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APPLICATIONS OF DIGITAL HEALTH: AN ASSESSMENT OF THE U.S AND SOUTH AFRICAN MARKETS

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An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health 2020.

Abstract

APPLICATIONS OF DIGITAL HEALTH: AN ASSESSMENT OF THE U.S AND SOUTH AFRICAN MARKETS

By Emily Paffhausen

Digital health is the use of innovative technologies to create health-related solutions. The term has expanded over the last decade and today includes products such as wearables, telemedicine, artificial intelligence, mobile applications, genomics, and digital medical devices. These products have been shown to provide several benefits, such as, improving access to healthcare services and knowledge, cost savings, and health services delivery.[1] Furthermore, the field of digital health has seen continuous market growth and venture capital interest in the U.S. since 2011.

The proliferation of mobile phone access across sub-Saharan Africa gave rise to the use of mobile phones for health-related purposes. Due to its lower infrastructure requirements and cost, digital health has been hailed as a potential solution to aid in sub-Saharan Africa's achievement of universal health coverage. The purpose of this study is, therefore, to examine the growth of digital health in the U.S. market and how this may affect the application of digital health in sub-Saharan Africa through both entrepreneurial and investor lenses.

Ultimately this analysis finds that South Africa, and broadly sub-Saharan Africa, offer both entrepreneurs and investors numerous positive opportunities for growth in digital health products. However, their investment markets and entrepreneurial mindset are still developing. Interviewees report there are two gaps in funding size requests. These gaps cause barriers for entrepreneurs to grow and scale their companies. Without enough successful entrepreneurial ventures, it becomes more difficult to convince investors to enter the market. This creates a cyclical paradox for the overall innovation landscape. South Africa's early phase of entrepreneurial investment makes it difficult to strongly conclude that digital health will be a worthwhile investment for health systems in the region long-term. It will be critical for international investors interested in the region to seek healthcare specific venture capital funds to facilitate the growth of the broader entrepreneurial ecosystem on a local level.

Key words: digital health, mobile health, venture capital, international investment markets, sub-Saharan Africa investments.

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CHAPTER ONE: INTRODUCTION

The field of digital health has grown substantially in the past two decades. Today the term digital health has expanded to include a much broader view of health-related technologies, such as wearables, telemedicine, artificial intelligence, mobile applications, genomics, and digital medical devices. Furthermore, the application of digital health has grown to include health tracking, diagnosis, treatment, clinical support, care management, and care delivery. Digital health has been shown to provide several benefits, improving access to healthcare services (especially in hard-to-reach areas), knowledge and access to health workers and health information, cost savings, and health services delivery.[1] Due to this growth and diversity of nomenclature and products, in 2018 the World Health Organization released a detailed classification framework and vocabulary for digital health interventions implemented globally.[2] Investment in the digital health sector globally and within the U.S. is also increasing. In the U.S. funding increased from $4.4 billion in 2016 to $6 billion in 2017 and $8.1 billion in 2018.[3] This highlights the growing market for health-related technologies. In 2017 there were over 300,000 mobile applications and 300 wearables alone - with approximately 200 new apps added to the market each day. Coupled with the 571 published effectiveness studies examining digital health and mobile apps in 2017, this provides evidence that digital health is set to accelerate innovation and positively impact human health.[4] Since 2011 there have been over $30 billion in U.S. venture capital dollars invested into U.S. digital health companies. Assuming that investors expect to receive approximately four times their initial investment over ten years, the market is expected to grow to $120 billion in the next four to six years within the U.S.[3]

Venture capital funding has been hailed as a critical driver of economic development in the United States - funding some of the most innovative companies in the world.[6] In 2011 a study

found that increased venture capital funding was associated with higher income, higher employment, and more new businesses in U.S. cities.[7] Given the positive effects of venture capital investment within the United States, many investors have turned to emerging markets in developing nations. This has given rise to an increasing interest in impact investing; investments made into organizations and funds with the intent to generate a beneficial social or environmental return as well as a financial return.[7] This interest coupled with the increased proliferation of mobile phone access has led to many new entrepreneurial endeavors throughout developing nations, especially throughout Africa where mobile phone penetration is approaching 80%.[30] African venture capital investments have grown substantially in the past five years, 2015 - 2020. According to WeeTracker's Venture Investments Report 2018, venture capitalists invested $725.6 million USD across 458 deals* - a 300% increase in total funding compared to 2017. In 2019 investments continued to rise with a record breaking $1.340 billion USD in investments through 427 deals.[8]

The impact of venture backed technology companies in Africa is already affecting local economies. Rwanda, for example, has become a technology hub housing many successful digital companies, an innovation hub - FabLab, and plans for the Kigali Innovation City. Furthermore, many African nations' economies are growing at impressive rates. According to the International Monetary Fund, in 2019 Uganda's gross domestic product rose by 6.1%, Rwanda's increased by 8.5%, and Libya by an impressive 17.8%.[9] This emphasis on technological innovation and growing economies presents an evolving entrepreneurial market and opportunity to utilize digital health innovations to improve health outcomes beyond the U.S. and throughout Africa. There are, however, challenges to investments into developing economies. Unstable political structures,

* A venture capital deal is an investment transaction between a venture capital firm and startup company where the investor invests a certain amount of money into a startup in exchange for ownership. Deals can be of any size.

high transaction costs, and limited exit opportunities are all barriers to entry that foreign investors face.[43]

In this paper I will examine (1) the current entrepreneurial and venture capital ecosystem in the U.S. and Africa, (2) the potential financial impact of digital health technologies and investments in Africa, and (3) the challenges and opportunities for international investors interested in African venture capital investments.

This paper's target audience is the healthcare venture capital community and relevant stakeholders who may propose and implement global digital health innovation. Therefore, this research is significant to investors interested in healthcare and broadly the global health field as it serves as an educational example for the potential impact of venture capital and entrepreneurial investing on global health initiatives. Often times global health initiatives have less sophisticated financial analysis as entrepreneurial ventures, thus this paper aims to demonstrate how the two fields can positively impact each other.

CHAPTER TWO: LITERATURE REVIEW

2.1 Timeline of Digital Health

In 2000 Seth Frank first formally introduced the field of digital health as internet-focused applications designed to improve three business service areas within the healthcare industry: content, connectivity, and commerce.[10] Frank theorized that access to the internet and internet based applications would produce positive impacts on healthcare faster than any previous technology or communications tool. Although the formal term was introduced in 2000 there were digital health applications throughout the 1990s. For example, the LOINC (Logical Observation Identifiers Names and Codes) database was developed at The Regenstrief Institute at Indiana University School of Medicine in 1994.[11] Initially intended as a classification for laboratory assays, the system expanded to include clinical classifications and provide a standard for health data interoperability.

Noting the growing digitization of patient records, in 1996 the US signed into law the US Health Insurance Portability and Accountability Act (HIPAA) setting standards for the confidentiality and security of personal health information. HIPAA also includes Title II, known as the Administrative Simplification Act. Title II encourages the healthcare industry to become more efficient by advocating the use of electronic transmission for certain patient administrative data. To make the public feel more secure with electronic transmission of data, the government developed new privacy and security rules.[12] This gave way to the new industry of digital health.

The field of digital health has grown substantially in the past two decades. Today the term has expanded to include a much broader view of health-related technologies. For the purpose of this paper I will refer to digital health in eight distinct categories:

1. genomics and sequencing

2. wearables and biosensing
3. telemedicine
4. analytics and big data
5. digital medical devices
6. population health management
7. personal health tools and tracking
8. electronic health records (EHR) and clinical workflow

Over the period of expansion, digital health has been shown to provide several benefits, including: improved access to healthcare services (especially in hard-to-reach areas), improved knowledge and access to health workers and health information, cost savings, and improved health services delivery.[13] Digital health is able to target more parties in the healthcare industry, such as: health providers, payers, pharmaceutical companies, medical device companies, employers, and patients. In a 2019 study, 94% of healthcare executives reported that the pace of innovation in their organizations had increased in the past three years due to emerging health technologies.[14] Furthermore, in 2019 healthcare was named one of the most vulnerable industries for future disruption according to Accenture's Disruptability Index[14]; making it an ideal industry for innovation. For these reasons, digital health's popularity is on the rise and U.S. venture capital investments saw a steady increase from 2011 to 2018 (Figure 1).

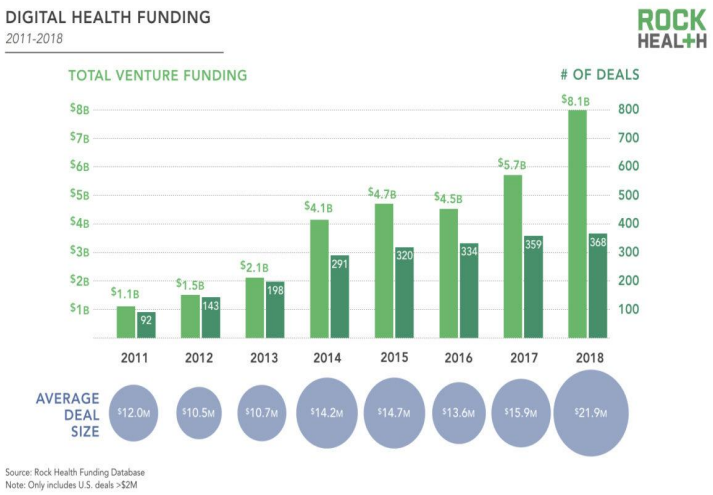


Figure 1: Total venture capital finding in U.S. based digital health companies from 2011 to 2019. Source: Rock Health.[*]

2.2 Digital Health Investments

The majority of digital health companies are funded by venture capital dollars.[15] In 2019 global venture capital funding in digital health, including private equity[*] and venture capital[*], contributed $8.9 billion in funding for 615 deals (a 6% drop compared to $9.5 billion in 698 deals in 2018). Total corporate funding[*] for digital health companies (including venture capital, debt financing[*], and public market financing[*]) contributed $10.1 billion. Overall, digital health

[*] Rock Health is an early stage digital health venture capital firm and research entity.
[*] Private equity refers to investment funds, generally organized as limited partnerships, that buy and restructure companies that are not publicly traded. Private equity firms utilize both equity and debt structures and are not limited to any industry. They typically will buy 100% of a company.
[*] Venture capital is a form of private equity financing that is provided by venture capital firms or funds to startups, early-stage, and emerging companies. Venture capital typically only utilizes equity structures and focuses on specific industries, such as, technology, biotechnology, and clean technology.
[*] Corporate funding refers to the broader area of finance that contains funding and investing structures, such as venture capital. Corporate funding's goal is to increase shareholder value.
[*] Debt Financing refers to when a firm raises money for capital by selling bonds, bills, or notes to individual and/or institutional investors. In return for lending the money, the individuals or institutions become creditors and receive a promise to repay principal and interest on the debt.
[*] Public market financing refers to a company that has held an initial public offering (IPO) and whose shares are traded on a stock exchange.

companies have received a global total of $58 billion in investments from 2010 to 2019 with $44 billion in venture capital funding in over 4,500 deals and almost $14 billion in debt and public market financing (including IPOs).[16]

The most prolific digital health investors have changed over time. In 2016 Khosla Ventures was the most prolific investor with 24 deals in one year (Table 1). In 2019, over 850 investors contributed funding to CB Insights 150 top digital health companies. The most active firms funding this cohort in 2019 were F-Prime Capital (31 deals), New Enterprise Associates (30 deals), and Google Ventures (29 deals) (Table 2).

MOST PROLIFIC INVESTORS

Firms with 6+ investments in 2016

ROCK HEALTH

	Location	# Deals 2011-2016	2016 Investments	
.406 Ventures	Boston	12	· Annum Health · axial Healthcare · CloudHealth	· Healthsense · HealthTell · Nomad Health
ANDREESSEN HOROWITZ	SF Bay Area	21	· Accolade · Benchling · Cardiogram	· Honor · PatientPing · Zipline
GE VENTURES	SF Bay Area	15	· Caremerge · Evidation Health · Chrono Therapeutics	· Human Longevity · Jiff · SilverVue
khosla ventures	SF Bay Area	24	· clear labs · Color Genomics · CrossChx	· Lumiata · Neurotrack · PatientBank
UPMC	Pittsburgh	6	· Cernostics · Health Catalyst · Lantern	· MedCPU · Omicia · Vivify Health

Source: Rock Health Funding Database
Note: Only includes U.S. deals >$2M; data through December 31, 2016

Table 1: The most active digital health investors in 2016.
Source: Rock Health Funding Database 2016.

Investor	Number of deals
F-Prime Capital	31
New Enterprise Associates	30
Google Ventures	29
Venrock	28
Founders Fund	27
Khosla Ventures	27
GE Ventures	22
Social Capital	20
.406 Ventures	19
Andreessen Horowitz	18

Table 2: Top 10 most active venture capital investors within CB Insights 2019 Digital Health 150 cohort (out of 850 unique investors). Source: CB Insights 2019 'Digital Health 150: The Digital Health Startups Redefining the Healthcare Industry' report.

However, in 2018 the digital health sector came under scrutiny for a lack of exits and initial public offerings (IPO) with 110 digital health company exits via acquisition but no IPOs for both 2017 and 2018. A lack of exits indicates startup and early stage companies are struggling to sell their companies, grow to high enough value to be listed on a public market, and/or provide investors with an alternative way to 'cash out' and receive their return on investment. In 2018 alone, investors put $8.1 billion into digital health companies, a 42% increase from the $5.7 billion invested in 2017. This was done through 368 digital health deals and an average deal size of $21.9 million in 2018. Therefore, despite the lack of exit scrutiny, investors were still confident that new entrants could make it in the digital health industry as half

of the investments in 2018 were seed* and series A* rounds.[3] Meaning investors were still confident enough that they will receive a return on their initial investment to invest into early stage rounds of fundraising. Assuming these investors expect a 4x return over 10 years on their initial investments (standard practice), the U.S. market is predicted to grow to $120 billion between 2022 and 2024.

In 2019 digital health provided six public offerings: Livongo, Health Catalyst, Phreesia, Change Healthcare, Peloton, and Progyny. While the performance of these IPOs has been mixed (Figure 2), it could be indicative that U.S. based digital health companies are carving out a stable and more mature niche in the healthcare market. This assumption regarding maturation and stability is because it is incredibly difficult for a company to successfully complete an IPO. This typically only happens when a company is mature enough to uphold Securities and Exchange Commission (SEC) regulations and satisfy public shareholders. Historically, companies will pursue an IPO when they have achieved a private valuation of $1 billion. Therefore, to have six public offerings in one year could be a sign that the digital health industry is growing into a more mature market.

* A seed round refers to a series of investments in which a small amount of investors "seed" a new company with anywhere from $50,000 to $2 million. This money is often used to support a startup's initial market research and early product development.

* A series A round refers to a company's first significant round of venture capital financing. Typically, a series A round will fund anywhere from $2 million to $15 million and is followed by subsequent rounds: series B, C, and potential D.

ROCK HEALTH'S DIGITAL HEALTH PUBLIC COMPANY INDEX

Q3 2019

ROCK HEALTH

TICK	Company	IPO Year	Cap	Q1 2019 Open	Q3 2019 Close	YTD % Change
MODN	Model N	2013	Small Cap	$13.05	$27.76	112.72%
NVTA	Invitae	2015	Small Cap	$10.76	$19.27	79.09%
VEEV	Veeva Systems Inc	2013	Big Cap	$87.55	$152.69	74.40%
SLP	Simulations Plus	1990s	Small Cap	$19.90	$34.70	74.37%
TDOC	Teladoc	2015	Mid Cap	$48.19	$67.72	40.53%
MDSO	Medidata Solutions Inc	2000s	Mid Cap	$65.91	$91.50	38.83%
STRM	Streamline Health Solutions Inc.	1990s	Nano Cap	$0.80	$1.10	37.50%
MB	Mindbody	2015	Mid Cap	$7.32	$10.02	36.89%
NH	Nant Health	2016	Micro Cap	$0.54	$0.72	33.33%
CERN	Cerner Corporation	1980s	Big Cap	$51.46	$68.17	32.47%
IQV	Iqvia Holdings Inc	2014	Big Cap	$114.41	$149.38	30.57%
OMCL	Omnicell, Inc.	2000s	Mid Cap	$60.26	$72.27	19.93%
INOV	Inovalon	2015	Mid Cap	$13.98	$16.39	17.24%
IRTC	iRhythm	2016	Big Cap	$67.89	$74.11	9.16%
HSTM	HealthStream, Inc.	2000s	Small Cap	$23.89	$25.89	8.37%
NXGN	Nextgen Healthcare Inc	1980s	Small Cap	$14.95	$15.67	4.82%
PTON	Peloton Interactive Inc	2019	Mid Cap	n/a	$25.10	-2.56%
PHR	Phreesia Inc	2019	Small Cap	n/a	$24.24	-3.43%
CPSI	Computer Programs and Systems	2000s	Small Cap	$24.80	$22.61	-8.83%
TRHC	Tabula Rasa HealthCare Inc	2016	Small Cap	$62.29	$54.94	-11.80%
HCAT	Health Catalyst Inc	2019	Small Cap	n/a	$31.64	-19.22%
CHNG	Change Healthcare Inc	2019	Small Cap	n/a	$12.08	-19.47%
FIT	Fitbit	2015	Small Cap	$4.87	$3.81	-21.77%
WORX	Scworx Corp	n/a	Nano Cap	$3.23	$2.40	-25.70%
CSLT	Castlight Health Inc	2014	Micro Cap	$2.14	$1.41	-34.11%
VCRA	Vocera Communications Inc	2012	Small Cap	$38.84	$24.65	-36.53%
CRCM	Care.com Inc	2014	Small Cap	$18.95	$10.45	-44.85%
BNFT	Benefitfocus	2013	Small Cap	$45.01	$23.81	-47.10%
LVGO	Livongo Health Inc	2019	Small Cap	n/a	$17.44	-54.23%
EVH	Evolent	2015	Small Cap	$19.70	$7.19	-63.50%

Source: Rock Health Digital Health Public Company Index
Note: For companies that went public in 2019, the YTD % Change column is % change since IPO

Figure 2: Digital health public companies index at Q3 2019.
Note: Progyny is not included in this index as it had not formalized its IPO at this time.

2.3 Trends in Digital Health

As digital health continues to grow as an industry within the United States, new trends within funding emerge. In 2016, Genomics & Sequencing was the most funded category with $410 million venture capital dollars, followed by Analytics & Big Data ($341 million), Wearables & Biosensing ($312 million), Telemedicine ($287 million), Digital Medical Devices ($268 million), and Population Health Management ($198 million).[15] However in 2019, investments have shifted as CB Insights and Rock Health have both identified behavioral health, women's health, senior care, and telehealth as some of the leading trends for 2019 and 2020.[19, 20]

While CB Insights and Rock Health identify these as separate sectors, this paper will address them all broadly as population health management and personal health tools and tracking.

Accenture further breaks down emerging trends into the technologies powering them. In a 2019 report Accenture states DARQ (Distributed ledger technology, Artificial intelligence, Reality [virtual, augmented], and Quantum computing) technologies will become the foundation for next-generation products and services (Figure 3).[21] When healthcare executives were asked to rank which of the DARQ technologies will have the greatest impact on their organization over the next three years, 41% ranked artificial intelligence (AI) number one.[20] Healthcare organizations are already using AI technologies to change how patients are interacting with healthcare providers, such as, performing diagnosis based on retinal scans, facial features, and speech. Overall, artificial intelligence is helping to alleviate workload for healthcare professionals. The majority (68%) of healthcare executives agree that within the next three years, every employee in their organization will have access to artificial technology to help them finish their work.[20]

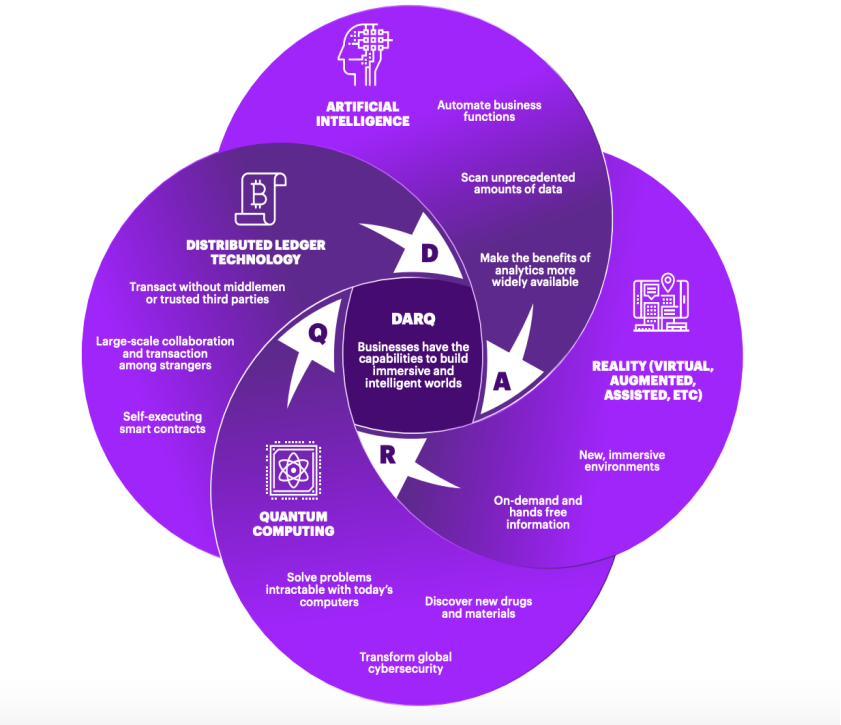


Figure 3: Visualization of various DARQ (Distributed ledger technology, Artificial intelligence, Reality [virtual, augmented, etc], and Quantum computing) technologies. Source is Accenture Digital Health Technology Vision 2019 report.

2.4 Success in Digital Health

For the purpose of this paper I will broadly define digital health success as *a service or product's ability to meet a healthcare need by utilizing an innovative technological platform*. However, defining success for digital health companies is increasingly complex. This is because the healthcare market has become very disjointed and cumbersome. A company's ability to meet a healthcare need through technological innovation will not be enough to move the industry long-term.

Moreover, success for digital health companies has been inconsistent and many times short lived. For example, digital health startup Zeo, developed a headband and accompanying app to give users their own sleep coach. The company quickly raised over $30 million from

investors. Despite its devoted users the company went out of business a few years later in 2017.[22] Many industry experts believe that companies, like Zeo, struggle because direct to consumer models have traditionally failed in digital health. This is because consumers do not control the bulk of funding for the U.S. healthcare market. Liz Rockett from KP Ventures states "if you believe your insurance should pay for it, it's a hard mental hurdle for folks to get over, myself included."[22] In Zeo's case, they acquired a devoted set of early adopters as customers but struggled to gain the larger, mainstream customer base.

Additionally, experts, such as Dr. Paul Yock from Stanford University, suggest digital health companies are mistakenly being run like a technology start up. The strategy cultivated in the technology sector has been to rush to market with a minimally viable product and then refine based on feedback from users. However, healthcare is a far more complex and regulated industry. Digital health companies must appeal to not only an end user but oftentimes doctors, hospitals, regulatory agencies, and insurers. This makes it more difficult to initially get to market and far more complex to iterate on products once they are in the market. Due to these difficulties, 61% of digital health companies that begin as direct to consumer business will pivot to become business to business.[23] Pivoting to business to business is important because it shifts the financial stakeholdership and business model. For example, 23andMe has become a popular digital health company where consumers are able to provide personal information based on home genetic testing kits purchased online. 23andMe has sold thousands of these kits direct to consumers, but it is not their main revenue source. Their larger business model is based on partnering with pharmaceutical companies for drug development.

Thus, the definition of success will likely evolve as the industry expands and matures. From an investor perspective, success for digital health companies will be determined by their

ability to provide a return on investment and their long-term ability in the market. From a consumer perspective, success will be defined as the ability to provide innovative solutions that address stakeholders' top needs and that positively impact the healthcare industry. However, neither of these outcomes can be determined in the short run and digital health companies will need to be assessed by investors and consumers over the next decade to truly see their long-term impacts.

2.5 Digital Health & Universal Health Coverage

Most of the global population now has access to a mobile phone and service. Due to its versatility and affordability digital health has been put forth as one mechanism to address healthcare inequalities and access in developing nations. For example, in regions where healthcare is scarce and infrastructure is limited, short message services (SMS) are widely used to provide health information and health services. In Africa, text messages are sent out to cell phone users regarding HIV/AIDS prevention and education. In India, women receive text messages reminders to conduct their own breast examinations.[29] Furthermore, in 2017 a systematic study of mobile phone use during an illness in rural China and India suggested mobile phone use is generally associated with better access to healthcare.[53]

The application of digital health provides a great opportunity for the global achievement of universal health coverage (UHC). UHC means that individuals and communities are able to receive the quality healthcare they require without suffering from financial hardship.[24] WHO (World Health Organization) has stated that achieving UHC is essential for the attainment of SDG (Sustainable Development Goal) 3 put forth in 2015 by the United Nations. UHC largely

embodies three objectives: equity in access to health services for all who need them, a standard of quality for health services, and protection against financial risk for using health services.[24]

Achieving UHC requires countries to strengthen their existing health systems. However, in regions where healthcare workers and health infrastructure are limited this is a difficult task. WHO states the most cost effective way to achieving UHC will be through investments into primary healthcare. They define primary health care as an approach to health that is centered on the needs and circumstances of individuals, families, and communities.[24] Primary health care involves the whole person, including physical, mental, and social health. This means that healthcare systems will require a horizontal approach.

A horizontal approach is a comprehensive public health strategy that seeks to treat underlying conditions and causes for ill health. A vertical approach in comparison is a disease specific approach that aims to treat a single condition. Both approaches are valuable within the public health paradigm, however it is traditionally easier to secure funding for vertical approach initiatives. This is because vertical initiatives have easier to measure results and a quicker implementation. Horizontal initiatives involve building health systems that are meant to function autonomously; this can take decades to accomplish.

Digital health is still largely in an experimentation phase globally. Therefore, it makes sense that most digital health applications have taken a vertical approach, such as SMS messages to remind women to conduct their own breast examines.[29] This allows for easier analysis of the initiatives. However, digital health has the potential to fill many gaps in developing nations progress towards UHC. As it evolves digital health may be able to utilize mobile phone access to create a multi-sector health system that contains various digital health applications within it. One example of this budding integration is South Africa's MomConnect. MomConnect started as an

SMS application that pregnant women could sign up for and receive maternal health information. The system is now run by the South African National Department of Health and offers free phone calls to a helpdesk and registration for all new pregnancies into South Africa's public health database.[36] This is not a robust horizontal approach, but it is the start of digital health integrating into a country's large health system and aiding in the access of healthcare.

2.6 Mobile Health & Sub-Saharan Africa

Mobile health refers to the use of mobile communication technology to promote health by supporting various healthcare practices (i.e. health data collection, delivery of healthcare information, or patient observation).[25] This differs from the broader scope of digital health which is not confined to the use of solely mobile devices. Therefore, mobile health is a subset of digital health innovation. This is notable because in the last decade mobile phone penetration in sub-Saharan Africa has risen dramatically. In 2016, two-fifths of individuals in sub-Saharan Africa owned mobile devices.[26] However, it is difficult to accurately estimate the number of unique subscribers and those who may not own a phone but have access. For example, in 2013, 58% of Kenyans who did not own a mobile phone reported they shared a mobile device with someone else.[27] This increased access to mobile phones has given way to positive impacts in multiple industries, including healthcare. Dr. Kharma Rogo, lead health specialist at the World Bank and head of the bank's Health in Africa Initiative, explains in the documentary, *The Great Escape*, "Mobile technology is disrupting every layer of society at an unprecedented pace. The biggest social equalizer now in this part of the world [Africa], I believe, is a cell phone."[28]

A 2011 World Health Organization (WHO) report found that 83% of the 112 member states who participated in the survey reported at least one mobile health initiative in their

country. Figure 4 shows that call centers or healthcare helplines and emergency telephone services were the most common global mobile health initiatives. Almost half (48%) of the participating member states reported the use of mobile devices for emergency and disaster situations. However, the African region reported that only 28% of countries offered emergency mobile phone services (compared to 42%-75% in other regions). WHO speculated that this difference in the use of mobile health could be due to insufficient infrastructure to respond effectively to emergency calls (i.e. lack of hospitals, lack of ambulances, and lack of paved roads). Furthermore, the study went on to outline barriers to mobile health implementation for each WHO region. The African region reported operating costs and knowledge as the largest barriers compared to the reported global barriers of knowledge and policy (Figure 5).[29]

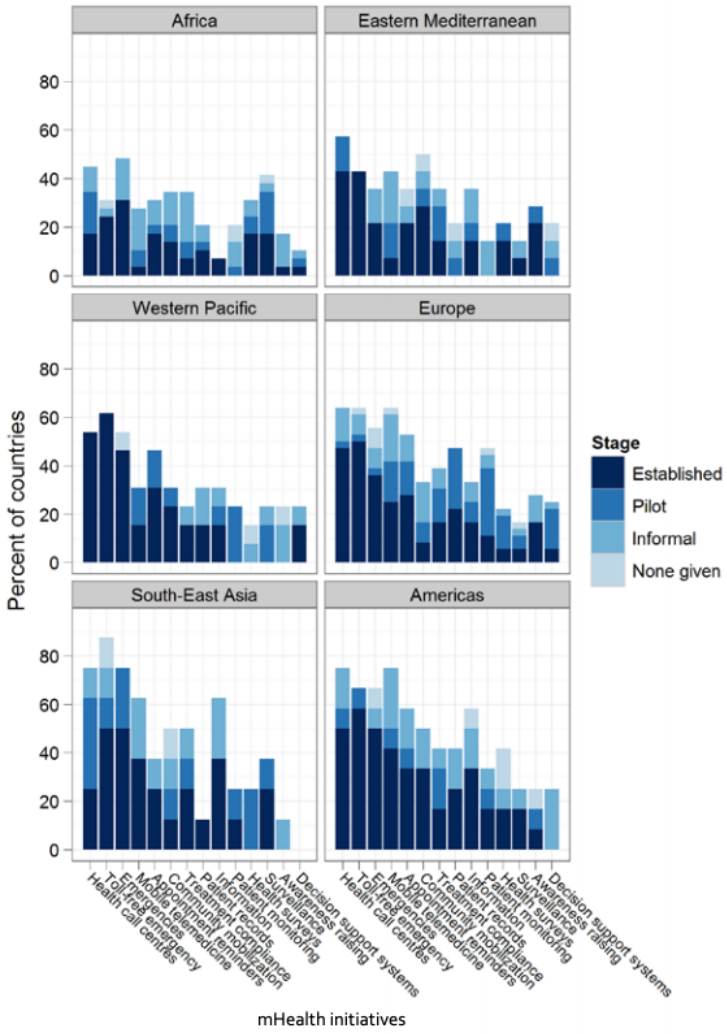


Figure 4: Status of mobile health initiatives by category for each WHO region. Source is WHO 'mHealth New horizons for health through mobile technologies' 2011 report.

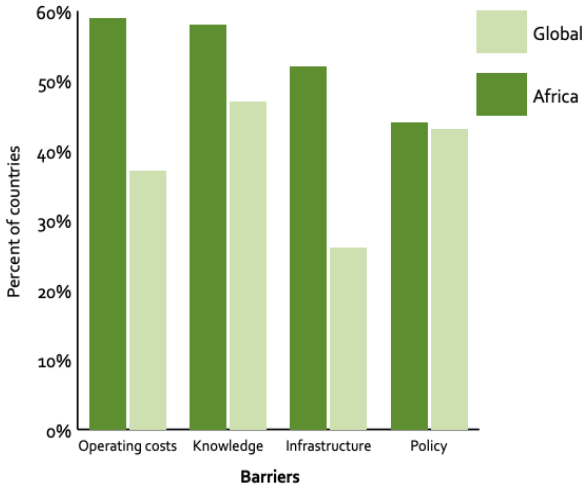


Figure 5: Barriers to implementing mobile health initiatives in WHO African region compared to global reported barriers. Source is WHO 'mHealth New horizons for health through mobile technologies' 2011 report.

In 2019 mobile phone penetration was approaching 80% throughout sub-Saharan Africa.[30] In 2017 the World Bank cited mobile phone infrastructure as the most advanced infrastructural development in Africa.[31] This robust development in telecommunications has resulted in populations utilizing their mobile devices for not only basic communications, but also for integrating business and healthcare. Initially, mobile health utilized SMS-message reminders and received positive affirmation in the literature for its impact on self-management of chronic diseases in low to middle income countries such as South Africa[32] and Bolivia.[33] Today, mobile health has expanded to include mobile apps connected to sensors that diagnose malaria without a blood sample[34], rapid one-on-one responses from a physician[35], and personalized information for mothers at every step of pregnancy.[36] Thus, mobile health is quickly evolving throughout sub-Saharan Africa and poses the potential to allow African countries to leapfrog healthcare hurdles other regions have faced. For example, the rapid proliferation of mobile phones in sub-Saharan

Africa allowed the continent to leapfrog the development of landline infrastructure that other parts of the globe experienced.

2.7 Venture Capital Investments in Africa

In 2019 there were 427 venture capital deals in Africa with an overall funding value of $1.340 billion USD. This is the highest amount of venture capital funding in Africa to date and a $614.4 million USD increase from 2018. This jump can be in part attributed to a few large transactions outside of the digital health industry, such as, Visa taking a 20% equity stake in Nigerian company Interswitch for a total of $20 million USD.[8]

Africa also saw a surge in seed deals in 2019. A total of $104.99 million USD or 30.68% of overall funding was invested through 131 deals in 2019 compared to only 16% of funding going towards seed rounds in 2018.[8] This growth in available seed funding is exciting because this is typically the first round of funding a startup faces. This growth could be indicative of a growing accessibility to funding for African entrepreneurs. Similar to Seed funding, Africa experienced a dramatic (277.73%) rise in series A funding compared to 2018. A total of $300.44 million USD was invested into 43 Series A deals. Most notably, Carepay, a Kenyan digital health startup, raised $45 million USD for their Series A funding cycle from IFHA-ll, ELMA Investments, and The Dutch Ministry of Foreign Affairs.[8]

Overall digital health deals received $74.96 million USD over 49 deals, the third largest sector after FinTech ($678.73 million USD) and CleanTech ($145.24 million USD).[8] This is a 389.94% increase in funding from 2018.[35] Top deals in the health sector include Carepay ($45 million USD), MPHARMA ($9 million USD), and 54gene ($4.5 million USD). The countries

with the highest investments were Nigeria with $5.73 million USD over 12 deals, South Africa with $4.57 million USD over 8 deals, and Egypt with $1.68 million USD over 10 deals.[8]

Alongside the increases in African venture capital funding, the continent experienced a decline in grant and prize money.[8] Historically grant and prize funding have been core forms of financial support for African entrepreneurs. In 2018 $27.5 million USD was awarded as grants and prize money through 195 deals. In 2019 this decreased to only $9.45 million USD awarded through 73 deals.[8] However, non-financial assistance increased in 2019. Wee Tracker states that many early stage ventures in Africa received non-financial support, including free working spaces, mentorship, and fundraising guidance.[8] These deals are not included in the venture capital funding analysis.

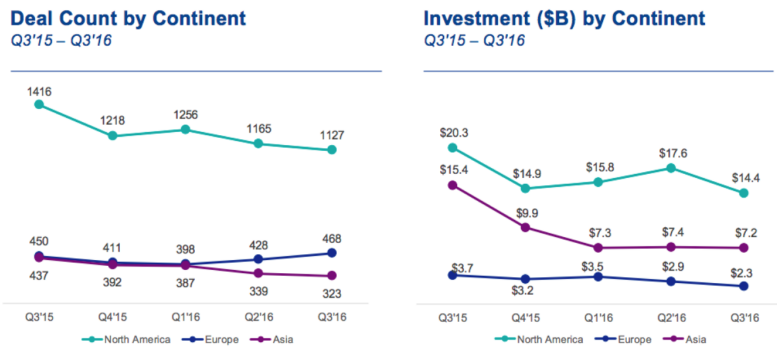
The most prolific investors across all industries in Africa for 2019 with over 9 investments were Samurai Incubate (Japanese venture capital firm with branches in Tokyo, Rwanda and Tel Aviv) and 500 Startups venture capital firm (based in Silicon Valley).[8] Next, with 7 investments was Goodwell Venture Partners (based in Bosie, Idaho) and Algebra Ventures (based in Cairo, Egypt).[8] The most active investors for the healthcare industry were Africa's first biotechnology incubator program, BioCiti Programme and Merck Accelerator (based in Germany).[8]

It is also worth noting external, non-financial events from 2019 that are shaping the entrepreneurial ecosystem in Africa. Senegal became the second African country after Tunisia to pass a Startup Act. The new legislation aims to promote innovation and entrepreneurship by providing tax incentives, startup financing, and a legal framework for registering and labeling new ventures.[38] Jack Ma, ex-chairman of Chinese Alibaba Group, hosted the first year of his Africa Netpreneur Prize Initiative (ANPI) which awarded $1 million USD in prize money to 10

entrepreneurs across Africa. Ma has committed to running the competition for the next ten years.[39] Nigerian e-commerce company, Jumia, successfully listed itself on the New York Stock Exchange in April 2019. This made Jumia the first African startup to list on a major global exchange.[40]

2.8 Challenges to International Investments

More than 80% of startups seek funding from their home countries.[41] However, the ease of capital movement in today's markets has opened up the opportunity for many entrepreneurs to consider international investments - especially entrepreneurs from countries with larger capital opportunity. In 2016 CB Insights data showed that for every dollar available to a European startup, there were six dollars available to their U.S. counterparts. In the last quarter of 2016, Europe closed 468 deals and Asia closed 323 deals compared to 1,127 deals completed in the U.S. over the same timeframe (Figure 6).[41] Furthermore, Gust reports that the U.S., France, and Canada received the most international applications for funding in 2016 (Figure 7).[42]



Venture Pulse, Q3'16, Global Analysis of Venture Funding, KPMG International and CB Insights (data provided by CB Insights) October 13th, 2016.

Figure 6: Venture capital investments per continent in 2016. Source: CB Insights.

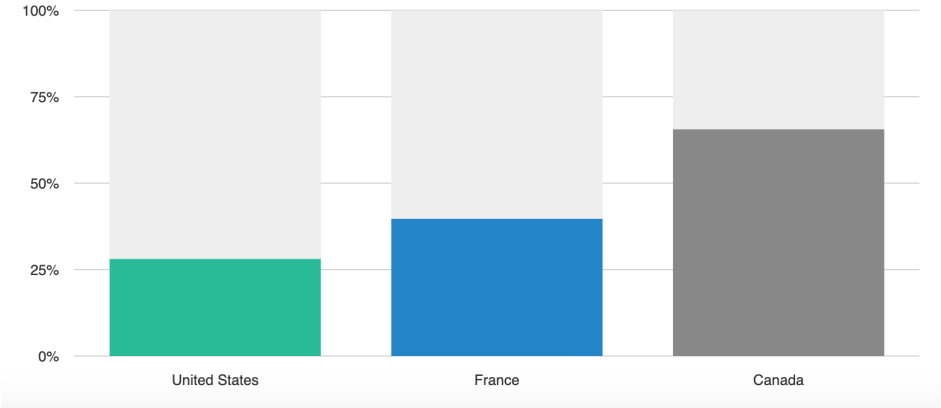


Figure 7: Percent of international funding applicants from July to December 2016. Source: Gust Startup Funding Trends End of the Year 2016.

Through interviews with multiple entrepreneurs who have successfully raised funds abroad and in their home countries, Startupbootcamp, an international accelerator network, compiled the key challenges to international funding: (1) cost to raise funds: raising funds in a foreign country can be expensive as some deals could take weeks or months to close. Financing this way can become more expensive for entrepreneurs than it would be to raise funds in their home countries; (2) perceived risk in emerging markets: foreign investors may not be keen on international investments as they may not fully understand the potential and may perceive a higher risk with emerging markets. For example, U.S. investors typically prefer to invest in U.S. incorporated companies as they understand the laws and tax regulations; (3) domestic success: early stage investors will want to see domestic success or proof of concept.[41]

Furthermore, international investors face higher transaction costs than domestic investors. Specific costs are unique to the international market such as stamp duties, levies, taxes, clearing fees and exchange fees.[43] On top of these, international investors have to account for currency volatility. For example, a U.S. investor will need to convert USD to a foreign currency at the current exchange rate to invest. If the investor holds the investment for three years, they will then

need to convert the currency back to USD. The uncertainty of the future exchange rate poses a risk to the return on investment. Finally, international investors may face liquidity risks. This is when an investor is not able to sell or exit an investment in a timely or profitable manner.

2.9 Digital Health's Future

Digital health is gaining momentum as a solution for multiple healthcare inequalities and consumer pain points in the U.S. and Africa. In the U.S. current trends suggest a larger emphasis is being given to personal health tracking and population health. In Africa trends are evolving from vertical SMS utilization to horizontal systems applications built in tandem with national governments. Moreover, investments have been steadily increasing for both regions. The industry of digital health is still in its infancy as the bulk of U.S. venture capital investments have only been in market for eight years (2011 – 2019).

This review of research and literature has attempted to capture the success and applications of digital health at this moment in time, but the industry will need constant evaluation over the next decade to understand its role in the healthcare system. The subsequent case analysis will examine the role of digital health in South Africa with the aim to provide contextual background for both investors and entrepreneurs.

CHAPTER THREE: METHODS

3.1 Peer Reviewed Articles

An initial search of original research and review articles was conducted via PubMed and Google Scholar using the terms “digital health” and “United States,” “digital health” and “venture capital,” and “mHealth” and “Africa” in the title or abstract. The search was limited to these terms to narrow the focus of the review. The articles were also limited in publication years 2015 to 2020 to cultivate the most up to date analysis and attempt to identify programs that are still active today. This yielded a total of 17,765 Google Scholar articles and 601 PubMed articles. Using exclusion criteria of mHealth studies conducted outside of sub-Saharan Africa, patents, clinical trials, books, and documents yielded a total of 456 articles. Finally, article abstracts were reviewed for reference to digital health’s history in the U.S. market, venture capital investments in the digital health industry, mHealth programs in sub-Saharan Africa, and African entrepreneurial financing frameworks. This selection process yielded a total of 76 articles. Additional internet searches were used to provide background information relevant to the review as well as popular press articles for current financial and legislative analysis.

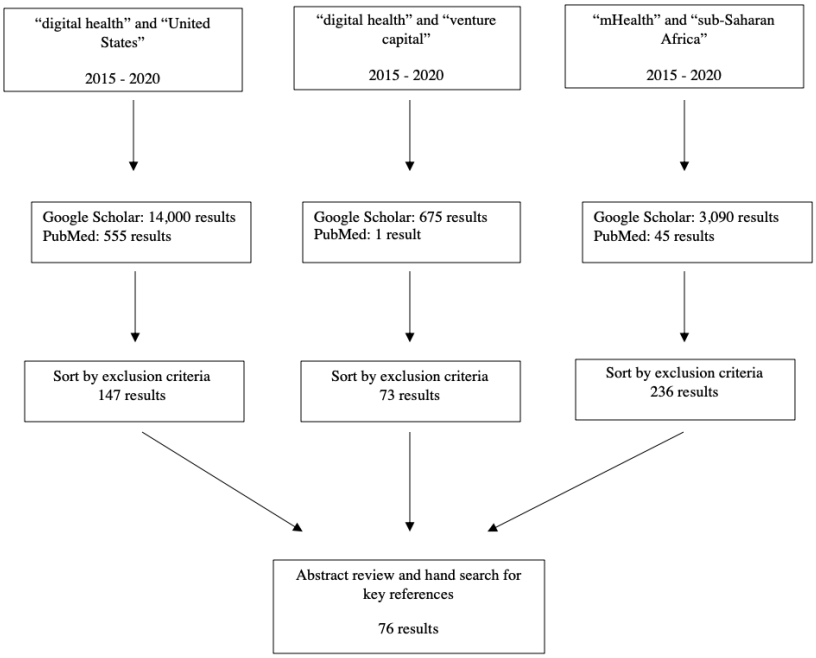


Figure 8: Methodology tree demonstrating the selection process for peer review cited works in this analysis.

3.2 Non-Peer Reviewed Articles

Digital health and its applications in the U.S. and abroad are continuously evolving. Due to this, non-peer reviewed articles and documents were sourced to provide up-to-date information and insights for this paper. An initial search utilizing the terms "digital health" and "United States," "digital health" and "venture capital," and "mHealth" and "Africa" was done via Google. Articles were then sourced using the following inclusion criteria: (1) article from an established popular press entity (i.e. New York Times); (2) information sourced from a government or acclaimed international organization website (i.e. WHO); (3) interview with industry experts in either digital health or venture capital investments; (4) data reports from leading industry research entities (i.e. Rock Health and CB Insights).

3.3 In-Depth Interviews

To supplement the literature review, in-depth interviews (IDI) were conducted with key informants with experience in entrepreneurship and investing throughout Africa. The interview questions are included in the Appendix. Interviewees were identified via personal contacts and were chosen for their various backgrounds and expertise (Table 3). The qualitative insights gained during these interviews was used to inform the South African case analysis and Conclusion and Discussion of this paper.

	Description of key informant's role and expertise
1	Managing partner at European healthcare company and investor into multiple South African companies. Lives half of the year in South Africa and half of the year in Switzerland.
2	South African biotech entrepreneur with experience in Ghana and South Africa.
3	American scientist and entrepreneur with robust experiences in South Africa drug delivery and entrepreneurship programs.

Table 3: Key informants for in-depth interviews

CHAPTER FOUR: SOUTH AFRICA CASE ANALYSIS

In order to examine the opportunities and risks in global digital health, a case analysis was implemented. Global digital health initiatives are so dynamic and unique in nature that it is unlikely a single research paper can generalize the risks and opportunities for the totality of sub-Saharan Africa. Due to the authors accessibility to key informants and experts, South Africa was chosen for a more in-depth examination with several points applying to many other African countries. The subsequent case analysis aims to (1) provide a brief economic background for South Africa, (2) examine the risk and opportunities from an international investor's perspective, and (3) analyze the challenges and support given to South African entrepreneurs. Many of the insights and analysis provided in this case have been drawn from multiple interviews with entrepreneurs and investors in South Africa.

4.1 South African Demographics & Economy

The Republic of South Africa is located on the southern tip of the continent of Africa. It is bordered by Botswana, Lesotho, Mozambique, Namibia, Eswatini, and Zimbabwe. The eastern half of the country is more densely populated than the west with the population concentrated along the southern and southeastern coast, and inland around Pretoria. South Africa has a population of approximately 56,463,617 according to a July 2020 estimate.[44] The country is predominantly black African (80.9%), followed by colored* (8.8%), white (7.8%,) and Indian/Asian (2.5%). There are 11 official languages with the top three being: isiZulu (24.7%), isiXhosa (15.6%), and Afrikaans (12.1%).[44] English is spoken by approximately 8.4% of South Africans and is ranked the 6th most common household language.[44]

South Africa declared independence May 31, 1961 and is a parliamentary republic with three capitals: Pretoria (administrative capital); Cape Town (legislative capital); Bloemfontein (judicial capital).[44] The current chief of state and head of government is President Matamela Cyril Ramaphosa (since 15 February 2018) and Deputy President David Mabuza (since 26 February 2018).

South Africa is a middle-income emerging market with Africa's largest stock exchange (top 20 in the world). The country has an abundance of natural resources, well-developed financial, legal, communications, energy, and transportation systems. Their largest industries are mining (they are the world's largest producer of platinum, gold, chromium), automobile assembly, metalworking, machinery, textiles, iron and steel, chemicals, fertilizer, foodstuffs, and commercial ship repair.[44] They have a labor force of approximately 22.19 million, an unemployment rate of 27.5%, and a GDP per capita of $13,600 according to a 2017 estimate.[44]

4.2 Venture Capital Funding in South Africa

After reaching an all-time high of $241 million USD over 108 deals in 2018, venture capital in South Africa declined in 2019 to $67.34 million USD over 96 deals. In 2019 there were 33 deals in FinTech, 15 deals in analytics, and 8 deals in digital health.[8] The highest value deals were a public safety startup, X RapidDeploy ($12 million USD), Spartan ($6.75 million USD), and Lulalend ($6.5 million USD). An emerging trend to note is that 34% of venture capital backed companies in South Africa are FinTech. Furthermore, 52% of the companies in FinTech are performing a type of lending operation. Out of the top five deals by value, two are small and medium business (SMB) lending firms - Spartan and Lulalend.[8]

Interestingly, Africa is the only continent where more female than male entrepreneurs are seeking funding. In 2019, 2.41% of the deals that received funding were led, founded or co-founded by women. In total, female led companies raised $159.90 million USD or 11.93% of the overall venture capital funding raised in 2019.[8] Nigeria and South Africa had the highest number of female-led startups with 12 and 9 companies receiving funding, respectively. Regarding industries, agritech had the highest number of female-led startups and digital health had the second-highest number.[8]

4.3 Investment Opportunities

Positive economic development in Sub-Saharan Africa has acted as a driver for stakeholders to support entrepreneurial expansion and create digital health solutions. In 2018 Deloitte forecasted Africa as the fastest growing region in the world,[30] highlighting the economies in East, West and Southern Africa for their continuous GDP growth rates. Despite South Africa's recent decline in GDP growth (Figure 9), ease of doing business in the region is improving. In the 2018 Deloitte report, employment rates and access to credit has increased rapidly in the southern regions.[30] Especially, noteworthy for the digital health industry is governmental health care spending in South Africa is expected to increase as the economy grows.[30]

Figure 9: South Africa GDP annual growth rate from 2017 to 2020. Source: Trading Economics.

South Africa is the largest healthcare market in Sub-Saharan Africa, followed by Nigeria, Ghana, Uganda and Kenya. South Africa's GDP is the largest in the Southern region, with high pharmaceutical expenditures and mHealth programs.[30] This aids in the digital health landscape as interviewed entrepreneurs and investors believe that digital health is more understood and yields a better chance of success in South Africa than in other countries in sub-Saharan Africa. Additionally, vibrant tech hubs being developed in Rwanda, Nigeria, and Kenya that have been instrumental in not only attracting international business but also increasing the uptake of technology-based entrepreneurship.

Furthermore, the South African workforce is continuously growing. The World Economic Forum estimates fifteen to twenty million individuals will join the sub-Saharan African workforce every year for the next two decades. By 2030, the continent is expected to be home to more than a quarter of the world's population under 25 and 15% of its total working-age population.[45] This poses an immense opportunity for South Africa to utilize this growing workforce in the technology industry where infrastructure requirements are lower and already have an established track record in country.

4.4 Investor Risks & Challenges

International investors interested in investing in Africa's emerging market may face legal, financial, political, and proximity challenges. The following topics were discussed as top challenges with interviewees.

1. **Legal and regulatory risk:** Investors are typically more inclined to invest in their own region because they are more familiar with the laws and regulations surrounding investing. If an international investor wishes to invest in an African entrepreneurial business, they will need to do substantial (and costly) research on the differences in legal and regulatory systems for each country and often receive complex legal advice during the due-diligence and contracts process. South Africa poses a comparatively low risk among African countries in this regard, as the legal system is well established, and regulatory standards are transparent.

2. **International finance:** While it has become easier in recent years to invest globally, international investors still face high transaction costs and currency volatility. As discussed above, this could severely impact the return on investment. Furthermore, interviewees report a difficulty in transferring money out of South Africa. For example, South Africa maintains an Annual Foreign Investment Allowance which prohibits South Africans or permanent residents to hold investments out of the country of more than $10 million Rand ($553,761.36 USD) per pear. Citizens and residents must obtain a tax clearance certification and maintain good standing with the South African Revenue

Service. Legislation such as this could pose risks to international investors being able to exit an investment in the timeframe they expect (typically 5-10 years). In addition, the foreign exchange-risk can be high due to large fluctuations of exchange rates.

3. **Political instability:** Political stability and security are integral factors in attracting investors. Much of Africa's recent economic growth in the past few years has been attributed to developments in the larger African political sphere. For example, South African President Ramaphosa stated 2019 has been "a good year for the consolidation of democracy across the continent,"[44] which he believes will persuade investors to invest more funds into the continent and increase economic growth. However, many countries, such as neighboring Zimbabwe, still face political instability and could cause risk to international investments. Interviewees state that some potential investors in South Africa shy away due to fears of nationalization that an opposition party within the governing ANC is trying to pursue.

4. **Proximity yields understanding**: To mitigate risk, venture capitalists set up dedicated funds for specific industries according to their skills and experience. In South Africa, there is a very limited amount of funds with a healthcare focus, let alone with digital health focus. Fund managers generally try to be geographically close to the companies they are investing in, especially if the investee is an earlier stage company or a start-up. Thus, ideally the investor has an office in or close to the country where the investments are being pursued. Moreover, South Africa is lacking an active healthcare investment hub with several specialized incubators, similar to what has developed in the U.S. and

Europe. Generalist venture capital funds will find difficulty investing in South African digital health as healthcare requires a specific set of knowledge and experience to implement due to its complexity; generalist funds are typically not equipped for this. In addition, the broad access of companies to mentors still has to be developed.

4.5 Entrepreneurial Risks and Opportunities

South Africa provides multiple investment opportunities for entrepreneurs and early stage companies. However, interviewed entrepreneurs expressed difficulty in raising capital for early and mid-growth phases of a company; identifying two financing gaps approximately between $300,000 - $400,000 and $8 - $10 million. Furthermore, interviewed investors and entrepreneurs report that larger funds of approximately $20 - $50 million seemed easier to attain through large-scale impact investment firms, such as DEG, a subsidiary of Germany's state-owned bank KfW. The most common forms of entrepreneurial funding for healthcare (including digital health) are governmental funds, foundations and grants, prize money (typically from pitch competitions), national impact funds, high net worth individuals, and venture capital and private equity firms.

1. **Governmental funding:** Entrepreneurial funding from the government through entities such as the Industrial Development Corporation (IDC) is reportedly readily accessible to South African entrepreneurs. Typically, it is structured as a loan with an interest payment. The IDC funds entrepreneurs at many stages of development and at many different levels of capital.

2. **Global Foundations**: Global foundations such as the Draper Richards Kaplan Foundation (DRK) offer healthcare specific grants for South African entrepreneurs. DRK offers $300,000 of unrestricted capital over three years to selected entrepreneurs and is many times their first institutional investor. Furthermore, DRK offers guidance and mentorship to early stage companies by joining their boards of directors and works to aid in the growth of the company. However, interviewees note that global foundations may also require investment stipulations, such as, a high return on invested capital. For example, non-dilutive funding is a type of financing offered where entrepreneurs do not need to give up ownership in their company and are not held to delivering a return on investment. Typically, grants would be considered non-dilutive but various foundations across the world are beginning to operate as traditional venture capitalists in regard to requiring higher returns on their initial funding.

3. **Prize money:** Prize money has historically been one of the most commonly reported routes to achieving entrepreneurial funding. It offers an initial financial start to an entrepreneurs funding journey, but the funding associated with pitch competitions is usually not high enough to produce (1) a full proof of concept and (2) enough business infrastructure to begin operation. Thus, pitch competitions alone are not enough to get a fledgling company off the ground.

4. **National Impact Funds:** National impact funds are national investment funds or national development banks that divert funds to smaller funds in South Africa - typically through a regional office in South Africa. For example, Holland's Entrepreneurial Development

Bank, FMO, manages funds for the Ministries of Foreign Affairs and Economic Affairs for the Dutch government to maximize the development impact of private sector investments. FMO is licensed as a bank and supervised by the Dutch Central Bank. FMO invests directly into long-term South African projects through their office in Johannesburg. They typically do this by investing into smaller venture capital and private equity firms in South Africa or directly into larger projects in the country. There are a few active national impact funds mentioned by interviewees, such as: DEG from Germany, SIFEM (Swiss Investment Fund for Emerging Markets) which invests into funds focused on emerging markets, and Norfund from Norway which invests, among others, into South Africa venture capital firm, Spear Capital.

5. **High Net Worth Individuals:** Various high net worth South Africans operate family offices throughout South Africa with the aim to fund South African entrepreneurship. For example, Johann Rupert is a South African businessman with an estimated net worth of $6.5 billion. Rupert and his family operate an investment company, Remgro Limited, which invests in multiple African industries, including healthcare. Other examples noted include Nicholas Oppenheimer (net worth $7.5 billion) and his investment firm Oppenheimer Partners which invests in early stage healthcare companies and inventor Mark Shuttleworth (net worth $500 million).

6. **Venture Capital & Private Equity:** There are multiple venture capital and private equity options for South African entrepreneurs. However, there are very few designated funds with a healthcare, let alone digital health, focus. Firms with an identified focus on

healthcare and technology include private equity firm Spear Capital with offices in South Africa, Zimbabwe, and Norway and the new venture capital firm OneBio based in South Africa.

It is also important to note non-financial challenges South African entrepreneurs may face. Often cited by interviewees is a lack of the entrepreneurial investor mindset and availability of mentorship. Interviewees state that entrepreneurial and executive ability is not lacking, but experience is. This could be attributed to a difficulty in securing mentorship. An interviewee and South African investor states that in Europe it is fairly easy to find mentorship and guidance for young entrepreneurs and companies. However, in South Africa her experience is that it is incredibly difficult to find such guidance. Seeing as how experience and mentorship are critical components to building a company, this poses a significant challenge to South African entrepreneurs.

CHAPTER 5: DISCUSSION & CONCLUSION

The previous chapters shared findings from the literature review and case analysis to ultimately examine the core research aim: provide a comprehensive risk and opportunity profile for potential digital health investments in Africa. In this section the key takeaways and implications of these findings will be discussed. This discussion will also heavily utilize insights and commentary collected in the three interviews with investors and entrepreneurs in South Africa.

5.1 Key Takeaways from U.S. Digital Health Market Analysis

Digital health has grown substantially since the term was first coined in 2000. Over the past two decades (2000 - 2020) it has been shown to provide several benefits, including: improved access to healthcare services (especially in rural areas), improved knowledge and access to health workers and health information, cost savings, and improved health services delivery.[13] Moreover, digital health applications are able to target multiple parties in the healthcare continuum, such as: providers, payers, pharmaceutical companies, medical device companies, employers, and patients. For example, Medxoom a digital health startup based in Atlanta, Georgia, has developed a single platform that simultaneously interacts with patients, employers, and insurance providers to provide improved patient experiences with health insurance. Digital health's reach, yet limited required infrastructure, has made digital health a fast-growing health solution in the U.S.

Digital health venture capital investments have also been on the rise each year since 2011. In 2011 digital health received $1.1 billion in venture capital investments with an average deal size of $12 million. In 2018 total venture capital investment had increased to $8.1 billion for

the year with an average deal size of $21.9 million.[3] In addition to rising investments and increasing startups in the market, digital health has begun to show signs of a maturing investment market with an uptick in IPOs, exits, and continued repeat investors. This is critical for the industry as multiple exits for investors means that investors are receiving a return on their invested capital and digital health companies are achieving enough financial success to provide this return. To further investigate this concept, in 2019 digital health had a net liquidity overhang (NLO) of $29.4 billion. NLO represents the amount of funding that has been invested into digital health but has yet to be returned to investors - or is still awaiting a liquidity event. Thus, from 2011 to the second financial quarter (Q2) of 2019, digital health in the U.S. had received $36.3 billion in investments. $6.2 billion of that invested capital has already been realized by investors through exits such as acquisitions and IPOs - leaving an NLO of $29.4 million as of July 2019.[3]

Understanding the NLO of digital health is important because as the industry continues to mature investors and entrepreneurs will be concerned with both the overall health of the market but also the feasibility of exits in the future. Thus, the NLO represents the exit pressure of the digital health market. An NLO of $29.4 million in 2019 meant that 81% of invested capital since 2011 was still awaiting a liquidity event. Considering most venture capital deals are structured with the idea that investors will receive a return on their investment between five and ten years, an NLO of 81% in eight years is quite good.

Finally, digital health has been gaining popularity with not only investors but with the general public as well. For example, wearables such as the FitBit or Apple Watch have surged in popularity. U.S. consumer use of wearables increased from 9% to 33% in just four years (2014 - 2018).[49] This increasing popularity among the general public has placed a larger spotlight on the digital health industry and its potential solutions for the healthcare marketplace. Moreover, as

consumers become increasingly familiar with digital health solutions, the demand for them will rise and evolve. The rise in wearables popularity has spurred insurers to think about how they can utilize their members wearable technology for potential cost savings; incentivizing members to practice healthy behaviors for discounted rates.[49] As each of the categories* within digital health continue to evolve, their dynamic applications will continue to expansion of the term digital health in the U.S.

5.2 Key Takeaways from Global Digital Health Applications Analysis

Developing nations typically face infrastructure deficiencies, limited access to healthcare and health information, and a shortage of healthcare workers. Due in part to this, their populations experience a higher burden of disease. In comparison, digital health requires little infrastructure compared to more traditional healthcare solutions (i.e. hospitals, clinics, urgent care centers, etc.). For this reason, it has been hailed as one potential healthcare solution for developing nations. Specifically, mHealth (a subset of digital health) has been implemented throughout sub-Saharan Africa to improve medication adherence, health worker communication, maternity care, and more.[25] mHealth refers to the utilization of mobile phone technology to enable health information and services. Thus, it has been particularly successful throughout sub-Saharan Africa as there is a high mobile phone penetration across the region (approximately 80% in 2019).[30]

Furthermore, the goals of UHC are shaping the global healthcare agenda. WHO has stated that achieving UHC is essential for the attainment of SDG 3 put forth in 2015 by the

* Digital health can be broken into eight separate categories: genomics and sequencing, wearables and biosensing, telemedicine, analytics and big data, digital medical devices, population health management, personal health tools and tracking, electronic health records (EHR) and clinical workflow.

United Nations. Africa's ability to leapfrog other nations in telecommunications has made it the ideal region for mHealth initiatives aimed to achieve UHC. Initially mHealth utilized vertical programs throughout sub-Saharan Africa, addressing only one health problem at a time (i.e. SMS medication reminder messages for chronic conditions). As the field of mHealth has expanded, it has started to move from the experimentation phase, utilizing vertical solutions, to a maturing multi-sector health system that contains numerous mHealth solutions within it. In this regard, mHealth should be seen as a mechanism or strategy to overcome healthcare barriers versus a direct mode to achieve a desired health outcome. Therefore, in order for mHealth to become a critical tool in the achievement of UHC, the industry must emphasize the need for interoperable, multi-system solutions.

In 2015 the WHO conducted the third Global Survey on eHealth, with a special emphasis on the use of eHealth* to support UHC. 75% of the participating member states, including South Africa and Ethiopia, noted that they have both a UHC policy or strategy as well as a national eHealth policy or strategy.[54] This is the first step towards digital health being regarded as mechanism for strengthening health systems. As countries begin to incorporate digital health into their UHC roadmaps it will be critical for each to find innovative ways to incorporate the technology used into their national health databases and broader systems – focusing on interoperability. For example, South Africa's MomConnect is operated by the South African Department of Health and informs their national database of new pregnancy registration while aiding mothers with access to maternal care services. To begin further utilizing this program in the achievement of UHC, the program could be leveraged to reach South African mothers for health purposes in addition to maternal care. South Africa and neighboring countries will need to

* eHealth is another phrase referencing the same applications that have been defined as mHealth in this paper.

partner with entrepreneurs in early stages of digital health innovation to ensure that as new programs emerge, such as MomConnect, they are easily layered into the existing system. Partnerships such as these coupled with a horizontal approach to the global implementation of digital health will decrease the likelihood of technologies being siloed into single, vertical health initiatives.

This transition to health systems must begin with investors; without guidance more financial resources will continue to be funneled into single solution technologies. Furthermore, mHealth to achieve UHC is a good investment. The prevention of poor health will lead to longer and more productive lives yielding higher earnings and avoided healthcare costs. Improved disease surveillance systems will aid in stopping epidemics that ultimately hurt economies. mHealth and more broadly, digital health, has the potential to positively affect health systems in developing nations but the implementation and investments into the field must continue to shift to a horizontal systems approach to provide long term impacts.

5.3 Key Takeaways from South African Case Analysis

South Africa is a middle-income emerging market and the most industrialized country in sub-Saharan Africa. The Johannesburg Stock Exchange (JSE) is Africa's largest stock exchange with 388 listings as of April 2020. Moreover, the JSE is one of the world's top 20 equity markets, top 10 derivative markets, and top 5 bond markets. [50] South Africa offers a number of world-class universities and technical colleges alongside a growing young workforce, positive economic development, and the largest healthcare market in sub-Saharan Africa.[30] Thus, the country offers an exceptional financial system and growing workforce of talented individuals.

Alongside the growth in South Africa's financial system, venture capital investments have also been rising. In 2019 South Africa received $67.34 million in venture capital investments over 96 deals; 8 of which were in digital health companies.[8] In addition to venture capital, South African entrepreneurs interested in healthcare are able to access financing through government funding, global foundations, entrepreneurial pitch competitions, national impact funds, high net worth individuals and private equity firms. However, interviewees report there are two gaps in funding size requests between $300,000 to $400,000 and $8 to $10 million. These gaps cause barriers for entrepreneurs to grow and scale their companies. Without enough successful entrepreneurial ventures, it becomes more difficult to convince investors to enter the market. This creates a cyclical paradox for the overall innovation landscape: without investors entrepreneurs cannot demonstrate success but without success investors are hesitant to invest capital. Thus, South Africa's scarce investment infrastructure is likely due to (1) a lack of experience in investing discussed above and (2) the fact that Sub-Saharan Africa is in the early stages of developing an entrepreneurial and venture capital investing mindset.

In order to foster an ecosystem for innovation both entrepreneurs and investors will ultimately need to become less risk averse over time. For example, the U.S. has the largest venture capital market in the world today, but this was not the case forty years ago.[52] In the early 1980s venture capital backed companies, such as Apple and Genentech, experienced highly visible public successes in the market. This success gave rise to a proliferation of venture capital firms from just a few dozen firms in 1980, to over 650 firms by 1989. The amount of venture capital funding managed by these firms increased from $3 billion to $31 billion in the same timeframe (1980 - 1989). Former Wharton Professor Andrew Metrick refers to the first 15 years of the venture capital industry (1980 - 1995) as the "pre-boom period." Subsequently, the dot

com boom in the U.S. brought with it the venture capital industry boom lasting through the bursting of the Internet bubble in 2000.[52] Two decades later the U.S. has emerged as a hub for innovation and entrepreneurship. In 2016 CB Insights data showed that for every dollar available to a European startup, there were six dollars available to their U.S. counterparts. In the last quarter of 2016, Europe closed 468 deals and Asia closed 323 deals compared to 1,127 deals completed in the U.S. over the same timeframe.[41] However, it took the U.S. approximately forty years to evolve and grow to this. It is likely that South Africa, and broadly sub-Saharan Africa, is in its "pre-boom period" currently.

Therefore, sub-Saharan Africa is likely evolving in a similar fashion to the U.S. The rise of vibrant technology hubs in Rwanda, Nigeria, and Kenya coupled with Nigerian company, Jumia's, successful IPO in 2019 has ignited the entrepreneurial mindset within the region. However, sub-Saharan Africa possesses challenges that the U.S. did not have to face. Sub-Saharan Africa is made up of 46 unique countries with approximately 1500 to 2000 languages spoken.[46] This means that creating a cohesive investment market for the region is difficult due to vast differences in regulatory, political, language, and proximity challenges.

International investors will face the additional challenges discussed above, but high net worth individuals could be the key to kickstart the system. Sub-Saharan Africa possesses the financial means necessary for wealthy individuals to fund venture capital and entrepreneurial investing. Nigeria, Egypt, and Kenya were all named in Wealth-X ten fastest growing high net-worth individuals list in 2019.[48] Additionally, New World Wealth reported the number of high net worth individuals (those with assets over $1 million USD) in Africa increased at twice the rate as the rest of the globe in the past 15 years[47] and South Africa's Business Report states there are more than 40,000 millionaires in South Africa[48]. Yet, Africa's most wealthy are hesitant to

invest. Forbes suggests this could be because there are more stable returns in other industries. For example, Nigeria's treasury bills have higher returns than the average annual growth of the U.S. stock market and newly built apartment buildings developing in Accra, Ghana are promising a 17.5% annual return.[48]

In order to encourage these high net-worth individuals to invest into local entrepreneurship, South Africa should expand its financial investing incentives. The government currently offers a few incentives, such as South Africa's Section 12J of the Income Tax Act which makes investments in funds that invest in small business 100% tax deductible.[48] However, this is not enough to offset the more stable returns that South African investors could find elsewhere. It would be advantageous of the government to expand incentives to include tax breaks for early stage companies, venture capital funds, and incubators within the 12J tax deductions. This could give local investors more range with the types of entrepreneurial ventures they can invest into beyond established small businesses. Additionally, this could offset the decrease in return on capital investors might experience by choosing entrepreneurial investing over more stable returns.

In addition to more robust tax incentives, South Africa needs a larger emphasis on digital health investments. The government has committed to an eHealth strategy yet has not partnered with local entrepreneurs to aggregate the innovation in this industry. For example, the Rwandan government set out to foster technology innovation and ease of business throughout the country. To do this they are creating a vibrant technology hub in Kigali and have positioned themselves as the epicenter for expanding technology companies in Africa. South Africa has the largest healthcare market in sub-Saharan Africa which gives it the ideal platform to become Africa's leading digital health hub. Through the creation of incubators and accelerators entrepreneurs can

receive not only the funds they need to innovate, but also the mentorship required to grow their companies.

Furthermore, the South African government could ensure interoperability by financing this emphasis on digital health. It is critical for new innovation to complement existing technology or solve critical health problems. Aggregating digital health innovation into technology hubs helps to facilitate collaboration among not only entrepreneurs and investors but also with the existing government health system. Involving the South African government in the innovation ecosystem is very different than U.S. and European methodologies but it could provide resources and stability to incentivize South African investors to join.

5.4 Conclusions & Recommendations

The rise of digital health and its potential solutions for emerging markets in sub-Saharan Africa are dynamic and evolving each day. This paper has analyzed only a single piece of the investment landscape that will make up the region's financing models. Since the target audience of this paper was primarily digital health venture capital investors and global health practitioners in the digital health field, it only provides a limited analysis of digital health financing models. Sub-Saharan Africa possess a complex regulatory environment with many stakeholders and unique challenges.

The critical role of international investors is to aid in sub-Saharan Africa's emerging markets through financing local innovation. Those interviewed for this paper have already begun to see differences in the way's international investors approach South Africa, for example. Foundations have shifted away from lump sum grants and replaced them with longer term funding coupled with mentorship and support (i.e. DRK grants). National impact funds have

begun to invest into local funds that support smaller innovative ideas versus large scale infrastructure projects alone (i.e. Holland's FMO). Interviewees say that this shift aids in the development of not only strong investment systems, but the strengthening of the entrepreneurial mindset.

The shift from funding large scale infrastructure projects through governments to smaller investments in local innovation is also more effective according to interviewees. Choosing to fund an entrepreneur versus a state government project has reportedly cut down on misuse of funds. The aim of venture capital investments is to spur innovation, create long term jobs, and grow the economy. Interviewees believe this is working, but investors will need to be patient. For example, experts suggest that it was the early successes of venture capital backed startups that spurred the explosion of venture capital in the U.S. This is a critical piece that is still growing and evolving in sub-Saharan Africa. An investor who works in both Europe and South Africa reports that even the EU does not yet have the same entrepreneurial mindset as the U.S. There is still a fear and stigma around entrepreneurial failure; if you have too many, or even one, "failure" on your CV this can negatively impact your chances of receiving funding. This, of course, happens in the U.S. as well but the difference is the ideology. Typically, in the U.S. investors have stated that they prefer to fund an entrepreneur who has failed once - it means they learned something. It is this deeply ingrained mindset of entrepreneurship that takes decades to grow alongside an investor market. This must be cultivated in sub-Saharan Africa for a similar ecosystem to flourish.

To grow this ecosystem investors will need to become less risk averse and adopt extended investing timelines. Traditional venture capital investors expect to see returns within 5 to 10 years, but sub-Saharan Africa is still developing. This means early stage businesses and

entrepreneurs may take longer to get a foothold in their market and scale the business. Given healthcare's notoriously complex ecosystem this will be especially pertinent in regard to digital health. Interviewees suggest timelines may be 15 to 25 years versus 5 to 10 years. Due to the increased risk of an extended timeline and existing challenges for international investors, it may be more advantageous for interested international partners to seek out locally managed funds.

In addition to the issues discussed above, the digital health landscape in sub-Saharan Africa also includes traditional global health financing models and entities. Venture capital investing was the sole focus of this paper, but it is only a fraction of the larger global health investing ecosystem. Multi-national organizations and non-profits such as the World Bank or CARE International should be seen as partners in the cultivation of sub-Saharan Africa's market and not separate industries. Traditional global health financing is via grants, loans, or philanthropy. These are critical funds to aid in the development of the healthcare industry. However, these funds traditionally do not interact with private venture capital funding. Venture capital has a track record of funding unproven, high risk technologies and demonstrating their clinical benefits. It would be advantageous for the two sides of the global financing models to come together in larger discussions concerning allocation. Venture capital traditionally tackles innovation in the technology sector while global health financing typically addresses healthcare access and delivery initiatives. The rise of digital health comes at the intersection of these two schemes.

Both venture capital and traditional global health finance can learn from each other to tackle the funding gaps in sub-Saharan Africa. Global health non-profits and multi-national organizations have far more experience in sub-Saharan Africa's healthcare ecosystem. They bring to the table unparalleled knowledge and creditability within the health community. Venture

capital brings with it the knowledge and ability to grow risky ideas into impactful businesses. As sub-Saharan Africa works towards the achievement of UHC it will be critical for both of these entities to communicate. Global health financing could adopt investing mechanisms to support innovation while channeling returns into new initiatives. Venture capital could learn to address early stage companies with a horizontal global health lens. The resulting collaboration will help prevent valuable funds being siloed into single solution technologies and aid in the execution of a horizontal approach to the implementation of digital health.

In 2018 Deloitte forecasted Africa as the fastest growing region in the world.[30] This paper has demonstrated that the region provides ample investments opportunities and specifically the potential value of digital health investments and applications. While this paper has focused heavily on venture capital systems in sub-Saharan Africa and its role in digital health innovation, there are many modes of innovative financing being applied to the region. It is the aim of this paper to encourage conversation between global health professionals and investors alike. Neither party should be beholden to the financing mechanisms discussed here. However, the global health and investment communities should continue to explore opportunities for investors to innovatively support African health initiatives.

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APPENDIX

Figure 1A: Map of South Africa.
Source: CIA World Factbook South Africa.

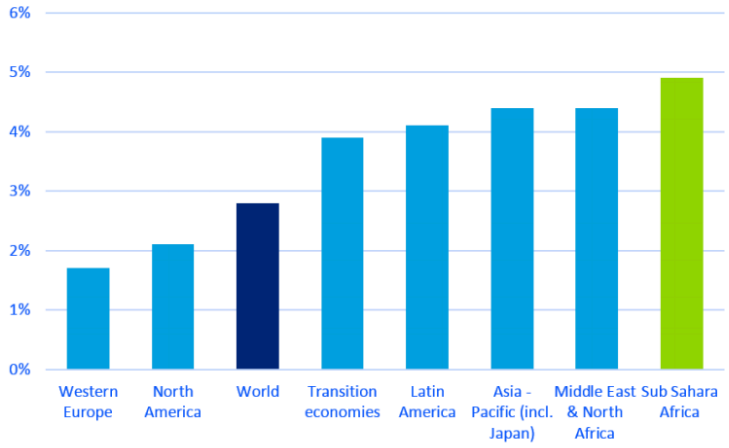

Figure 2A: Average annual forecast growth per region (2011-2015).
Source: Deloitte 2018 report "The mHealth opportunity in Sub-Saharan Africa: The path towards practical application."

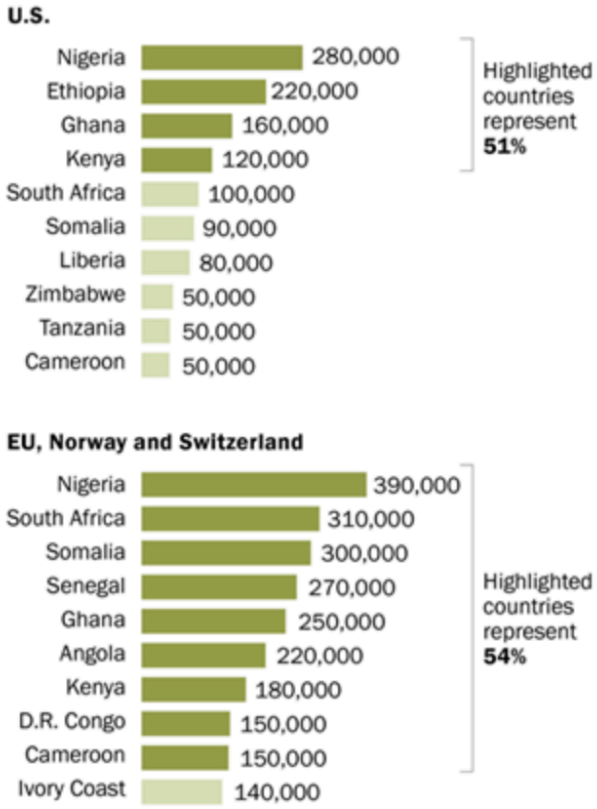

Figure 3A: Top countries of birth for sub-Saharan African migrants living in the U.S. and the European Union in thousands in 2017.
Source: Pew Research Center.

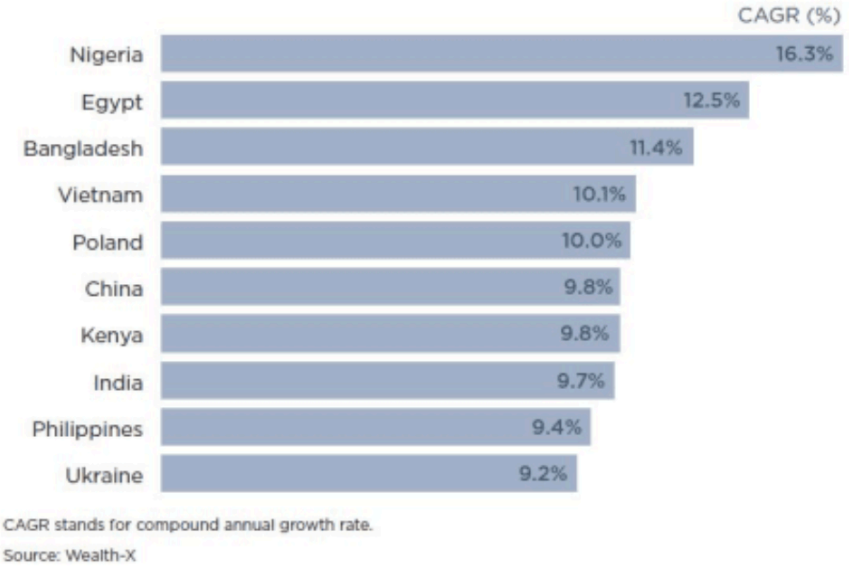

Figure 4A: List of the 10 fastest growing high net-worth individuals in 2019.
Source: Wealth-X.[47]

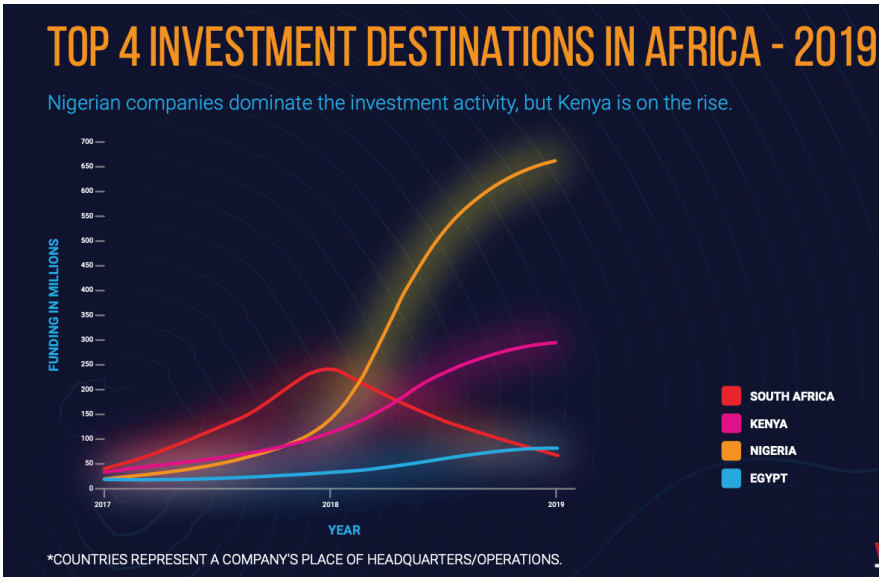

Figure 5A: Top four African countries that received venture capital funding in 2019. Source: Wee Tracker's Decoding Venture Investments in Africa annual 2019 report

In-Depth Interview Guide

PURPOSE

Thank you for participating in this interview. Your responses will be used to supplement and aid in my understanding of venture capital funding and entrepreneurship in sub-Saharan Africa, specifically, South Africa. I am a graduate student at Emory University in Atlanta, Georgia, United States studying global health, finance, and business. Specifically, I am interested in the emerging digital health industry and its global potential impact on healthcare in emerging markets. I am interviewing a few key experts in venture capital, entrepreneurship, and biotechnology; specifically located in South Africa to elevate my knowledge of startup financing in sub-Saharan Africa.

CONFIDENTIALITY

All information that we discuss will be de-identified and only used for the purpose of informing this thesis. Certain commentary and ideas may be used to enhance both the case study and discussion section of this paper, though all comments will remain anonymous.

Core Discussion Questions

1. How would you describe the healthcare investor landscape in South Africa in terms of 'ease of finding funds' and key players (i.e. domestic, international, private vs multilateral)? Are these characteristics unique to South Africa or are there any regional trends you have noted?

2. Do you see many US investors in local digital health companies? What are the challenges and barriers for US investors (i.e. regulatory, money management, communicating with entrepreneurs in a different country, etc.)?

3. What is the (typical) process for gaining international funding (i.e. government funding, regional funding, etc.)? How are African entrepreneurs connecting with their international investors initially? Are there benefits and drawbacks for entrepreneurs who receive international funding?

4. What strategic partnerships and operation channels are available in your market?

5. What do you believe are the reasons behind a lack of venture capital structures in South Africa?

6. In your opinion, what is the best course of action moving forward to facilitate more venture capital funding in South Africa?

Additional Discussion Questions

1. Grant and competition prize funding dropped in 2019. Do you believe this is indicative of a change in the funding landscape?