# CREATING HEALTHY LIVES-THE FUTURE OF MEDICAL INNOVATION

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The 2019 edition of the Global Innovation Index (GII) focuses on the theme *Creating Healthy Lives—The Future of Medical Innovation*. In the years to come, medical innovations such as artificial intelligence (AI), genomics, and mobile health applications will transform the delivery of healthcare in both developed and emerging nations.

The key questions addressed in this edition of the GII include:

- What is the potential impact of medical innovation on society and economic growth, and what obstacles must be overcome to reach that potential?
- How is the global landscape for research and development (R&D) and medical innovation changing?
- What health challenges do future innovations need to address and what types of breakthroughs are on the horizon?
- What are the main opportunities and obstacles to future medical innovation and what role might new policies play?

Five key messages emerge:

 High quality and affordable healthcare for all is important for sustainable economic growth and the overall quality of life of citizens. While significant progress has been achieved across many dimensions over the last decades, significant gaps in access to quality healthcare for large parts of the global population remain.

- 2. Medical innovations are critical for closing the gaps in global healthcare provision. These innovations are happening across multiple dimensions, including core sciences, drug development, care delivery, and organizational and business models. In particular, medical technology related innovations are blossoming, with medical technology patents more numerous and growing at a faster path than pharmaceutical patents for the last decade. However, some challenges need to be overcome—notably, a decline in pharmaceutical R&D productivity and a prolonged process for deploying health innovations due to complex health ecosystems.
- 3. The convergence of digital and biological technologies is disrupting healthcare and increasing the importance of data integration and management across the healthcare ecosystem. New digital health strategies need to focus on creating data infrastructure and processes for efficient and safe data collection, management, and sharing.
- 4. Emerging markets have a unique opportunity to leverage medical innovations and invest in new healthcare delivery models to close the healthcare gap with more developed markets. Caution should be taken to ensure that new health innovations, and their related costs, do not exacerbate the health gap between the rich and poor.
- 5. To maximize the potential for future health innovation, it is important to encourage collaboration across key actors, increase funding from public and private sources, establish and maintain a skilled health workforce, and carefully evaluate the costs and benefits of medical innovations.

The section has benefited from comments by Hans Georg Bartels, Kyle Bergquist, Ridha Bouabid, Amy Dietterich, Carsten Fink, Mosahid Khan, Charles Randolph, and Ola Zahran, all at WIPO, Bruno Lanvin, INSEAD, and Bertalan Mesko, Author, *The Medical Futurist*. It draws on all outside chapter contributions that follow.

#### The impact of medical innovation a high-stakes policy matter

Over the last century, improvements in healthcare have led to a doubling of life expectancy in both high-income and developing economies.<sup>1</sup> This increase in life expectancy has helped expand the global workforce, drive economic growth, and improve the quality of life for many.<sup>2</sup>

Innovations—on both technological and non-technological fronts—have contributed to better health and economic development. Improved hygiene, enhanced public health planning, the persistent pursuit of R&D in the medical field, and the increasing role of information technologies have been key. In particular, the decades after World War II are often considered the "golden age" of medical innovation. Many of the tools of modern medicine were developed between 1940 and 1980, including antibiotics, the polio vaccine, heart procedures, chemotherapy, radiation, and medical devices such as joint replacements.<sup>3</sup>

The benefits of improved health via innovation are becoming accessible to a growing number of people within and across developed and developing countries. As societies get richer, wealth buys better health and a higher quality of life, with more people in low- and middle-income economies having access to functioning health systems.<sup>4</sup>

Indeed, over the last decade, global spending on health has been growing faster than gross domestic product (GDP)—at roughly double the rate.<sup>5</sup> Health spending has been growing even more rapidly in low- and middle-income countries—close to 6% on average—than in high-income countries, which average 4%. In 2018, global healthcare expenditures amounted to US\$7.6 trillion, accounting for around 10% of global GDP (Figure T-1.1).<sup>6</sup> By 2020, estimated global health expenditures will reach close to US\$9 trillion.<sup>7</sup> While significant progress in global healthcare has been made over the last couple of decades, there are major challenges that remain. A large proportion of the world's population lacks access to quality healthcare. Increasing health costs are also an issue, in particular, out-of-pocket payments by private households without complete medical insurance.

Medical innovation is expected to contribute to increased cost-effectiveness in the healthcare sector in the years to come. It is also key to the realization of the health-related United Nations Sustainable Development Goals (Box T-1.1).<sup>8</sup>

Now the logical question for economists and policymakers is how health innovations will continue to drive well-being and economic growth in the future.

At a glance, upcoming health innovations and their possible contributions are impressive. Policy and news reports abundantly cover much-anticipated innovations in health and medicine and the resulting improvements that patients will see.

If history is any guide, one has to avoid unwarranted optimism as to how fast health innovation arises and how efficiently it is deployed. Productivity in healthcare R&D has slowed in some respects.<sup>12</sup> Also, traditionally, innovation in health has diffused more slowly relative to other sectors.<sup>13</sup> This is due to the complex health innovation ecosystem and the seriousness of the outcomes that healthcare addresses: the life and well-being of people.<sup>14</sup>

While there is significant potential for new medical innovations, several obstacles must be overcome. Though the demand for innovation is high, there are concerns that the golden years of medical innovation may be behind us, as measured by decreases in major medical advances by year,<sup>15</sup> drug approvals,<sup>16</sup> and research productivity.<sup>17</sup>

#### BOX T-1.1

## Sustainable development goals—innovation, health, and the United Nations

The United Nations (UN) Sustainable Development Goals (SDGs) are a collection of 17 global goals that seek to make significant progress on global matters, including health, by 2030. Specifically, SDG 3 sets global health targets in several areas. Importantly, it specifies the goal of universal health coverage—including access to essential healthcare services—and sets targets to support R&D for vaccines for communicable diseases, for example.<sup>9</sup>

To reach the 2030 goals, the UN General Assembly adopted health-related political declarations.<sup>10</sup> The SDGs and the ensuing declarations recognize the critical role of innovation and R&D. As a result, SDG Indicators were set up to monitor innovation and R&D progress—for example, SDG Indicators

9.5.1-2 measure gross domestic R&D expenditure on health (health GERD) as a percentage of gross domestic product, and the number of health researchers is measured in full-time equivalents (FTEs) per million inhabitants.<sup>11</sup>

In September 2019, the United Nations High-level Political Forum (HLPF) on Sustainable Development will convene to review the progress made on the first four-year cycle of the 2030 Agenda. The GII 2019—with up-to-date metrics on the underlying innovation systems—aims to be a useful guide, helping policymakers and other stakeholders engage in crafting coherent policies and implementation strategies to harness innovation for the achievement of SDG 3.

#### FIGURE T-1.1



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# **Evolution of healthcare expenditures over time, in US\$, and as a share of GDP**

6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 2000 2004 2008 2012 2016 ▲ Government spending on health Low income Upper-middle income as a % of GDP High income Lower-middle income Year

Source: Authors based on Xu et al., 2018; WHO data.

Pharmaceutical research is limited by rapidly increasing costs and a decline in major drug approvals over the past decade.<sup>18</sup> Cost increases are caused by multiple factors, including extensive research requirements, lengthier approval processes, longer development times, higher marketing expenditures, and a concentration of R&D investments in areas where the risk of failure is high.<sup>19</sup> To develop a drug for Alzheimer's, the process involves a commitment of nearly 10 years from research to use on patients—plus over 4 years of preclinical discovery and testing (Chapter 6–Eli Lilly and Company).<sup>20</sup> Diminishing returns on drug innovation may also be reducing incentives to invest in breakthroughs.

While later sections in this chapter point to a possible, recent turnaround in pharma R&D productivity, progress is generally slow with respect to some tenacious health challenges (Chapter 2–Bhaven Sampat). Many acute and chronic conditions have few treatment options beyond marginally mitigating disease progression and/or reducing discomfort resulting from symptoms. For some illnesses, such as cancer, depression, or Alzheimer's (Chapter 6), innovation has not yet produced breakthrough cures; failure rates and clinical trial setbacks are high.

Scientific advances in life sciences or biotech have often not been matched by a corresponding increase in medical innovation.<sup>21</sup> Efforts by pharmaceutical firms to overcome the pipeline challenge by buying biotechnology firms have not always produced the desired effect.<sup>22</sup> Gene development technologies have not created the breakthroughs many might have expected.<sup>23</sup> Moreover, new health-related research fields such as neuroscience are still in their infancy.

From the innovation diffusion perspective, the speed of adoption of existing medical innovations has been slow too, primarily due to complex interactions between actors in the health ecosystem.<sup>24</sup> Moving medical innovations "from bench to bedside" is a long process, sometimes extending over several decades. Multiple parties may be involved, such as private and public research actors, including medical technology, pharmaceutical firms, and universities; providers of healthcare, such as physicians and hospitals; patients; and payers, such as medical insurance companies.<sup>25</sup> Finally, the whole process is constrained by regulatory contexts and incentives, set by government or independent regulators to ensure safety and access.<sup>26</sup>

The fragmentation of healthcare across different actors—such as payers, insurers, providers, and manufacturers—leads to challenges (Chapter 8–GE Healthcare). The underlying innovation incentives for technology or new process adoption are regularly misaligned. Technologies to decrease the role of particular medical activities—such as minimally invasive surgery—might find lukewarm reception from a particular medical profession, slowing its deployment.<sup>27</sup> In addition, patients and insurers frequently have differing views as to the acceptable cost of new treatments.<sup>28</sup> Slow feedback and knowledge flow between the actors can slow collaboration—often due to a lack of communication channels or lack of shared standards on how to exchange data and information across silos. These inefficiencies can lead to wasted time. They can also negatively affect patient outcomes (Chapter 8).<sup>29</sup>

It is noteworthy that the slow diffusion of medical innovations is more than a developed versus developing country issue. Many innovations fail to achieve widespread and sustainable use, even in economies with advanced health systems. This is true although many medical innovations are about applying existing technologies from non-medical fields in new ways in the health sector.<sup>30</sup>

Medical innovations are only slowly gravitating to developing countries; large segments of the population in the developing world remain underserved in terms of access to medical technologies and basic healthcare.<sup>31</sup> A broader diffusion of existing technologies and practices would pay large dividends (Chapter 2). The development of drugs, vaccines, medical devices, and overall healthcare operations designed for low-resource settings is key (Chapter 11–PATH).<sup>32</sup> Currently, market forces still result in pharmaceutical R&D targeting diseases that are typical of affluent societies, to the detriment of developing economies.<sup>33</sup>

Furthermore, while the focus is often on access to medicines, inadequate attention is given to contributions that would ensure the functioning of health systems in developing countries. Investments in innovations aimed at the delivery of healthcare are needed (Chapter 12–Ministry of Health, Egypt and Chapter 13–Narayana Health, India).<sup>24</sup>

Finally, too much effort is still spent on fixing health problems rather than preventing them in the first place (Chapter 9–iamYiam).<sup>35</sup> Technological and non-technological medical innovations go a long way to remedy this situation and improve prevention.

## Medical innovations are changing the landscape of health

In the years to come, new technologies are likely to enrich the provision of healthcare at a rapid pace; they will help face some of the new medical challenges outlined in the section above while producing efficiencies and disrupting current ways of delivering healthcare.

This is not only about new technology. Innovation in health system organization—for example, how doctors are consulted, how monitoring is done, how diagnoses are established and shared, and how prevention takes place—is also on the way.<sup>36</sup>

These evolutions might help fix innovation obstacles in the health system, such as overcoming knowledge silos—created when specific medical actors keep data and information about patients to themselves—or allowing for a better assessment of the true impact of particular medical technologies or pharmaceutical inventions. Beyond increasing innovation at the corporate- and country-level, the geographical landscape of global medical innovation is changing too.

Historically, the markets for health innovation—as well as the innovation pipelines themselves—have been concentrated in high-income economies, mostly in Europe and North America.<sup>37</sup> Today, the most R&D-intensive health industry firms are still in Europe and the United States of America (U.S.): Switzerland, the United Kingdom (U.K.), and the U.S. are the top holders of pharmaceutical patents; the Netherlands and the U.S. lead in medical technology patents; and Switzerland and the U.K. lead in biotech patents.

However, the geography of medical innovation is changing to progressively include emerging economies. The demand for improved health services is growing in these regions, driven by a rising middle class and robust economic growth. This is not only true for large emerging economies such as China and India but also Mexico, Viet Nam, Indonesia, South Africa, Nigeria, and many others.<sup>38</sup> The innovation capacity in emerging markets is also growing, with increasing R&D, patents, and investment in these countries (Figures T-1.2 and T-1.3, and Table T-1.1). Accordingly, pharmaceutical companies based in emerging economies have shown strong growth in recent years.<sup>39</sup>

#### A resurgence of health R&D

After the financial crisis in 2009 and a significant slowdown across sectors, worldwide pharmaceutical R&D plateaued at around US\$135 billion for more than five years, including in 2013. Investment in health began a resurgence after 2013, reaching US\$177 billion worldwide in 2019.<sup>40</sup>

Overall, the healthcare sector is one of the most important investors in innovation, second to the information technology (IT) sector. Pharmaceutical, biotech, and medical device firms are among the top global corporate investors in R&D, spending over US\$100 billion annually; this represents close to 20% of global annual R&D expenditures by the top 2,500 R&D firms across all sectors.<sup>41</sup>

Health R&D is also a significant component of total private and public R&D expenditures, ranging from 10 to 12% of average annual R&D expenditures in high- and middle-income economies to about 14% in low-income economies.<sup>42</sup> In countries such as the U.K. and the U.S., governments place an even greater focus on R&D, allocating 20 to 25% of all government R&D expenditures on health.<sup>43</sup>

## Medical technology patents growing faster than pharmaceutical patents

Patents in pharmaceuticals, biotechnology, and medical technology have been growing strongly year-over-year for the last decade (Figure T-1.2). Medical technology patents grew the fastest at close to 6% per year. This puts medical technologies among the top five fastest-growing technology fields since 2016, with the other four being IT-related fields.<sup>44</sup> Consequently, medical technology patents are now as numerous—about 100,000 patents worldwide—as pharmaceutical

patents, with biotech at half that volume. Medical technology-related PCT filings are also nearly double the volume of pharmaceutical patents today, reflecting the increased importance of innovation in medical technology relative to pharmaceutical (Figure T-1.3). Finally, as evidenced in the 2019 Special Section on Identifying and Ranking the World's Largest Science and Technology Clusters, medical technology is now the most frequent field of patenting in these top clusters, overtaking pharmaceutical patents for the first time.<sup>45</sup>

Reflecting the increased spread of innovative capacity, Mexico and India are increasingly specialized in pharmaceutical patents relative to other patents—with India home to some of the top 10 pharmaceutical firms worldwide, such as Sun Pharmaceutical, Lupin, and Dr. Reddy's.<sup>46</sup> In absolute numbers of patents, China is also now the most important pharmaceutical patent origin (Table T-1.1).

As regards patent filings under the Patent Cooperation Treaty (PCT) at WIPO, medical technologies accounted for close to 7% of all applications in 2017 and were the fourth largest technology filing area in 2018, with IT-related fields topping this ranking.<sup>47</sup>

However, the above figures likely underestimate actual medical innovation activity. Health-related R&D and patenting are taking place in fields and firms as diverse as electrical and mechanical engineering, instruments—in particular, optics and measurement, chemistry, and the IT sector. Patents in the field of artificial intelligence are also forecast to be significant to future health systems.<sup>48</sup>

Furthermore, a number of the process and organizational innovations that are bound to have a positive influence in the health sector are not captured by R&D and patenting figures in the traditional health sector, as reported in the above data.

#### Is a revival of medical research productivity on the horizon?

While pharmaceutical research productivity might have been slower in past decades, more recently, new health-related patenting and drugs on the market are signaling a possible reversal of the productivity crisis outlined earlier in this chapter.<sup>49</sup>

Since 2015, the number of drugs in Phase I and II clinical trials has grown substantially.<sup>50</sup> The launch of new drugs, such as novel active substances, has increased in the last decade and is expected to continue growing. The drug approval rates at the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) increased in 2017 and 2018; they are considerably higher today than in prior years.<sup>51</sup> The pending lineup of immunotherapies and drugs with the potential to become blockbusters—for diabetes, hepatitis C, and cancer—is trending upward.<sup>52</sup>

Does this mean the end of the medical research productivity decline? This is hard to answer with certainty. The number of drugs in Phase III clinical trials has yet to reach the high levels seen during the golden times of pharmaceutical innovation; a large percentage of drugs still fail to make the transition from

### Patent publications by technology, 1980-2017



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Source: WIPO Statistics Database, March 2019.

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### Patent Cooperation Treaty (PCT) filings by technology, 2000-2018

▲ Patent publications

Year

Source: WIPO Statistics Database, March 2019.

### Overview of the top origins in health patent publications, 2010-2017

#### Top 10 in patent publications, 2010-2017

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Biotechnology	
Economy	Patent Publications
United States of America	126,581
China	92,107
Japan	33,818
Germany	24,094
Republic of Korea	21,045
Switzerland	15,750
France	15,292
United Kingdom	12,697
Netherlands	9,237
Denmark	7,942

#### Pharmaceuticals

Economy	Patent Publications
China	214,992
United States of America	204,057
Japan	45,850
Germany	38,279
Switzerland	33,694
Republic of Korea	28,036
France	25,814
United Kingdom	21,697
Russian Federation	11,566
Italy	10,286

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#### Medical technology

Economy	Patent Publications
United States of America	284,223
Japan	116,745
China	115,805
Germany	62,050
Republic of Korea	43,533
Netherlands	21,984
Switzerland	21,909
France	20,643
United Kingdom	19,643
Russian Federation	16,171

Source: WIPO Statistics Database, March 2019.

Note: Figures show the sum of patent publications from 2010 to 2017 for all economies.

#### The fastest growing middle-income economies in health patent publications, 2010-2017

Economy	Sum	Average	Compound growth
Biotechnology			
China	92,107	11,514	19.0%
Mexico	509	64	8.8%
India	2,341	293	1.4%

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Pharmaceuticals				
China	214,992	26,874	17.6%	
Turkey	2,164	271	11.7%	
Mexico	1,378	173	10.8%	
Ukraine	1,032	129	3.3%	
Russian Federation	11,566	1,446	0.9%	

Medical technology

China	115,805	14,476	29.7%
India	1,934	242	9.8%
Mexico	863	108	7.9%
Turkey	1,299	163	5.8%
Russian Federation	16,171	2,022	0.9%

Source: WIPO Statistics Database, March 2019.

Note: Economies considered for biotechnology show > 50 average patent publications from 2010 to 2017, and those considered for medical technology and pharmaceuticals show > 100 average patent publications over the period.

Phase II to Phase III. New pharmaceutical cures are harder to come by (Chapter 2).<sup>53</sup> While research expenditures are increasing, the return on drug-related R&D investments continues to be low.<sup>54</sup>

However, innovation is burgeoning in other increasingly health-related sectors, such as medical technologies or IT and software applications.<sup>55</sup> Over the last five years, regulatory agencies such as the FDA have announced record rates of novel medical device approvals for mechanical heart valves, digital health technologies, and 3D printing devices.<sup>56</sup>

Process and organizational innovations in healthcare delivery are also taking place due to increased automation and efficiency. These innovations are not necessarily captured by traditional R&D and patenting figures.

Finally, some important but less high-tech—and less measurable medical innovation is taking place in low- and middle-income countries. Countries in Africa, Central and Eastern Asia, and Latin America have witnessed the novel use of existing technologies—"frugal" or "adapted" medical innovations—with considerable impact in low-resource contexts. For example, clean "delivery kits" contain essential items that allow doctors in low-resource contexts to deliver babies more safely, while many other examples arise in countries such as India.<sup>57</sup>

## Upcoming breakthroughs in medical and health innovation

Novel ways to improve healthcare, to diagnose health problems, and to cure diseases are imminent (Chapter 4-National Institutes of Health, U.S. and Chapter 7–Dassault Systèmes).58 Health-related technologies and organizational innovations have the potential to disrupt existing business models, to lower healthcare costs, and to improve overall healthcare efficiency (Chapter 3–ZS Associates and Chapter 5–Tencent, China).<sup>59</sup> Many of these medical innovations are relevant to developing countries, whether they are technological, such as 3D printing; new tools to diagnose infections, such as malaria, in Brazil (Chapter 14–CNI and SEBRAE);<sup>60</sup> organizational, such as the improved screening for non-communicable diseases in Egypt (Chapter 12); or remote telemedicine applications in Rwanda (Chapter 15–Ministry of Health, Rwanda).<sup>61</sup> While medical breakthroughs and their diffusion are tough to predict, the sections below describe several possible scientific and technological breakthroughs, developments in process, and organizational innovations.62

#### Identifying promising fields

The fields of genetics and stem cell research, nanotechnology, biologics, and brain research are promising domains for scientific breakthroughs. Breakthroughs may also come from prevention techniques and cures through new vaccines and immunotherapy, new pain management techniques, and cures for mental diseases. A large number of innovations are pending in the areas of medical devices, medical imaging and diagnostics, precision and personalized medicine, and regenerative medicine. Organizational and process innovations are also improving healthcare delivery through novel approaches to research and clinical trials and new ways of delivering healthcare. These medical innovations could have a significant impact by helping overcome fragmentation of the healthcare ecosystem across different sectors—payers, insurers, providers, and manufacturers—and improving healthcare efficiency (Figure T-1.4).

IT and big data are often at the source of these innovations. New technologies, such as virtual modeling and AI techniques, enable new ways of conducting medical research (Chapter 5), facilitating breakthroughs, and increasing invention efficiency.<sup>63</sup> Many IT-enabled innovations have the potential to affect the delivery of healthcare and mitigate rising health costs (Chapter 14). Supported by the appropriate technology, health can be monitored in real time, conditions tracked remotely, data analyzed and shared, new modes of diagnosis applied, and treatments personalized. Individuals can also have access to their health data for the first time in history.<sup>64</sup>

These technologies have also begun impacting mobile health possibilities, some of which are critical for prevention and health monitoring. The technologies are starting to support a shift from a "react and revive" focus on ill-health to a "predict and prevent" model of wellness (Chapter 3, Chapter 7, Chapter 9, and Chapter 17–Thailand).<sup>65</sup> Examples include telemedicine applications, remote monitoring, portable diagnostics, and the delivery of medicines via drones. The surveillance of public health threats and the availability of data to drive policy and planning are key to optimizing health services in low-resource contexts (Chapter 12, Chapter 13, and Chapter 15).

The novel and better use of health data plays an important role in this context. Through big data analytics, machine learning, and AI, patient harm—and unintended consequences—may be predicted before they occur, and interventions can be provided to caregivers. Integrated data can help overcome silos and support medical professionals and care providers with insights that enable more predictive and efficient care (Chapter 5 and Chapter 8).<sup>66</sup>

The data-driven shifts in health policies and strategies could be a core driver in reordering the relationships among—and processes between—health services providers, medical equipment manufacturers, patients, governments, public research, social security, and financial/insurance companies. In this setup, the patient is at the center of better feedback flows.

As the same time, as more innovation is geared to enriching the data intensity of medical equipment and processes, it is to be expected that the relative power of those who have the ability to collect, combine, and analyze large data sets will increase relative to that of traditional players in the health and medical arena. This may have important consequences, such as increased inequalities between the haves and the have nots of relevant technologies or a rising reliance on algorithms to make medical decisions, which may generate distrust vis-à-vis the medical profession.

#### FIGURE T-1.4

### Promising fields for medical innovation and technologies





Sources: Gll 2019 chapters, in particular Collins, 2010; Collins, 2019. Also, Kraft, 2019; Nature, 2018; Nature, 2019; Frost & Sullivan, 2018; Frost & Sullivan, 2019; European Commission, 2007; Medical Futurist, 2017; Mesko, 2018.

## Opportunities and policy imperatives enabling healthy futures

Business and policy imperatives are key to creating a strong foundation for medical innovation systems—ranging from stable and predictable funding to technology transfer, skills, and regulation.

#### Ensuring sufficient medical innovation funding

The social returns of medical innovation expenditures far exceed the private returns of R&D.<sup>67</sup> For this reason, government R&D spending is still the primary source of scientific health research worldwide. Health-related R&D in public research institutes is of paramount importance. In fact, many state-of-the-art technologies behind healthcare innovations are initially developed as basic research projects carried out or financed by the public sector (Chapter 10–CERN, European Organization for Nuclear Research).<sup>68</sup>

It is thus vital to prioritize public funding—in particular, basic R&D. This holds true in middle- and low-income economies where health R&D expenditures are still relatively low, but also in high-income economies that have faced declining public R&D budgets—notably in health-related public research institutions—in recent years.<sup>69</sup> Discontinuities in public funding for health R&D can lead to brain drain and training gaps for qualified staff, not to mention the obsolescence of equipment (Chapter 14).

Government investment can help set up large funds to advance particular fields of research and to create health research centers or clusters, such as the Thai Center of Excellence for Life Sciences (Chapter 17), the Brazilian SENAI Innovation Institutes (Chapter 14), or the Iranian dedicated science and technology parks (Chapter 16–Iran).<sup>70</sup> More can be done to promote international research collaborations, which play a vital role as basic research ideas are translated into useful medical applications and solutions in the marketplace.<sup>71</sup>

There is also a need for innovative funding approaches especially in the earliest and riskiest phases of drug discovery research (Chapter 6).<sup>72</sup> Often companies have difficulty funding early stage or strongly disruptive technology. The ability of academic spin-offs to become sustainable ventures is uneven; they remain highly dependent upon venture capitalists, who tend to foster short-term financial growth and whose understanding of healthcare challenges and needs remains incomplete.<sup>73</sup>

Funding for product R&D, outcomes research, and market analyses of uses for health technologies in low-resource settings remain insufficient (Chapter 11).<sup>74</sup> This is not a new consideration and positive developments are on the way.

Entities such as the Bill & Melinda Gates Foundation and Gavi an organization bringing together public and private actors to deliver vaccines to children in low-income countries contribute significantly to the financing and deployment of medical innovation.<sup>75</sup> Still, new ideas and incentives are required to address certain health problems, particularly those affecting the least developed countries. R&D for such health innovations should be encouraged, along with special incentives and funding programs to encourage investment in health and medical research (Chapter 2).<sup>76</sup>

Finding solutions to these challenges requires multi-stakeholder consultation and coordination. The WIPO Re:Search public-private consortium, for example, shares valuable intellectual property and expertise with the health research community to promote the development of new drugs, vaccines, and diagnostics for neglected tropical diseases, malaria, and tuberculosis.<sup>77</sup>

## Building functional medical innovation systems: from "bench to bedside"

Once significant health R&D is financed and carried out, effective medical innovation—and its diffusion—depend on linkages between public and private actors to translate basic research into medical applications. This is often a "giant leap" (Chapter 10).<sup>78</sup>

Businesses and policy actors need to focus on the translation of research into commercially viable applications, which may require initiating public-private collaborations, building a culture of entrepreneurship in public research bodies, stimulating academic spin-offs, and creating business incubators and centers of excellence.<sup>79</sup>

The actors involved in shaping medical innovation need to be reconsidered. Academic healthcare organizations, such as university hospitals, have traditionally been boundary-spanning organizations between care and science.<sup>80</sup> The critical role of hospitals and doctors in future demand-led health innovation is undeniable.<sup>81</sup> In health innovation systems, patients could also have a more central role in leading the direction of innovation.<sup>82</sup> The same is true for insurers. Building on the information they have for individual patients and the impact of particular treatments, insurers could contribute more toward raising awareness, informing patients, and preventing diseases—moving from a payer to a more active health system player.<sup>83</sup>

In sum, hospitals, insurers, patients, and regulators will need to cooperate more to influence the rate and direction of innovation by identifying prioritized needs and redefining modes of financing that incentivize the creation and diffusion of health solutions.<sup>84</sup>

For this to materialize, the various health system actors will have to create and use better channels and to transmit relevant information and feedback.<sup>85</sup> Improving knowledge flows across the different health actors will help. Practically speaking, this will require understanding differing needs and improving shared data infrastructures to overcome significant gaps in intersectoral communication.<sup>86</sup>

More funding instruments need to be made available to fund the stage between prototype and final product. Public-private partnerships can help in this precompetitive stage. Awards to particular researchers or research teams to encourage high-risk, high-reward research are promising (Chapter 4), as is launching prize competitions aimed at finding innovative solutions to major health challenges.<sup>87</sup> Other new possibilities include crowdfunding and funding through patient advocacy groups.

Policymakers can also strongly influence the translation and diffusion of research to medical applications through demand-side policies that specify innovation targets and focus areas. Moreover, governments can exert influence on the funding of innovation by influencing prices and reimbursements for health costs and by helping to align the costs and benefits of new technologies and related incentives.<sup>88</sup>

#### Moving from cure to prevention

Generally, as mirrored in this year's GII chapters, attention should also gravitate from curing diseases and health conditions to preventing them in the first place. Of course, prevention goes beyond medical research and innovation. Environmental, agricultural, and infrastructure policies with an impact on clean air, clean water, or functioning sewage systems, for example, also have a well-documented impact on overall health and well-being, as well as on the incidence of disease. All too often, however, health-related policies, including those governing R&D, are treated separately—condemning medical research to a perpetual game of catch-up with diseases and conditions that are triggered or aggravated by environmental pollutants.<sup>89</sup>

#### Advancing skills and science education

The most important resource for the future of medical research will be having a workforce with the right skill sets (Chapter 4 and Chapter 7). Serious medical staff shortages exist in both developed and emerging markets. In addition, medical staff and researchers will need new sets of skills. The responsible implementation of health innovations requires local healthcare providers who are appropriately trained to use the latest technologies (Chapter 11 and Chapter 13).

To act as a bridge between research and the application of innovation in a real-life context, medical professionals with experience in research, training in the use of new hardware and software, and training in advanced research technologies such as 3D modeling—are needed (Chapter 7 and the Australian Commonwealth Scientific and Industrial Research Organisation, CSIRO, 2017). Workforce planning is required to ensure that professionals and staff are equipped with the appropriate types of skills to put new health technologies into practice.

To ensure better transfer of knowledge, researchers and medical professionals should also move more freely between research and business contexts. Research institutes should be incentivized to employ a higher proportion of experienced industry professionals, while researchers should be encouraged to spend time in industry.<sup>90</sup> These exchanges will also help with the translation of research to applied medical solutions.

#### Supporting new data infrastructure and regulatory processes

Healthcare stakeholders will require increased health data sharing to increase their efficacy. At the same, time, patients will want greater access and control over their health data, along with assurances that their information is safe.

The security and privacy of health information have been confirmed as top priorities, and regulations on personal health data are being progressively harmonized (Chapter 7). Digital health strategies that create strong data infrastructure—as well as new processes for efficient and safe data collection, management, and sharing—will be required. Agreements will also be required to define how to design and operationalize electronic health records and how to create standards and interoperable technologies.<sup>91</sup>

How to harness the promise of big data medical research while respecting the security of data and honoring patient privacy? System security and data security principles need to be established for healthcare institutions (Chapter 5). Otherwise, a lack of data governance could decrease transparency and raise concerns about security and trust (Chapter 4, Chapter 7, and Chapter 12).

In addition to data infrastructure, new regulatory processes are needed to overcome the increasing duration and complexity of clinical trials. Breakthroughs in therapy have almost always been coupled with breakthroughs in regulatory standards (Chapter 6). Yet, current regulations and health regulation agencies may not be equipped for health innovation, while current processes may be too cumbersome (Chapter 14).<sup>92</sup> Developing countries, in particular, may not have the capacity to deal with multiple national regulatory regimes (Chapter 11).

#### Improving cost-benefit assessments of medical innovation

To prioritize and foster the diffusion of research and medical technologies, cost-benefit assessments must be improved.<sup>93</sup>

Going forward, health technology assessments will be increasingly important as a tool to foster industry accountability, cost-efficient solutions, and outcome-oriented innovations in healthcare.<sup>94</sup>

The idea of better assessing health innovation is not new. Sweden and Switzerland, for example, have been at the forefront of health technology assessments for many years.<sup>95</sup> In the U.K., the National Institute for Health and Care Excellence provides evidence-based guidance on metrics, including on new medical technologies.<sup>96</sup> More can be done to spread these approaches to more countries. Better collection, analysis, and sharing of outcomes and cost data—and possibly mandating a better tracking of technology-specific health outcomes will help in this regard.<sup>97</sup>

#### Debating risks, social values, and the value of life

New technologies will bring new possibilities but also new risks and uncertainties—some of which will challenge current ethics and societal values (Chapter 4). This is the case for novel approaches in the field of genetic engineering in particular. As in the past, possibilities in the field of medical innovation will entail adaptable oversight and risk management functions, and possibly higher levels of precautionary oversight. To avoid a race to the bottom—in which countries will adopt the lowest-common safety or ethical denominator—international coordination is needed.

The challenges raised by novel approaches are not simply technical issues, but larger questions that will require discussion and agreement on matters at the core of ethics. Decision-making structures must be developed to encapsulate the far-reaching impacts on societal values. Similarly, as costs for new technologies increase exponentially, the potential for further challenges—to equity or access—may grow. Are there limits to the preservation of human life "at any price" and over an increasing life span? What are the limits to the cost of developing a new technology and under what circumstances should these limits be imposed?<sup>98</sup> These questions are beyond the scope of this edition of the GII research; nonetheless, societies around the world will increasingly have to confront them in this nexus between technology and health.

#### Conclusion

The future of medical innovation, and the role of medical innovation in improving health outcomes going forward, will depend crucially on the policies and institutions created by national and global actors to support research and innovation. There are important issues for policymakers to consider carefully, given the transformative economic, social, and health impact new medical technologies have had historically and the enormous potential value of further health improvements for current and future generations.

Some overarching observations are useful in the particular case of developing countries. While developing countries face many of the same constraints as developed countries, these low-resource contexts may have access to opportunities that developed countries lack. One indicator of this possibility is that some of the more interesting examples of new health technology applications have recently come from developing countries in fields such as telemedicine, real-time diagnostic tools, and even the establishment of electronic health records.

In the optimal scenario, developing countries might "leapfrog" their current health systems, due to lower sunk costs related to existing infrastructure and equipment, lower fixed costs from not building overcapacity, and possibly less regulatory constraint. They also have at their disposal technological innovations, alternative operating and financing models, and legal frameworks that were not previously available to developed countries. As a result, new health solutions might be deployed quickly and with immediate impact in developing

countries—possibly without the need to proportionately increase healthcare facilities and professionals. The disruption of established health systems in developed countries is more challenging.

#### Several caveats apply:

First, although leapfrogging implies the closing of a health gap between the rich and the poor, there are risks that costly new health innovations will exacerbate the health gap rather than narrow it. This will require careful monitoring. Diffusion should be encouraged, proper financing made available, public-private partnerships created, and technologies fostered (Chapter 2).

Second, new health innovations aside, the true challenge to developing countries is the lack of minimally functional health systems and not necessarily a need for more R&D or new technologies. The most pervasive unmet need in the developing world is still providing basic and affordable healthcare at scale (Chapter 3).<sup>99</sup> Technology is not always the remedy. The mere availability and training of nurses that can go door-to-door looking for signs of childhood diseases such as diarrhea, malaria, and pneumonia have been shown to have widespread and sustainable impacts in countries such as Mali.<sup>100</sup> Basic but impactful improvements of this kind are not necessarily devoid of technology. Often the contrary is the case: low-tech or adapted technology applications can save more lives than the latest high-tech solutions.

Third, evidence-based decision-making and assessments will be particularly important in developing countries. As new technologies, such as drones for the delivery of medicines, are much discussed, and hyped to some extent, a sober evidence-based look at the true costs and benefits of these innovations will bear great value.

#### Notes:

- 1 Roser, 2019; Ma, 2019; Shetty, 2019.
- 2 WIPO, 2015a; Sampat, 2019.
- 3 Gordon, 2012, 2014; WIPO, 2015a, 2015b; Sampat, 2019.
- 4 Kenny, 2011; WIPO, 2015a.
- 5 Deloitte, 2018a; EIU, 2017, 2018.
- 6 Deloitte, 2018a; Biot et al., 2019.
- 7 Deloitte, 2018a; EIU, 2017, 2018; Frost et al., 2019.
- 8 Dutta et al., 2019.
- 9 It also sets up targets aimed at specific challenges including, for example, maternal mortality, AIDS, tuberculosis, malaria and neglected tropical diseases and a goal to support R&D for vaccines and medicines for communicable and non-communicable diseases.

- 10 First in 2016, the Political Declaration on Antimicrobial Resistance and the Political Declaration on HIV and AIDS; and in 2018, the Political Declaration on the Fight against Tuberculosis and the Political Declaration on Non-Communicable Diseases.
- 11 To illustrate the cross-border dimension, and the need for specific research aimed at developing countries, SDG Indicator 3.b.2 monitors, the Official development assistance (ODA) for medical research and basic health sectors as a % of gross national income (GNI) and as a % of all ODA, by donor country.
- 12 Sheiner et al., 2016.
- 13 Nelson, 2003.
- 14 Bartfai et al., 2013; Andrade et al., 2019.
- 15 Casadevall, 2018.
- 16 Scannell et al., 2012.
- 17 Bloom et al., 2017—While most of the economic literature confirms this prospect of declining R&D pharmaceutical productivity, some contributions question the extent finding that the above trends are exaggerated as R&D costs are seriously overstated. Measuring the R&D productivity of a sector, let alone the overall productivity, in a field such as health is daunting. Invariably metrics are imperfect.; Cockburn, 2006—e.g., by failing to account for inflation in R&D input costs; Schmid et al., 2005.
- 18 Vijg, 2011—In one study, the total out-of-pocket R&D costs per new approved drug are estimated to be around US\$1.9 billion.; Pammolli et al., 2011; DiMasi et al.,2016.
- 19 Cross, 2018.—The development of a new health product is a risky activity; estimates indicate that the percentage of drugs that reach the market after starting clinical trials, which is already an advanced phase of R&D in the sector, varies between 6% and 13.8% depending on the estimate.
- 20 Ricks et al., 2019.
- 21 Hopkins et al., 2007; Singh, 2018.
- 22 Comanor, 2013.—Note that recent mergers have indeed contributed to the observed decline in pharmaceutical innovation.
- 23 R&D Magazine, 2018.
- 24 Abrishami et al., 2014; Penter, 2018.
- 25 Drolet et al., 2011.
- 26 Metcalfe et al., 2005.
- 27 Herzlinger, 2006.
- 28 Herzlinger, 2006.
- 29 Murphy, 2019.
- 30 Żaneta, 2019.
- 31 WHO, WIPO, and WTO, 2012, 2018.—Lack of access to medical technologies is rarely due to a single determinant. Important factors include: needs-based research, development, and innovation; intellectual property and trade policies; manufacturing processes and systems; regulatory environment; price transparency, pricing policies, and health system infrastructure; integrity and efficiency in procurement and supply chain management; and appropriate selection, prescribing and use.
- 32 Kaslow, 2019.
- 33 Murray et al., 2012; Woodson, 2016; von Philipsborn et al., 2015.—One study finds that diseases prominent in low-income economies cause about 14 % of the global disease burden. Yet they only receive about 1.3 % of health-related R&D expenditure.
- 34 Zaid et al., 2019; Shetty, 2019.

- 35 Puica et al. 2019.
- 36 Dewhurst, 2017.
- 37 Tannoury et al., 2017.
- 38 Frost et al., 2018.
- 39 EIU, 2017, 2018.
- 40 Evaluate Pharmaceutical, 2018; WifOR, 2018.
- 41 Hernández et al., 2018; R&D Magazine, 2018.—Top investors such as Roche (Switzerland), Johnson and Johnson (U.S.) and Merck US (U.S.) invested on average around US\$10 billion in R&D last year.
- 42 In some countries, the figures can be significantly higher—typically about 30% of total R&D—e.g. in selected African countries such as Kenya. Some high-income economies also stand out with a remarkably high share of health R&D; e.g. Singapore and Qatar (both 19%), but also the Netherlands (17%). Data drawn from Global Observatory on Health R&D of the WHO, with special tabulations made available to authors. The gross domestic expenditure on R&D (GERD) and GERD in the health and medical sciences (health GERD) are collected from the United Nations Educational, Scientific and Cultural Organization (UNESCO), the Organisation for Economic Co-operation and Development (OECD), and Eurostat, the statistical office of the European Union. They are reported using the most recent available data since 2010 by country (Note: not all countries have reported data on this indicator). See also https://www.who.int/research-observatory/monitoring/inputs/gerd/en/
- 43 Among high-income countries ranges vary greatly with, for example, France, Germany, Republic of Korea, and Italy between 5-10%, and other such as New Zealand, Spain, Denmark, Canada and Norway between 10-15%. Source: Authors based on OECD R&D Statistics.
- 44 WIPO, 2018.— see Patent applications and grants worldwide
- 45 Bergquist et al., 2019.
- 46 WIPO, 2018, WIPO Statistics Database, 2017; Retrived from https://www.wipo.int/ipstats/en/; Gokhale, 2017.
- 47 WIPO, 2018; WIPO, 2019b.
- 48 Cornell University, INSEAD, and WIPO, 2019; Ma, 2019; Bergquist et al., 2019; WIPO, 2019a; WIPO, 2019b.
- 49 Bloom et al., 2017.
- 50 Pharmaceutical Intelligence, 2019 ; Smietana, 2016.
- 51 Baedeker et al., 2018; Nature, 2019a; R&D Magazine, 2019; IQVIA Institute, 2019.—In 2018, the European Medicines Agency (EMA) had approved 84 (vs 94 in 2017) new drugs with 42 (vs 35 in 2017) of these being new active substances. At the same time, the US Food and Drug Administration (FDA) had approved 59 novel drugs and biologics in 2018 (vs 46 in 2017).
- 52 EIU, 2017; EIU, 2018; Casadevall, 2018.
- 53 Bloom et al., 2017; Vijg, 2011; Casadevall, 2018; Gordon, 2018.
- 54 R&D Magazine, 2018; Deloitte, 2018b.
- 55 Coffano, 2016.—gives an analysis of the dynamic field of medical device innovation.
- 56 FDA Statement from FDA Commissioner Scott Gottlieb, M.D., and Jeff Shuren, M.D., Director of the Center for Devices and Radiological Health, on a record year for device innovation, January 28, 2019.
- 57 On the delivery kits, see PATH, 2002; Beun et al., 2003; On frugal medical innovation in India, see Verma, 2017.
- 58 Collins, 2019; Biot, 2019.
- 59 Khedkar et al., 2019; Ma, 2019.
- 60 Andrade et al., 2019; Jewell, 2018.

- 61 Zaid et al., 2019; Uwaliraye, 2019.
- 62 See on this caveat: Gll 2019 chapters, in particular Sampat, 2019; Collins, 2019 and also earlier work on breakthrough innovation; WIPO, 2015a; WIPO 2015b.
- 63 Ma, 2019; Mahnken, 2018.
- 64 CSIRO, 2017; Basel et al.,2013.
- 65 Khedkar et al., 2019; Biot et al., 2019; Puica et al., 2019,; Boonfueng et al., 2019.
- 66 Ma, 2019; Murphy, 2019.
- 67 For pharmaceuticals in particular, see Lichtenberg, 2003 and Grabowski et al., 2002.
- 68 Anelli et al., 2019.
- 69 R&D Magazine, 2018; Research!America, 2018.
- 70 Boonfueng et al., 2019; Andrade et al., 2019; Fartash et al., 2019.
- 71 Anelli et al., 2019.
- 72 Ricks et al., 2019.
- 73 Lehoux et al., 2016; Foray et al., 2012.
- 74 Kaslow, 2019.
- 75 For more information see: https://www.gatesfoundation.org/What-We-Do; and https://www.gavi.org/
- 76 Sampat, 2019.
- 77 WIPO actively involves a wide range of stakeholders—from civil society, to academia, business, and more—in order to ensure that all members of society benefit from intellectual property. For its multi-stakeholder platforms, see https://www.wipo.int/cooperation/en/multi\_stakeholder\_platforms/
- 78 Anelli et al, 2019.
- 79 Gelijns et al., 1994; Thune, 2016.
- 80 Lander, 2016; Miller, 2016.
- 81 Gulbrandsen et al., 2016; Smits et al., 2008.
- 82 Llopis et al., 2016; The Medical Futurist, 2017, including the idea for a role of patients on the board of pharmaceutical companies.
- 83 See the Daniel Schmutz, CEO, Helsana, Interview at https://pharmaboardroom.com/interviews/interview-daniel-schmutz-ceo-helsana-switzerland/
- 84 Thune et al., 2016.
- 85 Barberá-Tomás et al., 2012.
- 86 Li et al., 2018.
- 87 Gandjour, 2011; Murray et al., 2012.
- 88 BCG and World Economic Forum, 2017.
- 89 There are many studies that tie air pollution in to increased rates of cardiovascular disease and death, for example. See https://www. eurekalert.org/pub\_releases/2019-03/esoc-apc030819.php for a study on the European Union.
- 90 CSRIO, 2017.
- 91 BCG and World Economic Forum, 2018.—In January 2017, the health ministers of OECD recommended that countries develop and implement health-data governance frameworks that secure privacy while enabling health data uses that are in public interest.

- 92 The Medical Futurist, 2017.
- 93 Thune, 2016.
- 94 Proksch et al., 2019.
- 95 See also: http://www.inahta.org/members/sbu/ and https://www.bag. admin.ch/bag/de/home/begriffe-a-z/health-technology-assessment.html
- 96 More information at https://www.nice.org.uk/about
- 97 BCG and World Economic Forum, 2017.
- 98 Mossialos, 2018.
- 99 Khedkar et al., 2019.
- 100 Mali's "astounding" community health programme should be emulated, By David Pilling, *Financial Times*, March 1, 2019.

#### **References:**

- Abrishami, P., Boer, A., & Horstman, K. (2014). Understanding the adoption dynamics of medical innovations: Affordances of the da Vinci robot in the Netherlands. Social Science & Medicine, 117, 125-133.
- Andrade, R. B., & Melles, C. (2019). A Brazilian Outlook on Health and Medical Innovation [Chapter 14]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.) Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation. Ithaca, Fontainebleau, and Geneva: Cornell, INSEAD, and WIPO.
- Anelli, G., Crilli, M., & Rassat, A. (2019). How Particle Physics Research at CERN Contributes to Medical Innovation [Chapter 10]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Baedeker, M., Ringel, M., & Schulze, U. (2019). FDA approvals hit all-time high — but average value slips again. *Nature Reviews Drug Discovery*, 18, 90.
- Basel, K., Knott, D., & Van Kuiken, S. (2013, April) The big-data revolution in US health care: Accelerating value and innovation, McKinsey & Company.
- Barberá-Tomás, D., & Consoli, D. (2012). Whatever works: Uncertainty and technological hybrids in medical innovation. *Technological Forecasting* and Social Change, 79(5), 932-948.
- Bartfai, T., & Lees, G. V. (2013). Chapter 7: Why is pharmaceutical a special industry? In T. Bartfai & G. V. Lees (Eds.), *The Future of Drug Discovery* (pp. 193-216). San Diego: Academic Press.
- Bergquist, K., & Fink, C. (2019). Identifying and Ranking the World's Largest Science and Technology Clusters [Special Section]. In S. Dutta, B. Lanvin, and S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation.* Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Beun, M. H., & Wood, S. K. (2003, December). Acceptability and Use of Clean Home Delivery Kits in Nepal: A Qualitative Study, *Journal of Health*, *Population and Nutrition 21*, (4), 367-373
- Biot, C., Johnson, P., Massart, S., & Pécuchet, N. (2019). Improving Patient Healthcare through Virtual Platforms [Chapter 7]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell, INSEAD, and WIPO.
- Bloom, N., Jones, Cl., Van Reenen, J., & Webb, M. (2017, September). Are Ideas Getting Harder to Find? (NBER Working Paper No. w23782). Retrieved from https://ssrn.com/abstract=3035132
- Boonfueng, K., Limapornvanich, C., & Suksaard, T. (2019). Social and Economic Aspects of Health and Medical Innovation in Thailand [Chapter 17]. In S. Dutta, B. Lanvin, and S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.

- BCG (Boston Consulting Group) and World Economic Forum. (2017, April). Value in Healthcare Laying the Foundation for Health System Transformation.
- . (2018, December). Accelerating the Pace of Health System Transformation.
- Casadevall, A. (2018). Is the Pace of Biomedical Innovation Slowing? Perspectives in Biology and Medicine, 61(4), 584-593.
- Cockburn, I. M. (2006). Is the Pharmaceutical Industry in a Productivity Crisis? Innovation Policy and the Economy, 7(2006), 1–32.
- Coffano, M. (2016, December 19) Innovation dynamics in the medical device sector: network of collaborations, knowledge spillovers and regulation. Thesis number 7257, École Polytechnique Fédérale De Lausanne.
- Collins, F. S. (2010, January). Opportunities for research and NIH. *Science*, 327 (5961), 36-37.
- Collins, F. (2019). Ten Opportunities for Biomedical Innovation over the Next Ten Years [Chapter 4]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation.* Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Comanor, W. S., & Scherer, F. M. (2013). Mergers and innovation in the pharmaceutical industry. *Journal of Health Economics*, 32(1), 106-113.
- Cornell University, INSEAD, & WIPO. (2019). *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation.* Ithaca, Fontainebleau, and Geneva.
- Cross, R. (2018, February 12). Drug development success rates are higher than previously reported. *Chemical and Engineering News*, 96(7).
- CSIRO. (2017, April). The Medical Technologies and Pharmaceuticals (MTP) Roadmap – unlocking future growth opportunities for Australia Commonwealth Scientific and Industrial Research Organisation. Canberra: Australia.
- Deloitte (2018a). 2018 Global health care outlook: The evolution of smart health care. Retrieved from https://www2.deloitte.com/content/dam/ Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-hc-outlook-2018.pdf
- (2018b). Embracing the future of work to unlock R&D productivity: Measuring the return from pharmaceutical innovation 2018. Retrieved from https://www2.deloitte.com/uk/en/pages/life-sciences-and-healthcare/articles/measuring-return-from-pharmaceutical-innovation.html
- Dewhurst, M. (2017, March). The next horizon of innovation for pharmaceutical. McKinsey Interview with David Epstein. Retrieved from https://www. mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/the-next-horizon-of-innovation-for-pharmaceutical
- DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics*, 47, 20-33.
- Drolet, B. C., & Lorenzi, N. M. (2011). Translational research: understanding the continuum from bench to bedside. *Translational Research*, 157(1), 1-5.
- Dutta, S., Escalona Reynoso, R., Wunsch-Vincent, S., Rivera Léon, L., & Hardman, C. (2019). Creating Healthy Lives—The Future of Medical Innovation [Theme Section]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- EIU (The Economist Intelligence Unit). (2017, June). World Industry Outlook: Healthcare and Pharmaceuticals. The Economic Intelligence Unit. Retrieved from http://www.eiu.com/FileHandler.ashx?issue\_ id=925683076&mode=pdf

- European Commission (2007) White Paper–Together for Health: A Strategic Approach for the EU 2008-2013, Brussels, Commission of the European Communities, 23.10.2007 COM(2007) 630 final.
- Evaluate Pharmaceutical. (2018). World Preview 2018, Outlook to 2024 (p. 22). London: Evaluate Ltd. Retrieved from http://info.evaluategroup.com/ rs/607-YGS-364/images/WP2018.pdf
- Fartash, K., & Elyasi, M. (2019). Iran's Experience in Developing High-tech Medical Innovations and the Path Ahead [Chapter 16]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Foray, D., Mowery, D. C. & Nelson, R. R. (2012). Public R&D and social challenges: What lessons from mission R&D programs? *Research Policy*, 41, 1697–702.
- Frost & Sullivan. (2018, January 12). Frost & Sullivan's 10 Healthcare Predictions for 2018. Retrieved from https://ww2.frost.com/frost-perspectives/ frost-sullivans-10-healthcare-predictions-2018/
- . (2019) 2019 Healthcare Predictions Growth Opportunities, Technology, and Trends. Global Healthcare Industry Outlook, 2019.
- Grabowski, H., Vernon, J., & DiMasi, J. A. (2002) Returns on Research and Development for 1990s New Drug Introductions. *Pharmacoeconomics*, 20, 11-29.
- Gandjour, A., & Chernyak, N. (2011). A new prize system for drug innovation. Health Policy, 102(2), 170-177.
- Gelijns, A., & Rosenberg, N. (1994). The dynamics of technological change in medicine. *Health Affairs*, 28–46.
- Gokhale, P., & Kannan, S. (2017). Patenting trends in Indian pharmaceutical industry. Annals of Library and Information Studies, 64(4), 260-267.
- Gordon, R. J. (2012). Is U.S. Economic Growth Over? Faltering Innovation Confronts the Six Headwinds (National Bureau of Economic Research Working Paper, No. 18315). DOI: 10.3386/w18315. Retrieved from https://www.nber.org/papers/w18315
- . (2014). The Demise of U.S. Economic Growth: Restatement, Rebuttal, and Reflections (National Bureau of Economic Research Working Paper, No. 19895). DOI: 10.3386/w19895. Retrieved from https://www.nber. org/papers/w19895
- Gulbrandsen, M., Hopkins, M., Thune, T., & Valentin, F. (2016). Hospitals and innovation: Introduction to the special section. *Research Policy*, 45(8), 1493-1498.
- Herzlinger, R. E. (2006, May). Why Innovation in Health Care Is So Hard. Harvard Business Review, 84(5).
- Hernández, H., Grassano, N., Tübke, A., Potters, L., Gkotsis, P. et al. (2018). The 2018 EU Industrial R&D Investment Scoreboard; EUR 29450 EN; Publications Office of the European Union, Luxembourg.
- Hopkins, M. M., Martin, P. A., Nightingale, P., Kraft, A., & Mahdi, S. (2007). The myth of the biotech revolution: An assessment of technological, clinical and organisational change. *Research Policy*, *36*(4), 566-589.
- IQVIA Institute (2019). The Global Use of Medicine in 2019 and Outlook 2023. Retrieved from https://intelligencepharma.files.wordpress. com/2019/01/the-global-use-of-medicine-in-2019-and-outlook-to-2023. pdf
- Jewell, C. (2018, June). Diagnostics for the Real World: point-of-care diagnosis made easy. *WIPO Magazine*.

- Kaslow, D. C. (2019). Overcoming Barriers to Medical Innovation for Low Resource Settings [Chapter 11]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Kenny, C. (2011). Getting Better: Why Global Development Is Succeeding— And How We Can Improve the World Even More. New York, NY: Basic Books.
- Khedkar, P., & Sahay, D. (2019). Trends in Healthcare and Medical Innovation [Chapter 3]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Kraft, D. (2019, January). 12 Innovations that will revolutionize the future of medicine. National Geographic magazine. Retrieved from https://www. nationalgeographic.com/magazine/2019/01/12-innovations-technology-revolutionize-future-medicine/
- Lander, B. (2016). Boundary-spanning in academic healthcare organisations. *Research Policy*, 45(8), 1524-1533.
- Lehoux, P., Daudelin, G., Williams-Jones, B., Denis, J. L., & Longo, C. (2014). How do business model and health technology design influence each other? Insights from a longitudinal case study of three academic spin-offs. *Research Policy*, 43(6), 1025-1038.
- Lehoux, P., Miller, F. A., Daudelin, G., & Urbach, D. R. (2016) How venture capitalists decide which new medical technologies come to exist. *Science and Public Policy, 43*(3), 375–385.
- Li, S. S., Fitzgerald, L., Morys-Carter, M. M., Davie, N. L., & Barker, R. (2018). Knowledge translation in tri-sectoral collaborations: An exploration of perceptions of academia, industry and healthcare collaborations in innovation adoption. *Health Policy* 122(2): 175-183.
- Lichtenberg, F. R. (2003). Pharmaceutical Innovation, Mortality Reduction, and Economic Growth. In K.M. Murphy & R.H. Topel (Eds.), *Measuring the Gains from Medical Research, an Economic Approach* (p. 102). University of Chicago Press,.
- Llopis, O., & D'Este, P. (2016). Beneficiary contact and innovation: The relation between contact with patients and medical innovation under different institutional logics. *Research Policy*, 45(8), 1512-1523.
- Ma, H. (2019). Application of Artificial Intelligence and Big Data in China's Healthcare Services [Chapter 5]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Mahnken, T. A., & Moehrle, M. G. (2018). Multi-cross-industry innovation patents in the USA–A combination of PATSTAT and Orbis search. World Patent Information, 55, 52-60.
- Mesko, B. (2018). The Medical Futurist: Technologies Shaping the Future of Pharmaceutical.
- Metcalfe, J. S., James, A., & Mina, A. (2005). Emergent innovation systems and the delivery of clinical services: The case of intra-ocular lenses. *Research Policy*, *34*(9), 1283-1304.
- Miller, F. A., & French, M. (2016). Organizing the entrepreneurial hospital: Hybridizing the logics of healthcare and innovation. *Research Policy*, 45(8), 1534-1544.
- Mossialos, E. (2018, January 17). Transforming health systems: Why innovation in health care is so hard? LSE China Lecture Series, Beijing, London School of Economics and Political Science.
- Murphy, K. (2019). How Data will Improve Healthcare without Adding Staff or Beds [Chapter 8]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation.* Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.

- Murray, C. J. L., Vos, T., Lozano, R., Naghavi, M., Flaxman, A. D. et al. (2012). 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. *The Lancet, 380*(9859), 2197-2223.
- Murray, F., Stern, S., Campbell, G., & MacCormack, A. (2012). Grand Innovation Prizes: A theoretical, normative, and empirical evaluation. *Research Policy*, 41(10), 1779-1792.
- Nature. (2018, March 8). Nature Outlook: The future of medicine. Retrieved from https://www.nature.com/collections/zfnjwhjjct
- . (2019a, January 15). 2018 FDA approvals hit all-time high but average value slips again. Nature Reviews Drug Discovery, 18, 90.
- —. (2019b, January 23.) Technology Feature Technologies to watch in 2019. Retrieved from https://www.nature.com/articles/d41586-018-02472-6.
- Nelson, R. R. (2003). On the uneven evolution of human know-how. *Research Policy*, 32(6), 909-922.
- Pammolli, F., Magazzini, L., & Riccaboni, M. (2011). The productivity crisis in pharmaceutical R& D. *Nature Reviews Drug Discovery, 10,* 428.
- PATH. (2002, March). Use of the Clean Home Delivery Kit in Nepal: A Qualitative Study. Seattle: Program for Appropriate Technology in Health (PATH).
- Penter, V, & Pfaffner, K. (2018). Why is innovation in health so hard? KPMG. Retreived from https://home.kpmg/bh/en/home/insights/2018/05/the-iword-paradox.html
- Pharmaceutical Intelligence (2019). Pharmaceutical R&D Annual Review 2019. Retrieved from https://pharmaintelligence.informa.com/~/media/informa-shop-window/pharmaceutical/2019/files/whitepapers/pharmaceutical-rd-review-2019-whitepaper.pdf
- Proksch, D., Busch-Casler, J., Haberstroh, M. M., & Pinkwart, A. (2019). National health innovation systems: Clustering the OECD countries by innovative output in healthcare using a multi indicator approach. Research Policy, 48(1), 169-179.
- Puica, L., & Bauersachs, J. (2019). Case of iamYiam—Innovating in Preventive Health Delivery [Chapter 9]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- R&D Magazine. (2018). 2018 Global R&D Funding Forecast, Winter 2018. Retrieved from https://www.rdmag.com/
- ——. (2019, March 19). The Marriage of Big Pharma and Biotech. Retrieved from https://www.rdmag.com/article/2019/03/marriage-big-pharma-andbiotech
- Research!America. (2018) U.S. Investments in Medical and Health Research and Development 2013–2017, Fall 2018. Retrieved from https://www. researchamerica.org/sites/default/files/Policy\_Advocacy/2013-2017InvestmentReportFall2018.pdf
- Ricks, D. A., & Matthews, B. R. (2019). Reaching New Frontiers for Alzheimer's through Research and Innovation [Chapter 6]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation.* Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Roser, M. (2019). Our World in Data: Life Expectancy. Retrieved from: https:// ourworldindata.org/life-expectancy
- Sampat, B. (2019). The Economics of Health Innovation: Looking Back and Looking Forward [Chapter 2]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation. Ithaca*, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Scannell, J. W., Blanckley, A., Boldon, H., & Warrington, B. (2012). Diagnosing the Decline in Pharmaceutical R&D Efficiency. *Nature Reviews Drug Discovery*, 11(3), 191.

- Schmid, E. F., & Smith, D. A. (2005). Keynote review: Is declining innovation in the pharmaceutical industry a myth? *Drug Discovery Today*, 10(15), 1031-1039.
- Sheiner, L., & Malinovskaya, A. (2016, June). Productivity in the Health Care sector. Hutchins Center on Fiscal and Monetary Policy at Brookings. Retrieved from https://www.brookings.edu/wp-content/uploads/2016/08/hp-issue-brief\_final.pdf
- Shetty, D. (2019). Innovations in Healthcare Affordability and Delivery— An Indian Perspective [Chapter 12]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Singh, G. (2018). Re-Innovation in Pharmaceutical Industry: Supergenerics and Biobetters [Chapter 23]. In D. Vohora & G. Singh (Eds.), *Pharmaceutical Medicine and Translational Clinical Research* (pp. 369-380). Boston: Academic Press.
- Smietana, K., Siatkowski, M., & Møller, M. (2016). Trends in clinical success rates. Nature Review 2016. Retrieved from https://doi.org/10.1038/ nrd.2016.85
- Smits, R. E. H. M., & Boon, W. P. C. (2008). The role of users in innovation in the pharmaceutical industry. *Drug Discovery Today*, 13(7), 353-359.
- Tannoury, M., & Attieh, Z. (2017). The Influence of Emerging Markets on the Pharmaceutical Industry. *Current therapeutic research, clinical and experimental*, 86, 19–22. doi:10.1016/j.curtheres.2017.04.005
- The Medical Futurist. (2017, June 20). The Top 10 Trends Shaping the Future of Pharmaceutical. Retrieved from https://medicalfuturist.com/ top-10-trends-shaping-future-pharmaceutical
- Thune, T., & Mina, A. (2016). Hospitals as innovators in the health-care system: A literature review and research agenda. *Research Policy*, 45(8), 1545-1557.
- Uwaliraye, P., Ndimubanzi, P., Muhire, A., & Lyle, V. (2019). Integration of Health and Medical Innovations in Rwanda to Promote Health Equity [Chapter 15]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent. (Eds.), *Global Innovation Index 2019: Creating Healthy Lives—The Future of Medical Innovation*. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Verma, S. (2017). Frugal innovation in medical devices: Key to growth in emerging economies. *Journal of Medical Marketing*, 16(2), 66–73.
- Vijg, J. (2011). The American Technological Challenge: Stagnation and Decline in the 21st Century. New York: Algora Publishing.
- von Philipsborn, P., Steinbeis, F., Bender, M. E., Tinnemann, P. (2015). Poverty-related and neglected diseases: an economic and epidemiological data analysis of poverty relatedness and neglect in research and development, *Glob. Health Action*, 382(2015), 7.
- WHO (World Health Organization), WIPO (World Intellectual Property Organization), and WTO (World Trade Organization). (2012). Promoting Access to Medical Technologies and Innovation, Geneva. Retrieved from https://www.wipo.int/edocs/pubdocs/en/global\_challenges/628/ wipo\_pub\_628.pdf
- WifOR. (2018, July). Understanding public and private funding for pharmaceutical R&D: Does society really pay twice?. Commissioned by the International Federation of Pharmaceutical Manufacturers and Associations, Berlin: Wirtschaftsforschung. Retrieved from https://www.ifpma.org/wp-content/ uploads/2018/06/Wifor-2018-RD-Activities-Footprint.pdf
- WIPO (World Intellectual Property Organization). (2015a). A Look Inside the Economic Growth Engine [Chapter 1]. World Intellectual Property Report 2015: Breakthrough Innovation and Economic Growth (pp. 21-46). Geneva: World Intellectual Property Organization.

- . (2015b). Historical breakthrough innovations [Chapter 2]. World Intellectual Property Report 2015: Breakthrough Innovation and Economic Growth (pp. 49-93). Geneva: World Intellectual Property Organization.
- —. (2018). World Intellectual Property Indicators 2018. Geneva: World Intellectual Property Organization.
- ——. (2019a). WIPO Technology Trends 2019: Artificial Intelligence. Geneva: World Intellectual Property Organization. Retrieved from https://www. wipo.int/edocs/pubdocs/en/wipo\_pub\_1055.pdf
- . (2019b, March 19). WIPO 20148 IP Services: Innovators File Record Number of International Patent Applications, With Asia Now Leading [Press release]. Retrieved from https://www.wipo.int/pressroom/en/articles/2019/article\_0004.html
- Woodson, T. S. (2016). Public private partnerships and emerging technologies: A look at nanomedicine for diseases of poverty. *Research Policy*, 45(7), 1410-1418.
- Xu, K., Soucat, A., Kutzin, J., Brindley, C., Vande Maele, N. et al. (2018). Public Spending on Health: A Closer Look at Global Trends (WHO/HIS/HGF/ HFWorkingPaper/18.3). Geneva: World Health Organization.
- Zaid, H., Salaheldein, A., Hassany, M., & Othman, M. M. (2019). Life is too short with HCV and NCDs—100 Million Healthy Lives Initiative [Chapter 12]. In S. Dutta, B. Lanvin, & S. Wunsch-Vincent (Eds.), *Global Innovation Index* 2019: Creating Healthy Lives—The Future of Medical Innovation. Ithaca, Fontainebleau, and Geneva: Cornell University, INSEAD, and WIPO.
- Żaneta, P. (2019). Innovation in the Polish health sector: a quality assessment (WIPO Economic Research Working Paper No. 47). Geneva: WIPO.