DIGITAL ACCESS TO SCHOLARSHIP AT HARVARD
DASH.HARVARD.EDU

HARVARD LIBRARY


Leveraging Pharma, Digital Innovation, and Partnerships to Increase Healthcare Access in China: A COVID-19 Case Study

Citation

Harrison, Vannessa Jean. 2021. Leveraging Pharma, Digital Innovation, and Partnerships to Increase Healthcare Access in China: A COVID-19 Case Study. Doctoral dissertation, Harvard T.H. Chan School of Public Health.

Link

https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37367926

Terms of use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material (LAA), as set forth at

https://harvardwiki.atlassian.net/wiki/external/NGY5NDE4ZjgzNTc5NDQzMGIzZWZhMGFlOWI2M2EwYTg

Accessibility

https://accessibility.huit.harvard.edu/digital-accessibility-policy

Share Your Story

The Harvard community has made this article openly available.
Please share how this access benefits you. Submit a story

This Doctoral Thesis, ***Leveraging Pharma, Digital Innovation, and Partnerships to Increase Healthcare Access in China: A COVID-19 Case Study***, presented by Vannessa Jean Harrison, and Submitted to the Faculty of The Harvard T.H. Chan School of Public Health in Partial Fulfillment of the Requirements for the Degree of Doctor of Public Health, has been read and approved by:

Richard Bolton Siegrist

Dr. Kimberlyn Rachael Leary

Dr. William Bean

Date: April 7, 2021

LEVERAGING PHARMA, DIGITAL INNOVATION, AND PARTNERSHIPS TO INCREASE HEALTHCARE ACCESS IN CHINA: A COVID-19 CASE STUDY

VANNESSA JEAN HARRISON

A Doctoral Thesis Submitted to the Faculty of

The Harvard T.H. Chan School of Public Health

in Partial Fulfillment of the Requirements

for the Degree of *Doctor of Public Health*

Harvard University

Boston, Massachusetts.

May 2021

"I had fainted, unless I had believed to see the goodness of the Lord in the land of the living. Wait on the Lord: be of good courage, and he shall strengthen thine heart: wait, I say, on the Lord."

Psalm 27:13-14, KJV

"Beloved, I wish above all things that thou mayest prosper and be in health, even as thy soul prospereth."

3 John 1:2, KJV

This Doctoral Thesis is dedicated to my mother, Marian Jean Lovett, whose love, support, and faith have carried me through the storms to the rainbows.

Thesis Advisor: Richard Siegrist Vannessa Jean Harrison

Leveraging Pharma, Digital Innovation, and Partnerships to Increase Healthcare Access in China: A COVID-19 Case Study

ABSTRACT

Background:

The COVID-19 pandemic disrupted healthcare systems globally and posed challenges for disease management, medication access, and adherence. Before the pandemic, digital healthcare had been increasing in China to address healthcare access and primary care inefficiencies. With COVID-19 pushing China's healthcare system to the brink, pharmaceutical companies had to quickly embrace digital solutions to continue providing life-saving care and medicines to patients, running clinical trials, and patient and physician engagement. Using COVID-19 and China as a case study, this project examines how Takeda can increase healthcare access through digital innovation and partnerships.

Objectives:

This doctoral project aimed to:

1. Explore how COVID-19 accelerated digital/technological innovation for health management and access in China.
2. Synthesize recommendations for Takeda on how to best utilize global partnerships and technology to increase healthcare access.

Methods*:*

A mixed-methods approach was used in which quantitative data provided an overview of the epidemiological disease burden and healthcare access statistics in China, while qualitative data provided insights into Takeda's digital health initiatives and opportunities for growth in China's

digital health ecosystem. Nineteen qualitative interviews were conducted. The ADKAR framework was used to conceptualize the results in the context of change management.

Results:

Cardiovascular disease, cancer, respiratory disease, and diabetes are top causes of death in China and increase the risk of severe COVID morbidity and mortality. Accelerated by COVID, internet hospitals saw a marked increase in users and daily consultations and provided e-prescriptions, Direct-to-Patient drug delivery, and offline hospital referrals. The qualitative thematic analysis revealed eight themes: healthcare system disruption, China's unique enabling environment, digital innovation type, cross-functional collaboration, data governance, therapeutic areas and assets, patient journey improvement, and digital innovation ethics.

Conclusion:

Takeda can increase healthcare access through digital innovation and partnerships through: 1) alignment of China's disease burden with Takeda's priority areas that better informs innovative digital solutions; 2) increased collaboration with key stakeholders (big tech companies, biotech startups, academia, HCPs, hospitals, and local governments); and 3) outreach to least resourced areas of China with pilots (e.g., rural areas with fewer than the average 1.96 physicians per 1,000 population, such as Guangxi, Anhui, Jiangxi, and Henan).

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

This doctoral thesis is for my ancestors, without whom I would not have been able to get my Doctor of Public Health degree at Harvard University. I thank God and my ancestors for all their sacrifices that afforded me the privilege of attending this great and coveted institution. You suffered slavery and genocide, and it is your strength and perseverance that enabled me to turn our collective pain into purpose. I thank my great-grandmother, the late Willie Cornelius James Cheney, who was born in 1887, had only a sixth-grade education, and cleaned houses for white people in Georgia for only $2 a week.

I thank my mother, Marian Jean Lovett, who has suffered and sacrificed so much to provide a better life for her only child, and whose kindness and patience know no bounds. I thank my aunt, Clintonia Samurita Lovett, who supported me and encouraged my love of reading and learning from an early age. I thank my grandmother, the late Sallie Mae Cheney Lovett, who helped my mother raise me from the time that I was born in Nashville, TN to adulthood. I thank my great aunt, the late Mary Lois Cheney, who taught school for 41 years and instilled a thirst for knowledge as well as a determined spirit in me. I also thank all of my immediate family members who stepped up to the plate and filled the space that my father's absence left. I would never have made it this far without you. Thank you for ensuring that I did not become a statistic.

I thank my doctoral committee members—Richard Siegrist, Dr. Kim Leary, and Dr. Bill Bean. Rick, thank you for being a wonderful and supportive advisor who gave me the freedom to carve my own path on this DELTA journey, and thank you for connecting me with my Takeda mentor. Also, thank you, Rick, for opening up your homes in Boston and Maine for our cohort retreats. Kim, thank you for always believing in me, helping me to embrace wicked problems and adaptive challenges, and nudging me to be a better version of myself. Your mentorship as well as

your Enabling Teams, Enabling Large Scale Change, and Exercising Authority classes helped me better understand my roles as a student, public health leader, and black woman in a world that demands transformative justice and healing. Bill, thank you for your endless support, enthusiasm, and stepping up when I needed a third committee member. Your Strategic Management class helped me be more thoughtful and comprehensive in my recommendations for Takeda.

To my host organization mentor and supervisor, Annette Schmid, words cannot express my gratitude for your time, love, gentleness, thoughtfulness, patience, and expertise. I could not have had a better DELTA experience because of you. You have helped me gain a sense of autonomy, mastery, and purpose in my work and life, and I am forever grateful. To the rest of my Global Science Policy & Public-Private Partnerships team at Takeda, thank you for your continued support and making me feel so welcome and appreciated at a new company.

To Cohort 4, my doctoral cohort, I have grown so much with you over these past four years. You have loved and held me through my traumas and pushed me to open my mind and heart in ways that I could not have conceived before I met you. Although we took a class called "Personal Mastery" the first summer that we met, you have provided a greater and deeper sense of personal mastery than one class alone ever could. A special thank you goes to Bryan O. Buckley, who has always encouraged me to step outside my comfort zone and took me on my first kayaking trip in Boston.

Thank you to the DrPH program for providing a unique opportunity for shaping the next generation of public health leaders and carving out a unique space in public health for the intersection of multiple disciplines. Thanks to this program, I was able to take my first international trip to Vietnam, and my Winter Immersion there sparked an interest in Asia emerging markets for both my Summer Immersion and DELTA Doctoral Project. The DrPH program at Harvard has

helped me turn pain into purpose and positioned me to help others from underprivileged backgrounds derive beauty from their ashes, too.

Last but certainly not least, my deepest love and gratitude go to the host of friends and family members who are too numerous to be named in this limited space. To my best friends, Tameir Holder and Qianyun Zhang, you are beautiful guiding lights and my world is much better after having met you both at Columbia. Just as our t-shirts at the end of the Mailman Core curriculum proclaimed, indeed, we are the future of public health.

1. INTRODUCTION

1.1. Background

First documented in Wuhan, Hubei Province, China in late 2019 and quickly spreading across the globe, the 2019 novel coronavirus disease (COVID-19) pandemic has caused shattering disruptions to global public health security. Global public health security is defined by the World Health Organization (WHO) as, "the activities required to minimize the danger and impact of acute public health events that endanger the collective health of populations living across geographical regions and international boundaries."[1] As of April 16, 2021, there were 138,688,383 confirmed cases and 2,978,935 confirmed deaths from COVID-19 globally.[2] From January 3, 2020 to April 15, 2021, there have been 103,185 confirmed cases of COVID-19 with 4,856 deaths in China.[3] As of April 5, 2021, 142,800,000 vaccine doses have been administered in China.[3]

In December 2019, multiple cases of pneumonia of unknown etiology were reported in Wuhan, Hubei Province, China.[4] Most patients were employed or lived near the local Huanan Wholesale Seafood market, which also sold live animals. In this pneumonia's early stages, severe acute respiratory infection symptoms were observed, with rapid development of acute respiratory distress syndrome (ARDS), acute respiratory failure, and other serious complications in some patients. On January 7, 2020, a novel coronavirus was identified by the Chinese Center for Disease Control and Prevention (CCDC) from a patient's throat swab sample, and the WHO subsequently named the virus 2019-nCoV.[4] The virus that causes COVID-19—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—is zoonotic, which was confirmed from environmental sampling from the Huanan Wholesale Seafood Market and others in the area, as well as through collecting detailed records on the type and source of wildlife species sold and destination of

animals once the market was closed.[5] Hubei province has 68,151 confirmed cases with 4,512 deaths as of March 7, 2021.[6]

The primary route of infection for SARS-CoV-2 is through respiratory droplet transmission, including aerosol transmission within a relatively short range (less than six feet) when an infectious person breathes, coughs, sings, sneezes, or talks (depending on prevailing ventilation).[7,8] It is also transmitted through direct contact with an infectious person (e.g., a handshake) or indirectly through fomites, when a person comes into contact with the virus on contaminated objects and surfaces and then touches their mouth, nose, or eyes.[7,8] However, fomite transmission is not thought to be the primary way that the virus spreads; although SARS-CoV-2 can remain on inanimate surfaces for days, there were unsuccessful attempts to culture the virus from these surfaces.[9,10] Airborne transmission has also been well-documented over long distances (greater than 6 feet) or times (typically hours).[7] There is mounting evidence that airborne particles and droplets can remain suspended in the air and be breathed in by others, and these airborne particles and droplets can travel distances beyond 6 feet.[9,10]

Because of population movement during Chinese New Year and Wuhan's status as a transportation hub, SARS-CoV-2 quickly spread throughout the country, and infected individuals were especially concentrated in cities that had the highest traffic volume with Wuhan.[5] Most of the recorded cases either had direct links to or were imported from Wuhan/Hubei. Extreme social distancing, aggressive case and contact identification (including quarantining of close contacts), very rapid diagnosis, and immediate isolation and management were implemented to interrupt transmission chains across China. Further, there was a remarkably high degree of understanding and compliance with these control measures in the population.[5]

There were 132 quarantine centers with a total of 12,571 beds opened throughout Wuhan, and some of the quarantine centers were converted from stadiums and convention centers.[11] Quarantined individuals included people who had had close contact with confirmed COVID-19 cases, patients with fever, and those with clinical syndromes that had not been confirmed yet. The Wuhan government also converted stadiums and convention centers into temporary hospitals to provide more beds for isolation areas. Patients were transferred from quarantine centers to temporary hospitals for prompt testing. Temporary hospitals were only for patients with mild symptoms and admitted patients could essentially care for themselves.[11]

Although people of all ages can be infected by SARS-CoV-2, there is an increased risk of severe morbidity and mortality for people 60+ and those of all ages with pre-existing non-communicable diseases (NCDs).[12] Cardiovascular disease (e.g., hypertension and heart attack), chronic respiratory disease (e.g., COPD), diabetes, severe obesity (body mass index [BMI] of 40 or higher), and cancer are included in these NCDs.[12,13] In China, a rapidly aging population with chronic diseases such as heart disease, cancer, and arthritis increases the demand for healthcare.[14] However, China had just 2.0 doctors for every 1,000 people in 2017—compared to 2.6 in the United States and 2.8 in the United Kingdom.[15]

Further, China has an uneven distribution of specialists at the expense of primary care physicians, so specialists are often overloaded with general duties.[14] The quality of primary care in China is suboptimal as there is a lack of qualified general practitioners in primary healthcare institutions, particularly in rural areas, and thus, the quality of diagnostic processes and outcomes is low.[16-18] Noncommunicable diseases such as hypertension and diabetes are often undertreated.[16,18] In addition to poor performance in controlling risk factors and inadequate qualifications and education of practitioners, China's primary healthcare system faces challenges

with turnover and aging of village doctors, financial incentives and subsidies that do not promote good performance and cost savings, fragmented health information technology systems, a dearth of digital data on routine clinical practice, and an inadequate quality measurement and improvement system.[18] Patients prefer tertiary comprehensive hospitals and secondary district hospitals over rural healthcare clinics and community healthcare centers.[17]

Before the COVID-19 crisis, digital healthcare technology was increasing in China to complement and optimize healthcare services.[19] However, the accelerated rise of digital health platform use in China was a defining marker of the COVID-19 outbreak.[20] Public-Private Partnerships (PPPs) are the foundation of many digital health responses in China, with digital technology providers leading innovation within a technological infrastructure and national enabling policy.[19]

1.2. Problem

With vaccine distribution still in the nascent stages, people must limit the spread of the contagion through social distancing. However, social distancing poses unique challenges for disease management, medication access, and adherence, particularly for those who are high-risk. This is where digital innovation and partnerships are key—for health management, reducing the risk of contracting the virus to healthcare workers and patients, and rapidly engineering new therapies and vaccines. Telemedicine, wearables and sensors, and drones for the delivery of medicines, spraying disinfectants, and transferring specimens and tests are just a few ways that digital technologies have transformed the public health response to COVID-19.[21] In addition to the response to COVID-19, these technologies have also transformed China's healthcare system because COVID-19 exposed the pre-existing inefficiencies and access to treatment challenges that were no longer sustainable. With COVID-19 pushing the healthcare system to the brink,

pharmaceutical companies had to quickly embrace digital solutions to continue providing life-saving care and medicines to patients, running clinical trials, and to collaborate to develop a safe and effective vaccine.

1.3. Research Question

Using COVID-19 and China as a case study, how do we increase healthcare access through digital innovation and partnerships?

1.4. Purpose

The aims of this Doctoral Project are as follows:

1. Explore how COVID-19 accelerated digital/technological innovation for health management and access in China.
2. Synthesize strategic recommendations for Takeda on how to best utilize global partnerships and technology to increase healthcare access. Seek to better understand the impact on the patient journey in the context of digital innovation. If feasible, assess whether there could be PPP (Public-Private Partnership) opportunities for Takeda to use digital innovation to mitigate health inequities in high-risk and marginalized groups.

2. ANALYTICAL PLATFORM

2.1. Host Organization Profile

Established in 1781, Takeda is a Japanese biopharmaceutical company that is the largest in Asia and is the 9th largest pharmaceutical company in the world by revenue.[22,23] With a global presence in 80 countries and regions, Takeda is a patient-focused, values-based, R&D-driven company committed to bringing Better Health and a Brighter Future to people worldwide.[23] At the heart of Takeda's corporate philosophy is what is abbreviated as PTRB—Patients, Trust,

Reputation, and Business. Takeda is committed to "Patients First" and hopes to transform the patient journey through deep patient engagement and the power of data and digital. Takeda has four Therapeutic Area Units (TAUs)—Oncology, Rare Diseases, Neuroscience, Gastroenterology—as well as targeted R&D investments in Vaccines and Plasma-Derived Therapies.[24]

The Global Science Policy and Public-Private Partnerships group wants to create a smoother path forward for healthcare innovation to benefit society, and seeks to achieve this through collaborations to foster a sustainable, value-driven, innovative ecosystem. The Global Science Policy and Public-Private Partnerships group at Takeda currently has more than 92 consortia-type partnerships (i.e., multiple organizations in a collaboration instead of a 1:1 partnership) between public and private entities, and there are hundreds of direct collaborations across Takeda. This provides a diversity of perspectives, new insights, and new ideas to solve complex healthcare challenges and accelerate new medicines to patients. Takeda looks for partnerships where patients and patient organizations have a voice in development and can help all stakeholders understand patient needs.[25]

2.2. Literature Review

2.2.1. Overview of Digital Solutions to COVID-19

Digital innovation, through telehealth, data science, and artificial intelligence (AI), has been China's biggest weapon to combat COVID-19.[26] BlueDot, an AI platform that monitors infectious diseases globally, identified a cluster of "unusual pneumonia" cases happening near a Wuhan market nine days before WHO released a statement on January 9, 2020 about a "novel coronavirus" found in a hospitalized pneumonia patient in Wuhan.[26,27] BlueDot's AI was also able to accurately predict where COVID-19 would spread by using machine learning algorithms

examining travel patterns to predict where those who had contracted SARS-CoV-2 would likely travel.[26]

To limit transmission of the virus, several companies and organizations have automated certain procedures that formerly required interaction between patients and medical staff.[26] Chinese firms used robots and drones to spray disinfectants in public areas and complete contactless delivery. Other robots checked people for fever and other COVID-19 symptoms as well as dispensed free hand sanitizer gel and foam. Within hospitals, robots delivered medicine and food to patients, cooked rice without human supervision, and disinfected their rooms, which reduced the amount of staff required to run the hospitals.[26]

AI has also been used to find COVID-19 diagnoses and treatments. China used big data and AI to improve contact tracing and manage priority populations.[5] Alibaba, one of China's biggest e-commerce companies, established an AI system that can identify COVID-19 in chest CT scans with 96% accuracy.[26] Data from 5,000 COVID-19 cases was used to train the AI, which can complete the test in 20 seconds compared to the 15 minutes for a human specialist to diagnose patients. Since AI can diagnose the bulk of clear cases for which the algorithm is trained, radiologists can focus on difficult and unusual cases.[26]

Taiwan was able to successfully curb the COVID-19 cases early on through big data analytics, new technology, and proactive testing.[28] Taiwan integrated its national health insurance and immigration and customs databases to create big data for analytics; this generated real-time alerts from travel history and clinical symptoms to support case identification during a clinical visit. Taiwan also employed new technology, such as QR code scanning and online reporting of health symptoms and travel history, to categorize travelers' contagious risks from flight origin and travel history over the past 14 days. Health declaration border passes via SMS (short message

service) were sent to low-risk individuals (no travel to level 3 alert areas) for faster immigration clearance; higher-risk individuals (recent travel to level 3 alert areas) were home-quarantined and traced through their mobile phone to confirm that they did not break quarantine during the incubation period. All Taiwan clinics, hospitals, and pharmacies were given access to patients' travel histories.[28]

2.2.2. Healthy China 2030 & AI Development Plan

Announced in 2016, Healthy China 2030 encompasses 29 chapters that cover five health areas, such as public health services, the medical industry, environment management, drug safety, and food safety.[29] It is China's most important national health action plan.[30] Healthy China 2030 embraces the 2030 United Nations Sustainable Development Goals (SDGs) 3 and 6: "Ensure healthy lives and promote well-being for all at all ages" and "Ensure access to water and sanitation for all," respectively.[29,31] Included in Healthy China 2030 are targets to reduce the percentage of out-of-pocket payments in total health expenditures to 28% by 2020 and 25% by 2030.[30] Healthy China 2030 is the fundamental national domestic population health policy, with population health as the critical goal of political reform and economic development.[32] Two targets are to increase disease prevention and improve healthy life expectancy and longevity, while other goals include improvements in health services and insurance (e.g., chronic disease mortality), lifestyle (e.g., regular exercise), the health industry, infant mortality, and the environment (e.g., air quality). Health equity is also a major priority since there are disparities in healthcare access to providers and services between the provinces in mainland China.[32] A visual depiction of the Healthy China 2030 framework can be found below (***Figure 1***).

Principles				
Health Priority	Reform and Innovation	Scientific Development		Justice and Equity
HC 2030: China's vision for health care				
1. Health Level	**2**. Healthy life	**3**. Health Services and Health Security	**4**. Environmental Health	**5**. Health Industry
The 13 Core Indicators				
A. The average life expectancy **B**. The mortality rate of infants **C**. The mortality rate of children below 5 years of age **D**. The mortality rate of pregnant women and mortality **E**. The proportion of those meeting the national physique determination standard among urban and rural residents	**A**. The level of health literacy among residents **B**. The number of people taking part in physical exercise	**A**. Premature mortality as a result of major non–communicable diseases **B**. The number of registered doctors per 1000 residents and registered nurses per 1000 residents **C**. The proportion of personal health spending in the total health expenses	**A**. Good air quality rate of all cities at prefecture level or above **B**. The rate of surface water quality better than III	**A**. The total investment scale of health services

Figure 1. Healthy China 2030 framework.

Source: Tan et al., 2017.[33, i]

The Chinese government has identified digital health as critical to reaching Healthy China 2030 goals, which center around making healthcare more affordable and accessible.[34] In April 2018, new guidelines on "Internet Plus healthcare" were approved at a State Council executive meeting, overseen by Premier Li Keqiang.[35] In line with the Healthy China 2030 blueprint, the focus was to establish a comprehensive internet healthcare system and strengthen data security oversight and service quality nationwide. Digital healthcare is meant to reform multiple problems within China's healthcare industry, such as difficulty seeking medical services, high medical costs, high costs of drug circulation, monopoly by public hospitals, fragmented healthcare management institutions, and a variety of frauds, wastes, and abuses. As a result, several recent policies promote AI, big data, and digital healthcare. Two big data policies were to create a unified, interconnected public health information platform and build 100 regional clinical data centers across China by 2020.[36]

[i] China's surface water quality is separated into 5 classes, with classes I-III considered good water quality and class I the best. In a May 2020 report by China's Ministry of Ecology and Environment, China's air and surface water quality improved from January-April 2020, and 81.2% of surface water quality was graded Class I to III, representing an increase of 6.3% compared to 2019.[148]

Although the Healthy China 2030 blueprint is quite aspirational, several challenges remain. One such challenge is the scientific basis for the indicators.[33] For instance, average life expectancy of residents in some cities is greater than 80 years, but according to the Healthy China 2030 blueprint, the target is 79 years by 2030. Furthermore, premature mortality caused by major noncommunicable or chronic diseases is not used as a disease surveillance indicator across China; so relevant government departments will have to consistently collect this data if they want to set reasonable, objective target values. A third challenge is that information bias will result if government departments adopt different ways of data collection and do not cooperate and communicate effectively.[33]

At the center of the Healthy China 2030 vision is the switch from the traditional, hospital-based care model to a sustainable primary healthcare system.[37] Healthy China 2030 emphasizes technology's importance in accomplishing China's healthcare reform strategy with a shift from treatment to prevention, and AI development is crucial to achieving this goal.[38] Big data also drives solutions for China's major development strategies.[38] AI-enhanced reading of scans and remote diagnostics has huge growth potential and is beneficial for treating chronic conditions such as diabetes and hypertension, which require much monitoring that can be performed virtually.[39]

In the "*New Generation Artificial Intelligence Development Plan*," China plans to build a domestic AI industry worth more than 150 billion yuan (USD$23 billion) and become the leading world AI power by 2030.[40] The ambition is to achieve this through an accurate, rapid intelligent medical system, smart hospital construction, surgical robots, intelligent clinic assistants, and R&D investment into wearable, biologically-compatible physiological monitoring systems, large-scale genome recognition, omics (proteomics and metabolomics),[ii] intelligent home health testing and

[ii] Omics (genomics, proteomics, etc.) are technologies that analyze data for molecules such as genes, proteins, or metabolites.[149]

monitoring equipment, and new drugs to promote intelligent pharmaceutical regulation. AI can accommodate a switch in health management from discrete to continuous monitoring and a shift from short-process management to long-process management. AI may also help construct smart old-age communities and institutions, improve the intuitiveness of products for the elderly, and develop physical auxiliary equipment, audio-visual aids, and other intelligent home care equipment, as well as mobile social and companion care service platforms for the elderly.[40] But what remains to be seen is the knowledge, attitudes, and behaviors around this new technology in elderly or other vulnerable populations, particularly in rural and low-income provinces. These populations and geographic regions will have to be closely studied to ensure that they are not left behind with technological advancements and to avoid exacerbating existing healthcare disparities.

2.2.3. Telemedicine

Telehealth, also known as digital health or telemedicine, refers to the virtual healthcare platforms that enable healthcare professionals and patients to meet via video platform or phone. If patients use telehealth for more routine, necessary care, this can free up local or specialized medical staff and equipment for seriously ill COVID-19 patients.[41] Further, not gathering in small spaces such as waiting rooms limits person-to-person transmission.[41] Quarantined physicians can cover emergency department tele-intake or direct-to-consumer care, which allows other physicians to perform care in person when needed.[42] A single remote clinician can cover multiple sites, which allows digital systems to be scaled up with lower workforce capacity constraints.[43,44] AI-powered medical assistants (chatbots) triage patients, analyze patient data, and route patient cases to live clinicians.[45,46]

As a novel telehealth model, internet hospitals are distinct but also intersect with telemedicine, online health, and mobile medical.[47] Internet hospitals are government-led, hospital-

led, or enterprise-led and offer four types of services: online medical services, telemedicine, convenience services, and related industries.[47] Online medical services enable patients to consult with doctors for health problems or receive diagnoses and prescriptions online for common and chronic diseases. Telemedicine involves inter-institution medical cooperation between hospitals when patients seek offline medical treatment. Convenience services use online technology to simplify offline procedures for patients and promote health literacy; they include health education, intelligent guidance, mobile payment, registration, inspection report and cost queries, and medical feedback. Related industries handle content that must be provided by a third party, including drug orders, drug distribution, and health records. The purpose is to alleviate medical waste and the shortage of medical resources.[47]

According to a comprehensive study of the 2017 telemedicine landscape in 161 tertiary hospitals across 29 provinces, autonomous regions, and municipalities in China, the telemedicine services with the highest hospital coverage rates were: teleconsultation (86.3%, 139/161), remote education (57.1%, 92/161), telediagnosis of medical images (49.7%, 80/161), tele-electrocardiography (37.9%, 61/161), and telepathology (33.5%, 54/161) [***Figure 2***].[48]

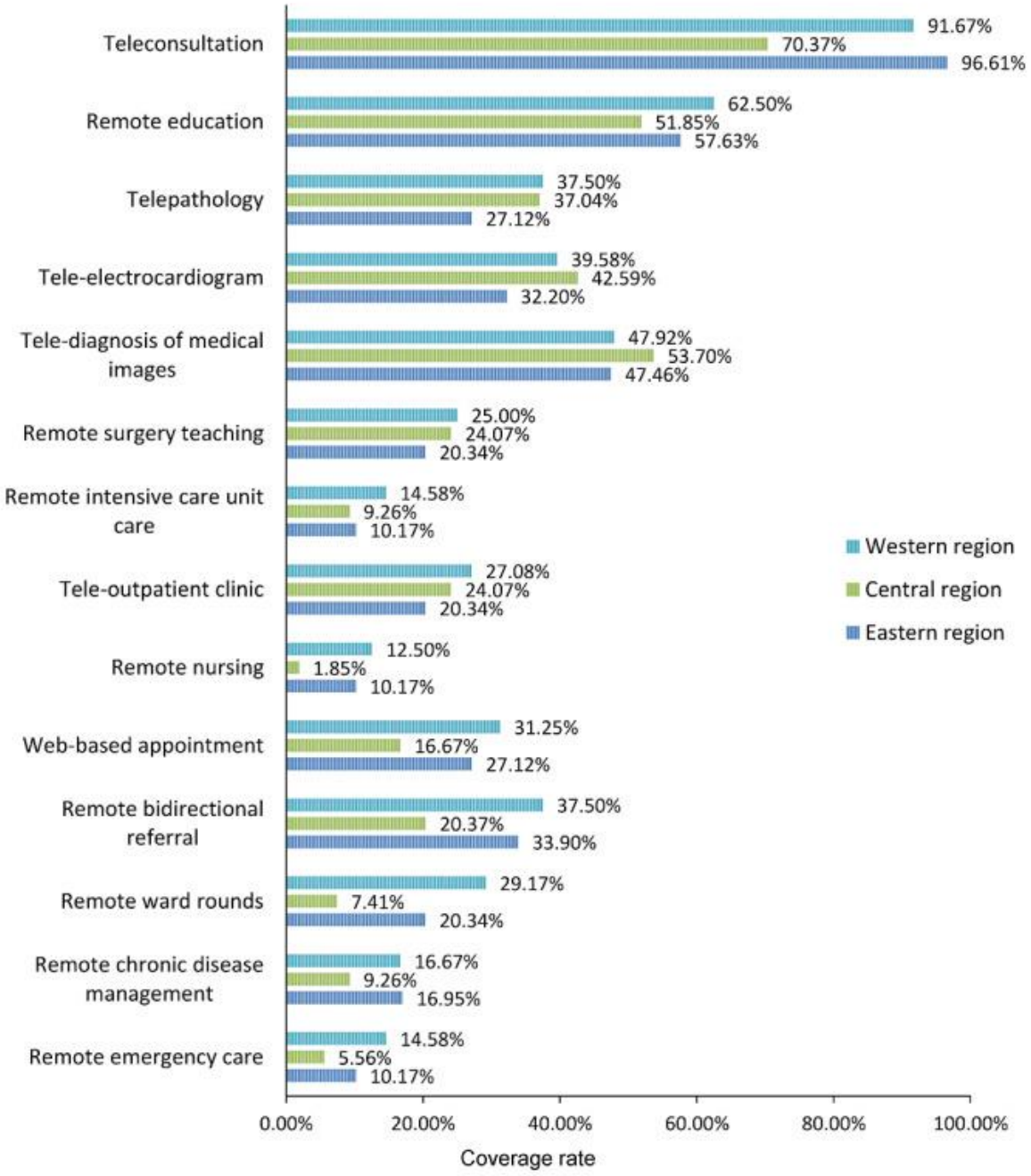

Figure 2. 2017 coverage rate of telemedicine services in tertiary hospitals, by different regions in China.

Source: Cui et al., 2020.[48]

There were significantly higher proportions of tertiary hospitals conducting teleconsultations and remote ward rounds in the eastern and western regions than in the central

region (P<.001 and P=0.02, respectively).[48] Telemedicine services had been implemented to some extent in most of China even before the pandemic, but this study does not include patients' attitudes towards telemedicine, which is important for expansion and sustainability of telemedicine.

As reported by the China Internet Network Information Center in April 2020, there were 904 million internet users in China, comprising an internet penetration rate of 64.5% of the population.[47] In China, online visits to National Health Commission (NHC) hospitals increased 17-fold during the peak of the outbreak. Shanghai launched 11 internet hospitals that were affiliated with offline public hospitals.[20] In just two months, there were 14,000 total visits to these internet hospitals and prescription volume surpassed 4,300. In local government, eight provinces integrated online Basic Medical Insurance (BMI) settlement for internet-based medical expenses.[20] With most people staying home and avoiding physical hospitals, users in China's internet healthcare sector were projected to surpass 60 million in 2020, generating over 700 billion yuan (USD$100.4 billion) in market volume.[49,50]

The first internet hospital platform in China was founded in 2012, led by the Guangdong Second Provincial General Hospital.[51] As of 2019, it had 700 licensed or assistant physicians from the Guangdong Second Provincial General Hospital and 19 county-level hospitals. Physicians on the platform provide online video consultations for approximately 14,000 community-based health providers that work in village clinics, health centers, pharmacies, and university health services in Guangdong. On average, 33,000 visits daily were made to the connected community health providers in 2018. Physicians using this online hospital are less inclined to overprescribe since patients have to fill prescriptions at local pharmacies or clinics, where the average cost of medications is 75% of the cost per prescription at Guangzhou, the provincial capital.[51]

Conversely, a potential consequence of fewer excessive prescriptions is lower income for community-based health practitioners, and this could disincentivize these practitioners from utilizing the internet hospital platform.[51] As such, an innovative incentive structure may need to be created to retain physicians. Concerns remain about financial sustainability because platform funding is sourced from the provincial hospital's funds, government grants, and a medical technology company. To address this issue, Guangdong province passed an action plan in June 2018 to ensure that primary health care via digital platforms will be reimbursed by insurance in the future.[51]

By January 2019, China had approximately 130 registered internet hospitals in 25 of 34 provinces—covering 73.5% of all provinces or province-level municipalities (***Figure 3***).[47] In January and February 2020, there were over 10 telehealth providers with over 200 public hospitals providing online healthcare services and more than 10 million consultations.[52] In the first half of February 2020 during China's COVID-19 peak, AliHealth (the healthcare platform of Alibaba) reported daily online consultations above 700,000.[52]

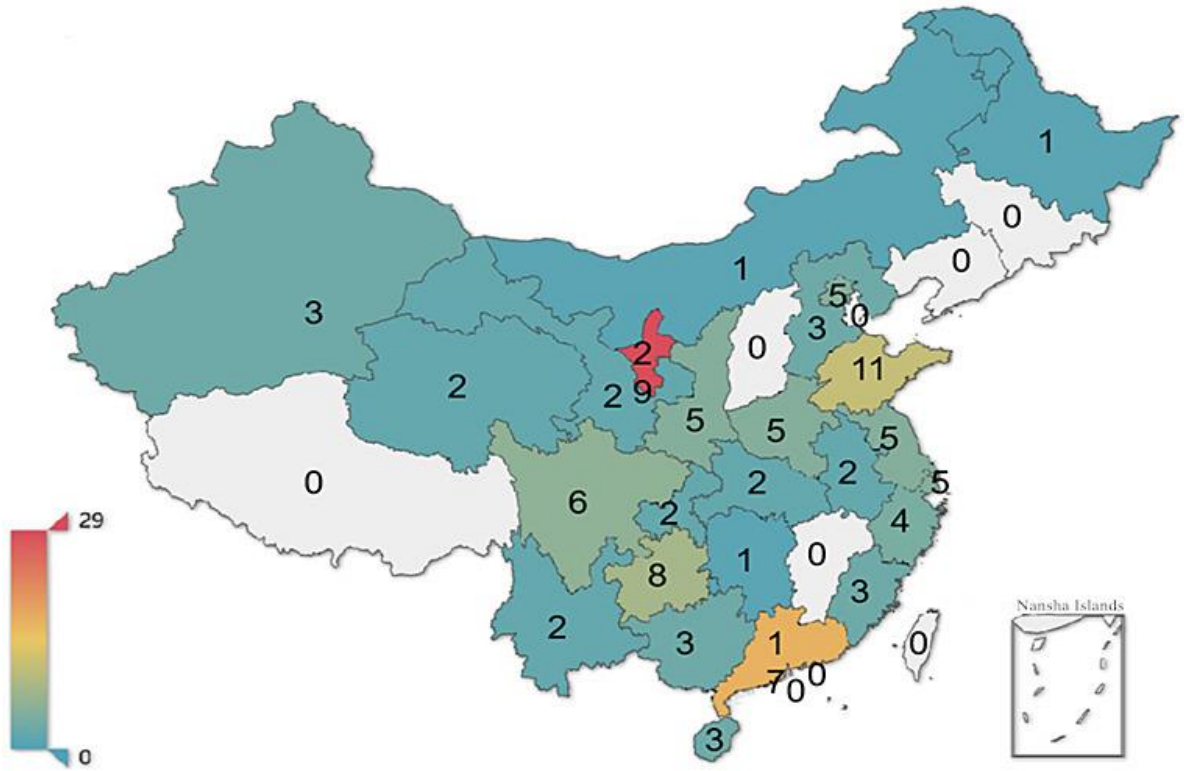

Figure 3. Heat map of the number of internet hospitals in Chinese provinces, January 2019. *Source*: Han et al., 2020.[47]

Physical hospitals contribute to much wider spread of SARS-CoV-2, and internet hospitals provide the advantages of non-contact treatment, greater efficiency at lower costs, and optimized health resource distribution.[53] Asymptomatic front-line workers can become accidental carriers to patients seeking care for other illnesses. Several hospitals canceled outpatient clinics to prevent cross-infection (except fever and emergency clinics).[53,54] During the height of the pandemic, all hospital beds in designated COVID hospitals were filled and the new Wuhan hospital had not been completed, so many confirmed patients stayed in general hospitals or went home for isolation, which increased morbidity and mortality.[54]

Therefore, internet hospitals were a necessity during the pandemic because they provided constant public medical services and prevented nosocomial virus spread.[53] WeDoctor, haodf.com, and several other internet hospitals offered free online COVID-19 consultation and guidance for

home quarantine during the epidemic, and this accounted for almost 20% of their online medical services. This is largely possible because the Chinese government has instituted policies to integrate long-term prescription and internet medical services into medical insurance.[53,55]

On March 15, 2020, "*Specification for online consultation service for infectious disease epidemic situation*," the first professional standard, was published on China's national group standard information platform.[56] It required internet hospitals to provide 24/7 online services to combat the epidemic, including pre-hospital services such as medical education and initial screening; intra-hospital services such as offline visit guidance and offline service appointment; and post-hospital services such as drug delivery services for chronic disease patients, report interpretation for reattending patients, post services for medical records, and psychological counseling. Further, internet hospitals established intact, traceable health files for each patient and shared the data with supervising departments such as local health commissions and the Centers for Disease Control and Prevention (CDC). These actions allowed internet hospitals to prevent and control the spread of COVID-19 through both primary and auxiliary functions (***Appendix A: Primary and Auxiliary COVID Internet Hospital Functions***).[56]

Despite the richness of services that internet hospitals can provide, they cannot replace several of the fundamental functions of offline hospitals.[47] For instance, they do not have physical infrastructure such as diagnostic equipment and sickbeds. Some medical services, such as first visit intake and treatment for severe illness, must be provided by physical hospitals while health consultation, non-clinical, and follow-up diagnosis can be serviced online.[47] Furthermore, users of internet hospitals do not reflect the entire population of China because of differences in public acceptance, ages, and internet accessibility.[56]

Bain & Company believes that COVID-19 will accelerate digitalization of China's healthcare system and reshape patient behavior.[57] COVID-19 made telemedicine more feasible and led to its growth from ~3% of the market up to 10% at its height.[39] From December 2019 to January 2020, Ping An Good Doctor had a ~900% increase in new users (***Figure 4***).[57] Founded in 2014 and the world's leading telemedicine platform, Ping An Good Doctor is a subsidiary of Ping An Insurance Group (which has a network of 3,100 hospitals and 7,500 pharmacies).[58] Chunyu Doctor, a telemedicine platform, and Ding Xiang Yuan (DXY), the largest online community for healthcare professionals, also experienced substantial increases in the number of online visits and users.[57]

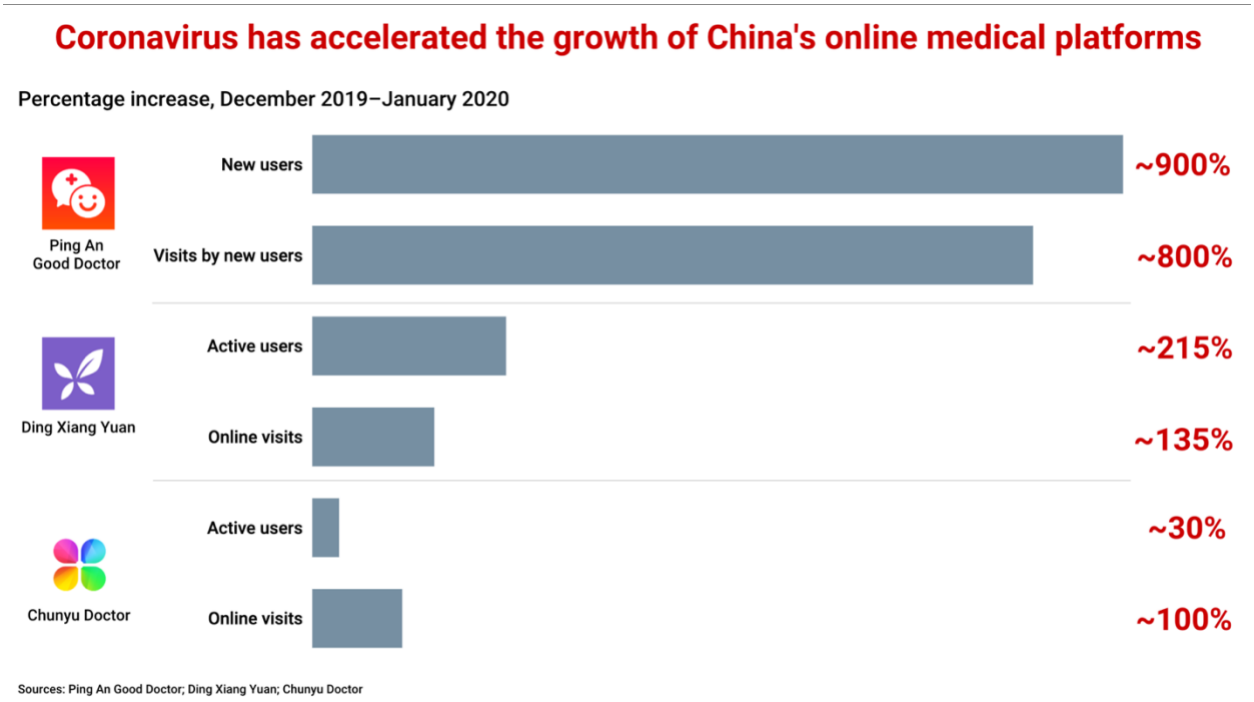

Figure 4. Accelerated growth of China's digital health platforms, due to COVID-19.

Source: Bain & Company, February 2020.[57]

But Bain & Company published this data in February 2020 for a period up to January, and it would be interesting to see how China's peak of cases in mid-February coincided with the usage

of digital innovation, as well as usage trends over the rest of the year once the worst of the outbreak subsided. Further data that shows growth, stagnation, or decline throughout 2020 for these platforms would paint a clearer picture of the potential staying power of digital health in a post-COVID world.

Prior to COVID-19, Chinese patients generally visited physical institutions for healthcare and digital adoption was lower; only 24% of Chinese respondents had utilized telemedicine, according to a Bain survey. Nevertheless, 97% conveyed interest in digital healthcare services, provided that costs were covered by an employer or insurance provider, and 64% anticipated using telemedicine within the next five years. According to a 2019 Bain Frontline of Healthcare APAC survey, over the next five years, telemedicine usage was expected to increase by 164%, long-term illness management by 98%, digital records use by 80%, usage of self-diagnosis apps by 52%, on-demand services by 33%, health/life insurance apps by 21%, and lifestyle/wellness monitors by 11% (***Figure 5***).[57]

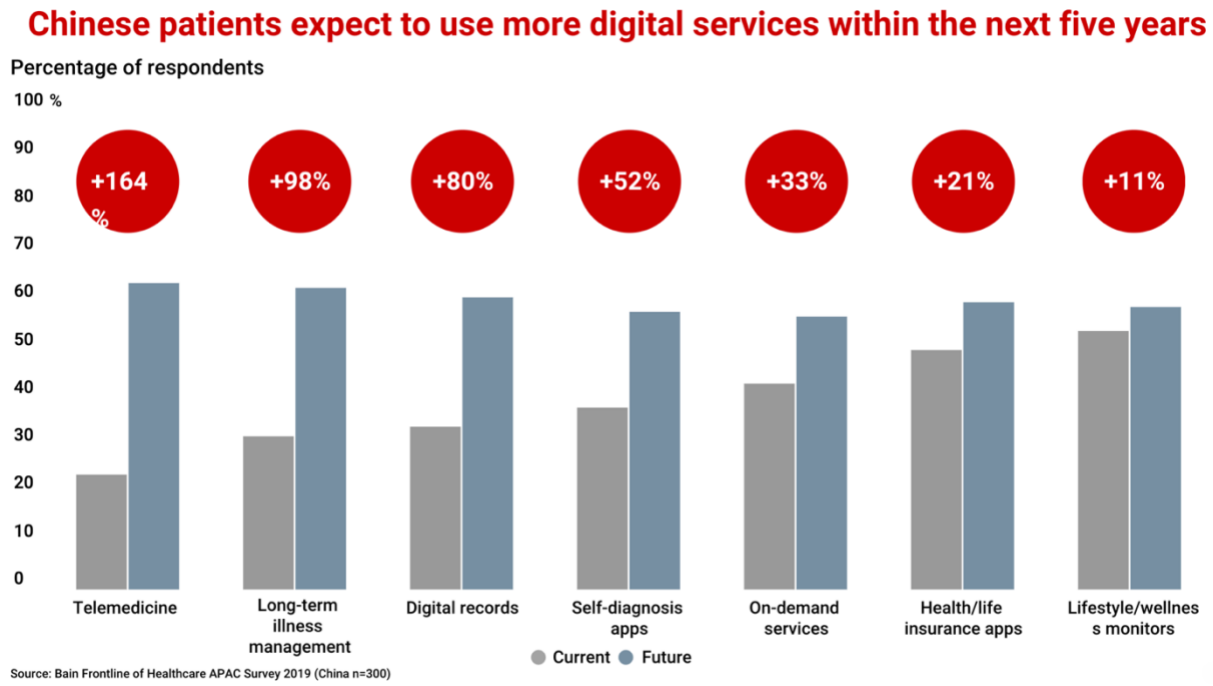

Figure 5. Use of digital services by Chinese patients over the next five years.

Source: Bain & Company, February 2020.[57]

However, the sample size of this survey was only 300 patients, so that is a relatively low number when compared to the 1.4 billion population in China. Further, it is unknown how random, geographically, or economically diverse this sample was and thus, how representative it was of the overall Chinese population. There could also be some bias from patients who may be more health and technology literate, and these factors could affect willingness to use digital health services in the near future.

Last but certainly not least, telemedicine also provides a safer environment for doctors by establishing physical distance between doctors and distressed patients. In China, patient-on-doctor violence has become more common over the years, typically when treatments fail.[59] According to the China Hospital Management Association, mob-style attacks and stabbings have risen an average of 23% a year since 2002.[59] This is a significant stressor for doctors since there is an average of an incident every two weeks across China.[59] In a study of judgment documents from the China Judgment Online System during 2013-2016, there were 459 criminal cases of patient-initiated workplace violence against healthcare workers.[60] The analysis showed a lower incidence of patient-initiated violence in western provinces versus central and eastern Chinese provinces. Primary hospitals suffered the highest rates of serious workplace violence, and doctors and emergency departments were at greater risk compared to other health workers and departments. Male farmers aged 18-44 with low education levels were primarily the perpetrators. The most frequent reasons for serious patient-initiated workplace violence were death-related issues (22.25%)—which included perceived medical malpractice by the attacker after patient death (8.38%), patient death with no other reason listed (7.59%), and failures of compensation negotiations after patient death (6.28%)—followed by dissatisfaction with treatment outcomes

(13.09%) and dissatisfaction with the treatment process (12.3%).[60] All pertained to perceived quality of care.

2.2.4. Pharma

According to a Deloitte report, favorable regulatory changes in China, such as accelerated drug approval and more dynamic and frequent adjustment of the National Reimbursement Drug List (NRDL), are creating unparalleled opportunities for quicker launch of innovative medicines and substantially larger market potential.[61] To implement a quicker and more transparent drug approval process, the Chinese FDA (CFDA) proposed various amendments to improve patient access to innovative medicines.[31] These include a reduced 60-day clinical trial application (CTA) approval process and establishment of an investigative new drug (IND) program, orphan drug system establishment, structured stakeholder-CFDA communication, and acceptance of foreign clinical data.[31]

Consistent with a March 2018 IQVIA market prognosis, the Chinese pharmaceutical market is forecast to grow at a compound annual growth rate (CAGR) of 5.5% between 2017 and 2022, and China is the largest emerging market with growth projected to reach $145 to $175 billion by 2022.[34,62] Advances in healthcare consumerism and digital technologies are re-engineering the path to success for pharmaceutical companies and altering China's healthcare system dynamic.[61] The emerging digital healthcare ecosystem is enabling innovative commercial models in pharma.[61] This ecosystem has patients who embrace digital and mobile technologies; newly registered users on Ping An Good Doctor grew 10 times from early January to mid-February 2020 during the peak of the COVID-19 pandemic.[50,61,63]

A 2019 Oliver Wyman "Health on Demand" study of 16,564 workers and 1,300 senior decision-makers in seven mature and six growth markets[iii] showed that respondents from Asian countries—China, Singapore, Indonesia, and India—are more enthusiastic about digital health (78% vs. 66% globally).[50] Further, 61% of Chinese consumers consider themselves "early adopters" of new technology, compared to 38% globally, and more Chinese consumers are willing to share personal data for healthcare purposes (94% vs. 85% globally).[50] In this same study, 76% of workers in China noted that they are responsible for a family member's healthcare (compared to a 53% average across all 13 countries), and as such, "companion robots or digital avatars that help elderly relatives stay healthy at home" was the most popular digital health solution, which ranked last or near last in all other 12 countries surveyed.[50]

The three largest Chinese big tech players—Tencent, Alibaba, and Baidu—have revolutionized digital health and provide new opportunities for pharmaceutical companies to partner in the space.[34] They have deep consumer understanding, advanced technical capabilities, and extensive pre-existing user pools.[34] Through their smart algorithms and big data technologies that can connect across all parts of the healthcare system, these digital health companies have an advantage over traditional healthcare players.[62]

Tencent runs China's largest social network, Alibaba is one of China's largest e-commerce retailers, and Baidu is the dominant search engine in China.[34] Tencent has over 1.1 billion users on its WeChat messaging app, and Merck and Tencent partnered to focus on increasing access and public health awareness through Tencent's digital platforms. Alibaba partnered with Pfizer to use QR scanning to detect low-quality and fake generic drugs. As part of the Baidu Doctor app, Baidu developed Melody, their AI health chatbot, to help patients determine if they needed an in-person

[iii] The growth markets were: Brazil, China, Colombia, India, Indonesia, and Mexico. The mature markets surveyed were Canada, France, Italy, Netherlands, Singapore, UK, and US.

consultation.[34] Further, several multinational pharma companies, such as Merck, Novartis, and Bayer, have launched innovation hubs in China to engage with local innovators and understand stakeholders on the ground.[34] In November 2017, Sanofi joined AliHealth to launch the Comfort at the Fingertips app, which enables chronic disease management, product traceability, and scientific knowledge of diseases for patients.[64,65]

In 2017, China was Bayer's second-largest market after the US, and Bayer also formed a partnership with AliHealth to utilize big data to follow health trends in Chinese patients and enhance health literacy in self-health care.[66] The collaboration allowed Bayer to offer personalized online medical consulting on health and diet via AliHealth's digital platform.[66] Bayer also has an R&D base in China and is deepening local cooperation with Chinese companies and academia (e.g., top research institutes such as Tsinghua University and Peking University) to accelerate innovative drug discovery.[62,67,68] In January 2020, 77 pharmaceutical companies received contracts with the Chinese government by reducing drug prices; Bayer reduced the price of its off-patent drug acarbose for diabetes (China has the highest prevalence of diabetics worldwide[iv]) by nearly 90%, and the new price is 78.5% lower than the Chinese government's price ceiling from December 2019.[67,69]

For Sanofi, China also is their second-largest market after the US and represented €2.4 billion of net sales (2018).[37] As of late 2019, Sanofi had more than 40 innovative drugs and vaccines, more than 9,000 employees, 12 locations, 3 manufacturing sites, 4 R&D sites, and supported 4 activities across China—primary care for chronic diseases, specialty care for rare diseases, vaccines, and consumer healthcare. Furthermore, Sanofi provides healthcare solutions

[iv] There are 113.9 million diabetic adults in China, accounting for 24% of patients with diabetes globally. In 2017, the healthcare cost associated with diabetes in China was 110 billion international dollars (purchasing power parity).[69]

for 7 of the 10 leading causes of death in China: cancer, cardiovascular diseases, cerebrovascular diseases, metabolic and endocrine diseases, diseases of the digestive system, diseases of the central nervous system, and contagious diseases (except tuberculosis).[37]

In 2019, Sanofi launched its fourth global research institute in Suzhou (a city west of Shanghai) after institutes in Europe and the US, as well as a new global R&D site in Chengdu—a tech-focused initiative to improve Sanofi's digital capabilities and speed up clinical trial analysis.[37] This initiative leverages the overhaul of China's regulatory framework and its extraordinarily rich native digital ecosystem. Sanofi collaborates with all important Chinese stakeholders in healthcare—hospitals, government, internet and technology companies, leading commercial insurance, as well as startups and academia—to create new digital health solutions. Sanofi has collaborated with AliHealth, and in November 2019, Sanofi announced a collaboration with Tencent in rare, immunological, neurological, and chronic diseases, as well as an agreement with Ping An International Smart City Technology to transform diabetes management and how diabetes patients interact with their physicians and healthcare stakeholders. Since 2011, Sanofi has invested in primary care in more than 1,600 rural Chinese counties and increased local initiatives for digital treatment solutions. As an example, Sanofi is developing a grassroots approach in Meishan (Sichuan province) on diabetes intervention in partnership with the China Diabetes Innovation Alliance, as well as private and public local stakeholders. Sanofi also signed an agreement with the Shenzhen Municipal People's Government to enhance access to innovative vaccines through digital health applications and technologies.[37]

In 2018, Merck and AliHealth formed a collaboration to concentrate on drug monitoring as well as internet health services in China.[70] This collaboration combined AliHealth's drug tracking platform with Merck's expertise in diabetes, heart diseases, and thyroid diseases for

secure and safe drug use. Merck and AliHealth also have plans for pharmaceutical e-commerce and AI-enabled healthcare applications.[70] In 2019, Merck formed a collaboration with Tencent to integrate patient-centric healthcare management and digital platforms, which helps Merck fulfill its mission of transforming 40 million Chinese patients' lives by 2025.[71] Merck and Tencent are working to create intelligent digital health services to increase public awareness of diseases and improve patients' health literacy for understanding symptoms and effective treatments. This partnership will also provide patients with smarter, more convenient services for better chronic disease management. Disease focus areas include allergies (digital services that enhance knowledge of allergy symptoms and support treatment plan adherence) and infertility (enhancing knowledge of disease and treatment options and helping patients needing fertility resources to shorten the medical treatment process). Merck and Tencent will also concentrate on diabetes, cardiovascular diseases, thyroid disorders, and oncology (e.g., metastatic colorectal cancer). In the future, Merck and Tencent plan to explore innovative medical service models based on "AI doctors" to provide better comprehensive disease knowledge and treatment services for metastatic colorectal cancer as well as other diseases.[71]

Pharma companies have also leveraged telehealth for patients to order prescriptions online or through apps in lieu of having to go into the pharmacy or hospital. This process was especially fast-tracked by COVID-19 since going to the hospital to get medicines could put vulnerable patients at high risk of contracting the virus. In partnership with online pharmacy Jianke Pharmaceutical and CausaHealth (health service platform of Yidu Cloud, leading AI medical technology company), Pfizer China accelerated the launch of its online chronic disease hospital in March 2020. This online hospital provides medication reminders, prescription refill and delivery services, telephone and online consultation through an AI-powered medical assistant, personalized

cardiovascular and cerebrovascular disease management, and enhanced scientific education for patients.[72-74]

In July 2020, Pfizer partnered with Alibaba Cloud and FinTech Academy to accelerate healthcare innovations across the Asia Pacific by forming the Healthcare FinTech Alliance.[75] Alibaba Cloud is China's largest provider of public cloud services, and it will offer technological expertise (cloud credits and mentorship) and infrastructure support to startups in this alliance. FinTech Academy is incorporated in Singapore for leading talent development programs that range from financial and fintech literacy awareness to fintech engineering courses with industry experts; it is thought to spur academia and industry experts to drive growth and innovation through venture building and talent development in support of innovators' journeys. Pfizer's role in this alliance is to provide a comprehensive understanding of healthcare systems across the Asia Pacific and the patient journey, as well as expertise regarding Pfizer's scientific and commercial knowledge for startups.[75]

The seven key focus areas of this alliance are: affordability (micro-financing and other financial models); value-based agreements (to connect payment schemes to a drug's effectiveness, utilization, or health outcomes); digital therapeutics (driven by software to prevent, treat, or manage a physical, behavioral, or mental condition); outcome monitoring (tracking and reporting of outcomes from patients, healthcare providers, R&D databases, remote devices, and real-world evidence); population health (managing patients' medical records and data insights using new technology to better understand population health characteristics); personalized healthcare (digital health solutions customized to patients' individual needs); and driving the adoption rate of innovative health tech devices (e.g., diagnostic tools to target reimbursement and access to medicines obstacles).[75]

In April 2020, Novartis launched their AI Nurse platform in partnership with Tencent and leading Chinese medical organizations.[76] This AI-enabled digital nurse platform could benefit 16 million heart disease patients in China. It serves as a 24/7 patient-centric intelligent platform to help patients, nurses, and physicians better manage heart disease. The goal of the AI Nurse platform is to reduce hospital readmission by linking a digital chronic disease management model with physician and hospital visits to allow more self-monitoring and management for heart failure patients. The AI Nurse platform is disease-specific as opposed to drug-specific, which means that it is a resource that can be used by any heart failure patient in China regardless of whether they are prescribed drugs by Novartis or other pharma companies.[76] Since July 2020, more than 300 of China's leading hospitals in more than 100 cities have started to integrate the AI Nurse solution in standard discharge protocol, and more than 25,000 patients have been recruited.[77]

Because of COVID-19, the AI Nurse platform was quickly remodeled to allow patients to better manage heart failure during lockdown, and basic COVID-19 facts, self-detection, and guidance on virus risk mitigation were embedded. Furthermore, the AI Nurse team made onboarding the patient easier and reduced the time needed from ~25 minutes to ~3.5 minutes, accelerated rollout from the original 50 planned hospitals per month to more than 200 in the first month to expand access, and provided in-hospital training for doctors and nurses with virtual technical support.[77]

In September 2020, AstraZeneca partnered with AliHealth to debut their anti-cancer drugs in AliHealth's direct online drugstores.[78] This partnership further enhanced access to and improved the adherence and convenience of anti-tumor treatment for cancer patients in China.[78] In November 2020, Pfizer, Novartis Oncology, and Servier China signed collaboration agreements with AliHealth at the China International Import Expo.[79] Bristol-Myers Squibb also signed an

agreement with JD Health to create a comprehensive tech platform for patients with liver disease, from early diagnosis to long-term disease management. The collaboration between Novartis Oncology and AliHealth seeks to create an innovative digital health model that combines Novartis' expertise in precision medicine with AliHealth's expertise in digital technology. This will provide one-stop, patient-centric services to cancer patients in online prescription, online medication purchase, payment, and medication compliance. Servier China[v] plans to utilize the Alibaba Health Pharmacy Platform for online chronic disease education to improve disease awareness and standard treatment, and to utilize the Alibaba Health Online Hospital for follow-up internet medical services. Pfizer's collaboration with AliHealth focuses on constructing a complete and full-chain online vaccination service. Using AliHealth's platforms, Pfizer will publicize vaccine information and promote online closed-loop service. This includes education, making appointments, and consultation.[79]

Also at the China International Import Expo, Microsoft in China and Novo Nordisk (a Danish multinational pharmaceutical company specializing in global diabetes care), announced their partnership to develop a Chinese-speaking AI chatbot for patients with diabetes.[80] The AI chatbot will launch in early 2021 on Novo Nordisk's digital patient support platforms, and Novo Nordisk and Microsoft have committed to a "healthcare + AI" model to set a new standard in AI-driven chronic disease management.[80]

The limitation with these pharma initiatives is that much of this information is derived from press releases given to media or information found directly on the companies' websites, which are designed to paint these initiatives in the best possible light. Much of the information is high-level and is absent of granularity about the specifics of the initiatives or investments, and information

[v] Servier is the largest independent French pharmaceutical company and was an early foreign presence in China. It has operated in China for 42 years.[150]

on technological, HCP (health care professional), geographic, and regulatory and policy challenges is not readily discussed. This is to be expected since this is proprietary data, as opposed to peer-reviewed public research, and these pharma + big tech partnerships are very complex and the digital healthcare space is a very competitive market. Since China has a fragmented healthcare system, it would be useful if companies posted about their challenges with digital implementation and both strengths and weaknesses of their platforms. It could also provide learning, growth, and collaboration opportunities with other pharma companies and tech players.

2.2.5. Rural Access

There are vast disparities between urban and rural care facilities; patients from the countryside often would rather travel long hours to get treatment in a tertiary hospital in Shanghai or Beijing than at a local primary care clinic.[59] As a result, millions of people in large rural territories are left without proper access to care.[59] According to the 2019 China Health Statistical Yearbook, there were only 1.8 doctors and nurses per 1,000 population in rural China in 2018, compared to more than twice that in urban areas (***Table 1***).[52]

Table 1. 2018 healthcare resources by geography in China (per 1,000 population).

	Number of hospital beds	Number of doctors	Number of nurses
Urban areas	8.70	4.00	5.08
Rural areas	4.56	1.80	1.80

Source: Xu et al., 2020; National Health Commission of the People's Republic of China (PRC).[52]

According to the 2020 China Health Statistical Yearbook, there are 1.48 beds per 1,000 population in rural township health centers.[81] In rural areas with limited medical resources, hospitals and the government wish to optimize resources with telemedicine; this would allow patients to connect with other remote doctors.[47] This also promotes the use of high-quality

healthcare resources in the East to meet the healthcare needs of Midwest patients; as a result, several internet hospitals exist in the western and central regions of China.[47]

With the internet hospital led by the Guangdong Second Provincial General Hospital, 55 of the 14,000 connected providers are Guangdong village doctors, who can consult higher-level hospital physicians and facilitate patients talking with physicians via the platform.[51] Additionally, the provincial government planned to expand this online hospital platform to 2,277 clinics in economically disadvantaged Guangdong villages, and there is financial support of 30 million Chinese Yuan (~$4.5 million USD).[51] However, it is not apparent whether this platform can relieve pressure on secondary and tertiary hospitals, maximize efficiency, and improve coordination of services.[51]

Due to the shortage of medical facilities in rural areas, patients flock to hospitals in neighboring cities and cause overcrowding.[82] A typical Beijing outpatient department sees ~10,000 patients daily. To counter this overcrowding in urban hospitals, more widespread adoption of AI should be integrated with investments in internet connectivity and primary care facilities in rural areas. This could increase healthcare access, affordability, and quality of life for people close to their communities.[82] Although China has seen rapid epidemiological and demographic transitions over the past four decades, with an economic boom that has rescued millions from poverty, health outcomes are still better in more industrialized, wealthier eastern provinces than more rural, impoverished western provinces.[32] In 2019, the poverty population in rural areas was 551 per 10,000 persons with a poverty headcount ratio of 0.6, down from 1,660 per 10,000 persons (ratio of 1.7) in 2018 and 16,567 per 10,000 persons (ratio of 17.2) in 2010.[81]

Because of the larger number of low-income groups in rural areas, healthcare utilization inequity is more prevalent in rural than urban areas.[83] For low-income groups, a low healthcare

utilization level can exhaust the majority of their income, so some elect not to see a physician when suffering illness. To relieve the rural healthcare utilization inequity, the government developed the New Rural Cooperative Medical Scheme (**NRCMS**) for Chinese rural residents in 2003. By covering a portion of the insured's medical expenses, NRCMS aims to decrease economic barriers in healthcare utilization and improve healthcare service equity for rural populations in the face of socioeconomic factors such as income, marital status, and education. While the coverage of NRCMS in rural populations has been over 90% since 2008, service coverage and financial protections were lower than those of the Urban Resident Basic Medical Insurance (URBMI) for urban populations. Therefore, the government developed the Urban and Rural Resident Basic Medical Insurance (**URRBMI**) to provide the same financial protections and service coverage to both rural and urban residents. In 2016, the central government stated that URRBMI had been progressively implemented nationwide in China.[83] In 2018, China's three social health insurance schemes—Urban Employee Basic Medical Insurance (UEBMI), URRBMI, and NRCMS—covered over 95% of the population with an average reimbursement rate of 70%.[52] URRBMI represents 66.74% of China's covered population, UEBMI represents 23.56% of the covered population, and NRCMS represents 9.67% of the covered population.[52]

Those insured by URRBMI often seek outpatient care in tertiary hospitals because they believe that URRBMI has a higher benefit, which causes higher medical expenses.[83] Most of those insured by NRCMS pursue outpatient care in village clinics. Though outpatient care expenses are lower in general, they are still unaffordable for some low-income populations.[83]

In 2019, Ping An Good Doctor launched the "Village Doctor Program" for impoverished rural areas nationwide to alleviate poverty and upgrade medical services for rural clinics, village doctors, and villagers.[84] By the end of 2019, Ping An Good Doctor had upgraded over 900 rural

clinics with advanced technology and trained more than 11,000 village doctors. The Village Doctor App includes over 160,000 auxiliary diagnosis and treatment cases, which help 10,000+ village doctors pair with national famous doctors to improve service capabilities and the standard of medical services with village doctors. In 2019, Ping An Good Doctor also coordinated free expert consultation and physical exams to improve villagers' health and carried out 570 on-site testing activities, which provided free medical consultation for over 63,000 people.[84] Of course, this source provides information released by Ping An directly, and there is no independent evaluation of data that shows the change in population health, medical resource numbers before and after Ping An's intervention in specific low-income areas, and specifics on how the quality of medical services was improved (e.g., earlier and more accurate diagnoses, treatment advice), along with HCP and patient perspectives.

2.2.6. Primary Care

China has 34 provincial regions with over 1.4 billion people (***Figure 6***), and in 2019, it had over 3.86 million doctors (2.76 per 1,000 population).[81,85-87] Almost 20% of the world's 7.67 billion population resides in China.

Figure 6. Geographic regions of China.

Source: UNICEF China.[87]

According to the 2020 China Statistical Yearbook, the urban population in China is 848,430,000 (60.6%), and the rural population totals 551,620,000 (39.4%).[81] China has a three-tier healthcare system, with primary care facilities designated for affordable first-contact care, and secondary and tertiary facilities providing specialist referral services.[51] Community health centers (CHCs), township health centers (THCs), and village/rural clinics are core primary care providers, while secondary (county or district) and tertiary (topmost) hospitals in urban areas accommodate specialist referrals.[17,85] However, there is no gatekeeping within primary healthcare, so patients

can choose freely from providers at any health facility.[17,51] As a result, many routinely choose outpatient services at hospitals for first-contact care, which means that patients with minor ailments, chronic conditions, and common diseases can always choose tertiary hospitals without being diverted to more appropriate primary healthcare institutions.[17,51] It is common for patients to wait hours for a five-minute face-to-face consultation.[58]

Primary healthcare services in China are plagued with many challenges, such as overprescribing diagnostic tests and profitable drugs, competition for patients when there is fee-for-service, and an aging population that drives an increasing demand for healthcare.[51] China's life expectancy increased from 69 years in 1990 to 77 today, and it is expected to reach 79 by 2030.[39] China has a more rapidly aging population than almost any country worldwide; by 2040, the United Nations estimates that China's 65+ population will reach ~303 million.[82] China's hospital-centric healthcare delivery system is very costly and fails to serve the aging population's changing needs as China goes through its epidemiological transition from high infant/child mortality and infectious disease epidemics to a high prevalence of chronic degenerative diseases.[16,88] Therefore, the Chinese government sees digital health as a solution to tackle these burgeoning issues by acting as a gatekeeper between primary healthcare providers and tertiary hospitals.[51] However, many tertiary hospitals allow patients to make online appointments directly and bypass primary health clinics, so this gatekeeping will need to be reinforced within digital health platforms to maximize their efficiency.[51]

Further pervasive gaps in the primary care system include suboptimal training and education of primary care practitioners, fragmentation of clinical care and public health service, a fee-for-service system that incentivizes treatments and testing over prevention, and insufficient continuity of care throughout the entire healthcare system.[16] Not only are primary care providers

in China usually not the point of first contact, but they also do not coordinate with specialty care.[16] In 2018, primary care institutions in China accounted for 53% (4.4 billion) of outpatient visits, declining from 62% in 2010, despite 2009 reform efforts to strengthen the primary healthcare system. In a survey of 17 provinces, poor skills and capacity of primary care practitioners were the predominant reasons that patients avoided primary care institutions when needing clinical care (32%). In a 2013 study, 26% of patients revealed that they did not trust community health centers, as opposed to 6% for hospitals. Furthermore, patients who knew or had seen community health center doctors were more inclined to have a negative view of and were unwilling to use community health centers than patients who had not seen these primary care doctors. Since local residents do not pursue care at primary care institutions, the ability of these institutions to execute public health duties under the National Basic Public Health Service Program could be considerably jeopardized.[16]

Healthy China 2030 prioritizes primary care and disease prevention, and COVID-19 highlighted the importance that primary healthcare could play in monitoring and screening for COVID-19 while maintaining routine care for chronic health conditions.[16] The Chinese government increased funding to institutions to prevent and manage chronic and infectious diseases from ¥19 billion (USD$2.9 billion) in 2008 to ¥197 billion (USD$30.2 billion) in 2018.[16] During the COVID-19 outbreak, the National Health Commission designated primary healthcare providers to do home quarantine monitoring, triage, and screening.[11,16] In mid-February 2020, a survey administered to 3,562 primary healthcare institutions in 31 Chinese provinces revealed that 90% of community health centers and 92% of township health centers had made these efforts during the outbreak.[16] Due to coordination between CDCs and hospitals, primary healthcare providers could screen patients early, give patients proper self-isolation training, and engage in

public education and community mobilization.[11,16] Primary healthcare providers also triaged patients to specialized or mobile cabin hospitals to reduce overcrowding and enable hospitals to prioritize limited resources for more serious cases.[11,16]

To combat COVID-19 in Hubei province, greater than 80,000 primary healthcare professionals comprised the frontline team for mass screening of its 59 million population.[16] In areas severely impacted by the epidemic, the entire workforce of community and township health centers performed multiple tasks to control and treat COVID-19. Among Wuhan's 203 primary healthcare institutions, 199 established fever clinics to perform screening and triage for individuals with suspected symptoms, 201 monitored contacts' symptoms, 173 delivered clinical care and public health service for those quarantined, 147 oversaw disinfection and sterilization at targeted spots, and 101 handled the remains of patients who had died at home. Three township and community health centers served as designated COVID-19 hospitals, 10 township and community health centers provided in-hospital management for suspected or confirmed COVID-19 patients, and workers from 70 primary healthcare institutions were enlisted to support the designated hospitals.[16]

In Zhejiang province, the local government prioritized COVID-19 control and prevention in the communities and villages.[16] In Kaihua County, 361,500 local residents and migrants were categorized by risk since Jan 20, 2020. In neighboring Hubei province, family doctors identified and successfully contacted 99% of 843 migrant workers who wished to travel home. Furthermore, 406 village and township doctors were mobilized to work on 392 inspection locations along country roads to check the temperature of and offer health education to drivers and passengers. Furthermore, several digital technologies were deployed to enhance the role of primary care to combat COVID-19 in China. Primary healthcare providers promoted online consultations, virtual

appointments, and drug delivery, which were substantial in maintaining access to care for non-COVID-19 patients during the epidemic. General practitioners used WeChat to establish instant messaging and social networking groups within villages for consultation and health education, and telephone follow-ups were conducted twice a day for home-isolating patients. Village doctors interviewed confirmed and suspected COVID-19 patients about their contact history and performed temperature checks for all patients. As soon as possible, patients exhibiting fever were transported to designated county hospitals, where isolation wards had been pre-arranged to minimize the risk of contact with suspected COVID-19 patients.[16]

To improve the efficiency and quality in primary healthcare institutions as well as the entire healthcare system, an integrated EHR (Electronic Health Record) system for all citizens is needed.[16] Li et al. recommend that China address the problems in the two core IT systems in primary care institutions—the Electronic Medical Record (EMR) system for clinical care and the Residents Health Record System for basic public health services. Clinical IT systems such as EMR should be available in all primary care institutions, especially village clinics. Further, clinical IT system development and deployment in primary care institutions need to be centralized, with standardized data structures, definitions, and suitable classification systems such as the International Classification of Primary Care, to ensure interoperability and integration. The Residents Health Record System that was employed nationally in the National Basic Public Health Service Program should be integrated with clinical care delivery; this will enable health data for efficient and proper clinical practice. To facilitate patient referrals, the EMR systems in primary care should be connected with systems used in secondary and tertiary hospitals.[16]

Li et al. also recommend that China work to build a learning primary healthcare system that is driven by data and technology, with a real-time, high-performance IT system that can

collect, organize, and standardize data from multiple sources, selectively grant access to data, maintain data securely, and rapidly analyze data.[16] Moreover, the healthcare system should guarantee that healthcare professionals are practicing at the highest training level, in accordance with IT support and the latest evidence. Based on the integrated data platform, three IT tools could employ innovative tech for staff training, quality control, and decision support. One IT tool could be in-service training tools through mobile apps and the internet. Online training could efficiently train millions of primary care professionals in such a huge country with widespread internet access. This digital training could facilitate personalized and adaptive courses built on individual abilities.[16]

The second type of IT tool that Li et. al. suggest is AI-enhanced decision support tools.[16] Together with the basic role of decision support tools—including dosage calculations, guideline recommendations, and contraindications warnings—AI algorithms can support these tools in producing new knowledge by analyzing data from ongoing care delivery. The third type of IT tool could be big data-based quality monitoring and feedback tools. Digital technologies can facilitate multiple systems data integration in quality monitoring, to provide insights on a broad range of the outcomes and process of care. Technologies can also facilitate timely and targeted analysis by determining performance benchmarks in consideration with primary care characteristics and local epidemiological profiles.[16]

Of course, the success of Li et al.'s recommendations would depend largely on the quality of training and support for primary healthcare professionals, especially in under-resourced areas. Although primary healthcare professionals in China must attend and earn a specific number of credits annually in Continuing Medical Education programs, more than 1/3 of nurses, physicians, and public health professionals in primary care institutions received none of this training in 2016.[16]

The reasons given by primary care practitioners were that they were too busy to attend training and even worse, the trainers were unqualified and content was poor. Perhaps some of these issues could be alleviated by the growing private healthcare sector collaborating with local governments and academic/medical institutions in China and abroad to provide financial support, technical support, and high-quality training for primary care practitioners, similar to what Ping An Good Doctor is doing with their Village Doctor program.[84,89]

2.2.7. Drones, Robotics, & Other Tech

China deployed robotic technology to combat COVID-19. In the first few months of 2020, service robots were deployed in publicly shared spaces and hospitals to take temperatures and deliver food, clean, and minimize contact between individuals.[90] The COVID-19 outbreak accelerated the clinical application of robotics technology for hospitals. Robots are a greatly needed priority in the medical sector to assist in areas such as surgery, nursing, and physical rehabilitation. The Chinese government has focused on the robotics industry to help care for patients since China has a shortage of healthcare workers, and a rapidly aging population is placing more demand on the healthcare system.[90]

During the outbreak, Shenzhen company Pudu Technology repurposed its catering robots in over 40 hospitals across China.[91] The robots helped medical staff deliver medicine and supplies to patients and limited healthcare workers' exposure.[91] The West China Hospital of Sichuan University in Chengdu, one of China's most esteemed medical centers, used a logistics robot to disinfect isolation wards during the COVID-19 outbreak.[90] This same hospital had utilized a ROSA robotic surgical assistant in 2018 for neurosurgery and in 2015, it had purchased a da Vinci robotic system for minimally invasive surgery. The da Vinci was approximately $3 million. Hospitals would like to use more robots, but only service robots (~$10,000) equipped to do basic

functions such as delivering food and medicine are affordable for hospitals and businesses currently. A disinfection robot for hospital use is typically $30,000-80,000. Yao Li, the founder of Borns Medical Robotics (based in Chengdu, China and Silicon Valley, California), noted that the Chinese robotics market needs to increase the number of homegrown Chinese robotics companies to stimulate demand and competition, which will lower costs.[90]

In 2011, China's central government outlined the push for robotics in its 12th five-year plan, which specified that robots should support society in varying roles, from aiding in medical rehabilitation and performing complex surgery to aiding emergency services during natural disasters and firefighting.[92] China's medical robotics research has grown progressively over the past two decades due to national planning needs that increased funding levels from the Ministry of Science and Technology and National Natural Science Foundation of China; the clinical utilization of robotics; and engineering advances in AI, medical imaging, precision mechatronics, and new materials to build robots. The number of da Vinci systems in Chinese hospitals jumped from 8 installations in 2018 to 59 in 2019. There was a government push in 2018 to encourage robotics research and its clinical application, and the central government planned to purchase and distribute 154 new robotic surgical systems nationwide by the end of 2020 (***Figure 7***).[92] In Hubei, the province hit hardest by COVID-19 in China, there were fewer than 3 robots installed and fewer than 8 planned by the end of 2020.

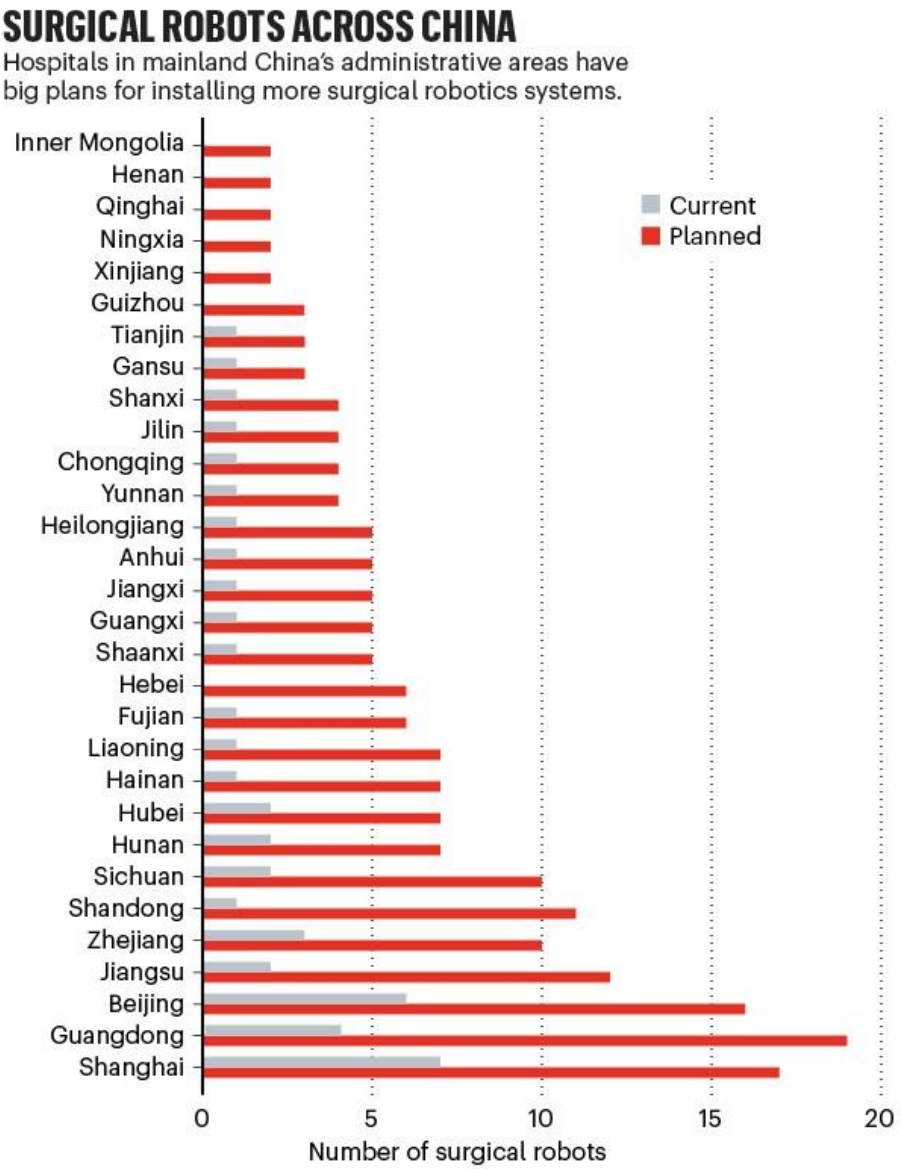

Figure 7. Allocation of surgical robots across China.

Source: National Health Commission, PRC; O'Meara, 2020.[92]

In addition to robots, drones were implemented in China's response to COVID-19. Drones originally created to spray pesticides were adapted to spray disinfectants in some public spaces and on epidemic prevention vehicles traveling between affected areas.[93] Drone spraying is more efficient and consistent than hand spraying, with drone spraying being fifty times more efficient depending on the application. To guarantee the safety of aerial disinfection processes, XAG

Technology (an agricultural drone company), DJI (Da Jiang Innovations) Agriculture, China Agricultural Machinery Distribution Association, China Agricultural University Research Center for Medical Equipment and Application Technology, and other relevant agencies collectively published a series of technical specifications and operational guidance to ensure that all efforts were conducted scientifically and safely and to communicate with local authorities.[93]

Using drones to deliver medical samples considerably reduces unnecessary contact during transport.[93] Drones can also accelerate feedback for critical tests that medical workers and patients need. Early in February 2020, a drone full of medical testing supplies departed the People's Hospital of Xinchang County, Zhejiang province and flew to the Chinese CDC located 3 km away. Thus, a trip that normally took 20 minutes by ground transport only took 6 minutes by drone, which cut delivery time by more than half. Since drones restrict the flow of people and limit contact, they prevent secondary transmission.[93]

Drones were also used for delivery of consumer goods; this ensured people's access to food and other goods while limiting human contact.[93] Even prior to COVID, consumer delivery was challenging in areas of China due to difficult geographies, such as Anxin's series of semi-isolated islands. In Anxin, routine grocery deliveries normally required three transport modes: products were shipped to a main pier, ferried to each island, and then disseminated by foot. When measures to counter SARS-CoV-2 suspended ferry service, driving along the peninsula's narrow and rugged road could take over 2 hours in a single trip to cover 100 km. Thus, drone delivery swiftly became a welcomed alternative. With local government support, JD (one of China's largest online retailers) deployed its drone team. The JD drone team rapidly conducted ground surveys, designed flight corridors, requested permission to access airspace, and executed final flight tests. Within a few

days, many drone delivery corridors were established, which replaced hours-long drives with a 2 km flight that could be done in only 10 minutes.[93]

To enforce the world's largest quarantine to contain the COVID-19 outbreak, the Chinese government co-opted and adapted industrial drones to ensure that ~50 million residents stayed home across a dozen cities.[94] The software flying the drones was rewritten to adapt their applications for crowd management and disease detection. The drones used high-definition zoom lenses, loudspeakers, thermal sensors, and chemical spray jets to disinfect large areas.[94]

Shenzhen company MMC (MicroMultiCopter) utilized drones equipped with megaphones to patrol the streets and warn groups of people without masks to disperse.[91] The drones can spray disinfectants in public places and measure individual thermal temperatures, which reduces the spread of SARS-CoV-2. The MMC drones also monitored traffic, enabling faster response rates and uncongested vehicle movement during medical emergencies. Outside of drones, Chengdu city in Sichuan Province gave epidemic-control workers high-tech smart helmets to automatically measure people's temperature within a five-meter range. The smart helmet sounds an alarm if a fever is detected.[91] Furthermore, facial-recognition cameras equipped with thermal sensors can detect people not wearing masks and those with fevers, and Tencent and Alipay developed mobile apps to inform users if they have been in contact with a SARS-CoV-2 carrier and if they should stay home or can be allowed in public spaces.[91]

While drone technology is promising, there are cybersecurity concerns that should be carefully evaluated. In a July 2020 article, the New York Times reported that cybersecurity researchers found a vulnerability in an app that control's the world's most popular consumer/commercial drones, made by DJI.[95] This Google Android app that powers the DJI drones captures large amounts of personal data that could be exploited by the Beijing government. In

December 2020, it was reported that DJI and SMIC (Semiconductor Manufacturing International Corporation, the most prominent chipmaker in China) were added to a US trade blacklist by the US government, due to the belief that DJI was involved in human rights violations in China and concerns that SMIC could use US intellectual property and manufacturing capabilities to support the Chinese military on ballistic missiles and soldier exoskeletons.[96] These privacy and human rights concerns tie into the ethics of digital and technological innovation in China, and they raise questions about other cybersecurity vulnerabilities that could be exploited for drones used to deliver medical samples and products.

2.2.8. Ethics

To quarantine and manage the spread of SARS-CoV-2, the Chinese government has integrated the social credit system.[97] China's social credit system is a set of initiatives and databases that monitor and evaluate how trustworthy individuals, companies, and government entities are.[98] Each gets a social credit score that rewards those with high ratings and punishes those with low ratings. China's economic planner, the National Development and Reform Commission (NDRC), the People's Bank of China (PBOC), and China's court system manage these databases. Most data is extracted from traditional sources such as financial, criminal, and government records, as well as data from registry offices and third-party sources (e.g., online credit platforms). Further, the Chinese government has begun capturing data from real-time data-transfers and video surveillance, which includes monitoring emission data from factories. The plan was first outlined by the State Council in 2014 to cover individuals, social interactions, businesses, and judicial administration; and system rollout is expected by the end of 2020.[98]

The social credit rating system compiles a score for individuals and businesses after gathering and analyzing data from multiple sources.[98] With businesses, information on partners

and suppliers is submitted to local and national authorities. Low trustworthiness, bad behavior, and ratings from customers and suppliers will affect a company's credit rating. Good ratings lead to rewards and poor ratings lead to sanctions and punishments. If individuals are deemed to be untrustworthy, they can face restrictions in areas such as education, travel by air and rail, and loans. To encourage good behavior, some local governments offer incentives such as waiving public housing rent deposits and prioritizing healthcare provision. Untrustworthy individuals and businesses will also be publicly named and shamed. People and businesses blacklisted for minor offenses can apply to have their social status restored when their debts have been repaid and they have maintained a good social credit record for a period of time. Serious violators will remain on the blacklist for a long time.[98]

Individuals who hide their COVID-19 exposure, such as through travel or medical history, can see their personal social credit scores deducted or end up on a blacklist.[97] Additionally, some cities have included behaviors such as hoarding products and spreading rumors as social credit infringements. Since SARS-CoV-2 was traced to live animal markets, the Chinese government also made the consumption of animals posing a risk of zoonotic diseases punishable within the social credit rating system. In Shenzhen, both individuals who eat and restaurants that serve dogs, turtles, snakes, and some wild birds are subject to social credit demerits and fines of 20,000 yuan ($3,061) to 200,000 yuan ($30,613).[97,99] Shanghai's Public Credit Information Platform blacklisted and city authorities took disciplinary action against those who evaded isolation for medical observation, concealed medical history and travel history to Wuhan and other hotspots, or concealed contact with suspected or confirmed patients.[100,101]

China's social credit system is controversial because it tracks behavior for individuals and gives citizens a credibility rating with data that is often incomplete or inaccurate, critics claim.[98]

Critics also claim that the government is trying to control every part of citizens' lives. Moreover, they express concerns about invasion of privacy, data protection, and data credibility because of weak regulations and law enforcement in China for the social credit system. It is estimated that just around half of the 1 billion individuals in the database had a complete social credit history because of improper tracking of data and records not consolidated among companies. Many irregularities exist in the personal credit market that could pose long-term problems for the rating system, and there are grey areas for overdue debt collection. Also, the system is vulnerable to data breaches from large data transfers with sensitive personal and technological information, which is particularly concerning to foreign firms. The European Chamber of Commerce in China is concerned that trade conflicts could occur from blacklisting "heavily distrusted market entities" for reasons such as fraud, malicious collaboration, endangering the public or national interest, coercion, and infringing on the legitimate interest and rights of consumers.[98]

China's "*New Generation Artificial Intelligence Development Plan*" (AIDP) informs AI ethics, with Confucian principles that place more emphasis on social responsibility and community and group relations while focusing less on individual rights.[38] Some risks accompany this approach. One risk arises from using AI to enhance the social service governance under the pretense of "improving people's lives."[38] Because China's population is rapidly expanding and aging, the government has significantly invested in the social informatization of healthcare and been linking behavioral and emotional data from social media—as well as daily healthcare data from wearables, Internet of Things (IoT)[vi] devices, carebots, implantables, and ingestibles—to electronic health records. The intention is to enable community care of the elderly, but it also

[vi] The "Internet of Things" is the concept of connecting any device with an on/off switch to the Internet and/or each other. This encompasses cellphones, wearables, washing machines, coffee makers, lamps, headphones, etc. This is also applicable to components of things, e.g., a jet engine of an airplane.[151]

enables China's culture of mass, state-operated surveillance, such as through the social credit rating system. With the social credit system, the same technologies that enable the aging population to remain independent in their communities could be used for social control to reduce the incidence of social diseases such as type II diabetes and obesity.[38]

Another risk arises from controversial CRISPR (clustered regularly interspaced short palindromic repeats) gene modification and AI.[38] CRISPR can alter the presentation of genes in living organisms to prevent or cure genetic diseases. CRISPR and AI are closely related because machine learning techniques can identify which gene(s) CRISPR needs to alter. This poses ethical issues since it is not always possible to determine the line between unmet clinical need and genetic control or human enhancement. When biophysics researcher He Jiankui successfully used CRISPR to genetically modify babies to limit their chances of contracting HIV, the November 2018 announcement sparked international outcry and condemnation of He's experiment by the Chinese government. However, China's goal to be a world leader in medical care, combined with the potential that gene editing offers for disease treatment, suggest that the Chinese government may respond differently in the future as global competition intensifies. With the US announcing clinical trial enrollment to cure a hereditary form of blindness and the UK launching the "Accelerating Detection of Disease" challenge to develop new AI approaches for biomarker discovery and early diagnosis, these initiatives create strong enticements for Chinese researchers to push regulatory boundaries for quick international successes. Further, China has filed the most patents in the world for gene-editing on animals.[38]

2.2.9. Gaps & Opportunities

Several leading MNC (multinational) pharmas have set aggressive launch targets in the next 2-5 years as innovative drugs spur their growth mechanism in China.[61] This is anticipated to

cause intensive competition in a crowded market from global and domestic pharma peers, and pharma companies already are trailing big tech giants in the digital healthcare space. Starting in 2021, China is projected to be the third-largest growth market for Takeda, after the US and Japan. So where can Takeda add value and innovate in an oversaturated digital health ecosystem, while being especially cognizant of ethical issues that could arise with technology in healthcare? How can Takeda most efficiently leverage technology and partnerships in this ecosystem to deliver innovative healthcare solutions to patients who need them most? Takeda has a unique array of drugs, cell gene therapies, and vaccines that would benefit millions of Chinese patients, especially those with complex (e.g., Inflammatory Bowel Disease), rare (e.g., Hereditary Angioedema [HAE]), and neglected diseases (e.g., dengue fever). Rare diseases pose significant challenges for the economy and healthcare system, and lack of rare disease awareness among the general public and significant delays in diagnosis are major problems in China.[102]

Over the next five years as part of Takeda's commitment to the Healthy China 2030 targets, Takeda plans to introduce more than 15 innovative medicines that will benefit around 10 million patients suffering from rare diseases, such as HAE and Gaucher disease.[103] Further in line with China's AI Development Plan, Healthy China 2030, and a rapidly aging population, should Takeda also consider robotic or other cutting edge technological solutions outside of just traditional therapies and telehealth platforms? This literature review provides an overview of China's rapidly expanding digital health ecosystem, and the qualitative interviews of key opinion leaders will address Takeda's digital strategy, needs, and challenges as the company ventures into this emerging market.

3. METHODS

3.1. Mixed Methods

This doctoral project uses a mixed methods concurrent triangulation approach, in which quantitative and qualitative data were collected in parallel.[104] To fully address the project objectives, the purpose of these mixed methods is to first showcase the epidemiological disease burden, as well as health resource challenges, in China before and after COVID-19. Elucidating the disease and access burdens then provides a roadmap for digital and technological innovation, which is needed to manage the pandemic as well as chronic diseases responsible for the greatest morbidity and mortality in China. The qualitative interviews add to the richness of the epidemiological data by highlighting themes, challenges, nuances, and internal and external digital health efforts that published data alone cannot provide. Together, this helps Takeda efficiently target therapeutic areas, provinces, and age groups for knowledge translation into science policy, Public-Private Partnerships, and digital health pilots in China.

3.1.1. Quantitative: Epidemiology & Healthcare Access Data

Descriptive epidemiology was used to showcase country-level cases and death rates for COVID-19 in China. Johns Hopkins COVID-19 database and DXY.cn were sourced for COVID-19 data on confirmed cases and deaths.[6,105] DXY.cn is the largest online physician community in China and sourced its data from various national, provincial, and municipal health commissions in China.[6,106]

Country-level morbidity and mortality rates for top chronic diseases in China were sourced from Global Burden of Disease (GBD) data. Deaths and DALYs (Disability-Adjusted Life Years) per 100,000 population from GBD data were used to quantify chronic disease burden for age groups and sexes in China.[107] DALYs represent the total number of years lost to illness, disability,

or premature death within a given population.[108,109] DALYs are calculated by adding the number of years of life lost (YLLs) to the number of years lived with disability (YLDs) for a certain disease or disorder.[108,109] As opposed to health expectancies, DALYs measure health gaps and the difference between a current situation and an ideal situation, in which everyone lives up to the age of standard life expectancy (and in perfect health).[110] Life tables set the standard life expectancy at birth to 82.5 years for women and 80 years for men.[110]

DALY = YLL + YLD

Where:

YLL = years of life lost due to premature mortality.
YLD = years lived with disability.

YLL = N x L

Where:

N = number of deaths.
L = standard life expectancy at age of death (in years).

YLD = I x DW x L

Where:

I = number of incident cases.
DW = disability weight.
L = average duration of disability (years).

For estimating YLD on a population basis, the number of disability cases is multiplied by the average disease duration and a weight factor that reflects disease severity on a scale from 0 (perfect health) to 1 (dead).[110]

Demographics, descriptive epidemiology, and multivariable analysis results for COVID-19 and associated comorbidities in China were sourced from two major studies with laboratory-confirmed COVID-19 cases. They are the most comprehensive analyses that stratify COVID-19 with comorbidities to assess the risk of serious adverse outcomes in patients (admission to ICU, invasive ventilation, or death). The first was a China CDC study that analyzed 44,672 COVID-19 cases in mainland China, and for triangulation, it was re-analyzed by another group of Chinese researchers to assess the risk of fatality.[111,112] This was the largest confirmed case series that was publicly reported by the Chinese CDC. The second study analyzed 1,590 laboratory-confirmed cases from 575 hospitals in 31 provinces, autonomous regions, or provincial municipalities across mainland China between December 11, 2019 and January 31, 2020; and it assessed composite endpoints of admission to ICU, invasive ventilation, or death.[113]

Health resource and mortality data of top major diseases in urban and rural areas were sourced from the 2020 China Statistical Yearbook from the Chinese National Bureau of Statistics, which covers 2019 data. At the time of writing this doctoral thesis, the 2021 China Statistical Yearbook had not been released. Health resource data was comprised of 2019 healthcare resources per 1,000 population in provinces most affected by COVID and least resourced provinces. The number of internet hospitals established by year in China and their health service capacity were sourced from a 2021 published study that assessed the internet hospital landscape during COVID-19 in 2020.[114] Utilization statistics of internet hospitals were extracted from 2020 financial reports of JD Health, Ping An Good Doctor, and Alibaba Health.

3.1.2. Qualitative Interviews

The qualitative component was comprised of 19 interviews with key opinion leaders (KOLs) at Takeda and external digital health stakeholders—18 semi-structured interviews

(including individuals from Takeda and the Harvard China Health Partnership) and 1 unstructured interview (McKinsey). These interviews were conducted from October 2020 – February 2021. The 19 key opinion leaders were divided into nine different categories for analysis (***Table 2***).

Table 2. Key opinion leader categorization.

KOL Category	Description	N=19
Digital	Various Digital groups at Takeda, comprising the Digital Advisory Board, China & Japan Enterprise Digital, China Incubator/Innovation Hub	5
Patient Engagement	Takeda group that focuses on engaging patients through patient advocacy/advisory groups	2
Emerging Tech	Subset of Digital, focusing specifically on emerging technologies & digital health partnerships	3
Public-Private Partnerships & Global Science Policy	Takeda R&D-focused group for global consortia-based Public-Private partnerships & science policy	1
Vaccines	Vaccines business unit at Takeda	1
Takeda Development Center (TDC) Asia	Drives the inclusion of Asia in Takeda's global development activities to bring transformative medicines to Chinese patients in a timely manner	1
Clinical Trials & Digital Solutions/Strategy	Groups focusing on strategy, innovation, and procurement of digital solutions for Takeda's clinical trials	4
Harvard China Health Partnership	Makes connections between Harvard T.H. Chan School of Public Health and peer institutions in China, such as universities, policy think tanks, socially-oriented entrepreneurs, and private sector innovators	1
McKinsey HealthTech Network	Global community of digital health startups, ASEAN chapter	1

Study participants were almost evenly split between sexes: 52.6% (n=10) were female and 47.4% (n=9) were male. For organization, 90% of participants were from Takeda and 10% were from external organizations. For location, 57.9% (n=11) were based in the US, 26.3% (n=5) were

based in Asia, and, 15.8% (n=3) were in Europe. Those living in Asia predominantly resided in China (15.8%, n=3), but 10.5% (n=2) were outside China at the time of the study. Regarding ethnicity, 42.1% (n=8) were Chinese or Taiwanese and 57.9% (n=11) were not Chinese or Taiwanese.

Study participants were chosen by convenience sampling, specifically snowball sampling. Interviews ranged from approximately 30 minutes to over an hour and were conducted with KOLs in the US, Europe (Switzerland, France), and Asia (Singapore, China, and Japan). Interviews discussed partnerships and digital health strategy and policy, including strengths, gaps, challenges, and future opportunities. A total of 6 interview guides were used, adapted for different expertise areas both inside and outside Takeda. Except for the McKinsey KOL (in which there was no recording), interviews were recorded with KOL consent through Microsoft Teams, Cisco WebEx, or Zoom. Otter AI transcription software was used to transcribe and edit the interviews for clarity and accuracy.

Once interviews were transcribed, Dedoose (v. 8.3.45) software was used to perform qualitative thematic analysis on ~235 pages of text that comprised the 19 interviews. A mixture of deductive (top-down coding with a predefined set of codes) and inductive (ground-up coding where codes are derived from the data) approaches were taken when deriving the coding structure.[115] After multiple reviews of the 274 excerpts that were coded, 8 themes were identified with 66 consolidated, underlying codes. No weights were attached to any codes or themes because no survey component or questionnaire was used in the study to rank strength or importance.

3.2. Framework for Change: ADKAR

The change management model used in this doctoral project is the ADKAR model, by Prosci founder Jeff Hiatt. It is based on his book, *ADKAR: A Model for Change in Business,*

Government, and Our Community.[116] This framework was chosen because Takeda aligns with a more sustainable form of capitalism that shifts from a short-term property model (in which shareholders are the only stakeholder) to a long-term entity model (in which businesses, governments, and communities are all stakeholders). COVID-19 demonstrated how crucial multi-sectoral collaboration was to combat the deadliest pandemic in history. Furthermore, each component of the ADKAR framework accentuates Takeda's "Patients First" corporate philosophy that is encapsulated in its PTRB acronym: Patients, Trust, Reputation, and Business.

ADKAR stands for:

- **Awareness** of the need for change
- **Desire** to support the change
- **Knowledge** of how to change
- **Ability** to demonstrate skills and behaviors
- **Reinforcement** to make the change stick

The AKDAR involves three states of change: current (**A**wareness and **D**esire), transition (**K**nowledge and **A**bility), and future (**A**bility and **R**einforcement).[117] (***Figure 8***)

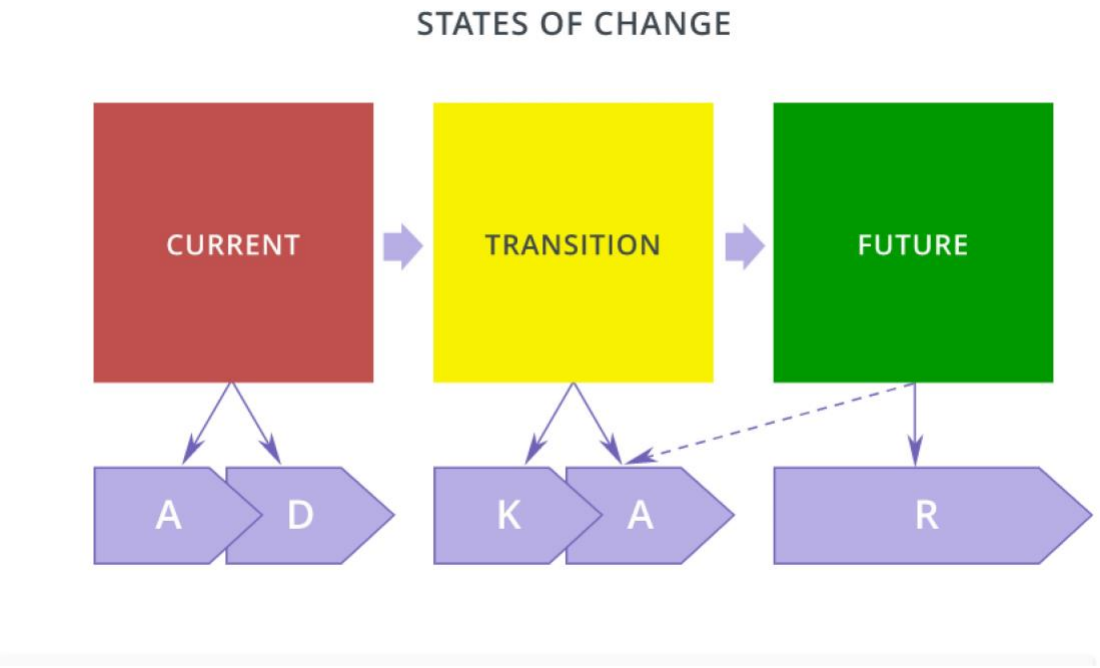

Figure 8. ADKAR states of change.

To progress from the current state, there needs to be awareness of the business need for change as well as a desire to support and participate in the change. Knowledge of how to change and the ability to implement the required skills and behaviors are needed to successfully move through the transition state. To sustain the change in the future, ability and reinforcement are needed.[117] ***Table 3*** highlights how the framework for change will be applied to the doctoral project objectives.

Table 3. Framework for change and methods by objective.

Objective 1: Explore how COVID-19 accelerated digital/technological innovation for health management and access in China.	
Framework	Current & Transition states: **A**wareness, **D**esire, **K**nowledge, **A**bility
Method	Semi-systematic literature review, qualitative thematic analysis, descriptive epidemiology
Data sources	Peer-reviewed journal articles, published reports/news, data repositories, qualitative interviews

Table 3 (Continued).

Outputs	Summary of research; tables of epidemiology, health resources, and themes; figures
Objective 2: Synthesize strategic recommendations for Takeda on how to best utilize global partnerships and technology to increase healthcare access. Seek to better understand the impact on the patient journey in the context of digital innovation. If feasible, assess whether there could be PPP (Public-Private Partnership) opportunities for Takeda to use digital innovation to mitigate health inequities in high-risk and marginalized groups.	
Framework	Future state: **A**bility**, R**einforcement
Method	Qualitative thematic analysis, descriptive epidemiology & health resource data
Data sources	Interviews, published epidemiological reports, and data repositories
Outputs	Recommendations for Takeda

4. RESULTS

4.1. Quantitative: Epidemiology & Healthcare Access Data

4.1.1. COVID and Chronic Disease Epidemiology

In both urban and rural areas in China, the diseases with the highest mortality rates are malignant neoplasms (cancer), heart diseases, cerebrovascular disease, respiratory diseases, endocrine, nutritional and metabolic diseases (e.g., diabetes), and digestive system diseases, according to China's 2020 Statistical Yearbook (***Table 4***).

Table 4. 2019 mortality rate of top major diseases in selected urban and rural areas in China.

	Urban		**Rural**		
Disease Category	**Mortality rate (1/100,000)**	**Percentage of all deaths (%)**	**Mortality rate (1/100,000)**	**Percentage of all deaths (%)**	**Mortality Rate % Difference**
Malignant neoplasms	161.56	25.73	160.96	23.27	0.37%

Table 4 (Continued).

Heart diseases	148.51	23.65	164.66	23.81	-10.31%
Cerebrovascular disease	129.41	20.61	158.63	22.94	-20.29%
Respiratory diseases	65.02	10.36	74.61	10.79	-13.74%
Endocrine, nutritional & metabolic diseases	21.44	3.42	17.80	2.57	18.55%
Digestive system diseases	14.86	2.37	14.49	2.10	2.52%
Nervous system diseases	9.14	1.45	8.60	1.24	6.09%
Genitourinary diseases	6.60	1.05	7.28	1.05	-9.80%

Source: National Bureau of Statistics of China, 2020.[81]

The mortality rate for genitourinary diseases, heart diseases, respiratory diseases, and cerebrovascular disease was 10-20% lower in urban compared to rural areas. However, there is not much geographical difference in mortality rates for digestive system diseases (2.52%) and cancer (0.37%). But for endocrine, nutritional & metabolic diseases, the urban mortality rate is ~19% higher than in rural areas. This could be due to diabetes diagnosis challenges in China, which would only be exacerbated in rural areas with poorer healthcare resources. Rural patients with diabetes have historically paid more out-of-pocket for diabetes treatment, and this could also deter rural residents from seeking health services.[118]

Previous studies show that approximately 61% of diabetic adults had not been previously diagnosed, and ~67% of diabetes patients had not been regularly examined as recommended by clinical guidelines.[118] According to a 2013 nationwide survey of 170,287 Chinese participants, only 37% of diabetic patients were aware of their diagnosis, and only 32% were being treated for

it.[16] Further, a national longitudinal survey from 2011 to 2015 showed a decrease from 76% to 70% in diabetes health education coverage and an increase from 79% to 81% in gaps in the use of diabetes examinations and treatments.[16] Being rural could also be protective since diet, urbanization, decreasing levels of physical activity, and obesity have been linked to China's rapid increase of diabetes.[118]

According to 2019 Global Burden of Disease (GBD) data for both sexes and all ages in China, cardiovascular diseases (CVD) were responsible for the greatest amount of death and disability, with 322.3 deaths and 6,463.47 DALYs per 100,000 (***Table 5***). In adults 70+ years old, cardiovascular diseases caused 3,057.82 deaths and 42,708.31 DALYs per 100,000. Deaths and DALYs for CVD were both higher in males than females (350.87 vs. 292.62 deaths and 7,450.76 vs. 5,437.54 DALYS, respectively).

Table 5. 2019 deaths and DALYs per 100,000 for most common chronic diseases in China.

	Cardiovascular Diseases		**Neoplasms**		**Chronic Respiratory Diseases**	
	Deaths (per 100,000)	DALYs (per 100,000)	Deaths (per 100,000)	DALYs (per 100,000)	Deaths (per 100,000)	DALYs (per 100,000)
All	322.30	6,463.47	190.99	4,747.06	76.30	1,583.33
Age (years)						
15-49	26.95	1,471.82	35.85	1,768.47	1.96	246.94
50-69	294.42	9,466.58	319.14	9,434.76	44.78	1,847.07
70+	3,057.82	42,708.31	1,176.11	17,613.21	838.86	12,551.17
Sex						
Male	350.87	7,450.76	241.32	6,012.78	86.69	1,760.11
Female	292.62	5,437.54	138.69	3,431.82	65.51	1,399.64

Table 5 (Continued).

	Neurological Disorders		Diabetes & CKD (Chronic Kidney Disease)	
	Deaths (per 100,000)	DALYs (per 100,000)	Deaths (per 100,000)	DALYs (per 100,000)
All	29.57	1,222.02	26.48	1,118.51
Age (years)				
15-49	1.50	834.73	3.75	482.13
50-69	14.95	1,246.60	32.79	2,012.43
70+	327.11	5,718.65	211.11	4,566.06
Sex				
Male	23.02	1,023.45	26.70	1,163.21
Female	36.38	1,428.36	26.25	1,072.06

Source: Institute for Health Metrics and Evaluation, 2020.[107]

The 2019 GBD data also shows that the greatest causes of death and disability in China are noncommunicable or chronic diseases. Cardiovascular diseases, neoplasms, and chronic respiratory diseases were the top three causes of death in both 1990 and 2019 (***Figure 9***).

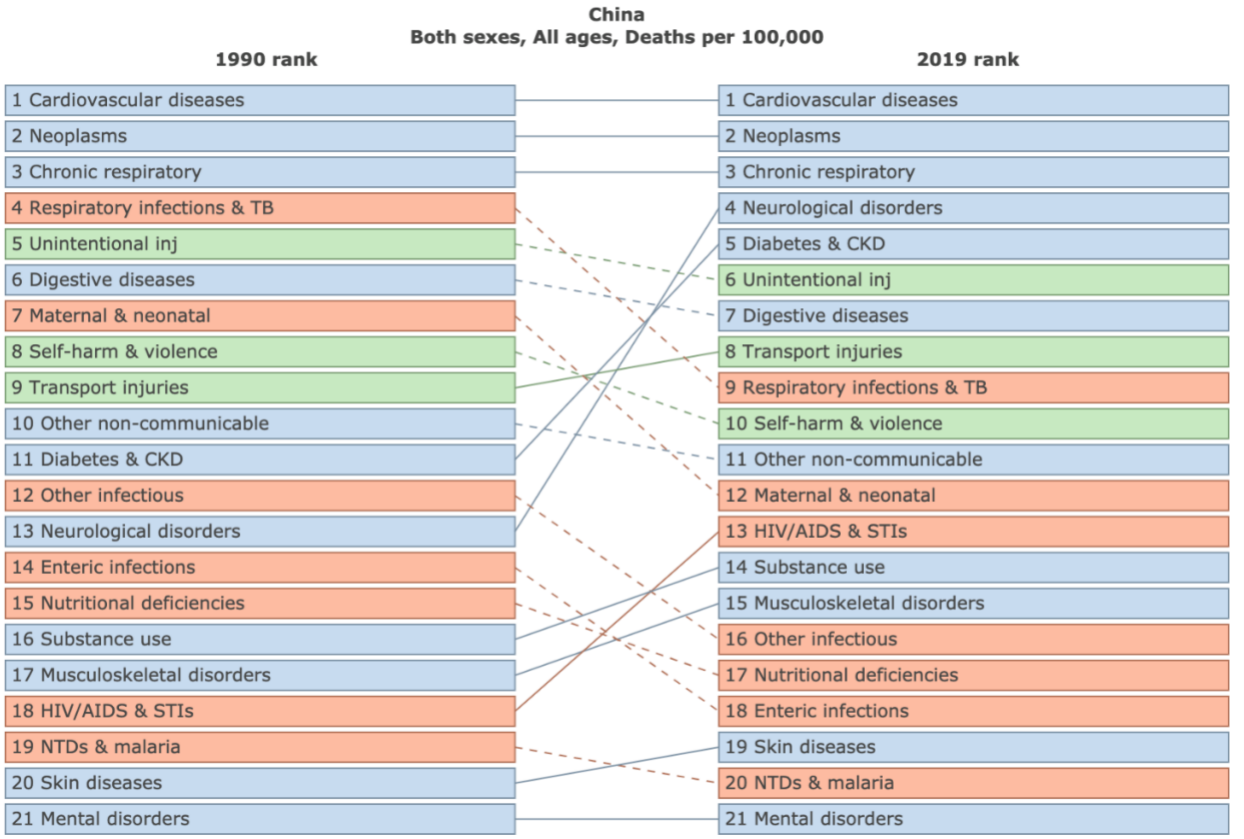

Figure 9. 1990 vs. 2019 ranking of most common causes of death in China for all ages and sexes. *Source:* Institute for Health Metrics and Evaluation, 2020.[107]

In 1990, cardiovascular diseases were the leading cause of DALYs, followed by respiratory infections and tuberculosis (***Figure 10***).

Figure 10. 1990 vs. 2019 ranking of most common causes of disability in China for all ages and sexes.

Source: Institute for Health Metrics and Evaluation, 2020.[107]

In 2019, there were no infectious diseases in the top 7 leading causes of disability (unlike in 1990), and cardiovascular diseases, neoplasms, musculoskeletal disorders, and chronic respiratory diseases were the top 4 causes of disability. This shows that the epidemiological transition from infectious to chronic diseases has been significant over 30 years.

However, when infectious and chronic diseases overlap, as with COVID-19, they exacerbate illness in the other. During the COVID-19 epidemic in China, cardiovascular disease, hypertension, diabetes, respiratory disease, and cancer were significantly associated with increased

risk of mortality from COVID, and the highest case fatality rates (CFRs) were in COVID patients with CVD, diabetes, and respiratory disease (***Table 6***).

Table 6. Demographics, severity, and comorbidity status of 44,672 COVID-19 patients in China.

Characteristics	**Confirmed cases, N (%)**		**Non-survivors**		**Survivors**	
Overall	44,672		1,023		43,649	
Age (years)	*n*	*%*	*n*	*%*	*n*	*%*
0-9	416	0.9	0	0.0	416	0.9
10-19	549	1.2	1	0.1	548	1.3
20-29	3,619	8.1	7	0.7	3,612	8.3
30-39	7,600	17.0	18	1.8	7,582	17.4
40-49	8,571	19.2	38	3.7	8,533	19.5
50-59	10,008	22.4	130	12.7	9,878	22.6
60-69	8,583	19.2	309	30.2	8,274	19.0
70-79	3,918	8.8	312	30.5	3,606	8.3
80+	1,408	3.2	208	20.3	1,200	2.7
Sex						
Male	22,981	51.4	653	63.8	22,328	51.2
Female	21,691	48.6	370	36.2	21,321	48.8
Occupation						
Service industry	3,449	7.7	23	2.2		
Farmer/laborer	9,811	22.0	139	13.6		
Health worker	1,716	3.8	5	0.5		
Retiree	9,193	20.6	472	46.1		
Other/none	20,503	45.9	384	37.5		
Province						
Hubei	33,367	74.7	979	95.7		
Other	11,305	25.3	44	4.3		
Wuhan-related exposure						
Yes	31,974	85.8	853	92.8		
No	5,295	14.2	66	7.2		
Severity*						
Mild/moderate	36,160	80.9	0	0.0	36,160	82.8

Table 6 (Continued).

Severe	6,168	13.8	0	0.0	6,168	14.1
Critical	2,087	4.7	1,023	100.0	1,064	2.4
Comorbidity**						
Hypertension	2,683	12.8	161	39.7	2,522	12.3
Diabetes	1,102	5.3	80	19.7	1,022	5.0
Cardiovascular disease	873	4.2	92	22.7	781	3.8
Respiratory disease	511	2.4	32	7.9	479	2.3
Cancer	107	0.5	6	1.5	101	0.5

Characteristics	Case fatality rate (%)	RR (95% CI)	P-value
Overall	2.3		
Age (years)			
0-9	0.0		
10-19	0.2		
20-29	0.2		
30-39	0.2		
40-49	0.4		
50-59	1.3		
60-69	3.6		
70-79	8.0		
80+	14.8		
Sex			
Male	2.8	1.67 (1.47-1.89)	<0.001
Female	1.7		
Occupation			
Service industry	0.7		
Farmer/laborer	1.4		
Health worker	0.3		
Retiree	5.1		
Other/none	1.9		
Province			
Hubei	2.9		
Other	0.4		

Table 6 (Continued).

Wuhan-related exposure			
Yes	2.7		
No	1.2		
Severity*			
Mild/moderate	0.0		
Severe	0.0		
Critical	49.0		
Comorbidity**			
Hypertension	6.0	4.48 (3.69-5.45)	<0.001
Diabetes	7.3	4.47 (3.49-5.61)	<0.001
Cardiovascular disease	10.5	6.75 (5.40-8.43)	<0.001
Respiratory disease	6.3	3.43 (2.42-4.87)	<0.001
Cancer	5.6	2.93 (1.34-6.41)	0.006

*Missing data (n=257 for Survivors)
**Missing data (n=617 for Non-survivors, n=23,073 for Survivors)

Sources: China CDC, 2020; Deng et al., 2020.[111,112]

However, since individual patient data was unavailable to the authors who re-analyzed the China CDC data, these risk ratios did not account for confounders like age, and older patients were more likely to have underlying comorbidities. This is in line with the 2019 greatest causes of death and disability pre-COVID in China (top 5 causes of death and top 10 causes of disability). The case fatality rate is just the death rate in those with confirmed COVID diagnoses, and it is not equal to actual number of people with COVID. Those more likely to get tested probably were the ones with the worst symptoms, which makes them more likely to have life-threatening complications. The risk ratio is a comorbid individual's probability of dying from COVID compared to a COVID patient without that comorbid condition (i.e., the CFR in those with a comorbidity compared to CFR in those without that comorbidity).[119]

In a 2020 study that analyzed data from 1,590 laboratory-confirmed COVID-19 hospitalized patients from 575 hospitals in 31 provinces across mainland China, the risk of a patient reaching the composite endpoints (admission to an intensive care unit, invasive ventilation, or death) was significantly 1.6-3.5 times higher in patients with hypertension, diabetes, COPD, and malignant tumors compared to COVID patients without those specific comorbidities—after adjusting for age and smoking status (***Figure 11***). Patients with 2 or more comorbidities had a significantly higher risk of the composite endpoints compared to those with only 1 comorbidity (hazard ratio of 2.6 vs. 1.8, respectively).

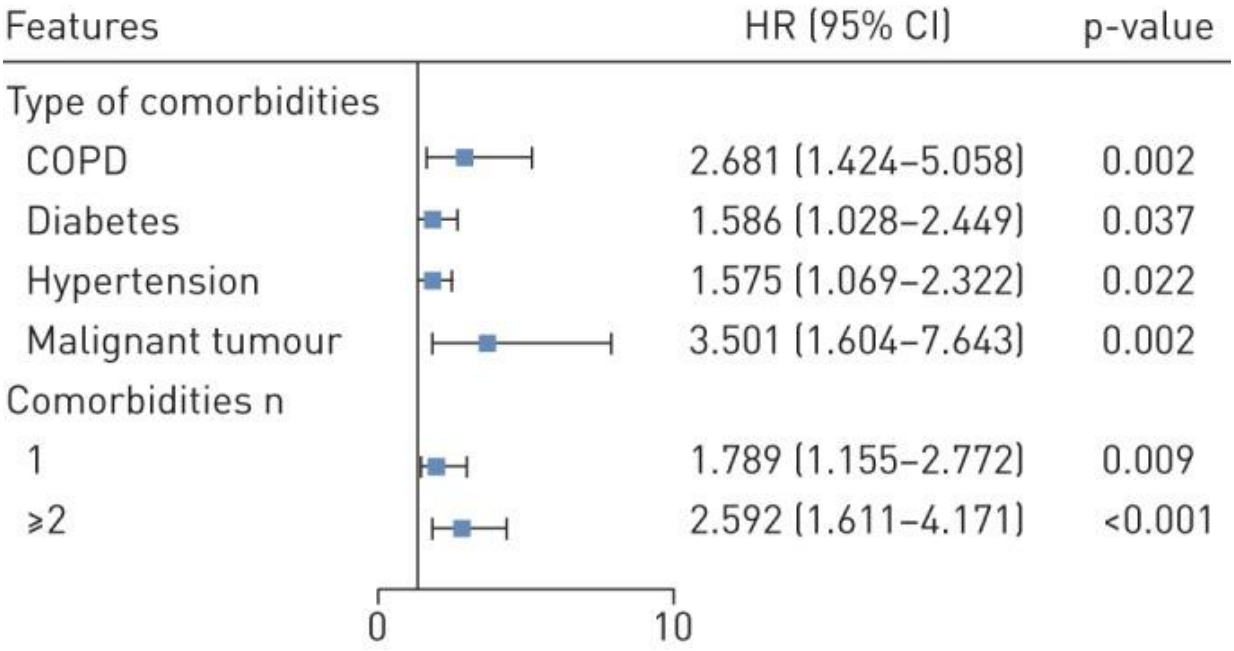

Figure 11. COVID-19 hazard ratios by type and number of comorbidities.

Source: Guan et al., 2020.[113]

4.1.2. Healthcare Resources & Internet Hospital Access Pre- and Post-COVID

Compared to rural areas, urban areas had 2.24 times the number of health tech personnel, 2.1 times the number of licensed physicians and physician assistants, 2.62 times the number of registered nurses, and 1.83 times the number of beds in healthcare institutions in 2019 (***Table 7***).

Table 7. 2019 healthcare resources per 1,000 population in China.

	Health Technical Personnel	Licensed Physicians & Physician Assistants	Registered Nurses	Beds of Healthcare Institutions
Urban	11.10	4.10	5.22	8.78
Rural	4.96	1.96	1.99	4.81

Source: National Bureau of Statistics of China, 2020.[81]

According to the 2020 China Statistical Yearbook, 39.4% of China's 1.4 billion population lives in rural areas.[81] Some of the provinces with the most COVID cases (Appendix ***Table 14***) also have the fewest resources in rural areas (***Table 8***). These are notably Anhui (44.2% rural), Jiangxi (42.6% rural), and Henan (46.8% rural) [Appendix ***Table 15***]. Anhui has a rural population of 28 million, Jiangxi has a rural population of 20 million, and Henan has a rural population of 45 million.

Table 8. 2019 urban and rural healthcare resources per 1,000 population, by provinces most affected by COVID and with fewest rural resources.

	Health Technical Personnel		Licensed Physicians & Physician Assistants		Registered Nurses		Beds of Healthcare Institutions		Beds of Township Health Centers
Provinces with most COVID-19 cases*	Urban	Rural	Urban	Rural	Urban	Rural	Urban	Rural	Rural
Hubei	10.24	4.97	3.63	1.91	5.14	2.14	8.99	5.28	1.94
Guangdong	11.34	4.36	4.13	1.64	5.23	1.82	7.26	3.58	1.3
Shanghai	14.5	-	5.27	-	6.61	-	10.42	-	-
Zhejiang	13.19	7.91	5.05	3.24	5.84	3.15	9	5.24	0.71
Henan	12.7	3.99	4.52	1.62	6.21	1.52	11.01	4.24	1.27
Hebei	8.45	5.02	3.49	2.56	3.78	1.61	6.73	4.74	1.34
Heilongjiang	10.75	4.49	4.02	1.89	5.02	1.49	12.78	4.42	1.09
Hunan	12.97	5.29	4.63	2.08	6.56	2.45	12.66	5.44	1.78

Table 8 (Continued).

Beijing	18.46	-	7.18	-	7.84	-	8.72	-	-
Anhui	8.26	3.61	2.94	1.48	4.11	1.47	7.44	3.69	1.21
Xinjiang	13.75	6.84	5.34	2.43	6.15	2.76	11.7	7.27	1.54
Jiangxi	8.92	3.97	3.02	1.5	4.43	1.64	7.86	4.32	1.5
Shandong	11.11	5.63	4.32	2.36	5.21	2.25	8.24	4.92	1.47
Sichuan	9.52	5.05	3.42	1.9	4.65	2.07	8.6	6.03	2.27
Jiangsu	10.34	6.16	3.85	2.71	4.88	2.48	8.3	5.11	1.66
Provinces with fewest rural resources**									
Guangxi	9.36	4.35	3.23	1.43	4.52	1.78	6.61	3.99	1.77
Anhui	8.26	3.61	2.94	1.48	4.11	1.47	7.44	3.69	1.21
Jiangxi	8.92	3.97	3.02	1.5	4.43	1.64	7.86	4.32	1.5
Chongqing	9.31	3.65	3.3	1.51	4.56	1.37	8.78	4.64	2.67
Guizhou	9.38	4.65	3.31	1.51	4.64	2	8.16	4.91	1.19
Henan	12.7	3.99	4.52	1.62	6.21	1.52	11.01	4.24	1.27
Hainan	14.63	4.53	5.11	1.63	7.29	2.01	10.44	3.45	0.85
Guangdong	11.34	4.36	4.13	1.64	5.23	1.82	7.26	3.58	1.3
Fujian	10.84	4.58	4.11	1.72	5.02	1.91	7.22	4.06	1.18
Liaoning	11.05	4.05	4.29	1.75	5.23	1.58	10.34	4.93	1.46
Gansu	10.17	4.76	3.38	1.76	5.04	1.89	9.08	5.35	1.42
Yunnan	13.82	5.6	4.87	1.83	6.82	2.53	10.41	5.62	1.36
Heilongjiang	10.75	4.49	4.02	1.89	5.02	1.49	12.78	4.42	1.09
Sichuan	9.52	5.05	3.42	1.9	4.65	2.07	8.6	6.03	2.27
Hubei	10.24	4.97	3.63	1.91	5.14	2.14	8.99	5.28	1.94

* Excludes Hong Kong and Taiwan
** Provinces under the average 1.96 rural physicians and physician assistants per 1,000 population

Sources: National Bureau of Statistics of China, 2020; DXY.cn, 2021.[6,81]

As of July 2020, there were a total of 711 internet hospitals in China, and 215 (30.2%) were created in 2020 after the COVID-19 outbreak (***Table 9***). The majority of the 215 created in 2020 were in January, February, and March (n=167, 77.7%).

Table 9. The number of internet hospitals established by year in China.

Year	N	%	Nov.	Dec.	Jan.	Feb.	Mar.
2020	215	30.24%			61	66	40
2019	206	28.97%	32	42			
2018	52	7.31%					
2017	40	5.63%					
2016	22	3.09%					
2015	15	2.11%					
Before 2015	5	0.70%					
Unknown	156	21.94%					
Total	**711**						

Source: Xu et al., 2021.[114]

Internet hospitals in China are run by three types of entities: enterprise (74%), hospital (20.1%), and government (5.9%). Each province has at least one internet hospital, but they are mainly concentrated in the East and Southern coastal provinces. The most common patient consultation method was SMS text messaging using graphics, followed by video consultations and telephone consultations. As of July 2020, most internet hospitals offer medical prescription, drug delivery, and medical insurance services (***Table 10***).

Table 10. Type, services, and patient consultation methods of internet hospitals in China during and after the COVID-19 outbreak.

Type		Service		Patient Consultation Method	
Government	42 (5.91%)	Drug delivery	411	Video	18
Hospital	143 (20.1%)	Epidemic prevention & control info	327	Video + graphic	124
Enterprise	526 (74.0%)	Epidemic situation dynamic assessment	29	Video + graphic + phone	106
		Fever clinic	316	Telephone	132
		Medical insurance	335	Graphic	190
		Medical prescription	419		
		COVID-19 myth-busters	64		
		Psych counseling	186		
		Donation to epidemic areas	17		

Source: Xu et al., 2021.[114]

JD Health, Ping An Good Doctor, and Alibaba Health all saw marked increases in registered or annual active users, monthly active users, and/or average daily online consultations (***Table 11***).

Table 11. Operating performance for major digital healthcare companies, 2019-2020.

	Number of Registered/Annual Active Users (millions)			Average daily online consultations			Monthly Active Users (millions)		
	6/30/19 or 9/30/19*	**6/30/20 or 9/30/20***	**% Inc.**	**6/30/19**	**6/30/20**	**% Inc.**	**6/30/19**	**6/30/20**	**% Inc.**
JD Health	53.5	72.50	35.51%	14,835	86,100	480.38%			
Ping An Good Doctor	289.30	346.20	19.67%	656,000	831,000	26.68%	62.70	67.30	7.34%
Alibaba Health*	48.00	65.00	35.42%						

*=specific to Alibaba Health

Sources: JD Health, 2020; Ping An Good Doctor, 2020, Alibaba Health, 2020.[78,120,121]

From the available data, Ping An Good Doctor had the largest amount of registered users on their platform both before and after China's COVID outbreak. JD Health and AliHealth had the largest percent increases in users to their platforms, and JD Health saw a massive 480% jump in average daily online consultations from June 2019 to June 2020. China peaked in its COVID cases in mid-February 2020, and data for all platforms listed shows that patients were still heavily utilizing telemedicine platforms for months after the outbreak.

AliHealth distributed COVID-19 information through AliPay (Alibaba's mobile and online payment platform) and Taobao and offered free consultation on both platforms.[122] As of September 30, 2020, Alipay had over 35,000 contracted medical institutions, with 4,000 tier 2 and tier 3 hospitals.[78] Over 700 tier 3 hospitals in 27 provinces had been connected to medical insurance reimbursement services. Driven by measures to provide convenient and easy services during the

pandemic (including online medical consultation and COVID-19 education), there were more than 330 million users of Alipay's healthcare channel from April to September 2020.[78]

AliHealth's pharmaceutical direct sales business (Alibaba Health Pharmacy and Alibaba Health Overseas Flagship Store) saw over 65 million annual active users, as of September 30, 2020. The direct sales business operated the Chronic Disease Welfare Program, which provides lifecycle solutions for chronic disease management, follow-up drug consultations, patient education, and telemedicine follow-up services. AliHealth reported that the membership coverage rate for chronic disease patients, average drug use duration, and user experience all improved during the reporting period.[78]

Due to COVID-19 causing a surge in demand for online consultation, JD Health accelerated its telemedicine business by rapidly adding more physicians to the network.[122] JD Health became a major channel for standard telemedicine as well as processing the purchase of medical products, and it also provided front-line COVID-19 triage services for Chinese citizens nationwide. Using prescribed questions (set by government protocol), telemedicine physicians could assess whether a caller was likely positive for COVID-19. If a given caller was considered at risk of COVID-19, they were connected with a local hospital for a physical checkup. JD Health also introduced a smart epidemic assistant to share official information pertaining to the SARS-CoV-2 virus and offered online psychological services.[122]

JD Health offers 24/7 comprehensive internet healthcare services, ranging from online consultation, chronic disease management, prescription renewal, family doctor, and consumer healthcare.[120] JD Health was the first company in China to provide online appointments for COVID-19 nucleic acid testing. As of June 30, 2020, JD Health had over 9,000 third-party merchants on their online marketplace, and their omnichannel initiative covered more than 200

cities in China and offers same-day, next-day, and 30-minute delivery services to meet patient needs for urgent medication. This complete online+offline, closed-loop model has strong partnerships with hospitals and presence in retail channels, and it is convenient for patients to be able to receive consultations from physicians, manage their disease, and then purchase medicines, health & wellness products, as well as medical supplies and devices all on one platform (***Figure 12***). JD Health's direct sales pharmacy business operates through JD Pharmacy, which was the largest online retail pharmacy in China in 2019.[120]

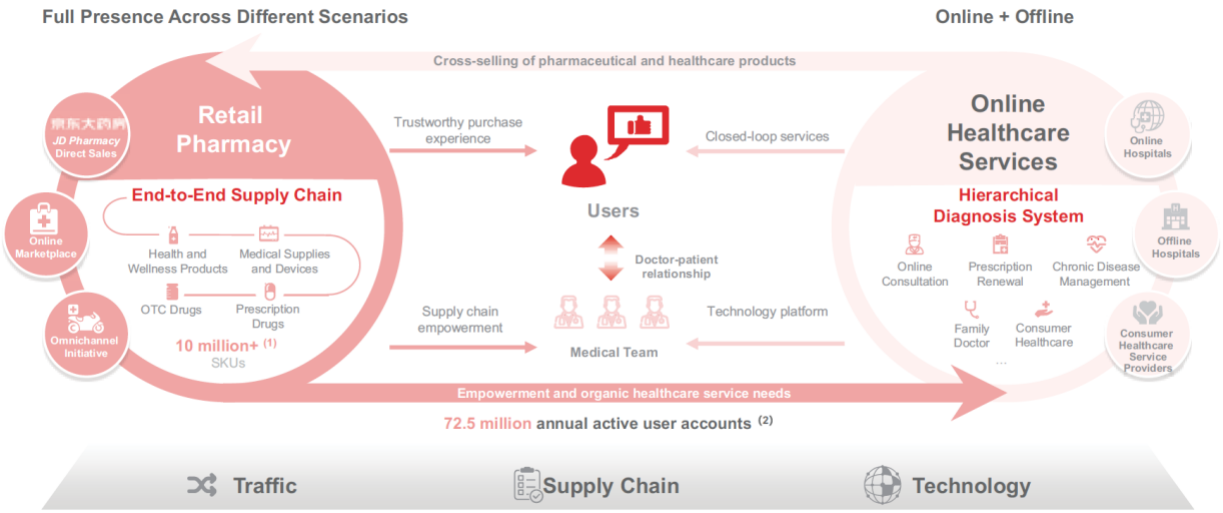

Figure 12. JD Health's closed-loop online healthcare service model.

Source: JD Health, 2020.[120]

As of June 30, 2020, Ping An Good Doctor had 1,836 in-house medical staff members, which represented an increase of 30.3% from December 31, 2019. Also a closed-loop service, Ping An Good Doctor's platform includes a smart severe disease monitoring platform, smart AI-based medical system, smart medical safety monitoring platform, and Prescription Automatic Screening System (PASS).[121] The medicine atlas has over 600,000 records and the AI-based system covers 3,000 diseases. The online consultation satisfaction rate was around 97% in 2020. As of June 30, 2020, Ping An Good Doctor had more than 820 million consultation records, which helps increase

the accuracy of the AI technology. Ping An Good Doctor has partnerships with 3,700 hospitals, including 2,000 tertiary hospitals. To provide delivery services for drugs prescribed during online consultation, they also collaborate with over 111,000 cooperative pharmacies that cover 371 cities in 32 provinces. During the COVID-19 outbreak, the platform was able to collect medical history of COVID, used AI algorithms to conduct precise consultation triage, had a knowledge base of over two million health Q&As to improve the efficiency and accuracy of their in-house medical team, and processed more than one million consultations daily (during the peak). By mid-August 2020, Ping An Good Doctor had partnered with 17 offline hospitals to build internet hospital platforms and obtained social health insurance qualification licenses from Hubei province and Yinchuan city.[121]

Throughout 2020, Ping An Good Doctor continued working closely with local governments to advance rural healthcare through the Village Doctor app.[121] As of June 30, 2020, the company had trained almost 1 million doctors in rural districts and offered free healthcare services to more than 66,000 rural residents. In keeping with the goals of Healthy China 2030, Ping An Good Doctor has significantly relieved the medical resource shortages in rural areas while drastically improving the quality of medical services and population health in low-income regions. The AI-based medical system assists village doctors in improving initial diagnosis accuracy as well as referral efficiency through integrated data functions and online registration.[121]

4.2. Qualitative Thematic Analysis

The eight themes that arose from the qualitative interviews were: COVID-19 disruption to the healthcare system, China's unique enabling environment, digital innovation type, cross-functional collaboration with health ecosystem, data governance, therapeutic areas and assets,

improvement of the patient journey, and ethics of digital innovation. ***Table 12*** shows a list of the themes and their accompanying codes.

Table 12. Qualitative thematic analysis on digital innovation and healthcare access in China.

Theme 1: COVID-19 disruption to the healthcare system.	**Theme 2. China's unique enabling environment.**	**Theme 3. Digital innovation type.**	**Theme 4. Cross-functional collaboration with health ecosystem.**
Acceleration of digital innovation (continuity of care & physician engagement)	Internet + healthcare; AI government policy (Insurance/ Reimbursement)	Telemedicine/ telehealth (internet hospitals)	Big Tech players (Tencent, AliHealth, Ping An Good Doctor, JD Health, Dīngxiāng Yuán)
Social distancing/lockdowns & COVID triage (interruption in care)	Early adopters of digital health and technology	Artificial Intelligence (AI) - algorithms, machine/deep learning, chatbots/virtual assistance, augmented/virtual reality	Public-Private Partnerships (Government, regulators, consortia)
Transforming drug delivery	Chinese government	Wearable, Remote Patient Monitoring, IoT devices	HCPs, KOLs, hospitals & health departments

Table 12 (Continued).

Theme 1: COVID-19 disruption to the healthcare system.	**Theme 2. China's unique enabling environment.**	**Theme 3. Digital innovation type.**	**Theme 4. Cross-functional collaboration with health ecosystem.**
Lowering the threshold for digital adoption	Large population size	Apps	Biotech startups/scale-ups
	Online + offline care integration	Virtual/hybrid clinical trials	Academia
		Big data (Real-World Data/ Evidence)	Chinese suppliers/local vendors
		ePRO (Electronic Patient-Reported Outcomes), E-diary	Payers
		eConsent	Inter-pharma
		eCOA (Electronic Clinical Outcomes Assessment)	Accelerators/ Incubators
		Electronic Health Records & decision support systems	
		5G	
		Robotics	
		Drones	
		Lifestyle management for chronic disease	
		QR codes for primary vaccine vials	
		Vaccine temperature monitoring	

Table 12 (Continued).

Theme 5. Data governance.	Theme 6. Therapeutic areas and assets.	Theme 7. Improvement of the patient journey.	Theme 8. Ethics of digital innovation.
Data access, sharing, ownership (siloed data)	Rare disease (Hereditary Angioedema/HAE)	Patient engagement - Patient community, advocacy/advisory groups; elderly care	Data privacy and trust
Data security	Neurology/neuroscience - Narcolepsy, Parkinson's, cerebrovascular disease, Alzheimer's, mental health	Better clinical trial design, conduct, recruitment - Reducing clinical trial burden; trial flexibility, continuity, resiliency; decentralized clinical trials	Quality of care/treatment
Data transparency	Oncology	Health equity - Increasing access to treatment (affordability, rural/remote areas), clinical trial diversity	Inequity of access - Treatment eligibility, population left behind
Better data quality (passively-acquired data)	Inflammatory Bowel Disease (IBD)/Gastrointestinal (GI)	Health literacy/disease awareness	Intention (profit vs. patient)

Table 12 (Continued).

Theme 5. Data governance.	**Theme 6. Therapeutic areas and assets.**	**Theme 7. Improvement of the patient journey.**	**Theme 8. Ethics of digital innovation.**
Anonymization	Chronic disease - Diabetes/metabolic, Hypertension/cardiovascular disease, COPD	Early diagnosis and treatment	Biased or incorrect algorithms/models
	Vaccines	Improved health outcomes/wellness (medication adherence)	Downstream effects
	Injectables/infusions	Home health care	Social credit rating system
	Cell gene therapy & omics	Improving primary healthcare	Manipulating behavior
	Surgery	PTRB (Patients First)	
		Closed-loop care/end-to-end network	

Many themes and codes overlap with one another; the highest overlap is between digital innovation type and improvement of patient journey (n=67 excerpts), followed by digital innovation type and therapeutic areas and assets (n=57 excerpts), and therapeutic areas and assets and improvement of the patient journey (n=56 excerpts). This code co-occurrence shows that across themes, these concepts were most frequently discussed together. Of the digital innovation types used to improve the patient journey and specific therapeutic areas, telemedicine/telehealth was mentioned most frequently. Neurology and rare disease were the therapeutic areas most frequently mentioned when discussing different types of digital innovation. When using digital

innovation to improve the patient journey in specific therapeutic areas and assets, rare disease was mentioned most often. For therapeutic areas and assets, improvement of the patient journey was discussed most often in the context of patient engagement and health equity.

4.2.1. Thematic Area 1: COVID-19 disruption to the healthcare system

COVID-19 caused a major strain on the healthcare system in China, and the government, public health and healthcare professionals, technology companies, and multi-national pharma companies quickly rose to the challenge. Respondents described four main ways that COVID-19 disrupted the healthcare system: acceleration of digital innovation, social distancing/lockdowns and COVID triage, transforming drug delivery, and lowering the threshold for digital adoption. To control the pandemic, the government instituted strict lockdowns, and many people could not go to the hospital to receive care or medicines because all resources were devoted to triaging COVID patients during the outbreak. Other provinces sent their healthcare workers to Wuhan, which means that many hospitals outside Hubei province were only doing emergency care and general outpatient treatment was shut down for many weeks. Further, many citizens were simply afraid of going to the hospital and contracting COVID, so they would have practiced social distancing even if it had not been enforced.

Specifically, primary care was compromised because many primary care providers had been mobilized to do emergency COVID response. As one KOL described the situation:

> *"Our understanding is that chronic disease management and some of these routine things that primary healthcare is doing, probably during that time has been compromised. People who should be getting chronic disease management like hypertension, diabetes, they may not be getting the routine care, the regular monitoring, etc."*
>
> *– KOL #2*

However, chronic diseases such as hypertension and diabetes were not the only ones that suffered an interruption in care; oncology, gastrointestinal, other disease areas did as well. The

total impact of delays in diagnosis and treatment, or the total number of patients who deferred care for acute conditions or stopped seeking care for chronic conditions, is not yet known. Other KOLs stated:

> *"If I look at the care pathway of a patient, especially in oncology or other disease area…how many patients that are supposed to be diagnosed, they're not diagnosed today because of COVID-19? How many patients that are supposed to be taking treatment—go to hospital to take it—they didn't, because of COVID-19, because of the lockdown? Or how many patients because of the economic impact, they couldn't afford to buy their own medicine; they had to make trade-offs?"*
>
> *– KOL #11*

> *"In IBD (Inflammatory Bowel Disease), Entyvio is [administered by] injection…most moderate to severe patients in IBD would have biologics and most biologics [need to be injected by] IV in the hospital, at least in China…if all the hospital beds and ICUs were full with or used by COVID patients, the IBD patients wouldn't be prioritized, right? If you have to prioritize, maybe you prioritize chemotherapy or oncology, and then you leave the chronic diseases a bit later."*
>
> *– KOL #12*

Although this interruption in care due to social distancing and lockdowns was certainly deleterious, COVID also disrupted the healthcare system in many beneficial ways that increased access to healthcare and medicines for millions of Chinese citizens. COVID-19 accelerated digital innovation, transformed drug delivery (direct-to-patient), and lowered the threshold of adoption for digital healthcare. The threat of COVID-19 accelerated digital innovation by creating a dramatic shift from physical consultation to virtual consultation, and it increased the number of patients using telemedicine in China substantially. COVID's transformation of patient behavior was described by one participant as:

> *"Before COVID-19, [the] patient is always going to the hospital, especially for the tertiary hospital because in China, we do not believe [trust] the family doctor very much... I think government want to build the family doctor system, it's also written into five years [plan]. So the team of family doctors, they are growing, but I think the adoption for the Chinese patient is not so good. Before COVID-19, every patient is going into the offline tertiary hospital to want to get the best treatment of their disease, and I think after COVID-19, the first thing change is they really think they can meet their physician online…through the internet hospital."*

– KOL #13

Inside Takeda, COVID-19 brought forward very unique challenges that disrupted research and commercial operations, which translated into tailwinds that brought digital innovation front and center. This included elevating digital innovation as a priority for senior executives and accelerating internal development to address the challenges that COVID brought forward. COVID also accelerated digital initiatives and external partnerships to address some of the access and treatment challenges, such as allowing clinical trials to continue or launch, as well as deploying home nurses so that IBD patients could continue ENTYVIO® infusions:

> *"A couple of examples for this is Takeda's endorsement and adoption of digital clinical trial platforms. Another example is, our patients who are dependent on intravenous drugs, like IV Entyvio, where subcutaneous Entyvio has not been approved yet, we're looking into leveraging digital for connecting them with providers that can do infusions at home, or help them navigate the infusion journey, infusion experience with minimal exposure to COVID."*
>
> *– KOL #9*

> *"The other area we're exploring because of COVID-19 is the hybrid virtual clinical trial model. So we've heard from patients directly that some of them value the in-person visits in clinical trials because sometimes that's the only care that they receive from the healthcare system. Other patients have cited that they're concerned to participate or go into a hospital setting in COVID-19, rightfully so.*
>
> *So this is something that's not new to the industry. It's something that the entire industry has been thinking about, but it's really COVID-19 that's accelerating this need to do a virtual clinical trial or hybrid model. So this would involve digital wearables, having devices on mobile phones to collect e-diary, so all sorts of different digital ways of collecting information when keeping the trial running."*
>
> *– KOL #16*

In addition to enabling continuity of care and clinical trials, the acceleration of digital innovation due to COVID-19 also provided a way for Takeda to continue physician engagement. Before COVID, HCPs could meet with Takeda's medical science liaison or medical preventive care manager. But COVID caused Takeda and other pharmaceutical companies to halt all offline

engagement with physicians for months during the outbreak, and Takeda moved to omnichannel[vii] digital engagement to keep in touch with and provide precision content to physicians. This engagement with HCPs is necessary to educate them about pharmaceutical products:

> *"Our traditional modalities of walking to the physician office due to COVID is no longer possible. So we are looking into performing advanced analytics for micro-segmentation of the physicians to inform what type of messages can we deliver to them through the different communication channels to be more effective and most effective, to educate them on our latest assets that are going to be released into the market."*
>
> *– KOL #9*

Another positive disruption to the healthcare system is the transformation of drug delivery. With internet hospitals rapidly growing, they have been coupled with solutions that allow online prescriptions and direct-to-patient drug delivery. Takeda also launched new medicines online during COVID-19. For prescription drugs, patients can receive an online consultation through the internet hospital and the doctor will give them the prescription to buy the drug online. For non-prescription drugs, patients can easily choose from a variety of e-commerce and online pharmacy websites to purchase their medicines. Many pharmaceutical companies began collaborating with internet hospitals to sell their medicines online. Online availability of medicines and direct shipment has greatly reduced the patient burden in China:

> *"For the drug delivery, the patients who have the chronic disease have to go to the hospital like every month to get the drug and the medicine. And after COVID-19, they can get the prescription online and delivered to their home. So this also changes the medicine purchase behavior of the patient."*
>
> *– KOL #13*

For both healthcare professionals and pharma, the threshold of adoption for digital healthcare was significantly lowered and much of the hesitation around using digital was no longer a factor. To maintain the same quality of patient care, Takeda had to adapt and move the adoption

[vii] Omnichannel engagement involves engaging the patient through multiple channels—desktop and mobile phone, websites, apps, social media, email, SMS and other messaging platforms, and IoT devices.

mode to leverage digital. This was particularly true for prompting teams at Takeda to adopt virtual clinical trials:

> *"So I do think that previously, there was a kind of sluggish mindset where, okay, we have to get on board with virtual clinical trials, but someone else can do it first. And it's not been tried and tested and oh, our patients are different. But I think that most teams have embraced it now because they've seen that especially in the context of COVID, it's really helped them keep going with their clinical trials. And a lot of the barriers and issues that we thought would present themselves have probably not had the same impact that we thought they would have."*
>
> *– KOL #5*

> *"And the silver lining for Takeda here with COVID was we saw an opportunity to accelerate the digital transformation. And what I mean by that is these digital tools initially were nice to have. And even though we had conviction and evidence to say that these would make our clinical trials run more efficiently, that there was a demand for patients to have these tools, change is hard. People prefer the status quo in many ways. They prefer the devil they know [rather] than the unknown Angel.*
>
> *You cannot run a clinical trial in the global pandemic, where people are quarantined, and cannot come to a site to enroll, or cannot communicate with their doctor…you're required to put the study on hold, or you cannot launch new studies. It was a must-have if you wanted to continue your clinical trial or actually launch your clinical trial."*
>
> *– KOL #6*

4.2.2. Thematic Area 2: China's unique enabling environment

China is a prime candidate for digital and technological healthcare innovation for several reasons. Respondents discussed China's "internet plus" healthcare policy and reimbursement mechanisms, Chinese citizens being early adopters of digital health and technology, the Chinese government and large population size, and online + offline care integration in the health system.

As part of the Healthy China 2030 strategy, the government has been encouraging innovative, digitalized platforms to support future health. In 2018, the Chinese government endorsed "internet plus" healthcare policy, which enables HCPs, hospitals, pharma, and technology companies to integrate digital services into patient care. In February 2020, China

released guidelines to control the COVID-19 pandemic and these included broadening the scope of medical insurance payment to include "Internet +" medical service fees, allowing designated medical institutions to provide contactless ("no-face") drug purchase services, improving handling services for medical insurance payments, medical behavior supervision, and prescription review services; continuously improving the level of informatization by strengthening network security of internet medical insurance services to prevent data leakage; strengthening the supervision of medical insurance funds; and ensuring the smooth and orderly development of work (system launching, reports, and evaluation during the epidemic, and promotion to qualified designated medical institutions and regions).[55]

> *"With the regulation, patients who had the service from the internet and bought the online drug, now they are able to reimburse those expenses from those national insurance companies. So that will help patients to participate more in the digital initiatives."*
>
> *– KOL #14*

Before COVID, hospital services usually were only reimbursed if they were offline. With the revised policy, every offline hospital should have an online component:

> *"So they have a lot of favorable regulation. I know that they just came out with a new regulation about internet hospitals to allow insurance reimbursement for the online hospital service. [Now that they] try to have some regulation to allow patients to claim their service in the network online, the regulation will help to speed up the digital innovation and internet healthcare."*
>
> *– KOL #14*

The government's National Reimbursement Drug List (NRDL) has already reduced the overall cost for patients, even though this has reduced a lot of benefit in the profits for pharmaceutical companies. But this has forced many pharma companies to change their strategic focus from just focusing on general medicines to also focusing on oncology and rare disease areas to cure more patients. Takeda has been working with some insurance companies to provide reimbursement of medicines for patients in China.

Entyvio® (vedolizumab), a Takeda drug for IBD (ulcerative colitis and Crohn's disease), was part of the 2020 NRDL negotiations that successfully made it into China's 2020 drug catalog.[123] Of the 2800 total drugs included in the 2020 drug catalog, 1,426 (51%) are Western medicines.[124] The price of successfully negotiated drugs was reduced by an average of 50.64%, according to China's National Healthcare Security Administration.[124] Under this policy, all provinces must strictly implement this drug catalog, and they are not allowed to formulate their own catalogs, use flexible methods to add drugs in the 2020 drug catalog, or adjust the limited drug payment scope in the catalogs.[125] The 2020 drug catalog officially went into effect on March 1, 2021.[125]

Respondents also saw Chinese citizens as early adopters of technology. The digital and technological penetration rate in the Chinese population was already very high, and this paved the way for successful digital innovation in pharma:

> *"In China, the mobile internet penetration rate is definitely more than 95%. And recent research shows that more than 70% of the internet users, they already are digital health users."*
>
> *– KOL #18*

China's mobile internet penetration rate was 99.1% in June 2019, 99.3% in March 2020, and 99.7% in December 2020.[126] By contrast, the 2020 mobile internet penetration rate in the United States was only 83%.[127] The general internet penetration rate in China was 61.2% in June 2019, 64.5% in March 2020, and 70.4% in December 2020.[128] China was the very first market that implemented 5G, which is critical for having a robust telemedicine platform. China is leading the rest of the world in terms of digital health adoption by patients, HCPs, and other pharma companies. Another KOL mentioned that there is more prominent receptivity to use technology in China than we are used to in the US:

"I hear from my cousin, who lives in Shanghai, that she's never carried physical cash before. She's even seen, for instance, someone who's homeless and asking for money having a mobile phone to ask for money…people there don't just don't carry cash, they haven't done so in years. So a lot of the digital presence and expectation of what digital can do is very much ingrained in how they operate day-to-day."

– KOL #16

Another attribute of China that enables digital innovation is the Chinese government. Because China is a capitalist market with a communist government, innovation can be easily mandated:

"Decisions are made from the top that we want to go digital, or we want to transform the way we deliver care, or we want to be more ecological. The decisions are made top-down, the country follows."

– KOL #11

This means that the government can mandate not only "internet plus" healthcare policy nationwide but also strict testing and tracing to reduce the spread of COVID-19 in the population. If someone was out shopping in China when they were supposed to be quarantined, they could get arrested. It is quite likely that the power of the Chinese government is the reason why China had fewer infections and deaths compared to the US.[viii] One KOL explained this stark comparison very candidly:

"The reason why test and trace works in China is basically because…of [its] regime, where people don't have the choice…they had to have that app on their phone. But at the end of the day, it helped decrease the virus… And you get a country that I'm in right now, for example, France, where they do have a test and trace system. The government have been doing a campaign around it saying, 'Please download this app,' but then you don't have to. It's not compulsory. So basically, no one's doing it."

– KOL #5

Due to its large population size (1.4 billion people), the Chinese government employs technology for mass surveillance of citizens. Although KOLs were concerned about the fact that

[viii] As of April 15, 2021, there were 31,029,700 confirmed COVID-19 cases and 558,238 deaths in the US, compared to 103,185 confirmed cases and 4,856 deaths in China.[3,152]

the Chinese government has access to everyone's data and information, some found the monitoring to have the potential to improve the lives of patients. One KOL discussed the opportunity to use technology to help patients be diagnosed and get treatment earlier:

> *"And I think because China does a lot more monitoring of their population, for better or for worse, we can use that to help patients get treatment. Imagine if you were to develop an algorithm that uses all of these CCTV cameras that are present to monitor the population, to maybe detect signs of stroke, or detect signs of Parkinson's disease, or detect many different disease conditions that manifest in changes in gait, changes in facial expression."*
>
> *– KOL #4*

China's large population size means that there are many individuals who suffer from the same diseases. This also makes China a good use case to test digital health. A higher burden of disease means a more pressing need to bring innovative solutions and medicines to patients who need them most. KOLs explained that this not only fulfills a Takeda business need to increase geographic access to care but also an economic need for the Chinese government to reduce healthcare expenditures:

> *"I think China has just demonstrated to the world how much they can innovate. [The] market in itself is huge. And China as a country is huge. So that, in itself, I think creates a lot of potential and opportunity for all of us to tap into."*
>
> *– KOL #10*

> *"I think China is a big market. It's a…very big country. When you think about access, not only about access in terms of resources, money, but also geographic access, digital intervention will be very important because it will reduce inequality in terms of access to care. And that's one example. Second example is how to maintain a large population healthy, because it costs money if they are sick, if they have diabetes, or COPD, or other diseases. And I think there is almost an economic driver for them to adopt digital."*
>
> *– KOL #11*

Telehealth is not only used for patients to have an online consultation but also to connect them with offline care if they need it. Online and offline care integration is the final example of how China enables digital healthcare to be successful, and it presents itself in three ways: two

involve connecting facilities and HCPs and one involves connecting physicians and patients for follow-up care and Directly-Observed Therapy. China's healthcare system is very fragmented and before COVID, many patients were overcrowding tertiary/specialty hospitals and bypassing primary health centers because primary healthcare is so suboptimal in China. Online and offline care integration means that 1) patients can receive online screening from an internet hospital and then doctors transfer them to Center of Excellence (COE) tertiary hospitals, or 2) patients can go to a primary healthcare center or less advanced hospital and be connected online to a more advanced hospital. This greatly improves access and reduces waiting times. To date, one of the greatest problems with primary care in China is that primary care providers often do not coordinate with specialty care and primary care is usually not the first point of contact.[16]

Therefore, this online and offline care integration enhances primary and specialty provider coordination as well as strengthens primary care as the first point of contact in the healthcare system. For very rare diseases like hereditary angioedema (HAE) in which China has potentially 28,000 patients, this increase in collaboration across tiers is necessary to diagnose and treat patients early. The Emerging Tech group at Takeda developed an AI use case to work with internet hospitals to help doctors do patient screening and predict patients who will be at high risk for HAE. This will help physicians transfer those patients to the Center of Excellence (COE) hospital:

> *"Not many people really know this disease and we only identify seven hospitals who have capability to confirm and diagnose HAE through their C1 testing. So, once the internet hospital help to do the patient screening and predict the patient who might have a possibility of HAE, then we transfer those patients to COE hospital to confirm and to make a diagnosis. So that's for the rare disease early diagnosis."*
>
> *– KOL #14*

> *"The other [approach] that is very popular in China is linking up big hospitals, advanced hospitals, with less advanced hospitals in the rural areas or even community health centers, so that they can do online consultation. The patient will still go to these primary health care centers or a district hospital in the rural areas.*

But they can then turn on the video, get connected to larger hospitals who have more specialists to then do online consultation."

– KOL #2

The third way that online and offline care integration works is to create a "virtual bridge" between physician and patient to enable online follow-up of the patient. For instance, patients can receive care at a tertiary hospital and physicians can follow up online with patients after they return home, especially if they traveled far from rural villages. Better communication between physician and patient leads to better health outcomes:

"I heard a lot of physicians complain about the specialist of oncology, they are all in the tertiary hospital. And they are all focused in Shanghai, Beijing, Guangzhou [Guangdong province]…So the patient will go to this tertiary hospital to get diagnosis and then go back to their own hometown to treatment. So the specialist always complained [that] when the patient go back home, there'll be disconnect between the patient and the physician. And the physician really want to know what reaction and what feedback or [the] response [to] their treatment."

– KOL #13

4.2.3. Thematic Area 3: Digital/technological innovation type

Participants described several types of digital and technological innovation that can be utilized across a wide range of therapeutic areas in pharma. These covered 7 main categories: apps and telemedicine/telehealth platforms, emerging technology, data science, health information systems, virtual/hybrid clinical trials, lifestyle management for chronic disease, and vaccine technology. Emerging technological innovation included: AI, IoT devices (wearables and remote patient monitoring [RPM]), 5G, robotics, and drones. Big data, including real-world data and real-world evidence, comprised the data science category. Health information systems included Electronic Health Records (EHR), Immunization Information Systems, and Clinical Decision Support Systems. For virtual and hybrid clinical trials, respondents discussed electronic Patient-Reported Outcomes (ePRO) and e-diary, eConsent, and electronic Clinical Outcomes Assessment

(eCOA). Vaccine technology included QR codes for primary vaccine vials and vaccine temperature monitoring.

Telehealth and apps

In China, telehealth platforms are considered the primary type of digital innovation in healthcare. Telemedicine/telehealth platforms were also the most frequently talked about innovation with all KOLs interviewed; out of 115 excerpts tagged for the theme of digital innovation type, 42% (n=48) were for telemedicine/telehealth platforms. Having a telemedicine platform is practically a necessity to succeed in digital healthcare in pharma.

Internet hospitals are run by physical hospitals with both offline and online services as well as big tech companies such as Alibaba, Tencent, and Ping An Good Doctor. For Takeda, this provides a broad range of innovative opportunities in patient care, especially in rare disease and oncology:

> *"They [China] have a rapidly growing telemedicine and virtual hospital systems. Large investments from Tencent Health, Alibaba Health, rapid growth companies like WeDoctor…present unique opportunities to find effective ways to care for our patients in China, especially in our focus areas oncology and rare disease, where access to medications remains a big challenge."*
>
> *– KOL #9*

Internet hospitals can provide online consultations, diagnoses, prescriptions for patients, and direct-to-patient shipment of medicines. Patients save more time by utilizing internet hospitals because this reduces long commutes to tertiary hospitals (unless a doctor on a telemedicine platform determines that an offline referral is necessary). Many internet hospitals are growing in China to improve primary healthcare since physicians are concentrated in tertiary hospitals:

> *"Healthcare resources mainly focus on the specialty and big hospitals. So then the IT startups created a concept called internet hospital, [and this] platform mainly focus on the primary care… So that's [the] main reason that China has so many growing internet hospital area."*
>
> *– KOL #15*

Telehealth is much broader than just internet hospitals and can include any apps and platforms (including virtual clinical trial platforms) that provide digital health services to patients, as well as continuing medical education, provider training, and administrative meetings.[129] It also includes allowing providers in rural areas to perform diagnostic tests and send images to centralized imaging centers to be read:

> *"Many of these district hospitals or community health centers, they previously do not have a lot of capacity to do sophisticated diagnostics. So patients would have to go to large hospitals very far away. And now patients can just go to the nearby hospitals, do the tests and the test would be then sent to some centralized imaging centers to be read. And then the result would be sent back to the patient and assigned to the providers at a lower level."*
>
> *– KOL #2*

For over 1 billion users in China, Tencent's WeChat app is the predominant form of communication—for social media, mobile payment, messaging, and healthcare. WeChat mini-apps/programs are sub-applications within the WeChat ecosystem (similar to the App Store for Apple or Google Android), and the WeChat Health Mini Program received access to the digital healthcare reimbursement system in 2020.[130] HCPs spend a lot of time on WeChat because it is one of the key channels of online engagement between patients and HCPs. Many of the mobile apps used in China are through WeChat, since most of the population uses WeChat as the central "super app":

> *"And within WeChat, they can pay, they can order food, they can access their health care information, they can receive some of the therapies through their mobile app."*
>
> *– KOL #17*

Companies also choose not to develop new apps because everything is done through WeChat:

> *"With WeChat, we can do almost everything and within WeChat, there's also a very big ecosystem. Actually, the WeChat ecosystem is no smaller than the Apple App*

Store, because so many people or many brand owners or many companies chose to develop WeChat-based mini-app, rather than develop a pure new app."

– KOL #18

For many disease areas in China, the first barrier is that there are still so many patients unaware of the disease or who are aware of the disease but it is not managed (e.g., hypertension and diabetes).[16] Therefore, apps are also a powerful tool for health literacy, home disease management, and medication adherence—even amid side effects. They have the potential to improve the patient journey, wellness, and health outcomes by conveniently empowering the patient to take charge of their own health. For instance, one KOL spoke of how an app could send reminders to non-small cell lung cancer patients to eat certain types of foods at certain times to reduce nausea and vomiting from their treatment:

"And so we were thinking that we would create an app that would give notifications to patients, 'did you eat your breakfast this morning? What did you eat for breakfast? Did you follow the guidelines?' So the guidelines would be, for example, a low-fat breakfast and not to have a high-fat breakfast, and especially not to have no breakfast. So it would remind them of that, and then it would explain… Here's why you should [adhere to this type of diet]. And the ultimate goal is that you stay on your treatment. Ultimately, you'll live longer, right?"

– KOL #5

In addition to telehealth and disease management, apps can be used for vaccine reminders and safety surveillance. For example, this could make Takeda's dengue vaccine launch more successful since it is a two-dose vaccine and an app reminding people to get their second dose would be important for vaccine effectiveness and herd immunity. This app could also be utilized to allow vaccinated individuals to report adverse events. Outside of vaccines, mental health is another therapeutic area where apps have great benefits to patients. Mental health-focused apps allow, for example, Cognitive Behavioral Therapy (CBT) to be delivered through a mobile platform, which makes therapy more accessible and portable. Self-harm and violence was the tenth cause of death in China in 2019.[107]

AI, Wearables & Other Emerging Tech

Artificial intelligence (AI) was the second most mentioned type of digital innovation, comprising 27% (n=31) of 115 excerpts for the theme of digital innovation type. This was followed by wearables, RPM, & other IoT devices with 25% (n=29) of 115 excerpts tagged. AI algorithms are useful for predicting disease, preventing worsening of symptoms and disease progression,[ix] and predicting how patients respond to different treatments and devices. AI and big data can train algorithms to quickly diagnose rare disease patients:

> *"So if we can use AI or big data to train some algorithm to quickly diagnose the patient, even quickly diagnose the high potential patient, that'll be very good for… screening patients to let them know, maybe they have this kind of disease and then they can go to the hospital to get further treatment."*
>
> *– KOL #13*

For Takeda's lysosomal storage disease franchises, deep learning can be performed on facial images to predict whether a patient has a genetic or hereditary condition. Takeda also supports initiatives that have very high value, including several machine learning solutions across the molecule lifecycle. For injectables and home health care, augmented reality can assist patients in assembling the injector and preparing injection medications (such as for HAE) to ensure that they are getting the correct dosage consistently. Virtual reality can be useful for distraction therapy, either during infusions or for Takeda's oncology patients who are enduring pain secondary to their cancer.

Wearables, implantables, digestibles, and other IoT devices that support digital biomarkers are useful for developing digital endpoints in virtual/hybrid clinical trials across a variety of disease areas, such as neurological and gastrointestinal disorders:

> *"For our narcolepsy assets, we are looking into using wearables to track sleep patterns, [also] to look at the efficacy of our assets that are currently in early phase*

[ix] Feedback from data can be used to advise patients in better managing their symptoms. For instance, AI could analyze an IBD patient's diet and suggest healthier diets to prevent flares and disease progression.

one trials for Parkinson's disease in Japan. We're using wearables to look at clinical outcomes of our patients to better care for them. For oncology, we're looking into using wearables to predict morbidity."

– KOL #9

Wearables or other IoT devices are a great tool for passively-acquired data, which ultimately is more accurate than patient recall or self-reporting. However, digital data from these tools is typically almost overwhelming in terms of quantity, so Takeda needs to identify biomarkers that suggest disease or health and are sensitive to the change that researchers are trying to induce or describe. At Takeda, these tools are chosen by fit-for-purpose analyses for inclusion in trials. These analyses assess feasibility from a technical perspective, clinical perspective, and patient perspective. For instance, a clinical trial team at Takeda has a project that uses visual capsule endoscopy, where patients have to swallow a very large pill that has a camera inside of it. The camera takes a picture of their intestine so that a clinician can look through and assess any intestinal damage:

"Well, if you tell a patient, 'Could you swallow that?' It's probably not something they would want to do. Except, if you put it in context of well, it's either that or…this endoscope that's like three and a half feet long to…look in your intestine…It changes completely the value proposition, right?"

– KOL #4

These digital tools for innovation often overlap and enable each other to work. Supplemented by AI, apps and IoT devices are useful lifestyle management tools for patients with chronic diseases, especially after COVID-19 hit China and chronic disease care was interrupted at facilities:

"After COVID-19, I think patients are willing to change their life behavior to get their disease under control, and also use some digital tools to help them get the behavior. Like wearing some devices to track their heartbeat or to track their diet, or their fitness frequency, and to provide some personal care. So, I think this…changes the patient journey."

– KOL #13

Digital lifestyle management tools are examples of employing digital technology as a service (vs. digital as therapeutics) because they may play a big role in behavioral change, which leads to better health outcomes than medicines alone:

> *"If I take China for instance, or US or India, one of the big problems they have is diabetes and all those different lifestyle-related diseases today. And one of the most important innovations you can do in digital, it's lifestyle management. It's how you can change the habit…if you look to COPD, and cardiovascular disease, and diabetes, I think lifestyle management is the most important piece because you want to change the habit and you want to keep people healthy and prevent they are sick. And digital can help a lot."*
>
> *– KOL #11*

Drones and robotics are also becoming a trend in China for digital transformation. Drones would be quite useful for last-mile delivery of vaccines in remote areas and would drive more uptake of vaccines. The combination of robotics and 5G technology allows for highly-detailed and precise surgeries to be performed remotely with little to no time lag:

> *"We saw an experiment for surgery. In the past, we never imagined that a doctor can do the surgery [remotely] because there's still time latency in this area and your video resolution should be very high [to] make sure that most person can see it very clearly. And then the time latency should be very, very short. So with 5G, we saw that it is possible. And there was a doctor that operated the bot, or machine, to finish the physical operation remotely. And with 5G, we can make it possible."*
>
> *– KOL #18*

Big data

Big data describes large, complex, and/or fast volumes of data that are used for advanced analytics and decision making. Real-world data (RWD) and real-world evidence (RWE) are two subsets of big data. RWD is data relating to patient health status and/or the healthcare delivery routinely collected from sources such as EHRs, product and disease registries, mobile devices, claims and billing, and patient-generated data from home IoT devices.[131] Derived from the analysis of RWD, RWE refers to clinical evidence regarding potential benefits, risks, and usage of a medical product. RWE is generated from RCTs (Randomized Controlled Trials), pragmatic trials,

and observational studies.[131] Two of Takeda's digital strategic priorities are an enterprise data backbone and RWE platform, to validate that digital therapies will work for patients. One of Takeda's RWE studies is a multiple melanoma study with the medical affairs team in China.

Big data is also being used for an HCP micro-segmentation project to improve Takeda's internal efficiency and understand academic trends and needs of physicians in China. Furthermore, partnerships that focus on AI are useful to analyze big data, and big data companies can provide data scientists to build algorithms for Takeda in particular treatment areas.

Health Information systems and vaccine technology

For vaccines, QR codes are on secondary containers that hold packs of vaccine vials but not primary, individual vials. The innovation of having QR codes for primary vaccine vials is something that WHO has been trying to get resolved for decades. This would mean that a child or adult could go in for a vaccination, the vial would be scanned, and that individual's vaccination information could be fed into an Immunization Information System that records the antigen, manufacturer, lot number, date, volume, and other details. This would allow for more accurate Immunization Information Systems that could link immunization history with various clinical outcomes (e.g., allergic reactions) if connected to Electronic Health Records. QR code digitization of the Immunization Information System and linking it to EHR would provide opportunities to understand vaccine safety as well as effectiveness, and know when a certain level of herd immunity has been reached, who was vaccinated, what age groups were vaccinated, and which geographic areas have been missed:

> *"One of the big issues in developing countries is that when you try to track who's gotten vaccinated, who needs another dose…all that information is recorded in these huge logbooks. And we've heard that the pressures of time at some of these immunization sites… some of the entries are just made up, they don't put in the entries, or the logbooks can get messed up for legitimate reasons. It would be so much simpler if you could have this information that is being handwritten into a*

logbook just by scanning the code, and entering a child's name and ID…all of that just gets accurately and automatically entered."

– KOL #7

Vaccine temperature or cold chain monitoring is another useful application of digital technology. Vaccines must be kept within certain temperature limits and when vaccines are shipped, there is a recording device called a temp tail, which continuously monitors the temperature inside the box. This can be downloaded later to see if there have been any temperature deviations. An innovation in vaccine temperature monitoring once vaccines have reached health facilities could be smart refrigerators:

"In a way similar to that temp tail, if there was a way to really monitor that continuously, send[ing] warnings to an app that the nurse or doctor has… I would think that [a] built-in system like that might be attractive to practitioners. If a company could kind of own that kind of integrated system, that would potentially be attractive. So temperature monitoring, cold chain monitoring would be another application."

– KOL #7

Virtual/hybrid clinical trials

Accelerated by COVID, Takeda leverages e-clinical trial platforms that can help run clinical trials in a more decentralized, patient-friendly manner. For decentralized or hybrid clinical trials, at least one clinical assessment is done outside of the clinic. These employ digital tools such as eConsent, ePRO (electronic Patient-Reported Outcomes) and e-diaries, and eCOA (electronic Clinical Outcomes Assessment). It is more convenient for patients or care partners to do many evaluations from home, such as ePRO. For example, e-diaries are useful for helping care partners of patients with seizures log the type and frequency of seizures:

"We have a recent concept of a team in TDC Asia that wants to engage with care partners, for two rare diseases for seizures and epilepsy. And from their phase two clinical trial feedback from their KOLs… it's really important for care partners of these individuals with seizures to be able to distinguish what type of seizures. So when they design the phase three trial, they can use e-diaries in order for the care

partners to log in the type of seizures and the frequency in which the seizures happen."

– KOL #16

An ePRO is easier for a patient to remotely complete compared to a paper PRO and it can also improve data quality, and research has shown that mean compliance rates are higher in patients keeping electronic diaries versus paper diaries.[132] During the outbreak in China, WeChat was used by research institutes, biotech companies, and healthcare media to organize webinars on different R&D approaches to support ongoing clinical trials or developing a treatment.[39] The most popular ePRO platforms are currently mobile apps and the WeChat Mini-Program.[132]

Intelligent clinical platforms can also obtain patient data in multiple ways.[132] As an example, remote data monitoring systems (including file scanning devices and the Patient Management app) allow self-reporting of patient data, and the WeChat Mini-Program platform features ePRO, DTP (Direct-to-Patient), and visit reminder utilities. Full-process intelligent clinical platforms also offer pharmacovigilance, safety, regulatory submission, and AI image evaluation functions.[132]

To streamline the virtual clinical trial process and follow the corporate philosophy of PTRB ("Patients First"), Takeda focuses on using suppliers that have multiple capabilities all on one platform instead of having a fragmented offering, such as starting as a telehealth company and then adding on eConsent or ePRO through the acquisition of other companies:

"And the feedback we got was, while they worked, they're not great. And we focused on suppliers that built their platform from the ground up with all of those functionalities already in mind. So the three suppliers we're using, built their platform from scratch with eConsent, telehealth, ePRO, eCOA, and streaming of data from wearable devices from the get-go."

– KOL #6

4.2.4. Thematic Area 4: Cross-functional collaboration with health ecosystem

For digital innovation to be successful, cross-functional collaboration with various health ecosystem stakeholders is crucial. Most respondents mentioned pharma collaboration with big tech players, Public-Private Partnerships, healthcare professionals (HCPs), biotech startups/scale-ups, and academia. The type of partnership depends on the specific needs and purposes of various teams at Takeda. In October 2020, Takeda held a China Digital Innovation summit with leadership team members and seven digital healthcare ecosystem players. This summit received much media attention and successfully established Takeda's image as a pioneer in digital innovation in China. Takeda China and these seven digital players committed to build a digital innovation ecosystem together, address major challenges, and create value for patients and healthcare providers.

Big Tech

When discussing partnerships, big tech players represented 42% (n=30) of the 72 excerpts that were coded for the theme of health ecosystem collaboration. Tencent WeChat and WeDoctor, Alibaba Health (AliHealth), and Ping An Good Doctor were the top 3 discussed big tech companies. Big tech partners are useful because they provide digital and technological expertise, scale, and it is incredibly difficult for a pharma company to build their own platform and roll it out system to system:

> *"We need to be quite clear about what we need from these partners. For example, if we are asking or expecting a lot of internet traffic, then we definitely need to partner with those big internet giants because they have a lot of traffic. And they also have a material competence."*
>
> *– KOL #18*

Some KOLs thought that it is necessary to partner with a big tech company to be successful in China's digital healthcare space:

> *"Since I think everything is just run through those kind of super apps, I think we're going to have to. I think that also provides you with some scale that you wouldn't*

get if you were to try to do this on your own, and rolling it out from system to system there is really hard. And so I think utilizing a big tech partner, one) may be mandatory, but two) will certainly help from a scale perspective…the larger the partner is, it may be one of the only approaches that we have there."

– KOL #17

"To be a fast mover or quick mover is very important because in China, they have many digital health companies, but they have a small number of main players. For example, Baidu, Alibaba, they already have like e-commerce or search engine platform, then they created the healthcare tech solution on top of it…so it's very important to be a partner with these large companies."

– KOL #15

Takeda has also run some pilots in China through WeChat, such as to support IBD patients on Entyvio® for improved health outcomes. Integrated personalized care with embedded telemedicine solutions helps patients care for themselves better:

"And we're seeing an example of this with our product Entyvio…the common cause of exacerbations is essentially the inability to recognize the symptoms that are going to lead to an exacerbation…And you know, we are developing solutions, one of them is in production. It's a WeChat app that helps patients recognize those early on and then engage their physicians through WeChat for them to care for themselves better."

– KOL #9

Essentially, all MNC (multinational) pharma companies are partnering with big tech companies in China, but these partnerships seem more 1:1 than consortia that include multiple pharma companies:

"Merck also have the innovation incubation in China and they are also able to build the ecosystem to collaborate with some startup and also with some big technology company. And for the big technology company like JD, Alibaba, Tencent… every MNC company in China, they are all collaborating with these companies. Novartis is collaborating with Tencent to build the digital therapy for the patient. And I think…Novo Nordisk….are also collaborating with Alibaba to build the ecosystem. And for Sanofi, they are also collaborating with Ping An Technology to build the digital therapy for the type two diabetes patients as well as leverage the Ping An technology; they are building the CDSS for the hospital. CDSS stands for the clinical decision support system for the hospital."

– KOL #13

Not only have many pharmaceutical companies collaborated with big tech internet hospitals to provide telemedicine services, but they also collaborated to sell their medicines online and to follow up with patients to improve their Directly-Observed Therapy (DOT):

> *"Pfizer, they invest on one internet hospital, they are putting a lot of money for that internet hospital and they are also putting a lot of virtual reps on their internet hospitals. So this is kind of the trend. And for other pharmaceutical company like Sanofi, like Novartis, they are collaborating with multiple internet hospitals like Jingdong, like Alibaba. They kind of defined the internet hospital as a role of the drug seller."*
>
> *– KOL #13*

Biotech startups/scale-ups

One KOL stated that if the focus is commercial, big tech partnerships are useful since they have a bigger pool of data and more experience in digital healthcare. But on the R&D side, biotech startups and scale-ups are great for building custom solutions geared toward specific therapeutic area needs:

> *"But from the development perspective, we may not necessarily leverage on Ali and Ping An for such information, but somehow we may be focusing on the specific therapeutic area. For example, a rare disease, then we might be focusing on the startup biotech or smaller companies, which is specialized in the areas [and] which is more focused."*
>
> *– KOL #8*

However, the startup regulatory landscape in China may not be as mature as in the West and the fragmentation of China's healthcare system can make it challenging to implement digital solutions from startups across various geographies in China:

> *"If you want to build applications, scalable applications, you do have the big partners that can build more table stakes solutions. But if you want to build custom solutions that address the specific needs of patients across our therapeutic areas, it's harder to achieve that because the market for developing such solutions, the landscape of startups, is not as mature as you would find in West—and with regards to how you implement that, associated with the fragmentation of the healthcare system, the clinical workflows, how they run the adoption needs."*
>
> *– KOL #9*

When discussing the benefits and potential of startups, some KOLs discussed how startups may not have enough financial resources to commercialize their solutions (even if they have the proof of concept), but Takeda is interested in partnering with them because their technology could help address unmet needs in specific disease areas:

> *"There are a ton of very cool, small—some well-funded, some not so well-funded—startups that are focused on… all points along the patient journey. So whether it's a mobile app, or whether it's a symptom checker or something that helps the patient get to a faster diagnosis, if it's a rare disease…There are so many interesting companies out there. I think we can really capitalize by partnering with them, learning from them. It's a win-win for us, it's a win-win for the company, it will certainly be a win for the patient."*
>
> *– KOL #17*

> *"I think we aim to build the ecosystem of the health industry in China. I think Takeda is playing the role to building that ecosystem. So for that ecosystem, one part [that] is really important is to bring new ideas, new initiatives, and new technologies into our company. That's the reason we want to leverage the startups in China, because…they're very booming in China and also have a lot of advanced tech knowledge."*
>
> *– KOL #13*

Public-Private Partnerships

Public-Private Partnerships (PPPs) represented the second most discussed type of health ecosystem collaboration, with 37.5% (n=27) of 72 excerpts tagged for the theme of health ecosystem collaboration. When most respondents discussed PPPs, they focused on 1:1 partnerships (e.g., Takeda and a local municipal government) as opposed to consortia. For certain projects, Takeda has collaborated with non-profits such as the China Red Cross Foundation, which is government-operated. As with the big tech companies, it is considered prudent to partner with the Chinese government in some capacity if MNCs want to be successful in the digital healthcare ecosystem. Sub-national entities can be evaluated throughout the country for PPPs that align with the local government's unmet needs and Takeda's therapeutic area interests, whether this is for public health purposes or running analytics for rare disease early diagnosis:

"Well, I think it's almost essential in China…where working with the Chinese government gets you a lot further along than in other countries, if you really have something they want. But it could be on a municipal level…When I was at [another pharma company], we were partnering with this anti-epidemic station in a particular province. And we chose that particular province and that particular anti-epidemic station because they were a good example of a well-functioning health department."

– KOL #7

"And with regards to Public-Private Partnerships, we are, for example, looking into starting a partnership with the government in a city …where 200 hospitals through the mandate of the government to that city has put together their medical records into one hub, which we help to tap into, to run analytics for rare disease early diagnosis, but also a number of other use cases."

– KOL #9

Consortia can bring together a dozen partners to more than 80 partners in a single project. When speaking about how consortia could help advance Takeda's goals in China, one participant discussed how it may be easier to tackle challenges and raise awareness as a larger group than one or two individual organizations:

"One of the aspects that these consortia could help with is break[ing] down some of the barriers that might exist, and I think these barriers will vary from place to place…China's a really, really complex place... So, if you were trying to help patients in a really remote rural part of China get access to really quality care, where telemedicine, for example, could really help to give them that access…the other partners in the consortia could help to think of effective ways to facilitate that kind of access."

– KOL #10

In the neuroscience therapeutic area unit (TAU) at Takeda, a KOL discussed how PPPs were looking at the use of digital devices to collect data and help scientists develop therapeutics to address the needs of Parkinson's patients. PPPs (such as a pharma company and academic institution) can also create a good use case or case study in innovative healthcare solutions; this case study outcome can then be brought to a government and help them fine-tune their policy based on new scientific evidence. If this outcome can be used in other clinics and hospitals, Takeda can

publish this case study as a white paper or another publication for physicians to learn and apply it to their daily work.

HCPs, KOLs, hospitals, health departments

The third most mentioned type of partnership was with HCPs, KOLs, and hospitals or health departments. This type of partnership represented 31% (n=22) of 72 excerpts tagged for health ecosystem collaboration. This collaboration is useful for educating HCPs to understand the intricacies of therapies at Takeda, such as how protein cell line inhibition therapy or injection therapy (e.g., Ninlaro® for multiple myeloma) can improve patient outcomes. This will help HCPs understand the potential value of Ninlaro® or other Takeda brands for patients. Collaboration with public health teams, such as at health departments, can help Takeda understand their specific needs and current trends to determine where to add value with digital transformation.

Physician societies and KOLs can help Takeda really understand patient needs in specific therapeutic areas as well as the gaps and challenges that arise with implementing digital solutions in certain provinces, municipalities, and rural areas. For rare diseases or other specialty areas where awareness is sorely lacking, Takeda can help educate physicians and KOLs through online campaigns so that they can better diagnose and treat patients and in turn, educate patients and the public. Collaboration with physician societies and KOLs could produce an online broadcast that brings widespread awareness of disease as well as telemedicine or other digital solutions that Takeda has for specific therapeutic areas. This could then be picked up by news outlets and covered nationwide (such as when Pfizer launched their cardiovascular disease internet hospital with CausaHealth). KOLs talked about partnering with Dīngxiāng Yuán (DXY), which is the largest online physician community in China and is backed by Tencent.[133] DXY began as a knowledge-

sharing platform for doctors but later incorporated wellness advice and medical consultation for the public:

> *"They're also some partners providing physician education capabilities. For example, like DXY...in China, it's very famous. DXY is the largest physician community of online digital. So they provided a precision-targeted approach for pharmaceutical companies based on their understanding of all the big online physician fields, as well as their data."*
>
> *– KOL #18*

Furthermore, to do initiatives with multiple hospitals, it is important to engage with local government or else solutions will not scale across geographies:

> *"Of course, the hospital is very important. KOLs, key opinion leader, as well as local government. If we want to do some initiative [with] more than one hospital, we need to engage with local government. Can be city government, different county government or prefecture government, province government. Because without government support, solution will not scale across the geography."*
>
> *– KOL #15*

Academia

Collaborating with academia is also necessary for pharmaceutical companies to maximize their potential in China's digital healthcare ecosystem. Universities have concentrated research capabilities in specific disease and innovative technology areas. They are considered important future drivers of innovation trends, can also provide mass storage for big data, and professors can give guidelines on the correct path for the health tech industry:

> *"So, I think this [academia] is the backbone of our knowledge base of our innovation. And also, I think Harvard or other university, they are standing in front of the high technology happening. So they know very detailed about what's happening globally... I think they also can bring us this new idea – what they see [are] the trends for the particular areas like 5g or IoT device. I think they [are] kind of like a lighthouse for us to let us know whether this is possible or whether that is not the trend of the health industry."*
>
> *– KOL #13*

Takeda has been in discussion with multiple research universities in China, such as Shanghai Jiao Tong, Fudan, and Tsinghua universities. These universities are leading the way and

are well advanced in health technology; much research in data and AI is coming from China. One participant discussed collaborating with a physician and academician who specializes in HAE patients. He has a catalog of 500 HAE patients and is the sole physician to which HAE patients are referred:

> *"And he's an academician in one of these hospitals. So yes, we are looking into partnerships with academia. But I would say that, that is evolving a little slower. And to activate such partnerships, we have to build relationships with the senior administrations of those universities and affiliated training hospitals. And also, if we're going to tap into patient data, coming to agreements with the local governments, but that takes time to build."*
>
> *– KOL #9*

4.2.5. Thematic Area 5: Data governance

Data is critical for good digital intervention; otherwise, it is just a service. Data provides a feedback loop from digital tools and allows for more advanced analytics, scalability, and enterprise-level initiatives. Effective data governance is necessary to secure patients' personal information, ensure privacy, and get the best quality data. For this theme, the most talked-about issue was data access, sharing, and ownership, representing 54% (n=21) of 39 excerpts tagged. Data access, sharing, and ownership are barriers to entry for MNCs that wish to operate in China. Pharmaceutical companies cannot own the patient data or directly access data for Chinese patients, even when implementing their own telehealth or other digital solutions:

> *"As a pharma company, the government says…you don't own any of the data. And all healthcare system or governments, policymakers are sensitive, but in China, it's a clear cut 'NO…' We have to have very serious discussions with our external partners to have at least anonymized data, some sort of analytics to know how to improve the solution or just to get a sense of 'Are we on the right track or not?' So there's really a lot of resistance there on data ownership or data access."*
>
> *– KOL #12*

Since Takeda cannot access patient data directly, an external partnership with a local Chinese company is required. This affects the type of partnerships that Takeda can leverage. For

instance, Takeda is not always able to use some existing global partnership for China digital initiatives because some of the existing global vendors may have a relationship in the US, but they may not have operations in China. Thus, they cannot access data with Chinese patients:

> *"For example, the HAE algorithm, we do know a few global company, they might have an HAE algorithm, but because they don't have office in China, they cannot bring the data outside of China… so that is another challenge, looking for the partnership to work on some digital initiative."*
>
> *– KOL #14*

> *"I think the government has a very strict regulation on the data accessibility. So also when we work with different third-party, we actually need to ask if they can share any HCP or patient data and they all say the answer is no…this is a very serious regulation."*
>
> *– KOL #14*

An added layer of difficulty is that all patient data are stored in individual hospitals in China and controlled by the hospital. Data is very siloed in China and is not portable outside of China or from hospital to hospital:

> *"From what I understand, it is still very siloed from hospital to hospital, and they have them in a very tiered structure… depending on the cities and the size of the populations. So I do think the data piece of this is really difficult in China…Data is not necessarily portable, it's very siloed there."*
>
> *– KOL #17*

Data governance typically also encompasses data transparency issues, such as who will see it, for what purposes it will be used, and for how long and where it is going to be stored. This transparency increases trust, allows patients to be involved in digital solutions, and lets patients know that Takeda respects them. Data transparency is also closely tied to data privacy, and explicitly stating why Takeda is using particular devices helps alleviate patients' concerns about data leaks and unintended consequences. For example, for narcolepsy (orexin agonist) studies as part of the neuroscience TAU (Therapeutic Area Unit), patients sleep with a special bonnet that measures EEG waves and directly reports the sleep quality or duration of the previous night:

"So for the example of sleep that I gave earlier, that was actual feedback we got, it's kind of creepy that you're going to be monitoring my sleep every night. But if we explain to them that people are notoriously bad at self-reporting quality of sleep, and there's data out there to show that people wake up in the morning, say, 'Oh I had a terrible night.' But if you look at the sleep data, they actually had a beautiful REM cycle. And they went in and out of the four stages of sleep, and they got at least seven hours. So it wasn't great, but it wasn't terrible."

– KOL #6

If devices are going to be used in a seemingly invasive way, it is important to let patients know that Takeda is doing this to provide better data quality (since self-reporting is often inaccurate) and collect a more representative sample from passively-acquired data. Passively-acquired data also reduces the patient burden. If patients know these things, this increases clinical trial enrollment, retention, and completion. Passively-acquired data also allows clinical trial teams to shorten the study time:

"Frequently, we require you to report two months of sleep data. But if we can get more accurate, more reliable data, instead of monitoring sleep for two months, we can monitor it for a week. And that's a concrete example given to me by a supplier. For a study that they worked with another sponsor, one week of directly recorded sleep data was of such better quality…it saved them two months of self-reporting. So when patients hear that, they said, 'brilliant, I would wear it in a heartbeat. If you're telling me I don't have to fill out a form every morning for two months, instead, I just need to wear a cap for two weeks or a week, sign me up. I'm in.'"

– KOL #6

Therefore, passively-acquired data from wearables and other IoT devices is key to better clinical trial design, conduct, and recruitment. According to the aforementioned KOL, it can allow a team to finish their study six months earlier and get the statistical power with half as many patients (in one example) because the data is of higher quality from direct monitoring, as opposed to self-reporting. However, the challenge is understanding how to analyze the continuous data and which data points are meaningful.

Takeda engages data transparency and data sharing colleagues to advise and ensure that everything is being done to protect and secure patient data. Privacy breaches carry significant

media attention and could greatly affect Takeda's reputation, which would impact patient participation in trials/patient programs, public trust, and shareholder confidence. This is especially important for consortia-style PPP projects where Takeda may contribute data and samples. Takeda has very stringent processes and SOPs (Standard Operating Procedures) for data security, is transparent about them with patients, and frequently does proactive evaluations on technology to ensure that privacy is being protected and any vulnerabilities are identified and rectified early:

> *"As we reached out to patients early on as part of this co-creation process, there were worries about being monitored, they were concerned of being lab rats and constantly watched—kind of a big brother feeling. And so we asked them, What would help you mitigate for this? What would make you more likely to say yes to this, and they said two things: sharing the steps you've taken to ensure our data security and data privacy. And that's an easy one, Takeda is very stringent from both a legal perspective and a quality assurance perspective.*
>
> *All our suppliers are audited, and we make sure that all our suppliers meet the highest standards, not just the bare minimum, but the highest standards. So with regards to have you done penetration testing recently, have you hired an external group to try to hack your system so you know where your vulnerabilities are? You're not reacting. You're proactively identifying where those vulnerabilities are. What is your downtime? Where are your backup servers? When was the last time you tested your backup service?"*
>
> *– KOL #6*

One way that Takeda works to secure data privacy is through anonymization. Once data comes into Takeda, there is not only carefully defined and limited sharing of that data during a clinical trial but the data is associated to a code number (not a patient), as is standard in the industry:

> "*And I think if you can convince patients that everything is being done, that it's possible to secure their data, and make sure they understand what the data is that's going to be collected and what it's going to be used for, then I think, generally, they're fine with it, especially if you're making them aware that it's going to be de-identified, and aggregate data is going to be what's analyzed… I think they're quite comfortable with it."*
>
> *– KOL #5*

On the other hand, if medical records are anonymized, aggregate data can be analyzed by AI but the outcomes cannot be brought back to patients in a personalized way. Each patient's pain points or symptoms can be different, so there needs to be a balance between protecting patient privacy and bringing the value back to the patient. Part of this is addressed by the fact that the patient management is being provided by the medical care team in the clinic, and this team knows and closely follows the patients. However, the determination of the efficacy and safety is part of the clinical trial conduct which may be at a distance, especially in sponsor-run clinical trials.

4.2.6. Thematic Area 6: Therapeutic areas and assets

Digital innovation can essentially benefit all therapeutic areas and assets. However, the ones that were mentioned the most by participants were rare disease, neuroscience, oncology, and gastrointestinal diseases (e.g., IBD), which are important TAUs (Therapeutic Area Units) at Takeda.

Rare disease comprised 37% (n=34) of 92 excerpts for the theme of therapeutic areas and assets. One of the five strategic pillars for the Digital Advisory Board (which develops the strategic digital agenda at Takeda) is rare disease early diagnosis. Takeda patient engagement teams have presented at CORD (China Organization for Rare Diseases) meetings and noted how the China FDA (CFDA) was very open and forward-thinking to what the patient community was needing and wanting in terms of accelerating rare disease pathways to approval:

> *"It was only very recently that China started looking at requirements for trials to be conducted in China, versus global trials that had sufficient evidence of safety and efficacy in Chinese patients. And so there's been a pretty rapid evolution in the openness to global trials and every trial that is FDA or CFDA approved doesn't have to be conducted necessarily in China if it meets certain criteria."*
>
> *– KOL #1*

One of Takeda's treatments for HAE (hereditary angioedema) is Takhzyro®. KOLs expressed that much of Takeda's efforts surrounding rare disease early diagnosis are focused on

HAE. One digital innovation to identify HAE patients is using an AI algorithm to help confirm HAE diagnosis. In addition, during and after COVID-19, several academic meetings were launched online instead of offline to secure continued support, and online academic meetings will provide a very good opportunity for Takeda to understand and also lead the trends of the health industry in areas such as HAE. There are limited physicians and hospitals that can treat HAE in China, and online education campaigns can increase awareness and efficiency in diagnosis and treatment:

> *"So based on the previous interview with a patient for HAE, it will take the patient like 7 to 10 years to go to the right physician and the right hospital. So I really think the digital online part can improve this efficiency, can direct the patient to the correct physician and hospital to get the right treatment."*
>
> *– KOL #13*

Because of this delay in diagnosis due to lack of familiarity with the conditions, Takeda is exploring innovative ways to identify rare disease patients, such as by applying machine learning to medical records. This involves putting forward patient-facing solutions to collect ePROs (electronic Patient-Reported Outcomes) that can infer whether a patient is a rare disease patient.

Neurological disorders represented 24% (n=22) of 92 excerpts for the theme of therapeutic areas and assets. These include narcolepsy, Parkinson's, cerebrovascular disease, Alzheimer's, and mental health. Digital innovation for Parkinson's includes wearables to determine, for example, reaction times or mobility to see if the drug is efficacious. While most digital innovation is patient-facing (e.g., sleep bonnet to measure EEG waves in narcolepsy patients), some of it also revolves around internal digital innovation capabilities to share insights about different diseases from the patient perspective with other teams across R&D and the enterprise, as well as across different regions and disease areas. An example of internal-facing Takeda innovation is a digital AI platform that acts as a research analyst and database to pull together insights to address a particular question

through natural language processing, and tagging of work products that are uploaded into that system:

> *"And in that way, we would have access to many more insights across the organization to inform the team that's looking at questions, like what do we know about how narcolepsy is perceived in China, and the patient experience in that culture, as opposed to the patient experience in the US or the UK, for example."*
>
> *– KOL #1*

Oncology also represented 24% (n=22) of 92 excerpts for therapeutic areas and assets. As described by participants, digital health can improve both the diagnosis capabilities as well as the long-term care plan and patient follow-up for oncologists. One digital initiative at Takeda is providing some diagnostic AI tools for physicians to interpret results of gene mutation testing and improve usage of such data within hematology and solid tumors (lung cancer). Another digital oncology initiative is to build machine learning-based micro-segmentation models to understand the needs and knowledge of HCPs, in order to provide educational information on Takeda's multiple myeloma drug Ninlaro®. This is the first step in providing a pathway to patient access to vital drugs. In addition to educating our physicians on the latest new oncology modalities that are made available, digital innovation is also important for sharing efficacy data of our medications and looking into label expansion opportunities since several medications are now targeting mutation-specific cancers.

For oncology in general, traditional clinical trial endpoints (such as survival rate after a certain number of months or the size of tumors) do not capture a full picture of the patient's wellbeing, so efforts are made to explore digital tools that could help capture more meaningful data about the quality of a patient's life while on treatment:

> *"Saying that someone survived the next six or eight months on a cancer drug doesn't tell me if those six or eight months were happy, productive, meaningful six or eight months or were miserable, right? So I think we can leverage tools or we can build digital tools that can almost non-invasively, or minimally invasively, give*

us these data and show us that maybe we're only extending a patient's life by four months instead of six. But those four months are happy and meaningful, rather than miserable in the hospital. And I would imagine that, that would be more important."

– KOL #4

However, oncology is an area where digital endpoints are less developed. While the above is aspirational and could tremendously transform patients' qualify of life, there is still a long way to go, even though Takeda is working on RWE and with regulators to find new ways to improve oncology digital endpoints.

Gastrointestinal (GI) disorders, including IBD and Cyclic Vomiting Syndrome, comprised 21% (n=19) of 92 excerpts for the theme of therapeutic areas and assets. For Cyclic Vomiting Syndrome (CVS), Takeda's patient engagement advisory board has brought wearables to patients to seek out their perspective and include it into the design of the clinical trials. The process of choosing appropriate wearables factors in patient comfort for wearing a device for a certain duration of time during the CVS trial in addition to other aspects (e.g., ease of use, accuracy and reproducibility of the data, and technical and clinical validation of such tools). For IBD, digital devices can be at-home fecal or blood tests that personalize the care when collecting patient data. Flares in IBD are very serious and home devices and AI algorithms for predicting flares have the potential to greatly improve patient lives. AI and other tools can also be applied to the analysis of patient diets for studies in Takeda's large GI portfolio. For example, patients do not have to take time and write a food diary because they may instead take a picture of what they ate.

4.2.7. Thematic Area 7: Improvement of the patient journey

Digital and technological innovation considerably improve the patient journey by empowering patients to have more control over their lives and be more involved in their own healthcare. Takeda is thinking of the following areas in the context of improving the patient

journey, such as: patient engagement, health equity, better clinical trial design, conduct, and recruitment, health literacy and disease awareness, early diagnosis and treatment, improved health outcomes and wellness, home health care, improving primary healthcare, and closed-loop care. Improvement of the patient journey represented 45% (n=122) of the total 274 excerpts, which was the largest proportion out of all 8 themes. This indicates that improvement of the patient journey was at the forefront of all participants' minds when discussing digital innovation, which aligns with Takeda's values of "Patients First."

Patient engagement

Representing 41% (n=50) of 122 excerpts tagged under this theme, patient engagement involves Takeda co-creating the patient journey with patients across demographic groups and patient communities, advocacy, and advisory groups. It also refers to better communication between pharma companies, physicians, and patients. Within Takeda, the Patient Engagement Office actively works with patients, patient caregivers, and patient advocacy groups and has a patient advisory board on digital tools. While patient advocacy organizations in China advocate for patients, we are not aware of stakeholders in patient engagement in the way that we typically think of it in the US and Europe. According to KOLs, patient engagement is nascent in China and vendors helping to support patient engagement with pharmaceutical companies are less established. Although there are a few patient advisory groups (PAGs) in China for some specific diseases, many disease areas still do not have a PAG. One participant explained:

> *"Maturity of patient advocacy is very different from country to country. Like US and Europe, patient advocacy is very mature, then they have a very strong voice to government and various pharma companies. They have also been involved in [discussions with] regulators [and] policymaking... But I am not sure that the patient advocacy is mature enough in China. So we need to check the maturity of these stakeholders."*
>
> *– KOL #15*

Engaging with patients is needed to dispel assumptions on how patients actually feel about digital tools. Although patients generally welcome digital tools and feel that they do indeed reduce the patient burden, digital tools that constantly collect information can not only make them wary about privacy but can also increase anxiety about their disease. While health literacy and disease awareness are very important to helping patients make truly informed decisions about their illness, some may consider that ignorance is bliss. This is why there needs to be constant interaction between innovators such as Takeda and patient populations to really understand what the unmet need is for the patient population:

> *"There was an idea that an algorithm could be created if they were willing to put information into an app. And putting this information in the algorithm would identify for them that they were at risk for having an event related to their disease. And the overwhelming response from the patient population was, '**I'd like a disease holiday**,' meaning if I don't have to be paying attention to the management of my disease, I don't want to be thinking about it because when I have the event, I need to visit my physician anyway. So I don't want to know."*
>
> *– KOL #3*

The elderly are an important population for patient engagement, and pharma companies should take great care to make sure that older and/or visually or auditorily impaired individuals are getting the extra support and education that they may need to enable greater use and benefit from technology. Some devices may be technically difficult for them to set up in the home, may need regular maintenance (e.g., batteries to charge), may need to be taken off when showering, or may be uncomfortable. Therefore, engaging with elderly patients is important to build trust to convince them to wear the devices for sometimes quite long durations during a trial. Not only is elderly care part of the Healthy China 2030 and AI development plans (see ***Healthy China 2030 & AI Development Plan***), but remote patient monitoring devices for elderly patients can save lives in times of emergency:

> *"We were providing some elderly people some AI speakers at home, like a health front door to use this AI speaker to help the patient at home if they have some emergency, or they can use this AI Speaker to regularly communicate with their physicians and also to remind them to take medicine. So I really think the at-home hub really can help the patient, and this hub is also a digital tool for them to control their disease."*
>
> *– KOL #13*

Health equity

Health equity comprised 37% (n=45) of the 122 excerpts for improvement of the patient journey. Health equity involves increasing access to treatment, through affordability and coverage of underserved communities in rural/remote areas. Affordability is very important to Takeda and society but presents a big challenge, especially for rare diseases. So Takeda is looking into finding ways to embed digital solutions with insurance (through China's revised reimbursement policies for "internet plus" healthcare) to provide patients medicines that they can afford. To increase affordability for rare disease patients, Takeda will have to successfully negotiate with the Chinese government to get drugs into the rare disease medicine list as part of the NRDL. As mentioned in ***Thematic Area 2: China's unique enabling environment***, the price of successfully negotiated drugs was reduced by an average of 50.64% for pharma companies' drugs that were included in the 2020 drug catalog.

Field force refers to representatives that pharmaceutical companies deploy in the "field" to generate sales (e.g., medical reps, pharma reps, Medical Science Liaisons, and regional market access managers). To expand access to medicines in remote areas, Takeda deployed a digital field force solution to increase field representative coverage in remote areas since offline physician engagement was interrupted due to COVID:

> *"But for those remote, broader areas, they face a problem that the field force may not be able to cover a broader territory. Because the physicians might be very remote and for example, like a very small hospital or even we might not have a hospital, but like a village clinic. And so their coverage efficiency is not that high,*

we just deployed field force digital… this digital model can be add[ed] on to those field force so it can also adjust the coverage, coverage efficiency, and frequency issues."

– KOL #18

Increasing diversity in clinical trials is another way of providing access to larger demographics of patients and promoting health equity. Having a very narrow patient population is a historic problem in clinical trials because it is not representative of all the people who would eventually be seeking treatment with the medicines. One of the main reasons is that many people cannot afford to take a day off to go to a site visit. Therefore, many participants discussed expanding the geographic reach of trials through telehealth because this engages a broader population that is more representative of the population that will actually take the medication:

"Not everybody can afford the time from their families or work to complete all the trial requirements. But if we expand the geographic footprint with telehealth and you don't have to travel anymore, and if we give you flexibility, because many of these tasks you can do on your own time, then we stand a really good chance of improving the diversity of our clinical trials, which is something that is really important to Takeda right now."

– KOL #6

"With regards to patient access, especially in the rare disease area, a lot of the patients may be in geographical areas or in rural areas where it's been traditionally difficult to access these people. And then it's costly as well…if you've accessed a patient in a rare population, to get them to a study center, to get them enrolled in a clinical trial and have them followed up for the timeframe that they need to be followed up for. So I do think that patient access has just been, will just be massively accelerated using digital."

– KOL #5

"Allowing patients to participate in a trial from the comfort of their homes would tremendously increase diversity, at least geographic diversity…I think around three-quarters of patients in trials right now live within two hours of a large academic center. Well, guess what? A very small portion of the population of the world lives within two hours of a large academic center."

– KOL #4

Health literacy/disease awareness

Health literacy represented 16% (n=20) of the 122 excerpts for improvement of the patient journey. Digital communication tools to address health literacy disparities and needs may also increase diversity in clinical trials; trial materials need to be communicated in ways that can be understood by the target communities. While important efforts are ongoing across the industry, there is clearly still room for improvement. Educational videos and materials to increase awareness of drug development and clinical trials aim to foster understanding and are important for earning trust with patients. Having very clear, short, and understandable Terms of Service on apps and utilizing eConsent for clinical trials can build out the toolbox to address health literacy needs. Traditional Informed Consent Forms (ICFs) are typically very lengthy and difficult to understand, so videos can explain components of the clinical trial:

> *"And it's not necessarily about education, because there's gonna be people who are PhD educated and honestly don't understand ICF. So it's around sort of understanding what you're being asked when you participate in clinical trials. And we want to make sure that people understand what they're getting into before they sign the Informed Consent Form.*
>
> *So very recently, we collaborated with organizations to call a script to come up with a video that explains what the different parts of a clinical trial could be in a generalized manner. And we're intending to put that on a platform where as a pilot, we can put not only videos but the actual Informed Consent Form or different resources prior to someone signing up for a clinical trial."*
>
> *– KOL #16*

In addition to study-related materials, digital innovation can increase patients' knowledge about their illness and help them become more physically involved in their own story. Through wearing devices such as an ECG patch on the chest or wearing headbands to record their EEG during the night for orexin agonist studies in treatment of narcolepsy, patients can become much more connected to their body via the device:

> *"So then they start asking themselves, you know, if I'm recording my heart, why are we doing that? How does it relate to me and my illness? And what will that data show?"*
>
> *– KOL #5*

Better clinical trial design, conduct, recruitment

Representing 23% (n=28) of 122 excerpts for improvement of the patient journey, better clinical trial design, conduct, and recruitment is centered around trial flexibility, continuity, and resiliency, reducing the clinical trial burden on the patient, and decentralizing clinical trials (where at least one assessment is done outside the clinic or at a medical facility closer to a patient's home). Trial flexibility is important because the burden of having to travel to sites or do things on a highly regimented timeline limits who can participate in a clinical trial:

> *"The other thing that patients have been asking for, that they explicitly told us was important to them was flexibility. And flexibility means that individuals… have a family life…They could be a mom or a dad and have childcare responsibilities. They have a job that they would like to keep… If we can give patients flexibility by giving them digital tools, that allows them to complete trial tasks on their own time within a defined window. So instead of having to drive today three hours to the site to complete XYZ, you can complete the task on your smartphone by completing a survey or answering these questions or doing this test."*
>
> *– KOL #6*

COVID made building more flexibility into trials a necessity to enable trial resiliency during the pandemic. Flexibility allows Takeda to capture more diverse subpopulations and design trials that will meet the individual's needs:

> *"Because of COVID, we now are crossing over into thinking about the statistical analysis plan that will allow us to have built in that flexibility into the trial design…we need to be able to communicate that there are a few options that patients can decide for themselves how they want to participate…and start to really build that into how we conduct a trial. Because for many different reasons, people are diverse, and we want to make sure to capture different needs—whether they're part of a subpopulation or mixture of many different subpopulations, giving them that decision making and flexibility is key."*
>
> *– KOL #1*

Another way that Takeda has decentralized clinical trials to reduce the patient burden and provide access to more patients is by deploying home health nurses in certain trials. Mobile health nurses can provide skilled assistance with home infusions as well as draw blood for tests:

> *"We used to send the patient to the clinic for every single thing. You need to go in between your infusions, for example, to get your blood drawn. And what we realized is because of COVID, patients didn't want to go to the hospital... So we turned into sending home health aides to be able to draw blood in the patient's home. And that simple step actually makes the clinical trial process much friendlier and much more accessible to a larger swath of patients—the elderly, those who may be living far away from a clinical site, those who don't have transportation. We're all of a sudden solving these challenges that we didn't really appreciate... But I think COVID opened their [clinical trial teams'] eyes."*
>
> *– KOL #4*

Similarly, some rare disease patients previously had to go to the clinical site weekly to get infusions to replace an enzyme that they do not naturally produce. Now there is a Takeda program where a nurse under the guidance of the primary physician can administer infusions in the patient's home and teach the patient how to do self-infusions. Instead of 52 weekly site visits, this reduces visits to quarterly increments. Only having to visit a site four times a year fundamentally changes the standard of care because patients can do this at home and get the same therapeutic benefit with a home nurse or by doing it themselves:

> *"Because if this drug is successful…patients do not need to go to a site or to their doctor every week to get an infusion…just quarterly site visits to check in to make sure everything's okay. You know, the site of infusion, the site of injection is clean, there's no abscess…That's where we see the biggest benefits of these digital technologies, integrating them with the digital ecosystem, direct-to-patient shipment of medicines, combining with home health care. And this is especially true for our rare disease patients."*
>
> *– KOL #6*

Early diagnosis and treatment

Early diagnosis and treatment represented 14% (n=17) of the 122 excerpts for improvement of the patient journey. While several pharma companies already have internet hospitals that focus

on primary care for chronic disease management, Takeda is committed to reducing the time to diagnosis in rare disease and is a leader in industry efforts with this aim (e.g., The Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease).[134] Thus, digital teams at Takeda are brainstorming a rare disease early diagnosis internet hospital to find HAE and other rare disease patients earlier, screen them, and then diagnose them. This will be much more convenient and save time for patients since it usually takes 7 to 10 years to find the right physician and right hospital, and a patient can see 7 different specialists in that journey. If a disease is diagnosed later, it may be harder to treat and there could be irreversible damage to organs or tissue, as well as many years of painful symptoms and missed work, school, and opportunities. A rare disease internet hospital could strengthen Takeda's reputation in China so that patients know exactly where to go to be connected with the right rare disease physicians and start their treatment journey sooner.

Improving primary healthcare

Since China has limited resources in primary care areas, digital health can provide much-needed additional support and simplify the process of seeking care. Ping An Good Doctor has been working to improve primary healthcare through telemedicine, especially in rural areas that do not have many healthcare resources:

> *"So platforms like Ping An or other telemedicine fulfill people's need in rural areas and also…provide easier access for consumers to talk with good doctors. In physical hospitals, it's not easy for consumers to access the good doctors. There are so many people who want to see the good doctors and also to get the appointment, they need to have a personal connection with the hospital…So physical consultation is very complicated and also time-consuming. But the telemedicine platform make these complicated processes very, very easy and simple, just paying extra."*
>
> *– KOL #15*

One reason that Chinese patients avoid primary care is because they do not trust the ability of the primary healthcare providers. So when primary care providers can be connected to tertiary facilities through telehealth, it may improve patients' perceptions of them and the quality of the services that they provide:

> *"So if primary health care provider can be connected to more advanced level of facilities so that they can get advice, they can get support from them, it would one) improve the actual quality, two) also improve the signal to the patients that the primary health care providers are actually supported."*
>
> *– KOL #2*

Trust in primary care doctors and their abilities also seemed to increase with their emergency response to COVID-19, where patients saw their dedication:

> *"During COVID-19, a lot of family doctors [were] playing their role of connecting patients. So this really improves their belief about the family doctor after COVID-19. We can see, especially in Shanghai, Beijing, these big cities, the people who are older than 60, they have all assigned one family doctor. So they can connect to their family doctor frequently and also during the COVID-19, this family doctor is collecting their symptoms and caring for this patient. So I also think this will improve their belief of the family doctor after COVID-19."*
>
> *– KOL #13*

Aside from increasing access to good doctors, new policies for internet hospitals mitigated many of the insurance challenges surrounding access to non-local physical facilities. With many patients traveling to tertiary hospitals for better treatment before COVID, patients faced issues getting coverage in provinces outside of the one in which they resided:

> *"The insurance coverages are governed at the provincial level. So if you're a patient at the Guangzhou Province, and you go to Shanghai, it's challenging for you to get coverage there for your medications."*
>
> *– KOL #9*

Now with the government's new COVID-induced policy on broadening medical insurance to include internet-based medical service fees, prescriptions, and drug delivery, these services became more affordable with reduced fees (***Table 13***).

Table 13. Consultation fees and number of doctors for internet hospitals in China in 2020.

	Minimum	5th percentile	25th percentile	50th percentile	75th percentile	95th percentile	Maximum
Number of available web-based doctors	1	3	11	43	172	1,496	563,881
Consultation fee of fever clinics, ¥[a]/consultation	0	0	0	0	0	9	50
Consultation fee of other outpatient clinics (i.e., excluding fever clinics), ¥/consultation	0	0	0	6	20	120	500

[a] Currency exchange rate of ¥1=US $0.15.

Source: Xu et al., 2021.[114]

The median consultation fee for fever clinics was USD$0, the maximum fee was only USD$7.5, and the fee was less than USD$1.35 for 95% of internet hospitals. For outpatient internet clinics, the median consultation fee was USD$0.90, the maximum fee was USD$75, less than USD$18 for 95% of internet hospitals, and less than USD$3 for 75% of internet hospitals.

Closed-loop care

When discussing their vision for improving the patient journey in China through digital innovation, several participants described a concept called closed-loop or end-to-end care, which provides care to the patient across the entire patient journey. Takeda's Digital Advisory Board has an Integrated & Personalized Care (IPC) program that provides full end-to-end patient care and identifies solutions that can improve patient life as well as the relationship between patients, HCPs, and caregivers:

"I think that the innovation operation model has to be connected with the internet hospital and also, the online drug management, then the reimbursement. So if we can connect all those channels together, then [the] patient doesn't have to go outside… to the hospital to get the consultation, to get a diagnosis, and go get the drugs, even to claim their insurance. So if we can connect all those online, it will change patients' journey, especially for some patient who has a disability, not able to move easily, and online healthcare is very important for them in their life."

– KOL #14

Embracing Takeda's "Patients First" philosophy, the Integrated & Personalized Care solution follows a prescription-devices-services model, which strives to envelop each one of Takeda's assets with a suite of digital solutions that enables the health ecosystem around the patient, so that the patient's journey will be seamless instead of fragmented:

"We don't want to be a company that puts an injector or a pill into a warehouse that gets distributed, we want to envelop that with a suite of solutions for patients to become more literate about their condition for us to be able to care for them, for us to enable the health ecosystem around them so they have a holistic treatment course, versus sporadic and fragmented."

– KOL #9

4.2.8. Thematic Area 8: Ethics of digital innovation

Digital innovation provides many opportunities for the advancement of healthcare and patient access to therapeutics, but it also presents many challenges. Several ethical concerns were brought up during interviews: data privacy and trust, quality of care, inequity of access, intention (profit vs. patient), biased or incorrect algorithms and models, and downstream effects.

The issue of most concern to participants was data privacy and trust, which represented 66% (n=27) of the 41 excerpts coded for the theme of ethics of digital innovation. Some patients have expressed that they are not necessarily comfortable using wearables because it feels very much like "Big Brother" 24-hour monitoring, and they may not know the extent of what is being monitored. This is why Takeda is committed to being transparent about the data that is being collected for clinical trials, why it is being collected, and how it will be protected. Takeda's consent

forms also provide opt-in, opt-out opportunities for patients and ask patients what they are willing to share. However, the culture in China around privacy is different from that in the West, and some participants thought that privacy seemed to be less of an issue in China than in the US and Europe:

> *"I mean, it's just people know that they are combining the ubiquitous cameras that are taking pictures of people wherever you go—the facial recognition capacity that they have. There's very little room for privacy in China, and people put up with it. Whether they like it or not, they have to."*
>
> *– KOL #7*

While it can be alarming that China has so much information on citizens, China has taken great measures to protect data. However, the access to such a wealth of data still produces an ethical argument that should be considered and closely monitored to prevent abuse or overreach:

> "*I haven't heard any news that patient information is leaking outside of the organization. So China is doing pretty well with data/information confidentiality and privacy. But of course government has all those data; our government knows everyone's information. So if you think about that… that's something that needs to be considered."*
>
> *– KOL #14*

Others discussed how privacy is a trade-off for convenience, the use of information that would benefit society, and saving vulnerable patients' lives. So privacy is an issue that has to carefully navigated and fit-for-purpose:

> *"And we have to make sure that we really constrain what are we recording - the time and whatnot, because it's just not pleasant to be continuously monitored. But at the same time, if you have a specific condition like children with epilepsy, where something can happen to them at any point in time, and if you have a system that can alert a caregiver or call 911 and essentially help you save a life, well, maybe you sacrifice some privacy for it. So again, it has to be fit-for-purpose."*
>
> *– KOL #4*

Abuse and overreach can lead to various downstream effects, where an employer or landlord could use health information against individuals. With the social credit rating system (see ***Ethics*** section) to encourage good behavior in citizens, there is concern that medical records can be linked with behavior information:

> *"You have this social rating. Will also they use your relationship to disease area or your behavior as a way to rate you and have these almost like a bonus model against you? I see that could be a risk, a limitation."*
>
> *– KOL #11*

If medical records are linked to someone's social credit score through technology, then this could lead to biased or incorrect models and algorithms. Critics of the social credit rating system claim that scores are determined with information that is often incomplete or incorrect.[98] Similarly, AI-based models and algorithms are only as good as the data that is fed into them, and there is already a lack of high-quality hospital data in China. When discussing home devices for predicting IBD flares, some physicians and patients are concerned that the AI algorithms could be incorrect:

> *"How do they know this algorithm works? How do they know the patient used the right data or used the kit to produce the right data? So there's maybe lack of education or just mistrust in how data coming from somewhere would be used for clinical decision making, and also for patients is the same."*
>
> *– KOL #12*

Even without being linked to social credit ratings, biased models could also manifest by favoring some patients over others, which in turn affects how patients are connected with providers and how those engagements with HCPs are managed. This could lead to inequity in access if some patients get access to care faster than others:

> *"With regards to algorithms, if we are using the data to make recommendations around care, you know, bias in the models could be favoring some patients over others. And with regards to managing the engagements, likewise, inherently the mechanisms developed, the piping you put in place could inform whether some patients living in certain geographies have an upper hand in getting access to care faster than others."*
>
> *– KOL #9*

Some local governments offer incentives already such as prioritizing healthcare provision to encourage good behavior and a higher social credit score.[98] Inequity of access can also manifest as issues with treatment eligibility if the government uses data against patients. With the rapidly

expanding advances in digital and technological innovation, it is important to consider ethical guardrails for not just the present but also the future:

> *"If you imagine the future in five or 10 years from now, it will be completely different. And the use of digital could be also different, because they might decide based on your data, based on your omics, genetics, and other data, they can predict basically in the future whether you will survive a cancer or not. And they can say, 'Oh, you have just a bonus of three years, three months. Should we give you a treatment, for instance, or just let you die?' What is an ethical guardrail to prevent these kind of things in the future?"*
>
> *– KOL #11*

The final ethical issues with digital innovation are quality of care and intention (profit vs. patient). Access to digital and technological innovation for healthcare is only good if it is of high quality. Otherwise, it could actually end up harming patients through misdiagnosis. If patients are paying for services that are not actually good care, it is not ethical. One KOL referred to quality as the most acute ethics issue that has not received enough attention yet:

> *"My sense is that the other challenges are, there's no question that internet health has provided a lot of easy access to care. But to what extent the quality of care, the standards of care, are actually high, I don't know. My sense is it is highly variable."*
>
> *– KOL #2*

This KOL went on to explain that big tech marketing is very powerful, their products are very attractive, but it seems as if tech companies do not always pay attention to the quality of their AI technology in the rush to get things to market. This could also pose problems with incorrect algorithms, which could lead to improper diagnosis and treatment advice for physicians. There is a delicate balance between having a big market and also a high-quality product:

> *"And so [one big tech company]'s strategy is to have a big market, which I think they are reasonably successful. But the product in my view is a bit shallow."*
>
> *– KOL #2*

> *"The other possibilities…is perhaps give primary health care provider AI-enabled decision support system. But some parts of China have tried that; it hasn't been that successful for the following reason: the AI algorithm hasn't been developed very well, number one. And a lot of commercial company is just too eager to expand and*

scale up and they basically just market and say that they have an AI support system that would help primary healthcare providers. But then when you really look at the algorithm, I mean, to what extent it's really improving primary healthcare ability, I think is a big question mark."

– KOL #2

An increasing number of apps on WeChat does not directly correlate to increasing the quality of care. The design of the apps is not always so clear or derived from the patient perspective:

"There are a lot of apps or WeChat mini-app is aimed to treating patients and to care for patients outside hospital in China. But the problem is that they do not think about the patient way…they are not using the patient journey to design this product, they are just putting a lot of function on the apps or on the mini-apps. So I think if I am a patient, I will be very confused about these apps, what they will provide to me and what is the benefit for me."

– KOL #13

Technology is a high-value industry, which makes it enticing to many stakeholders. The intention of HCPs, pharma, and tech companies has to be focused more on the patient than the profit. This ties into the quality issue because if companies just want to be the fastest to get products out to market, or to entice patients and HCPs with numbers of features on digital health platforms, then they could be tempted to cut corners to increase profits. There needs to be a clear balance of the social goals of Healthy China 2030 and UN SDG 3 (to promote healthy lives at all ages), with the profit-making agenda of key stakeholders:

"The National Health Commission, the National Health and Social Security Administration, their goal is to drive the policy agenda. They of course work in a way that is more bound by bureaucratic rules. Whereas a private entrepreneur, there's no question that they're much more flexible, creative, innovative, they move very fast. But working with them also have a challenge of how do you balance their profit-making goal and the social public purposes?"

– KOL #2

In China's fee-for-service system, two challenges with primary healthcare are competition for patients and overprescribing of diagnostic tests and profitable drugs. With more adoption of

digital healthcare and increasing revenues from it, physicians will have to take care to ensure that they are putting the patient first:

> *"The other concern is also to what extent physicians who have a main job somewhere else are using internet platforms to try to select patients or encourage patients to go to their offline office to actually do more, get more care, and whether those are necessary or unnecessary, I think it needs to be studied."*
>
> *– KOL #2*

Regarding pharma companies, we also have to make sure that we are engaging our physicians for the right reason—to improve the patient journey. There is already a heavy stigma in society that pharma companies just want to make money to please shareholders, and if digital innovation is used to promote a company's own brands at the expense of patients, this will reinforce that stigma and harm our reputation in society:

> *"So probably, because digital health is emerging, there are still some questions about…are we engaging our physicians for the right things? Or are we using digital to wrap around and kind of promote our own brands, which is a no go, but still, there's a little bit of customer engagement and ethics around intention."*
>
> *– KOL #12*

5. DISCUSSION & RECOMMENDATIONS

5.1. ADKAR Framework for Change

*Current state: **Awareness** of the need for change and **Desire** to support the change*

COVID-19 accelerated the awareness of the need for change and the desire to support more digital innovation in pharma. According to the ADKAR framework, a catastrophic disaster (and a worldwide pandemic would definitely fall under this category) builds organizational awareness of the need for change.[135] Takeda and other pharmaceutical companies were already aware of the need to transform both the healthcare system and patient journey with digital and technological innovation before COVID. Many pharmaceutical companies had been collaborating with big tech companies, local governments, payers, and academia on digital initiatives in China for years prior

to COVID (see ***Pharma*** section and Appendix ***Table 16***). Furthermore, Takeda and many others in the industry had been keen on innovating clinical trials for years, especially around digital and wearable technology. Although digital initiatives did not begin with COVID, they were massively accelerated because COVID revealed just how unsustainable the healthcare access and management challenges were in China.

As participants discussed, COVID disrupted the healthcare system as well as Takeda's clinical research, development, and commercial operations, so digital innovation went from optional to mandatory. Being generally risk-averse as an industry, COVID forced Takeda's hand to more boldly apply digital approaches with the buy-in of the health authorities in many regions. Takeda had to quickly adapt to continue to conduct clinical trials, modify the approach to physician field force engagement, and provide care and life-saving medicines to patients since patients could not go to the hospital to get medicines or see physicians for non-emergency services.

This awareness of the need for and desire to support the change came from both within Takeda—led by the Digital Advisory Board and Patient Engagement teams—and outside Takeda. China's unique enabling environment included favorable policy for "internet plus" healthcare, AI development, and insurance reimbursement. Chinese citizens were early adopters of digital health and technology, and telemedicine integrated online and offline care. Having a supportive government and advanced technological infrastructure during COVID lowered the threshold for adoption and made it easier to support digital changes to healthcare.

Takeda's Digital Advisory Board has five pillars: Real-world Evidence (RWE), Integrated Patient Care, rare disease early diagnosis, enterprise data backbone, and a Patient Engagement Platform. All of these pillars are centered around Takeda's fundamental desire to improve the patient journey through Takeda's "Patients First" philosophy. Patient engagement is foundational

to Takeda's work, especially clinical trials. Patients had expressed even before COVID that they wanted more flexibility to participate in clinical trials and would like to do some assessments at home away from trial sites. So Takeda began embracing decentralized, e-clinical trials to meet patient needs, broaden the geographic diversity of clinical trials, and reduce the trial burden.

*Transition state: **Knowledge** of how to change and **Ability** to demonstrate skills and behaviors*

Through this doctoral project, the knowledge of how to change is elucidated in the quantitative sections that showcase the epidemiological disease burden and healthcare resource statistics in China, as well as the qualitative thematic analysis. The epidemiological disease burden both before and during COVID-19 is highly skewed towards hypertension and cardiovascular disease, cancer, cerebrovascular disease, chronic respiratory diseases (e.g., COPD), diabetes, and gastrointestinal (GI) diseases. Takeda's four therapeutic focus areas are **oncology, rare diseases, neuroscience/neurology, and gastroenterology**. As a leader in GI, Takeda is also exploring a rare disease online hospital. Now that Entyvio® for irritable bowel disease (IBD) has been added to the 2020 National Reimbursement Drug List (NRDL) catalog, the ability to increase access, affordability, and improve health outcomes for millions of IBD patients has greater potential. But even when a rare disease online hospital launches, the ability to provide hereditary angioedema (HAE) patients affordable treatment is limited until Takeda can successfully negotiate with the government to add the HAE drug Takhzyro® to the NRDL list. Working with local governments to understand the needs and challenges with certain rare diseases, and compassionate use programs in the least resourced areas where medicines are provided free to patients would be great ways to gain local government and community support and credibility, as well as align with the Healthy China 2030 goals of making healthcare more affordable and accessible.

Since provinces such as Anhui (44.2% rural), Jiangxi (42.6% rural), and Henan (46.8% rural) were shown to have the fewest healthcare resources in rural areas and were also some of the hardest hit by COVID (***Table 8***), they would particularly benefit from digital initiatives to increase healthcare access. However, provinces with high proportions of urban populations would also greatly benefit from digital initiatives to reduce overcrowding from residents who live and seek medical attention there, in addition to those coming from other provinces. The provinces with the highest numbers of urban population are Shanghai (88.3%), Beijing (86.6%), Tianjin (83.5%), Guangdong (71.4%), Jiangsu (70.6%), and Zhejiang (70%), but most other provinces still have an urban population greater than 50% [Appendix ***Table 15***].

Jiangsu has only 3.85 urban physicians and physician assistants per 1,000 population, which is under the urban average (4.10) for China (***Table 7***, ***Table 8***). Jiangsu has an urban population of ~57 million, so their HCPs are significantly overburdened. If urban patients can utilize digital health platforms for primary or specialty care instead of waiting hours in a big tertiary hospital, then this would significantly reduce the patient and HCP burden. With 4.13 urban physicians and physician assistants per 1,000 population, Guangdong is over the urban average for China, but they are still under-resourced in rural areas, with only 1.64 physicians and physician assistants per 1,000 population (rural average is 1.96 physicians and physician assistants). With a total rural population of ~33 million, this is a major health disparity for Guangdong patients.

As demonstrated by the literature review, health resource data, and qualitative thematic analysis results, digital and technological innovations have considerably improved China's healthcare access and management challenges—which were exacerbated by COVID-19. Collaboration between various health ecosystem players in both the private and public sectors has been tantamount to mitigating these challenges. Since KOLs shared that they are looking into

starting a partnership with the government in one majority rural, Western province to run analytics for rare disease early diagnosis and other use cases, rural areas in provinces such as Guangxi, Anhui, and Jiangxi could also benefit from digital health initiatives to increase healthcare access and treatment. Meridian Medical Network Corp deployed an "Angel Robot" system to improve primary care for village doctors in Anhui province. The Angel Robot has two AI-powered CDSS (Clinical Decision Support Systems) to improve primary care physicians' diagnoses, high-quality videoconference telemedicine to connect primary clinics with higher-tier hospitals, and better management and utilization of health records.[136] Additionally, Ping An Good Doctor's Village Doctor Program has been transforming primary care in rural regions through upgrading rural clinics and improving the standard of basic medical services in impoverished regions.[121]

Doing fit-for-purpose analyses to identify the most effective and comfortable digital innovation types for specific therapeutic areas provides knowledge and the ability to implement digital health initiatives in chosen provinces. For instance, wearables and specific digital biomarkers have to be chosen carefully to collect accurate and meaningful data from patients. So if clinical trial teams want to measure muscle activation of the diaphragm and muscles in the abdomen (e.g., to assess incidence of nausea and vomiting in Cyclic Vomiting Syndrome patients), electrodes could be a bad choice for obese patients because they can slip. They need to be placed on muscle or else measurements will not be accurate. But in other scenarios, electrodes could be a good choice if teams want to measure muscles in the upper chest because people do not generally have too much visceral fat there.

But regardless of the knowledge to support the change, the ability to demonstrate skills and behaviors is impacted by significant barriers to entry and operation for foreign companies. These barriers are intentional by design, as Jessica Tan, co-CEO of Ping An stated: "We aim to establish

strong technological competition entry barriers by building a closed-loop ecosystem of health care services."[137] Although China has a robust healthcare infrastructure that enables digital innovation, being unable to access patient data and needing a Chinese external partner pose challenges for multinational pharma companies. As shown in ***Thematic Area 5: Data governance***, even if partnerships for these initiatives have been identified and an algorithm (e.g., for HAE) has already been developed by a global company, if they do not have an office in China, then they cannot access raw patient data. Rare disease early diagnosis is one of the Digital Advisory Board's five pillars at Takeda, and having to search for a Chinese company to implement an HAE algorithm could delay diagnosis and treatment for patients.

Because the startup regulatory landscape is not as developed in China as you would find in the US, this also poses a quality risk if Takeda's existing global partnerships would have a more advanced algorithm than a Chinese startup. Being forced to look for a Chinese company with similar quality can waste precious time and resources for the Digital teams at Takeda, especially since rare diseases such as HAE are largely unknown in China. As respondents mentioned, choosing a big tech company for custom solutions may not be the best choice for specific therapeutic areas because although they have the scale and reputation, they have their own priorities and interests, and Takeda may have limited influence. However, every other major MNC pharma has partnerships with big tech players, which may be a productive avenue to mitigate competition entry barriers set by both the government and big tech players (Appendix ***Table 16***). For Takeda to thrive in this space with other big pharma companies, likely a mix of both big tech partnerships (for scale, reputation, and technological expertise) and startups (for custom solutions in focused therapeutic areas) will be needed. Partnerships with leading research academic

institutions and Chinese medical associations will also enable better digital innovation at Takeda with refined therapeutic area expertise in Takeda's key focus areas.

Clinical trial teams at Takeda also use global companies as suppliers when appropriate, but they were able to mitigate the lack of portability of Chinese participant trial data by using a supplier that could put servers in China. If a company has a server in China, special exemptions apply where this data permanently resides on a Chinese local server but can be analyzed in Takeda or vendor offices outside of China. But issues still exist for eConsent, which can greatly improve the patient journey by increasing health literacy, reducing the clinical trial burden, and allowing patients to have a more convenient, decentralized trial experience if it is accompanied by virtual trial educational materials. Clinical trial teams at Takeda have not been able to use eConsent in their trials in China. But perhaps a way to move forward and demonstrate the benefits of eConsent is through partnering with a Chinese company that does eConsent. Dong Ma (Taimei Medical Technology) has an ePRO app that encompasses eVisit, eSource, eConsent, and EDC (Electronic Data Capture) capabilities.[132] Patients can download the app and register through an invitation code sent by the investigator. The patient then watches an introductory video and has to pass a test on the informed consent process to sign the electronic Informed Consent Form. Afterward, the patient enters the ePRO system and completes reports based on protocol requirements. The system sends out reminders to submit data and queries from the investigator, and it intelligently detects and conceals patient privacy information.[132]

Another challenge to data governance and improving digital solutions is the lack of a robust EMR system across China. There is a lack of high-quality hospital data in China, which makes it challenging for Takeda to build the algorithm and run some big use cases very quickly in China. The EMR system in China is not as mature as EMR in the US since each hospital in each province

often has its own EMR solutions. In the US, many hospitals' EMR systems are already standardized and can be connected with each other. But in China, connecting one hospital's EMR with another hospital is challenging since the EMR standardization might show different hospitals' unmet needs, and some hospitals do not want to share EMR data with other hospitals. To make matters more complicated, some hospitals in China still keep paper records. This makes it difficult for even third-party partners to create a longitudinal profile of the patient's clinical status with a true 360-degree patient view that would allow granular analytics to be performed on clinical characteristics, phenotypical characteristics, and sociodemographic or social determinants of health. Therefore, to enable robust EMR interoperability across China and have the best quality data for digital solutions to be built at Takeda, policy endorsements are needed for the EMR access and control to be standardized across different regions and hospitals.

To demonstrate the effectiveness of new digital therapeutics and services as well as raise disease awareness across China, Takeda could launch a digital broadcast with medical associations, top KOLs, and government officials to advocate for rare disease, IBD, oncology, and/or neuroscience online management. Pfizer's post-coronavirus CVD online hospital broadcast was viewed by almost half a million people and gained front-page news coverage on People's Daily, the largest newspaper group in China.

*Future state: **Ability** and **Reinforcement** to make the change stick*

Although COVID is hopefully not here to stay, digital health transformation in the healthcare industry is likely to be the future. As the ADKAR framework explains, people have a natural tendency to revert to what they know, so sustaining change can be even more difficult than making a positive change.[135] Not only is collaboration necessary for enabling digital expertise to be implemented, it is also critical for sustaining these changes so that they can be scaled up across

China and are not one-off initiatives. However, this does not just mean collaboration with external partners but also inside Takeda. Several digital health efforts are ongoing at Takeda but many of them are siloed across departments. The goal of the qualitative research was to interview people across various departments at Takeda to glean insights about digital health projects in different groups, find the synergies, and then share knowledge across the organization in a white paper. This will make it easier for those in different groups to know the digital needs, progress, and gaps for different therapeutic areas and teams, so that they can reach out across groups to collaborate and move projects forward in a faster, more comprehensive, and more streamlined manner.

Furthermore, while it is important to keep patients and HCPs engaged with digital healthcare changes, it is equally important to keep employees who are driving these changes engaged. For instance, one of the challenges that Takeda has been facing is employee turnover. So for PPP projects that were initially strongly supported by a particular team or functional group, several people may have left a few years down the road or transitioned to other roles. Then it may become difficult to identify other colleagues who have similar expertise, passion, and are willing to engage. Therefore, teams will have to develop innovative ways to engage new people to sustain and reinforce commitment to projects. One participant suggested that a best practice could be identifying a core group at the start of a project but also other people on their team. This way, if one person transitions out of the role, there will be someone else who is still engaged and can help move the project forward instead of an entirely new group of people who are unfamiliar with it. If at least one person is showing passion and leadership for a project for which they are familiar, this can help new team members become excited as well.

Even with employee turnover, Takeda will continue to implement and advance digital health initiatives because of our “Patients First” philosophy, which always puts the patients before

revenue and the business. One participant called COVID the "great revealer and accelerator" and said that COVID helped pharma realize how much distrust and inequity there is in the industry. So Takeda plans to address these problems very intentionally for not just the shorter term, but long-term as well. For Takeda's momentum in China's digital health ecosystem to be sustainable, we will have to be especially vigilant to ethics to ensure that we do not create monsters that we will regret down the road.

One major risk is producing a market for human care. In China, over 95% of the population has basic medical insurance, and individuals have the option to pay privately for higher quality or quicker treatment.[38,138] This aligns with Confucian principles, which encourage individuals to use private resources for the benefit of oneself and one's family. Ping An Good Doctor has approximately 1,000 unmanned minute clinics across China, where patients can walk in, provide medical history and symptoms, and receive automated diagnosis and treatment plans. These plans are followed up by human clinical advice only for new customers. So this poses a future risk that only those who can pay can access human clinicians. For those unable to afford human care, this could cause a significant negative impact on the quality and level of healthcare access throughout the population. Emotional care and involvement in healthcare decision-making are frequently as important as the analytical inference of a diagnosis.[38] As one KOL said, people need people and they need to be touched. So COVID has really brought to the fore that there is no replacing the human aspect of care for patient engagement, which includes reading cues from being in the room with someone that would not be observed from behind a computer or phone screen.

In putting patients first, it is also important to ensure that digital innovation in healthcare does not leave vulnerable populations behind, such as the elderly, rural populations, or those who may not be as technologically literate. Although the mobile and internet penetration rate in China

is high, there are still some people who may not have technology or may not be as technologically literate. Tech knowledge is different in different cities, and the technology setup can be quite different as well. For those who may not be as technologically literate, being inundated with apps, functions, and digital biomarkers could just confuse them and after an initial pilot, they may stop using these tools.

Therefore, it is not just about having affordable digital tools that are of reliable quality and great partnerships to increase access to these tools, but Takeda also needs to make sure that the people who need them actually want to use them. If they do not or cannot, then this could lead to a population that is left behind, which would create inequity of access to better care. Part of China's AI Development Plan is creating physical auxiliary equipment, audio-visual aids, other intelligent home care equipment, and mobile social and companion care service platforms for the elderly.[40] Digital health literacy campaigns, more direct patient engagement, as well as observational and longitudinal studies on knowledge, attitudes, and behaviors, will have to be launched as the adoption of digital tools is accelerated. These efforts will provide knowledge of how to revise digital tools for ease of use, enable higher adoption rates in the elderly and other groups, and ensure that these adoption rates are sustained over the long-term.

But aside from concerns about adoption with certain patient groups, adoption by some HCPs also remains a challenge because it is hard to change behavior. Older doctors (especially in rural areas) who were trained in a classical medical curriculum and are not as familiar with using AI algorithms for treatment decisions, may not be as keen on adopting digital solutions. Even if they receive training from Takeda and partner tech companies or academic institutions, they still may be reluctant to use these solutions in their daily practice for the long-term. Therefore, if Takeda is going to implement digital solutions in rural areas with the least healthcare resources,

then they will have to prove the increased benefits to rural HCPs and offer incentives to make changes stick:

> *"Then there are other places that like in the rural areas, I think the village doctors for many years, they're not used to these kind of digital systems. So they need some behavioral change to understand how this is helpful to them. Most of the village doctors are in their 50s and even 60s. It's not whether they know how to use it, it's about the attitude, the acceptability as well. They feel for 40 years, I have been practicing the way I practice. I mean, it's hard to change behavior."*
>
> *– KOL #2*

Nevertheless, Takeda will have to be vigilant that any incentives for digital adoption are ethical and will not be used to increase profit for HCPs at the expense of patients. With more HCP adoption, digital health literacy campaigns could be delivered through primary care physicians (especially barefoot or village doctors) and community health workers. By seeing the extensive efforts of primary care physicians to treat patients, educate citizens, and mitigate the COVID outbreak, patient trust in their ability may increase and can be leveraged to sustain digital innovation.

Patients will only continue to use digital services if they are of high quality and provide both ease of use and accurate diagnosis and treatment advice. Thus, there need to be patient satisfaction surveys and studies that show improved health outcomes, not just improved access. These studies take time, and one big limitation with the private sector in China is that it has difficulty integrating tech with policy. The private sector in China moves very fast and big tech companies are very good with rolling initiatives out in a few months. However, policy experts and academic researchers provide understanding of the policy aspects for using a product, as well as scientific proof that a product is reliable and high quality, which takes time. Digital health initiatives will not be sustainable for the long-term unless they can integrate well with policy. So Takeda's initiatives will have to be consistently evaluated to align with the Healthy China 2030,

AI Development Plan, and other government agendas. Collaborating with academic institutions that have China health policy experts will be a way to ensure that Takeda is appropriately aligning with policy and demonstrating proven quality instead of rushing to get a digital product or service out on the market. This can also help avoid expensive and time-consuming missteps through regulatory hurdles.

Another way to improve sustainability is through inter-pharma collaboration. From the literature review as well as the qualitative interviews, there does not seem to be a lot of inter-pharma collaboration, and this appears to be a major gap. However, this provides a unique opportunity for Takeda and other pharma companies to collaborate on shared interests and unmet needs to create value for patient populations in the same therapeutic area, as well as hold each other accountable. Considering the barriers to entry for MNCs, stronger inter-pharma collaboration could help increase access for patients while also giving pharma companies more leverage to negotiate with the Chinese government. Of course, this is only a positive thing if that negotiating power is used to the benefit of patients and not to increase profits.

5.2. Recommendations for Takeda

1. **Partner with Big Tech players in the China digital health ecosystem.**

   Benefits are scale, reputation, technical expertise, and trust within the Chinese patient population and the government. All of the big tech players have their platforms integrated nationwide and have a strong first-mover advantage over pharma companies, and the vast majority of internet hospitals (74%) are enterprise-led. Therefore, Takeda would be able to achieve scale much faster without trying to integrate a new platform in provinces with varying technological capacities. This would remove a significant barrier to entry for Takeda as an MNC and also save time. Numerous other big pharma companies

have partnered with big tech (see Appendix ***Table 16***). For instance, Tencent is used by more than 1.1 billion of China's 1.4 billion population, so integrating Takeda's digital health solutions with Tencent provides care within an easily accessible and familiar social media platform, which will also make things more convenient for patients. Ping An Good Doctor has made great strides to improve medical services in rural areas through their Village Doctor Program.

2. **Partner with Harvard's China Health Partnership to leverage consortia-style PPPs.**

The China Health Partnership spans partners covering the gamut of healthcare stakeholders in China—from the government (National Health Commission) to tech (Tencent WeDoctor and Meridian Medical Network Corp.) to universities and hospitals, and donor and multilateral organizations such as Gates Foundation and World Bank.[139] This could be beneficial for establishing some consortia-style Public-Private Partnerships. Such PPPs will also make it easier to connect with top academic institutions, come to agreement with local governments, and build enduring relationships. Most of the pharma collaborations seem to be 1:1 (e.g., pharma: local government, pharma: big tech). Navigating any regulatory hurdles is probably easier to tackle as a group with various ecosystem stakeholders than as an individual organization.

3. **Collaborate with other pharma companies.**

Due to the barriers to entry for foreign MNCs, inter-pharma collaboration would be a chance to learn best practices, create shared value, and share lessons learned across companies. Inter-pharma collaboration could also strengthen collaboration with big tech companies, where challenges such as ownership stake, intellectual property, and competing agendas could arise. Key partnership attributes for other pharma candidates could be those

with a “Patients First” philosophy, strong patient and physician engagement in China, expertise in launching digital initiatives in rural areas, and the same therapeutic areas as Takeda.

4. **Regarding digital health platforms, try the Novartis approach in providing access to patients in a particular therapeutic area, regardless of whether they are on our medications.**

With Takeda’s “Patients First” philosophy, this would provide innovative, transformative healthcare to the greatest number of patients. Novartis’ AI Nurse platform is available to any heart failure patient in China independent of a Novartis prescription. This could also foster inter-pharma collaboration because digital health platforms would be disease-focused instead of brand-focused, which could improve pharma’s reputation in society.

5. **Launch digital health initiatives in provinces that are under-resourced by traditional methods.**

In addition to providing rare disease early diagnosis and closed-loop health management for GI, oncology, and neuroscience, this would increase diversity and access in clinical trials and provide a broader reach to patients who would traditionally be outside clinical trial sites. Patients in rural areas with lower access to care could already have advanced illness manifestations because of delays in diagnosis, and they could have a worse prognosis and be too sick to travel 500+ miles to participate in a trial or receive care. A broader, more realistic patient population would increase real-world effectiveness and external validity of clinical trial results. After market launch, this would also allow patients to participate in online drug prescription and delivery, so they would not have to travel to

hospitals. See ***Table 8*** and ***Table 15*** for provinces with the fewest rural resources and proportion of rural residents by province.

6. **Partner with biotech startups that are integrating drone healthcare delivery and robotics.**

There is much benefit to drones and robotics, but so many other pharma companies are focused on telehealth implementation. Drones could be a better way to deliver innovative, transformative medicines and robots could provide more efficient healthcare to patients in underserved areas. Surgical robots are becoming increasingly popular in China and one KOL discussed the combination of 5G and surgical robotics to assist doctors in remote areas. These technologies would not only help defend against pandemics like COVID-19 but would relieve the burden on overworked doctors, nurses, and other medical personnel in China. Partnering with some of these companies (see ***Drones, Robotics, & Other Tech***) could make these emerging technologies more affordable for hospitals and strengthen relationships with hospital administrations and HCPs, which could, in turn, make it easier for Takeda to collaborate on digital initiatives for patients, such as the Integrated & Personalized Care platform.

7. **Partner with companies that focus on technological innovations for vaccine uptake.**

Takeda's Vaccines business unit anticipates launching the dengue vaccine in China in the next few years. Drones could transform delivery in remote areas and ensure greater access. Drone delivery service Zipline partnered with the government of Ghana to deliver COVID-19 vaccines to remote areas.[140] China also has several domestic drone companies. In addition to drones for rural vaccine delivery, QR codes for primary vaccine vials are something that WHO has wanted for decades. Digitizing the Immunization Information

System through QR code scanning and linking patient vaccine records to Electronic Health Records could revolutionize vaccine distribution and information systems. For vaccine smart refrigerators, the Weka Smart Fridge has a dedicated IoT platform that collects data from multiple sensors in real-time, which means that it can understand vaccination rates per location as well as ensure that vaccines are always stored at the right temperatures.[141] The connection to Microsoft's Azure machine learning platform can alert doctors and nurses if vaccines are running low or if there are temperature changes from power outages or doors left open.

5.3. Limitations

Although qualitative interviews are primary research, the quantitative sections are all secondary research. The biggest limitation of using secondary research is that analysis or re-analysis of the data cannot be done, and if there are any errors in the original collection and/or analysis of data, secondary reporting will just compound any errors or biases. Meta-analysis was not done in this project to analyze clinical determinants of mortality for COVID-19 patients due to insufficient sample size and overlapped cases in different articles, which would create an inaccurate scientific record.[112,142] Further, a meta-analysis poses the risk of producing an ecological fallacy (i.e., making inferences about the individual based on group observation), since it analyzes data on an aggregate level as opposed to individual-level patients.

Another limitation is that health access data for the big tech players was not linked to health outcomes, so there is no way to assess population impact. In their financial reports, revenue, average daily consultations, and/or the number of monthly/annual users were reported, but there were no statistics showing a decrease in incidence or prevalence of disease. Detailed information on patient satisfaction and statistics about medication adherence would have also been helpful to

measure the effectiveness of these platforms in improving health outcomes. For instance, Ping An Good Doctor stated that their online consultation satisfaction rate was around 97% in 2020, but they did not go into details of what constitutes patient satisfaction, how it was evaluated, or what issues the 3% of patients who were not satisfied with online consultation had.

In China, there is a dearth of rigorous research that examines how hospital characteristics correlate with patient satisfaction, even though attention has been increasing on healthcare quality from the public and government.[143] A 2020 study showed that for offline hospitals, patients under Urban and Rural Resident Basic Medical Insurance and New Rural Cooperative Medical Insurance tend to have lower satisfaction with their inpatient experience compared to patients under the Government Insurance Scheme (for government officials and employees). Hopefully, patient satisfaction will be evaluated for reimbursement and quality improvement more in the future, especially for internet hospitals, which are majority enterprise-led.

Since this doctoral project was focused on Takeda's place in China's digital health ecosystem, the majority of KOLs interviewed were from Takeda. There were no interviews held with any big tech players, venture capitalists, or digital health leaders at other pharma companies. The project would have been strengthened by having firsthand perspectives from these ecosystem players to learn their motivations and glean more opportunities for partnerships.

6. CONCLUSION

Using COVID-19 and China as a case study, this project addressed the research question of how Takeda, as a big pharma company, can increase healthcare access through digital innovation and partnerships. To analyze this question, a mixed-methods approach was used in which quantitative data provided an overview of the epidemiological disease burden and healthcare access statistics in China, while qualitative data provided insights into Takeda's digital

health initiatives and opportunities for growth in China's digital health ecosystem. The qualitative thematic analysis revealed eight themes to understand COVID-19's impact on digital innovation and healthcare access in China: COVID-19 disruption to the healthcare system, China's unique enabling environment, digital innovation type, cross-functional collaboration with health ecosystem, data governance, therapeutic areas and assets, improvement of the patient journey, and ethics of digital innovation (***Table 12***).

Takeda can increase healthcare access through digital innovation and partnerships in **three main ways**: 1) alignment of China's disease burden with Takeda's priority areas that better informs innovative digital solutions; 2) increased collaboration with key stakeholders (big tech companies, biotech startups, academia, HCPs, hospitals, and local governments); and 3) outreach to least resourced areas of China with pilots. These include both rural areas with fewer than the average 1.96 physicians per 1,000 population (e.g., Guangxi, Anhui, Jiangxi, Henan) and urban areas with fewer than the average 4.10 physicians per 1,000 population in China (e.g., Jiangsu, Sichuan, Hubei, Chongqing).

Impact on public health

Takeda's digital innovation efforts and transformative medicines in rare disease, oncology, gastroenterology, and neuroscience can transform the lives of millions of Chinese patients with complex, rare, and neglected diseases. These efforts will also advance the government's vision for Healthy China 2030, which emphasizes technology's importance in transitioning from hospital-based models of care that focus on treatment, to a sustainable primary care system that focuses on prevention. Through big data, AI, digital biomarkers, and telemedicine, earlier and more accurate diagnosis and treatment decrease the incidence and prevalence of diseases that disrupt patients' lives and wellbeing. An increase in population health leads to a healthier and more productive

workforce, which in turn leads to a healthier economy. Without public health, there is no economic health.

Since pandemics have the power to shut down society for an undetermined amount of time, it is of utmost importance that we prioritize innovative digital solutions and partnerships for pandemic preparedness and response, as well as health access and management. This will greatly decrease disruptions to society and the individual as well as empower governments, businesses, and communities to see each other as friends rather than foes. Efforts to increase elasticity between infectious and chronic disease prevention and treatment initiatives will safeguard global health security and reduce the burden on the healthcare system.

As advances in digital health are expanded globally, it is important to consider the tradeoffs between innovation and the emotional connection in care, inability to physically examine patients, and privacy. A trade-off for more efficiency and convenience is the emotional connection in care if chronic disease management is moved to home care. The warm handoff, or transfer of care between two members of the health care team, is an important part of the clinical patient experience as it builds trust and can reduce anxiety for patients.[144] At primary care clinics, patients are transferred from the receptionist, to the nurse, to the physician, and it is easier to pick up on nuance and read cues in person than it is behind a screen. AI virtualized assistants and chatbots in telehealth or robots delivering food and medicines in the hospital can seem relatively cold in comparison. To restore some of the emotional connection in care, plans could be implemented for regular touchpoints where a nurse reaches out to patients to check in on them or home health nurses could be used to guide elderly patients through the telehealth and wearable process. Another tradeoff for efficiency and convenience is the inability to physically examine patients and having

to rely on self-reports for telehealth, which may be inaccurate since people have varying levels of comfort with their bodies as well as levels of health literacy.

A tradeoff for better, more accurate AI algorithms and earlier diagnoses is privacy. As mentioned in the literature review, Chinese patients are much more comfortable sharing personal data for healthcare purposes than those in the West (especially the United States), and better AI involves the use of big data and adding more use cases to improve diagnoses. In China, big tech companies are first movers in driving digital healthcare, but American-owned big tech companies such as Facebook have had numerous data privacy breaches. A recent breach involved the personal information of 533 million Facebook users in 106 countries being publicly leaked to a hacking forum.[145] Therefore, American patients have valid reasons for not trusting these companies with their personal data. There needs to be stronger accountability and government oversight of American big tech companies to minimize data breaches in the future if patients are going to be more trustful of data in their hands. More direct patient and physician engagement will also be needed to help patients and physicians navigate and acclimate to some of these tradeoffs, especially as this innovation is expanded in countries such as the United States.

Impact on the host organization

As part of Takeda's Public-Private Partnerships & Global Science Policy group, this doctoral project aimed to break down silos across the organization regarding digital innovation and to understand how it impacts healthcare access in China. This will stimulate teams to collaborate with each other on digital initiatives, draw on the strengths and expertise of other groups, navigate any policy and regulatory hurdles more easily, and be stronger digital health leaders in China. More internal collaboration will enable better collaborations with external players

in China's digital health ecosystem, as opposed to fragmented efforts that would only complicate matters in an already fragmented healthcare system.

The COVID-19 pandemic is shining an even brighter spotlight on big pharma, and multi-sectoral, innovative healthcare solutions are needed to safely and fully reopen economies and society—as well as mitigate the impact of the next pandemic. Furthermore, given the numerous social pressures against big pharma, access to medicines is a critical topic of interest. Using China as a case study, digital technology could reshape health systems globally and fill several access gaps across a multitude of therapeutic areas. In the 2021 Access to Medicine Index, Takeda ranked 6 out of 20 overall but was ranked first in governance of access because of Takeda's clear access to medicine strategy.[146] Greater collaborations with both the public and private health sectors in China and a continued commitment to improving access to medicines will increase the public's trust of and respect for Takeda. Takeda and other for-profit stakeholders need to ensure that there is a balance of the profit-making goals with social good if they are to achieve the UN's SDG (Sustainable Development Goal) 3—access to safe, effective, quality, and affordable essential medicines and vaccines for all by 2030.

Takeda's approach to digital innovation engages patients at every step of the R&D process and commercial operations. Continued patient engagement will be necessary for sustainable digital solutions. While integrating digital healthcare with China's constantly evolving regulatory system may present challenges, patients will always remain Takeda's north star. Takeda is unwavering in commitment to delivering solutions that hold the best value for patients, and this will make it easier to adapt to changes and solve wicked problems along the way. As one colleague stated, "I've been in meetings where we've gone around in circles and couldn't come to an answer. And somebody at the end said, 'Well, we have five more minutes…what's best for our patients? Let's do it.'"

7. BIBLIOGRAPHY

1. World Health Organization. Health security. WHO Web site. https://www.who.int/westernpacific/health-topics/health-security. Accessed Oct 8, 2020.

2. World Health Organization. WHO coronavirus (COVID-19) dashboard. WHO Web site. https://covid19.who.int. Published April 16, 2021. Updated 2021. Accessed Apr 16, 2021.

3. World Health Organization. China: WHO coronavirus disease (COVID-19) dashboard. WHO Web site. https://covid19.who.int/region/wpro/country/cn. Updated 2021. Accessed January 6, 2021.

4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. *The Lancet*. 2020;395(10223):507-513. https://doi.org/10.1016/S0140-6736(20)30211-7. Accessed Oct 17, 2020. doi: 10.1016/S0140-6736(20)30211-7.

5. World Health Organization. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). WHO Web site. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf. Published February 2020. Updated 2020. Accessed October 9, 2020.

6. Dīngxiāng Yuán. Global COVID-19 epidemic map - Doctor Dingxiangyuan. DXY Web site. https://ncov.dxy.cn/ncovh5/view/pneumonia. Published March 2, 2021. Updated 2021. Accessed March 7, 2021.

7. Centers for Disease Control and Prevention. Scientific brief: SARS-CoV-2 and potential airborne transmission. CDC Web site. https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-brief-sars-cov-2.html. Published October 5, 2020. Updated 2020. Accessed Oct 18, 2020.

8. World Health Organization. Transmission of SARS-CoV-2: Implications for infection prevention precautions. WHO Web site. https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions. Published July 9, 2020. Accessed Oct 18, 2020.

9. Centers for Disease Control and Prevention. Coronavirus (COVID-19) frequently asked questions. CDC Web site. https://www.cdc.gov/coronavirus/2019-ncov/faq.html#Spread. Published February 11, 2020. Updated 2020. Accessed January 6, 2021.

10. The Lancet Respiratory Medicine. COVID-19 transmission—up in the air. *The Lancet Respiratory Medicine*. 2020;8(12):1159. https://doi.org/10.1016/S2213-2600(20)30514-2. Accessed Feb 20, 2021. doi: 10.1016/S2213-2600(20)30514-2.

11. Jin H, Lu L, Liu J, Cui M. COVID-19 emergencies around the globe: China's experience in controlling COVID-19 and lessons learned. *International Journal for Quality in Health Care*. 2020. https://doi.org/10.1093/intqhc/mzaa143. Accessed Dec 27, 2020. doi: 10.1093/intqhc/mzaa143.

12. World Health Organization. Information note on COVID-19 and NCDs. WHO Web site. https://www.who.int/publications/m/item/covid-19-and-ncds. Published March 23, 2020. Updated 2020. Accessed Oct 8, 2020.

13. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19): People with certain medical conditions. CDC Web site. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Published February 11, 2020. Updated 2020. Accessed Oct 13, 2020.

14. Campbell C. How the coronavirus is helping to fix China's broken healthcare system. Time Web site. https://time.com/5832584/coronavirus-covid19-telehealth-online-healthcare/. Published May 6, 2020. Updated 2020. Accessed Oct 9, 2020.

15. Organisation for Economic Co-operation and Development. Health resources - doctors - OECD data. OECD Web site. http://data.oecd.org/healthres/doctors.htm. Accessed Apr 15, 2021.

16. Li X, Krumholz HM, Yip W, et al. Quality of primary health care in China: Challenges and recommendations. *The Lancet (British edition)*. 2020;395(10239):1802-1812. http://dx.doi.org/10.1016/S0140-6736(20)30122-7. doi: 10.1016/S0140-6736(20)30122-7.

17. Yu W, Liu X, Zhao F, Li M, Zhang L. Control of unreasonable growth of medical expenses in public hospitals in Shanghai, China: A multi-agent system model. *BMC Health Services Research*. 2020;20:490. https://dx.doi.org/10.1186/s12913-020-05309-z.

18. Li X, Lu J, Hu S, et al. The primary health-care system in China. *The Lancet*. 2017;390(10112):2584-2594. https://doi.org/10.1016/S0140-6736(17)33109-4. Accessed Mar 12, 2021.

19. World Health Organization. COVID-19 and digital health: What can digital health offer for COVID-19? WHO Web site. https://www.who.int/china/news/feature-stories/detail/covid-19-

and-digital-health-what-can-digital-health-offer-for-covid-19. Published April 10, 2020. Updated 2020. Accessed Oct 9, 2020.

20. Chen S, Le Deu F, Then F, Wu K. How COVID-19 is reshaping China's medtech industry. McKinsey Web site. https://www.mckinsey.com/featured-insights/china/how-covid-19-is-reshaping-chinas-medtech-industry#. Published May 7, 2020. Updated 2020. Accessed October 9, 2020.

21. Budd J, Miller BS, Manning EM, et al. Digital technologies in the public-health response to COVID-19. *Nature Medicine*. 2020;26:1183–1192. https://doi.org/10.1038/s41591-020-1011-4.

22. Sagonowsky E. The top 20 pharma companies by 2019 revenue. FiercePharma Web site. https://www.fiercepharma.com/special-report/top-20-pharma-companies-by-2019-revenue. Published April 20, 2020. Updated 2020. Accessed Oct 10, 2020.

23. Takeda Pharmaceutical Company Limited. Company information. Takeda Web site. https://www.takeda.com/en-us/who-we-are/company-information/. Accessed Oct 10, 2020.

24. Takeda Pharmaceutical Company Limited. Areas of focus | takeda. Takeda Web site. https://www.takeda.com/what-we-do/areas-of-focus/. Accessed Dec 22, 2020.

25. Rauscher H. Accelerating medicines and jump-starting treatments: Public-private partnerships enlist Takeda and other biopharma companies in the fight against serious diseases. Association of Strategic Alliance Professionals Web site. https://www.strategic-alliances.org/blogpost/1143942/339732/Accelerating-Medicines-and-Jump-Starting-Treatments-Public-Private-Partnerships-Enlist-Takeda-and-Other-Biopharma-Companies-in-the-Fight-

Against-Serious-Diseases. Published January 31, 2020. Updated 2020. Accessed October 11, 2020.

26. Dickson B. AI is among our most effective tools in the fight against coronavirus. TechTalks Web site. https://bdtechtalks.com/2020/03/09/artificial-intelligence-covid-19-coronavirus/. Published March 9, 2020. Updated 2020. Accessed Oct 9, 2020.

27. World Health Organization. WHO statement regarding cluster of pneumonia cases in Wuhan, China. WHO Web site. https://www.who.int/china/news/detail/09-01-2020-who-statement-regarding-cluster-of-pneumonia-cases-in-wuhan-china. Published January 9, 2020. Updated 2020. Accessed February 20, 2021.

28. Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: Big data analytics, new technology, and proactive testing. *JAMA*. 2020;323(14):1341-1342. http://jamanetwork.com/article.aspx?doi=10.1001/jama.2020.3151.

29. Tan X, Wu Q, Shao H. Global commitments and China's endeavors to promote health and achieve sustainable development goals. *J Health Popul Nutr*. 2018;37(1):8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5898031/. Accessed Dec 22, 2020. doi: 10.1186/s41043-018-0139-z.

30. Fu W, Zhao S, Zhang Y, Chai P, Goss J. Research in health policy making in China: Out-of-pocket payments in Healthy China 2030. *BMJ*. 2018;360:k234. https://doi.org/10.1136/bmj.k234.

31. Kantel V. Healthy China 2030: China's healthcare journey. Bayer Web site. https://pharma.bayer.com/healthy-china-2030-chinas-healthcare-journey. Published June 25, 2018. Updated 2019. Accessed December 29, 2020.

32. Zhou M, Wang H, Zeng X, et al. Mortality, morbidity, and risk factors in China and its provinces, 1990–2017: A systematic analysis for the global burden of disease study 2017. *The Lancet*. 2019;394(10204):1145-1158. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30427-1/fulltext. Accessed Dec 26, 2020. doi: 10.1016/S0140-6736(19)30427-1.

33. Tan X, Liu X, Shao H. Healthy China 2030: A vision for health care. *Value in Health Regional Issues*. 2017;12:112-114. https://doi.org/10.1016/j.vhri.2017.04.001.

34. Phelan H. 3 reasons why pharma is heading to China. HealthXL Web site. https://www.healthxl.com/blog/3-reasons-why-pharma-is-heading-to-china. Published March 1, 2019. Updated 2019. Accessed Oct 20, 2020.

35. Xu W. Nation to promote internet plus healthcare. State Council of the People's Republic of China Web site. http://english.www.gov.cn/premier/news/2018/04/12/content_281476109872514.htm. Published April 12, 2018. Updated 2018. Accessed February 20, 2021.

36. Zhong N. Innovating healthcare for tech edge. China Daily Web site. https://www.chinadaily.com.cn/business/2017-09/25/content_32447314.htm. Published September 25, 2017. Updated 2017. Accessed April 14, 2021.

37. Sanofi. Unlocking the potential of technology for the benefit of health in China. Sanofi Web site. https://www.sanofi.com/about-us/nos-recits/2019-11-15. Published November 15, 2019. Updated 2019. Accessed Jan 2, 2021.

38. Roberts H, Cowls J, Morley J, Taddeo M, Wang V, Floridi L. The Chinese approach to artificial intelligence: An analysis of policy, ethics, and regulation. *AI & SOCIETY*. 2020. https://doi.org/10.1007/s00146-020-00992-2.

39. Wincuinas J. Could Healthy China 2030 also be a blueprint for investment opportunity? The Economist Web site. https://eiuperspectives.economist.com/financial-services/could-healthy-china-2030-also-be-blueprint-investment-opportunity. Published October 22, 2020. Updated 2020. Accessed Jan 4, 2021.

40. State Council of the People's Republic of China. Notice of the state council issuing the new generation of artificial intelligence development plan. Foundation for Law and International Affairs Web site. https://flia.org/wp-content/uploads/2017/07/A-New-Generation-of-Artificial-Intelligence-Development-Plan-1.pdf. Published July 8, 2017. Updated 2017. Accessed January 5, 2021.

41. Schwamm LH. Can telehealth help flatten the curve of COVID-19? Harvard Health Publishing Web site. https://www.health.harvard.edu/blog/can-telehealth-help-flatten-the-curve-of-covid-19-2020032419288. Published March 24, 2020. Updated 2020. Accessed Oct 10, 2020.

42. Hollander JE, Carr BG. Virtually perfect? telemedicine for COVID-19. *N Engl J Med*. 2020;382(18):1679-1681. https://doi.org/10.1056/NEJMp2003539. doi: 10.1056/NEJMp2003539.

43. Greenhalgh T, Wherton J, Shaw S, Morrison C. Video consultations for COVID-19. *BMJ*. 2020;368:m998. https://doi.org/10.1136/bmj.m998.

44. Monaghesh E, Hajizadeh A. The role of telehealth during COVID-19 outbreak: A systematic review based on current evidence. *BMC Public Health*. 2020;20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7395209/. Accessed Oct 8, 2020. doi: 10.1186/s12889-020-09301-4.

45. Steger A. Can AI help patients take control of their care? HealthTech Magazine Web site. https://healthtechmagazine.net/article/2019/10/can-ai-help-patients-take-control-their-care-perfcon. Published October 31, 2019. Updated 2019. Accessed Oct 11, 2020.

46. Wittbold KA, Carroll C, Iansiti M, Zhang HM, Landman AB. How hospitals are using AI to battle COVID-19. *Harvard Business Review*. 2020. https://hbr.org/2020/04/how-hospitals-are-using-ai-to-battle-covid-19. Accessed Oct 11, 2020.

47. Han Y, Lie RK, Guo R. The internet hospital as a telehealth model in China: Systematic search and content analysis. *J Med Internet Res*. 2020;22(7):e17995. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7424477/. Accessed Oct 14, 2020. doi: 10.2196/17995.

48. Cui F, Ma Q, He X, et al. Implementation and application of telemedicine in China: Cross-sectional study. *JMIR Mhealth Uhealth*. 2020;8(10):e18426. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7647817/. Accessed Feb 22, 2021. doi: 10.2196/18426.

49. China Daily. Internet-based healthcare helps fight against epidemic. Asia News Network Web site. https://asianews.network/2020/03/04/internet-based-healthcare-helps-fight-against-epidemic/. Published March 4, 2020. Updated 2020. Accessed Oct 11, 2020.

50. Lee K, Zafra M. COVID-19 makes digital care the norm in China. Oliver Wyman Web site. https://health.oliverwyman.com/2020/04/covid-19-makes-digital-care-the-norm-in-china.html. Published April 29, 2020. Updated 2020. Accessed Oct 8, 2020.

51. Wu D, Hesketh T, Shu H, Lian W, Tang W, Tian J. Description of an online hospital platform, China. *Bull World Health Organ*. 2019;97(8):578-579. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6653824/. Accessed Oct 13, 2020. doi: 10.2471/BLT.18.226936.

52. Xu W, Wu J, Cao L. COVID-19 pandemic in China: Context, experience and lessons. *Health Policy Technol*. 2020;9(4):639-648. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7451009/. Accessed Jan 4, 2021. doi: 10.1016/j.hlpt.2020.08.006.

53. Sun S, Yu K, Xie Z, Pan X. China empowers internet hospital to fight against COVID-19. *J Infect*. 2020;81(1):e67-e68. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7129532/. Accessed Nov 22, 2020. doi: 10.1016/j.jinf.2020.03.061.

54. Zhang H. Early lessons from the frontline of the 2019-nCoV outbreak. *Lancet*. 2020;395(10225):687. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7135082/. Accessed Nov 23, 2020. doi: 10.1016/S0140-6736(20)30356-1.

55. National Health Commission of the People's Republic of China. Guiding opinions of the national medical insurance administration and the national health commission on promoting the development of "internet +" medical insurance services during the period of prevention and control of the new coronary pneumonia epidemic. NHC Web site. http://www.gov.cn/zhengce/zhengceku/2020-03/03/content_5486256.htm. Published February 28, 2020. Updated 2020. Accessed November 22, 2020.

56. Gong K, Xu Z, Cai Z, Chen Y, Wang Z. Internet hospitals help prevent and control the epidemic of COVID-19 in China: Multicenter user profiling study. *Journal of Medical Internet Research*. 2020;22(4):e18908. https://www.jmir.org/2020/4/e18908/. Accessed Nov 23, 2020. doi: 10.2196/18908.

57. Chang K. As the coronavirus spreads, healthcare goes digital. Bain Web site. https://www.bain.com/insights/as-coronavirus-spreads-healthcare-goes-digital-snap-chart/. Published February 26, 2020. Updated 2020. Accessed Dec 28, 2020.

58. Digital Health Central. China and telehealth in a post-COVID-19 world. Digital Health Central Web site. https://digitalhealthcentral.com/2020/11/13/china-and-telehealth-in-a-post-covid19-world/. Published November 13, 2020. Updated 2020. Accessed Dec 27, 2020.

59. The Medical Futurist. China is building the ultimate technological health paradise. Or is it? Medical Futurist Web site. https://medicalfuturist.com/china-digital-health/. Published February 19, 2019. Updated 2019. Accessed October 14, 2020.

60. Cai R, Tang J, Deng C, et al. Violence against health care workers in China, 2013–2016: Evidence from the national judgment documents. *Human Resources for Health*. 2019;17:103. https://doi.org/10.1186/s12960-019-0440-y.

61. Xiao C. China as a digital transformation sandbox: A prescription for pharma multinationals. *Deloitte China*. 2020. https://www2.deloitte.com/content/dam/Deloitte/cn/Documents/life-sciences-health-care/deloitte-cn-lshc-digital-transformation-sandbox-en-200715.pdf. Accessed October 20, 2020.

62. Liu Z, Liang K. Bayer looking to strengthen R&D focus, innovation. China Daily Web site. https://www.chinadaily.com.cn/a/202001/04/WS5e0fd06da310cf3e355826ad.html. Published January 4, 2020. Updated 2020. Accessed January 5, 2021.

63. Ng E. Ping An Good Doctor, China's largest health care platform, reports jump in users amid coronavirus, smaller than expected annual loss. South China Morning Post Web site. https://www.scmp.com/business/article/3050074/ping-good-doctor-chinas-largest-health-care-platform-reports-jump-users. Published February 12, 2020. Updated 2020. Accessed Oct 13, 2020.

64. Xie D, Li X. A new view on China's digital health care: Launching innovative biopharma in China. Deloitte Web site. https://www2.deloitte.com/content/dam/insights/us/articles/r722480_new-view-on-chinas-digital-health-care/DI_A-new-view-on-Chinas-digital-health-care.pdf. Published 2019. Updated 2019. Accessed November 3, 2020.

65. Zhao S. Sanofi committed to innovation for its efforts in 'empowering life'. China Daily Web site. https://www.chinadaily.com.cn/cndy/2018-01/10/content_35472407.htm. Published January 10, 2018. Updated 2018. Accessed November 3, 2020.

66. Wang Y. Bayer forms strategic partnership with AliHealth. China Daily Web site. https://www.chinadaily.com.cn/business/2017-10/21/content_33522563.htm. Published October 21, 2017. Updated 2017. Accessed January 5, 2021.

67. David M. Bayer in China: How the pharma giant gained the strong approval of Chinese consumers. Daxue Consulting Web site. https://daxueconsulting.com/bayer-in-china/. Published July 31, 2020. Updated 2020. Accessed January 5, 2021.

68. Bayer China. Bayer china - divisions. Bayer China Web site. https://www.bayer.com.cn/index.php/AboutBayer/BayerChina/2nd/SubGroups?l=en-us. Published March 8, 2021. Updated 2021. Accessed March 10, 2021.

69. Li Y, Teng D, Shi X, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: National cross sectional study. *BMJ*. 2020;369:m997. https://doi.org/10.1136/bmj.m997.

70. Bie E. Merck KGaA, Alibaba Health collaborate on digital healthcare services in China. S&P Global Web site. https://www.spglobal.com/marketintelligence/en/news-insights/trending/bvmvmbtknuyzg-7usdhpfa2. Published June 20, 2018. Updated 2018. Accessed January 6, 2021.

71. Merck. Merck KGaA, Darmstadt, Germany, and Tencent announce collaboration on intelligent digital healthcare services in China. Merck Web site. https://www.emdgroup.com/en/news/tencent-partnership-china-23-01-2019.html. Published January 23, 2019. Updated 2019. Accessed January 6, 2021.

72. Koh D. China's online healthcare platform jianke.com enters into strategic collaboration with Pfizer. MobiHealthNews Web site. https://www.mobihealthnews.com/content/chinas-online-healthcare-platform-jiankecom-enters-strategic-collaboration-pfizer. Published November 29, 2018. Updated 2018. Accessed Oct 11, 2020.

73. PR Newswire. China's online healthcare platform jianke.com upgrades its Jianke doctor brand and enters into strategic cooperation with Pfizer. PR Newswire Web site. https://www.prnewswire.com/news-releases/chinas-online-healthcare-platform-jiankecom-upgrades-its-jianke-doctor-brand-and-enters-into-strategic-cooperation-with-pfizer-300757534.html. Published November 29, 2018. Updated 2018. Accessed Oct 11, 2020.

74. Causa Health. Causa Health: Trusted professional chronic disease management platform. Causa Health Web site. https://www.causahealth.com/. Accessed February 22, 2021.

75. Pfizer. Alibaba Cloud, Fintech Academy and Pfizer partner to accelerate healthcare innovations across Asia Pacific. Pfizer Web site. https://www.pfizer.com.sg/alibaba-cloud-fintech-academy-and-pfizer-partner-accelerate-healthcare-innovations-across-asia. Published July 6, 2020. Updated 2020. Accessed January 6, 2021.

76. Novartis. AI nurse set to transform standards of care for heart failure patients in China. Novartis Web site. https://www.novartis.com/news/ai-nurse-set-transform-standards-care-heart-failure-patients-china. Published April 30, 2020. Updated 2020. Accessed Mar 11, 2021.

77. Novartis. AI nurse evolving for health failure patients in China. Novartis Web site. https://www.novartis.com/stories/patient-perspectives/ai-nurse-evolving-health-failure-patients-china. Published January 7, 2021. Updated 2021. Accessed Mar 11, 2021.

78. Alibaba Health. Alibaba Health 2020 interim report. Alibaba Health Web site. https://doc.irasia.com/listco/hk/alihealth/interim/2021/intrep.pdf. Published November 25, 2020. Updated 2020. Accessed March 11, 2021.

79. Zhou W. Pharmaceutical companies sign deals with China's tech giants. China Daily Web site. https://www.chinadaily.com.cn/a/202011/08/WS5fa7b230a31024ad0ba83cf7.html. Published November 8, 2020. Updated 2020. Accessed January 6, 2021.

80. Microsoft. Novo Nordisk and Microsoft will introduce an educational Chinese-speaking chatbot for diabetes patients. Microsoft Web site. https://news.microsoft.com/apac/2020/11/11/novo-nordisk-and-microsoft-will-introduce-an-educational-chinese-speaking-chatbot-for-diabetes-patients/. Published November 11, 2020. Updated 2020. Accessed January 6, 2021.

81. National Bureau of Statistics of China. 2020 China statistical yearbook. National Bureau of Statistics of China Web site. http://www.stats.gov.cn/tjsj/ndsj/2020/indexeh.htm. Published 2020. Updated 2020. Accessed January 20, 2021.

82. Ho A. AI can solve China's doctor shortage. Here's how. World Economic Forum Web site. https://www.weforum.org/agenda/2018/09/ai-can-solve-china-s-doctor-shortage-here-s-how/. Published September 17, 2018. Updated 2018. Accessed Dec 26, 2020.

83. Wang Z, Chen Y, Pan T, Liu X, Hu H. The comparison of healthcare utilization inequity between URRBMI and NCMS in rural China. *Int J Equity Health*. 2019;18:90. https://doi.org/10.1186/s12939-019-0987-1.

84. Ping An Good Doctor. Ping An Good Doctor issues 2019 sustainable development report, platform visits hit 1.11 billion during epidemic. PR Newswire Web site. https://www.prnewswire.com/news-releases/ping-an-good-doctor-issues-2019-sustainable-development-report-platform-visits-hit-1-11-billion-during-epidemic-301005828.html. Published February 17, 2020. Updated 2020. Accessed Jan 4, 2021.

85. Ding L, She Q, Chen F, et al. The internet hospital plus drug delivery platform for health management during the COVID-19 pandemic: Observational study. *Journal of Medical Internet Research*. 2020;22(8):e19678. https://doi.org/10.2196/19678. Accessed Oct 20, 2020. doi: 10.2196/19678.

86. National Health Commission of the People's Republic of China. China reports rapid growth in number of medical doctors. NHC Web site. http://en.nhc.gov.cn/2020-08/20/c_81451.htm. Published August 20, 2020. Updated 2020. Accessed November 1, 2020.

87. United Nations Children's Fund, (UNICEF). Geographic regions of china. UNICEF China Web site. https://www.unicef.cn/en/figure-11-geographic-regions-china. Accessed January 24, 2021.

88. McKeown RE. The epidemiologic transition: Changing patterns of mortality and population dynamics. *Am J Lifestyle Med*. 2009;3(1 Suppl):19S-26S. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805833/. Accessed Dec 27, 2020. doi: 10.1177/1559827609335350.

89. Ping An Healthcare and Technology Company Limited. Ping An healthcare and technology company limited announces 2020 interim report. PR Newswire Web site. https://www.prnewswire.com/news-releases/ping-an-healthcare-and-technology-company-limited-announces-2020-interim-report-301116232.html. Published August 21, 2020. Updated 2020. Accessed Jan 4, 2021.

90. O'Meara S. The robot recruits in China's health-care system. *Nature*. 2020;582(7813):S49-S51. https://www.nature.com/articles/d41586-020-01793-9. Accessed Dec 20, 2020. doi: 10.1038/d41586-020-01793-9.

91. Dujmovic J. How China used robots, drones and artificial intelligence to control the spread of the coronavirus. MarketWatch Web site. https://www.marketwatch.com/story/how-china-used-robots-drones-and-artificial-intelligence-to-control-the-spread-of-the-coronavirus-2020-05-01. Published May 1, 2020. Updated 2020. Accessed Dec 28, 2020.

92. O'Meara S. Medical robotics in China: The rise of technology in three charts. *Nature*. 2020;582(7813):S51-S52. https://www.nature.com/articles/d41586-020-01795-7. Accessed Dec 20, 2020. doi: 10.1038/d41586-020-01795-7.

93. Yang J, Reuter T. 3 ways China is using drones to fight coronavirus. World Economic Forum Web site. https://www.weforum.org/agenda/2020/03/three-ways-china-is-using-drones-to-fight-coronavirus/. Published March 16, 2020. Updated 2020. Accessed Dec 28, 2020.

94. Liu Y. China adapts surveying, mapping, delivery drones to enforce world's biggest quarantine and contain coronavirus outbreak. South China Morning Post Web site. https://www.scmp.com/business/china-business/article/3064986/china-adapts-surveying-mapping-delivery-drones-task. Published March 5, 2020. Updated 2020. Accessed Dec 28, 2020.

95. Mozur P, Barnes JE, Krolik A. Popular Chinese-made drone is found to have security weakness. NY Times Web site. https://www.nytimes.com/2020/07/23/us/politics/dji-drones-security-vulnerability.html. Published July 23, 2020. Updated 2020. Accessed February 22, 2021.

96. British Broadcasting Corporation. Chinese drone and chip makers added to US banned list. BBC News Web site. https://www.bbc.com/news/technology-55367163. Published December 18, 2020. Updated 2020. Accessed February 22, 2021.

97. Koty AC. China's social credit system: COVID-19 triggers some exemptions, obligations for businesses. China Briefing Web site. https://www.china-briefing.com/news/chinas-social-credit-system-covid-19-triggers-some-exemptions-obligations-businesses/. Published March 26, 2020. Updated 2020. Accessed Dec 4, 2020.

98. Lee A. What is China's social credit system and why is it controversial? South China Morning Post Web site. https://www.scmp.com/economy/china-economy/article/3096090/what-

chinas-social-credit-system-and-why-it-controversial. Published August 9, 2020. Updated 2020. Accessed Dec 7, 2020.

99. Li Y. Shenzhen issues blacklist, whitelist on animal consumption amid COVID-19. China News Service Web site. http://www.ecns.cn/news/society/2020-02-26/detail-ifztvsqr0582549.shtml. Published February 26, 2020. Updated 2020. Accessed December 8, 2020.

100. Borak M. Hiding your coronavirus history can give you bad social credit. South China Morning Post Web site. https://www.scmp.com/abacus/news-bites/article/3049568/hiding-your-coronavirus-history-can-give-you-bad-social-credit. Published February 7, 2020. Updated 2020. Accessed Dec 8, 2020.

101. Shanghai Municipal People's Congress. News! The Municipal People's Congress standing committee voted to pass decisions on epidemic prevention and control. Shanghai Municipal People's Congress Web site. http://www.spcsc.sh.cn/n1939/n1944/n1945/n2436/u1ai205298.html. Updated 2020. Accessed February 7, 2020.

102. Li X, Lu Z, Zhang J, et al. The urgent need to empower rare disease organizations in China: An interview-based study. *Orphanet J Rare Dis*. 2020;15:282. https://doi.org/10.1186/s13023-020-01568-5.

103. Wei H. Takeda set to unveil slew of innovative medicines in China. China Daily Web site. https://www.chinadaily.com.cn/a/202011/09/WS5fa8f270a31024ad0ba85e6e.html. Published November 9, 2020. Updated 2020. Accessed Feb 22, 2021.

104. Creswell JW, Clark VLP. *Designing and conducting mixed methods research.* Sage Publications, Inc.; 2007.

105. Center for Systems Science and Engineering at Johns Hopkins University. COVID-19 dashboard. Johns Hopkins Coronavirus Resource Center Web site. https://coronavirus.jhu.edu/map.html. Published March 7, 2021. Updated 2021. Accessed Mar 7, 2021.

106. Thomala LL. Confirmed, death and recovery cases of COVID-19 in greater China 2021, by region. Statista Web site. https://www.statista.com/statistics/1090007/china-confirmed-and-suspected-wuhan-coronavirus-cases-region/. Published March 3, 2021. Updated 2021. Accessed March 7, 2021.

107. Institute for Health Metrics and Evaluation. GBD compare | IHME viz hub. IHME Web site. http://vizhub.healthdata.org/gbd-compare. Accessed Nov 27, 2020.

108. National Institute of Mental Health. What are DALYs? NIMH Web site. https://www.nimh.nih.gov/health/statistics/global/index.shtml. Accessed November 27, 2020.

109. Murray CJL, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: A systematic analysis for the global burden of disease study 2010. *Lancet.* 2012;380(9859):2197-2223. https://pubmed.ncbi.nlm.nih.gov/23245608/. Accessed Nov 27, 2020. doi: 10.1016/S0140-6736(12)61689-4.

110. World Health Organization. The global burden of disease concept. WHO Web site. https://www.who.int/quantifying_ehimpacts/publications/en/9241546204chap3.pdf. Accessed December 22, 2020.

111. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — china, 2020. *CCDCW*. 2020;2(8):113-122. http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.032. Accessed Feb 17, 2021. doi: 10.46234/ccdcw2020.032.

112. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care*. 2020;24:179. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7187660/. Accessed Feb 17, 2021. doi: 10.1186/s13054-020-02902-w.

113. Guan W, Liang W, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in china: A nationwide analysis. *The European Respiratory Journal*. 2020;55(5):2000547. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7098485/. doi: 10.1183/13993003.00547-2020.

114. Xu X, Cai Y, Wu S, et al. Assessment of internet hospitals in China during the COVID-19 pandemic: National cross-sectional data analysis study. *Journal of Medical Internet Research*. 2021;23(1):e21825. https://www.jmir.org/2021/1/e21825/. Accessed Feb 17, 2021. doi: 10.2196/21825.

115. Delve. The essential guide to coding qualitative data. Delve Web site. https://delvetool.com/guide. Accessed Apr 15, 2021.

116. Hiatt JM. *ADKAR: A model for change in business, government and our community.* 1st ed. Loveland, Colorado: Prosci Learning Center Publications; 2006.

117. Prosci Inc. Applications of the ADKAR model for change. Prosci Web site. https://www.prosci.com/adkar/applications-of-adkar. Accessed Mar 8, 2021.

118. Mao W, Yip CW, Chen W. Complications of diabetes in China: Health system and economic implications. *BMC Public Health*. 2019;19:269. https://doi.org/10.1186/s12889-019-6569-8.

119. Lipsitch M, Donnelly CA, Fraser C, et al. Potential biases in estimating absolute and relative case-fatality risks during outbreaks. *PLOS Neglected Tropical Diseases*. 2015;9(7):e0003846. https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0003846. Accessed Mar 17, 2021. doi: 10.1371/journal.pntd.0003846.

120. JD Health. JD health global offering. Hong Kong Exchanges and Clearing Web site. https://www1.hkexnews.hk/listedco/listconews/sehk/2020/1126/2020112600117.pdf. Published November 26, 2020. Updated 2020. Accessed March 11, 2021.

121. Ping An Healthcare and Technology Company. Ping An healthcare and technology company 2020 interim report. Ping An Good Doctor Web site. http://asia.blob.euroland.com/press-releases-attachments/1247655/HKEX-EPS_20200909_9435932_0.PDF. Published August 20, 2020. Updated 2020. Accessed March 11, 2021.

122. Lin C. In the face of lockdown, China's E-commerce giants deliver. *Harvard Business Review*. 2020. https://hbr.org/2020/04/in-the-face-of-lockdown-chinas-e-commerce-giants-deliver. Accessed Jan 4, 2021.

123. Liu A. Merck, Bristol Myers, AstraZeneca and Roche lose bid to expand PD-1/L1 reach in China. Fierce Pharma Web site. https://www.fiercepharma.com/pharma-asia/pd-1-l1-drugmakers-merck-bristol-myers-astrazeneca-and-roche-lose-bid-to-expand-reach. Published December 29, 2020. Updated 2020. Accessed February 23, 2021.

124. National Healthcare Security Administration. The National Medical Security Administration and the Ministry of Human Resources and Social Security issued the 2020 National Medical Insurance drug catalog. NHSA Web site. http://www.nhsa.gov.cn/art/2020/12/28/art_14_4221.html. Published December 28, 2020. Updated 2020. Accessed March 3, 2021.

125. National Healthcare Security Administration. Notice of the Ministry of Human Resources and Social Security of the National Medical Insurance Administration on issuing the National Basic Medical Insurance, Work Injury Insurance and Maternity Insurance drug catalog. NHSA Web site. http://www.nhsa.gov.cn/art/2020/12/28/art_37_4220.html. Published December 28, 2020. Updated 2020. Accessed March 3, 2021.

126. Thomala LL. Penetration rate of mobile internet users in China 2008-2020. Statista Web site. https://www.statista.com/statistics/255552/penetration-rate-of-mobile-internet-users-in-china/. Published February 9, 2021. Updated 2021. Accessed Mar 6, 2021.

127. Statista Research Department. Mobile internet user penetration in the United States from 2015 to 2025. Statista Web site. https://www.statista.com/statistics/275587/mobile-phone-internet-user-penetration-us/. Published February 4, 2021. Updated 2021. Accessed April 15, 2021.

128. Thomala LL. Penetration rate of internet users in China 2008-2020. Statista Web site. https://www.statista.com/statistics/236963/penetration-rate-of-internet-users-in-china/. Published February 9, 2021. Updated 2021. Accessed Mar 6, 2021.

129. Office of the National Coordinator for Health Information Technology. What is telehealth? How is telehealth different from telemedicine? HealthIT.gov Web site. https://www.healthit.gov/faq/what-telehealth-how-telehealth-different-telemedicine. Published October 17, 2019. Updated 2019. Accessed March 3, 2021.

130. EqualOcean. WeChat's health mini program has access to healthcare reimbursement. EqualOcean Web site. https://equalocean.com/briefing/20200911230003665. Published September 11, 2020. Updated 2020. Accessed Apr 16, 2021.

131. U.S. Food & Drug Administration. Real-world evidence. FDA Web site. https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence. Published November 30, 2020. Updated 2020. Accessed Mar 4, 2021.

132. Liang Y. Remote clinical trials in China during the COVID-19 pandemic. DIA Global Forum Web site. https://globalforum.diaglobal.org/issue/june-2020/remote-clinical-trials-in-china-during-the-covid-19-pandemic/. Published June 3, 2020. Updated 2020. Accessed Dec 4, 2020.

133. Liao R. Tencent backs Chinese healthcare portal DXY in $500M round. TechCrunch Web site. https://social.techcrunch.com/2020/12/28/china-dxy-500-million-funding-tencent/. Published December 28, 2020. Updated 2020. Accessed Mar 5, 2021.

134. Global Rare Disease Commission. Global commission to end the diagnostic odyssey for children with a rare disease. Global Commission Web site. https://www.globalrarediseasecommission.com/. Accessed April 16, 2021.

135. Prosci Inc. Change management articles | prosci | ADKAR. Prosci Web site. https://www.prosci.com/resources/articles/tag/adkar. Accessed Mar 10, 2021.

136. Meridian Medical Network Corp. Meridian "angel robot" intelligent medicine service system. Meridian Web site. https://en.mmednet.com/product/angeldoctor. Accessed March 13, 2021.

137. Ping An Group. Ping An unveils health care ecosystem strategy - A growth engine for the group empowered by world-leading healthtech. Ping An Web site. https://group.pingan.com/media/news/News-2020/Ping-An-Unveils-Health-Care-Ecosystem-Strategy.html. Published September 23, 2020. Updated 2020. Accessed Feb 20, 2021.

138. National Healthcare Security Administration. 2019 statistical bulletin of the national medical security development. NHSA Web site. http://www.nhsa.gov.cn/art/2020/6/24/art_7_3268.html. Published June 24, 2020. Updated 2020. Accessed March 13, 2021.

139. Harvard T.H. Chan School of Public Health. Partners - China Health Partnership. Harvard China Health Partnership Web site. https://sites.sph.harvard.edu/china-health-partnership/partners/. Accessed Mar 13, 2021.

140. Balasubramanian S. Drones are now being used to deliver COVID-19 vaccines. Forbes Web site. https://www.forbes.com/sites/saibala/2021/03/06/drones-are-now-being-used-to-deliver-covid-19-vaccines/. Published March 6, 2021. Updated 2021. Accessed Mar 13, 2021.

141. Fearn N. IoT smart fridge revolutionising vaccine care. Internet of Business Web site. https://internetofbusiness.com/iot-smart-fridge-vaccine-care/. Published August 17, 2016. Updated 2016. Accessed Mar 13, 2021.

142. Bauchner H, Golub RM, Zylke J. Editorial Concern—Possible reporting of the same patients with COVID-19 in different reports. *JAMA*. 2020;323(13):1256. https://jamanetwork.com/journals/jama/fullarticle/2763371. doi: 10.1001/jama.2020.3980.

143. Hu L, Ding H, Liu S, Wang Z, Hu G, Liu Y. Influence of patient and hospital characteristics on inpatient satisfaction in China's tertiary hospitals: A cross-sectional study. *Health Expectations*. 2020;23(1):115-124. https://doi.org/10.1111/hex.12974. Accessed Apr 3, 2021. doi: https://doi.org/10.1111/hex.12974.

144. Agency for Healthcare Research and Quality. Warm handoff: Intervention. AHRQ Web site. http://www.ahrq.gov/patient-safety/reports/engage/interventions/warmhandoff.html. Accessed Apr 11, 2021.

145. Bowman E. After data breach exposes 530 million, Facebook says it will not notify users. NPR Web site. https://www.npr.org/2021/04/09/986005820/after-data-breach-exposes-530-million-facebook-says-it-will-not-notify-users. Published April 9, 2021. Updated 2021. Accessed Apr 11, 2021.

146. Access to Medicine Foundation. 2021 ranking - Access to Medicine Index. Access to Medicine Foundation Web site. https://accesstomedicinefoundation.org/access-to-medicine-index/report-cards/takeda-pharmaceutical-co-ltd. Accessed Mar 15, 2021.

147. Xiao H, Zhang Y, Kong D, Li S, Yang N. Social capital and sleep quality in individuals who self-isolated for 14 days during the coronavirus disease 2019 (COVID-19) outbreak in January 2020 in china. *Med Sci Monit.* 2020;26:e923921-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7111105/. Accessed Feb 20, 2021. doi: 10.12659/MSM.923921.

148. China Global Television Network. China's air and surface water quality improved January-April. China Global Television Network Web site. https://news.cgtn.com/news/2020-05-20/China-s-air-and-surface-water-quality-improved-January-April-QE5NXu1wSQ/index.html. Published May 20, 2020. Updated 2020. Accessed Feb 20, 2021.

149. Ward SL. Omics, bioinformatics, computational biology. AltTox Web site. http://alttox.org/mapp/emerging-technologies/omics-bioinformatics-computational-biology/. Published July 3, 2014. Updated 2014. Accessed Apr 15, 2021.

150. Servier. Servier China: Committed to care for 40 years. Servier Web site. https://servier.com/en/communique/servier-china-committed-to-care-for-40-years/. Published April 16, 2019. Updated 2019. Accessed January 6, 2021.

151. Morgan J. A simple explanation of 'the internet of things'. Forbes Web site. https://www.forbes.com/sites/jacobmorgan/2014/05/13/simple-explanation-internet-things-that-anyone-can-understand/. Published May 13, 2014. Updated 2014. Accessed Dec 26, 2020.

152. World Health Organization. United states of America: WHO coronavirus disease (COVID-19) dashboard with vaccination data. WHO Web site. https://covid19.who.int/region/amro/country/us. Published April 15, 2021. Updated 2021. Accessed Apr 15, 2021.

8. APPENDICES

8.1. Appendix A: Primary and Auxiliary COVID Internet Hospital Functions

For primary functions, internet hospitals reduced overcrowding in physical hospitals through online education and psychological interventions, as well as reducing repeat in-person visits.[56] The online medical services taught the public essential COVID-19 prevention skills and helped also alleviate social panic and relieve hypochondriac suspicions, which enhanced psychological resilience and reduced unnecessary physical hospital visits. Furthermore, internet hospitals run by public hospitals offered online triage services and guided patients to corresponding offline departments based on their symptoms. This routed suspected cases through isolated channels to specialized outpatient clinics, which reduced contact within hospitals and chances of infection. Furthermore, this protected medical staff from unnecessary workplace exposure and being overburdened with patients. Internet hospitals also integrated online resources with offline epidemic control efforts executed by epidemiologic investigation organizations and community offices. By screening and identifying all symptomatic patients and close contacts who were required to be in self-isolation, internet hospitals facilitated supervision offline for potential undocumented cases and promoted social distancing.[56]

For auxiliary functions, internet hospitals provided basic medical assistance to the public throughout the epidemic.[56] Numerous non-emergency outpatient hospital departments were closed, which caused most physical clinics to be inaccessible to the public. Therefore, internet hospitals allowed patients to remain connected with attending doctors. For patients with new mild symptoms, physicians could safely provide advice on self-management of treatment and care. For severe patients, online clinicians could direct them to visit offline hospitals quickly. During

individual self-isolation, internet hospitals also improved quality of life by reducing anxiety through social workers and psychotherapists providing online help and support.[56,147]

8.2. Appendix B. Additional Tables: COVID Burden, China Population Statistics, & Pharma Digital Collaborations

Table 14. COVID-19 cases and deaths in Greater China as of March 7, 2021, by region.

	Currently confirmed	Cumulative Cases	Deaths	Incidence Rate (per 100,000)	Case Fatality Ratio (%)
Total	461	102,080	4,848		
Hubei	0	68,151	4,512	115.18	6.62
Hong Kong	259	11,090	202	147.93	1.82
Guangdong	43	2,229	8	1.96	0.36
Shanghai	36	1,811	7	7.47	0.39
Zhejiang	7	1,322	1	2.30	0.08
Henan	2	1,305	22	1.36	1.69
Hebei	0	1,317	7	1.74	0.53
Heilongjiang	0	1,610	13	4.27	0.81
Hunan	5	1,037	4	1.50	0.39
Beijing	8	1,049	9	4.87	0.86
Anhui	0	994	6	1.57	0.60
Xinjiang	0	980	3	3.94	0.31
Jiangxi	0	935	1	2.01	0.11
Shandong	1	869	7	0.86	0.81
Sichuan	37	918	3	1.10	0.33
Taiwan	25	967	10	4.06	1.03
Jiangsu	2	704	0	0.87	0.00
Chongqing	0	591	6	1.91	1.02
Fujian	4	551	1	1.40	0.18
Shaanxi	8	555	3	1.44	0.54
Liaoning	2	406	2	0.93	0.49
Inner Mongolia	1	367	1	1.45	0.27
Tianjin	15	361	3	2.31	0.83
Guangxi	0	267	2	0.54	0.75
Yunnan	3	234	2	0.48	0.85
Shanxi	2	240	0	0.65	0.00

Table 14 (Continued).

Jilin	0	573	3	2.12	0.52
Gansu	0	187	2	0.71	1.07
Hainan	0	171	6	1.83	3.51
Guizhou	0	147	2	0.41	1.36
Ningxia	0	75	0	1.09	0.00
Macao	1	48	0	7.39	0.00
Qinghai	0	18	0	0.30	0.00
Tibet	0	1	0	0.03	0.00

Sources: DXY.cn, Johns Hopkins COVID-19 Dashboard.[6,105]

Table 15. 2019 urban and rural population in China, by province and region.

	Total Year-End Population (10,000 persons)	**Urban**		**Rural**	
		Population	**Proportion**	**Population**	**Proportion**
National Total*	140,005	84,843	60.60	55,162	39.40
Eastern					
Beijing	2,154	1,865	86.60	289	13.40
Tianjin	1,562	1,304	83.48	258	16.52
Hebei	7,592	4,374	57.62	3,218	42.38
Liaoning	4,352	2,964	68.11	1,388	31.89
Shanghai	2,428	2,144	88.30	284	11.70
Jiangsu	8,070	5,698	70.61	2,372	29.39
Zhejiang	5,850	4,095	70.00	1,755	30.00
Fujian	3,973	2,642	66.50	1,331	33.50
Shandong	10,070	6,194	61.51	3,876	38.49
Guangdong	11,521	8,226	71.40	3,295	28.60
Hainan	945	560	59.23	385	40.77
Central					
Shanxi	3,729	2,221	59.55	1,508	40.45
Jilin	2,691	1,568	58.27	1,123	41.73
Heilongjiang	3,751	2,284	60.90	1,467	39.10
Anhui	6,366	3,553	55.81	2,813	44.19
Jiangxi	4,666	2,679	57.42	1,987	42.58

Table 15 (Continued).

Henan	9,640	5,129	53.21	4,511	46.79
Hubei	5,927	3,615	61.00	2,312	39.00
Hunan	6,918	3,959	57.22	2,959	42.78
Western					
Inner Mongolia	2,540	1,609	63.37	931	36.63
Guangxi	4,960	2,534	51.09	2,426	48.91
Chongqing	3,124	2,087	66.80	1,037	33.20
Sichuan	8,375	4,505	53.79	3,870	46.21
Guizhou	3,623	1,776	49.02	1,847	50.98
Yunnan	4,858	2,376	48.91	2,482	51.09
Tibet	351	111	31.54	240	68.46
Shaanxi	3,876	2,304	59.43	1,572	40.57
Gansu	2,647	1,284	48.49	1,363	51.51
Qinghai	608	337	55.52	271	44.48
Ningxia	695	416	59.86	279	40.14
Xinjiang	2,523	1,309	51.87	1,214	48.13

*Data in the table are estimates from the 2019 National Sample Survey on Population Changes. National total population was adjusted on basis of sampling and non-sampling errors. No adjustment was made to regional figures.

Source: National Bureau of Statistics of China, 2020.[81]

Table 16. Pharma companies and their corresponding digital health initiatives and partners in China.

Pharma Company	Partner	Initiative	Therapeutic Area	Type
Pfizer	Alibaba Health/ Cloud	QR scanning to detect low quality/fake generics	Multiple	Big Tech
		Full-chain, online, closed-loop vaccination service	Vaccines	
		Healthcare FinTech Alliance (affordability, value-based agreements, digital therapeutics, outcome monitoring, population health, digital personalized healthcare, driving adoption rate of innovative health tech devices)	Multiple	
	Yidu Cloud (CausaHealth) & Jianke Pharmaceutical	Online hospital for personalized chronic disease management - medication reminders, prescription refill and delivery services, telephone and online consultation service, AI-powered medical assistant	Cardiovascular disease, cerebrovascular disease	Big Tech, Online Pharmacy

Table 16 (Continued).

Sanofi	Ping An Good Doctor/ Smart City	Transform diabetes management & interaction between patients & physicians, healthcare stakeholders (using Ping An Smart City Technology)	Diabetes	Big Tech/ Insurance
	Tencent (WeDoctor/ WeChat)	Innovative digital solutions for unmet medical needs, improve disease awareness, health literacy, & management	Rare, immunological, neurological, chronic diseases	Big Tech
		Smart Community Chronic Disease Management (robotic doctor assistants, AI medication reminders, electronic patient files)		
	Alibaba Health/ Cloud	Comfort at the Fingertips app (product traceability, health literacy, health management)	Chronic disease	Big Tech
	Suzhou (Jiangsu province)	Global research institute	R&D	Government
	Chengdu (Sichuan province)	Global R&D site - tech-focused operation to strengthen Sanofi's digital capabilities and speed up clinical trial analysis	R&D	Government
	Meishan (Sichuan province) and China Diabetes Innovation Alliance	Grassroots diabetes intervention	Diabetes	Government
	1,600+ rural Chinese counties	Digital treatment solutions for primary care	Multiple, Primary Care	Government

Table 16 (Continued).

Sanofi	Shenzhen Municipal People's Government (Guangdong province)	Vaccines access using digital health applications and technologies	Vaccines	Government
Merck	Ping An Good Doctor	Personalized digital chronic disease management & intelligent healthcare services, disease awareness & prevention	Chronic diseases, infertility	Big Tech/ Insurance
		"Medical Health + Insurance" platform		
	Tencent (WeDoctor/ WeChat)	Patient-centric chronic disease management & intelligent digital platforms, health literacy	Allergies, infertility, diabetes, CVD, thyroid disorders, oncology	Big Tech
		AI doctors		
	Alibaba Health/ Cloud	Drug safety monitoring & internet health services	Diabetes, heart, & thyroid diseases	Big Tech
		Pharmaceutical e-commerce & AI-enabled healthcare apps		
Novartis	Tencent (WeDoctor/ WeChat)	AI Nurse platform (support heart failure patients, digital chronic disease management model + hospital & physician visits) - Available to any patient independent of Novartis prescriptions	Cardiovascular disease	Big Tech
	Alibaba Health/ Cloud	Patient-centric digital health model (online prescription, medication purchase, payment, & medication compliance)	Oncology	Big Tech

Table 16 (Continued).

Bristol-Myers Squibb	JD Health	Comprehensive tech platform (early diagnosis to long-term disease management)	Liver disease	Big Tech / Online Pharmacy
Bayer	Alibaba Health/ Cloud	Big data for health trends, health literacy, personalized online medical consulting	Multiple, Health & diet	Big Tech
	Tsinghua University, Peking University, Shanghai Institute of Organic Chemistry	Innovative drug discovery, improve China's R&D capabilities & pharmaceutical innovation	R&D	Academia
Novo Nordisk	Microsoft in China	Chinese-speaking, AI chatbot for diabetic patients - "Healthcare + AI" model	Diabetes	Big Tech
AstraZeneca	Alibaba Health/ Cloud	Debut anti-cancer drugs in Alibaba Health's direct online drugstores	Oncology	Big Tech

Sources: See ***Pharma*** section of literature review.

8.3. Appendix C. Interview Guides

8.3.1. Default qualitative interview guide

Intro: I'm part of Takeda's Public-Private Partnerships & Global Science Policy group. We are aiming to break down silos across the organization regarding digital innovation and understanding how it impacts healthcare access. While my specific focus is on COVID-19's impact on digital innovation and healthcare access in China, I would like to learn from your broader perspective.

1. Can you tell me about your role at Takeda?

2. How do you define digital innovation and how does your role connect to the larger digital strategy at Takeda?
    a. Probe→Examples: accelerating diagnosis and treatment/therapies, innovation, patient journey, engagement, access; better data governance
    b. How did COVID-19 accelerate or impact digital innovation at Takeda?
3. What about China makes it a prime candidate for digital innovation in pharma?
4. What therapeutic areas, assets, or clinical trial aspects do you believe could benefit the most from digital innovation?
    a. Why? (*Alt*: How could it transform them?)
    b. What types of digital innovation would be best suited? (Probe→Examples: wearables, telemedicine, etc.)
5. What are the biggest challenges to the successful implementation of digital innovation in China?
    a. How could these be mitigated?
6. How can partnerships enhance digital health efforts in China?
    a. Which partnerships do you feel will have the most impact and why?
        i. Probe→Examples: big tech players in China such as Alibaba/AliHealth, Ping An Good Doctor, Tencent; Public-Private Partnerships
    b. How could Public-Private Partnerships help minimize any implementation hurdles?
        i. Probe→Examples: Academia: Harvard telemedicine training for physicians on digital health platforms, especially in rural areas; patient advocacy organizations

7. What are some of the gaps in patient access in China that digital innovation could address?
    a. What is working and what is not?
    b. Who are the biggest stakeholders in patient engagement in China?
    c. Who else should be engaged to improve the patient journey?
        i. Probe→How are they innovating (or how should they innovate) in the digital healthcare space?
8. What is your sense of how COVID-19 has affected the patient journey and access in China?
9. What are some of the ethical issues with digital healthcare that we should be aware of? How can patients trust that their data will be safe?
    a. Probe→Examples: privacy, data integrity/protection
10. What is your vision for improving the patient journey in China?
    a. Probe→For digital health and the future of Takeda?
11. To your knowledge, how does Takeda's approach to foster, implement, and accelerate the use of digital innovation compare to other companies and players in the space? Are there any learning opportunities that you're aware of?
12. Before we close, is there anything else that you would like to add? Who else should I reach out to, to gain more insight?

8.3.2. Qualitative interview guide for patient engagement and clinical trials teams

Intro: I'm part of Takeda's Public-Private Partnerships & Global Science Policy group. We are aiming to break down silos across the organization regarding digital innovation and understanding

how it impacts healthcare access. While my specific focus is on COVID-19's impact on digital innovation and healthcare access in China, I would like to learn from your broader perspective.

1. Can you tell me about your role at Takeda?
2. How do you define digital innovation and how does your role connect to the larger digital strategy at Takeda?
    a. Probe→Examples: accelerating diagnosis and treatment/therapies, innovation, patient journey, engagement, access; better data governance
    b. How did COVID-19 accelerate or impact digital innovation at Takeda?
3. What are some of the gaps in patient access in China that digital innovation could address?
    a. What is working and what is not?
    b. Who are the biggest stakeholders in patient engagement in China?
        i. *Alternative*: How can digital innovation enhance patient engagement in China?
    c. Who else should be engaged to improve the patient journey?
        i. Probe→How are they innovating (or how should they innovate) in the digital healthcare space?
4. How could digital innovation be used to increase health literacy in patients?
5. How could digital innovation increase diversity and access in clinical trials?
    a. How could it improve how clinical trials are designed and conducted?
6. What is your sense of how COVID-19 has affected the patient journey and access in China?

7. What are some of the ethical issues with digital healthcare that we should be aware of? How can patients trust that their data will be safe?
    a. Probe→Examples: privacy, data integrity/protection
8. What is your vision for improving the patient journey in China?
    a. Probe→For digital health and the future of Takeda?
9. To your knowledge, how does Takeda's approach to foster, implement, and accelerate the use of digital innovation compare to other companies and players in the space? Are there any learning opportunities that you're aware of?
10. Before we close, is there anything else that you would like to add? Who else should I reach out to, to gain more insight?

8.3.3. Qualitative interview guide for Vaccines business unit

Intro: I'm part of Takeda's Public-Private Partnerships & Global Science Policy group. We are aiming to break down silos across the organization regarding digital innovation and understanding how it impacts healthcare access. While my specific focus is on COVID-19's impact on digital innovation and healthcare access in China, I would like to learn from your broader perspective.

1. Can you tell me about your role at Takeda?
2. How do you define digital innovation and how does your role connect to the larger digital strategy at Takeda?
    a. Probe→Examples: accelerating diagnosis and treatment/therapies, innovation, patient journey, engagement, access; better data governance
    b. How did COVID-19 accelerate or impact digital innovation at Takeda?
3. What about China makes it a prime candidate for digital innovation in pharma?

4. What are the biggest challenges to the successful implementation of digital innovation in China?
    a. How could these be mitigated?
5. What therapeutic areas, assets, or clinical trial aspects do you believe could benefit the most from digital innovation?
    a. Why? (*Alt*: How could it transform them?)
    b. What types of digital innovation would be best suited? (Probe→Examples: drones for vaccine delivery, wearables, telemedicine, etc.)
6. What are some of the ethical issues with digital healthcare that you think we should be aware of? How can patients trust that their data will be safe?
    a. Probe→Examples: privacy, data integrity/protection
7. To your knowledge, how does Takeda's approach to foster, implement, and accelerate the use of digital innovation compare to other companies and players in the space? Are there any learning opportunities that you're aware of?
    a. Probe→Example: Sanofi signed a strategic collaboration with the Shenzhen Municipal People's Government to improve vaccines access using digital health technologies
8. From your perspective what are some of the largest health care access challenges in China?
9. How can digital innovation make the dengue vaccine launch or other vaccine launches more successful?
10. What are some of the gaps in vaccines development and access and treatment of infectious disease in China that digital innovation could address?

a. Who are the most vulnerable or underserved groups?

b. Who are the biggest stakeholders in vaccine development and delivery in China?

11. What is your sense of how COVID-19 has affected vaccines access in China?

12. How can partnerships enhance digital health efforts (for vaccine development, delivery, and uptake) in China?

    a. Which partnerships do you feel will have the most impact and why?

        i. Probe→Examples: big tech players in China such as Alibaba/AliHealth, Ping An Good Doctor, Tencent; Public-Private Partnerships

    b. How could Public-Private Partnerships help minimize any implementation hurdles?

    c. Probe→Are you aware who could function as a facilitator?

        i. Examples: Similar to IMI (Europe), fNIH or C-PATH (US), or other neutral entities that bring together academia, pharma, biotech/tech, government, patient organizations, etc.

13. What is your vision for improving the patient journey in China?

    a. Probe→For digital health and the future of Takeda?

14. Before we close, is there anything else that you would like to add? Who else should I reach out to, to gain more insight?