renewed for an unlimited number of successive 10-year periods, as long as the mark is in use. An IP asset that may never expire can be an incredibly valuable asset.

Given the low cost and quick return, it might seem that one should consider protecting a trademark immediately upon its creation. However, securing trademark protection typically requires proof that the mark has been used in commerce for a period of time. It therefore can be beneficial to use the mark first, before seeking formal protection in order to avoid delays, although an application for federal registration can be made based on a genuine intent to use the mark in the future. In addition, before seeking trademark protection it is advisable to conduct a search to ensure that a desired mark is not already in use or confusingly similar to another, existing mark. It does not make financial sense to attempt to obtain a trademark for a brand name or logo that already exists and is being used by another company. Given that trademarks are also protected by common law, it is not necessary for trademark protection to be pursued immediately. The costs associated with trademark protection can be deferred for a period of time without losing any rights.

Trade Secret Considerations

We hear it all of the time, the idea that trade secret protection is free and never expires, so a company has elected to protect its core technology as a trade secret, rather than seek other forms of IP protection for it. Admittedly, this is an attractive option for a startup company working with limited funds. However, as the saying goes, nothing is ever as simple as it seems.

One cannot obtain meaningful trade secret protection simply by declaring something as a trade secret. Meaningful trade secret protection (*i.e.*, protection that is defensible in a court of law) requires one to contractually obligate everyone (*everyone*) who knows of the trade secret to keep it secret. Those people must be monitored after they leave the company to ensure that they do not go to a competitor and begin using the trade secret. Additionally, one cannot "infringe" a trade secret. To prevail in a court of law, one must prove the intentional act of *theft* of a trade secret. Thus, the company would have to prove that a competitor knew of, and intentionally stole, the company's trade secret. This isn't impossible, but can be very difficult and expensive. Further complicating the matter is that, if the competitor can prove that it developed the company's trade secret independently, without knowledge of the company's trade secret, there may be no recourse against the competitor. Also, if a third party reverse engineers an item that is freely distributed in the marketplace, not knowing it is a trade secret and not obligated to maintain the item as a trade secret, that third party may be able to freely make, use and sell the trade secret. It may not be possible for the company to prove the intent required for theft.

The foregoing does not mean that the creation of trade secrets is impossible or that they are not valuable IP assets, they simply require a large amount of effort at the outset. A trade secret is only as good as the measures that are put in place to keep it secret. As you might expect, timing is critical. A trade secret must be identified as such virtually immediately, to ensure that all of the people who know of the trade secret are available to sign a confidentiality agreement. Thereafter, extreme care must be taken to minimize the number of people who obtain knowledge of the trade secret. Additional confidentiality agreements must be signed as needed. And perhaps most importantly, the technology that will be maintained as a trade secret must not be readily capable of being reverse engineered.

The creation of an asset that could be protected as a trade secret may occur at any time. As such, they are difficult to plan for. What is required instead is for a company to be ready for them to occur at any moment. Confidentiality agreements need to be at the ready. It would also be wise to include a provision relating to trade secrets in an employment contract. The earlier they are considered, the better.

Patent Considerations

Patent protection is more expensive than copyright or trademark protection and will almost always take significantly longer to obtain. For a small entity, filing a utility patent application currently costs US $785 and obtaining protection can take up to

3 years or more. However, the real cost associated with a utility patent application is in its preparation. There are numerous formal requirements that must be met in the application upon filing, making the preparation of a patent application the most expensive part of filing. On average, you can expect to pay anywhere from US $5000–30,000 for a properly prepared utility patent application. Because of that, a careful analysis of the company's patentable core technology is essential. It is almost always cost prohibitive for a startup company to attempt to obtain patent protection for transient IP, like software that will be regularly updated. However, if your core technology includes a hardware device or a software program that will maintain a given functionality and exist for years, then patent protection is the most important form of protection one can seek.

As with a trade secret, timing is critical for a patent application. To be patentable, the subject of an application must be both novel and inventive. "Novel" is a legal concept meaning that the technology must never have been made publicly available. This is where many inventors get into trouble. Depending on the circumstances, simply discussing technology with a small number of people can be legally considered a public disclosure. When one considers how enthusiastic a developer of new technology can be—how could she not want to discuss her new technology with everyone she sees, or publish her results?—not having a plan for patent protection can have a disastrous outcome.

For most countries of the world, a public disclosure prior to the filing of a patent application eliminates the applicant's ability to obtain patent protection in that country. This is because the invention is no longer "novel," it has been placed in the public domain. Some countries have grace periods for their citizens, allowing a citizen to file a patent application after a public disclosure, but those grace periods are enacted by local laws and do not extend to other countries. Patent protection will be limited to the country granting the grace period—the rest of the world will consider the public disclosure fatal to the patentability of the invention. Therefore, an inadvertent public disclosure can reduce what could have been a global patent portfolio to protection in just one country. Having a plan to file a patent application before any possible public disclosure is made can stave off disaster.

The plan here is simple in concept, but can be difficult in practice: all new technology must be kept secret until a patent application is filed. No public presentations, no discussions, no publications, nothing that is not done under an obligation of confidentiality, until a patent application is on file. Patent protection is too valuable to jeopardize it with one seemingly harmless discussion. Plus, inadvertently placing core technology in the public domain outside of your home country can be disastrous for a global marketing plan and will scare off investors.

Enforcement

A final consideration is enforcement of the IP rights obtained. IP rights are offensive rights, meaning that the owner must actively seek out infringers (or a trade secret thief) and sue them in a court of law to get them to stop what they're doing. One

cannot get an issued patent and then sit back and assume that others will come to her, asking to license the patent. That rarely occurs.

The strength of an IP asset should also be considered when making the decision to expend the funds to protect it. Stronger IP rights are easier to enforce and will thus be more valuable to a company. A company would be well-advised to engage IP counsel early, to help the company evaluate the strength of their IP assets.

Final Considerations

It is clearly critical to not only understand the types of IP protection available and what they cover, but also to know when to consider seeking IP protection. A carefully crafted plan, based on a thorough review of a company's IP assets, that is prioritized and includes realistic cost estimates, can help a company plan for the future. Additionally, a comprehensive plan can help impress and attract investors, who typically like to invest in sophisticated companies that understand the importance of protecting IP rights. Walking into an investment meeting with a burgeoning IP portfolio will give you an advantage in your efforts to raise capital.

Lastly, IP rights can help distinguish a company from its competitors and establish its place in the market. They are enormously valuable assets that can help increase the value of a startup company. IP can be expensive to obtain, but the rewards a company experiences from a strong IP portfolio can often far exceed the costs to obtain it. Good luck!

Chapter 10
FDA and Digital Health

Jason Sapsin

For the purpose of this chapter we'll accept the U.S. Food and Drug Administration's ("FDA's" or "the agency's") current interpretation of digital health: "The broad scope of digital health includes categories such as mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine."[1]

FDA has been rapidly changing its approach to "digital health products" ("DHP"s) over the last 5–10 years. By regulation, by policy and most notably by legislation, some DHPs once regulated by FDA are no longer. Health and wellness mobile medical applications are an example: policy, regulation and legislation have all changed in an effort to keep up with this quickly evolving segment. Other products have emerged with which FDA has no previous experience, for example "additive manufacturing" ("3D Printing") devices relying on computer-generated schematics and computer control; and there are still other, more familiar products, for which FDA has not yet been able to provide detailed guidance.

This chapter introduces basic legal concepts in medical device regulation; FDA's organization with respect to medical device regulation; different types of FDA documents which Digital Health Entrepreneurs ("DHE"s) may encounter; the routes by which medical devices (including DHPs) enter the market; product classification; basic elements of FDA pre-market submissions; and, finally, restrictions on marketing and advertising of which DHEs must be aware. We try to provide examples, along the way, of actual digital health products to illustrate different points in the discussion.

[1] https://www.fda.gov/MedicalDevices/DigitalHealth/default.htm, last accessed September 2, 2018.

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Legal Concepts for Regulating Devices

This chapter will deal with statutes, regulations, guidance documents and (indirectly) court opinions. What follows is a very brief description of the legal structure and some definitions used for regulating medical devices.

The Federal Food, Drug, and Cosmetic Act ("FDCA") governs device development, manufacturing, testing, approval and marketing. Its authority is based on "interstate commerce," i.e., the presumption that medical devices move between states and so fall within the federal government's jurisdiction. In addition to its explicit, general, prescriptive requirements, the FDCA also empowers FDA to create much more specific laws through rulemaking. The resultant "rules" or "regulations" can, like provisions within the FDCA itself, be enforced directly by FDA and also through judicial proceedings, almost always with the assistance of the Department of Justics. In the course of these proceedings courts interpret and apply both the rules and the FDCA and create an additional body of interpretive law which will apply both to FDA and industry.

Adulteration and Misbranding

The concepts of "adulteration" and "misbranding" form the backbone of all medical device regulation. A device is "adulterated," for example, if it has been prepared under unhygienic conditions; if it has not been manufactured under appropriate standards and controls; if it fails to perform as intended; or if it requires a pre-market clearance[2] or approval[2] and has none. A device is "misbranded," for example, if its label is false or misleading; if it is misleadingly named; if it lacks adequate directions for use; if it was manufactured in an unregistered establishment; if its advertising is false or misleading; or if it does not bear its required labeling.

Selling or offering for sale an adulterated or misbranded device violates the FDCA. Intent is not required; like a speeding violation, the act alone is sufficient to establish legal culpability. Almost every violation of the FDCA constitutes a criminal misdemeanor and, when committed with intent, a felony. DHEs must be aware of and comply with the FDCA and applicable regulations in order to avoid these and other, purely economic, results.[3] A study of recalls due primarily to software defects occurring from 2011 through 2015 found that 627 software devices (a total of

[2] Discussed below.

[3] FDA very rarely initiates criminal enforcement proceedings. It is far more likely that the agency will demand a product's removal from the market or require a company to change its manufacturing or marketing approach. Any of these can cause the company's revenue to fall, jeopardizing both future growth and future outside investment.

1.4 million individual products) had been recalled with a little over 10% involving high risks.[4]

"Label" Versus "Labeling"

A device's label appears on the device or its packaging, presenting the information required by law and any other information which the law permits manufacturers to add. A device's "labeling" is a broader set of materials. It includes the label and, also, any other material accompanying the sale of the device. This can include the package insert, for example, but also any materials or other information associated with displaying the device or used to procure its sale. A device can be misbranded by virtue of any of its labeling.

Overview of FDA's Organizational Structure

DHEs working with medical devices who are new to FDA-regulated products tend to regard the agency as a monolith. The reality is very different. FDA—part of the U.S. Department of Health and Human Services ("DHHS")—is comprised of six primary centers of expertise: The Center for Food Safety and Applied Nutrition ("CFSAN"); The Center for Drug Evaluation and Research ("CFSAN"); The Center for Devices and Radiological Health ("CDRH"); The Center for Biologics Evaluation and Research ("CBER"); The Center for Veterinary Medicine ("CVM"); and The Center for Tobacco Products ("CTP"). Each Center exhibits both its own character and even its own procedures. Above them all sits the Office of the Commissioner along with the Offices of Foods, Global Regulatory Operations and Medical Products and Tobacco. These offices together coordinate policy and operations agency-wide under the authority of the Commissioner who, in turn, represents the Secretary of DHHS.

In the process of developing a new medical product it's easy to focus on FDA's science mission to the exclusion of the other pillars supporting the agency's work: public policy and law. The work of each Center combines all three. This chapter attempts to place the practicalities of bringing digital health devices to market into the context of that law and policy.

[4] J Ronquillo and D Zuckerman, "Software-Related Recalls of Health Information Technology and Other Medical Devices: Implications for FDA Regulation of Digital Health," *Milbank Quarterly* Vol. 95, Issue 3 (pp. 535–553) (September 12, 2017).

Office of Regulatory Affairs

The Office of Regulatory Affairs ("ORA") operates as FDA's enforcement arm. Traditionally the largest agency component, if not by budget then by numbers of staff, ORA inspects products entering-into the U.S., inspects foreign and domestic medical device facilities and investigates clinical trials and researchers. ORA has very little discretion to make decisions based on the interpretation or analysis of agency policy or law. Instead, it develops the facts necessary for CDRH and the Office of the Commissioner to make those decisions. Consequently, if ORA personnel enter your facility to review your software design history and validation files (regarding, for example, high risk software applications or interpretive imaging applications) ORA's observations are relevant, important and should be respected, but they are not ultimately binding on FDA and cannot alone determine the outcome of your inspection.

Center for Devices and Radiologic Health

CDRH is responsible for regulating medical devices during all stages of their lifecycles. A medical device, under the Federal Food, Drug, and Cosmetic Act, typically is any primarily "mechanical" product which is:

1. Intended to diagnose, cure, mitigate, treat or prevent disease in man or other animals (and operates through physical action); and/or
2. Intended to affect the structure or function of the body of man or other animals primarily without chemical action or metabolism.

The requirement that a device be a "mechanical" product (as opposed to a chemical, a tissue product or a clinical method) can be confusing. Some DHEs are not even aware that their products will be regulated as medical devices because they are not necessarily tangible, "mechanical" items. However, the law interprets products such as software, for example, to be "contrivances" or "other similar or related articles" so FDA can regulate them (Fig. 10.1).

Intended Use

DHEs commit one of their most common errors by approaching new products as if they must first meet some "ideal" of a medical device product in order to be regulated by FDA. Public policy and the law underlying medical device regulation allow the agency to reach much further. To be classified as a medical device, a product—even an electronic or digital product—need only have an "intended use" to diagnose, cure, mitigate, treat, prevent disease or otherwise affect the body's structure or function.

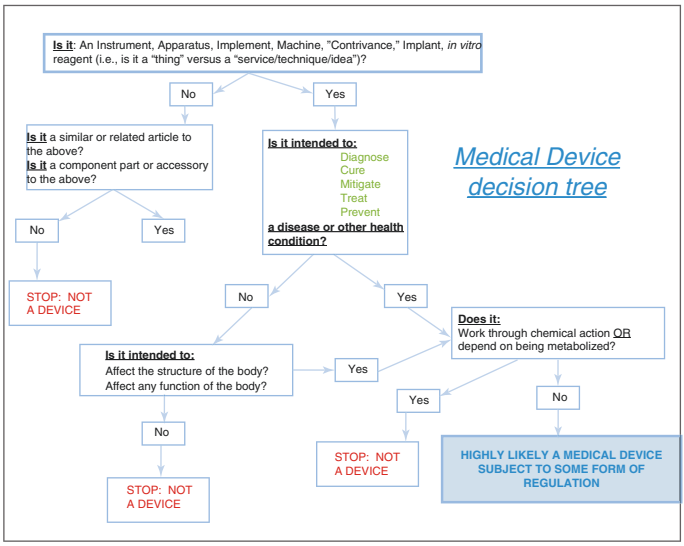

Fig. 10.1 Medical device decision tree

This concept of intended use may be the most important element of the FDCA. It is incredibly flexible and therefore incredibly powerful in allowing FDA to reach new and innovative health products—including, and perhaps even especially due to their unusual nature, digital health products.

Rulemaking Basics

Understanding how the agency develops, drafts, revises and promulgates rules helps to clarify the status and authority of the many different types of agency documents a DHE will face. DHEs must know how to draw distinctions between agency rules and agency guidance.

The easiest way to understand what we mean by a rule is that it is a legal obligation enforceable against private actors under threat of government sanction.[5] Most important new agency documents, in the modern era, are not rules at all. They articulate principles, policies and recommendations which are not mandatory; the agency has no power automatically to sanction industry if they are disregarded. Consequently, for situations in which these documents do not fit well with new products actually being developed and sold, DHEs can (and sometimes should) pursue different paths.

[5] Sanctions take many forms, including but not limited to the seizure, detention or registration revocation of medical devices.

A typical, informal rulemaking procedure[6] requires that FDA drafts a set of regulations. These will be circulated within a variety of offices and functions in the agency and also within DHHS and the White House Office of Management and Budget. Generally they are offered for public comments, which may be submitted by anyone and any entity. Depending on the subject of the rule, combining comments from an entire sector (such as digital health) can give the comments more force and influence FDA (or even Congress). The agency may also hold forums or meetings for public comments which can provide opportunities for more direct engagement. FDA is required by law to consider these comments and offer reasoned responses before it may publish the final, formal rules.

Uses of Guidance, Public Statements, Letters to Industry, and Warning Letters

The rulemaking process described above is extremely vulnerable to delay, complication and politicization. Consequently, guidance documents, statements of policy, letters to industry, "Dear Doctor" letters and Warning Letters have become FDA's favored communication methods for the last two decades or more. None of these are binding even though they may be developed using relatively formal procedures. Guidance documents, for example, typically undergo months of internal and public review as "Draft Guidances." Many (and, recently, most) Draft Guidances never actually become "final." FDA's guidance on "Clinical and Patient Decision Support Software" (December, 2017) is an example of "draft" guidance in the digital health space.

DHEs (or any other medical device developers) should guidance documents as FDA's statements of how it believes—under then-prevailing circumstances—legal compliance can best be achieved. Some final guidance documents, measured against the pace of digital innovation, may quickly become outdated. FDA's guidance on "Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data" was first issued in draft form in 2009 and finalized in 2012, for example. The agency's "General Principles of Software Validation" final guidance, something that should be a fundamental building block for digital health, was issued in 2002. Many industry actors treat guidance documents as if they are binding. FDA knows this and, consequently, will use new guidance documents to prod industry into behaviors the agency would like to see but cannot require.

[6] Strictly speaking there are two types of rulemakings: Formal and informal. Federal agencies in the modern era hardly ever follow formal rulemaking procedures. Because, for example, they involving hearings and the introduction of testimony under very strict procedures, formal rulemakings are incredibly easy to delay by affected industry actors and highly inefficient. Agencies instead prefer to use the "informal" rulemaking procedures briefly described here.

The agency uses public statements and letters to industry similarly. These require primarily internal review only and allow FDA to act (indirectly) and disseminate information more quickly. Warning Letters represent FDA's determination that a company's or individual's conduct violates the FDCA. In addition to putting the recipient on notice, FDA can use Warning Letters to signal to industry more broadly how the agency intends to enforce the law, its priorities and those practices FDA considers clearly illegal. Warning Letters should not be underestimated as valuable sources of information for health product entrepreneurs, including in digital health. For example, before FDA developed guidance on mobile medical applications—and before Congress enacted new law excluding some types of medical software—Warning Letters were important guideposts to how FDA viewed medical software products and might attempt to regulate them.

FDA's Regulatory Classifications and Pathways to Market

Example: When "Medical" Software Isn't "Medical" at All

So far we've discussed only the mechanisms FDA can use to (a) subject products to regulation; and (b) order (or strongly advise) industry to manufacture and market those products in ways the agency believes are necessary to comply with law. But it's equally important to understand that the "science" pillar of FDA's mission—i.e., the technical characteristics of a device, how it works and even what it is intended to do—must sometimes defer to the policy or legal pillars. Certain types of medical software provide perfect examples of this relationship.

Before December, 2016—when Congress enacted a statute entitled "The 21st Century Cures Act"—FDA had established non-binding criteria to determine when software used in providing healthcare services would be regulated as a medical device. However, an entirely new, evolving field for health-oriented software—medical records, healthy lifestyle analytics and reminders, electronic medical references and even basic weight loss recommendation applications—didn't fit the scheme particularly well. So in 2014 FDA also created special guidance directed at the burgeoning field of "mobile medical applications" and, additionally, for medical device data systems (hardware or software products transferring, storing, converting and displaying data from medical devices). These documents were intended to lighten the regulatory burden—within limits—on these products without promulgating new rules.

Within the only 2 years Congress passed the 21st Century Cures Act, exempting most or all of these types of products (21 USC § 360j(o)) from regulation as medical devices. Software for patient records; for providing "healthy habits" tracking, tips and data; for displaying clinical laboratory test results; and even for assisting clinicians in their decision-making may no longer (under most circumstances) be considered medical devices even though they may be intended, at least in theory, to be

used in diagnosing, mitigating and treating health conditions. This provides a good example for DHEs of how rapidly the field evolves, not just because of industry's technical sophistication but also due to overriding changes in law based on policy judgments. It is also a crucial reminder that every product idea must be carefully evaluated from inception in order to identify legal obstacles in its path to market.

Product Classification

The law has recognized medical devices as a distinct category of regulated products for only about 40 years. Up until that time (1976, the year the Medical Device Amendments ("MDA") were passed) they were regulated, when regulated at all, under the legal fiction that they were drugs. In creating a separate structure in order to deal with medical devices, Congress and the agency faced the problem of how to treat all of the devices which had been on the market up until that point in time. The solution, simplified, was to divide devices into two categories: those which were "pre-amendment" and those which were "post-amendment." Pre-amendment devices would continue to be marketed, at least temporarily, as they always had been. Post-amendment devices, on the other hand, could be marketed if they were "substantially equivalent" to existing, pre-amendment devices. The MDA originally required only that manufacturers notify FDA that they had marketed a qualifying device—there would be no pre-market review—and section 510k of the FDCA implemented this "pre-market notification" requirement. It was thought that, over time, FDA would deal wholesale with entire categories of devices as new ones continued to be marketed and old, pre-amendment, devices came up for review.

In 1990 Congress introduced huge changes to this framework by requiring FDA to review medical devices before they went to market. The new law defined all post-amendment devices as "new" and, like drugs, treated them as adulterated if they had not received some form of pre-market review. But the law also provided an escape clause. Manufacturers could demonstrate that their devices actually were not "new" by showing that they were "substantially equivalent" to pre-amendment devices *or other existing, legally marketed devices*.[7] For more complicated devices or devices with more complicated uses, FDA would need to agree with their manufacturers beforehand. The 510k notification—originally just a notice requirement—instead became the triggering event for FDA to determine whether or not the manufacturer's determination of substantial equivalence was sound. This is why medical device developers now speak of new devices as requiring "510ks."

The concept of predicate devices lies at the core of every 510k review. Device developers must select the right predicates because these provide the baseline stan-

[7] Pre-amendment devices or other existing, lawfully marketed medical devices to which the new device will be compared are referred to as "predicate devices" or, simply, "predicates."

dard against which their devices will be measured. FDA recognizes the importance of this selection and provides guidance on the subject.[8] The comparison between the new device and its predicate compares legal and technical evaluations of the new product to the predicate to determine whether they are substantially equivalent:

Scenario 1:

- Do they have the same intended use? *(yes)*
- Do they have the same technological characteristics? *(yes)*

Alternatively, even if they have differing technological characteristics[9]:

Scenario 2:

- Do they still have the same intended use? *(yes)*
- Do the technological characteristics of the new device raise different questions of safety or efficacy? *(no)*
- Does the developer's evidence demonstrate that the new device is at least as safe and effective as the predicate? *(yes)*

FDA will consider new devices falling within either Scenario 1 or Scenario 2 "substantially equivalent" to their predicates and legally marketable under the FDCA.

Classification Dilemmas for Digital Health Products

It's probably obvious that DHPs present problems for this framework, if not least because historically they have tended to have few predicates. Making matters worse, some DHPs regarded as relatively simple by current technological standards can be expected to develop a robust body of predicates only after several generations. Until then these products would, by definition, be "new" medical devices and require FDA's full pre-market review. Furthermore, both consumers and product developers seem to have acclimated to greater sophistication in common, everyday products (e.g., the mobile phone/computer) and services (e.g., web-based tools and applications). So some DHPs, which could qualify as medical devices under the FDCA, can appear from a commonsense viewpoint as if they shouldn't. Treating them as medical devices requires an expenditure of time and resources, both by the agency and by DHEs, out of proportion to their perceived degrees of risk and complication.

[8] E.g., "How to find and effectively use predicate devices," https://www.fda.gov/medicaldevices/deviceregulationandguidance/howtomarketyourdevice/premarketsubmissions/premarketnotification510k/ucm134571.htm, last accessed September 8, 2018. Fortunately FDA is not graded on grammar.

[9] Significant changes in materials, design, energy sources or other physical traits.

"Mobile Medical Applications" (the phrase used by FDA) exemplify this difficulty. FDA struggled with several versions of policy and guidance, over a number of years, attempting to help developers understand whether and how their products might be regulated as medical devices and, if so, what criteria they must meet. The agency also had to distinguish between mobile applications which use their hardware counterparts (e.g., a mobile phone) simply as platforms and those which cause the hardware counterpart to function, itself, as a medical device when the application runs.[10] Congress eventually codified some of FDA's guiding principles directly into the FDCA via the 21st Century Cures Act (mentioned above) formally taking large chunks of common, consumer-facing DHPs out of FDA's jurisdiction entirely and so reconciled scientific, policy and legal conflicts.

Device Classes I, II and III

FDA categorizes all medical device types roughly according to the risks they present, where Class I products theoretically pose the lowest risk and Class III products the greatest, and regulates them accordingly. Categorizing a medical device type is largely a function of two factors: (1) its intended use; and (2) its technical characteristics. This deceptively simple structure provides DHEs extremely powerful opportunities to control the progression (and reception) of their products in the market.

Class I devices, because they are lowest risk, are the easiest (i.e., the least expensive) to get to market. Class III devices, because they usually involve the highest risk, are the most difficult (i.e., often—but not always—the most expensive due to more extensive design and testing requirements) to get to market. Since device classification is essentially the function of the two variables "use" and "characteristics," DHEs can to a large extent control their products' classifications. For example, by promising less for a product—in other words, claiming less complex uses cases and specific health outcomes for it—DHEs can reduce the amount of testing their products require before going to market. This ultimately affects the cost of and time spent in bringing the product to market. DHEs then must weigh these potential cost savings against, potentially, losses in profitability. Take (non-electronic) scalpels as an example: Very broad, general uses (e.g., a device used for cutting tissue) with very limited promises of specific results (e.g., the scalpel cuts) means it is very easy to get to market and risks becoming a commodity item.

Classification therefore necessarily has specific legal and economic consequences for medical device developers. Entrepreneurs, including DHEs, chart their best paths to market by making efficient, opportunity-maximizing decisions regarding intended uses and technical characteristics along the development pathway (Fig. 10.2).

[10] E.g., the "Smart Dongle Blood Glucose Monitoring System," which includes a blood glucose meter, test strips and a mobile platform (in this case the iPhones 4 through 6s Plus) for calculating and displaying results. See https://www.accessdata.fda.gov/cdrh_docs/pdf16/K162382.pdf (last accessed September 9, 2018).

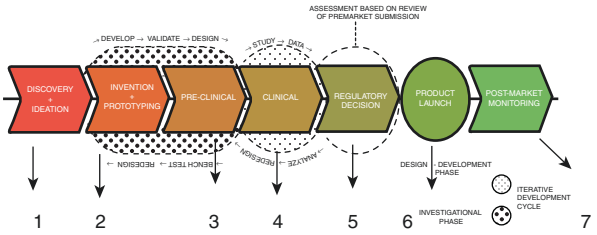

Fig. 10.2 Every stage of medical device development relies on the product's intended use and technical characteristics

Obstacles to marketing can be erected or removed based on DHEs' choices of intended uses and technical characteristics. Often compromises are required in order to avoid FDA's classification decisions from triggering breakdowns at steps 4 and 5, for example when new and different data might suddenly be necessary or the standard of review for the device simply becomes too high for it to pass scrutiny. If this happens a product can get stuck—instead of progressing to step 6 it must re-run step 4 (even, in drastic cases, returning to Step 2)—resulting in more time-to-market and dramatically increased costs. Further venture capitalization may be jeopardized because Step 5 is very often the second, critical point at which DHEs seek additional funding. It is only then that they have a product which is marketable; revenue projections will have become more certain and stable after this point because the product's intended uses and technical characteristics have been established.

A second, indirect consequence of classification is that the market value of a device *tends* to correlate with its level of "riskiness." In the example above we noted that manual scalpels have very broad, general uses and do not over-promise health care outcomes; they are also technologically relatively unsophisticated. They are Class I—they are not terribly risky in that they are relatively easy to produce in large quantities, their performance and specifications can be fairly easily measured, they do not require a lot of clinical study and they tend not to malfunction absent blatant manufacturing failures. On the other hand, products in the "digital health" space—let's take, for example, 3D customized prostheses manufactured using 3D printing systems employing software, scanning and laser fabrication—are generally considered much higher in risk due to their novelty, possible variations in performance and manufacturing, risk of failure and the critical functions they might play within the body. They are, in other words, more complex, more "risky," more costly to produce, harder to get to market and therefore can command a higher price. A DHE makes choices by adjusting the characteristics of his or her product either to (a) "down classify" the device (reducing costs and time to market) or (b) "up classify" the device (potentially increasing returns on investment).

Class I and General Controls

The fundamental point underlying the concept of a "Class I" product is that it is so basic (technically straightforward) and so common (its uses so general and widespread) that it presents very little risk other than the risk of straightforward manufacturing

defects. “Tongue depressors” are another example. Their purposes are simple and do not involve serious injury risks in the ordinary course of use. They are, however, still considered “medical devices.”[11]

While more complicated than a tongue depressor, software to analyze (retrospectively) data collected by a continuous glucose monitor is an example of a DHP which FDA regulates as a Class I medical device.[12] In general, in order to qualify as a Class I medical device, the DHP must not:

1. Be intended to support or sustain life;
2. Be intended to contribute significantly to preventing impairment to life; and
3. Present a “potential unreasonable risk of illness or injury.”

The law specifies a basic set of standards which all medical devices must meet referred-to as “general controls.” Class I devices—unlike Class II and III devices—are bound only to these standards. General controls include, but are not limited to, “good manufacturing practices” (“GMP”s) (discussed below), complete and accurate labeling, device “listing” requirements (discussed below) and, relatively rarely, premarket notification (discussed below).

Class I Exempt Devices

Most Class I medical devices are considered to be of such low risk that, unlike most Class II devices and almost all Class III devices, their developers need not notify FDA before marketing the product. The DHP mentioned at the beginning of this section—analytic software for continuous glucose monitors—is an example of a Class I exempt device. While still subject to most general controls, it is specifically exempted from the premarket notification requirement. DHEs can only be certain about whether their products must meet the pre-notification requirement of the general controls when one of two things happens: (1) either the law (statute or regulation) specifically exempts their type of product; or (2) FDA explicitly states its intention not to prosecute developers who do not pre-notify. It is likely that approximately 10–20% of Class I devices are exempt from the pre-market notification requirement of § 510k of the FDCA. FDA maintains a list of Class I (and II) exempt devices at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/315.cfm.

Class II and “Special Controls”

Class II devices present greater risks than Class I. “Risk”, as discussed here, should be understood in terms of the safety and efficacy concerns accompanying their intended uses and technological characteristics. A Class II device, at least theoretically, requires more regulatory oversight to ensure that it is safe and effective.

[11] 21 CFR § 880.6230.

[12] 21 CFR § 862.2120.

This does not mean that Class II (or Class I or III) devices must be perfectly safe or perfectly effective, i.e., that they must produce the exact effect intended at every instance of use with no adverse events. The legal standard requires that the device present a "reasonable assurance of safety and efficacy."[13] Class II devices achieve this by fulfilling the requirements of "special controls" applicable to their device type and establishing that they are very much like other devices with which FDA (and the market) already has experience. Special controls are measures imposed by law in addition to the general controls applicable to all medical devices. They can, but do not have to, include measures such as (a) performance standards; (b) conformance to recognized standards; (c) post-market surveillance for adverse events/failures in efficacy; (d) specific labeling requirements; and (e) pre-market data requirements.

Special Case: Conformance to Recognized Standards (e.g., ISO Documents)

Recognized industry standards play an important role in medical device development. Standards—for example those developed and adopted by the International Organization for Standards (ISO) or the American National Standards Institute (ANSI)—help FDA reduce its own workload (resulting in quicker reviews). But even more importantly, they simplify device development by incorporating, through regulation, explicit industry standards or performance measurements into "special controls."

DHPs lend themselves particularly well to this approach. A Bluetooth-dependent, noninvasive blood-pressure monitoring system might, for example, show conformance with IEC 80601-2-30 (Requirements for safety and performance of automated, non-invasive sphygmomanometers) and ISO 11073-10407 (Health informatics—personal health device communication, blood pressure monitor). This is a Class II type device[14] which, while not life-saving or life sustaining, must function consistently and accurately. Meeting consensus standards like these assures FDA that the product should function properly and gives the DHE objective criteria against which he or she knows the product will be measured.

FDA currently participates in an effort to develop a unified international approach for risk-classifying "software as a medical device" which also will eventually address some quality and performance characteristics.[15]

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[13] Cite.

[14] 21 CFR § 870.1130.

[15] See "Global Approach to Software as a Medical Device" at https://www.fda.gov/MedicalDevices/DigitalHealth/SoftwareasaMedicalDevice/ucm587925.htm (last accessed September 9, 2018).

Class III

Class III devices theoretically present the most risk. For new DHEs they may also present the greatest conceptual difficulty. The most important point to remember about Class III devices is that, as the FDCA now stands, every device is automatically assigned Class III until demonstrated otherwise to FDA's satisfaction. "Demonstrating otherwise" is the function of the 510k (discussed above), but not every device can.

Conceptually, Class III devices:

1. Support or sustain life;
2. Are of substantial importance in preventing impairment; or
3. Present a potential, unreasonable risk of illness or injury.

Not all new medical devices will necessarily, in actuality, meet any of these three criteria. But the law assumes they will.[16] If a given DHP cannot be demonstrated substantially equivalent to a predicate (or predicates) the DHE must provide sufficient, valid scientific evidence to offer reasonable assurance that the device is safe and effective under the conditions of use presented by its labeling. This requires pre-market approval ("PMA").

PMA requires that a medical device pass the most stringent review even though the outcome of the PMA process should be the same as that for a 510k: reasonable assurance that the device is safe and effective for its intended use. But the two approaches arrive at that point by different routes. In the case of the 510k, the DHE shows substantial equivalence to an existing, legally marketed product which has either itself—or through a daisy chain of previously cleared devices—been demonstrated reasonably safe and effective. In the case of the PMA, the DHE demonstrates reasonable assurance of safety and efficacy by building an evidentiary base from the ground-up.

Types of FDA Submissions

Unless a DHP is Class I Exempt the DHE will have to submit one or more of: (1) an application for an Investigational Device Exemption; (2) a Pre-Market Notification under Section 510k; or (3) an application for Pre-Market Approval. This section reviews, briefly, these three main types of pre-market submissions. We'll start with the Investigational Device Exemption ("IDE") because it can be a necessary precursor to either of the other two.

[16] The failsafe mechanism for situations presenting a disjunction between a product's legally mandated classification of a product and its actual degree of risk is the "De Novo" 510k. See below.

IDEs

Investigational Device Exemptions ("IDEs") allow "significant risk" medical devices which FDA has not cleared or approved to be moved in interstate commerce for the purpose of being used in clinical (i.e., human health care) applications. These almost[17] always attempt to gather data regarding the product's safety and performance in order to allow FDA to conclude, in addition to other types of data, that the device presents a reasonable assurance of safety and effectiveness. An IDE may be required in order to gather data in support of PMAs and 510ks though, as discussed below, IDEs are necessary for 510ks in a much more limited number of instances than for PMAs.

As suggested above, only "significant risk" devices require that FDA approve an IDE before their use in clinical trials. A significant risk device mirrors a Class III device: it can be an implant, a product to support or sustain human life or a product of substantial importance in diagnosing disease, treating disease or preventing health impairment. Nonsignificant risk devices do not require that FDA approve an IDE—the Institutional Review Board overseeing the clinical study exercises a kind of *de facto* IDE approval when it approves the study. However, even nonsignificant risk devices must comply with most of the IDE regulations. Finally, the law also considers that some devices pose so little risk that they are "IDE exempt" and need not comply with any of the IDE regulations.

Time and Costs

Every entrepreneur wants to know how long it will take and how much it will cost to get an IDE. The answer, unsurprisingly, is "it depends." It is difficult to measure the actual amount of time because FDA measures time according to the number of days an IDE is actually under review—periods of time during which sponsors are preparing answers to agency questions, for example, may not count. However, in general, it is probably not unreasonable to expect a decision within 90 "actual" days of submitting an IDE (and sometimes much sooner).

The costs of IDEs really are too variable to estimate. Compiling the submission is not the most expensive element—far more expensive, for example, are designing and conducting one or more studies, successfully moving through IRB review and developing the manufacturing specifications and quality controls for the test devices.

Technical Requirements

The basic elements of an IDE application include the developer's identification; disclosure of prior investigations; an investigational plan; manufacturing information; investigator agreements and patient informed consent documents; the device's

[17] Limited cases of other, legitimate uses for IDEs exist but aren't immediately relevant here, e.g., "compassionate use."

labeling; and the names of the IRB overseeing and institution(s) hosting the clinical trial. A complete IDE application can be several dozens of pages or several hundred, depending on the complexity of the device and the proposed clinical study.

Developers should almost always request a pre-submission conference with FDA, but it is particularly important for first-time IDE submitters. A pre-submission conference offers the opportunity to consult and reach an understanding with FDA about the type of scientific evidence required and the clinical trial design most likely to provide that evidence. "Determination" meetings are less formal, less exacting (in terms of presenting FDA with information) and have less precedential value. "Agreement" meetings, on the other hand, require more detail about the device and will evaluate a clinical protocol. If FDA and the developer reach an agreement a written document will be placed in the administrative record for the device.

Standard for Approval

The default result of submitting an IDE application is approval—in other words, the developer may begin the clinical trial if FDA takes no action on an IDE within a specified time (30 days) after it has been submitted. The agency may also explicitly approve the IDE; it may disapprove the IDE; or it may request further information. The most important substantive reasons upon which FDA bases its disapproval relate to whether the risks to participants outweigh the benefits of the study and the scientific soundness of the study itself. One of the great benefits of the IDE pre-submission meeting is that these two issues can be addressed and taken off the table.

510k Submissions

510ks submissions can run from dozens to several hundreds of pages and, without considering the specific device involved, costs estimates are similarly variable. A fairly simple, straightforward 510k submission (for a Class I device, for example) might—after label and package design, pre-clinical bench testing and compiling the submission—cost around $100,000. A Class II device with clinical trial data requirements could run several hundreds of thousands.[18]

In the late 1990s and early 2000s it was more common for 510ks to move through clearance reviews with a minimum of data, review effort and time. Starting toward the end of the first decade of the 2000s, however, data requirements for and scrutiny of 510ks began to increase to previous levels. While 90 days remains the target time for 510k clearance, 180 calendar days is the more common experience. Almost all 510ks can expect to be cleared within about 12 months. As a general rule of thumb, 6 months (180 days) represents a reasonable approximation of the median clearance time.

[18] Again, clinical testing will be the primary cost driver.

Technical Requirements

510k submissions include the same basic elements as IDEs with the addition of information relevant to determining substantial equivalence: Device name, intended use, device engineering (including specifications, special controls and standards), proposed classification, labeling, predicates and the "510k Summary" which sums-up the argument for why the device is substantially equivalent to an existing, legally marketed device.

Using Clinical Data

Some new devices require performance data beyond engineering performance, sterility, shelf life, software validation, etc. (i.e., beyond the "non-clinical" data). Clinical performance data becomes more important as a device moves further away from precisely replicating the indications for use and technological characteristics of its predicate.

For example, some medical devices can be coupled with software to display and analyze anatomical or physiological data. If a DHE develops new software performing the same diagnostic function as its predicate—but by using a different algorithm—the "technological" differences between the two pieces of software would likely require clinical performance data to support the argument that the new software was as effective as the predicate. In other words, a new question of efficacy would arise because the software relied on a different procedure or set of calculations; while it might be possible to challenge the software using a modeled set of patient data, it could be far more relevant to test the software's functioning with the device under real-world conditions.

"De Novo" 510ks

The "de novo" 510k provides an alternative to the 510k review and the PMA for devices which should receive an automatic Class III designation but which, while novel, can still appropriately be risk-classified by FDA into either Classes I or II. In order to down-classify these devices from automatic Class III into Classes I or II, FDA must determine that those lower classes of devices are subject to enough regulatory controls reasonably to ensure that the new product is safe and effective. Simplified, the de novo 510k is a mechanism by which a developer can declare that—while novel and therefore a Class III device by default—sufficient controls can be applied under either Class I or Class II such that the device can be reviewed by FDA and cleared for marketing under less than a pre-market approval.

Two examples[19] of digital health products which have gone to market using this route are a software/hardware device[20] for home use which (a) measures a patient's breathing patterns and (b) moves the patient's jaw, using a computer-controlled motor, to improve airflow while collecting data and measuring the results; and a software device[21] for detecting significant diabetic retinopathy based on images captured by a fundus camera. FDA had automatically classified the first (apnea) product into Class III because there was no such type of pre-amendment device and there was no post-amendment Class I or Class II predicate device. FDA then reclassified the product under a de novo 510k into Class II and identified as special controls, among others, clinical performance testing of the algorithm, wireless compatibility and electrical safety testing and software verification, validation and hazard analysis. Regarding the second product, rather than requiring a PMA, FDA determined that the product and others of its type—which FDA now defines as "retinal diagnostic software devices"—should be classified as Class II with special controls (among others) of software verification and validation documentation, and clinical performance data for sensitivity, specificity and both positive and negative predictive value.

Premarket Approval

FDA describes premarket approval as "the most stringent type of device marketing application required by FDA. [ ] An approved PMA is, in effect, a private license granting the applicant (or owner) permission to market the device."[22]

Notwithstanding this, PMAs share the same purpose with 510ks—to demonstrate reasonable assurance of safety and efficacy. A Class III product requiring a PMA does this not by showing substantial equivalence to another product but, instead, by building an evidentiary case for safety and efficacy from the ground-up. This is both more time consuming and more expensive and the time-to-market is longer.

Predicting times and costs for PMAs runs into the same difficulties as making predications for 510ks. However, much of the time a PMA can be granted in about

[19] These products are being used only as examples of digital health products recent cleared under de novo 510ks—no endorsement is made or implied and the authors have no affiliations with the companies.

[20] The "MATRx plus" produced by Zephyr Sleep Technologies, Inc. (Calgary, Alberta (Canada)). The company "designs, develops and manufactures medical devices for the diagnosis and treatment of sleep-disordered breathing," https://www.zephyrsleep.com/company/about-us/.

[21] The "IDx-DR" produced by IDx, LLC (Coralville, IA). The company describes itself as "focused on developing clinically-aligned autonomous algorithms that detect disease in medical images," https://www.eyediagnosis.net/.

[22] https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketApprovalPMA/default.htm, last accessed September 8, 2018.

12 months (give or take a couple of months). Given the PMA's more extensive evidentiary requirements—including clinical studies—it would not be unreasonable to expect to spend several hundreds of thousands of dollars along the way.

Technical Requirements

PMA applications are extensive. In addition to the usual items (developer name and address, device name, indications, labeling, etc.) the application will contain detailed analyses of clinical and non-clinical studies including written defenses of their methodologies and conclusions with comparisons to recognized industry best practices and standards. The developer will also have to discuss pre-submission interactions, if any, with FDA and how previously-identified concerns have been addressed. The application must include a table of contents, a bibliography with "copies of key articles," a formal "summary" section, full clinical protocols for each study conducted and a discussion of how and whether FDA guidance recommendations have been followed (and, if not, how the same objectives have been achieved). These represent only a few of the basic elements.

PMAs, because of their complexity, go through three separate review steps of increasing intensity. Each PMA application must first be "accepted" (a review for administrative completeness), then "filed" (a review to assess "the basic adequacy of" the technical elements of the PMA such that it can be substantively reviewed) and finally the actual approval review ("in-depth review") itself. The application can be rejected or be the subject of additional requests for information at any of these steps.

FDA automatically refers almost all PMAs for devices which are first-in-kind to FDA's "Medical Devices Advisory Committee." The Committee is actually 15 mini-committees referred-to as panels and established according to specialty. So, for example, there is a panel for anesthesiology and respiratory therapy devices; a panel for circulatory system devices; a panel for neurological devices; a panel for orthopaedic and rehabilitation devices; and a panel for general and plastic surgical devices, among others. There are no "software" or "digital health products" panels. Instead, DHPs are reviewed by the panel responsible for their intended use(s). The "retinal diagnostic software device" mentioned above, for example, would probably go before the ophthalmic devices panel if it required a PMA.

Outcomes

The PMA has four possible outcomes: (1) an approval order; (2) an "approvable letter"; (3) a "not approvable letter"; and (4) an denial order. Outcomes (1) and (4) represent the agency's final determination—a decision has been made which can be appealed. Outcomes (2) and (3) represent the agency's tentative conclusion that either the application can and will be approved if additional information is provided or, unless the PMA is significantly amended or supplemented, it cannot and will not be approved.

Example

FDA received the PowerLook® Tomo Detection Software[23] device's PMA application in April, 2016 and granted approval in March, 2017.[24] It is used by radiologists while reading GE Senoclaire breast tomosynthesis exams, detecting soft tissue densities in three-dimensional images which can then be integrated with the two-dimensional images on mammography workstations. FDA noted that there was no other computer-assisted concurrent read detection software for radiologists interpreting either two-dimensional mammography or digital breast tomosynthesis.[25]

The company appears, based on FDA's summaries,[26] to have conducted validation testing using an internal database of medical records to compare the software's performance against a human reader. But this product is a good example of how the PMA process can channel companies into far larger investments—attempting to substantiate new performance claims and indications—then they might otherwise undertake were they to follow in the footsteps of predicate devices. Ultimately the company designed a 603 record study which, after filtering, resulted in 240 records being read by physicians both with and without the software. The purpose was to allow the company to demonstrate: (a) that using the software provided results as good as reading images without it; (b) that using the software reduced reading time per image; and (c) that, for marketing purposes, radiologists using the software were better in detecting cancerous lesions.

This last question of marketing—what can be said about a product and what is required in order to say it—leads to the final topic in this chapter.

Marketing and Advertising

Every developer wants, at the end of the process, to bring his or her product to market so that it can be sold to and used by health care providers. Advancing patient health while offering funders returns on their investments go hand-in-hand in the world of commercial medical device development. Entrepreneurs, in order to accomplish these intertwined objectives, must tell potential purchasers that the device exists and describe its capabilities. The questions of when, how and (for specific performance claims) even whether this can be done form the subjects of this section.

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[23] This product is being used only as an example of a digital health product approved through the PMA process—no endorsement is made or implied and the authors have no affiliations with the company. PowerLook® Tomo Detection Software is a product of ICAD Inc. of Nashua, N.H.

[24] See https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160009, last accessed September 8, 2018, for basic information and links to FDA's summary of approval.

[25] FDA did not refer the product to an advisory panel (for radiological devices) because the panel had already reviewed duplicate information.

[26] See n. 22, above.

Entrepreneurs tend to be impatient people. Arguably this may be even more true for digital health entrepreneurs. The digital world moves at such a rapid pace, and innovation can take such sudden and surprisingly large leaps, that these individuals and their investors demand that products to move to market, gain acceptance and generate ROI as quickly as possible. Those expectations can be further heightened when the players are new to the field of medical device development. Consequently digital health entrepreneurs can face both enormous internal desires and external pressures aggressively to market and advertise their products. These impulses can lead to marketing and advertising activities which are legally impermissible if not properly planned and understood.

Regulators' Jurisdictions

FDA is not the only regulator involved. FDA has jurisdiction over the products themselves and their manufacturers. Selling or offering to sell a misbranded or adulterated medical device in interstate commerce violates the FDCA, exposing the manufacturer to civil and criminal penalties.

However, DHHS arguably plays an even more important role through its enforcement of statutes related to federal health care programs, e.g., Medicare and Medicaid. In the simplest legal terms possible, the federal government considers that it has been defrauded if it reimburses providers under Medicare or Medicaid for misbranded or adulterated medical devices. In fact the government need not actually have paid for the products; it's enough that a "false claim" (a claim for such a product) has been submitted. These violations fall under the jurisdiction of DHHS and are prosecuted by the U.S. Department of Justice.

Consistency with Labeling and Pathway

Every device (digital or not) may only be promoted consistent with its labeling. The FDA- cleared or approved indications and claims for the device provide the outermost boundaries of what can be said. Exceed those boundaries and the device is misbranded (and adulterated); ask a federal program to pay for it and risk liability under the False Claims Act.

Suppose we imagine a hypothetical product—a vertebral spacer—which we will design and fabricate using detailed, three-dimensional analyses of medical images so that it fits the precise contours of a patient's vertebrae. We believe that the product will help orthopedists deliver better patient care and that it will produce better results, and we plan on making these points in our product's labelling and marketing. Let's assume that, as a vertebral spacer, we believe we can get the product cleared under a 510k but that we will need clinical performance data because (a)

we're using our new, 3D modeling software; and (b) we want to make "comparative superiority" claims to existing vertebral spacers in Class II.

We design and execute a study under an IDE, first, to demonstrate that the product can be made consistently and reliably and will perform at least as well as existing spacers. Assuming that's true, the study also looks at whether the customized spacers will allow orthopedists to complete their surgeries faster (representing savings for physicians and reduced risks to patients). Finally, we measure whether the spacers produce better long-term results because they better integrate, over time, into the patient's vertebral column.

We complete our study and find that the product is at least as good as existing vertebral fixation devices. We also find that physicians using the product are faster in completing surgeries and, as a result, patients spend a clinically significant lower amount of time under anesthetic. Unfortunately, however, our evidence is inconclusive about whether the spacers produce better long term results. Patients using our spacer ultimately do no better or worse over the long term than patients using existing spacers. So FDA approves our product without that claim.

Consistency with Labeling

FDA's decision does not mean that our product can't, actually, improve long-term patient outcomes. It also does not mean that there is no evidence that our product can't improve outcomes (perhaps we have an earlier, pilot study, demonstrating that it does). All it means is that, at this time and under this 510k, FDA cannot conclude that our product produces superior long-term outcomes. Consequently, FDA clears it only as a device for intervertebral body fusion also intended to reduce surgical time. The practical effect is that we cannot now go to the market and say that our product is for improving long-term patient outcomes. A suggestion that orthopedists should buy and use the product for that purpose would demonstrate our intent that the product be used for a purpose for which it has not been cleared—an "off-label" use. That would render the product misbranded and adulterated, violating the FDCA and requirements of federal healthcare programs.

Consistency with Pathway

The distinction between 510ks and PMAs now also affects our marketing. Products brought to market under 510ks have not been determined to be safe and effective for their indications. The products instead have only been found to be substantially equivalent to some other product with the same/similar characteristics and indications. Because our presentation of the product must not be false or misleading, any implication that our product has been determined safely and effectively to achieve intervertebral body fusion with reduced surgical times will be false and/or

misleading, thereby misbranding the product even if we never mention an ability to improve long-term patient outcomes.

Dissemination of Scientific Information Related to Unapproved/ Uncleared Uses

Finally, suppose that an independent group of investigators conducts their own study and finds evidence of improved outcomes using our spacers. Can we provide that information to third parties—not, we say, in order to drive sales—but because it is potentially useful data, developed by people outside the company, which may be of interest in the market?

FDA's view is that all information from a manufacturer is promotional unless it is "legitimate scientific exchange." The first question here, particularly where off-label information is involved, is whether it is published in scientific or medical publications. FDA issued in 2014 a guidance document on this point entitled "Distributing Scientific and Medical Publications on Unapproved New Uses—Recommended Practices."[27] It lays out extremely detailed prescriptions for using scientific and medical publications including, for example, that they be peer reviewed and that complete, unabridged copies are provided.[28] Returning to our hypothetical, we also should not unilaterally "push" that material out to the market—doing so provides evidence of our intent that the product be used to achieve a purpose (superior long-term outcomes) for which it has not been cleared or approved. We can only safely provide the material in response to unsolicited requests; the material should only be "pulled" from us.

Commentators vigorously debate how much power FDA has to regulate promotional activity when, under U.S. Supreme Court precedent, the First Amendment protects commercial speech. Expert consensus appears to be that FDA's ability to pursue enforcement action against companies only engaged in truthful, non-misleading speech—and not pursuing other, "non-communicative" off-label promotional practices—gradually is contracting. Some federal courts have adopted a vigorous approach to enforcing commercial free speech rights which would permit any truthful, non-misleading communications regarding off-label uses. However, it's probably not commercially advisable for a DHE to offer him- or herself as a test case.

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[27] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM387652.pdf (last accessed September 9, 2018).

[28] See n.25, e.g., "[a] scientific or medical journal article that includes information on unapproved uses and is distributed by manufacturers should first have been published by an organization that has an editorial board that uses experts who have demonstrated expertise in the subject of the article under review by the organization. Experts should be independent of the organization and should review and objectively select, reject, or provide comments about proposed articles."

"Appropriate" Promotional Materials

Manufacturers will of course disseminate promotional material. These materials must fulfill basic conditions. For example, unless they are unsolicited "scientific information," the materials should only discuss on-label uses. They also may not be "false or misleading in any particular." For example, they may not make misleading statements about other products; they cannot misleadingly manipulate data, even if related to on-label uses; and they may not omit or minimize serious risks associated with using the product.

Over the last several years there appears, at least anecdotally, to have been a significant increase in FDA's use of open-ended letters of inquiry related to promotional activity as opposed to outright prosecutions. These can ask companies for time-consuming and extensive document productions or responses to questions. Even when it does not result in enforcement an FDA inquiry can be time consuming and expensive. State law enforcement has also become increasingly active. Off-label promotion cases have proven lucrative for states and the number of single-state enforcement actions (actions brought in the name of one state) has been increasing. Some data suggests that the number of state settlements actually exceeds the number of federal settlements, on an annual basis, over the last 10 years.

Conclusion

The goal of this chapter has been to provide a brief introduction to the law's and FDA's organizational structure for medical device regulation; the types of information FDA provides through rules and recommendations and whether they are mandatory; considerations relevant to bringing new products to market; the basic administrative processes of bringing new products to market; and, finally, the kinds of restrictions on—and risks of—marketing and advertising new products once they are on the market. These topics are extremely complex and have justified entire books by themselves but, hopefully, enough basic material has been presented here to allow digital health entrepreneurs to get an overall sense of the landscape with the many opportunities and pitfalls it presents.

Chapter 11
Getting Reimbursed for Digital Health

David D. Davis

Overview

Reimbursement in the digital health world can come from two types of payers, the individual user or a third party, for instance an insurance company or a Government program, i.e. Medicare. Typically, we do not think of the individual user when discussing reimbursement but, in this case it is relevant. Third party payers have been hesitant to reimburse for digital health in the past however we are on the cusp of change.

Reimbursement within digital health is a two-edged sword, as entrepreneurs want the freedom to build and create, payment by a third party always creates more regulations, rules and/or medical policies that could prohibit or slow this creation. There are many believers within digital health that believe this industry does not need third party reimbursement to survive. However, there are many that believe the only way to forward their technology and receive the reimbursement they are looking for will only come from third party payers.

Digital health faces challenges to reimbursement from within the reimbursement framework that is built today. So much of our reimbursement system is built on the role the provider plays within the procedure or service. Digital Health is built to disrupt this model but at the same time is asking to be rewarded for the disruption. In a pay for performance system where the provider is rewarded for performing tasks, what task does the physician perform in order to be reimbursed in the digital health world? Implantable sensors where the physician is implanting a device within the patient fits nicely within todays reimbursement frame work or a remote monitoring sensor where the physician has data to be reviewed on a daily, monthly or quarterly basis is another area where this plays nice within today's framework.

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An external sensor where there is no feedback loop to the physician and the physician has no role with the technology is not one that fits today's reimbursement framework. I think it is important to point out that we are seeing a major change within digital health as we speak. Medicare is now proposing to pay for digital health and remote monitoring services they have not paid for in the past. In the most recent CPT meeting, almost 20% of all new codes coming through the CPT process can be classified as having a digital health component. We are on the cusp of digital health becoming mainstream.

Will your product be used and sold as a medical device or as a commercial product? This decision should be decided early in the development process. These are two distinct paths that are difficult to change course once your strategy has been developed. Once your device shows up at the local drugstore for a $10 price point, no insurance company will pay you over this amount as a medical device. Think early on in the development process, will this be a medical device or a consumer product.

Introduction to Medicare

Medicare is the primary payer in the US for medical technologies. Medicare's payment system is well documented and updated annually at its website, www.cms.gov. Many of the commercial insurers have mimicked or adopted many of its payment policies in their decisions as well. Due to this fact, Medicare is the gold standard when discussing reimbursement.

Medicare is the federal health insurance program for:

- People who are 65 or older
- Certain younger people with disabilities
- People with End-Stage Renal Disease (permanent kidney failure requiring dialysis or a transplant, sometimes called ESRD)

The different parts of Medicare help cover specific services:

Medicare Part A (Hospital Insurance):

Part A covers inpatient hospital stays, care in a skilled nursing facility, hospice care, and some home health care.

Medicare Part B (Medical Insurance):

Part B covers certain doctors' services, outpatient care, medical supplies, and preventive services.

Medicare Part C (Medicare Advantage Plans):

A type of Medicare health plan offered by a private company that contracts with Medicare.

Medicare Advantage Plans provide all Part A and Part B benefits.

Medicare Advantage Plans include:

- Health Maintenance Organizations
- Preferred Provider Organizations

- Private Fee-for-Service Plans
- Special Needs Plans
- Medicare Medical Savings Account Plans

Medicare Part D (prescription drug coverage)
Part D adds prescription drug coverage to:

- Original Medicare
- Some Medicare Cost Plans
- Some Medicare Private-Fee-for-Service Plans
- Medicare Medical Savings Account Plans

These plans are offered by insurance companies and other private companies approved by Medicare. Medicare Advantage Plans may also offer prescription drug coverage that follows the same rules as Medicare Prescription Drug Plans.[1]

Commercial Payers

Private medical health insurance within the US. Commercial health insurers can be publicly traded companies as well as non-profit. Examples include Blue Cross Blue Shield, Aetna, United Healthcare.

What Is Reimbursement?

Reimbursement for medical services is typically defined as any third party that pays the provider. Reimbursement has three main aspects, coding, coverage and payment, without one of these components it is impossible to have reimbursement. For example, a three legged stool needs all three legs to work appropriately to support the top of the stool, reimbursement is exactly like the stool without one of its legs it will not be supported and you will not have reimbursement.

Coding

The transmission of services from the provider to the payer is performed by using a coding system. Coding is all about telling a story to the insurer through the coding systems. Basically, there are two types of codes, procedure codes or what service the physician is performing and diagnosis codes, why did the patient come in for the

[1] Centers for Medicare and Medicaid Services (2018) Medicare Consumer Information. https://www.medicare.gov/sign-up-change-plans/decide-how-to-get-medicare/whats-medicare/what-is-medicare.html, Accessed 1 Aug 2018.

service. When you place what and why together, you are telling the story through codes. This system is called HCPCS (hick-picks) or the Healthcare Common Procedural Coding System. The same legislation that created HIPAA (Health Insurance Portability and Accountability Act of 1996) also formally cemented our code sets. Prior to HIPAA, many insurance companies created their own codes, this created a nightmare situation, as many providers were not sure what code to choose for what insurance company. The code sets today classify medical diagnoses, procedures, diagnostic tests, treatments, equipment and supplies. Each service or treatment is identified by a unique code, this code is then placed on a billing form and sent electronically to the insurance company.

CPT

CPT stands for Current Procedural Terminology. This coding manual was created and is maintained with annual updates by the American Medical Association. The CPT provides procedural codes that are performed by a licensed medical professional.

Category 1 CPT codes describe proven technologies that are FDA approved and available in the market place today.

Category 2 CPT codes describe well established measurements that are supported by medical societies and/or national guidelines as well as evidence based measurements.

Category 3 CPT codes are procedures or services that are currently or recently performed in humans.

ICD-10

ICD-10 stands for International Classifications of Diseases, 10th Edition. The book is updated annually and is maintained by the World Health Organization. This book has two distinct parts, CM (clinical modifications) these are diagnostic codes. PCS (Procedural Coding System) these are inpatient procedure codes.

Physician Coding

Physicians are always paid and coded separately. If a physician performs a service in an office that is privately owned or in the hospital setting they will code the exact same way and expect to receive a separate payment for their services. The physician will code a CPT code that will describe the service or procedure and an ICD-10-CM code which will describe the diagnosis of the patient.

Table 11.1 Coding system by place of service

Place of service	CPT	ICD-10-CM	ICD-10-PCS
Physician service	X	X	
Hospital inpatient		X	X
Hospital outpatient	X	X	

Hospital Coding

Before choosing the correct code in a hospital setting, one must choose if the patient is an inpatient or an outpatient. Historically, the provider decided if this patient was likely to stay in the hospital for greater than 24 h. Medicare changed this rule and instituted a "2 Midnight Rule". Now, if a patient is in the hospital for 2 midnights or more this patient is now an inpatient. Patients that are in the hospital for less than 2 midnights are considered outpatient. Table 11.1 illustrates the coding changes between an inpatient and an outpatient.

Coding Challenges Within Digital Health

One of the issues with Digital Health and the coding system is first trying to find where it fits. If you think of a wearable sensor that displays information to a mobile device so the patient can take action or can track activity you see that the physician is left out of the picture. Therefore, there is nothing to code and nothing to reimburse. However, if the design of the device was to keep the physician in the loop and all of the information was sent to his office, via email, then we have a physician activity which can now be reimbursed. Sensors that are easily placed on the outside of the body by a nurse that do not require a physician may not receive a code for the placement of a sensor. However, a sensor that is placed under the skin may receive a CPT code. Digital Health entrepreneurs should always design products with the physician in mind if reimbursement is desired.

Coverage

Insurance coverage is not the same as coverage in the reimbursement world. We are assuming, that each patient has some sort of insurance coverage. Reimbursement coverage would be defined as, the act of the payer recognizing the medical services of the provider as appropriate within the medical policy of the insured. One important point to remember, FDA coverage does not equal CMS or commercial insurance coverage. FDA coverage does not automatically mean you will receive CMS or commercial insurance coverage.

Medicare Coverage

> "Medicare coverage is limited to items and services that are reasonable and necessary for the diagnosis or treatment of an illness or injury (and within the scope of a Medicare benefit category). National coverage determinations (NCDs) are made through an evidence-based process, with opportunities for public participation. In some cases, CMS' own research is supplemented by an outside technology assessment and/or consultation with the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC). In the absence of a national coverage policy, an item or service may be covered at the discretion of the Medicare contractors based on a local coverage determination (LCD)."[2]

The Social Security Act of 1965 created what is known today as Medicare, within the act Congress authorized Medicare to pay for services that meet the criteria of "medically necessary and reasonable". This standard was determined by the physician performing the service. While this standard is still the overall theme of Medicare, legislation has been created that allows Medicare to determine "medically reasonable and necessary" by examining the services more closely and using outside sources to assist as necessary.

National Coverage Determination National Coverage Determinations are made through an evidence-based process, with opportunities for public participation.[3] Any manufacturer or entity can request an NCD through a formal request to the CMS. The downside risk of using this process is if the device or service in question receives a national non-coverage decision then the product or service will not be covered by Medicare and possibly no other insurer as well. All National Coverage Decisions can be found on the CMS website.

Local Coverage Decision In the absence of a NCD, each local Medicare administrative contractor (MAC), may cover services at their discretion. Medicare is flexible with these coverage decisions since it is known that all medical decisions may vary by geography. The downside for applying for an LCD is much less than an NCD. A denial at the local level will not allow you to serve beneficiaries within that region until you can show better evidence. A negative response at one MAC will not carry over to the next MAC. One would still be allowed to apply at another region. A positive response would only apply in the region that it was accepted this would not be a nationwide acceptance. All local coverage decisions can be found on the CMS website.

MAC Medicare Administrative Contractors are commercial health insurers that have been awarded a geographic jurisdiction process to process claims on behalf of Medicare. The Medical Directors at these MAC's will be the gatekeepers to the

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[2] Centers for Medicare and Medicaid Services (2018) Medicare Coverage Determination Process. https://www.cms.gov/Medicare/Coverage/DeterminationProcess/index.html, Accessed 1 Aug 2018.

[3] Centers for Medicare and Medicaid Services (2018) How to Request an NCD. https://www.cms.gov/Medicare/Coverage/DeterminationProcess/howtorequestanNCD.html, Accessed 1 Aug 2018.

local coverage decisions. Currently, there are 12 MAC's that process Part A and Part B claims.

Commercial Payers

Commercial payers tend to follow Medicare on coverage decisions. A positive coverage decision by Medicare will most likely result in a positive coverage decision for commercial payers. Commercial payers can and should be involved with your digital health device early on in development. Commercial payers have more leniency and are not bound to legislation that may inhibit Medicare covering your digital health service. Commercial payers may be the only coverage you are trying to obtain for your service if you are targeting pediatrics or obstetrical services. There are many examples of collaborations between commercial payers and digital health today and this number will only grow exponentially into the future.

Coverage Challenges to Digital Health

Digital health services primary challenge when working on coverage will be the high hurdle that has been set by the Medicare program. This is no different than with any other medical device and is not unique to the digital health platform. Proving that your platform works and having the data to substantiate claims is the best way to overcome any coverage challenge.

Payment

A specific amount of funds being transferred from the payer and the patient to the provider to perform a unique medical service, procedure, or test. The patient, in most cases, will owe a copayment for the service. This can be important as well because if the copayment is too high this can limit uptake of the digital health service.

Medicare Payment

Medicare has many different payment structures that have been developed to determine the appropriate price to pay physicians and hospitals. Understanding the basics of these payment systems will assist you in developing a reimbursement strategy for your digital health platform. The payment structures that we will cover are for the

following places of service: physician facility payment, physician non-facility payment, hospital inpatient, and hospital outpatient.

Physician Payment

Physicians are paid within the rules of the Physician Fee Schedule (PFS). The PFS is updated on a quarterly basis. The physician fee schedule is based on RBRVS or (Resource Based Relative Value System), this system is designed to pay the appropriate amount for the resources used during the procedure or service. There are three components used: Physician work is defined as the skill, work and effort required to complete a procedure, practice expense (office resources utilized during the procedure or service), Professional Liability Insurance. Each service is relative to another, for example you would expect an open heart procedure to pay more than a cardiac catheterization.

Physicians can perform services within their offices where they will utilize and pay for the resources used to complete the procedure, however, this is not the same at the hospital. The hospital will pay for the equipment, utilities, and the building, these are called facility expenses. Medicare does not want to pay the physician for these expenses they are not incurring. In the PFS, these are broken out into two categories, facility and non-facility. The facility payment is the payment the physician will receive when they are performing services at the hospital. Non-facility payments will be paid when the physician is performing services within their office setting.

Hospital Inpatient Payment

Hospital payment is based off of a rate per discharge. The system Medicare uses is called the Medicare Severity-Diagnosis Related Group or MS-DRG. There is only one MS-DRG per discharge. The hospital sends to Medicare all of the ICD codes mentioned in the previous section. Medicare then uses a grouper software that will combine all of the diagnoses and procedures that were performed during the hospitalization and it will group this into one MS-DRG that will be paid to the hospital. The hospital does not choose a MS-DRG to send to Medicare, this is a common misnomer within the industry.

Hospital Outpatient Payment

Hospital Outpatient Payment is paid by APC or Ambulatory Payment Classification. This system is based off of CPT codes, as previously mentioned. Each CPT is placed into an APC category and that is the amount that Medicare will pay. There are multiple CPT codes placed into APC's. Medicare will pay for multiple APC's but these services will be reduced at 50% after the most expensive APC is paid.

Payment Challenges to Digital Health

If your digital health service is a disruptor and completely eliminates the physician or reduces resources used by the physician then within the current RBRVS system one can expect a lower payment. Our current payment systems are not tied to the amount of savings that you are attempting to deliver to the system. If you have an implantable that can performed in an office setting and paid as a non-facility payment then you will be creating a new procedure in the office for the physician and this is looked upon favorably by the physician community.

In the hospital setting, since the hospital is paid on a MS-DRG it would be beneficial if you can lower the cost of the procedure or create a savings to an existing procedure. If your service adds hospital costs to a procedure this will likely be a tough sell to hospitals.

The current payment system is not favorable to stand alone digital health services today. This is one reason the large medical device companies have all embraced digital health with an implantable device. This way the service can be paid appropriately and it will fit nicer into the payment schema used today. For example, each pacemaker/ICD today is sold with a remote monitoring component. The remote monitoring hardware is bundled into the cost of the implantable device. Once the implant is performed the hardware is then sent to the patient's house, where the device will be monitored for appropriate battery usage, any events that may have occurred, and heart failure symptoms. This is sent to the physician's office for review and the physician is allowed to bill for monitoring of the device and the patient. Another example of this would be continuous glucose monitoring, the patient is implanted with a sensor that will allow them to monitor glucose. The physician is also sent a report and the physician can bill for monitoring the device and patient. These are good examples of keeping the physician within the loop of your digital health platform.

Now that we understand all of the reimbursement concepts and the major players within the ecosystem it is time to put this all together and see how it will affect Digital Health and specifically your company's product or service. Next, we will see if we can appropriately build a strategy around Coding, Coverage and Payment to achieve reimbursement for digital health.

Creating Your Strategy

Think About Reimbursement Early

Most entrepreneurs and medical device executives always consider FDA qualifications and will set out an FDA strategy while ignoring reimbursement. It is rare for executives to plot out a reimbursement strategy early although it is just as important as the FDA strategy. Remember, if your service was considered as a 510(k) then it is similar in nature to the predicate device and most likely will receive the same

reimbursement. It is imperative to always start and plan the reimbursement strategy at the same time as the FDA strategy. Start early! Too many devices have been shelved because they could not obtain reimbursement after receiving FDA clearance. If you are thinking about the reimbursement strategy after FDA clearance, it is too late.

Talk to the Payers

There are many private payers today interested in working with digital health partners. Many private payers see the savings that are being produced from these existing digital health initiatives and they want to participate as well. Set appointments with the medical directors to discuss your new technology and to discuss the benefits the payer will experience with your product or service. During these meetings with payers find out what level of evidence they would like to see for your service to obtain coverage through their system.

Clinical Trials

First, as you build your clinical trial for FDA approval always include as many elements of economic data as possible. This data will serve many purposes but we will want to build a cost effectiveness story to include for our discussions with the payers. Since we are collecting clinical data is not very difficult to include costs, reimbursements, quality of life measures, etc. All of these measures are appropriate for future white papers and health economic studies which all can support reimbursement of the data health service. For some reason, if you do not have to complete a clinical trial for FDA purposes, we will still need these measures mentioned above for our discussion with payers. Find an appropriate way to collect these measures as early as possible.

Creating Appropriate Codes for Your Service

First, you will need to decide if there are any appropriate codes that will fit your technology today. If you find a code that describes your service and you feel this may be a fit for your product, you will need to call the specialty society that your technology would fall under and ask them to verify the code for your technology. A written verification will be needed so your customers will feel comfortable selecting the code and they may want to verify with the specialty society as well. Also check the diagnosis/procedure codes in ICD-10, are they specified enough to match your technology. ICD-10 codes are much easier to obtain than CPT codes.

If your digital health service is not described by a code today then you will need to fill out a CPT application for your service. You will have two choices that we described earlier in the chapter, a Category 1 code or a Category 3 code. In order to apply for a Category 1 code, we must have the following:

- All devices necessary for performance of the procedure of service have received FDA clearance or approval when such is required for performance of the procedure or service.
- The procedure or service is performed by many physicians or other qualified health care professionals across the United States.
- The procedure or service is performed with frequency consistent with the intended clinical use (i.e., a service for a common condition should have high volume).
- The procedure or service is consistent with current medical practice.
- The clinical efficacy of the procedure or service is documented in literature that meets the requirements set forth in the CPT code-change application.

The following criteria are used by the CPT Advisory Committee and the CPT Editorial Panel for evaluating Category III code applications:

- The procedure or service is currently or recently performed in humans AND

At least one of the following additional criteria has been met:

- The application is supported by at least 1 CPT or HCPAC Advisor representing practitioners who would use this procedure or service (or)
- The actual or potential clinical efficacy of the specific procedure or service is supported by peer reviewed literature which is available in English for examination by the CPT Editorial Panel (or)
- There is:
- At least 1 Institutional Review Board approved protocol of a study of the procedure or service being performed
- A description of a current and ongoing United States trial outlining the efficacy of the procedure or service or
- Other evidence of evolving clinical utilization

Which would you choose?

A CPT code takes approximately 2 years to obtain depending on when your application was received.

If the decision is made to apply for a Category 3 code, Medicare will automatically issue a non-coverage decision at the local level. This will force us into individual conversations for coverage at the local level. A service cannot move from Category 3 to a Category 1 until all of the criteria are satisfied for a Category 1 code.

As you can see, in some instances it may better to wait and apply for a Category 1 code instead of choosing a Category 3 and being issued non-coverage decisions which could be difficult to overturn with no data and damage your reimbursement chances for longer than 3 years. This is an important choice to make within your strategy.

Once we have a CPT 1 code, the AMA and CMS then take the code through the RUC (RVS Update Committee) process and apply the appropriate resources to the CPT code so it will have a payment amount. Category 3 codes have no payment attached and are not involved in the RUC process.

Obtaining Coverage for Your Service

Coverage strategy first requires research. The first task you want to tackle is to review coverage for Medicare and the top 20 commercial payers in the US. Identify the policies for services that are similar to yours. Place the findings in a spreadsheet so that they are easy to compare. Some questions that will need to be answered within the course of this research:

- Will your service be considered as a fit for an existing medical policy?
- Is there a similar service that has received a negative medical policy? If so, how can you highlight the differences in your technology so it will not be viewed in the same manner as the negative policy.
- What is the gold standard today that is used for the same diagnosis?

Coverage research is also a good opportunity to see how the payers are recommending coding of a service. All of the appropriate CPT/ICD-10 codes will be included in the coverage policy so if you are unsure about which codes to pick for a service this can always be used as a hint.

Once your research is complete you may need to take action if your service does not have a medical policy. You will want to create a roadmap. Here are some possible questions to assist in your coverage roadmap.

- What does success look like?
- Which payers should we contact first?
- Large or small commercial payers?
- Which geography do we want to approach first?
- Which Key Opinion Leader do we want to use to assist?
- Are there patient support groups that can be tapped into for advocates?
- Are there local TV or radio stations that may want to report the story of this new digital health service?

Next put your roadmap into action, one of your first steps undoubtedly will be to contact the payers. No matter what demographic you are serving I would recommend approaching commercial payers first. Research the medical directors of the commercial payers and try to contact them individually and schedule an appointment to review your technology. Be prepared with clinical data, health economic benefits, society benefits and any argument that you will be able to make that shows your device is better than the gold standard today. Also, you will want to be prepared to share what other payers may be paying for your service as well. Whenever

possible, use an advocate to tell the story for you, telling the story yourself can seem self-serving and not helping the greater good of the community.

Physicians using your product that are considered Key Opinion Leaders (KOL) in your field will make excellent advocates. Insurance executives want to please the physicians that are under contract with the insurance company. Many of these KOL's will have knowledge on who to contact and may already have a professional relationship with this individual. Use the KOL to explain why he wants to use your service, the benefits that he is seeing in his patients, what is the defined patient population that he uses to.

Patients can be used as an advocate for your procedure or service. If a patient is using a service and it has been denied by the insurance company, use the patient's appeals to get in front of the medical directors. First, you will need to make sure you or your company representatives have correct HIPAA forms in place to share health data. Be in contact with your physician offices to see if your service is being paid or denied by the insurance company. If there are denials taking place, the patients "explanation of benefits" will explain how to correctly appeal the claim. Make sure the claim is getting appealed by the physician's office. This allows your technology to be reviewed by more senior personnel each time within the insurance company. This is an excellent way to prove that your service is working and should be used on more patients.

Coverage can take many years to be successful. A best case timeframe will be approximately 1 year. There are many great technologies that have been shelved due to lack of coverage. Most of these technologies, the entrepreneur did not have a reimbursement plan and started working on reimbursement after FDA approvals. You may be wondering, if I have a CPT code doesn't that guarantee coverage? The answer is no. There are many medical devices/services in use today that do not have coverage but have been successful in obtaining a CPT code.

Payment

Payment can be the afterthought in this process since the data will prove the correct price for your product. Medicare will use the submitted data for the claims on its patients to set the payment for the digital health service. The data that was submitted during a clinical trial for instance will be used to determine the payment. Therefore, if you are giving away your service for free or at a reduced charge to collect data this could negatively affect the payment. Always attempt to receive full payment for your service before payment is finalized within the reimbursement system. Once payment has been established it is difficult to raise. Consider the negative effects of discounting before making the business decision to discount to see if the risk outweighs the benefit. Payment should never be the primary driver of the price of your product or service. Always price your product to the value that it brings to the marketplace and try to increase payment, if possible.

Conclusion

Building the key reimbursement elements for any service is not easy but it is rewarding to know that your service can now be utilized by patients and paid for by the insurer. Coding, coverage and payment should be thought of for any service that is demanding or needing reimbursement from commercial or government payers. Remember to develop your reimbursement strategy early and update as necessary as you move along the reimbursement pathway. Always find a way to introduce a payer to your technology, too many entrepreneurs are hesitant to share the technology with the payer community. Sharing your story can lead to many opportunities to increase your chances of reimbursement success.

Chapter 12
Legal Environment of Digital Health: Rules, Regulations and Laws That Govern Digital Health Business Design and Ownership

Jonathan A. Mintz

Introduction

The risks to all involved in digital health entrepreneurship are plentiful, limited only by one's imagination. They include, but are not limited to: product liability, breach of contract, director and/or officer liability, personal injury, personal guarantees, trademark and copyright infringement, unfair business practices, regulatory risks, etc. In the U.S., these risks often manifest themselves in civil litigation, with a significant risk of a large jury verdict.

Unlike most common law countries such as the U.K. and other Crown Dependencies, the U.S. gives potential plaintiffs easy access to the courts in two significant ways: (1) Contingency fees, which permit lawyers to accept cases with little out of pocket cost to the plaintiff (typically only the nominal filing fees required to file a complaint); and (2) No "loser pays" consequence for unsuccessful plaintiffs. In most common law jurisdictions other than the United States, the loser in litigation must pay the winner's costs, including legal fees, which is a significant deterrent to bringing frivolous litigation. Thus, there is little or no financial deterrent to file a lawsuit, and yet it costs tens of thousands or even hundreds of thousands of dollars for the defendant get out of a lawsuit—even where that suit has no merit!

Perhaps just as significantly, as a general rule many Americans do not accept that sometimes bad things just happen (i.e., it's always someone else's fault), and juries frequently accept as their role redistributing wealth from those who have it to those who have been injured. Thus, one can do absolutely nothing wrong and still find themselves on the wrong side of a very large judgment.

As a result, the United States is one of the most litigious countries in the world, and many times juries award large judgments in cases where the facts establishing liability

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are scarce. Moreover, the laws of many states (like California) tend to favor creditors over debtors, with the result that those with any wealth are a target, and the greater the wealth the larger the target. Therefore, protecting one's hard-earned wealth should be a critical component of their estate planning. For digital health entrepreneurs, this includes strategic business formation and ownership planning as well.

Fortunately, many of these risks can be addressed through insurance and legal structures. This chapter explores these solutions in greater detail.

Insurance

The first line of defense against many of the risks faced by digital health entrepreneurs is frequently insurance. For example, practicing physicians obtain malpractice insurance against claims of malpractice, whether real or fabricated. Similarly, directors and officers of digital health entrepreneurship companies can protect against claims against them in these capacities through Directors and Officers (D&O) Liability Insurance or Errors and Omissions (E&O) Liability Insurance.

Moreover, all digital health entrepreneurs should consider umbrella liability coverage for all of their activities. Umbrella liability coverage is an inexpensive first or second line of defense for all types of potential claims faced by digital health entrepreneurs, including claims that arise from activities both in and out of their business. For example, if the digital health entrepreneur owns rental properties in her name (a bad idea, as discussed below) and a tenant is injured on the property, an umbrella policy *may* provide coverage against any claims arising from that injury. Note the italicized "may"—the downside with umbrella coverage is there are typically exclusions that preclude coverage; for example, most policies exclude coverage for intentional acts, such as a crime.

Further, while it is relatively inexpensive and thus all digital health entrepreneurs should purchase as much umbrella coverage as possible, umbrella policies have relatively low policy limits, typically $5 million or less. Thus, for larger claims, umbrella insurance will only serve as leverage for settlement. For catastrophic claims umbrella coverage will simply be inadequate and other assets will likely be available to satisfy the claim. The rest of this chapter will focus on legal structures digital health entrepreneurs can implement to minimize the risk of frivolous—and real—claims that can and frequently do have a devastating financial effect absent proactive planning.

Legal Structures

What follows is a discussion of the legal structures available to digital health entrepreneurs. The information provided below is very general in nature, and thus it should not be construed as legal advice; digital health entrepreneurs should seek the advice of a qualified professional based upon their particular facts and circumstances.

Business Entities (Corporations and LLCs): The First Step

Most digital health entrepreneurs understand the risk associated with a new venture. Thus, most new ventures are housed in a legal entity designed to limit legal exposure to the digital health entrepreneur's investment in the business. This explains why most new ventures are created as either a Limited Liability Company (LLC) or, if outside investors are contemplated, a C corporation.

These legal entities are an excellent first step in protecting against the risks associated with any new venture, digital health entrepreneur or otherwise. But housing the venture in an entity is only a first step. There are several additional steps one should take to protect against creditors of the business, often referred to as "inside creditors."

Corporations vs. LLCs

Most digital health entrepreneurs realize that running their venture through a legal entity protects them from personal liability for claims arising within the business. In other words, the legal entity limits their liability to the business itself, absent an "alter ego" claim. Alter ego claims most frequently arise when the separate legal existence of the entity is not respected; i.e., when the entity is used as one's personal "piggy bank."

Historically, corporations and partnerships were the only entity types available to limit one's liability to their investment in the business. Corporations provide limited liability to all shareholders, but restrict the business' ability to segregate ownership and control—all voting shareholders have equal voting rights.

Alternatively, limited partnerships permit limited liability for limited partners, but the general partners of both general and limited partnerships have unlimited liability—i.e., all of their personal assets are available to satisfy a claim against the business.

In response to the perceived weaknesses of both corporations and partnerships, beginning more than 40 years ago in Wyoming, states began adopting LLC statutes that are hybrids between corporations and limited partnerships; LLCs provide limited liability for all members (owners), and through the use of a Manager or Managers, LLC permit the separation of ownership and control. Let's explore the advantages and disadvantages of C corporations and LLCs in greater detail, since these are the two most commonly used legal entity types by digital health entrepreneurs.

C Corporations

The advantages of C corporations are significant, particularly where the business contemplates outside investors. These entities:

- Permit numerous shareholders
- Permit multiple classes of stock (e.g., preferred and common, voting and non-voting)

- Have a low 21% corporate tax rate for retained earnings

Conversely, the disadvantages of C corporations are also significant:

- Subject to double taxation—retained earnings are taxed again upon distribution to the corporation's shareholders
- No asset protection for ownership (discussed in more detail below)
- Requirement of corporate formalities

The requirement of corporate formalities is not onerous (i.e., notice of and holding an annual meeting of shareholders, minutes from that meeting, etc.), but the failure to uphold corporate formalities can be the grounds for a claim of *alter ego*, which would permit a creditor to seek personal liability from a controlling shareholder.

Note that S corporations are similar to C corporations except that with an S corporation the annual profits and losses flow through to the shareholders' personal income tax returns, rather than being subject to tax at the corporation level. However, S corporations are different in that they are limited to 75 shareholders; prohibit nonresident, non-U.S. citizen owners, and are very restrictive as to the types of owners. Thus, S corporations are infrequently used in this context.

LLCs

The advantages of LLCs are also numerous. This entity type:

- Permits numerous/all types of shareholders
- Permits multiple classes of ownership interests via "Series LLC"
- Can elect pass-through taxation or as a C Corp
- Charging order protection (discussed in more detail below)

The disadvantages of LLCs are less significant:

- Generally taxed at owner's tax rate (if a passthrough) but can elect corporate taxation if desirable
- Owners can't defer tax on income to reinvest

Thus, in this author's view LLCs (particularly Series LLCs, discussed below) provide the highest degree of flexibility, especially if established in the right jurisdiction. That said, historically C corporations have been used more often than not in this context, particularly where outside investors are considered. But because LLCs may elect to be taxed as a C corporation, it is possible to combine the flexible legal structure of the LLC with the tax benefits of a C corporation where retained earnings are contemplated.

Protecting Business Assets from Inside Creditors

What if a claim arises within the business? As a general rule a creditor of the business may attach any assets of the business, including real estate, equipment, intellectual property, or any other assets owned by the business. Thus, it is

imperative to also structure the business itself in such a way so as to reduce the risk of a business creditor taking the business's most valuable assets.

Therefore, it is *never* a good idea for the business to own the real estate upon which the business operates. The real estate should be owned by a separate LLC, which in turn is ideally owned by the type of trust described below. The business should then enter into a long-term lease to occupy the property, memorialized by a written lease agreement. In this way the digital health entrepreneur can retain the cash flow from the lease, if desired, upon a sale of the business. Alternatively, the real estate can also be sold, but at an additional cost to the buyer because of the long-term lease. (Note that this general rule about real estate also applies to the digital health entrepreneurs' investment real estate as well. Investment real estate, whether residential or commercial, should be owned by an LLC so that if liability arises on the investment property the risk of loss is limited to that property alone. Conversely, if the digital health entrepreneur owns the property in his or her personal name *all* personal assets will be potentially available to satisfy the claim.)

Similarly, expensive equipment (e.g., medical equipment) should be owned by a separate LLC and leased to the business, and high-risk assets like vehicles should be owned by yet another LLC so that these assets don't "taint" the business and trigger liability.

Moreover, the businesses intangibles such as goodwill, copyrights, trademarks, customer lists, etc. can all be owned by a separate LLC, with the operating business paying a royalty for the use of these intangibles. All of these separate LLCs can be bundled and sold together, or the digital health entrepreneur can retain one or more for enhanced cash flow upon the sale of the operating business.

In this way we can isolate the operating business so that all assets that would otherwise be attractive to a potential creditor of the business are unavailable. And again, the ownership interests of all of these separate LLCs should held by the trust described above.

If we structure the business in this manner the creditor's only remedy would be against the operating business, which is largely dependent upon the people running that business. This gives the business owners significant leverage to settle a creditor claim for far less than any judgment.

Protecting Business Assets from Outside Creditors

The above discussion addresses creditors from within the business. What if the creditor comes from outside the business, such as with a successful alter ego claim or as the result of a car wreck. In most U.S. jurisdictions, if you own interests in a legal entity such as a corporation or LLC and you have a personal creditor, the courts will transfer your corporate shares or LLC interests to satisfy the creditor's claim. In other words, you will lose your ownership interest to that creditor!

For decades Delaware was the best jurisdiction for corporations because Delaware law was the best in the U.S. in this area. As a result, the vast majority of corporations were created in Delaware, regardless of where the investor(s) lived. It is important to note that one is not restricted to creating a legal entity in her own

state, and it behooves one to "forum shop" to pick the best state's laws to establish a legal entity.

In addition to forum shopping, the type of legal entity is significant. As previously mentioned, historically most ventures that intend to raise capital from outside investors are established as C corporations (S corporations restrict the type and number of investors, so they are infrequently used for this purpose). Unfortunately, in nearly every jurisdiction in the U.S., shares in a corporation will be available to satisfy a personal creditor's claim. A simple example will help explain this risk.

Example: Anne is the majority shareholder in a new venture that uses blockchain technology to house digital health data. Anne was one of the first to market and thus she has a significant competitive advantage, and the venture already has significant value. Unfortunately, after working long hours, Anne was involved in a car accident on her way home, and Susan (a young professional), was killed. After a jury trial Anne was found to be at fault and a large judgment was entered in favor of Susan's estate. Due to the value of the corporation, Susan's executor asked the court to foreclose on Anne's shares, which the court granted. As a result, Anne's shares were transferred to Susan's estate to the extent necessary to satisfy the claim, and Anne lost control of *her* business.

What could Anne have done differently? Since shares in a corporation are rarely protected from creditors, did the entity have to be a corporation? Again, historically we've used C corporations when outside investors are used or contemplated, but other entities might work better in these circumstances.

If outside investors are not contemplated an LLC established in the right jurisdiction is a far better choice than a corporation. This is because in several states (including, Delaware, Nevada, South Dakota and Wyoming), the sole remedy of a creditor against an LLC interest is what's known as a "charging order." Such sole remedy jurisdictions dot not allow a creditor to foreclose on the LLC interest like it can with shares in a corporation. Instead, the creditor's sole remedy is to receive whatever distributions the LLC member would have received absent the creditor.

Thus, if the LLC makes no profit distributions to the debtor the creditor gets nothing! (Note, however, that this does not preclude the LLC from paying management fees to the LLC member debtor, although these may be attached under certain circumstances.) If the debtor can avoid making distributions the debtor can use this as leverage to settle with the creditor, often on favorable terms.

Moreover, LLCs established in these jurisdictions provide the highest degree of privacy in that only the information for the LLC's in-state agent for service of process (typically a corporate agent) is available in the public record. Thus, in these states one cannot simply search by the digital health entrepreneur's name to learn what entities he or she owns.

What if the business contemplates outside investors with different rights (e.g., preference for distributions), such that a typical LLC will not be satisfactory? In this case the entity could be a legal entity offered in only a few jurisdictions, a Series LLC. As depicted in Fig. 12.1 below, a Series LLC acts like a holding company and subsidiary LLCs all wrapped up into one LLC, with the entity having different

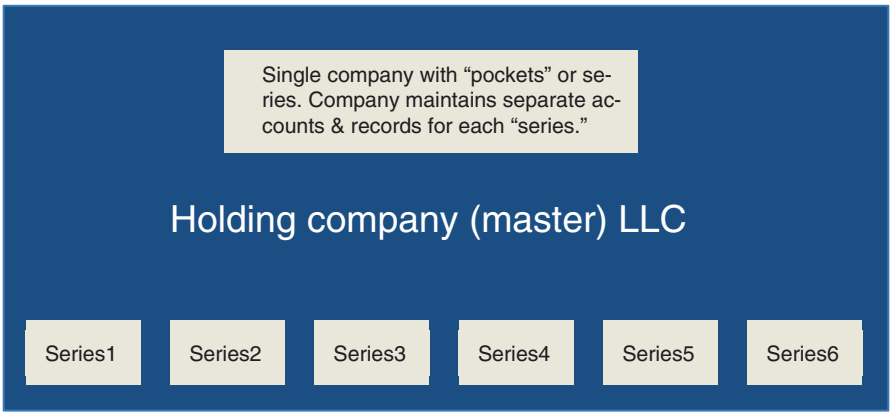

Fig. 12.1 Series LLC structure

"series" for different investors with different rights. But again, Series LLCs are relatively new and only offered in a handful of jurisdictions.

As a result, it behooves the new business venture to be very intentional as to where it is established.

What about existing businesses and entities? Fortunately, existing entities can be "domesticated" into a state with the sole remedy of charging order protection, as either a traditional LLC or Series LLC as needed, so this analysis is also very relevant to existing businesses.

Is There an Alternative Ownership Structure?

Is there anything the founder can do to protect her ownership interest? What about the investors who have no say in the type of entity used, or the state in which it is established. Can they somehow protect their shares or LLC interests?

Fortunately, there are several steps digital health entrepreneurs can take to protect their assets, including their interests in the venture itself. Recall that only assets one owns personally are available to satisfy a creditor claim. Thus, if one doesn't own the assets yet has a beneficial interest in those assets, can we protect the assets from a potential creditor?

The answer is yes, but a more detailed explanation is warranted.

As a general rule only assets we own are available to satisfy our creditor's claim. Alternatively, if we live in a community property state, the creditor of either spouse may be able to attach community property (e.g., in California), or community property may only be available to a creditor of both spouses (e.g., Texas).

If we transfer our ownership interest away, however, that asset may be protected from creditors. I say may because in all states one cannot transfer assets for less than fair or adequate consideration to avoid, hinder or delay a creditor. Thus, one the eve

of a jury verdict against them one cannot transfer their assets and have them protected from creditors. The "fraudulent transfer" or "voidable transaction" rules in every state prohibit this—the transfer can be undone so that the asset is available to the creditor.

However, what if we proactively transfer our assets when the proverbial waters are calm, when there are no claims against us and we have no reasonable knowledge of facts giving rise to any claims? Can this protect these assets from creditors?

Historically one could only transfer assets to others, or to a trust for those others, presuming the fraudulent transfer rules did not apply. However, for up to 20 years several states have permitted one to transfer assets to a trust in which the transferor is a beneficiary, and still have those assets protected from the transferor's creditors (again, presuming the fraudulent transfer rules do not apply).

Moreover, in several states the transferor can even serve as "Investment Advisor" over trust assets, such that she can have total and exclusive control over the investment decisions for the assets owned by the trust. In this way one can transfer assets proactively to protect them from future creditors yet retain total investment control over those assets.

The transferor cannot, however, retain control over distributions, as this would subject the assets to the claims of the transferor's creditors. This function is often left to an independent resident or corporate trustee in the jurisdiction where the trust is created, or the transferor can select an independent "Distribution Advisor" to initiate distributions from the trust.

Note, however, that not every state permits these types of trusts, so once again the correct choice of law for the trust is critical.

A continuation of the prior example will help explain this concept. Suppose that long before her car accident Anne transferred her interests in her blockchain company to a trust along the lines of what we've been describing established in the State of Wyoming. Presuming Anne transferred her interests long enough ago so that the transfer is not subject to the fraudulent transfer statute of limitations, Anne could be a trust beneficiary and the Investment Advisor, so that she continues to control the company as majority shareholder and yet her interests would be protected from her creditors.

Figure 12.2 depicts this structure, using a Wyoming trust to own the membership interests in the startup Wyoming LLC.

In this way we can protect the ownership *and control* of all intangible assets (those that do not have a physical presence), such as interests in LLCs, as well as many tangible assets such as shares in a corporation. Similarly, we may be able to protect real estate, particularly if that real estate is owned by an LLC.

The Role of Estate Planning

Under current law, a U.S. resident or citizen can transfer up to $10 million (indexed for inflation to $11.18 M in 2018) during their lifetime or at death free of U.S. federal gift or estate tax. However, if one transfers more than $15,000 to any one

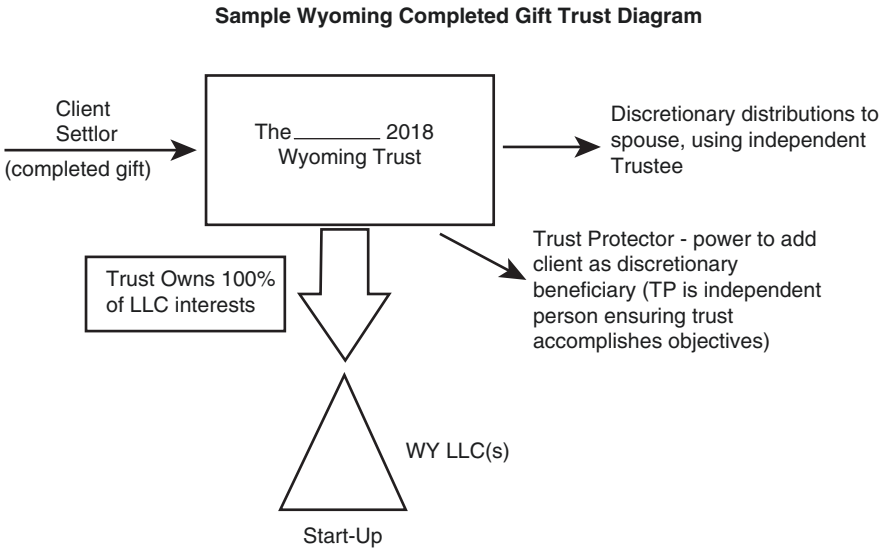

Fig. 12.2 Sample asset protection structure

individual in a calendar year during lifetime, the transferor must file a gift tax return (Form 709) that uses up some of the $10 million exemption. Transfers above this exemption threshold are subject to a 40% tax.

Example: Let's assume Anne's blockchain business is worth $5 million. Under current law, she can transfer the entire business to her children free of federal gift or estate tax. Note that depending upon Anne's state of residence, however, she may be subject to *state* gift or estate tax.

Alternatively, if Anne's blockchain business is worth $20 million and she desires to transfer it to her children, she cannot transfer all of the business without incurring federal transfer tax (gift or estate tax) totaling **$3,528,000** (i.e., 40% of $20 M less $11.18 M).

One must value the transfer at the current fair market value (i.e., what a willing buyer would pay a willing seller). What if, instead of waiting until the business had significant value, Anne transferred the business before it reached its current fair market value? During the start-up phase, Anne's business was worth very little, if anything; at inception a start-up has nominal value. Therefore, at inception, if Anne transferred all of her ownership interests to the type of trust described above, where Anne could be a beneficiary and control the trust's assets as Investment Advisor, Anne could remove the value of the business completely from her estate for estate tax purposes. In other words, even if the business grew to $1 billion, all of that wealth would not be subject to federal estate tax.

Moreover, because of the protections provided by this structure, the $1 billion would also be protected from Anne's creditors (with the exception of a fraudulent transfer claim discussed above). Therefore, it is critical that digital health entrepreneurs

proactively plan to protect their business interests from confiscatory taxes and creditors and predators.

And while they're at it, digital health entrepreneurs should also do their foundational estate planning: a revocable trust to avoid probate and control assets in the event of disability, plus powers of attorney for property and medical decisions, should be the foundation for every digital health entrepreneur's estate plan.

Importance of Succession Planning

The above discussion emphasis the importance of estate planning for digital health entrepreneurs. However, as with many entrepreneurs, the business may be one of the entrepreneurs most valuable assets, if not *the* most valuable asset. Where the business has significant value it is also imperative that the owners implement a carefully considered succession plan, particularly one that addresses the disability or death of owners working in the business.

Thoughtful, carefully documented planning that strategically blends business planning, asset protection, estate planning, and business succession planning must take into consideration the delicate balance of the health and protection of the venture while maximizing protection and value for each owner.

Conclusion

Digital health entrepreneurs face many risks and significant potential liability arising from those risks. However, with proactive planning using carefully considering legal structures, typically a combination of legal entities and trusts, digital health entrepreneurs can significantly reduce the business' and their personal potential exposure resulting from these risks. Moreover, with additional proactive planning, the digital health entrepreneur can protect their ownership interests (and potentially control) from being lost to one or more potential creditors, while ensuring they pay no gift or estate tax even if the value of the business skyrockets.

Chapter 13
Digital Health Intrapreneurship

Uli K. Chettipally

Definition of an Intrapreneur

From the previous chapters one has an understanding of what Digital Health is. Here we will talk about Intrapreneurship. An intrapreneur is "a person within a large corporation who takes direct responsibility for turning an idea into a profitable finished product through assertive risk-taking and innovation" as defined by the American Heritage Dictionary. The terms intrapreneur, intrapreneuring and intrapreneurship were coined by Gifford Pinchot III in 1984 [1]. It was later popularized in business magazines and in business literature where case studies were published.

Introduction

There are typically two ways companies can grow into new areas of business. One is where the company acquires or merges with another company that has the desired product, service, talent or customers in the market. The idea is that there is a potential to increase the market share by increasing the product or service line. Here the difficult work of innovation and finding a market for the offering is already done and has been tested to a degree where the risk of failure is minimized by the company that is being acquired. And hence the value of the company that is being acquired is significant. The ultimate result of this is to grow into new areas of business and increase the value of the acquiring company.

The second way is to innovate through new product and services developed by the company. Typically, the leadership of the company sets the agenda and direction

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of the new growth. It could be set up as a specific business unit to develop a specific product or service. Sometimes it may not be clear which areas have potential for growth. Then it becomes a broader search for these areas of growth.

Typically, companies that have reached a certain level of maturity are the ones exploring these options. These companies need to be in a strong position with mature markets. Let's look at the life cycle of a company to understand why investment in innovation is imperative for companies to grow and thrive.

Life Cycle of a Company

Every company has a life cycle [2]. It starts with the formation of the company and ends with decline and death. This may not be evident when we observe companies for short periods of time, as some companies may have long lives sometimes lasting more than a century. There are five stages in a company's life cycle:

1. **Launch**. This is where the entrepreneurs come up with the idea for a product or a service and start building the company. The capital needs are high. And there is no revenue coming in. The idea needs to be turned into a product or service of this new company. The market needs to be tested. There is a need for investment in sales and marketing. The cash flow is negative. This puts immense pressure on the company to create value and generate income.
2. **Growth**. In this stage revenue starts to grow. So also the need for capital. There may not be any profits, as the money that is made will need to be put back into building growth. This is the phase when the company is bringing in good revenue, but the expenses are still high and at some point will break even and go into a positive cash flow situation.
3. **Shake-out**. During shake-out competition will increase. The market will reach its saturation point. And the revenues will peak. Cash flow is positive and profits are good, but there will be pressure from the competition. There may be some mergers and acquisitions. Companies that gain a strong foot hold will survive this stage.
4. **Maturity**. The company has succeeded in warding off competition and gotten into a solid financial situation where the revenues and profits are stable or decrease. Cash flow is good. During this phase companies need to figure out how to continue to grow. They need to look at new markets or new offerings.
5. **Decline**. During this phase the company's products and services loose relevance in the market place. The sales, revenues and profits decline, and the company's infrastructure becomes a burden. This leads to decline and ultimately the death of the company.

In order to maintain a company's market, revenues and profits, it needs to continuously reinvent and reimagine their product or service strategies. This could be done by creating new business units for specific products or services, when the direction has been set by the leadership. This is often the strategic pursuit of organic

growth within their core offerings. Sometimes the direction may not be clear or the company may want to explore opportunities outside of their core business. Then it is imperative for the company to set up a business unit that oversees innovation and intrapreneurship. Here, intrapreneurship can be seen as a process where individuals working for a company or organization create and develop new innovations that can potentially lead to new areas of business growth for the company. They sometimes can be paired with outside talent, but mostly work on their own internally.

Organizations that have a formal and a deliberate process and priorities are more successful in translating innovation from their internal projects [3]. The success of their innovations are tied to the effort and thought they put into the process of formalizing it, even though it is a challenge to do. Having the support roles like including research, information technology, finance and marketing coordinated will improve the rate of commercialization. Thus, strong leadership plays a crucial role at every stage and the ultimate success leading to commercialization of winning products or services.

Healthcare Industry's Challenges

Healthcare is a complex industry. It is also the largest employer of people in the USA. It consumes nearly 20% of the GDP. But, compared to other industrialized nations, the quality of care and health outcomes do not match the amount of money spent on healthcare.

To summarize the challenges facing healthcare today, refer to "Quadruple Aim" [4]. Quadruple Aim consists of four components: (1) improving the individual experience of care. (2) Improving the health of populations. (3) Reducing the per capita cost of care and (4) Improving the experience of providing care. Each of these four goals are critical to improving the status of healthcare as an industry. Although the business model of healthcare may be at the heart of the problems facing the industry today, digitization of the processes is seen as a solution to achieving all of the above aims. Any digital health solution that does not involve one of the aims may not be seen as an improvement.

Digital Health

According to Mesko et al. [5], Digital Health can be defined as "the cultural transformation of how disruptive technologies that provide digital and objective data accessible to both caregivers and patients leads to an equal level doctor-patient relationship with shared decision-making and the democratization of care". Technologies that provide objective data, whether it is vital signs, genomic or social, plays an important role. Access to data is not only available for the physician, but also to the patient. The decisions are made by both the doctor and the patient, together. The

ability to avail descriptive data, assess predictive information and access prescriptive knowledge for both the doctor and the patient is the key to improving health while decreasing costs. A sure way for the healthcare industry to attain these goals is through digital health.

Innovation as a Strategy

Healthcare companies have enjoyed a good run of healthy growth over the past few decades. They did not have to change much in terms of how they did business. Now they are being forced to change. There are several reasons to innovate [6]:

1. **Increasing competition**. Existing competitors are innovating to capture a larger market share. Nimble startups, pharma companies, technology companies and global competition are some of the forces that are increasing the pace of innovation. Healthcare companies that have had a stable business with huge infrastructure are facing challenges from new companies that are lean and technology driven. Technology has helped speed up globalization and thus increase competition.
2. **Consumer expectations**. Consumers now have access to more knowledge and services, thanks to technology. They are now expecting personalized, efficient and inexpensive services. Companies that can provide all of the above with convenience are going to be the winners. Consumers can now share information through social media which drives more engagement for the companies that can innovate in this area and reap the benefits.
3. **Advancing technology**. It is now possible to automate a lot of the processes that used to take manual labor to accomplish. Technology is getting smarter, faster and cheaper. Legacy companies that do not have modern technology will be at a disadvantage, not only due to lack of sophistication but with increased cost and inefficiency, they become less profitable. With smarter technology the cost of doing business decreases due to increased efficiency and decreased need for human labor.
4. **Aging population**. With improving conditions, populations are living longer. As population gets older, their health deteriorates and the cost of taking care of them increases. It may take five to ten times the cost to take care of an older patient compared to a younger patient. This puts an additional burden on legacy companies that have nurtured their patients over the past few decades. With increasing cost of medical technology and newer, expensive drugs the pressure keeps mounting.
5. **Changing environment**. There are several external factors that are changing the business environment where healthcare companies operate. From regulatory hurdles to changing business models, companies are faced with difficult decisions like embracing their core competencies versus venturing into new areas of business. If they make no changes, there is the risk of becoming obsolete and irrelevant. If they make changes, there is the risk of that venture failing in the market.

How to Do Innovation

One thing is for sure—companies cannot stay where they are and expect to conduct business as usual and still remain in business. So, what are the ways companies can grow and remain relevant in the market place? There are three things that companies can do to stay relevant, grow into new markets and thrive amongst competition [7]:

1. **Increase investment capacity**. This can be done by revitalizing their core businesses. These are the services and products that have helped them succeed so far and generate revenue. The systems need to be made more efficient. Costs need to be trimmed. New technology needs to be used to automate or speed up processes. Make a firm commitment to their customers to buy their loyalty.
2. **Foster innovation internally**. Encouraging the current employees to participate in the innovation process. People working in the front lines understand the problems intimately. They may also come up with solutions that can solve the problem. Encouraging them by giving them protected time to innovate and changing the overall culture to nurture innovation at various stages is helpful.
3. **Create synergies between old and new**. Once new lines of product or service are created, building synergies to support the new and move the old towards the new moves the whole organization forward. Using existing support services to support the new business and repurposing some of the resources can have a beneficial effect on the newly created service or product lines. Sometimes they may have to let some of the old processes die to make room for new processes.

A Good Innovation Process

Here we are describing the innovation process as not just coming up with ideas or solutions, but to actually create a product or service that can be commercialized [8]. Innovation involves taking risks. A good innovation process should be designed to decrease the risk of intrapreneurship. We can look at innovation process as a funnel. Not all ideas can solve problems. Not all solutions can become products and not all products can be commercialized or scaled. As we go from product to a scaled product, there will be many ideas that cannot reach the market, which is the ultimate destination. In other words, there is a risk of failure or risk of not reaching the ultimate goal. A lot of work needs to be done before an idea becomes a product. This process is called de-risking. Methodologies like the Lean Start-up that have become popular in de-risking the startup process can be used in an Intrapreneurship program.

There are three main components of the Lean Start-up Process [9].

1. **Business model canvas**. Here the intrapreneurs sketch out what their hypotheses are while they are just starting out on their projects. The creation of the traditional business plan is discouraged. And the reason for that is the numbers and

projections in a business plan are based on assumptions. So it is better not to get too far in planning before those assumptions are tested to be true. The idea is to clearly express the value one is creating for the company and its customers.

2. **Customer development**. In this phase the intrapreneur has to go out and talk with several potential customers, distributers and partners. One is trying to understand how and whether the solution that is being proposed satisfies or solves a customer problem. By talking with customers early on, one might get a better understanding of the market fit of the solution. Customer development can also tell early on whether there is a problem and whether the solution being proposed will be successful or even needed. A lot of emphasis is put on customer research to come up with features and pricing for the product before it is built.
3. **Agile development**. Developing the product and features iteratively is the core work that occurs during this phase. It goes hand in hand with the previous phase where customer feedback helps design and develop the product. This reduces unnecessary expenditure of effort and resources on features that are not needed. It also helps in reaching the stage of minimum viable product or MVP. The idea is to go to market with a product with just the basic features and give it to customers. As one gets feedback from the customers, then develop more features that the customer actually needs. It is designed to decrease time to market and wasted money on product development.

The Purpose of an Intrapreneurship Program

Research has shown that a formal and structured process that has been set up deliberately to promote innovation and entrepreneurship is more successful [3]. The lack of a formal process fails to bring ideas to reach commercial success. The principles behind these processes are to:

1. **Decrease the risk**. Innovation is a risky business. Seventy-five to ninety percent of the start-ups fail. The purpose of an intrapreneurship program is to decrease this risk. Starting from problem discovery to commercial success, there are several steps that need to be completed to de-risk the process. The idea is to invest in the journey incrementally as the idea progresses through various steps to ultimately become a successful product.
2. **Make evidence-based decisions**. Research should be a closely intertwined with the intrapreneurship process. Research may involve qualitative research like speaking with customers, getting input from focus groups to quantitative research like doing retrospective data study or doing an outright clinical trial to evaluate tools developed. All decisions should be based on evidence.
3. **Figure out the business model**. Business model has to be thought through and decided upon, before launching the product. Even the greatest product may not survive if the business model picked is not right. This may require detailed

analysis of the value proposition for the customer and the company. If a product cannot be sold while making a profit, it cannot survive in the market.
4. **Be O.K. to fail**. Processes should be designed in such a way that if an idea is going to fail, it will fail early. There should not be any negative consequences attached to failure. In fact early failure should be encouraged. This saves a lot of effort, money and time. The team can pursue other ideas and not waste their time on something that may not work out in the end.

Structure of an Intrapreneurship Program

There are several types of formal structures that organizations can set up to encourage innovation and support intrapreneurship. The type of structure depends on what stage of innovation journey the organization is going through and how seriously it is pursuing this. Here are the most common ones in the order of involvement and investment:

1. **Innovation lab**. An innovation lab is a dedicated space allocated for the purpose of encouraging innovation. The theme for innovation is loosely structured. There are no rigid rules about what projects can or cannot be a part of the lab. There are no timelines or financial support other than having basic supplies. Outcomes may not be tracked. The downside of this structure is that there is no serious thought to what happens to the innovations if they are successful. Some critics call this "Innovation Theater" for this reason.
2. **Incubator**. An incubator is a more formal structure where innovators are given more support. The duration may be well defined and there is a definite end point. The support typically includes mentoring, meeting and office space, access to experts and investment networks. They may not provide financial support directly to the projects. They may offer to fund some of the projects that have proven to be successful.
3. **Accelerator**. An accelerator may have all the support structures with the addition of early stage financing and a competitive application process. The timeline is comparatively shorter and has a regular calendar with a definite graduation day. If successful, the team is expected to launch the company and raise funding from angel and venture capital groups. An equity stake is taken by the host company. And there are various combinations and variations of the above models.

Creating Space for Innovation

Ultimately, the level of support that the organization provides to its intrapreneurs depends on the strategic priority of innovation for that organization. Innovators and intrapreneurs in established companies face tremendous cultural challenges.

What is needed to run a company's core business is very different from running an innovation space. Ultimately, it boils down to leadership. There are several "spaces" that company leaders need to create for an intrapreneur, other than the physical space, to succeed in a corporate setting according to Tendayi Viki [10]:

1. **Strategic space**. Innovation and intrapreneurship should be part of the main strategy that the company is planning to grow in the future. If that is not the case, then innovations are bound to stagnate once created. Leaders need to have a clear vision on the strategic growth areas that intrapreneurs can then focus on exploring.
2. **Portfolio space**. Portfolio space refers to making space for products whether they may be core vs. adjacent vs. transformational. Having a vision of the future on how the current company portfolio will change based on market opportunities is a leadership function.
3. **Financial space**. Providing protected financial support to these ventures is critical to their success. Some entities have made that decision by separating the innovation arm from the main company with separate leadership. Sometimes these projects need longer term support than the annual cycles that organizations have.
4. **Management space**. Intrapreneurs use very different methods compared to running a typical business. There is a lot of experimentation and iteration that needs to happen. So, there are different set of tools that help intrapreneurs guide their journey through product development.
5. **Time space**. Innovation needs protected time for intrapreneurs to use. A lot of frustration ensues when that is not available. Companies that can provide this dedicated time for innovation have seen more successes. Again, it falls on the leaders to provide this time to encourage innovation.
6. **Learning space**. Intrapreneurs need to learn and develop new skills. The traditional ways of working that helped them in their previous jobs may not be useful in their innovation journey. Investing in building these new skills needs to be a priority to be able to use time productively. Creating mentorship is one way to do this.
7. **Space to fail**. Innovation is about taking risks and trying out various ideas. Not all ideas succeed. Having this knowledge and putting it into practice creates a space for intrapreneurs to not get scared and to try a variety of ideas. The more ideas one goes through and learns from, the higher the chance of success of the next idea.
8. **Space to scale**. Innovation process may help develop products successfully, but the product needs to find a place to be implemented and to grow. Finding a fertile environment becomes critical for the new product to flourish. Sometimes, the organization cannot find a way to scale it or is unwilling to scale it. There may be several reasons for it. The product may not fit with their current strategy, or it may make current, successful product obsolete. This is a very frustrating place to be. This is why having an innovation strategy is so important even before anything is built, so that valuable resources are not wasted on something that will not be needed or used.

As we can see, all these "Spaces" need to be created by the leadership. It has to be planned deliberately, if the company is taking innovation seriously. Many times, organization's leaders do not think that far or that wide. This leads to frustration on the part of the intrapreneur because it takes up valuable time and effort to educate and convince leadership on this. Ultimately, they end up spending a lot of energy in managing the leadership.

Skills Needed for a Digital Health Intrapreneur

As discussed in the previous section, leadership plays a very important role in innovation and intrapreneurship. There are several tasks that intrapreneurs need to learn to be successful in their endeavors:

1. **Manage stakeholders**. The first task that intrapreneurs have is to manage the stakeholders. Leaders of the company being the most important stakeholders. Managing involves educating, demonstrating value, casting a vision and disseminating the success stories about the innovation. It is probably the most important responsibility, as the ultimate success of the project depends on leadership. It is also important to note that the culture of the company plays an important role. The users of your product or your customers are the second most important stakeholders. Trying to understand their pain points and problems, educating them on the benefits of your product and showing them how important they are to the innovation process goes a long way towards the success of the project. The third most important stakeholders are the funders. Keeping them updated on your progress or challenges is an important element to maintain relationship and build goodwill. Managing interpersonal relationships with managers is important to keep ego, jealousy and dogma out of the way.
2. **Learn continuously**. Intrapreneurship is a new skill. It is not taught in a clinical school curriculum. It is up to the person to learn about the technology, the business and the clinical aspects of the solution. One's prior expertise in clinical medicine is not enough to tackle intrapreneurship. It is a very different environment to work in. Things are not as clear. One needs to become comfortable dealing with uncertainty and taking small risks. Build the solution in small steps and taking time to decrease risks at each level. Learning from potential customers is key to finding the pain point and developing a solution that they will use. Once they have the product in hand, one needs to learn how they are using it and what would make it better. Also, one needs to learn from the leadership. What are the problems they are tackling? What are the priorities? Where are the budgets moving to? This knowledge will help align one's project with the organizational goals.
3. **Start small**. Starting with small projects is a great way to test the waters and also to see if it is a good fit for one's strengths and ambitions. The project could be building a new feature for a current core product or creating a small new application which is not mission critical. This experience will help develop new

relationships, provides an opportunity to learn new skills and getting comfortable doing projects that have uncertainty built into it. Not everyone will be able to thrive under these circumstances. Starting small is also a good way to show the leadership your capabilities. One can build trust and reliability through their work. This helps in getting and doing larger projects.

4. **Work smart**. It takes a tremendous effort to create something that did not exist before. It takes a special person to do the work without the guarantee that the product will work. Many hours of sweat goes into it. The satisfaction one gets from seeing a new product that one created in action is unmeasurable. But, one must be prepared to kill the project when it is not successful. It can sometimes be hard to kill one's "baby", due to the emotional investment that goes into it. Being aware and prepared of this possibility is important. Sometimes, intrapreneurs will be tempted to get into conflict with others when their project is not given the green light. It is important to remember that one is still an employee of the company and one should not attempt anything that will jeopardize their relationships, career or financial wellbeing. Frustration is a common feeling when things don't proceed the way they should or people don't understand the importance of one's project for the company. Maintaining one's physical and mental health is important. Using help when needed is critical. One does not need to do everything to get the product out. Programmers, statisticians, analysts and project managers can be hired. Some of the development work can be outsourced. It is better to avoid being the only person on the project for the above reasons. A team-based approach may be helpful to the overall success of the project.

Working with Legacy Systems

Adoption of the Electronic Health Records (EHR) have been boosted in the late 2000s with incentives from the federal government. A wealth of data resides in the EHR systems. Although these systems have not kept up with the latest advances, the data in the systems can be used for innovation in digital health. FHIR (Fast Healthcare Interoperability Resources) Specification, a new standard for exchanging healthcare information electronically from HL7 can be used to access data [11]. One needs to be aware of intellectual property issues when working with EHR companies. Variables such as access, effort and time need to be considered when working with EHRs, which may complicate some innovation projects.

Future of Digital Health

The future of digital health has amazing potential. Healthcare being one of the last industries to be digitized, there will be tremendous opportunities to grow in this field. One may or may not pursue a formal training or fellowship in informatics.

Understanding the basic principles is important. Some in the field have felt more comfortable getting a formal training. Some, who have been doing projects and are more confident in learning on the job have thrived also. The rate of change and introduction of new technologies makes any new learning obsolete very quickly. One has to be on a continuous cycle of learning. There are exciting new technologies on the horizon like machine learning/artificial intelligence, blockchain, genomics, robotics etc. that make this a very exciting time to be in business as an intrapreneur. These new technologies promise to change healthcare as we know it and bring in an era of health for our patients and wellness for our physicians and staff.

Conclusion

Intrapreneurship is a great way to make a contribution to the company's growth while fulfilling one's curiosity and building a skill set which ultimately leads to tremendous job satisfaction. It is a challenging journey, but ultimately rewarding. Preparing for it, learning about the process, managing stakeholders and keeping one's perspective on the mission will result in a successful career in intrapreneurship.

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Chapter 14
Growth Hacking Health: Scaling Your Venture

Mussaad Al-Razouki

Working Out Unit Economics Before Running

Before we jump into scaling, it is important to emphasize a tried and true analogy, that of comparing a venture to a car or plane (or flying car). Consider yourself, the founder, as the main driver with your fellow co-founders as the highly caffeinated co-pilots that will join you on a long cross country drive/flight towards the vision you have collectively set in your pitch deck. Now, before the investors can come and fill up your tank with the gas that you will most certainly need to speed towards your vision (or build more carplanes), you must first make sure that the vehicle you have built actually works. In fact, I personally love the car analogy because as any serial entrepreneur or seasoned investor worth their salt would admit, there is often a lot of "wheel spinning" that has to occur before the company finally gets on track. The good news is, that formula one cars as well spin their wheels on the start line just before they zoom off down the circuit.

Figuring out what type of fuel you need and how far each gallon of fuel will take you are the building blocks or unit economics of any venture. Simply put, these are the direct costs and expected revenues on a per unit basis. In digital health that can mean the customer acquisition cost and the life time value of a PMPM (per member per month) user or a SaaS (Software as a Service) enterprise client or the margin you make on reselling a wearable sensor plus associated software.

Remember, your product or service is the base number and growth hacking is only the multiplier. Always start with the customer in mind. Understand who your core customer is, find users like your ideal customer congregate (both in the real world and online) and figure out the best way to get in contact with them. Once you have both your customer and unit economics out, rev up your engines and start your path towards your vision. The faster you fly down that entrepreneurial pathway; the

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more investors you will attract as proverbial hitchhikers begging you for a ride. Once you have the right investor on board, he or she will make sure you accelerate and shift gears through the multiple rounds of financing needed to continue to scale your business. I find that the best investors take a literal back seat to the founders, but are ever ready to point out dangerous roadblocks or nifty short cuts to ensure a quick and safe journey towards success.

The final use of the car analogy comes by taking the infamous *Toyota Production System* (TPS) into consideration. TPS is as close to a panacea as one could get when it comes to process development and improvement. An integrated socio-technical system, developed by the world's largest car manufacturer by volume, Toyota, the TPS combines eastern management philosophy and modern day manufacturing practices that can be easily transmogrified into the digital realm.

Originally called "just-in-time production", TPS builds on the approach created by the founder of Toyota, Sakichi Toyoda, his son Kiichiro Toyoda, and the engineer Taiichi Ohno. TPS is usually a good place to start because in its most basic form—it reminds entrepreneurs that the earlier you discover a problem, the less likely that problem itself will grow as you scale your business, resulting in a higher chance of success for your startup.

The main objectives of the TPS are to design out overburden (*muri*) and inconsistency (*mura*), and to eliminate waste (*muda*). Therefore, it is easy to see that the most significant effects on delivering value to your end user can be achieved by first designing hardware or software that is capable of delivering the required unit economics smoothly; by designing out all that "mura" (inconsistency). It is also crucial to ensure that your venture is as flexible as necessary without stress or "muri" (overburden) since this will eventually generate "muda" (waste). In the case of digital health, this stress should be considered as both the biological stress on the co-founder and the technical stress on the software code or physical stress on the digital devices (hardware). Founders must realize that any tactical improvements in waste reduction or the ideal elimination of muda are very valuable to the venture. And the earlier the better. There are eight kinds of muda documented in the TPS, digital health entrepreneurs need only occupy themselves with the top two: Waste of Overproduction and Waste of Time on Hand.

When it comes to Waste of Overproduction, we must consider both waste when it comes to the production of physical hardware or waste when it comes to the deployment of a digital campaigns. Indeed, the beauty of the internet is that the costs of selling more software is negligible and closer to zero than industry could ever get.

When it comes to Waste of Time on Hand, here it's all about reducing waiting, a term notoriously associated in the collective patient psyche with spending hours in doctor waiting rooms buried in decrepitly old magazine. Annihilating the waiting room is a petrous premise of a great many digital health ventures. Indeed, it is also important to eliminate waiting time from the U/X or User Experience perspective, meaning that all your digital users should experience the same seamless integration of all software modules—the all illusive intuitive patient pathway, but founders must also take into consideration the utilization of their team and digital resources—

especially the multiple marketing channels used during a digital campaign. Orchestrating the storm should be seamless as well.

The elimination of waste must come to dominate the thinking of any successful digital health entrepreneur, especially given the large amount of waste currently enjoyed by the global healthcare system, which many experts estimate to be close to 30% [1] or two trillion dollars of the global seven trillion dollars spent.

Don't Be Afraid of the Dirty Back-End

A seamless final product is the ultimate goal of any enterprise, however, in a "just-in-time" lean startup world, the Minimal Viable Product or (MVP) is paramount. As, *PayPal Mafia* alumnus and *LinkedIn* Founder, Phil Hoffman astutely notes: "if you are not embarrassed by the first version of your product (website or app) then you haven't launched early enough."

Many digital entrepreneurs also struggle with the concept of maintaining a seamless storefront online and then marrying that well designed digital window to the world with a manual back-end. Think of that medieval *Mechanical Turk*—it may look like a sophisticated automaton on the outside, but there is a person inside pulling all the strings. This same spirit should be employed by digital health founders when building their own MVPs. If you have to prioritize (and entrepreneurship is all about prioritization) then prioritize a clean front end to attract your customers and don't be afraid to keep the back-end manual and dirty.

This same dirty mindset should also be employed when you first start advertising your products or services. You must do it manually (yes, as slow as one email or customer at a time) before you decide to automate the process and blast your campaign onto the World Wide Web.

The Psycho Is King

Like the classical tale of Dr. Victor Frankenstein, it is very easy for passionate digital health entrepreneurs, to get caught up in the creation of their solution without an objection consideration of the final outcome. Whether it's a funky new augmented reality/virtual reality (AR/VR) platform that encourages patients to lead healthier lives or a new nanotech diagnostic tool that shifts the wait time of an incumbent technology from days to seconds, all that hard work and innovation is absolutely worthless if the market for said product or service does not exist—i.e. is there a customer and would they (or someone else e.g. their employer or insurance provider) be willing to pay for it.

As alluded to earlier, yes, you may have the unit economics figured out, but do you really know your customer? The days of demography have gone the way of the dinosaur. Enter instead, the brave new world of psychographics (Fig. 14.1) [2].

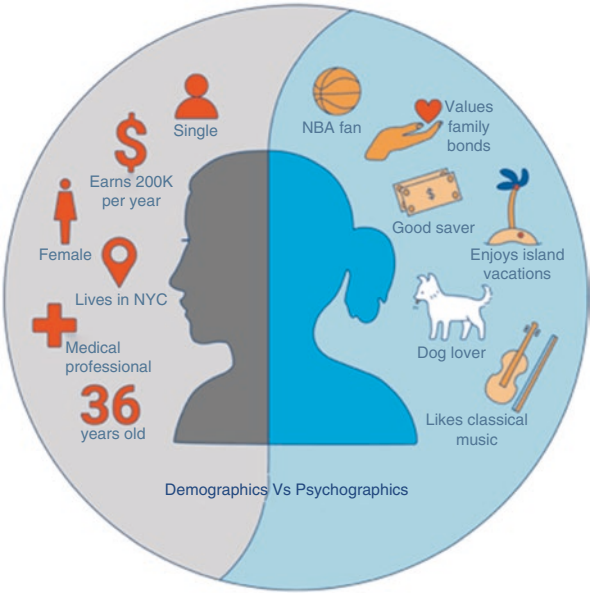

Fig. 14.1 Demographics vs. psychographics (Courtesy of CB Insights)

Psychographics is the study of consumers based on their activities, interests, and opinions (traditional marketers call these AIOs). It goes beyond classifying people based on general demographic data, such as age, gender, or race.

Instead of dull demographics, psychographics focuses on understanding cognitive attributes, such as customer emotions, values, and attitudes, among other psychological factors. Digital health founders must leverage this approach to create "psychographic profiles" of their consumers. These profiles will help entrepreneurs understand consumer motivations and opinions that can then drive messaging tactics.

This way digital health entrepreneurs can beat those in traditional healthcare delivery to the proverbial punch by moving beyond blanket advertising techniques like direct mailers, television ads, and billboards. These approaches tend to target entire demographic groups, such as "males 18 to 34," "females 50+," or "upper-middle-class suburbanites", which is so 2000 and late. There is a great deal of variation in personality traits within traditional demographic groups, making this kind of blanket advertising a very blunt tool. Digital health founders need to be sharper than a surgeon's scalpel.

In contrast, a psychographic profile contains specific information around a person's interests, hobbies, emotional triggers, and lifestyle choices, among other data. This provides insight into *why* someone might buy a specific product, support a given cause, or vote a certain way.

There are several different ways to gather and analyze psychographic data. Some methods include the use of:

- Traditional focus groups/interviews of initial beta users

- Surveys/questionnaires/quizzes (obviously online versions are paramount to the paper based variety)
- Psycholinguistic dictionaries
- Website analytics (e.g. Google analytics)
- User Browsing Data
- Social Media (i.e. likes, clicks, tweets, posts, etc.)
- Third-party analytics

With each data source, and obviously with the appropriate user permission, founders can gain important insight into their customer's preferences either directly or indirectly. And while the data collection methods are time consuming, it is well worth it as the trove of information gathered can be game-changing, again, all the while respecting user's privacy and patient confidentiality.

For example, disgraced political consulting firm *Cambridge Analytica* created a psychographic profile that placed people in a particular market segment according to the presence or absence of five personality traits: openness, conscientiousness, extraversion, agreeableness, and neuroticism (popularly known as the OCEAN model of personality).

To see how this works in practice, let's look at a digital health companies using psychographic modeling to revolutionize the wellness industry—*CoreHealth Technologies* and *PatientBond*.

CoreHealth Technologies is a corporate wellness software company and platform that provides services to over 1000 companies (including many Fortune 500 companies like Cigna and Sun Financial), representing more than two million employees worldwide. CoreHealth a good example of how psychographics helps entrepreneurs refine and deploy their services to their core customers.

In her 2017 annual newsletter, CoreHealth founder and CEO Anne Marie Kirby predicted that artificial intelligence, psychographics, and personalization will be key sites of innovation for companies like her own in 2018. Considering CoreHealth's wellness focused business model, it was important to find ways to increase employee participation in its clients' workplace wellness programs, screenings, and health interventions.

To this end, CoreHealth partnered up with PatientBond, a "platform for driving digital personalized engagement" using email, text message, and Interactive Voice Response (IVR). PatientBond promised behavior change by bringing together psychology and technology.

But PatientBond did not simply rely on the OCEAN model. Instead, together with CoreHealth, they customized their own five-factor psychographic segmentation model, categorizing potential users as:

- Self-achievers
- Balance Seekers
- Priority Jugglers
- Direction Takers
- Willful Endurers

Using this customized psychographic model, PatientBond then provided each of its users with the appropriate behavioral nudge to increase engagement with CoreHealths products and services, resulting in some impressive immediate results. PatientBond claims to have increased participation in biometric screenings among blue-collar workers at Midwest employers by 82%, achieved 72% enrollment in a 12-week metabolic syndrome program among eligible employees in Fortune 50 companies, and increased the number of employees among their clients who have chosen a primary care physician by 20% [2].

The Three Pillars of Scale

Now that you have built your MVP and understood your customers through psychographics, it's time to focus your entrepreneurial energies outward. Founders must focus on these three pillars if they are to grow their respective ventures and turn the corner from barely surviving to fully thriving:

1. People
2. Processes
3. Technology

It's the People, Stupid

Nauseating but true, all successful business magnates claim that their success and the success of their enterprises can be easily factored and derived back to the people they hired. As Cyrus Massoumi, founder and former CEO of digital health behemoth ZocDoc once quipped that he spends 50% of his time as a CEO on hiring (and firing) talent, summing it up with the mantra "slow to hire, quick to fire."

Founders also need to fire themselves. Not from their companies (this usually happens to unlucky founders when their vision event-horizons nebulizes far from that of their 'back seat slipping into the front seat' investors). Founders need to fire themselves from certain roles that other newly hired employees or fellow entrepreneurial crusaders are more qualified to do. Always look to hire people that are smarter (and ideally harder working) than you. This is the single most important use of your time as a founder, especially when your company is ready to scale.

As the number of people grows so do the number of roles. Founders must be ready to create new roles and shift employee or departmental responsibilities from the typical early flat organization into a more hierarchical one. Your first full time hire may have the role of 'VP of Everything,' but all subsequent hires should be readily slotted into predefined roles and departments. Keep in mind though, that the

organization chart is a living organism. It must evolve and adapt to the needs of your growing company.

Traditionally, entrepreneurs have been constrained by "the Rule of 150" coined by Anthropologist, Robin Dunbar, and popularized by Malcom Gladwell in his seminal business book "*The Tipping Point.*" The rule of 150 is defined as the "suggested cognitive limit to the number of people with whom one can maintain stable social relationships and thus numbers larger than this generally require more restrictive rules, laws, and enforced norms to maintain a stable, cohesive group". Basically, it's difficult for one person to stay in close contact with more than 150 people due to the way we are hardwired biologically. In a corporate setting, the theory has ramifications when companies grow to over 150 employees as cohesion between business units tends to break down with hierarchy, thus hindering communication and diluting company goals. Sir Richard Branson famously prefers to spin off each batch of 150 employees into their own company, a major reason why his Virgin Empire boasts over 400 different companies (although with over 70,000 Virgin employees the company average is closer to 175). Thankfully, you have chosen to build a company during the fourth industrial revolution where the internet has singularly solved the issue of mass communication and cohesion. If anything, the challenge many modern day moguls face is more to do with over-communication than miscommunication.

Process Is Power

Neonate startup companies tend not to focus on institutionalizing and documenting the way they do business. Small teams are by their very nature cohesive, especially those that are forged in the fires of the early bootstrapping, hand-to-mouth months of the venture. If you want your startup to grow into a real company, then start writing things down. Human Resource Manuals, Payment Protocols for Vendors, Benefits Onboarding Decks, Employee Stock Option Plans etc. Remember, the strength of the Roman Empire depended just as much on their strong administrative protocols and their stone roads as it did on the strength of their army (and definitely more than the Caesars' cult leadership). Beware the Ides of Entrepreneurial March my dear founder, set up your startup for success by making sure that from day 1, the empire has the ability to outlast the emperor.

Technology, Technology, Technology

Since this is a book focused on Digital Health Entrepreneurship, this pillar will be the focus on this chapter. We will spend a bit more time here and start with your digital window to the world; your startups landing page.

Landing Page

A landing page is simply the first page that pops up when a user accesses your platform (website or application) on the internet, whether via a browser or native application. Eventually, it is the first page that your users will "land on" after clicking through on a digital marketing or social media links and calls-to-action. But hold onto your entrepreneurial horses' compadre, we must first design the stable before we go out corralling for customers. The landing page is an essential component of any well-crafted, effective, inbound growth strategy. First impressions do count, as there is no refresh button when it comes to a user's initial perception. The idea is to convert as many visitors as possible into leads and as many leads as possible into eventual paying customers or loyal Daily/Monthly Active Users (DAU/MAUs) that would generate plenty of lucrative Big Data.

Landing pages are oxymoronic in that they must be both catchy and simple. As with minimalistic architecture, your goal should always be to eliminate as many distractions as possible, but still be pleasing to the eye and fulfilling to the soul, especially since your platform must have multiple landing pages as all great landing pages should target a specific customer or (since you are now an expert) psychographic profile. However, all landing pages must align to your company's branding, imagery and positioning. The user should be greeted with a relevant welcome message, memorable or attention-grabbing headline, image or video. A great way to check if your landing page is snappy enough is the 'Blink Test'—i.e. will your visitor know what your company is offering, why you and only you are the best at offering it, and why it's valuable to them in a blink of the eye (under 5 s)?

A landing page can either have a call to action, for example, allowing your visitors to download more content/tech or a simple sign up form for future offers; this is called a Lead Capture Form (LCF). For most digital companies, the LCF and more importantly its length, is the most crucial element of the landing page. Designing the optimal form is important as you need to collect as much information as is relevant to your core service while not losing your customer to a lengthy mind numbing form filling process. Some digital health platforms might only require a simple form that asks for a user's name and email address. Other's might require a phone number in order to send an OTP (One Time Password or Pin) for added security. The goal of the LCF is to try and sort the different visitors into actionable leads for your sales staff or loyal users that your customer service or development teams can interact with.

Another important consideration is the type of copy (text) that is on your call-to-action button that is usually at the bottom of the landing page and directs your visitors to take a desired action. That's why words like "Submit" or "Register" are not only boring but they are in their nature too vague. Digital Health founders need to be specific, by using actionable words and phrases such as "Access Your Wellness Profile Immediately" or "Download Your Diabetes Shield Now" or "Sign Up for Free Access." Remember, it's not the steak that sells, it's the sizzle!

Speaking of sizzle, another common technique to jazz up your landing pages is to showcase "Social Proof." This can be a bit tricky in health care as we have to be

concerned with the Health Insurance Portability and Accountability Act (HIPAA), however getting patients permission or including actual user's first name only or blocking out their eyes in a picture from their featured testimonials is a great way to convert other visitors into users. Beyond user testimonials, digital health companies, especially those focused on the enterprise or B2B business models, can use case studies, whereby their innovative technology solution provided Hospital X with Y% of savings over the course of Z months. Another two less effective forms of social proof include embedded social media posts as well as download or user visit counters.

As with any technical development, optimizing your landing page is an ongoing process. Knowing where your users clicks and how long they spend on each screen will allow you to tailor your landing page to their needs. To do this, there are a variety of "heat-mapping" techniques that founders must employ.

Heat Mapping

A heat map is a data visualization tool that showcases how visitors interact with a web page using a color-coded system. Cast your eyes at maybe the most well-known heat map of all-time (at least by digital marketers), which shows that people read in an F-shaped pattern on the web [3].

In most heat maps, the red and yellow portions of the map indicate a highly viewed areas with red signifying the highest, and the blue areas are where visitors looked the least.

This particular data was gathered by the *Nielsen Norman Group* from an eye-tracking study that monitored visitors' gaze as they encountered text on a web page.

Heat maps from eye-tracking experiments are the most accurate, but they're also the costliest and most inconvenient to produce. Studies like the Nielsen Norman one above usually take place in a controlled setting (lab, in-house) with a research team or pricey hardware that *observes your visitors' eyes* as they interact with your web page. These can cost upwards of several thousands of dollars to run.

Because hiring an entire team of researchers is out of the question for most businesses, many entrepreneurs instead turn to mouse (the hardware not the device)-tracking software. As opposed to monitoring actual eye movements, mouse-tracking software monitors visitor *mouse movement*, including details such as clicks, scrolls, and hovers. Haptic equivalents for mobile apps exist as well.

Since this method doesn't require a formal laboratory setting or a hefty chunk of a business's budget, it's much more readily accessible. Today, you can install mouse-tracking software and begin monitoring visitors' behavior immediately—and some research shows that mouse tracking is even nearly as accurately as formal eye-tracking studies do.

The heat map on the left was produced from a formal eye-tracking study, while the one on the right was generated with mouse-tracking. According to *ClickTale*, experiments in which both techniques were administered simultaneously have shown there's an 84–88% correlation between their results [3].

A final type of heat map is the Scroll Heat Map. In his very enlightening *Slate* article "You won't finish this article," Farhad Manjoo revealed findings from a joint heat map analysis between *Chartbeat* and the online magazine. There is no surprise that very few people read all the way through.

Even though an impressive 86.2% of engagement took place below the fold, only 25% of people scrolled past pixel number 1600 (most Slate articles are around 2000 pixels long) [3]. The take home message to digital health entrepreneurs are that insights like these are what scroll maps are helpful for uncovering—particularly on longer pages.

In landing page terms, that's most likely to be a sales page. These expertly drafted persuasive pieces of marketing collateral can grow to behemoth proportions, especially in the world of medical content online.

But how could the very top of a page be viewed less than the middle? Well, research from Chartbeat shows that many people tend to start scrolling before a page even loads, which means they'll miss the very top, a term known as "Scroll Depth".

Two important takeaways that founders must internalize from scroll map tests are:

1. With a scroll map, you won't know why people are scrolling as far as they are. You and your team will have to do some hypothesis testing to figure it out.
2. Sometimes you don't necessarily need to know why people drop off where they do. The goal isn't *always* to get people to scroll deeper

Ultimately, the goal of heat map analysis is to discover real-life visitor(s) behavior and utilize that information to optimize the user experience for them. It is also important to remember that heat maps aren't data; they simply *organize data* in an easily digestible way. They show clicks, scrolls, and hovers. What those mouse movements mean is up to you to determine.

Email List Campaigns and Newsletters

One of the most valuable tool in a marketer's tool kit is the email list(s). The money is in the list [4]. Consider it a living document that should be continuously updated and curated. You will most certainly start by having one email list of all your contacts, which you should eventually start to divide up into a separate list of customers/users, vendors/partners and eventually investors. Don't be afraid to add people you have only met briefly (or for those more aggressive entrepreneurs, even vendors or investors you have not met yet), so long as they have a chance to opt out. In terms of frequency of email barrages, once a month to once a week is usually the case for most technology startups. You don't want to be the founder that cried wolf.

Some quick email math. The average open rate can range from 10 to 30% [4]. The typical CTR or Click Through Rate is usually much, much, lower around 1–3% for links embedded inside the email message. In general, you can expect that around

15% of clicks will convert into paying customers or vendors. This is unfortunately a bit lower in digital healthcare.

There are multiple bulk email service providers, the most popular include *Constant Contact, MailChimp, Sail Thru, Drip, ConvertKit, AWeber, GetResponse, ActiveCampaign*. There are also multiple 'sales by emails' service provides such as *Reply, Streak, Sidekick, Mailmatch, Discover.ly, Boomerang, Nova, Crystal, Conspire*, that are also worth considering, especially for those e-commerce minded digital health entrepreneurs.

Most of these bulk email service providers will allow you to A/B test different email campaigns. They could also provide feedback on the best time to send an email campaign based on previous campaigns as well as who exactly opened your email, what they clicked on and how long they spent on the landing page. Many even provide automated services that help tailor the content of says your newsletter to meet the interests of your users. For example, if your previous newsletter contained a highly viewed story on "10 New Radical Treatments for Diabetic Foot Ulcer" and a low viewed article on "Roses and Rhinoplasty: How to Select the Best Surgeon", the software will make sure those users who clicked on the Diabetic Foot Ulcer article will get more articles on Diabetes, Diabetic Foot Ulcers and Radical treatments in future newsletters for example while those users who clicks on the Rhinoplasty article will get more information on plastic surgery in future newsletter.

If you don't have an email list, you have to start building one today.

A/B Testing

The beauty of adapting a "just-in-time" mindset to digital entrepreneurship is that we can easily deploy multiple versions of the same email list or landing page and see which one sticks best to our core consumer (or other fringe consumers we may want to target down the line). A/B testing must be employed continuously by companies looking to scale.

Founders are encouraged to launch multiple email campaigns and landing pages that target different randomized segments of your core customers. For example, using the heat maps we discussed earlier, you may find out too many people click on the navigation bar on the top instead of clicking the conversion button (e.g. link to *AppStore* and *Google Android Play Store*). You therefore decide to do a few of A/B tests based on the theory of removing the "distractions" around the conversion button. And less distractions should hopefully result in a more seamless user experience and more users.

The data you collect from your landing pages and email list campaigns will help you develop a positive feedback loop to improve future email campaigns and landing pages. But you first need to know what to measure. Are you interested in generating leads, selling a product or just testing your user experience? This answer will determine the conversion action you target, whether it be downloads, registrations or sales. Founders must set the end point even before they begin. Whether you

choose a time period or number of conversations, you must set a deadline. If your test does not produce significant changes after a reasonable deadline, simply end it and move on. You must also test the most "disruptive" elements first, these are the campaign or landing pages' most obvious and prominent elements such as the headline, image, form and call-to-action (CTA) button. You must also test one of these elements at a time. Testing multiple elements simultaneously will produce indecipherable results. It will be virtually impossible to pinpoint which change actually affected your conversion rate.

Finally, don't compare results from different time periods. A/B testing is all about discovering statistical difference in behavior over a given time period. Comparisons between different time periods are not valid as any number of outside influences could impact the results of the ad campaign.

Search Engine Optimization (SEO)

Remember those landing pages we talked about. Well, each time you publish a new landing page, you are adding one more indexed page to your website. The more indexed pages you have the higher your ranking on search engines which would drive more traffic to your website or application via what's known as organic search i.e. user's searching for generic terms such as "diabetes type II." This is why you have to design landing pages that are "search-friendly" or "SEO friendly." To do this, you must optimize the title, headlines, Uniform Resource Locators (URLs)—you know, that words that come after the http://www.yourcompanyname.com/index.html/, with target "Key Words."

Avoid the temptation, don't use spammy ways to speed up the process (automated software like *RankerX, GSA SER and ScrapeBox; link wheels; PBNs; hacking domains*; provides instructions to create spam or spin content), but it only works in the short-term. Remember, building your digital health venture is a marathon, not a sprint.

Start your SEO journey, by getting your landing page to rank highly for one keyword that isn't your brand or company name. Ideally, use long-tail keywords i.e. something very exact, intention-driven keywords with lower competition e.g. Rhinoplasty. This is usually the easy part in healthcare focused ventures. Next, plug each keyword into keyword generator services such as *UberSuggest* to come up with at least 1500 keywords. You can then export those 1500 keywords to the *Google Keyword Planner* to come up with estimates on future traffic level. Next, you should search for those keywords with the *SEOquake* browser plug-in installed to analyze the true keyword difficulty. Eliminate the most competitive ones and keep at least five or ten keywords (depending on your budget) that will bring in the highest traffic. Next, you must search for a SEO checklist and make sure your landing page is optimized accordingly. Finally, founders must build links to their landing pages using the profiles and status pages of all the startups social sites including *Twitter, Instagram, Github, YouTube, Medium, Wordpress, Blog, Tumblr, Facebook*.

Another cool tool, to use is *Buzzbundle* which helps entrepreneurs engage in conversations about your keywords across almost all platforms. Remember to be contextual and to ultimately bring value; only mention your product if it makes sense. It is important to make comments that are personal, rather than just spewing out automated spam.

Seducing the Fourth Estate

Reporters, like users and vendors, need to see social proof before they plug you or your venture into their own media machine. In simple terms, if other people write about you, you are worth writing about. Reporters most often don't like products or direct product pitches, but they usually love missions. What is your burning platform? What part of healthcare are you disrupting? What disease are your trying to eradicate? Talk about what you're doing, why you're doing it, who is doing it as well and why it needs to be done.

It is also important to have a Press Kit in your arsenal. This could be a simple pitch deck or presentation/word document with a general company overview in the form of an elevator pitch, founder photos, logos, press mentions, product screenshots/videos/photographs and most importantly, that all important founding story.

Needless to say, your intro email to a journalist should be short and sweet, sent under that basic premise of "We're here. Are you interested?" There is no need to put links in the initial email, seduction takes time.

Once the initial fourth estate flirtations are over, it's time to go for goal by creating a list of the top 100 (or ideally 1000 blogs) in the disease or subsector of healthcare you are trying to disrupt and to simple start contacting them one by one. Another important tool to install the *Scraper Chrome Extension*. Feel free to double check by searching your categories in *Alltop* and *Blogrank*. You can then use the Scrapper to extract a list of hundreds of blogs relevant to your chosen topic or subindustry.

Another method to create a list of blogs is to go to digitalmethods.net/Dmi/ToolGoogleNewsScraper and scrap the *Google News API* using your keywords. This tool however requires the use of the Firefox browser and a Firefox plugin.

Another cool too is *Buzzstream* which you can use to send prepopulated but personalized intro emails to as many journalists as you need to with a limited of 500 emails per day.

Social Media Strategies

We live in a social media crazed world where both users and vendors are spending more time glued to their phones than out in the real world. But hey, that's why you decided to start a digital health venture. Your presence on social media should not be an afterthought, as many (if not most) of you users and vendors will first come across your platform on the social web (vs. the searchable web). This is why the

only advice that I give entrepreneurs when choosing the brand name of their venture is for the name to be available in a .com as well as in all social media outlets. No sense in having a companyname.com if your Instagram handle is @company-name123 or @companynamehealth.

Remember, as with all outward communication, the difference between spam and initiating a conversation is the thought and effort you put into it. Be genuine. Be real. Also, be very selective about whom you follow. If you are following a lot of people, check if they actually enjoy your feed. If not, you are doing something wrong and following the wrong accounts.

Let's tackle the Gram first. Instagram is (as of the course of this writing) the fastest growing social media platform in the world. A great method to bring visitors to your account is to follow and like, like, like. Go to the most recent section for the hashtag you choose to target or use in your upcoming campaign, and simply select the top picture. Follow that account. Go to its photos, and like the most recent photos. 1 in 4 should follow back. Consider it an insta-courtesy. Also, remember that when you send people to a link, add the comment "link in bio" to a photo and change the link in your profile.

Use marketplaces like *Shoutcart* and *Instafluence* to find influencers in your disease or subindustry space and *Audiense* is the tool to be used to find individual influencers. But note that spending all your advertising budget with a few well known influencers can be expensive. A better strategy is to spread the wealth. Find Instagram handles with large yet untapped audiences. In my opinion it is better to use 20 accounts with 50,000 followers and pay $10 per shout-out rather than finding that one account with one million users and paying them the standard $1000. As of this writings, it generally costs around $1 for every 1000 users.

Another strategy is to try and convince or simple pay accounts with a big reach to like your photos for a lower premium than you would pay for a shout-out or direct post. You could also just simple 'steal' an influencer's post by reposting it in your own feed. Regramming works well but ask for permission before you do it. If you are lucky, some influencers might even regram your posts to return the favor.

Maximize the reach of your own feed by employing the most relevant hashtags. *Tagsforlikes* is a great tool to find popular hash-tags. Don't be afraid to drop comments full of hash-tags in the first 10–15 min to maximize your reach and don't be too proud to ask your loyal follower base for some extra help. Posts that work endlessly include those that have a call-to-action: "Double tap if you X!" "Tag someone who Y!"

Employ a similar strategy while running competitions or giveaways on your Instagram. Maximize those coupons or free samples, by making sure the winner of the competition has to infect as many other Instagram users as possible with your hashtag or handle.

To utilize your Instagram most effectively, use photo-editing services like *Canva* to create your images and customize your posts. Use post scheduling services such as *Hootsuite* or *Buffergram* to schedule 100 posts in advance. Most of these services will also allow you to control your feed on both Twitter and Instagram as well. Also

be sure to avoid the temptation of buying fake followers (and even fake likes) or bots (like *FollowLiker*) which may work well initially to assuage any social proof concerns, but they are not recommended in the long run as users can easily look at the number of likes or comments on a post and compare it to the number of (fake) users you have.

Next, let's tackle the granddaddy of all social media platforms, Twitter. Favoriting and retweeting tweets works but it is a sloth-slug strategy. Also, gaining followers (on both Twitter and Instagram) is not the end game, they are the means to the end of gaining more users on your own platform. Manually following other users is the best, but again slowest, way to gain followers. But if you do decide to do it, be sure to create a search syntax that finds the right users to follow. For example: search for "internal medicine" if you are selling software that promises to reduce hospital readmissions. Make sure to click "All" to get the most recent results instead of the top results of people who have the most followers. Using semi-manual following software like *FollowLiker* works but be sure to use it with your startups twitter handle and not your own personal profile as it will definitely destroy the (any?) enjoyment of using Twitter. A great tool to aid you in your quest for authentic communication with people across the Twitterverse is software like *TweetDeck*, which allows you to respond instantly to any tweet. Again, don't let this become a rote copypaste script. Consider each tweet or retweet as an unparalleled opportunity to engage in an authentic, one-on-one conversation with a would-be user or vendor. *Twitter Cards* are an easy way to allow a Twitter user to perform an action without actually leaving the Twitter interface. Use them. Again, similar to Instagram, use Audiense to search for the most relevant Twitter profiles and reach out to them in bulk, again using Hootsuite or Buffer. As always, avoid the temptation to simple copy and paste. Make each reach out message unique. It will be worth the effort. For example, tag influencers for retweets by emphasizing how awesome they are: "here's what I learnt from Person X."

A final key image based social media network that should be featured in any digital health company's social media strategy is Pinterest a web and mobile application company that operates a software system designed to discover information on the World Wide Web, mainly using images and on a shorter scale, GIFs and videos. From a growth perspective, think of Pinterest as a discovery engine. Entrepreneurs are encouraged to follow a lot of people and like some of their pins to make them take notice. This strategy is especially relevant for women's health startups or digital health ventures focused on hardware, specifically wearables. Founders can create boards full of beautiful pins and encourage others to follow your boards by pinning their content. These are strategies that definitely work and stand out. But to really make your product explode on Pinterest, create a legitimate and active account, constantly interacting with others in your healthcare niche. Create great pins with a tacit endorsement comment and join group boards (usually by invitation or board swap), and be sure to leverage those audiences as best as you can. *Pingroupie* is a great way to find relevant group boards.

Shifting from social media platform that are primarily concerned with images (although all are moving into a world of video and even live broadcasting) all

digital health entrepreneurs must employ similar social media strategies to platforms that are known for video content. On YouTube be sure to find and employ keywords the same way you did for your general SEO. There are as well two more YouTube specific tools that you can use, such as, *Google Display Planner* or *YouTube Autosuggest* (simply type your keywords and see what YouTube recommends you search for).

All your corporate YouTube videos should have descriptions that are 300–500 words of text in length with a 2–5% keyword density [4]. You can test for keyword density at http://smallseotools.com/keyword-density-checker/. It is also important to make sure to name the actual video files with your keywords even before you upload your videos to YouTube. It is also equally important to spend a decent amount of time on adding a good thumbnail (remember, first impressions do count). Be sure to include closed captions, especially for product demos or when using complex medical terms. You should also put annotations to other videos so that people keep watching your videos on YouTube. Also, create your own keyword-based playlists. Inject your videos in it, and drive traffic to that playlist—which just so happens to contain your video, which again just happens to include and link to all of our content.

Finally, encourage your viewer to subscribe to your YouTube channel or give your video the thumbs up at the right moment in your video, again remember, your videos are a means to the end of getting more traffic to your website, so don't get lost in the Bermuda Triangle of YouTube cyber-celebrity.

The final social media platform we will discuss is Snapchat, the poison préféré of the selfie generation. This ephemeral messaging app definitely attracts younger users but has been losing ground to its arch nemesis Instagram. Nevertheless, digital health entrepreneurs, especially those in the wellness space, should certainly tap into Snapchats social web to boost their brands recognition. One feature in which Snapchat reigns supreme are its geotags. Geotags are composed of a logo and a location tag, which your users can add it to their snaps. Digital health founders could also utilize Snapchat to build that first pillar of scale—People. Feel free to introduce any new vendors or staff members in your company or network. You can also feature "a day in the life with a ____", such as a vendor, user, staff member to really drive home why your USP is so unique. Feel free to also use the ghost to update your users and build awareness for different diseases or illnesses that you focus on in your startup. Don't be afraid to celebrate the holidays, for example, highlight labor and delivery nurses or OB/GYNs on Mother's Day.

Most importantly, before going on a snapping spree (or going crazy on any other social media outlet), remember that as an entrepreneur in healthcare, our first responsibility is to HIPAA laws and respecting patient confidentiality. Make sure you always get formal consent and release forms from patients and healthcare providers to avoid any future problems or litigation.

Finally, a big part of your social media strategy should involve content marketing. Remember, you need to build your platform as the Authority Site when it comes to the disease or subsector of healthcare that you are disrupting.

For starters, don't be ashamed of catching users with compelling click-bait. "8 ways to Lose Weight before Valentine's Day", The Secrets of Psychiatrists", "10 Trends in the Revenue Cycle Management Space that will Revolutionize the Healthcare Industry", "Hacking HIPAA 101: Everything You Need to Know". I know you wished that you could have clicked on every one of them right? I do to.

Post your thought leadership articles on *Reddit* first, tweak it until it is good enough with the feedback of the Reddit community, then post it to Medium.com or on your corporate Blog/website. If you decide to present your thought leadership to a group of SMEs (subject matter experts) or industry influencers in the physical world, then be sure to leave a digital trace by using *Meetup* and *Eventbrite* to book presentations. This should also help boost your SEO.

A great list of tools to check for getting people to your platform for free to check out your amazing content include: *Import.io, Hunter, Voila Norbert, Spaceship.rocks, SellHack, Mattermark, Mention, Fresh Web Explorer, Gainful, LeadFuze*.

Next, here is a list of free tools to maximize visitors' value once they're on the site such as: *HelloBar, SalesIQ, Inboundgeo, Leadfeeder, Intercom*.

In general, when it comes to content marketing, Pareto's Principle comes to mind: spend 20% of your time writing content and 80% distributing your content. Build a social following and always cross-post across multiple social media channels where possible. For example, LinkedIn allows you to share an article with up to 50 *LinkedIn* groups at once and services like *Hootsuite*, allow you to both schedule and send the same post across multiple platforms.

App Store Optimization

Now that you have optimized your landing page(s) and A/B tested it to death, there is some extra value that can be squeeze by optimizing the way your app is uploaded to the app stores. From the get go, be sure to put your keywords in the title and description.

Next, to boost your ranking, all you have to do is directly ask people if they enjoyed the app or found it useful. If they do, then simply ask them to rate it. If they do not, ask them for feedback.

Another way to boost your profile on the app store is the competitors hack. Brush up your list of competitors. Find the ones that don't have an app (you will be surprised how many traditional healthcare providers don't) and then simply list them subtly in your app's description. You can even add a cheeky line like: "The best app alternative to Healthcare Provider X". Remember, be bold.

Another tactic that works quite well to boost your apps profile on the app store is to buy a lot of downloads on the day you launch your app. It is, after all, all about social validation and first impressions. You can use 'click farm' services such as *Tapjoy* to pay for downloads. This however, should not be your long term strategy.

How to Win at Paid Search Marketing

Speaking of paying, let's talk about spending that limited marketing budget more appropriately than simply buying downloads. The gold standard of paid digital marketing is **Google AdWords** (Google Pay-Per-Click search advertising solution). First, you must focus on the quality of your ads. (i.e. Quality Score) in order to win bidding contests cheaply. The way Google AdWords' advertising system works is that you, the advertiser bid on certain keywords in order for your clickable ads to appear in Google's search results. This is how Google makes money from search. It is not tied directly to Search Engine Optimization. Similar to your bulk email campaigns, your goal should be to maximize your CTR (Click-Through-Rate). In general terms, 8% is a good CTR. 3% is bad, 15% is great [4].

Start by testing a dozen different ad variations on day 1 with a low $3–$5 daily budget per ad. Simple repeat on day 2 with 12 new and optimized ad variations (same budget). Next, repeat on day 3 with 12 new and optimized ad variations (same budget). This should be enough to get a good CTR. Start low and slow and eventually you will get where you need to go.

Be sure to use the keyword that you are advertising in the text of your ad. A great list of keywords that signal commercial intent can be found on https://github.com/growth-austen/intent-keywords. Use them. Founders should also take the time to search for keywords that nobody bids on using tools like *Ubersuggest*. Finally, make sure to have proper tracking in place to know where the clicks are coming from.

Measuring Success: How to Track Almost Anything

Now that you know how to grow, here is what you have to show. Investors (both current and future) will hound you for these metrics, most importantly your LTC/CAC and DAU/MAU.

Fundamental Law of Growth

Like Newton's laws of gravity or momentum, most tech start-ups who sell directly to their customers—both enterprises and consumers—must eventually obey the Fundamental Law of Growth: LTV/CAC > 3. There's a lot of nuance as to why [5], but suffice to say that the LTV/CAC ratio speaks to a start-up's revenue trajectory, capital needs, and in turn, how much irrational exuberance is demanded of its investors [5]. The lower the LTV/CAC ratio, the less efficient a company is at deploying

capital and the more money it needs to fuel growth; conversely, the higher the LTV/CAC ratio, the more efficient the company is and thus the more value it creates for the same amount of capital. Though this can be derived, many before me have empirically observed that 3× is roughly the threshold needed to build big, sustainable businesses [5].

Exceptions to the Fundamental Law of Growth include companies whose value is not predicated on revenue (e.g., disruptive technologies, monopolies, social networks, intellectual property) as well as companies where revenue is achieved indirectly (e.g., ad-tech networks, certain marketplaces, certain viral growth start-ups) or discontinuously (e.g., government contractors) typically do not follow this rule [5].

As we will later cover, assessing a company's valuation is a discipline on its own and growth is only one factor in that calculation. However, for simplicity's sake, one can assume that tech companies who don't obey the Fundamental Law of Growth will eventually lose access to capital, drastically slow their growth, and watch their valuations plummet [5].

The following are two case studies of digital health companies and how they fared against the Fundamental Law of Growth:

Case Example: Clover Health, Health Insurance Payor

Clover Health is a new age health insurance company currently valued at just under $1 billion USD with a focus on utilizing technology, services and data to humanize healthcare. Let us apply the Fundamental Law of Growth to Clover Health:

Customer Lifetime—Clover is a Medicare Advantage plan, so when seniors switch to a plan, they tend to stay there, so let's use 3 years even though the true lifetime may be longer

Average Revenue Per User—Medicare Advantage average payments are publicly available and average around 10,000 USD per user

Margin %—incumbent healthcare insurance payors have gross margins in the 5–10% range with a maximum of 15% as mandated by Obamacare, so we will assume 15%

Customer Acquisition Cost (CAC)—Medicare Advantage fixes broker commissions on a state by state level (<$550); additional channels such as direct-to-consumer are likely more expensive, so we will assume $800 for the blended CAC.

$$\textbf{Valuation Cap} = \textbf{Equity Valuation}$$

Further potential upside should also be looked forward to as costs are expected should fall as Clover expands across the United States and works more directly with Healthcare service (provider) networks.

Case Example: ZocDoc, Online Doctor Reservations

ZocDoc is an online platform where patients can find in-network neighborhood doctors, instantly book appointments online, see reviews by other patients, get reminders for upcoming appointments and preventive checkups, and fill out part of their paperwork online. ZocDoc is also based in New York City and is currently valued at 1.8 billion USD. Let us apply the Fundamental Law of Growth to ZocDoc.

Customer Lifetime—ZocDoc has traditionally targeted standalone physician practices (they are now trying to target more established healthcare provider networks). These doctors typically opt out of the 300 USD per month subscription per physician once they established a sizable patient base with in a year. Again, to be conservative, we will assume 2 years

Average Revenue Per User (ARPU)—$3000 as reported publicly by ZocDoc

Margin %—since ZocDoc is a SaaS company at its core with light-touch customer service should probably achieve 60–80% margins, so let's assume a very high 80% margin

Customer Acquisition Cost (CAC)—Selling to physician practices must is challenging and the founders of ZocDoc have many incredible stories of being literally escorted out of physician offices by security, so like any high-touch inside sales operation, ZocDoc's CAC probably ranges from the $1–10K range; so we will assume $3K as it is closer to the bottom on the range [5].

$$\text{LTV} / \text{CAC} = 2 \text{ years} \times \$3000 / \text{year} \times 80\% / \$3000 = 1.60\text{x}$$

So we can see that even with a very conservative CAC and very optimistic profit margin. We must also keep in mind that as competition increases, customer lifetimes and pricing erode too, further driving down the LTV/CAC ratio. We can now clearly see why ZocDoc is shifting sales to hospital system customers which would probably result in a 1000× higher LTV and only 20× higher CAC [5].

It is important to note however, that there are also some VCs that believe that a lack of understanding customer acquisition costs and life time value is driving companies to premature failure and that focusing on a large LTV/CAC ratio can be a trap especially when the payback period may be long even if LTV/CAC is large.

So why do investors sometimes grant multibillion dollar valuations if the Fundamental Law of Growth displays an LTV/CAC below three? The answer is a most likely a combination of optimistic upside predictions of Brighter Days Ahead (BDA), downside protections and what can only be described as Fear of Missing Out (FOMO) [5] on a 'hot' company that is set to disrupt a market with a multibillion or even trillion-dollar Total Addressable Market (TAM).

Downside protections are when early stage investors insulate themselves from potential future losses using some techniques we will cover shortly. This allows VCs to hedge their large investments and at the same time, fully benefit from the positive press their investment will generate for the entrepreneurs and their venture.

With regards to optimistic upside predictions, both investors and entrepreneurs especially must always remain eternally optimistic—expecting CLVs would extend, ARPUs to increase, margins would expand, and CACs to decline [5].

The Stickiness Ratio

The Daily Active Users (DAU) to Monthly Active Users (MAU) Ratio is a great way to measure the stickiness of your platform—that is, how often people engage with your product or solution. DAU is the number of unique users who engage with your product during a 24-h window. MAU is the number of unique users who engage with your product over a 30-day window (yes including weekends).

Dividing the number of DAUs by the number of MAUs is a great way to show investors how active your user base is. All social consideration aside, the longer your user spend on your digital platform, the higher your stickiness, the more investors love you.

As one of the Godfather's of venture capital, Paul Graham, sums it up:

> If there's one number every founder should always know, it's the company's growth rate. That's the measure of a startup. If you don't know that number, you don't even know if you're doing well or badly. The best thing to measure the growth rate of is revenue. The next best, for startups that aren't charging initially, is active users. That's a reasonable proxy for revenue growth because whenever the startup does start trying to make money, their revenues will probably be a constant multiple of active users.

The stickiness ratio may be deceptively simple in an intuitive sense, but figuring out what to measure could be tricky. It all boils down to how you define 'active' for your product or service. Active could mean anything from a user making a purchase (for ecommerce based ventures), to a certain number of pages viewed/videos watched/comments (for content focused startups), or the number of product login/usage (for SaaS companies that rely on a PMPM model).

A variation of this metric is to swap the number of MAU with the total number of unique weekly active users (WAU). This gives you the DAU/WAU Ratio.

The stickiness ratio is helps you as a founder understand how valuable your product is to your users. It is a snapshot of user retention. For early stage startups, this is a helpful metric for evaluating traction and potential revenue. Using the ratio—instead of DAU or MAU alone—gives you the necessary context to understand the actual level of engagement.

The downside is that the Stickiness Ratio doesn't tell you *which* users are being retained and which users are churning (losing interest in you're a platform). This is where a cohort retention analysis is useful. A cohort can be any similar group of users you define—often categorized by a unit of time. Be sure to dig into the weeds.

Keep in mind that even multibillion dollar, super sticky and addictive social media apps do not have a 100% DAU/MAU ration. According to renowned Silicon Valley venture capitalist firm Sequoia, the standard DAU/MAU ratio in the digital world is 10–20% with only a handful of companies over 50%.

Finally, a few fire round tips and hints on how to track your performance from a technical perspective:

Google Analytics is the gold standard.

- Follow the Google Analytics setup guide here: https://support.google.com/analytics/answer/1008015?hl=en
- Set up e-commerce tracking here: https://support.google.com/tagmanager/answer/6107169
- You can find a perfect dashboard for a revenue generating site here: https://analytics.google.com/analytics/web/template?uid=nblAnxQXTqCqtWbdZMtjJg
- You can find a perfect dashboard for a non-revenue site here: https://analytics.google.com/analytics/web/template?uid=jfJLs1wqQTOS8L2OYGgiQ
- Use *Google Analytics URL* builder to track each and every campaign. https://ga-dev-tools.appspot.com/campaign-url-builder/
- Use the tool *FullStory* to make usability tests of your own website. This tool lets you record and play back as a video every session of users visiting your site.

Hybrid Health

Hybrid Healthcare is a term coined by digital health entrepreneur Sophie Smith, Founder and CEO of Nabta Health whereby healthcare must continue to be delivered by both traditional and digital means. Even though the future of quality healthcare is firmly set in the coalescence of the digital world with not just the physical world, but the biological one as well (what is known as the singularity) the healthcare industry and tis entrepreneurs must still be open to embracing a hybrid approach if they are to truly scale their business.

Since the days of Hammurabi, healthcare has always been affiliated with the physical world. Doctors would visit with patients the same way they do today, the only difference would be that these ancient Babylonian doctors were paid based on how many of their patients remained healthy, not the current fee for service model of 'sickcare.'

Today, some 4000 years after Hammurabi's famous coded tablet, digital health entrepreneurs must consider both hybrid models of healthcare finance and healthcare delivery. Coding the digital realm is not enough. To grow, healthcare entrepreneurs must dare to cross the digital divide and plunge headfirst into the archaic world of traditional healthcare delivery.

Cera Care

Cera Care (www.ceracare.co.uk) is a London-based technology-enabled home care company that was established by digital health entrepreneur Dr. Mahiben (Ben) Maruthappu, a physician, researcher, and health policy specialist, and Marek Sacha,

an engineer and entrepreneur to allow families to arrange, schedule and manage home care for elderly relatives, it uses an on-demand digital platform to match people seeking in-home assistance with professional carers.

During their early days, Cera raised seed money from notable angel investors including David Buttress, the former CEO of JustEat, and Peter Sands, the former CEO of Standard Chartered. With £1.3 million raised, at the time it was the largest seed-round funding in European healthcare history. Cera Care raised an additional £1.4 million in funding in April 2017.

Cera transitioned into a more integrated healthcare model in March 2017, when the largest of the NHS Trusts, the Barts Health NHS Trust, partnered with Cera to provide carers for elderly patients in their own homes. The Trust sought to prevent the bane of bed blocking by accelerating the patient's discharge from their five Barts Health hospitals. The partnership also allowed NHS staff to refer patients to carers through the Cera platform, potentially matching up to six million patients with caretakers. As the agreement with the NHS was finalized, Cera contracted hybrid technology behemoth (and world's most valuable startup) Uber, to transport both patients and carers. Following the launch of its partnership with Uber, Cera commenced another digital partnership with taxi service Gett to deliver items from London chemists to patients at home.

Not giving up on its digital roots, Cera introduced its Chabot, Martha, in May 2017. Created in partnership with Bloomsbury AI, Martha was designed to use artificial intelligence to review patients' digital records and provide health alerts based on data points gathered by Cera's care workers. A great example of the digital starting to coalesce with both the physical and the biological. Cera soon developed a patient care dashboard to provide patients with on-demand access to care, medications, transportation, food, and doctor's services via a tablet computer (take that Hammurabi). It also developed a platform that predicts patient deteriorations by computing the risk of events such as hospitalizations and pesky readmissions based on care worker input.

By the end of 2017, Cera had over 10 partnerships with NHS organizations, councils, and public organizations, including Age UK and the Dementia Action Alliance. It won a bunch of awards including the Health Startup of the Year award at the British Startup Awards, Dementia Care Provider of the Year at the LaingBuisson Awards, and the Digital Health Innovation of the Year award at the Global Awards. Cera Care was also included at the European Innovation Summit as one of the EU's Top 50 Startups.

For their dedication to patient care and corporate growth, Cera went on to raise an additional $17 million in Series A funding in May 2018 from renowned institutional investors such as is Guinness Asset Management (via its EIS fund) and Yabeo (which is the lead investor in Germany's biggest traditional care supply company Pflegebox), and Kairos. In addition, a number of Cera's original seed backers have contributed with follow on investments.

Continuing its a hybrid healthcare strategy, Cera is using its Series A funding to expand its digital services further across the U.K., launching in an additional three cities beyond London, namely Manchester, Leeds and Birmingham, via what it is calling a "buy and build" strategy. This will see Cera buy struggling homecare

agencies across the U.K.—many of which it says lack the technology to scale and grow independently—as a more rapid means of expanding [6].

According to Cera, "a fragmented market of over 8000 homecare providers, Cera has built the technology to quickly aggregate U.K. homecare businesses in a scalable manner, in what will be a U.K. first from a startup in this space. This model will also be used to drive Cera's expansion to Germany" [7].

The injection of capital will also support Cera's continued investment in AI, especially since its data lake or digital data set has grown to "over 1 million data points"—via 90% quarter-on-quarter increase—which it intends to feed into its machine learning-powered predictive analytics tool to help improve health outcomes and reduce preventable hospital admissions. This time, Cera is taking careful steps forward with respect to regulatory changes on data privacy in Europe known as the General Data Protection Regulation (GDRP). Cera is also doubling down on its hybrid healthcare strategy by working on a collaboration with the NHS 111 call center that would permit integration of data records between Cera and the NHS 111 helpline service. The hybrid healthcare startup is also working on Amazon Alexa integration and has formed an exclusive partnership with traditional media provider the Daily Mail Group, to offer home care to Daily Mail readers and users.

Nabta Health

Nabta Health (www.nabtahealth.com) is founded by digital health serial entrepreneur Sophie Smith with a very unconventional background for a techy—Sophie studied history at Cambridge. Nabta provides a comprehensive set of digital health services to women, which mirror the health-related challenges and concerns that accompany every major event in their lives; from birth, through puberty, marriage and pregnancy, to parenting, perimenopause and beyond. Nabta is one of the first next generation healthcare providers in the MEASA (Middle East, Africa, South Asia) region; a pioneer for Health 3.0, reimaging care pathways and plans to include Hybrid Healthcare as standard. For example, Nabta is currently creating a blueprint for Hybrid Antenatal Care, which will see half of all antenatal appointments substituted with virtual consultations, supported by a digital starter pack. The objective of Hybrid Healthcare here is to ensure that 100% of women in the MEASA region attend at least one antenatal appointment, thereby reducing the risk of early onset gestational diabetes, which currently affects one in four women in Saudi Arabia [8].

Another way Nabta is pushing towards the hybrid healthcare horizon is by integrating with various physical hardware devices that have been built to disrupt traditional healthcare services, such as the OvuSense by Fertility Focus.

Nabta partnered with Fertility Focus with a twofold objective: (1) to make OvuSense available to women in the MEASA region by integrating it seamlessly with Nabta Cycle—a period and ovulation tracker, that incorporates region-specific functionality and (2) to further improve the outcomes associated with the use of OvuSense through the application of Big Data Analytics and AI.

By developing a hardware and software hybrid service, Nabta Cycle with OvuSense provides real-time, 24-h advance predictions of ovulation with up to 99% accuracy (Fig. 14.2). In addition to this, at the start of each cycle, Nabta Cycle provides a full 8-day fertile window—these features help women to take back control of their planning for pregnancy.

Nabta uses its proprietary technology to create a "Health 3.0" experience for women. What this means is that the Nabta team is innovating simultaneously in two fields: in the medical field, with our R&D and smart medical devices, and in the technology field, with their hybrid healthcare provision (in-person consultations + telehealth), blockchain-based PHRs and our MI/AL healthcare assistant.

In addition to this, Nabta intends to be at the forefront of personalized (genetic) medicine and disrupt even traditional healthcare service providers using gene editing techniques such as CRISPRs/Cas 9 that will, as an example, prevent or cure diseases such as cystic fibrosis by eliminating faulty genes in children and adults.

Fig. 14.2 Nabta Cycle with the Ovusense

Vyltalize Health

Vytalize Health (www.vytalizehealth.com) was founded by four friends, two doctors and two self-proclaimed techies, Dr. Hasan Bayat, Dr. Amer Alnajar, Omar Elrabie and CEO Faris Ghawi in Hoboken, New Jersey as a hybrid healthcare provider of primary care for seniors that uses a combination of telemedicine and traditional in -home visits to services to Medicare recipients. Each patient receives their own Vytalize Health tablet (take that times two Hammurabi) that allows for 24/7 access to their care team via telemedicine, thereby reducing their need to have a cumbersome traditional healthcare visit. Upon signing up to Vytalizes service, a patient will automatically receive a Medicare approved Annual Wellness Visit, behavioral health assessment, and the option to enroll in Medicare's Chronic Care Management (CCM) program. Only if a patient enrolls into the CCM program, will they receive their Vytalize Health tablet. This program will assign a Vytalize Health care team to the patient which includes Medical Assistants, a Nurse Practitioner, and a Primary Care Physician.

Vytalize's goal is to decrease hospitalizations by keeping patients healthy through access, monthly check ins, and general high quality care of the hybrid variety. Even though this service is covered by Medicare, Vytalize Health was initially struggling to sign patients up even after spending over a year building the brand by hosting presentations at senior centers and communities, targeted digital marketing campaigns (to the caregivers), sponsoring events, etc. It was not until Vytalize Health acquired a small physician practice in Rockland County, New York for a mere $70,000 that it began to see traction. This practice had 177 patients, and each one of them opted in for all of Vytalize Health's services. With a lifetime value of $2600 per patient, the deal eventually payed back in spades. At this point, the 'one-to-many-deal' tipping point that every startup strives for, became a reality. Vytalize Health immediately acquired three more practices and partnered up with two over the next 12 months.

For Vytalize Health, the key trust factor here in building out their hybrid healthcare model is that ardent cornerstone of traditional healthcare delivery: the physician. Without this trust factor, without the physician buy in, Vytalize's patients would have been very wary to sign up for its service.

Conclusion

If the internet was the catalyst for Health 2.0—the interfacing of digital technologies with traditional healthcare—blockchain, as the enabler of patient-owned health data and truly patient-centric care, is the catalyst for Health 3.0.

Health 3.0 is the next generation of care, whereby the digital enablement of every stage in the care pathway—from healthy living, to prevention, diagnosis, treatment and rehabilitation—is assumed. In other words, what we term "telehealth" today

will, in future, be referred to simply as "health". Virtual consultations, blockchain-based Personal Health Records (PHRs) and digital prescriptions will become the norm; to provide a patient with a paper-based prescription will seem farcical, outdated. This normalizing and standardizing of technology-use in a clinical setting is what we refer to as Hybrid Healthcare—healthcare that streamlines and future-proofs traditional clinical practices by integrating them seamlessly with technology enablers such as smartphones, wearables and other smart devices.

It is generally accepted that moving the majority of healthcare spend from "diagnosis" and "treatment" to "healthy living" and "prevention" will not reduce costs in the long term [6]. If anything, preventing the onset of chronic illness will result in people living longer and costing the healthcare industry more in later life. Aaron Carroll refers to the "Iron Triangle" of healthcare—access, cost and quality—whereby increasing access to and quality of care will inevitably result in a corresponding increase in costs, and vice versa [9]. Therefore, the primary objective of Hybrid Healthcare is not to reduce healthcare expenditure in absolute terms, but to facilitate equal access to healthcare services in line with the United Nation's Global Goals.

There will always be a temptation to adopt a "all is grist for the mill" mentality when seeking ways to grow your digital health company. Remember, the single most important strategic decision a founder of a fast growing company needs to make; is learning when to say no.

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Chapter 15
Digital Health Trends

Rubin Pillay

Meet Alex. He's 42 years old and seemingly healthy. When walking his dog, Alex is alerted about a deviation in his health condition by his wearable device and advised to see a doctor. He schedules an appointment with his family physician in one click using his smart phone. The physician reviews Alex's patient history, including the most recent information from his wearable device, performs an examination and advises Alex to see a cardiologist. Using a registry of ranking specialists, Alex receives recommendations based on his personal preference and schedules an appointment. By giving the cardiologist access to Alex's patient history, Alex enables her to review all relevant information prior to the appointment. After her examination, the specialist adds her diagnosis to Alex's patient history. Comparing Alex's patient profile against a large set of patients with the same disease and similar health profiles, she can predict that the standard surgery for this disease would be risky for Alex. The analysis shows that for Alex's specific case, a certain drug can be expected to provide the best outcomes. Because Alex has given his consent to mapping his profile against ongoing clinical studies, he is matched to a clinical trial that has shown positive results and fewer side effects than with current drugs on the market. Alex decides to enroll in the clinical trial to benefit from the new drug and to contribute his data to the research study. As part of the trial, Alex downloads an app to track specific health parameters. He uses his monitoring device to manage his physical activity, and resumes life as before, knowing that he will be notified if anything urgent arises. Meanwhile, the smart care team consisting of doctors and supporting professionals remotely monitor Alex's progress in real time through the information provided by his wearable device. They use this information to advise him on his daily plan, if necessary, and motivate Alex to continue on his prescriptions and follow his health plan. Alex has also given his consent for his data to be used by researchers

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in different organizations for the creation of new drugs and the adaption of drugs in order to help improve the lives of patients just like him.

This is the patient journey in the digital age!

With 10 billion people—that's the global population projected by 2050, and with many enjoying longer lives—the services required by healthcare systems will have to adapt and grow. No one can be certain how the industry will evolve, but with new challenges come exciting solutions. What we can be certain of is that future trends will be driven by unprecedented access to big data and a greater involvement by the patient or healthcare consumer in shaping those services to their greater benefit.

Digitalization has reached every aspect of life today and is about to change how we as a society provide and consume healthcare services. Breakthrough technologies, such as the Internet of Things, artificial intelligence, blockchain, and cloud computing, have matured and are finding broader adoption in the healthcare world. Advancements in medical technology, such as genomics, health wearables, and sensors, show increasing success in medicine. And research around nanomedicine, robotics, and medical 3D printing is promising to deliver targeted, precise, and timely healthcare services.

This new era of true digital connection is giving people greater access to health information and resources. The convergence of three main drivers is the catalyst for many healthcare organizations to start their digital transformation, with the goal to create more value for patients along the continuum of care:

- Cost pressures, demographics, and the rise of chronic diseases
- A digital, empowered, "connected" patient, who shares valuable data with the wider community
- The emergence of digital technology and advanced medical devices, sensors, and wearables for extended monitoring and prevention and more fact-based care decisions

To respond to those driving forces and capitalize on the opportunities that digitalization brings along, the traditional healthcare value chain is evolving towards a digital healthcare network. This network connects patients, professionals, and providers in real time for more responsive, patient-centric care. The digital healthcare network will be the foundation for a new, consumer-centric healthcare system in which stakeholders respond more and more to mutual, shared challenges. Its open platform for communication and integration will enable shared, connected, and fluid data among all network participants.

The transition to digital healthcare offers many opportunities for both established organizations as well as new players. All future healthcare services will need to be designed in a way that promotes the following concepts:

- Value-based care: adapting structures focusing on optimal patient outcomes at the lowest possible cost
- Patient engagement: encouraging patients to take a more responsible role in disease management and prevention

- Personalized medicine: gaining groundbreaking insights into the human body at unprecedented, highly granular levels
- Participatory research and clinical trials: including more stakeholders and a higher number of participants
- Balanced demand and supply: optimizing service offerings and eliminating waste with real-time insight and predictive

Strategic Objectives Analysis

Current healthcare models are not sustainable. For digital transformation to have a maximal impact on creating more value in healthcare, it will require quick and ongoing adaptations by healthcare providers, insurers, and life sciences organizations. What is emerging is a healthcare ecosystem, moving beyond traditional hierarchies, in which all healthcare shareholders participate and benefit. Leaders will be inspired to re-evaluate business models, business processes, and workforce structures to meet key strategic objectives, including:

- *Enhancing the patient experience*: Every patient is a consumer, and consumer expectations are bleeding into healthcare. Digital technology is changing the traditional role of patients, enabling better-informed choices regarding health and well-being. Patients can more readily access health information and diagnose their own conditions or easily obtain test results and even receive better treatment. *How can we meet the expectations of the new healthcare consumers?*
- *Optimizing outcomes for each individual patient*: Today's patients need to see value from the insight into options they have for their specific health issues, based on key performance indicators and assessments of other patients facing similar circumstances. Pure statistics are not meaningful. The demonstrated outcomes must be specifically relevant to the individual patient and his or her particular context. *How do we provide healthcare services with optimized outcomes for each individual patient?*
- *Empowering healthcare workers*: Complexity is the enemy of workforce empowerment. It can drive up costs and slow down progress. New digital tools enable the workforce to reevaluate how they work and get the most out of their professional training, freeing them from paperwork to focus on patient care. *How can we restructure and empower our workforces to allow them to perform at their best?*
- *Increasing their organization's operational efficiency*: Providers are under constant cost pressures and resource constraints. A next-generation digital core will be the foundation for a smarter business—leveraging Internet of Things (IoT) and machine learning for higher automation and offering cockpits with embedded analytics, prediction, and simulation to ensure a more agile nervous system for the entire organization. *How do we remove unnecessary cost and waste and free resources for innovation and better patient care?*

- *Applying data-driven clinical innovations*: The most dramatic change in the digital economy will be driven by hyperconnectivity and Big Data science. These will transform nearly every business model in healthcare. The ability to monitor patients, collect health data, and react early to, or even predict, medical conditions, independent from physical constraints, will massively change the healthcare value chain and the way healthcare professionals deliver care to their patients. *How can we move from a mainly experience-based healthcare model to delivering personalized medicine based on real-world evidence?*

The starting point of the digital journey is the ability to reimagine everything. To help you reimagine your organization, you can think along three core dimensions: business models, business processes, and work environment. These dimensions can be evaluated by using the concept of value-based care and asking two basic questions:

- Are we improving patient outcomes?
- Are we reducing costs?

Business Model Trends

Healthcare is evolving from the optimization of single providers to building a community of specialists that collaborates in a wider ecosystem. By harnessing the flexibility of digital and, in particular, cloud-based solutions, the healthcare industry can find new ways to help professionals and consumers jointly create more comprehensive, patient-centric, and cost-effective healthcare.

Digital technology provides an opportunity to *integrate the care continuum* to elevate quality of care and health consumer interaction by orchestrating one-dimensional, single-step care providers into communities of care. The goal is to ensure targeted and personalized responses across the spectrum of service providers. Digital services can help patients navigate the healthcare system, foster prevention and manage chronic diseases, and empower them to take an active role in monitoring and and managing their health. Real-time analytics can provide insights into the population and trends and help clinicians and researchers make good decisions atthe moment of necessity.

Healthcare providers can lead in patient outcomes through *specialization* rather than offering a wide selection of services. To adopt this business model, organizations need to know their key strengths (such as units leading in patient outcomes), and identify noncore services to shed. This could include investing in clinical research, attracting new patients seeking specialized, highquality care, leveraging economies of scale through a higher volume and exchanging specialized knowledge within the ecosystem.

By harnessing digital technologies and electronic medical records from various sources, clinics can unveil new clinical insights from large populations beyond traditional clinical trials. This will help inform patient care with lessons learned from

previous cases, optimize and personalize clinical treatment and increase transparency of clinical outcomes.

Connectivity also enables providers to offer innovative healthcare services to address the needs of the new healthcare consumers by leveraging new channels and acessing new market segments like corporate health to help companies keep the workforce healthy and productive, medical tourism aimed at offering high-quality, specialized services at attractive prices to patients willing to get healthcare abroad and retail healthcare which will offer standard services at convenient locations and office hours.

Leveraging real-time digital platforms will also create opportunities aimed at eliminating inefficiencies in healthcare delivery by brokering resources within healthcare networks. Stakeholders can connect beyond traditional channels to match supply and demand better using the digital age to close the gap. These would include amongst others, optimizing appointments.

Business Process Trends

With new business models opening the doors to increased collaboration across the digital healthcare network, processes are arising that provide solutions at every stage of healthcare—preventative, curative, and educational.

Digital technologies, such as sensors and mobile devices, help the patient and the care team to monitor conditions and behavior in real time and react faster and more effectively. We will thus be able to create effective preventive healthcare by empowering and motivating patients to take responsibility for their health. Engaging patients in disease prevention will result in better health outcomes.

With digitalized solutions, healthcare professionals can underpin clinical decisions and diagnostics with real-world evidence. They can gain new insights into our physiology, biology, and anatomy. By sharing health information over the digital health network and combining it with relevant clinical research, we can rely less on experienced-based medicine and find the root causes of diseases [1]. This includes:

- Outsourcing of highly specialized diagnostics
- Identifying and accessing relevant clinical research
- Eliminating duplicate testing
- Making patients a trusted source of valuable health information

Remote patient monitoring is among the top ten use cases that will drive IoT growth through 2020 across all industries [2]. Through delivery of telemedicine services with digital and interactive technologies, organizations can virtualize care venues, continuously track relevant biological signals, and facilitate early detection and prediction of health issues—extending their impact beyond traditional borders.

Digital technology will also help us meet health consumer expectations for individualized care. Medication and treatment can be tailored to each patient, promising

better health outcomes, for example, by matching doses and active ingredients to individual genetic profiles rather than the general population. Leveraging the digital healthcare network, patients and providers will jointly define actionable health plans, agree on individual health goals, and use technology to monitor progress and react to deviations in real time.

When live data from all critical resource categories becomes available in the digital healthcare network, physical assets, care teams, and the patient can be planned simultaneously, even across organizational borders. Data capture can be automated through machine-to-machine communication and connected medical devices in real time. Advanced resource planning combines actual status with simulations and what-if scenarios thereby enabling us to manage resources smartly, efficiently, and in real time.

Connectivity also empowers the workforce with real-time insights and communication. Organizations can enjoy full transparency and real-time insights into all care activities and across all care team roles and care venues. New technology makes it possible to eliminate repetitive hand-over of tasks and error prone manual transmission of information. Lightweight, enterprise-grade communication tools provide professionals the same level of convenience they experience in their private lives.

The Future of the Work Environment

People working in healthcare do so because they feel it is their calling, even a dream job. Yet the burgeoning healthcare infrastructure prohibits them from giving hands-on, effective care. With digital technology, they will find new opportunities to do their job better and grow in their profession. They will also be able to actively contribute to the solutions of the future, creating the next cycle of proactive care.

In the new digital healthcare network, a physician's responsibilities will go beyond one-off diagnostics to include advising and coordinating along the continuum of care. Access to relevant clinical and research information combined with advanced clinical decision-support systems will help empower physicians to evolve into a new role of trusted facilitator. Whether rule-based or through insights from smart data, the digital health network will provide a new level of clinical decision support to healthcare stakeholders to make the best decision for each patient based on real-world evidence thereby driving better outcomes.

Human interaction will continue to be key in healthcare. Digitalization will enrich this interaction for better patient outcomes and more efficient deployment of scarce medical resources. Supporting technology, such as sensors, speech recognition, and automated documentation, releases nurses from traditional, routine tasks, freeing them up for more time with patients. They can focus on value adding activities, such as interaction, providing advice, and planning recovery, making for an improved patient experience.

Employers aim to create work environments that foster open communication across specialties. Mutual knowledge sharing based on proven patient outcomes will create a new generation that questions hierarchies and assumes shared responsibility. Digitisation encourages and faciltates the easy formation of collaborative and cross-functional care teams that then create clear and patient-centric key performance indicators.

Applying data-driven innovations will also extend and accelerate clinical research. Researchers use real-time analysis of clinical and genomic data, ranging from large patient cohorts down to the individual, anonymized patient. This capability allows researchers to validate hypotheses instantly and ask the best follow-up research question based on the results. Breakthrough research results can be generated in hours rather than years.

Redesigned applications enriched with machine learning and embedded analytics will not only automate back office processes, like patient billing. They will also relieve your workforce from related tedious routine tasks and help to overcome knowledge silos across departments. The automation of processes will result in smart and efficient operations.

Conclusion

Digital health has become synonymous with disruptive innovation in health care. Proponents say it has the power to transform every aspect of health and health care delivery, from improving patients' health status to the process of paying for a medical procedure. Despite that promise, digital health has yet to become ubiquitous in the U.S. health care system.

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Chapter 16
Future Entrepreneurship in Digital Health

Homero Rivas

Background

Medicine and entrepreneurship may have gone hand-in-hand since the earliest humans. For thousands of years, medicine has been practiced in many different ways: from very primitive interventions, like a skull trepanation, basic abscess drainage, hemorrhage control, etc., to the present implementation of very sophisticated diagnostic and interventional technologies, such as scar-less surgery, genomics and precision health, robotics, and artificial intelligence among many others. Throughout this progression, physicians have, in general, been entrepreneurs by default. Good or bad, we have been performing the trade called "medicine" by offering our services for something else, such as goods, other services, benefits, money, and in many cases just personal satisfaction. Sadly, during all these years, the core business model of medicine has remained greatly unchanged and quite antiquated. Usually and mostly in clinical practice, a physician can only serve a given patient at a time using a B2C (business-to-consumer) model or, more aptly, a P2P (physician-to-patient) model. This reflects the foundation of the doctor–patient relationship and what most people may think about when describing the practice of medicine. Unfortunately, this model is not scalable and is extremely limited, especially when having a limited number of care providers and an unlimited number of patients, and results in a very inadequate throughput and poor access to care. Certainly, preventive medicine conducted through public health strategies can reach much wider populations; however, such an approach represents high-risk investment and a long-term plan, with considerable uncertainty regarding the return on investment. As a matter of fact, and sadly, most government health budgets only allocate very little to prevention. As it has become evident in other chapters of this book, Digital Health has disrupted the way most people practice and receive

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healthcare and it truly empowers all stakeholders to potentially gain universal access to care in most if not all specialties.

The Perfect Storm in Healthcare for Entrepreneurship

Lately, due to multiple diverse factors that include, but are not limited to extremely busy clinical practices, increasingly more complex and older patients, intricate medico-legal issues, reduced pay, and universal implementation of electronic medical records, among many others; there is great dissatisfaction among clinicians and for many there is no incentive to remain in clinical practice. Additionally, attrition from medical school remains a challenge, along with concerns of poor quality of life among potential candidates debating to pursue a medical education or, alternately, some other less challenging careers with more attractive lifestyles. In many other cases, medical students may go through years of medical school with a plan to follow non-clinical pathways by joining a corporate workforce or becoming full-time entrepreneurs as soon as they graduate, if they ever do.

By now, this situation has been identified by a few medical schools and medical associations and has led to organized efforts to implement the concept of entrepreneurship in healthcare as part of the medical curriculum, vision, or core values. Hopefully, in the not so distant future, instead of being the exception this paradigm may be the rule in healthcare across the world. Much like the mass adoption of digital health technologies by younger generations, entrepreneurship in digital health will be inherent to a new generation of clinical workforce of digital natives that if anything, they may question why entrepreneurship and digital health were not fully embraced many years before.

For many, entrepreneurial traits may be natural while for many others such traits would have to be cultivated and nourished throughout their medical education. For this, all medical school curricula should soon include not only basic science and clinical skills, but also and just as importantly, innovation and business courses, providing physicians-in-training a solid foundation in innovation, design thinking, entrepreneurship, marketing, financial forecasting, creation of business plans, pitching, investing, among others. The present profile of a successful physician being risk averse to maintain optimal clinical outcomes will evolve into one more acutely sensitive physician who would gauge optimal risk and opportunity when it comes to innovating and creating novel value propositions in entrepreneurial ventures in healthcare.

Without a doubt, physician-entrepreneurs will be involved not only as consultants or investors of business ventures but, most importantly, as founders of numerous different healthcare startups. Our competitive advantage in medicine, together with sound business acumen, will make the physician-entrepreneur a key to success for these healthcare businesses. Indeed, there is no one better than healthcare providers to empathize with patients and to identify voids in this complex market. We are certainly the right stakeholders to ideate, innovate, and implement new concepts

and processes through startups in healthcare. Additionally, it is likely that successful physician-entrepreneurs will also venture outside healthcare, leveraging their leadership and business skills in non-medical startups.

The Future Patient-Physician Interaction, Patient-Experience, and New Medical Professions

Soon to be common are innovative business models that implement basic and advanced information and communication technologies along with advanced neural networks or engines of machine learning. A great portion of the patient–physician interaction will be automated and it will rely purely on digital health platforms. Patients will meet with physicians following well-curated differential diagnoses and respective potential treatments proposed by artificial intelligence (AI) platforms. Diagnostic specialties, such as radiology, pathology, dermatology, etc., would be the first to follow these procedures and, soon after, they may be followed by others where automated intervention would take place such as interventional radiology, surgical specialties, etc.

Innovative insurance and revenue models will engage patients and physicians into shaping better lifestyles and promoting a better state of wellness and disease prevention, in contrast to traditional models that support the treatment of disease but do not invest much on prevention. Fee-for-service models clearly incentivize physicians to treat more rather than to be investing in education and prevention. Such models will be the exception rather than the rule.

Regulation will have a paramount role on allowing the creation of innovative revenue models that would promote universal access to care through digital health platforms including telemedicine, genomics, precision medicine, robotics, brain-computer interfaces, etc. For example, genomics will change enormously the practice of medicine, including present insurance practices. In the not so distant future, all births, and even pregnancies *in utero*, will require extensive genomic coding to assess accurately the newborn's health forecast and propose personalized preventive and healthcare life plans. Thus, children would be spared from hereditary diseases before they are even born. Some professions will flourish, such as Geneticists, Artificial Intelligence Medical Informatics, etc., and some new medical super specialists will be created such as Genomic Planners, Genomic Curators, Genomic Editors, Tissue Engineers, Healthcare Designers, Brain Computer Interface Specialists, etc. Regulation within ethical boundaries should promote such an innovative and entrepreneurial spirit.

Probably since the inception of the concept of AI, there has been a general paranoia that AI may replace most professions, including medicine. In healthcare, with no doubt, physicians who do not embrace digital health technologies and AI may soon be replaced by those who do. This transition will be generational and geographic. Digital native generations of patients and medical providers will lead the

way as well as small, visionary countries. Places like the United Arab Emirates have already incorporated Ministers of Artificial Intelligence, Happiness, Future, etc. into their government cabinets, which will allow them to innovate at a much bigger scale by implementing such technologies. Other places, like Singapore or Kuwait, may do the same as they attempt to obtain genomic profiles of all their population. On the contrary and ironically, for larger countries, where most innovating technologies are being created every day like in the United States, their implementation strategies will be laggards in this race due to regulation, litigation, a risk-averse culture in healthcare, etc.

In the near future, the profile of the successful physician-entrepreneur will depict someone who navigates flawlessly through all digital health technologies previously described. On the other hand, not understanding them and not embracing them will take us away from business, as we would be replaced by others who actually do. In addition, the patient–physician interaction will be so different from what it has been until now. From before its inception, extensive, yet simple genomic planning will take place. Through genomics and AI, each of us will have personalized "life portfolios." Minimal viable genomic profiles will be pursued and healthcare providers will become medical curators of such profiles. Digital health literacy will become a must, being even as important as medical knowledge itself. Regular physical checkups would be obtained based on biometrics, wearables, implantables, other smart clothing, sweat analyzers, brain computer interfaces, etc., at any time, 24 h a day, 7 days a week, on demand and remotely through telemedicine. Similar to taking a car in for servicing, AI and genomic platforms will scan and screen patients using medical bots at home to identify any problems, suggest treatments, and if possible, such platforms would take automated action based on those suggestions. Many existing digital health technologies will become quintessential, including bio-3D printing, implantable bio-neuronal circuits, use of soft exoskeletons, among many others. Many diseases will then be curable, some others treatable, and some may not exist anymore.

Markets will evolve as well as the health of large corporations is evaluated up or down depending on AI-based "health indexes" of corporate members. Indeed, the sum of those AI/genomics health checks, which would change day by day, sometimes for the better, sometimes for the worse, could affect a company's value and, hence, its share price. Chief Medical Officers will truly become accountable for the health of their corporations not only for keeping them physically healthy, but also and more importantly, for keeping them financially sound. Everyone would be expected to be healthy and disease would be the exception rather than the rule.

Final Thoughts

A fully re-imagined healthcare delivery system based extensively on digital health, with novel revenue models, entrepreneurially trained physicians across the world, and empowered e-patients with nearly universal connectivity, will inevitably result

in extensive regulation changes that allow care providers and physicians from all over the world to engage with each other, regardless of location. Telemedicine, therefore, will be the rule and physical encounters would be limited to interventional procedures (i.e., surgery, obstetrics, etc.), where even automated procedures will be the norm. Genomics and artificial intelligence networks will work together not only to predict and diagnose disease but also to propose the best precision treatments, which may be manufactured through genomic curation, bio 3D printing, etc. Successful physician entrepreneurs will be those who embrace digital health.

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