# Digital Impact: The Future of Healthcare

- The healthcare sector is among the largest and fastest-growing in the world, with a value exceeding $8.45 trillion, according to the World Health Organization. According to the American Medical Association, in the sector represents approximate 18% of the U.S. economy. Given aging populations in many countries, spending on healthcare will likely continue to rise.
- Meanwhile, U.S. healthcare spending outpaces the rest of the world while health outcomes rank relatively poorly. Access to quality care varies based on location and demographics, with poorer, more rural, and non-white populations feeling the burden of this inequity.
- Digital healthcare holds tremendous promise for improving access to quality care. Developments such as telehealth, personalized (also called precision) medicine, remote monitoring, robotics, genomics, and wearable technology may provide the solution to making healthcare more widely available at a reasonable cost.
- In this report we explore a key element of the future of healthcare: digital health. We address the investment landscape while considering issues of health equity, the role of government, the promise (and worries) of artificial intelligence in healthcare, and the mental health challenges stemming from social media.

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# Table of Contents




Special thanks to Dr. Derek Yach for his guidance and contributions to this report. Derek explored many issues addressed here 25 years ago in his research article "Telecommunications for Health – New Opportunities for Action." [1] Decades later, the potential he saw for digital health is a reality.


Please note: When referring to specific demographic groups, we used the terms from the original sources. It is for this reason that there is inconsistent terminology in this report.

[1] Yach, Derek, "Telecommunications for Health – New Opportunities for Action," Health Promotion International, Vol. 13, December 1, 1998. https://doi.org/10.1093/heapro/13.4.339

# Introduction

Erika Karp, Executive Managing Director, Chief Impact Officer

**The healthcare sector is one of the largest and fastest-growing in the world.** Healthcare is the second largest sector in the global equity markets (MSCI World) behind information technology, representing 13% of the global market capitalization.[1] Within the MSCI World Healthcare index, there are 10 industry sub-groups representing 153 companies. For the five years leading into the pandemic, the S&P 1500 healthcare sector profits experienced compound annual growth 3.5 times greater than the full S&P 1500.[2]

**Demographics are among the key factors responsible for this growth.** For instance, the over-65 population in the U.S. has grown 62% since 2000 and is expected to grow another 30% over the next decade, according to a U.S. Census Bureau projection.[3] Additionally, as of 2021, U.S. birthrates have fallen by 4%.[4] An aging population in the U.S. and globally is likely to demand more and spend more on healthcare, which argues for a continuation of the trends underway.[5]

The broad healthcare sector offers opportunities to invest in companies producing lifesaving drugs, innovative treatments, medical devices, and healthcare services. Further, innovative solutions from the healthcare IT and digital space may offer ways to reach a broader population at lower costs. Such investments offer the potential to improve quality of life and raise productivity for millions of people.

However, the cost of healthcare in the U.S. keeps rising dramatically while the access to quality healthcare services for those most in need seems tenuous. Growth in U.S. health expenditure as a share of GDP outpaced comparable nations in the Organization for Economic Cooperation and Development (OECD), at 16.2% vs 17.8% between 2010 and 2021.[6] In 2021,The U.S. spent approximately $12,914 per person on healthcare, the highest per capita cost across the OECD, which spent less than $5,050 per person on average in 2021.[7] Yet there is a substantial portion of the U.S. population that lacks adequate access to healthcare, as we discuss in the section "Framing the Challenge (p. 10)."

**Clearly, there is an enormous market of people who need access to healthcare services,** especially those either underserved or not served by the U.S. healthcare system. This includes 85 million people on Medicaid as of December 2022, over 65 million people using Medicare in 2022, and 27.5 million nonelderly individuals who lacked health insurance in 2021.[8]

**Further, those with chronic conditions account for a larger proportion of the national healthcare spend.** By one estimate, 90% of the nation's $3.5 trillion in annual healthcare expenditures are for people with chronic and mental health conditions.[9] More than half of Medicaid spending is attributable to the highest-cost 5% of enrollees, primarily the elderly and individuals with disabilities, many of whom have chronic conditions.[10] Better access to healthcare services, which could lead to earlier intervention to control these chronic and mental health conditions, may reduce their toll on this segment of the population while reducing their cost to nation's healthcare system.

What types of investments can help provide better care for all, including underserved and medically vulnerable populations? How can costs be controlled while expanding the reach of healthcare to those in need?

## Investing in Health & Health Equity

Healthcare consumers typically interact with the health system only when they are sick or injured. But **the future of health may be focused more on well-being and prevention rather than just treatment**. Prevention and early diagnoses can reduce healthcare costs and improve health outcomes. Cost, quality, and access to care are key to the healthcare system. In the future, health is likely to revolve around sustaining well-being rather than just responding to illness.

Some major themes that capture this trend toward investing to sustain health include telehealth, personalized (also called precision) medicine, remote monitoring, robotics, genomics, and wearable technology. Innovative technology and improved processes may provide the solution to making healthcare more widely available at a reasonable cost.

With advances in lower-cost preventive, diagnostic, and disease management technologies comes an opportunity to address the significant inequities in access to health care. McKinsey stated that "Better healthcare is an absolute good" in a recent report in which they outlined a

framework for how pharmaceutical and life sciences companies can think about health equity.

So while we think about the technologies being developed, we also need to consider the populations being addressed. As with every sector of the economy, the analysis changes as we think through an equity lens. We must consider limited access to food, care, or medication; needs left unmet when innovation is misaligned with disease burdens; and communities that do not receive care commensurate with their needs. Addressing the issues has obvious benefits for patients, the pharmaceutical and life sciences companies that serve them, and investors who contribute capital toward these solutions.

## The Role of Government

Addressing the massive challenge to society in delivering health care requires a multidisciplinary approach. As illustrated in this report, contributions from various scientific fields, combined with insights from social science and advocacy, are coming together to redefine the future of health care.

Government investment also has a tremendous role to play. The recent creation of the Advanced Research Projects Agency for Health (ARPA-H) to support and fund research is modeled on the long-lived and highly productive DARPA – the Defense Advanced Research Projects Agency. We discuss DARPA and the promise of ARPA-H on p. 14 of this report.

## The Challenge of Data Governance

Overhanging the potential for digital technologies to revolutionize health care delivery is the very real issue of data governance. In the U.S., for example, federal health information privacy laws do not explicitly cover digital health records or applications (although some states do). Personal health data can become vulnerable to cyberattack or unauthorized use. As we highlight in our section "Using Digital Tech to Close the Gender Equity Gap in Health," concerns about privacy could pose a significant risk to investments in reproduction-focused apps.

Another challenge is the growing need for public health professionals to understand how to leverage the power of artificial intelligence to analyze massive amounts of data in a way that is both scientifically sound and anonymized. While these are critical concerns, they are beyond the scope of our report.

### ABOUT THIS REPORT

With the context of a severely stressed healthcare system and the urgent need for technology and digital transformation to address the daunting issues we face, Pathstone is offering this report as a reflection of how investors can deploy their capital to that end. **We have chosen to examine one portion of this enormous subject: Digital Health.** The National Institutes of Health defines "digital health" as the use of information and communication technologies in medicine, such as mobile health (mHealth), to manage illness and to promote wellness.[11] At the same time, we have tried to weave in discussions of Health Equity and Women's Health. As outlined in our next section, the Digital Health Investment Landscape, there are numerous investable solutions that hold promise to reshape healthcare in a meaningful way. We also highlight some of the innovative achievements of DARPA as a way to highlight to key role of public/private partnerships in developing solutions.

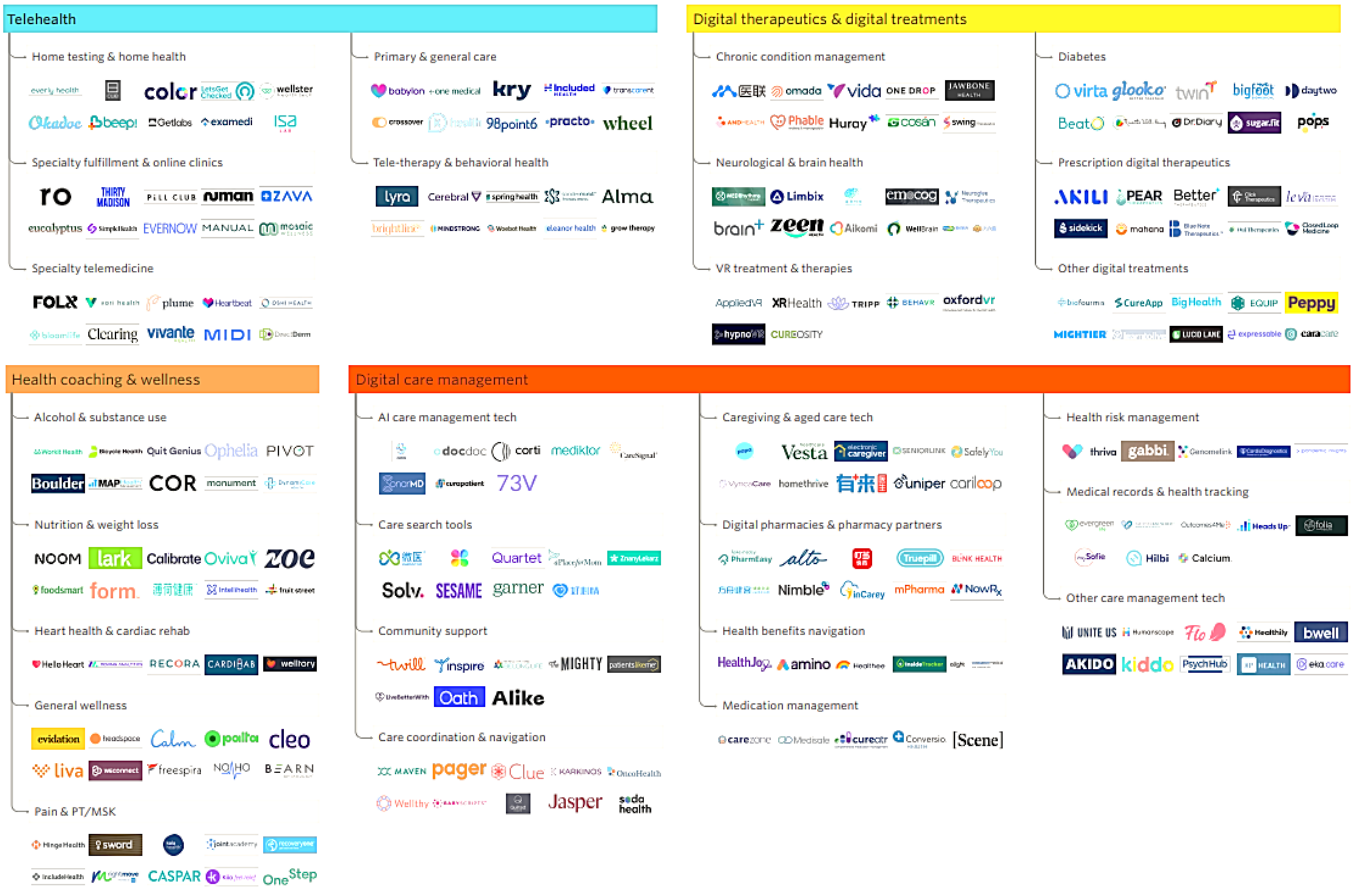
# The Digital Healthcare Investment Landscape

**AJ Levine, Associate Director | Sam Sterling, CFA, Senior Analyst**

Digital health and the future of healthcare broadly are investible, multi-sector themes. While there are many opportunities to create dedicated, concentrated exposure, we believe that investment managers with a broad perspective and understanding of intersectionality may be well positioned to invest over the long term.

Pitchbook, a private markets data and intelligence platform, tags over 5,900 companies with the "digital health" moniker. The system tracks more than 18,000 unique deals including venture capital investments, corporate M&A activity, and IPOs. As shown in the market map below, there are at least a half-dozen segments of the digital health market that have attracted at least $1 billion of venture capital funding.

**Digital Health Market Map**




Source: Pitchbook Q4 2022 Launch Report: Digital Health.

While upstream funding (venture capital) continues to be supportive of early-stage innovation, downstream acquisitions and new entrants are serving as bullish indicators for interested investors. Specifically, several of the world's largest technology companies, including Apple, Amazon, Google, and Microsoft, have entered the market in a meaningful way. Once considered the prime strategic acquirers for start-up technology companies, these businesses have increasingly flexed their size, scale, and significant cash balances to acquire healthcare-related solutions. Already today, these incumbent technology companies are active across pharmaceutical distribution (Amazon's PillPack), electronic health records (FitBit), medical/monitoring devices (Apple Watch), and full-stack AI and cloud-based solutions (Microsoft's Nuance Communications).

The competition to dominate the "healthcare cloud" is here and is unlikely to abate in the near term. As this competition and acquisition spree continues, the lines between technology, healthcare, and digital health companies will become further blurred.

## Public Markets

Healthcare investing emerged as one of the first sector-based investment strategies with the launch of the Fidelity Select Healthcare mutual fund in 1981. According to Morningstar data, there are 92 mutual funds and ETFs representing approximately $212 billion of assets that invest in a dedicated way to healthcare stocks. In the last year, we have seen the launch of three ETFs that are dedicated to digital healthcare investing. These launches are part of a bigger trend over the past three years of new healthcare strategies brought to market that focus on innovation and emerging healthcare trends, in which digital health plays a key role.

While ETF structures are the latest entrant to this theme, access to innovative healthcare companies has long been part of the alternative investing landscape. Forty-two hedge funds are investing in a dedicated manner as tracked by Hedge Fund Research, the oldest of which has an inception date of 1996. These funds have a variety of approaches, both long and short. Some of the most well-known include Eversept and HealthCor (acquired in Jan 2023 by Catalio Capital). Eversept's investment philosophy is based upon recognizing and capitalizing on emerging global healthcare trends and stock-specific opportunities ahead of the broader market. They believe that because healthcare is a complex sector, investor behavior shows persistent patterns of inefficiency. The partnership focuses the firm's research resources around those inefficiencies.

*Digital health investing is not limited to sector funds. Thoughtful active managers have been incorporating digital health trends into their investment decisions for years.*

Of course, digital health investing is not limited to sector funds. Thoughtful active managers, particularly those focused on investing in companies with innovative solutions, have been incorporating digital health trends into their investment decisions for years. A wider investment scope allows these investment teams to leverage their work in this theme across sectors.

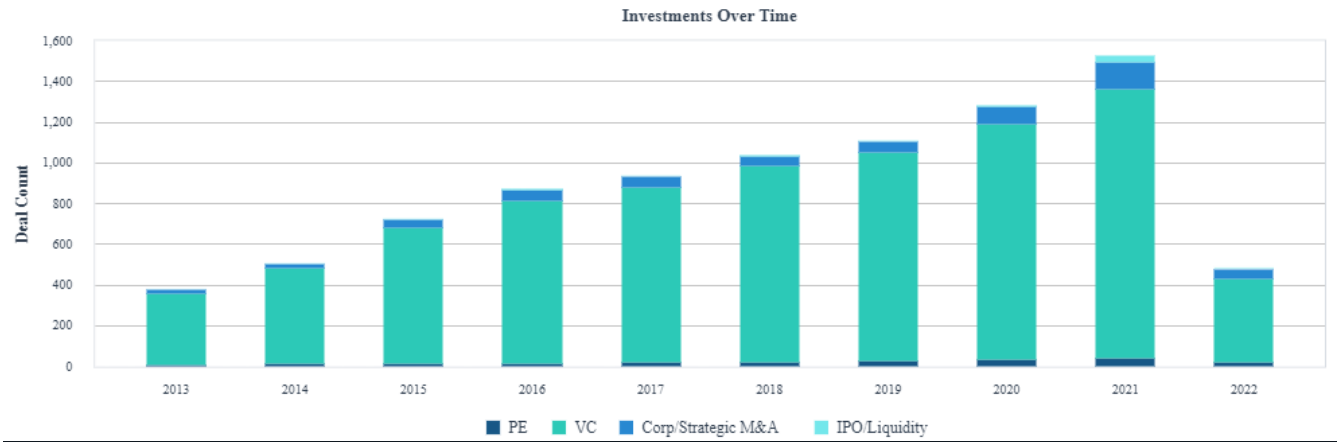
Examples include:

- Summit Partners' Sustainable Opportunities Fund invests in multiple innovative medical device companies leveraging technology-enabled solutions; one portfolio company, Inspire Medical Solutions, offers a revolutionary digital sleep apnea care device.
- TransMedics' Organ Care System (OCS) is a portable, multi-organ preservation and assessment technology that mirrors human physiology; OCS helps to maximize the potential of donor hearts, lungs, and livers, ensuring transplant teams can preserve organs in an optimal condition.
- Brown Advisory's Sustainable Growth Fund invests in Danaher, whose digital technology-enabled products support life sciences research as well as filtration and purification in clinical healthcare settings.

## Private Markets

We believe that there are significant opportunities in the private markets for investors to gain exposure to the themes discussed throughout this report. At the end of 2021, an average of 420 "health tech" venture capital deals — funding the earliest stages of company formation — had occurred over the previous two years. The total amount of capital raised across the 370+ deals in 2021 crossed the $20 billion threshold. (2021 venture capital activity is widely considered an outlier year across the venture capital ecosystem.) While there are signs that this market is maturing, with 2022 funding levels dropping from record-setting 2021 figures, deal activity levels remained in line with 2020.

**Private Market Deal Flow, 2013-22**

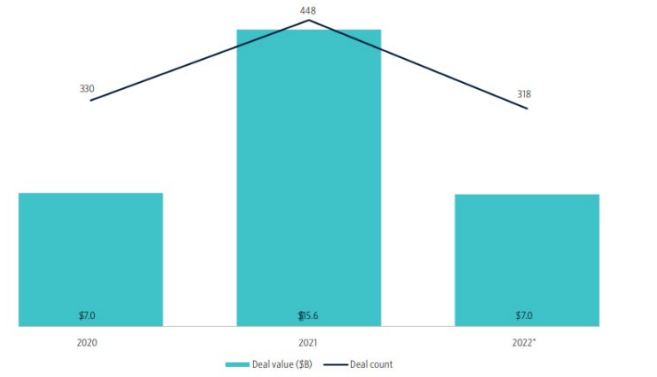



Source: Pitchbook.

While fundraising levels did not reach those of 2021 (as expected), deal activity in the health tech segment appears strong against a backdrop of deteriorating economic conditions. We expect that both investor demand and the opportunity set will remain robust for the foreseeable future. Both dedicated sector specialists and generalist funds are active in the market.

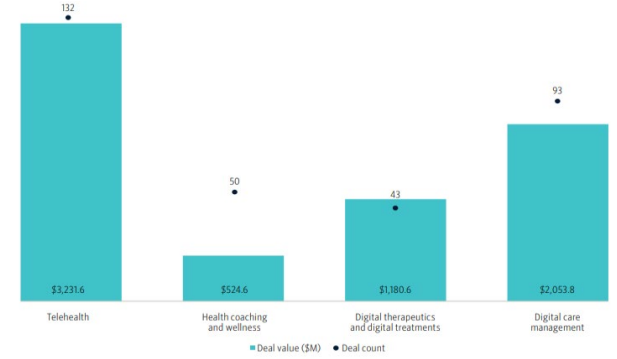
The current public market turbulence may limit strategic investment and M&A activity in the short term, however, as indicated by 2022 and early 2023 Pitchbook data. Experienced and well capitalized managers with operational capabilities may be better positioned to win access to deal flow in this market environment.

**Digital Health VC Activity**




Source: Pitchbook | Geography Global | As of 12/31/22.

**Digital Health VC Activity by Segment, 2022**

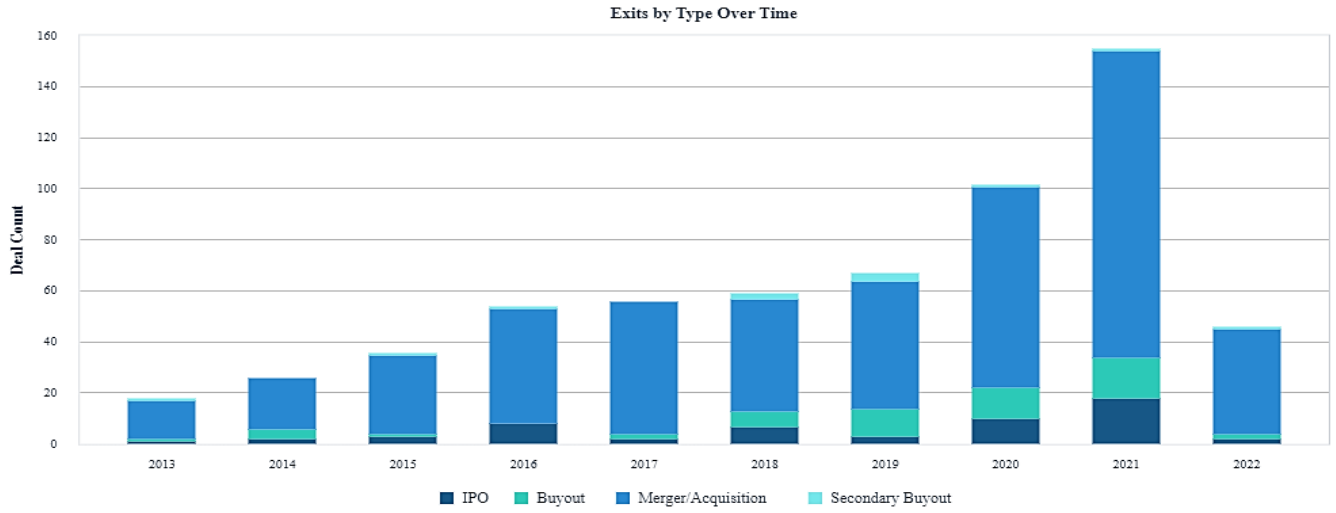



Source: Pitchbook | Geography Global | As of 12/31/22.

Recent exit activity in the private markets should also support continued momentum in the space. Total exit value exploded in 2021, up to north of $36 billion from the prior year's total of $5.4 billion. Significant IPO activity such as Bright Health Group (NYSE:NHG) at $10.2 billion in exit value, Oscar (NYSE: OSCR) at $6.5 billion, PolicyBazaar at $5.4 billion, Shuidi (NYSE: WDH) at $4.4 billion, and Clover Health (NASDAQ: CLOV) at $3.3 billion were the largest drivers of the elevated figure.

However, an active IPO window was not the only factor powering the market. In 2021, Pitchbook tracked 40 acquisitions and buyouts of VC-backed startups in the industry, the largest of which was Headspace's acquisition of on-demand mental health service provider Ginger. These outsized exits will likely now serve as proof points for early-stage entrepreneurs and investors alike of the ability of digital health companies to generate meaningful liquidity as well as returns for investors via a variety of exit routes: strategic sale, IPO, and peer-to-peer.

**Private Exits from 2013-2022**




Source: Pitchbook | Geography Global | As of 12/31/22

As exit activity tapered across the private market ecosystem broadly following 2021, the sub-sectors driving the future of healthcare transformation were not immune. Digital health deals generated only $200 million of total VC exit value in 2022, versus $11 billion in 2021 and $3.2 billion in 2020. While we do not expect activity to retest the highs of 2021 in the near term, we do expect a general uptrend in exit activity as macro headwinds abate and the companies underpinning these segments continue to mature.

*While the level of successful exit activity in the digital health segment has been noteworthy, and likely supportive of specialist funds, we believe that diversified mandates may also serve certain clients well.*

We believe that these conditions, and the need for continued innovation, will support further growth of the market. A review of 25+ market size estimates from various research outlets shows a median estimate of a roughly $500 billion total market in three to five years (2025-27).

This projected scale is expected to yield continued attention and likely specialized investment products. While the level of successful exit activity in the digital health segment has been noteworthy, and likely supportive of specialist funds, we believe that diversified mandates may also serve certain clients well.

Bright Health Group, which had generated the largest IPO at $10.2 billion, had previously raised investment capital exclusively from traditional early-stage venture capital firms. Firms such as Greycroft, NEA, and Redpoint initially backed the company before large, established firms such as Blackstone, Tiger Global, and T. Rowe Price all made commitments ahead of the IPO.

Where there are formative value-add opportunities at the early stages, we believe that sector specialists may be best positioned to capture outsized returns. However, as companies approach maturity and prospective public offerings, the expertise of those investors who live closest to the public markets can be invaluable. We continue to believe that thoughtful and diligent selection of investment managers is the key driver of successful investment outcomes.

Pathstone partners with several investment managers who focus either exclusively or in part on digital health opportunities. They range from those focused on early-stage start-ups, to public equity managers, to those proactively and intentionally seeking high-impact outcomes – and in some cases, all of the above. We have anecdotally observed mandate expansion, particularly among those focused on impact, to include digital health

in strategies previously focused only on environmental sustainability opportunities. We believe that investor demand, driven in part by factors such as recent U.S. Supreme Court opinions, the tense geopolitical environment, and the continued momentum for social justice reform, will likely continue to support this trend.

Generation Investment Management, a leading global investment manager, is an example of a firm that recently expanded the scope of its impact mandate to include digital health. Not only has this yielded greater investment opportunities, but it has also allowed Generation to more holistically and authentically pursue its stated mission "to ensure that sustainable investing drives the transformative change required for a net-zero, prosperous, equitable, healthy and safe society."

While many opportunities exist for investors to support significant innovation and enhanced patient outcomes, prudent due diligence and portfolio construction is critically important. As recent high-profile cases (e.g., Theranos, FTX) have demonstrated, exuberance can often obscure sound investment judgment. Given the implied link between positive health outcomes and advanced scientific innovation, these risks may be elevated for investors participating at the earliest stages of company formation. Sound analysis of all investment factors (often framed as "environmental, social, and governance" analysis) is critical to understanding such opportunities.

## ADDRESSING HEALTH EQUITY: CATALYTIC CAPITAL

Technology is not the only way to expand cost effective healthcare to underserved communities. Creative financing of targeted innovative initiatives offered at concessionary rates can also help close the gap in healthcare to communities of color and those in rural areas.

Program Related Investments (PRIs) are investment vehicles set up by foundations. Their primary purpose is to help further a foundation's mission - e.g., developing health clinics or affordable housing for a particular target population or area the foundation serves. While a PRI may generate income or appreciation, financial returns are not the primary purpose of the vehicle.[12] Foundations do expect returns on their investment within a specific timeframe, albeit often at a below-market interest rate. The benefit of a PRI to the recipient is access to needed capital at a below-market rate. The benefit to the funder or foundation is that the repayment can be recycled for another charitable purpose.[13]

### Case Study: Colorado Health Foundation

The Colorado Health Foundation (CHF) has invested over $60 million in its PRI portfolio since 2017. As is typical of many PRIs, financing structures include loans, notes, and other financial products offered at below-market rates. PRI funding is eventually returned to the Foundation and the funds are redeployed to new opportunities.[14]

Some examples of the CHF's current healthcare-oriented PRIs include:

- Center for Care Innovations - a $3.5 million initiative to establish a statewide network of safety net providers that will learn how innovations around the delivery of care can improve the quality of care to underserved Coloradans;
- indieDwell-Colorado - a $1.5 million investment in a 100,000 square foot modular housing factory in Pueblo, offering 175 good jobs and producing 1,000 units of high-quality, affordable housing per year;
- Mind Springs Health - a $4.25 million capital investment to support the construction of a new psychiatric hospital, significantly boosting available beds for acute psychiatric inpatient treatment in the region; and
- National Institute of Medical Assistant Advancement – an infusion of $245,000 in growth capital to educate and train medical assistants to strengthen the primary care workforce needed in underserved communities.[15]

### Case Study: Healthcare Georgia Foundation

The Healthcare Georgia Foundation invests along four pillars: rural health, maternal and infant health, chronic disease, and capacity building. Here are some examples of HGF's current PRIs:

- Community Health Center Capital Fund - $500,000 in a nationally focused Community Development Financial Institution (CDFI) to provide low-cost, fixed-rate, five- to seven-year term loans to Georgia's Federally Qualified Health Centers (FQHCs). The goal of the health impact investment to Capital Fund is to align its resources with the causes of poor health outcomes for Georgians, and generate a measurable, beneficial social impact with a financial return.[16]
- Community Health Coalitions – a $13.2 million investment to enable 11 rural Community Coalitions to implement their Community Improvement Plans.[17]

# Framing the Challenge: The Burden of Disease in the U.S.

**Erika Karp, Executive Managing Director | Akshika Patel, Senior Associate**

## The Burden of Inequity: U.S. Health Data

The U.S. ranks poorly in terms of key health metrics when compared to other developed nations, according to data from the Organization for Economic Co-operation and Development (OECD). The OECD has 38 member countries, mostly from the developed nations. For example:

- With an average of 5.7 deaths per every 1,000 births, the U.S. ranks 33rd.[18]
- The U.S. ranks 29th in life expectancy, with an average of 80.2 years for women and 75.5 years for men.[19]
- Our country's suicide rate ranks 34th with 14.5 per 100,000 persons, just behind Latvia. [20]
- Further, within the U.S. there are startling disparities in health status and access to healthcare based on demographics. Some statistics bear witness:
  - African Americans were 30% more likely than whites to die prematurely from heart disease in 2010, and African American men are twice as likely as whites to die prematurely from stroke.[21]
  - The U.S. Centers for Disease Control and Prevention (CDC) reports that 44% of African American men and 48% of African American women have some form of cardiovascular disease.[22]
  - Moreover, African American and American Indian/Alaska Native women have higher rates of stroke-related death than Hispanic or white women.[23]

While overall mortality rates have been declining nationwide, rural areas have seen a much slower decrease. According to the CDC, rates for the five leading causes of death in the U.S. — heart disease, cancer, unintentional injury (including vehicle accidents and opioid overdoses), chronic respiratory disease, and stroke — are higher in rural communities.[24]

## The Financial Burden: U.S. Healthcare Spending

While the U.S. lags developed peers on many health metrics, we outpace in healthcare spending. In 2020, the U.S. spent 2.56 times the average for all OECD countries — $12,914 per capita vs an average $5,050 per capita.[25] In 2020, the Institute for Health Metrics and Evaluation estimated U.S. spending at $11,027 per person. Spending on diabetes, heart disease, and low back and neck pain accounted for the highest amounts of spending by disease category.[26] On average, the healthcare cost of one stroke is estimated at $140,048.[27] This includes inpatient care, rehabilitation, and follow-up care. Rising U.S. healthcare expenditures over the past few decades have been primarily due to increases in healthcare service prices and intensity (a measure of the number, technical complexity or attendant services), as well as a growing and aging population.[28]

However, a tremendous portion of the spending by U.S. insurers and providers has gone towards administrative costs. A 2020 study done by the Annals of Internal Medicine Journal uncovered that U.S. insurers and providers spent more than $8 trillion on administrative costs alone, amounting to 34.2% of national health expenditures. [29] The U.S. spends roughly $940 per person on administrative costs — four times more than the average of other wealthy countries and significantly more than is spent for preventive healthcare.[30]

## DEATH AND CHRONIC ILLNESS: KEY CAUSES AND IMPACTS

Below we provide some high-level datapoints on major current causes of death and chronic illness in the U.S. and the disparities in their prevalence by key demographic factors. This is not intended to be a comprehensive review, but rather to provide context for our discussion of solutions and investments.

**Ischemic heart disease** (IHD), or coronary heart disease, is the leading cause of death in the U.S. In fact, according to the Centers for Disease Control and Prevention, one person dies every 34 seconds because of IHD.[31] Although IHD-caused mortality in the US is decreasing, there is a great deal of disparity within the country. States such as Arkansas and Florida have seen 227.42 deaths per 100,000 and 209.21 deaths per 100,000, respectively.[32]

**Lung cancer** is the leading cause of cancer death in the U.S. In 2022, lung cancer accounted for 21.4% of all cancer deaths.[33] Arkansas, Kansas, and West Virginia suffer from the highest rates of lung cancer in the U.S.[34] Notably, the cancer death rate has decreased substantially since the 1990s.[35]

**Chronic obstructive pulmonary disease (COPD)** is the third leading cause of death in the U.S. COPD is a group of debilitating diseases that obstruct airflow. COPD is caused by tobacco smoke, air pollutants, and respiratory infections. Recent evidence indicates that COPD prevalence has increased at a faster rate among women than men.[36] Also, COPD has been reported at a higher rate among older adults, American Indians/Alaska Natives, and rural residents.[37] On a positive note, the age-adjusted death rate decreased by 15% between 1999 and 2019.[38]

Every three minutes and 14 seconds, someone dies of **stroke**. Stroke is also the leading cause of serious long-term disability.[39] There are huge geographic disparities in stroke mortality. In fact, the southeastern part of the U.S., otherwise known as the "stroke belt", has a 30% higher mortality due to stroke than any other region in the U.S. Stroke is a predominantly caused by comorbidities, such as hypertension, which are also prevalent amongst the population in the "stroke belt".

Among adults aged 65 and older, **Alzheimer's** is the fifth leading cause of death.[40] By 2060, 3.3% of the population may have the disease, up from 1.76% in 2020. Among those diagnosed with Alzheimer's, African Americans have the highest prevalence of the disease at 13.8%, followed by the Latinx population at 12.2%.[41]

Like Alzheimer's, **chronic kidney disease** predominantly affects people aged 65 years or older. The most common causes of CKD are diabetes and high blood pressure. CKD is slightly more common in women than men and is most prevalent among non-Hispanic Black adults.[42] While the burden of CKD is increasing overall in the U.S., southern states, such as Mississippi and Louisiana, presented more than twice the burden seen elsewhere.[43]

Current projections show that the number of Americans suffering from **diabetes** will rise exponentially, from 11.3% of adult Americans in 2022 to 17.9% in 2060.[44] As with most diseases, women and people of color face higher prevalence levels. By 2060, 19.2% of women will likely have diabetes, versus 16.2% of men. Black women could see the highest prevalence of all demographics, 25.2%, by then.[45]

**Chronic conditions and diseases** also place a large burden on the population. For example, the 2017 Global Burden of Diseases study found that low back pain was among the leading causes of years lived with disability.[46] Yet care for chronic back pain within our healthcare system is not consistently effective or appropriate; for example, it is estimated that 32% of healthcare for low back pain in the U.S. did not follow clinical guidelines. A recent study by The Lancet estimated that in 2016 a total of $134.5 billion was spent in the U.S. on lower back and neck pain alone.[47]

**For people of color and the disabled,** the burden of disease is heavier relative to other demographic groups. According to the American Journal of Preventive Medicine, the major sources of death and disability for these populations are more similar to patterns in developing countries than to other U.S. populations.[48]

**Socioeconomic factors** also play an important role in discussions of health equity. One 2016 study found that men without insurance and those who relied solely on Medicaid faced a 58% increased risk of death in comparison with men who had insurance.[49]

**Rural Americans** face barriers in obtaining proper healthcare, including low rates of insurance and fewer healthcare facilities and professionals. Lower-income white Appalachians face the highest mortality rates of all Americans linked with heart disease, cancer, COPD, stroke, and diabetes.[50]

## Why Isn't Innovation Helping Reduce Healthcare Costs?

Expenditures continue to increase despite technological innovations in U.S. healthcare. This increase in overall costs may be due in part to a failure to improve net productivity. Healthcare delivery remains highly labor intensive. For example, during the Covid-19 pandemic, healthcare workers still need to operate ventilators on a one-to-one basis, same as in the mid-20th century.[51]

Other potential reasons why the U.S. spends more per person than other countries include the consolidation of hospitals, which leads to a lack of competition, and the inefficiencies derived from the complexity of our healthcare system, as noted above. Further, technological development may stimulate consumer demand for services even if they are not always cost-effective. Also, the promise of potentially expanding insurance coverage provides incentives to develop new technologies. These incentives may contribute to long-term growth in expenditure because the development costs of these products must be recovered by industry, leading to higher prices.[52]

Additionally, since passage of the 2010 Biosimilars Act, aimed at stimulating innovation and competition in the therapeutics markets, only seven new agents have made it to market. Biosimilars are generic versions of biological drugs, also referred to as biologics, that are remarkably similar (albeit not identical) to the original biologic. Under the act, biosimilars would not have to jump through the same costly hoops associated with getting a novel medicine approved initially.

However, 78% of drugs receiving new patents between 2005 and 2015 were "reissues." These are drugs that were previously approved, where the new patent reflects changes to the previously approved formula. Extending patent protection this way is particularly pronounced among blockbuster drugs. Extended patent protection means lower-cost generics cannot be manufactured and sold.

*Can technological innovation promote cost savings as well as expanding healthcare's reach to those most in need?*

Meanwhile, the costs of already-approved drugs have increased at rates between 4% and 7% annually.[53] Pharmaceutical companies increased prices on 857 drugs between January 1 and June 30, 2020, and adjusted the cost of 42 branded medicines by an average of approximately 3.5%.[54] According to the Interfaith Center on Corporate Responsibility, pharmaceutical companies typically raise prices on drugs twice per year, in January and July, often without any change in clinical efficacy. In other words, the companies are increasing prices without any improvement to the drug or to patient outcomes. Such increases may push costs out of the range of many patients. (Some companies have committed to staying below 10%. Merck, for example, has agreed to only increase prices by no more than the rate of inflation.)[55]

Going forward, can technological innovation promote cost savings as well as expanding healthcare's reach to those most in need? In this report we look at technological and process solutions that may provide an answer to this question.

## Major Breakthroughs Hold Promise for Solutions

Despite causing immense loss of life, the Covid-19 pandemic did yield positive developments in medical treatments, as well as overall drug and treatment advances. The urgency to develop Covid-19 vaccinations prompted governments to cut red tape to speed innovation. Also, private companies utilized emerging technologies to deliver healthcare that the public health system had failed to provide adequately. It is also thanks to these emerging technologies and practices that once-fatal diseases are now becoming easier to identify and treat.

Historically, vaccines have taken years to develop. Yet the Covid-19 vaccines were available to the public within a year, thanks to greater collaboration among pharmaceutical companies and governments. This process was further enabled by emerging technologies such as cloud computing, artificial intelligence, and machine learning. AI specifically will factor more into health monitoring and care delivery in the future. According to specialist marketing firm TechTarget, use of AI in the health market will reach $36.15 billion by 2025.[56]

The table below depicts examples of digital solutions that have been developed to address the top 10 causes of death in the US. Unfortunately, no digital solutions have been developed to directly address COPD, colorectal cancer, lower respiratory infection, or cirrhosis.

**Causes of Death and Examples of Corresponding Digital Solutions**

| Top U.S. Causes of Death | Digital Solutions |
|---|---|
| **Ischemic Heart Disease** | My mhealth, Elucid |
| **Lung Cancer** | Bio Passport |
| **COPD** | |
| **Stroke** | Elucid, Neeuro, Brainomix |
| **Alzheimer's disease** | MyndYou |
| **Chronic Kidney Disease** | Strive Health |
| **Colorectal Cancer** | |
| **Lower Respiratory Infection** | |
| **Diabetes** | Livongo Health, Omada Health, Onduo |
| **Cirrhosis** | |

Source: Examples provided by Dr. Derek Yach | As of 12/31/2022

Telehealth also saw significant growth during the pandemic. Previously, Medicare restricted telehealth to rural beneficiaries only, at one half the amount of an in-person visit.[57] The unprecedented demand triggered by Covid-19 caused the government to remove these coverage restrictions associated with telehealth. In 2021, 37% of U.S. adults used telehealth services.[58] Now, telehealth is a booming sub-industry that can reach populations previously missed or ignored.

In addition to emerging technology leading to medical innovation, improvements in the most fatal of diseases have occurred. Unlike a few decades prior, cancer is no longer a death sentence. Cancer deaths have declined by 27% in the past 25 years.[59] This decrease is largely due to improved prevention and screening, and earlier detection. It is also attributable to fewer people smoking.[60] More recently, there have been advances in immunotherapy, precision medicine, development of liquid biopsies, and the usage of machine learning.[61] [62] Thanks to innovations in detection and advances in molecularly targeted therapy, the cancer survival rate will continue to increase.

## The Role of Government-Funded Research: ARPA-H and Lessons from DARPA

Addressing the massive challenge to society in delivering health care requires a multidisciplinary approach. As illustrated in this report, contributions from various scientific fields, combined with insights from social science and advocacy, are coming together to redefine the future of health care.

Government investment also has a tremendous role to play. In the U.S., a March 2022 law authorized the create of the Advanced Research Projects Agency for Health (ARPA-H) to support and fund "high-potential, high-impact biomedical and health research that cannot be readily accomplished through traditional research or commercial activity."[63] While the agency is still quite new and just beginning to solicit project proposals, ARPA-H is modeled on the long-lived and highly productive DARPA – the Defense Advanced Research Projects Agency. [64]

DARPA, launched in 1958 by President Dwight D. Eisenhower in response to the Soviet launch of Sputnik,[65] is responsible for funding and supporting research into emerging technologies for military use. This pioneering entity was the early driver of the internet, weather satellites, GPS, drones, and the personal computer. In creating DARPA, Eisenhower recognized the need for an interdisciplinary approach to addressing extremely complex issues at scale. The agency brought together academia, industry, and government in collective efforts to explore, research, and develop technologies that would represent leaps forward in security, artificial intelligence, molecular science, autonomous systems, pandemic protection, micro-physiological systems, preclinical drug testing technology, climate change, and many more areas of exploration.

Unlike most governmental bodies, DARPA is a flat organization that has tenure-limited program managers with the autonomy to pursue innovative ideas.[66] By virtue of being truly independent within the Department of Defense and the Federal Government, being small and flat in organizational structure, and avoiding bureaucratic processes that can impede progress, DARPA has the flexibility that allows for rapid progress. DARPA states that its long history of successful innovation comes from four factors: 1) trust and autonomy; 2) limited tenure and the urgency it promotes; 3) a sense of mission; and 4) risk taking and tolerance for failure. With only 200 people, and Program Managers with autonomy and leadership strength, DARPA's mission is "to prevent and create technological surprise."

ARPA-H is following the DARPA operating model, functioning as an independent entity under the auspices of the National Institutes of Health. It seeks to pursue health breakthroughs in collaboration with other organizations and the private sector, applying key research principles: 1) expanding what is technically possible; 2) scalable solutions; 3) proactive health care; and 4) resilient, integrated healthcare systems.

DARPA has not been free of controversy given its role in the development of Agent Orange and, more recently, post-9/11 advances in surveillance using data-mining research.[67] That said, much good has come from its work. In this report, we have selected a few examples to illustrate DARPA's achievements in the realm of healthcare. Perhaps ARPA-H will yield similarly meaningful results over time.

### DARPA: INNOVATION IN BIOTECHNOLOGY

The mission of the Biological Technologies Office (BTO) is to foster, demonstrate, and transition breakthrough fundamental research, discoveries, and applications that integrate biology, engineering, computer science, mathematics, and the physical sciences. BTO's investment portfolio goes far beyond life sciences applications in medicine to include areas of research such as human-machine interfaces, microbes as production platforms, and deep exploration of the impact of evolving ecologies and environments on U.S. readiness and capabilities.

# Digital Health and Virtual Care: Key Subsectors

**Erika Karp, Executive Managing Director, Chief Impact Officer**

Digital health and virtual care are broad and fast-growing sectors covering a range of products and services including wearables, electronic health records, telemedicine, robotics, and artificial intelligence. The terms are often used interchangeably, but there are differences: Virtual care encompasses remote technologies to connect with patients, while digital health represents the larger universe of digital devices that support medically informed decision-making.[68]

Both digital health and virtual care aim to help patients and caregivers monitor and manage chronic conditions, lower the cost of healthcare, and tailor medicine to individual needs. Digital health tools could identify health problems earlier or track the progression of an existing issue. The use of these tools may help shorten the length of an illness and improve the quality of a patient's life. Another major benefit of both digital health and virtual care are their potential to close health equity gaps. Below, we discuss some key digital health developments, including their positive impact and potential drawbacks.[69]

## Telehealth and Telemedicine

Telehealth and telemedicine have expanded access to healthcare. Telehealth refers to the broad scope of remote healthcare services, including provider training, administrative meetings, continuing medical education, and clinical services. Telemedicine is the remote provision of clinical services via cellphone, tablet, computer or other digital device. Covid-19 brought telehealth to the forefront of medical access and caregivers can now be reimbursed for this type of service, even across state lines.[70]

Telehealth is not a panacea, but it can help expand services to those in remote or underserved areas and to people who are less mobile, thus expanding access to healthcare for the disabled population. Essentially, innovative technologies and services may help expand healthcare access to those most in need while possibly lowering the cost of delivery.

Since the start of the Covid-19 pandemic, telehealth has exploded as people have sought to avoid visiting the doctors' office. In 2020, the global telehealth market was $144 billion. This number is projected to increase to $636 billion in 2028.[71] The global telemedicine market was estimated to be more than $41 billion in 2019, and it is expected to experience at least a mid-teens compound annual growth rate for the foreseeable future.[72] An estimate by Fortune Business Insights projects a global market of over $185 billion by 2026. Services under the telemedicine umbrella include teleradiology, telepsychiatry, and telecardiology, among other services. End users range from Medicaid patients to regional healthcare facilities.[73]

There are a bevy of companies that have followed on or will follow on with IPOs in the telemedicine space. Teladoc is one well known company that went public in 2015 at a market capitalization of $758 million.[74] As of April 2023 its market cap was $4.16 billion.[75] Another emerging firm promising for its delivery of healthcare engagement and communication via mobile devices is mPulse Mobile, is a portfolio company of SJF Ventures' IV fund (approved on Pathstone's platform). The company focuses on empowering patients to retain their healthcare coverage, especially in Medicaid programs where patients need to reapply for benefits annually – a process known as redetermination. The solution has resulted in a 22% increase in the redetermination of members when using their solution.

### TELEMEDICINE IN THE HOSPITAL SETTING

According to Dr. Howard C. Mandel, President of the Los Angeles City Health Commission:

The Balanced Budget Act of 1997 balanced the federal budget by restraining the Medicare growth curve to be below real inflation. Hospital administrators attempted to insulate themselves from this market manipulation. As the number of Medicare and Medicaid patients has grown, cost pressures forced hospitals to increase revenues, decrease supplies and lower nursing/patient ratios. Hospitals that predominantly rely on Medicaid and Medicare have had to cut corners, underpay, and overwork their staffs and understock supplies to balance their budgets. Covid-19 blew up those systems, as was evident by the severe lack of Personal Protective Equipment (PPE) available. This critical shortage of PPE directly contributed and exacerbated the overwhelming number of Americans who died during the Covid-19 crisis. A large majority of those who died were either nursing-home residents or patients in chronically underfunded safety-net hospitals.[76]

Dr. Mandel refers to a Wall Street Journal article that highlights Banner Health, a Phoenix-based hospital system, which focused on controlling costs while moving patients away from hospital visits and toward free-standing clinics and surgery centers. Its efforts paid off in strong cash flow along with a strong corporate bond rating. But when Covid-19 hit Arizona, Banner did not have enough medical staff to adequately care for the burgeoning patient population. It had to turn to travel nurses, driving up the cost of healthcare workers out of the reach of poorer, safety-net hospitals. Short staffing can and has led to worse health outcomes and higher death rates in hospitals.[77]

Technology may help mitigate this trend. One hospital in New Hampshire, Dartmouth-Hitchcock, services medically underserved communities and special needs populations who lack convenient access to physicians via telemedicine. Before Covid-19, Dartmouth's network averaged only 30 outpatient telehealth visits per week. As of April 1, 2020, the system received 2,000 outpatient visits per week.[78]

Aside from Covid-19, some of the increase stemmed from the Coronavirus Preparedness and Response Supplemental Appropriations Act, which helped clear the way for 50 million seniors to use their Medicare benefits for telemedicine. Medicare claims for telemedicine nationwide jumped from 10,000 per week in March 2020 to well over a million per week the next month. Also fueling telemedicine growth in this period was state governments suspending rules that limit doctors' practices to the states they are licensed in; similar injunctions against writing prescriptions for out-of-state patients were also lifted.[79]

While the long-term upward trend in adoption of telehealth solutions is likely to continue, near term it may face some bumps. Major private insurers recently started rolling back the terms of their telehealth coverage. New rules vary in terms of reimbursements and charges. The confusion and complication of various types of coverage could encourage patients to switch back to in-person visits. This could lead to more infections during spikes in Covid and in flu season.[80]

## Benefits of telehealth and telemedicine

Telemedicine replaces in-person visits with an audiovisual connection via a digital device such as a cell phone, tablet, or computer.[81] Telemedicine may also involve a hospital to clinic connection that enables large, typically university centered hospital personnel in major cities to assist complex procedures at distant clinics and/or rural hospitals.

The benefits of telehealth and telemedicine include lower costs, improved access to care overall — particularly for disabled or older adults and those who are geographically isolated — and potentially improved utilization of the preventive care that is key to improving health outcomes. As shown during Covid-19, telehealth and telemedicine may help slow the spread of infections picked up at a doctor's office or clinic.[82]

### TELEMEDICINE AND CRITICAL CARE

Across many hospital systems, especially safety-net hospitals, there is a shortage of "intensivists," or critical care physicians. These are board-certified physicians who provide special care for critically ill patients.[83] As the U.S. population ages, there will be more demand for these types of specialists to provide care in hospital intensive care units (ICUs). An ICU can consume a quarter of a hospital's budget. Studies have shown that telemedicine can reduce the expense of intensive care and provide access to much needed but distant intensivists. However, the cost of equipping and running a single hardwired ICU room can be as high as $100,000 per year — prohibitive for many smaller (rural) hospitals. A less expensive option, a tele-ICU cart, costs about $12,000. The carts carry audiovisual equipment and can connect directly to the tele-ICU software from any hospital room.[84] The use of this technology can provide affordable remote access to medical experts, such as intensivists, for underserved communities.

### Downsides of telehealth and telemedicine

Telehealth may require providers to depend on patient self-reporting. Patients may leave out symptoms that could be noticed during an in-patient visit. From a doctor's perspective, telehealth may promote a "knee-jerk" reaction to prescribe an unnecessary medicine, e.g., an antibiotic for cold symptoms.[85] Technological issues could make it difficult to offer quality care.

Regulatory issues, particularly across state lines, may still hinder telemedicine services.[86] A team of legal analysts determined that only ten states required private insurers to reimburse virtual visits at the same rate and with the same freedom from restrictions as in-person visits. Tele-doctors could spend more time with fewer patients for less money.[87]

Many rural clinics and community hospitals fear that their already meagre medical staffing, and the revenues generated from procedures that can be performed on-site, will be further hollowed out by remote medicine. Another issue concerns patients who most need care — the old and the poor. Many don't have smartphones or broadband connectivity or cannot afford extra minutes on their wireless plan. Others do not trust an anonymous doctor.

Another issue concerns virtual doctors' visits, which can take longer than in-person ones. This may be due in part to the widely varying ability of patients to operate the necessary technology.

While telemedicine has a critical role to play in connecting patients to their providers, and thus include a greater number of individuals in the US healthcare system, a large population has been left unserved. The telemedicine services designed during the Covid-19 pandemic did not account for non-English speakers. Those who utilized available telemedicine services struggled, including platforms that provided translated information or integrated third-party interpreters.[88] According to the US Census Bureau, 26 million people have reported that they have limited English-language proficiency.[89] That is 8% of the U.S. population for whom current telemedicine services are largely unavailable.

## Remote Patient Monitoring

Remote Patient Monitoring (RPM) uses digital technology to collect medical and other data from individuals in one location, such as their home or a remote clinical location, and electronically transmit that information to a caregiver or medical professional in another location, or to a centralized monitoring system. This market is large and projected to grow rapidly over the next several years. Increased access to smart phones, wearable devices such as fitness trackers, and other digital gadgets is making RPM more readily available to a growing patient population. According to one estimate, the RPM market totaled $786 million in 2019 and is projected to experience compound annual growth of more than 14% through 2027 to reach an estimated size of $2 billion.[90]

There are a number of ways RPM can be used to improve health outcomes:

- It allows a healthcare service provider to track healthcare data from a patient who has been released to home or a care facility. One major goal is to reduce hospital readmission rates.
- It may also help older or disabled people to remain in their homes instead of entering a nursing home or hospital.[91]
- It helps with serving patients who live in rural or remote areas, traveling to a doctor's office may be inconvenient, expensive and/or difficult for those with disabilities.

RPM may be particularly advantageous for patients with chronic conditions, helping to enhance their access to healthcare, improve health outcomes, and reduce costs to care for such patients.[92] This may prove particularly true for patients with multiple chronic conditions – a common problem in the elderly and underserved populations. RPM is often used to keep tabs on patients with less severe cases of chronic or other diseases, thus preserving limited bed space for patients with severe cases. In many cases, RPM may help manage and minimize problems that would arise from chronic conditions that are not properly monitored. As an example, Dexcom is a biotech company that provides continuous glucose monitoring devices for diabetes management, which helps make remote visits more effective.[93]

While RPM can be highly effective for improving health outcomes, especially for those with chronic conditions, several things need to be considered. Companies should design this technology around patient and caregiver preferences. Both groups should be trained to use the equipment as older patients and even caregivers may not be familiar with this type of technology. Patients and clinicians will likely need resources to troubleshoot should technical difficulties arise. Beyond user design, poverty could also limit a patient's access to technology. Caregivers may need to figure out how to give access to needed devices and how to train patients to use the devices so that RPM can be successfully implemented.[94]

## INTERSECTION OF TECHNOLOGY, ARTIFICIAL INTELLIGENCE AND HEALTHCARE

For patients with heart disease symptoms, the process of obtaining an accurate diagnosis can be vague, time-consuming, and involve invasive tests such as angiograms. This procedure requires a catheter to be inserted through the bloodstream to deliver dye into the arteries, so they are visible in an x-ray. Over half the invasive coronary angiograms reveal no obstructive coronary heart disease. These invasive tests are expensive and may entail risk of complications for patients.[95]

Technology may provide a way to curb both deaths and costs associated with coronary heart disease by diagnosing the problem early and monitoring patients more effectively. For example, HeartFlow, a medical technology company focused on precision heart care, combines CT scanning with artificial intelligence (AI) to meet the need for accurate diagnosis of coronary heart disease in a non-invasive manner. (A CT scan is a medical imaging technique that uses a computer processed combination of multiple x-rays to produce a cross-sectional image inside a body without surgery).[96] Using data from a patient's CT scan, Heartflow's technology generates a 3D model of a patient's heart. HeartFlow then utilizes deep learning AI to find and predict the impact of one or more coronary artery blockages.

Studies have shown that HeartFlow's analysis is better at diagnostic performance vs. other non- invasive cardiac tests. Formerly, this high-quality examination was only possible with an invasive procedure such as an angiogram. Studies have shown that four of five patients are able to avoid any further tests or surgery, which reduces both healthcare costs and risks. For a $1,450 test, HeartFlow claims it prevents $4,000 in further costs. In the United States, commercial plans and Medicare pay for this test.[97]

## Personalized/Precision Medicine (PM)

Personalized medicine (PM), also called precision medicine, is the tailoring of medical treatment to the individual characteristics of each patient. A result of scientific breakthroughs in analyzing an individual's molecular and genetic profile, PM makes it easier to predict the potential for a patient's susceptibility to a particular disease and determine a safe, effective treatment.

PM encompasses risk assessment through genetic testing, prevention by prescribing lifestyle and/or treatment interventions, early disease detection, accurate disease diagnosis, targeted treatment, and active monitoring of treatment and disease progression. The approach is participatory, engaging patients in lifestyle choices and active health maintenance to compensate for genetic susceptibilities and has been effective in reducing mortality rates for various cancers and cardiovascular diseases. It has shifted the emphasis in medicine from reactive to preventive.[98]

*A result of scientific breakthroughs in analyzing an individual's molecular and genetic profile, PM makes it easier to predict the potential for a patient's susceptibility to a particular disease and determine a safe, effective treatment.*

In 2022, the global PM market was valued at $83.4 billion. By 2032, the PM market is estimated to grow to USD 254 billion, experiencing a compound annual growth of 12.1% from 2023 to 2032.[99] Some of the major players include Abbott Laboratories, Merck, and Novartis.

PM offers a promising approach to dealing with cancer, neurodegenerative diseases, and rare genetic conditions. A recent estimate from the American Cancer Society predicts that there will be over 1.9 million new cancer cases diagnosed and nearly 610,000 deaths in 2023[100]. Some of these cancers are the result of genetic predispositions. One form of PM is immunotherapy, a treatment that uses certain parts of a patient's immune system to fight cancer. Immunotherapy works to boost the immune system by either working with the body's own immune cells or by creating components similar to those found in the immune system.[101] The global market for immunotherapy oncology grew from $85 billion in 2022 to $96 billion in 2023, almost 50% of the overall oncology market. It is expected to grow rapidly, reaching over $154.42 billion in 2027.[102]

Alzheimer's and other types of dementia are among the leading causes of death in the United States. Over 6.7 million people aged 65 and older are affected,[103] and the disease cost the U.S. economy $321 billion in 2022.[104] The number of cases and the cost associated with the disease is expected to grow quickly and, unfortunately, it is not yet curable.[105]

*The potential for Alzheimer's therapeutics is enormous. One source projects more than $12.4 billion in sales by 2026.*

There is a strong genetic component to many forms of dementia. By combining genomics with clinical, pharmaceutical, and socioeconomic information, researchers can identify genetic variations to determine effective treatments. Clinical drug trials can then be implemented to test the resulting hypothesis. The hope is to find the best gene DNA to treat a genetic disease, or treatment for specific conditions on an individual basis.[106] The potential for Alzheimer's therapeutics is enormous. One source projects more than $12.4 billion in sales by 2026.[107]

SOPHiA GENETICS is one company bridging both the delivery of personalized and precision healthcare utilizing AI. A portfolio company of Pathstone's approved Generation Investment Management's Sustainable Solutions III fund, SOPHiA GENETICS uses AI and machine learning to analyze multiple healthcare data repositories to provide patients a targeted, personalized evaluation and experience with their healthcare professionals to improve outcomes by identifying cancers as well as rare and inherited diseases.

## Robotics

Robotics has been used to aid doctors in surgery since the 1990s. In 1999, Intuitive Surgical launched the da Vinci surgical system – one of the first robot-assisted surgical systems to gain FDA clearance. To date, the company claims its robots have assisted in over 6 million surgeries worldwide.[108] Overall, the global medical robot market was valued at $7.1 billion in 2019 and is expected to reach $20.7 billion by 2027.[109]

In addition to aiding doctors in surgery, robotics is likely to play a much larger role in the future of healthcare. Robots may be used to perform rehabilitation therapy for injured or disabled patients, dispense medication to patients in a hospital or clinic, disinfect hospital and operating rooms, and even draw blood from hospital patients. Robotic exoskeletons could even be used to help paralyzed patients walk again. Some robots might help provide companionship to the sick or elderly. Robots can be designed to carry out repetitive, monotonous, and even dangerous tasks, thereby freeing up human staff to spend more time on decision-making and care.

### DARPA CASE STUDY: NERVE AND MUSCLE INTERFACES FOR PROSTHETICS

DARPA's Reliable Neural-Interface Technology (RE-NET) program researched the long-term viability of brain interfaces and continues research to develop high-performance, reliable peripheral interfaces. These new peripheral interfaces use signals from nerves or muscles to both control prosthetics and to provide direct sensory feedback. Ongoing clinical trials present compelling examples of both interface types.

## Rapid Diagnostic Tests

Rapid diagnostic tests (RDTs) are tests designed for use at the point-of-care such as a clinic, doctor's office or even a drug store screening site. An RDT is low-cost, simple to operate and read, sensitive, specific, stable at elevated temperatures, and works in a short period of time. RDTs are already used for several conditions including strep throat, blood sugar in diabetic patients, Covid-19, and pregnancy. RDTs can be especially useful with patient samples that can be collected by minimally trained health personnel, such as community health workers. Body fluids that can be collected non-invasively, such as nasal swabs, urine, saliva, and tears, are preferred as these are relatively easy to collect with minimal training. RDTs are valuable epidemiological tools, in addition to their use in diagnostics. [110]

In 2018, the global RDT market size was $24.6 billion; some project it will reach over $48 billion by 2026. Factors stimulating growth include: the globalization of the food trade leading to increasing incidences of foodborne illnesses; rising patient demand for preventive medical care along with the rising frequency of lifestyle-related diseases, such as cardiovascular disease and diabetes; and the high burden of infectious diseases.

### DARPA CASE STUDY: DEVELOPING A NEW CLASS OF ANTIBIOTICS

Antibiotic resistance is on the rise and is recognized by both the CDC and the U.S. Military as a current – and formidable – global health threat. The U.S Department of Defense (DoD) has long documented the outsized risk of exposure to infectious disease, including the increasing number of multi-drug resistant (MDR) organisms that challenged military wound care in Iraq and Afghanistan. Despite this looming crisis, there has been a notable exodus of pharmaceutical companies from the antibiotic space, as well as several high-profile failures of biotechnology companies focused on antibiotic development. Current therapeutics to combat microbial infections, including MDR microbes and bacterial biothreats, are insufficient to meet the growing need, and existing methods to develop new treatments are too slow and/or costly to combat emerging drug resistance in pathogenic microorganisms.

# Artificial Intelligence in Healthcare

**Garvin Jabusch, Chief Investment Officer, Green Alpha Advisors**

From its uses in medical imaging, to its potential for use in detecting and diagnosing diseases, to new drug discovery, genomic analysis, and therapeutic discovery, the existing and emerging uses of artificial intelligence (AI) in healthcare are, in practical terms, limitless. This section focuses on just two examples from the realm of drug discovery.

One of the most promising applications of AI in drug discovery is in the identification of new drug targets. The ability to analyze large amounts of genomic data quickly and efficiently is something in which AI excels. This can lead to the identification of new drug targets, which could potentially lead to new drugs that are more effective and have fewer side effects. One such example is halicin, a new antibiotic compound. Halicin was discovered using a machine learning algorithm that screened a library of about 6,000 existing drugs to identify ones that could be effective against a range of bacteria. The algorithm found halicin, which was originally developed as a treatment for diabetes, to be highly effective against a number of bacterial strains, including some that are resistant to multiple antibiotics.

AI-powered tools can analyze vast amounts of genomic data to identify genes that are associated with disease. This information can be used to design new drugs that target these genes or to suggest gene-edited interventions to address the disease directly, as in the case of Crispr Therapeutics' intervention for sickle cell anemia. The company's therapy, called CTX001, uses CRISPR-Cas9 gene editing technology to modify a patient's hematopoietic stem cells (HSCs) in the lab. HSCs are the cells in the bone marrow that give rise to all other blood cells. If approved, CTX001 could be a major breakthrough in the treatment of sickle cell disease. The therapy has the potential to cure the disease and improve the quality of life for millions of people around the world.

AI played a significant role in the development of CTX001. AI was used to:

- Identify the HBB gene as a potential target for gene editing.
- Design the CRISPR-Cas9 guide RNA that is used to edit the HBB gene.
- Predict the efficacy and toxicity of CTX001 in preclinical studies.
- Monitor the safety and efficacy of CTX001 in clinical trials.

The use of AI in drug discovery is still in its early stages, but it has the potential to revolutionize the way that new drugs are developed. AI-powered tools can help scientists to identify new drug targets, design new drug molecules, and predict the efficacy and toxicity of potential drugs. This could lead to the development of new and more effective treatments for a wide range of diseases.

For the asset manager, the opportunity to gain market exposure to these revolutionary developments is as exciting as it is complicated. For research-intensive firms and analysts, I believe a carefully researched and curated basket of the world-leading firms at the intersection of AI and biotech may present generational growth opportunities. By staying informed about the latest advancements in AI and biotech and investing in a diversified portfolio of companies at the forefront of this field, investors can potentially capitalize on the growth opportunities offered by this exciting sector.

# Social Media and Internet Search Activity

**Erika Karp, Executive Managing Director, Chief Impact Officer**

In our discussion of digital technology and health, we would be remiss not to discuss the health implications of social media.

In recent years it has become clear that Meta, Twitter, and Google systematically amplify content that garners more attention, regardless of its nature. Facebook's algorithm has been shown to incite misinformation, hate speech, and ethnic violence. Twitter has been criticized for how its algorithms amplify political differences. Earlier this year, Google appeared before the Supreme Court for their algorithm radicalizing Islamic State terrorists. (The Court rejected arguments in favor of holding social media companies liable for their content.)

As the evidence of societal damage builds, the Seattle Public Schools (SPS) is taking steps towards holding social media companies accountable for the harm caused to students' social, emotional, and mental health. Their early 2023 complaint summarizes extensive evidence of the relationship between social media use and anxiety, depression, thoughts of self-harm, and suicidal ideation.

More recently, U.S. Surgeon General Dr. Vivek Murthy issued an advisory on May 23, 2023, about the impact social media is having on the mental health of young people. The advisory cites studies that have found a link between social media use and increased risk of depression, anxiety, and suicidal thoughts. The advisory also notes that social media use can lead to sleep deprivation, cyberbullying, and exposure to harmful content.

This evidence is strengthened by research published by Dr. Jean Twenge in her recent book, Generations. Dr. Twenge shows how Generation Z (born 1995-2012 and representing roughly 75 million Americans), which she calls the "iGen," has been deeply influenced by the arrival of smart phones and social media. Based on rigorously conducted survey data, she shows that the iGen cohort is more interested in a range of issues than Millennials (born 1980-1996): gender fluidity, free speech, physical and emotional safety, and racial awareness. They also report being more dissatisfied with life – and depressed at increased rates, to a greater degree than other current generations. This is reflected in dramatic increases in teen suicides over the last decade: the United Health Foundation released a report last year which showed suicides amongst teenagers aged 15-19 had jumped 29% between 2012 and 2020. .

Dr. Twenge systematically considers which factors could be driving these negative trends and concludes that the most likely explanation relates to the rise of social media between 2009 and now. She describes how the technologies attract and keep young people engaged. Recent research shows a close relationship between social media use and many aspects of mental health among youth: sleep deprivation, less time with friends, decreased physical activity, and a greater sense of pessimism; all leading to increased reports of online bullying, isolation, suicide, suicide attempts, and suicidal ideation.

The Seattle case and emerging evidence of harm associated with social media will likely lead to greater focus on regulations. The danger is that bad regulations could thwart the very real benefits that digital technologies are already bringing to address mental health. The challenge is heightened by the conflict between corporate goals of profit maximization and social goals of a stable, thriving, healthy economy. Arguably, the current business model of social media platforms is inconsistent with civil discourse.

And in terms of content moderation, Renee Diresta argues that the content dynamics are not an issue of speech, but "challenges of curation and network organization." There is limited capacity for attention in the world. Advertisers and social media must grab as much of that attention and advertising spending as possible. The best way to succeed along those metrics is to leverage the outrage amplification and polarization that is anathema to stability, prosperity, mental and physical health, and sustainability.

# Using Digital Tech to Close the Gender Equity Gap in Health

**Katherine Pease, Managing Director | Akshika Patel, Senior Associate**

Since the onset of Covid-19 in 2020, there has been a rapid increase in digital health investments (DHIs). However, domestically only 3% of DHIs focus on improving women's health,[111] even though women make up more than half the population and spend $500 billion per year on medical expenses.[112] On average, women spend $1,000-$3,000 per year addressing the effects of menopause and chronic conditions/disorders.[113]

Further, DHIs targeting women's health issues have largely focused on tracking menstrual cycles and managing pregnancy[114]. They also catered largely to mid-upper-class, cis, white, childbearing, able-bodied women.[115] Meanwhile, according to the Commonwealth Fund, the U.S.'s maternal mortality rate far surpasses that of any other developed country.[116] Further, Black women are two to three times more likely than white women to die in childbirth[117] and are more likely than white women to develop postpartum depression.[118]

Obviously, women's health is about more than fertility. Women are more likely than men to die from heart attack (and are 50% more likely to be misdiagnosed when they have heart disease)[119]; the creation of sex-specific digital diagnostics for heart disease could be an investible solution to level that particular gender gap.[120] Around 45% of women suffer from chronic conditions such as diabetes or the results of hormonal changes associated with menopause.[121] Women also display greater prevalence of conditions such as anxiety, depression, osteoporosis, breast cancer, autoimmune conditions, stroke, and irritable bowel syndrome.[122] While these chronic conditions adversely affect women at a greater rate than men, currently available digital technology solutions for women do not address them.

*Digital Health Interventions targeting women represent a long-term investment opportunity. By 2027, the women's digital health sector could be worth US$60 billion.*

This lack of DHIs targeting women beyond the scope of reproductive health represents a long-term investment opportunity. From 2019 through 2021, venture capital funding for solutions targeting menopause doubled. By 2027, the women's digital health sector could be worth US$60 billion.[123] By improving care delivery, enabling self-care, improving diagnoses, addressing stigmatized conditions, and creating culturally sensitive and tailored care, DHIs hold significant potential to boost health outcomes while providing new growth opportunities to investors.

## Inclusive Digital Health Innovations

Despite the severe lack of VC funding and support, there are a small number of startups that have created digital health technology products for women. Most of these startups have been supported by capital from women-led VCs that focus on digital healthcare for women.

- In 2021, Flo became the first startup addressing women's healthcare needs to achieve so-called unicorn status. The period tracker application secured $110 million in Series D investments.

- Another example is Ovia Health, a digital health platform offering support to women and parents. After being acquired by Labcorp in early 2021, the company secured a partnership with New York State's leading health plan, Capital District Physician's Health Plan, Inc (CDPHP). Through this deal, Ovia Health will support all eligible commercial and Medicaid members in New York.[124] This represents a potential increase of at least 251,067 customers in just one state.[125]

- In 2020, Bloomer Health Tech, a startup that uses wearable fabrics and machine learning for the detection and monitoring of chronic diseases such as ischemic heart disease, raised $3 million in seed funding.

- Rhia Ventures is a fund dedicated to investing in reproductive and maternal health, while uplifting marginalized communities. The firm's pipeline includes investments in companies such as Nurx, an online source of birth control products, Cadence, which is focused on bringing over-the-counter birth control pills to market, and AOA, an early cancer-detection platform.

As the use telehealth and DHIs expands, more companies are tapping into an unexplored consumer base of Black, Latinx, Asian-American, low-income, and disabled women. This requires more than simply integrating a gender equity lens. The gender gap in digital health intersects with inequities stemming from the failure to include a racial equity perspective. In other words, women of color are routinely ignored when it comes to the design of DHIs. For example, while Black and Hispanic/Latina women are "the least physically active", according to national medical studies, they typically are not accounted for in the design of DHIs focusing on physical activity.[126]

With thoughtful approaches to product research, design and marketing, DHI companies can make a significant impact on many of the most marginalized communities and ensure greater returns for investors.

## Legislative Landscape Creates Uncertainty for Gender-Focused DHIs

There have been several significant recent legislative developments that impact women's health, including the Momnibus Act of 2021, which mandated increased government spending on Black maternal health. Under the act, post-partum eligibility for the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is extended by 24 months. This is especially significant given the strong tie between postpartum nutrition and maternal mental health.[127] The bill also calls for increased government investment in digital tools to improve maternal health outcomes in underserved areas.[128]

In addition to the Momnibus act, four state governments have expanded Medicaid coverage to include doulas. Doulas are trained professionals who provide physical, emotional, and informational support to a mother before, during, and after childbirth.[129]

Even considering the positive legislative developments that took place during the pandemic, however, the overturning of Roe v Wade will change likely affect the evolution of digital health solutions for women and government funding for women's healthcare. In 2020, medication abortion made up 54% of all abortions.[130] With the overturn of Roe v Wade, medication abortion will likely make up most abortions. Beyond this, the reversal of Roe v Wade has sparked further concern for data privacy among consumers. Historically, period-tracking startups and companies have shared user data with third parties, for marketing and other purposes. Now advocates for reproductive healthcare fear that tech companies will share fertility and abortion-related data with governmental bodies or law enforcement. In a post-Roe world, consumers may find this lack of privacy intolerable; fears of reproductive health policing will be grounded in a new legal reality, and investors in digital health solutions for women will need to stay apprised of the repercussions of legislative developments that may hinder or help the growth of the industry.

# Digital Tech and Environmentally Linked Health Issues

**Mark Peters, Managing Director**

There are well-documented links between environmental conditions and rates of disease and death. In addition to technologies that directly address health, digital advances in other areas can indirectly impact the health of individuals and communities. For instance, digital technology can be instrumental in increasing renewable energy, improving transportation, and increasing the sustainability of mining and upstream production. According to the EU Science Hub, digital technology, when well utilized, could possibly reduce 15-20% of total greenhouse gas emissions. [131]

Social justice and climate justice benefits are intertwined within health solutions for many diseases, since low- and middle-income countries are bearing more than their fair share of the disease burdens of ischemic heart disease (IHD), chronic respiratory diseases, cancers, and unintentional injuries. In this section we highlight key studies and developments illustrating these interconnected issues.

## Diseases Linked to Environmental Factors

Research by the World Health Organization (WHO) indicated that in 2016, as many as 24% of deaths globally resulted from environmental factors that could be changed and modified, and many of these factors were related to changes in temperature and climate. They identified the following top ten diseases with significant environmental components:

| **Diseases with Strong Environmental Linkages** | **Number of Deaths**, 2016 |
|---|---|
| **Ischemic heart disease** | 2,433,735 |
| **Chronic obstructive pulmonary disease** | 1,675,273 |
| **Lower respiratory infections** | 1,478,582 |
| **Stroke** | 1,456,512 |
| **Other cancers*** | 1,088,891 |
| **Diarrheal diseases** | 828,645 |
| **Trachea, bronchus, lung cancers** | 724,484 |
| **Road injury** | 560,603 |
| **Diabetes mellitus** | 390,633 |
| **Malaria** | 354,924 |
| **Other unintentional injuries** | 330,601 |

### Heart Disease

A study of ischemic heart disease (IHD) found that, after adjusting for age, there was a 20-fold difference in IHD mortality by country that is directly correlated with income level. The study estimated that low- and middle-income countries account for more than 80% of IHD mortalities. The study noted that IHD is the leading cause of death worldwide, accountable for an estimated 12.7% of total global mortality in 2008.

An article focusing on pollution and the heart noted that the extent of the adverse impact of pollution is most likely undercounted in studies and has received scant attention. Despite the opportunity for pollution reduction to save millions of lives, most studies on cardiovascular disease have focused on individual behavior and metabolic risk factors.

Technologies such as wearables and smart monitors can measure both biological activity at the individual level as well as the environment in which the body is functioning. This data can be tracked across large populations and collected and assembled for analysis in a systematic manner.

Technology is enabling nascent healthcare systems to leapfrog conventional diagnostic approaches. For example, one journal article argues that the diagnostic ecosystem in African countries could be radically transformed by embracing digital molecular diagnostics rather than emulating the old-school laboratory models used in more resource-rich countries.[132]

## Temperature

A 2006 article in Lancet, Climate change and human health: present and future risks, provided a summary of past research and pointed to future opportunities to better understand how climate and health are interrelated.[133] The article highlights thermal stress as a heightened risk, with heat waves adversely impacting vulnerable and marginal populations, which tend to have higher levels of heart disease and asthma.

*Wearable devices can track exposure to extreme temperatures and provide real-time alerts when risks are high.*

Urban dwellers are at greater risk than others due to greater exposure to temperature extremes, reflecting the less thermally efficient built environment, along with an urban heat island effect during extreme rising temperature events. Wearable devices can track exposure to extreme temperatures and provide real-time alerts when risks are high, such as residents of nursing homes and assisted-living communities that lack insulation during cold spells or air conditioning during hot spells.

Heart disease, asthma, heat stroke, and hypothermia are not the only diseases related to temperature change. As illuminated by a systematic review of the climatic drivers of diarrhea, studies have found a significant positive correlation between the incidence of diarrhea and the level of temperature.[134]

From a wearable device perspective, temperature is perhaps one of the easiest metrics to measure and transmit on a regular basis.

## Air Pollution

As outlined in the article Environmental and Health Impacts of Air Pollution, the World Health Organization focuses on the following types of air pollutants:[135]

- Particulates
- Ozone
- Carbon Monoxide
- Sulfur Oxides
- Nitrogen Oxides
- Lead

These pollutants contaminate not only the air, but the water and the ground as well. The article describes how air pollution's long-term effects include chronic asthma, pulmonary insufficiency, cardiovascular diseases, and cardiovascular mortality. It points out how respiratory, cardiovascular, mental, and perinatal disorders that are contracted early in life may lead to infant mortality or chronic disease later in life. It goes on to note that air pollution is responsible for the largest amount of disability-adjusted life years lost (DALYs).

As noted in a study focusing on pollution and the heart, "Innovations in digital health technologies, such as platforms that integrate data from portable sensors and ground-level monitors, have the potential to further heighten awareness of air pollution, inform individual behaviors, and enhance the provision of individualized guidance."[136]

A recent Veterans Cohort Mortality Study looked into mortality rates of military veterans and how they related to exposure to air pollution. They found that "higher exposures and mortality risks associated with vehicular traffic posed environmental injustice for the black veterans."[137]

A recent Harvard study has linked air pollution from fracking to increased mortality rates based on proximity. For those 65 and older, the closer you lived to a well, the greater your risk of premature mortality, suggesting that air pollution surrounding the oil and gas wells pose potential health risks.[138]

Any discussion of air pollution should include a focus on short-lived climate pollutants, which have been called "near-term climate forcers" by the Intergovernmental Panel on Climate Change.[139] These pollutants only last a short while in the atmosphere when compared with other greenhouse gases such as carbon dioxide but are known to have a stronger warming effect. Immediate actions to reduce pollutants such as black carbon, tropospheric ozone, and hydrofluorocarbons can reduce warming in a cost-effective manner. In addition, given the toxic nature of many of these pollutants, technologies that reduce these emissions or exposure to these emissions will deliver the additional benefit of improved health outcomes.

Evidence of the adverse impact from air pollution is substantive. In its research of the benefits of cleaner cooking fuels, one study estimated that household air pollution is responsible for 3 to 4 million early deaths per year.[140]

A more recent comprehensive study within the U.S. published by the Health Effects Institute found a strong association between the risk of mortality and longer-term exposure to relatively low concentrations of air pollution, especially among elderly and other vulnerable populations.[141] According to the NY Times, the group examined data from 68.5 million Medicare recipients, concluding that as many as 143,000 deaths over a decade could have been prevented if allowable levels of soot were slightly lower.[142]

*Companies and federal, local, and state governments are teaming up to create and implement low-cost and efficient products which can actively monitor air quality in our communities.*

With accelerated environmental degradation and increased global temperature extremes, there is a clear necessity for innovative solutions. Companies and federal, local, and state governments are teaming up to create and implement low-cost and efficient products which can actively monitor air quality in our communities.

Airspec is one such company. Funded by NASA, NSF and NIH, their stated goal is "Protecting your health and the planet with our affordable high-quality fine and ultra-fine air pollution sensors." The devices measure exposure to hazardous air with great precision. Particulates enter the device and cast a shadow on the detector. By measuring the diameter of the shadow, the device can categorize the type of pollutant. Airspec has been utilized in many projects, including one that measured personal exposure to air pollution particulates in Delhi, India.

Researchers from the University of Michigan, Michigan State University, and Oakland University recently received a $2.78 million grant from the National Institutes of Health to study how a wearable device can detect particulate matter, such as soot and toxic metals, that are emitted from cars, trucks and factories.[143] Their first field research will be across neighborhoods throughout the Detroit metropolitan area.

Both outdoor and indoor air pollution can be monitored by these wearable devices and collected data can be utilized to improve health across communities.

According to many studies, indoor air pollution is more deadly than outdoor air pollution. One study notes that poor indoor air quality is the second major factor in India's relatively higher mortality rate.[144] The study noted that Wireless Sensor Networks and Internet of Things models are appropriate for real-time monitoring of exposures.

### Water Pollution

In poor countries, where there may be a lack of sanitation infrastructure, contaminated water and poor hygiene can result in widespread disease, including diarrhea. Storms exacerbate these issues.

In developed countries, communities such as Flint, Michigan have been exposed to harmful drinking water from mismanagement.[145] In addition, storms often result in spills from sewage plants, resulting in increased emergency room visits for gastrointestinal disorders.[146] Across the globe, human action and climate change present a threat to safe drinking water and sanitation services.[147]

Technology is available to monitor water quality, both in terms of drinking water and in terms of exposure through bath water. It is important to measure water quality in a comprehensive and systematic manner.

### Food

Dietary risks are preventable, and yet they contribute significantly to non-communicable diseases such as heart and respiratory illnesses, and diabetes. A study published in the Lancet examined the health effects of dietary risks in 195 countries over nearly three decades.[148] Their findings estimate that in 2017, 11 million deaths and 255 million disability-adjusted life-years were due to suboptimal dietary practices. The worst offenders were sodium, low grain consumption, and low fruit consumption.

Lists of ingredients contain a wealth of data that link back to specific dietary outcomes. Menus at restaurants and meals that are being prepared may open the door for specific and tailored positive or negative feedback. For example, wearable technology could be developed that measures biological conditions related to salt intake, as well as a lack of nutrients connected with grains and fruits. Perhaps an algorithm could be used to evaluate a photo of a meal, computing the health "rating" for the type of food and the quantity of food photographed.

Wearable technology that tracks location may also offer an approach to improve one's diet. Consumers could be encouraged to utilize an app that suggests they modify their behavior to reduce consumption of fast food. Perhaps the use of the app might be rewarded by their health insurer, just as insurance providers deliver safe-driver discounts to those that drive with a monitoring device onboard.

## Community Monitoring

### Community Engagement Using Inputs from the Internet of Medical Things

Creative technology can be used to monitor risk exposures and launch specific information campaigns designed to reduce negative behavior and boost positive outcomes. Such measures can reduce consumption of tobacco, alcohol, and processed foods, and can also foster movement and mobility to combat the increase in sedentary life that accompanies urbanization.

### Sewage Analysis

Wastewater-based epidemiology (WBE) is a way in which communities can monitor public health and important environmental data in real time to assess the risks and to identify areas for improvement. This type of monitoring can help facilitate interventions, such as those we saw with the Covid-19 recommended that future studies focus on the design and validation of biosensors in sewage.[149]

Using a data-driven approach to review areas of focus of WBE researchers, the authors found that WBE researchers have focused on monitoring and analyzing sewage for the presence of bacterial and viral diseases, pharmaceutical and personal care products, use of illicit drugs, and the use of legal drugs.[150] Recently the mention of SARS-CoV-2 has increased in frequency, and enterovirus, norovirus, and rotavirus are also mentioned. The most widely monitored illicit drugs include cocaine, methamphetamine, amphetamines, and new psychoactive substances. Common therapeutic drugs, such as antidepressants and cardiovascular drugs, have also been studied. These tools may be helpful in dealing with opioid and fentanyl crises as well.

Confirmation of the effectiveness of the WBE approach might be found in the testing done in a wastewater-treatment plant in Connecticut. In addition to other findings, the authors found "trends related directly to the pandemic (e.g., hydroxychloroquine, a drug publicized for its potential to treat Covid-19, had elevated concentrations in the week following the implementation of the US Emergency Use Authorization)."[151]

Low-income countries, which do not have the resources for centralized sewage processing, must employ different approaches to WBE. In these areas, the wastewater reservoirs may also be areas from which the viruses and diseases are spread. Decentralized approaches are required in these settings. Resulting insights may reveal the prevalence of disease, and also allow a prioritization of the main sources of spread in controlling the disease.[152]

## Geo-Focused Alerts for Community Advocacy

Data can drive decisions, and compelling arguments can sway behavior. On all levels, across continents and across streets, we can benefit from information that is monitored and shared in a way that can lead to better outcomes. Much of the globe is focused on a screen, and much of the globe can be provided with real-time alerts that get to the risk of extreme temperatures and other weather events, the prevalence of disease, and the risk of a poor diet and immobility, to name a few. Alerts can be tailored for the local community, and experts can be assembled to address the most at-risk communities. The experts can also congratulate those that have had success at moving toward better outcomes.

# Addressing Mental Health Through Digital Tech

**Akshika Patel, Senior Associate**

*"We must promote--to the best of our ability and by all possible and appropriate means--the mental and physical health of all our citizens." - President Kennedy, February 5, 1963*

*"Few countries spend very much on provision of mental-health services. The median spend on mental health is about 2% of total healthcare spending. Even in wealthier countries, the share is typically below 10%." - Generation Sustainability Trends Report 2021*

## A Crisis in Mental Health

In the U.S., poor mental health is widely viewed as a crisis. The U.S. spends $71 billion annually on depression treatment.[153] Since the onset of the pandemic, the prevalence of mental health disorders and diseases has increased exponentially. This is now reflected in the nation's declining life expectancy, with suicide and substance abuse being major contributors over the last two years. During the pandemic, suicide rates alone increased by 25%.[154]

Both adults and youth are affected, with 10-20% of youth experiencing mental health challenges. One in four people ages 1-24 have experienced a mental health episode in the past year. In 2019 alone, 13% of youth had a depressive episode.[155] Even more alarming, that 64%-87% of mental health issues in young people are undetected.[156]

Among the most vulnerable to mental health disorders and diseases are Americans with low socioeconomic status (SES), people of color (POC), sexual/gender minorities (SGM), and people with disabilities.[157]

The demand for mental health services is strong. In 2020, the mental health and substance abuse center industry was valued at $18.7 billion.[158] A data brief published by the National Center for Health Statistics revealed that the percentage of adults who received any mental health treatment increased from 9.2% to 21.6% from 2019 to 2021.[159] A comprehensive 2018 study of access to mental healthcare revealed that 56% of Americans either sought or wanted mental healthcare either for themselves or a loved one. The survey revealed that these individuals tend to be younger, come from a lower-income household and in many cases, had a military background.

*The percentage of adults who received any mental health treatment increased from 9.2% to 21.6% from 2019 to 2021.*

Individuals located in rural areas and lower-income households are less likely to have readily accessible mental health services. Also, lower-income Americans are less likely to know where to receive treatment. They are more likely to use a community center versus a qualified mental health center. Of the Americans who have not sought mental health treatment, the survey revealed that more than half were from low-income households.[160]

Further, there is an enormous mental health workforce shortage; only 27% of mental health is being met in health professional shortage areas.[161] Currently, more than half of adults who suffer from mental illness report being unable to obtain treatment.[162] This includes 54% of adults covered by insurance (around 27 million Americans) who did not receive mental health treatment.[163]

Regionally speaking, Ohio (2.24%), Nebraska (2.2%), Wyoming (2.2%), and Oklahoma (2.11%) saw the biggest increase in adults suffering from mental health illnesses or disorders.[164] Data from the Understanding America Study (UAS) revealed that individuals without pre-existing mental health conditions who lived in states with the most severe Covid-19 outbreaks suffered from increasingly worse mental health disorders and diseases.[165]

Covid-19 has also highlighted the frailty of the mental healthcare system. In New York State, roughly 400 psychiatric and 150 drug-rehabilitation beds were repurposed or closed to make beds available for Covid-19 patients in 2020. Hospitals also closed these beds in other states, including Illinois and Texas. As a result, healthcare workers noted that mental health patients were discharged early to free up space even when they still needed care, thus, exacerbating the mental healthcare crisis.

## Digital Solutions

Our country's approach to mental health is not working. The occurrence of mental health disorders will likely increase without investment into digital mental health services that encompass intentional design and work within the ecosystem of U.S. medical care. Thankfully, the rise in mental health focused Digital Health Interventions (DHIs) is an opportunity to transform mental healthcare delivery in a more wide-reaching and ultimately effective manner. Investors are well positioned to support DHIs to face the burgeoning mental health crisis in America.[166]

An overwhelming majority of Americans own smartphones. Those that do are interested in using technology to help manage their mental health. In fact, over two-thirds of American adults are willing to use their smartphones as a vehicle for health management.[167] Sixty percent of people with smartphones have downloaded a health application. While most of the smartphone applications purchased are free, Deloitte Global predicted that global spending on smartphone mental health applications would approach $500 million by the end of 2022.[168] This is a strong indicator of the investment potential in smartphone mental health applications. According to a 2021 Accenture report, 46% of patients prefer DHIs over in-person treatment.[169]

There are several examples of startups creating mental health technology that utilizes augmented reality and smartphone applications. One such firm, led by prominent mental health advocate Karan Singh, is Ginger. Leveraging smartphone-based technology, the platform identifies patterns of anxiety, stress, and depression.[170] In August 2022, Amazon entered a partnership with Ginger as a part of its Amazon Care program.[171] Prior to this, Ginger had merged with Headspace in fall 2019 to create a $3 billion company.[172]

*There are several examples of startups creating mental health technology that utilizes augmented reality and smartphone applications.*

With the heightened interest in virtual and augmented reality, VR-Eval is an example of an immersive platform that is specifically designated for victims of human trafficking. Designed by Dr. Brook Bello, Google Next Gen Policy Leader, VR-Eval is an example of technology used to provide mental healthcare to a marginalized community.[173]

A key component of addressing mental health concerns is identifying them to begin with. One solution, Ellipsis Health (a portfolio company of private market firm SJF Ventures), focuses on the early identification of stress, anxiety, and depression. Ellipsis uses human voice as a biomarker for mental health and wellbeing along with machine learning and AI. Ellipsis Health assesses the severity of clinical anxiety and depression, as well as a sub-clinical assessment of the severity of stress.

While DHIs cannot completely replace in-person care, they can help address more immediate mental health concerns that are not severe enough to warrant immediate in-person medical attention. Since the U.S. government is the biggest procurer of medical technology, one of the most profitable and meaningful ways for the wider implementation of DHIs is through the Veteran's Administration (VA). Importantly, a recent study comparing in-person diagnosis of mental health issues with online remote diagnosis demonstrated extremely high concordance. However, it is too early to be sure that DHIs lead to better health outcomes. Some studies are hopeful. In 2020, the VA conducted a study that found video tele-psychotherapy is as effective as in-person office-based care.[174]

### DARPA CASE STUDY: NEW COGNITIVE SCIENCE TOOL TO SHED LIGHT ON MENTAL HEALTH

Since Sept. 11, 2001, more than 30,000 active-duty members and veterans have taken their own lives – four times as many as those killed in post-911 military operations.[1] Current methods to detect early signs of behavioral and mental health risk factors rely on self-reporting and screening questionnaires, which cannot reliably predict suicidality. Effective behavioral health assessment is a mission-critical capability requiring novel tools to identify and help those at risk.

Recently, DARPA announced the Neural Evidence Aggregation Tool (NEAT) program. NEAT aims to develop a new cognitive science tool that identifies people at risk of suicide by using preconscious brain signals rather than asking questions and waiting for consciously filtered responses. "NEAT is a proof-of-concept effort attempting to develop a new tool for mental and behavioral health screening that moves us beyond historical and current methods of questions and consciously filtered responses," said Greg Witkop, a former Army surgeon and current program manager in DARPA's Defense Sciences Office. "Using the preconscious will hopefully enable us to detect signs of depression, anxiety, or suicidal ideation earlier and more reliably than ever before."

The veteran community is not the only community that could stand to benefit from DHIs. A qualitative 2019 study, conducted by Carpenter-Song et al, found that across diverse communities, there was a high level of interest in using DHIs to support patients affected by mental illnesses.[175]

Mental health disorders cover a very wide spectrum of specific diseases with varying levels of severity. Many are characterized by requiring long-term support well beyond the initial crisis. DHIs are well addressed to do this. Emerging technologies can continuously assess mental health status, alerting providers to patients' needs. They could be used widely to triage patients to therapists as needed.

## Careful Design a Critical Concern

The interest in and need for the integration of DHIs is clear. DHIs have the potential to completely revolutionize how mental health disorders and diseases are treated in America. They allow individuals to take their care into their own hands, which helps personalize medicine. Yet, this requires intentional and inclusive design to capture key populations. And it requires new means of assuring referral to trained therapists when needed.

However, there are clear distinctions to be made in evaluating DHIs. There are six categories that mental health (mHealth) apps must meet for therapists and physicians to be willing to integrate them into their process of care: self-management, cognition improvement, skills training, social support, symptom tracking, and passive data collection. Beyond this, there are an additional 17 frameworks for evaluating mHealth apps. A 2019 **study** found that only 3.4% of mHealth startups had conducted research on the efficacy of their technology, and this research was not peer evaluated or done together with an academic institution, medical facility, or government agency. According to the same study, fewer than 31% of mHealth applications had development input from mental health experts.[176] In 2020, the Organization for the Review of Health and Care Apps (ORCHA) found that only 30% of the available mHealth smartphone applications met the quality and efficacy threshold.

As John Tourous, associate professor of psychiatry at Harvard Medical School, has put it, "with direct-to-consumer advertising and marketing, companies will sometimes exaggerate what these apps can do".[177] To properly meet the challenges of the mental health crisis, consumers need more than just an abundance of choices when it comes to mHealth apps and DHIs. They need HIPAA-compliant solutions that can be integrated into the medical care process.

Many start-ups in the DHI space are driven by innovative engineering entrepreneurs with depth in computer science, digital applications, and AI. They rarely include people with mental health expertise. This influx of

innovative entrepreneurs needs to be carefully supported (not overregulated) given the early stage of many of the interventions.

In addition to integrating peer-reviewed research and institutional partnerships, a focus on diversity, equity, and inclusion (DEI) and user-centered design are important to ensuring the success of mHealth apps and DHIs more broadly. A 2020 US-based study showed that more than half of people of color (POC) would choose virtual visits over in-person treatment in order to access medical providers of color.[178] Given that this study is representational of national demographics, that means a large proportion of the country's POC may be interested in purchasing a mHealth application or DHIs.

*To properly meet the challenges of the mental health crisis, consumers need more than just an abundance of choices when it comes to mHealth apps and DHIs. They need HIPAA-compliant solutions that can be integrated into the medical care process.*

While the initial appetite for mHealth apps and DHIs is strong, integrating user-centered design is paramount for sustaining a long-term consumer base. According to a meta-study done by Karyotaki, almost 70% of youth patients stop using mHealth and DHIs before three-quarters of the intervention is complete. [179] A huge reason for this is poor user interfaces.

Investors who want to help address the U.S. mental health crisis should look to funds investing in mHealth technology that seeks to integrate into clinical settings, and thus create participatory methods that properly function in the context of the greater healthcare ecosystem.[180] Not only is this more effective, but it could also open the door to greater capital via insurance coverage. As DHIs become more popular in a post-pandemic world, insurance companies will slowly move toward providing coverage for phone and video therapy.[181] The future of mental healthcare lies in intentionally designed and researched mHealth applications and DHIs.

## Disclosures

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