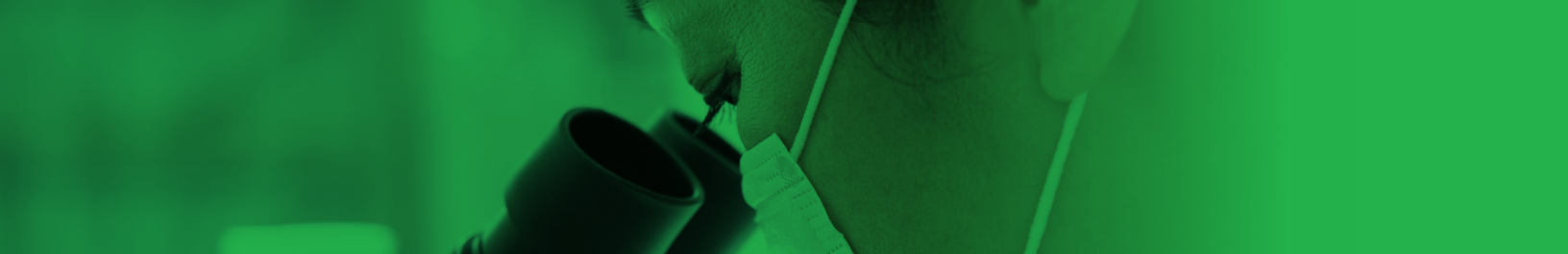




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Crowell & Moring

WASHINGTON, D.C. + SINGAPORE



GLOBAL HEALTH: A LOOK AHEAD AT TRENDS IN SEVEN KEY AREAS



2022



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GLOBAL HEALTH: A LOOK AHEAD AT TRENDS IN SEVEN KEY AREAS

More than ever, health is top of mind around the world. In its 2021 report, “Global Expenditures on Health,” the World Health Organization noted that between 2000 and 2019, the 192 countries that WHO surveyed doubled their total expenditures on health and increased the average percentage of GDP targeted to health from 8.5% to 9.8%.

Not surprisingly, since the emergence of COVID-19, WHO reports an even more substantial rise. This growth is evident in the work of scientists, industry, governments, regulators, the health workforce, NGOs, and educators, united in their efforts to address global health issues and scale innovative solutions. And that, we believe, makes the information we are releasing in this new series of global health reports particularly compelling.

Crowell & Moring International (CMI) serves clients at the intersection of the public, private, and nonprofit sectors on a wide range of critical global health policy, market access,

and regulatory issues. Our work affords us a unique perspective on trends we believe will positively transform and improve health for people around the world. With a clear-eyed view of present and potential roadblocks, we work to help policymakers, regulators, and industry partners visualize ways around them.

With this knowledge and these insights in mind, we cast an eye in these reports on important developments we believe will take place in seven key areas: vaccines, health financing, antimicrobial resistance, oncology/cervical cancer, women’s health, rare diseases, and artificial intelligence/digital health.

We hope you find the analysis presented in these reports helpful, and we look forward to sharing additional perspectives with you going forward.

Best wishes,

Ambassador Robert Holleyman
President & CEO
Crowell & Moring International





Vaccines

PUSHING THE PACE OF CHANGE

Despite challenges, innovation will continue in immunization research, development, and infrastructure.

THE DEVELOPMENT OF CONSISTENT MESSAGING ON THE VALUE OF VACCINATION ACROSS THE LIFE COURSE REMAINS A PRIORITY FOR ALL STAKEHOLDERS.

Nothing in recent years has focused the world's attention on the development, use, and efficacy of vaccines more than COVID-19. Through efficient public-private partnerships, global R&D platforms generated several highly effective COVID-19 vaccines and governments around the world rallied to approve and administer them within their populations.

But there were bumps in the road. Supply chain problems tied to delivery, trade barriers, and cold chain issues slowed down distribution. Vaccine hesitancy—borne not only from misinformation but also from limited access and understanding of the value of vaccination—put downward pressure on vaccination rates globally. By the end of 2021, nearly a year after multiple vaccines were approved, less than half the world had been vaccinated and significant differences persisted in vaccination rates between countries.

Some governments and companies responded by requiring vaccination and implementing other restrictions designed to encourage vaccine uptake. At the same time, rates for non-COVID child, adolescent, and adult vaccinations fell as the pandemic reduced routine provider visits. Despite these challenges, key developments in vaccine research and commitment to improved healthcare by a range of stakeholders foreshadow continued innovation and public health impact, highlighted by the following.

CONSISTENT MESSAGING WILL DRIVE VACCINATION RATES—AND MORE

Though the situation varies among countries, the development of consistent yet tailored messaging regarding the value of vaccines has become especially important. For routine vaccinations, the focus will remain on developing consistent messaging for both providers and patients, especially around adult immunizations, supported by policymaking aimed at increasing access for all communities. For COVID-19, key steps will remain countering misinformation while developing culturally competent messaging to be used with diverse global populations.

Tailoring these messages to a rapidly changing environment will be especially important as new variants emerge and the science advances. The audience for these messages will go beyond those to whom the vaccine is administered, extending to all stakeholders—including government—focused on immunization financing and policy interventions to sup-

port innovation in both vaccine development and delivery.

PUBLIC-PRIVATE PARTNERSHIPS WILL SPEED CHANGE

Developing and fostering partnerships between the public and private sectors, along with collaboration among local and international NGOs and other nongovernmental entities, will be a key driver of both local and global efforts to shape core messaging. Public-private partnerships have had and will continue to have a critical role in pandemic response, not just in communication, but also in building the infrastructure necessary to streamline delivery by identifying and solving challenges related to health system capacity.

A common theme across countries will continue to be increased focus by governments on sustainable immunization infrastructure, particularly financing, through cooperation among government health regulators, trade officials, and customs officials. Now and in the future, the lessons learned and infrastructure developed through the response to COVID-19 can be leveraged for all vaccination programs across the life course.

NEW VACCINES WILL EMERGE—AND NOT JUST FOR COVID-19

What helped drive the rapid development of the COVID-19 vaccines was not just the prior R&D investments in existing vaccine and therapeutic platforms, but also reduced administrative barriers, increased funding, and streamlined regulatory approval processes. Inspired by this, there will be an expansion of the use of innovative vaccine technology platforms for other novel indications, such as HIV and other infectious diseases.

This will build on existing innovation in the vaccine pipeline that predates the COVID-19 pandemic.

This spirit of innovation will go beyond the COVID-19 vaccine platform to place much-needed global emphasis on adolescent and adult vaccination, which will be critical as people begin to travel again and are exposed to other infectious, but preventable, diseases. There will also be an emphasis on innovation in the delivery of immunizations, including to address supply chain and distribution challenges, such as cold chain for rural communities, to support broad public health impact.

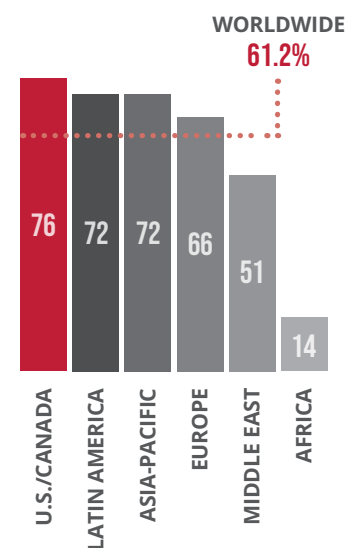
COVID-19 WILL MOVE FROM PANDEMIC TO ENDEMIC IN FUTURE YEARS

The ultimate goal of the COVID-19 vaccine is to reduce the impact this deadly, highly contagious virus has on the health and well-being of the world by stemming transmission, improving health outcomes following infection, and preventing hospitalization and death. Emerging variants have hindered progress in pandemic response, as have such forces as supply chain issues and vaccine hesitancy.

While many believe that 2022 will see a continuation of COVID-19 as a pandemic, the effects of global progress in the forecasts above is likely to bend the arc of COVID-19 in future years. As COVID-19 transitions to the endemic phase in future years, continued emphasis on sustainable immunization financing, building global health systems capacity, developing consistent messaging on the value of vaccination, and public-private partnership in policymaking will remain critical for responding to public health needs across the immunization life course.

VARYING RATES OF COVID-19 VACCINE COVERAGE

Percentage of population that had received at least one dose of a COVID-19 vaccine by January 14, 2022, by region



72% of these shots were administered in high- and upper-middle-income countries. Only 1% were administered in low-income countries.

Source: *Our World in Data*, University of Oxford, published by *The New York Times*



Health Financing

INNOVATIVE APPROACHES DRIVING OUTCOMES

Although public financing hasn't kept pace with need, countries now understand the importance of boosting investment.

WHILE PUBLIC FINANCING FOR HEALTHCARE REMAINS ESSENTIAL, THE PRIVATE SECTOR IS USING NEW, INNOVATIVE FINANCING TECHNIQUES TO COMPLEMENT PUBLIC FUNDING AND CLOSE GAPS IN ACCESS.

It's fair to say that the current state of health financing is mixed. On the one hand, outside of pandemic-related funding, public financing hasn't kept pace with the increasing need for healthcare, due to rapidly aging populations and the rising incidence of noncommunicable diseases. In addition, there is more emphasis on responding to health problems than on preventing them, and political will to take important funding measures is in short supply.

On the other hand, country-level appreciation of the need to boost investment in healthcare is rising; there is positive movement in private-sector solutions; and the pandemic has helped foster recognition that a well-financed healthcare system can strengthen economic health.

The following are four key trends that we see in health financing during 2022.

PRIVATE-SECTOR ENGAGEMENT WILL RISE

Private-sector efforts are growing, and increasingly, they are taking the form of innovative partnerships. Prominent among these efforts are blended capital and health impact bonds.

Blended capital is funding contributed by multiple sources that may include governments, international organizations, and private-sector entities. A blended instrument is structured to address two primary objectives: achieving a specific health outcome and generating an ac-

ceptable return for investors.

One of the best-known examples is Maternal Outcomes Matter (known as MOMs), which aims to improve maternal health in sub-Saharan Africa and South Asia, where women are dying at high rates from complications of pregnancy and childbirth. Launched in 2019 with a commitment of \$50 million in debt and grant financing, MOMs is a collaboration of the U.S. International Development Finance Corporation, MSD for Mothers, Credit Suisse, and the U.S. Agency for International Development.

Health impact bonds are a form of blended capital that combines elements of impact investing, private-sector partnerships, and results-based contracting. The Utkrisht impact bond, for instance, has raised around \$50 million to support private healthcare facilities in Rajasthan, India, to help reduce maternal and newborn mortality. The Brookings Institution reports that there are 32 active health impact bonds worldwide.

NEW SOURCES OF FINANCING WILL ADDRESS GLOBAL PANDEMICS

The global fight to control the coronavirus and prepare for future pandemics got a potentially big boost from the G20 nations in 2021. In October, G20 health and finance ministers announced the formation of a Joint Finance-Health Task Force to forge greater cooperation and support sustainable financing by member states.

We're optimistic the task force can be a catalyst for meaningful action by the G20 and the world. More specifically, we are looking for five developments in 2022:

- Creation of a new financing facility with the flexibility to complement multilateral development banks
- Establishment of a financial intermediary fund, along with a common understanding about how its funds will be managed
- Commitment by member states to provide a level of funding commensurate with the scale of need
- Recognition that governments must mobilize increased domestic resources on a sustained basis
- Efforts to leverage the capabilities of the private and philanthropic sectors

MORE COUNTRIES WILL ADOPT UNIVERSAL HEALTH COVERAGE

Universal health coverage (UHC) isn't universal: Some nations offer healthcare to their citizens at little or no cost, but others don't. While there is growing interest in attaining UHC, doing so will require sufficient, sustained, equitable, and creative funding together with an openness to developing new partnerships.

The United Nations has adopted 2030 as its target date for global UHC and will host a meeting in 2023 to review the progress that has been made so far. But achieving the 2030 goal isn't assured, and diverse financing approaches will be needed. We see the biggest obstacles as insufficient funding and the political calculus in many governments that getting to UHC simply isn't feasible.

Our hope is that in 2022, the combination of momentum at the UN and the massive damage wrought by COVID-19 can push more countries toward their UHC goals.

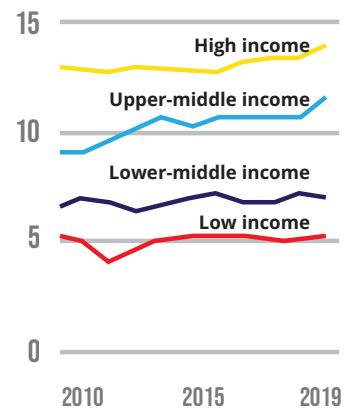
DATA WILL HELP FIGHT RARE—AND NOT-SO-RARE—DISEASES

Historically, the diseases whose treatments have gotten the most financial attention are the Big Three: HIV/AIDS, malaria, and tuberculosis. Funding is much lower for rare diseases (extremely debilitating illnesses that affect a relatively small number of people). While treatments for rare diseases are expensive to develop and bring to market, their effectiveness could have lasting gains for society in terms of mortality and economic productivity.

Data is playing an increasingly important role in fighting rare diseases. New tools to analyze disparate and complex data sets are accelerating efforts to diagnose and treat rare diseases. Big data analytics is also being used for more common diseases. Pharmaceutical giant Roche, for example, is using its data on the costs and usage of innovative cancer treatments to help improve insurance coverage for cancer therapies and diagnostics in China. We expect this data sweet spot—at the intersection of healthcare and insurance—to attract more interest going forward.

DESPITE THE NEED, GOVERNMENT HEALTHCARE SPENDING HAS REMAINED RELATIVELY STAGNANT

Median government health spending (% of total government spending)



Note: Median values are presented to minimize the influence of extreme values.

Source: WHO Global Health Expenditure Database, 2021.



Antimicrobial Resistance

FIXING A BROKEN SYSTEM

As more antibiotics are rendered ineffective, there is a recognition that the problem—and the solution—is market-driven, not scientific.

THE SEARCH FOR LASTING SOLUTIONS TO THE BROKEN AMR MARKET IS LEADING TO ACTIONS SUCH AS PAYING FOR ANTIBIOTICS BASED ON THEIR VALUE TO HEALTHCARE, RATHER THAN USAGE.

Antimicrobial resistance (AMR), which is making a growing range of antibiotics ineffective, is an increasingly critical problem. Driven largely by the improper use of antibiotics, AMR causes more than 1.2 million deaths every year. As this resistance grows, it is eroding the power of a cornerstone of modern medicine. And if nothing is done, that figure is expected to reach 10 million deaths a year by 2050.

The problem is not new, and many in healthcare and government have been sounding the alarm for some time. Nevertheless, there has been little progress in producing new classes of antimicrobials. This is largely a market problem, rather than a scientific challenge. Antibiotics are ideally taken for short periods of time, which makes them less lucrative than drugs intended for extended use. Unable to make this work commercially, many pharmaceutical companies essentially stopped developing new antimicrobials years ago. In short, our approach to antimicrobial innovation is broken.

There are no simple solutions to AMR, but in the coming year, growing awareness of the problem may lead to action in several key areas.

GOVERNMENTS WILL INCREASE THEIR FOCUS ON INNOVATIVE INCENTIVES

Governments understand that they are

key to finding lasting solutions to the broken AMR market. This is leading to actions such as a pilot program that pays for antibiotics based on their value to healthcare, rather than usage, and proposals to allow governments to compensate companies that create new antimicrobials by granting fast-approval status to their other, more lucrative drugs.

In late 2021, the G7 finance ministers released a statement on antimicrobial resistance, saying “We are committed to strengthen and intensify our action across the G7” and “recognizing that this is a multiyear and multistakeholder effort.” Such a statement from finance ministers—as opposed to health ministers—underscores the growing recognition of the need to address the economic side of the problem.

In addition, the U.S. Congress is considering the Pioneering Antimicrobial Subscriptions to End Upsurging

ANTIMICROBIAL RESISTANCE

Resistance (PASTEUR) Act, which has a good chance of becoming law in 2022. This legislation would create a program in which companies that develop new antimicrobials can offer their drugs on a subscription basis that provides revenue without requiring high levels of drug usage. Altogether, these efforts send a clear signal that governments are ramping up efforts to find new ways to incentivize antimicrobial development.

COUNTRIES ARE SET TO RENEW AMR EFFORTS

When the 2015 WHO Global Action Plan on Antimicrobial Resistance called for countries to develop national AMR action plans, many countries—including a significant number of lower- and middle-income nations—responded with plans that typically run for three to five years. Now, these plans are coming to an end, and those nations are poised to renew them. Thus, 2022 will see increased activity in countries' efforts to assess the impact of their efforts, incorporate the lessons learned into new plans, and spell out how they will build response plans and surveillance capabilities and improve stewardship to rein in the unnecessary use of antibiotics.

Efforts to shape these new national plans in the coming year will be critical to the future of AMR, because they will drive the on-the-ground work that is key to translating ideas into action.

PRIVATE SECTOR EFFORTS WILL INCREASE

The pharmaceutical industry has recently become more active in pursuing

AMR solutions. For example, a few years ago the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) launched the Antimicrobial Resistance Industry Alliance (AMRIA), which includes more than 90 member companies. The group works on several fronts, such as promoting research into new drugs and stewardship to slow the emergence of AMR drugs.

Looking forward, the alliance and its members are likely to keep expanding their efforts. This could include improving the collection and sharing of AMR surveillance data, which a 2021 alliance report cited as an area for potential improvement. In addition, we are likely to see activity in the area of responsible manufacturing and reducing the “leakage” of antimicrobials into the environment. While members typically perform well on that front, the report says, there is now an opportunity to extend those gains into their supply chains.

Separately, the IFPMA formed an AMR Action Fund in 2020—essentially, a venture capital fund that aims to invest \$1 billion in startups, with the goal of creating up to four new antimicrobial drugs by the end of the decade. To date, the fund has been working to organize and identify opportunities—and in the coming year, it is likely to start making investments to support clinical research, where there is often a funding gap. This type of action will be important, but as the fund itself notes, its main impact will be to buy time for governments to implement the innovative policies needed to address the fundamental market problems that drive AMR.

ROOM FOR IMPROVEMENT

Despite more nations committing to taking action on AMR, only:

53%

have a standardized national AMR surveillance system aligned with global standards

20%

actively monitor the implementation of their national plans

50%

have a functional AMR multisectoral coordination mechanism

9%

have formally incorporated AMR into healthcare worker training

Source: World Health Organization, 2021



Oncology/Cervical Cancer

CANCER RETURNS TO THE FOREFRONT

Although many cancer-fighting efforts have been sidelined by COVID-19, new approaches and initiatives will have an impact.

WHILE THE TRUE TOLL OF COVID-19-RELATED DISRUPTIONS IN CANCER CARE MAY ONLY COME TO LIGHT IN 2022 AND BEYOND, AWARENESS CAMPAIGNS, ADVANCED TECHNOLOGY, AND NEW PLANNING EFFORTS HAVE THE POTENTIAL TO MITIGATE THE PROBLEMS THIS DISRUPTION HAS CAUSED.

Historically, the World Health Organization (WHO) has led extraordinary efforts to eliminate, and even eradicate, highly communicable diseases such as malaria and smallpox in low- and middle-income countries. The UN-based agency, however, has increasingly turned its focus to noncommunicable diseases, acknowledging the burden that cancer, diabetes, and heart and respiratory diseases are placing on emerging economies.

Cancer emerged as a key topic in 2017 when WHO member states unanimously adopted a landmark resolution, committing to make cancer prevention and control a global public health priority. The following year, the International Cancer Control Partnership—a consortium of cancer control groups from around the world—announced its goal to reduce deaths from noncommunicable diseases, such as cancer, by one-third by 2030.

In February 2020, the WHO released a 180-page report outlining a plan to save 7 million lives from cancer over the next decade by mobilizing stakeholders and strategically using limited resources in low- and middle-income countries.

At the time, however, the attention of national health authorities shifted to the growing threat of the novel coronavirus disease (COVID-19) that had already been reported in Asia, Australia, Europe, and the U.S.

Just four weeks after the report was released, the WHO declared the COVID-19 outbreak a global pandemic.

COVID-19-RELATED DISRUPTIONS WILL RESULT IN ADDITIONAL CANCER DEATHS

The COVID-19 pandemic has resulted in major setbacks for cancer-fighting efforts around the globe. Not only are cancer patients at higher risk from COVID-19, but 42% of countries reported disruptions in cancer treatment because of the pandemic's strain on their healthcare systems, according to the *International Journal of Cancer*.

Cancer screening programs were particularly affected. One study showed breast cancer screening rates in Taiwan down by more than 20%. In the Netherlands, colonoscopies fell by 45%. Lung cancer scans in the U.S. dropped by more than 70%.

The widespread impact will become more evident in 2022. UK researchers project significant increases in premature cancer deaths due to missed screenings over the next five years, estimating as many as 150,000 more deaths from colorectal cancer, 95,000 from lung cancer,

65,000 from breast cancer, and 32,000 from esophageal cancer in the UK alone.

NEW APPROACHES TO AWARENESS AND DETECTION WILL EMERGE

With global health officials optimistic that COVID-19 could begin to recede as a public health emergency in 2022, countries are urged to develop COVID-19 recovery plans that address disruptions to health services in the short term, while also promoting long-term policies to build more resilient healthcare systems in preparation for future pandemics.

Awareness and early detection will continue to play a key role. Increased availability of telehealth services is a much-needed health policy intervention to bolster awareness campaigns. They can be aided by increased deployment of at-home screening tests for several cancers as well as community-based programs for cancer screenings that cannot be performed at home. The use of wearable devices to monitor patients undergoing cancer therapy should become more common.

However, with government resources and healthcare workforces depleted by COVID-19, government health ministries alone cannot launch a holistic post-pandemic response. A multistakeholder approach that ensures the best use of limited resources, pools expertise, and considers different perspectives will be needed.

The WHO's February 2020 cancer report specifically called on countries to adopt more effective National Cancer Control Plans (NCCPs) by including private sector and nonprofit organizations in their design and implementation.

A robust NCCP should tackle the range of cancer-related interventions: primary prevention, screening and early diag-

nosis, access to treatment and services, and evaluation, governance, and monitoring of implementation. It also requires convening representatives from industry, academia, and patient advocacy and provider groups, along with health ministry officials, to identify the highest priorities and the most cost-effective responses.

CERVICAL CANCER WILL PAVE THE WAY FOR OTHER SPECIFIC CAMPAIGNS

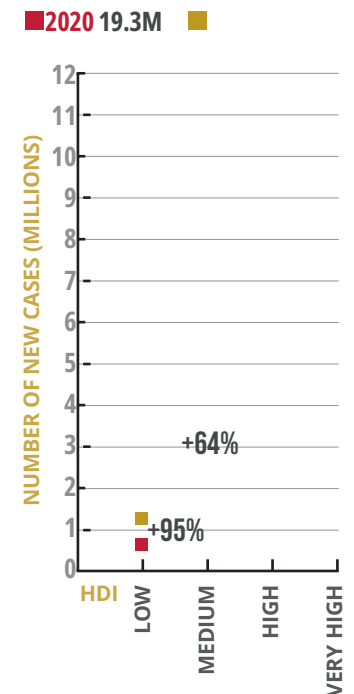
While efforts to fight all kinds of cancer will get renewed attention, efforts to eliminate cervical cancer will be heightened in 2022.

In 2018, the WHO called for the elimination of cervical cancer by 2030 through a combination of increased access to screenings and treatment as well as widespread uptake of vaccination against the human papillomavirus (HPV), which causes the vast majority of cervical cancers.

Though vaccination and screening campaigns were hindered by the pandemic, numerous organizations are poised to redouble their efforts in the coming year. For example, in August 2021 the Asia-Pacific Economic Cooperation (APEC) forum, with 21 member economies, issued a road map for forming multisectoral partnerships to defeat cervical cancer. The strategic objectives aim to support APEC economies in accelerating and scaling prevention of cervical cancer through HPV vaccination of eligible populations and effective screening and treatment of pre-cancerous lesions, expanding the application of health-systems tools to improve the quality of treatment and palliative care and improving health infrastructure to support improvements in prevention and care.

Look for the most successful strategies in this effort to be employed in other cancer-fighting campaigns in the future.

EMERGING HDI COUNTRIES WILL EXPERIENCE THE HIGHEST INCREASE IN NEW CASES OF CANCER



The rising burden of cancer will not affect all countries the same. While emerging markets, which rank lower on the **Human Development Index**, currently have lower rates of cancer than countries that rank higher, they are likely to see a greater increase in cancer cases over the next two decades due to demographic and lifestyle changes, increased life expectancy, and more reliable screening and diagnosis. These shifts will not only impact public health ecosystems, but they will also have significant economic impacts, demanding innovative new frameworks, partnerships, and perspectives.

Source: GLOBOCAN 2020



Women's Health

RESUMING PROGRESS AS COVID-19 RECEDES

In the pandemic's wake, organizations, governments, and advocacy groups are working to push women's health initiatives forward.

WHILE COVID-19 HAD A NEGATIVE IMPACT ON WOMEN'S HEALTH AND WELL-BEING WORLDWIDE AND STALLED PROGRESS ON A NUMBER OF CRITICAL WOMEN'S HEALTH INITIATIVES, GLOBAL PUBLIC HEALTH AUTHORITIES ARE HOPEFUL THAT SEVERAL ISSUES WILL COME TO THE FOREFRONT IN 2022.

No look ahead at women's health issues in 2022 would be complete without a discussion of the continuing impact of the COVID-19 pandemic. COVID-19 death rates are significantly higher among men, but—for reasons experts are still trying to understand—women are as much as four times as likely to suffer from “long COVID,” with symptoms such as fatigue, insomnia, and cognitive dysfunction persisting after the infection has resolved.

Available evidence suggests that women's emotional well-being has also taken a bigger hit from COVID-19. In a survey by the international humanitarian organization CARE, 27% of women reported pandemic-related mental health challenges such as anxiety, loss of appetite, and inability to sleep, compared to 10% of men. Women's health advocates attribute this to women's outsized role as unpaid caregivers for sick family members as well as children forced to stay home due to school closures. Women also make up 70% of the frontline health-care workforce, which has consistently reported highly elevated levels of stress and burnout throughout the pandemic.

COVID-19 has not only negatively impacted women's health and well-being worldwide, it has also stalled progress on a number of women's health initiatives. However, with global public health authorities hopeful that COVID-19 will at least partially recede as a global health emergency in 2022, look for several is-

ues to come to the forefront once again.

SEXUAL AND REPRODUCTIVE HEALTH EFFORTS WILL BE RENEWED

The United Nations Population Fund estimated in April 2021 that a disruption in contraceptive services due to the pandemic had resulted in 1.7 million unintended pregnancies worldwide. One study revealed significant increases in maternal death, stillbirth, and maternal depression globally, citing limited access to maternal services and reduced health-care-seeking behavior as major contributing factors, especially in low- and middle-income countries.

The issue took center stage in mid-2021 at the UN-organized Generation Equality Forum, where participants pledged a cumulative \$40 billion to accelerate gender equality efforts in the face of COVID-19 setbacks. That included \$1.4 billion from the Gates Foundation, \$1.2 billion from the government of Norway, and \$83 million

from the Ford Foundation to boost sexual and reproductive health efforts worldwide.

The infusion is expected to jump-start Generation Equality's efforts toward its stated five-year goal of delivering quality sexuality education to 50 million additional adolescents, providing access to contraceptive services to 50 million more women, integrating comprehensive sexual and reproductive health access into health systems in 20 additional countries, and advancing legal and policy reforms to support sexual and reproductive health access in at least 10 additional countries.

Expect a progress report when many of the organizations at the Generation Equality Forum gather in Kigali, Rwanda, for the Women Deliver conference in 2023.

MANY COUNTRIES WILL FOCUS ON LOW FERTILITY RATES

At the same time, governments around the globe are raising the alarm about dramatically declining fertility rates, which are largely linked to increased educational attainment and access to contraception among women.

According to demographers, the pandemic accelerated a drop in global fertility rates that had already been occurring, and some believe that nearly every country could see shrinking populations by the end of this century. More important, populations are expected to get significantly older, with more people turning 80 than being born in 2100.

Many governments worry that this could dramatically increase the burden on the working-age population to support non-working, older adults, drive up taxation rates, and foster political and social instability.

In 2022, policymakers are expected to

place more emphasis on fertility issues in an attempt to bounce back from the pandemic baby bust. Given the parallel efforts being made to increase access to education and contraception for women, however, developing the correct policy responses to low fertility rates will be complex as well as critical.

Some countries have already begun offering housing and childcare subsidies to encourage births, along with requiring employers to offer paid maternity leave and flexible work scheduling. Several governments in Europe and Asia have recently begun subsidizing fertility treatments such as in-vitro fertilization. China's health commission has set a goal of having at least one institution offering IVF for every 3 million people by 2025.

CERVICAL CANCER WILL BE TARGETED FOR ELIMINATION

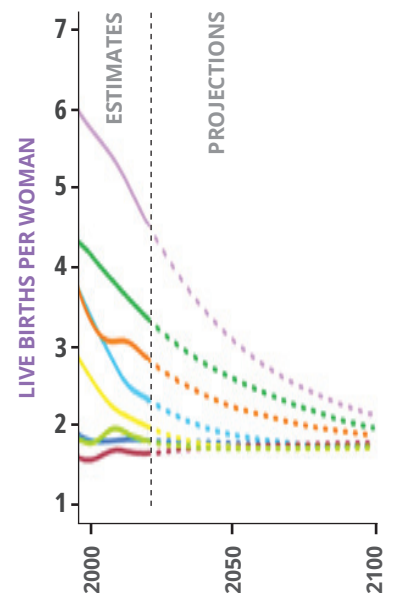
Increasingly, advocacy groups are touting women's health initiatives as important for economic prosperity, enabling women to participate fully in the workforce.

The current global push to prevent and control cervical cancer could serve as a case study for that rationale. Most commonly diagnosed between ages 35 and 44, cervical cancer often strikes women in their prime earning years, as well as during the time that they are most needed as caregivers to children and elderly family members.

Cervical cancer is also highly preventable through vaccination for the human papillomavirus, screenings for early detection, and treatment of precancerous lesions. Though the pandemic sidelined vaccination and screening programs in many countries, look for a comeback in 2022 as these countries aim to meet the UN's targets for the elimination of cervical cancer by 2030.

TOTAL FERTILITY RATE BY REGION

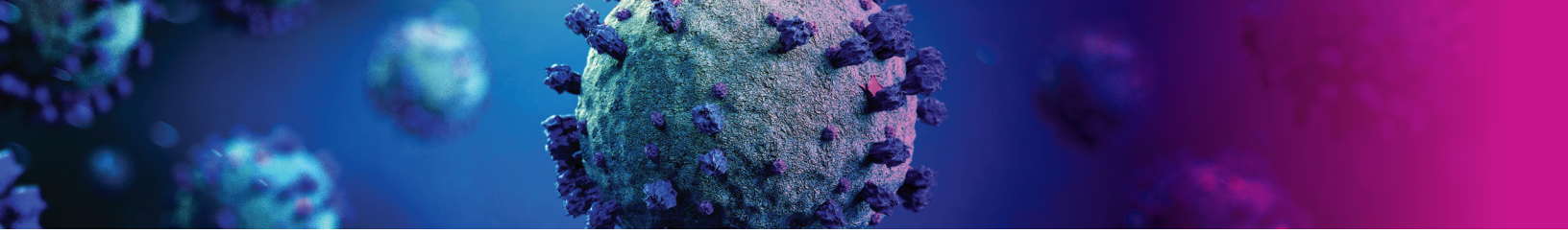
Estimates and Projections, 2000-2100



- Sub-Saharan Africa
- Northern Africa and Western Asia
- Central and Southern Asia
- Eastern and South-Eastern Asia
- Latin America and The Caribbean
- Australia and New Zealand
- Oceania excluding Australia and New Zealand
- Europe and North America

Global fertility rates have dropped significantly since 1950, a trend that is projected to continue in most regions through the rest of this century.

Source: United Nations Department of Economic and Social Affairs, Population Division (2019a). *World Population Prospects 2019*.



Rare Diseases

THE OUTLOOK BRIGHTENS

Despite steps to incentivize development and accelerate treatment, challenges remain. But barriers are beginning to fall.

THE OUTLOOK FOR FIGHTING RARE DISEASES IS BRIGHTENING AS A RESULT OF SCIENTIFIC ADVANCES, RISING GLOBAL AWARENESS, REGULATORY MOMENTUM, AND ATTENTION FROM INSTITUTIONAL PAYORS.

Rare diseases are considered rare because they affect relatively tiny numbers of people: up to 200,000 in the U.S., for example, and less than one in 2,000 in the European Union. While individually they are uncommon, collectively they are not. More than 300 million people live with one of about 7,000 identified rare diseases globally, including 25-30 million in the U.S., according to EURORDIS-Rare Diseases Europe and National Institutes of Health.

Historically, the combination of complex genetic etiology, small patient populations, large development costs, and regulatory and reimbursement uncertainty has limited the development of treatments for rare diseases. Regulatory authorities in the United States, the EU, and other developed markets have taken steps to incentivize development and accelerate approval of treatments for rare diseases, but challenges remain. Gene therapy, which could offer durable cures for many rare diseases, brings its own mixture of promise and complication. Overall, we believe that the outlook for rare-disease treatments is brightening and see several trends driving positive momentum.

SCIENCE IS ADVANCING

After decades of research, gene therapy has taken a monumental leap from the lab bench to the bedside over the past

several years, unlocking the possibility of curing some of the rare diseases caused by a defect in a single gene. While Fierce Pharma notes that the U.S. Food and Drug Administration has approved only two gene therapies for rare diseases for sale in the U.S., the American Society of Gene + Cell Therapy reports that 998 gene therapies for rare diseases are currently in the preclinical-to-preregistration stages of development worldwide.

Clinical trials for more gene therapies are reaching advanced stages. Many are generating favorable data for safety and efficacy—an encouraging sign for patients, caregivers, regulators, researchers, and manufacturers alike.

GLOBAL ATTENTION IS RISING

The fight against rare diseases is gaining attention worldwide from patients, medical providers, nongovernmental organizations, and—most importantly—

regulators and institutional payors (e.g., health insurers and governments).

A major milestone occurred in December 2021, when the United Nations adopted its first-ever resolution recognizing the more than 300 million people living with rare diseases and their families. While the resolution was symbolic, its recognition of rare diseases' seriousness set a marker of sorts for others to join the fight and take concrete action.

Ultimately, each country must determine its own approach to rare diseases, ideally with a formal national action plan. Few such plans yet exist: Chile drafted one in 2021, and Malaysia and Peru are working on their own. Several Latin American countries (Argentina, Brazil, Chile, Colombia, Mexico, and Peru) have passed legislation specific to rare diseases since 2010.

The Asia-Pacific region is working on a promising regional initiative. In 2018, the Asia-Pacific Economic Cooperation forum (APEC) launched its Action Plan for Rare Diseases to provide APEC's 21 member economies with a framework for policy action. The plan calls for members to improve economic and social inclusion of people with rare diseases and sets precise targets for achievement by 2025.

REGULATORS ARE ADJUSTING

Regulators represent one of the biggest potential opportunities for the introduction of new rare-disease treatments—and not simply because their approval is required. Historically, regulators have made approval decisions based on large-scale participation in clinical trials that often last for years and generate huge volumes of patient data. In order to most efficiently review new drug applications to treat rare diseases, however, regulators must

rethink their methods and processes to adjust for potentially smaller trials, alternative endpoints, and real-world data. Gene therapy adds further complexity.

The good news is that regulators are increasingly aware of the need to change. This is particularly true in the U.S., Europe, Japan, and China, where most of the new treatments are in development and regulators are already reviewing trial data. Regulatory agencies in emerging markets—notably Brazil, Chile, Indonesia, Mexico, the Philippines, and Saudi Arabia—are closely monitoring their larger-nation counterparts to see how they will need to adjust.

Regulators in many smaller countries face additional pressures to act both from elsewhere and at home. On an external level, they see increasing access to new treatments in larger nations and want the same for their own populations. Domestically, they face well-organized groups of patient advocates whose increasingly vocal demands for new and improved medicines cannot be ignored.

PAYORS ARE PAYING ATTENTION

The economics underpinning the value and cost of treatments for rare diseases are unique and complicated, and they can pose tough challenges for institutional payors as well as individuals covering out-of-pocket costs. Payors will have to reassess how they manage their reimbursement risk when the number of potential patients is low. Gene therapies pose especially big actuarial challenges for insurers.

Fortunately, payors are beginning to explore, design, and pilot innovative funding and financing mechanisms to accelerate access to rare-disease treatments, including for gene therapies.

RARE DISEASES: BY THE NUMBERS

7,000

Identified rare diseases in the world

300 MILLION+

Affected by rare diseases

25 MILLION+

In the United States

200,000

Or fewer Americans have a specific rare disease

1 IN 2,000

EU residents have a specific rare disease

Sources: EURORIDS-Rare Diseases Europe; National Institutes of Health



Artificial Intelligence/Digital Health

MEETING THE INCREASED DEMAND

Fueled by the pandemic, tools, policy, technology, and data are coming together to produce opportunities for digital healthcare.

ADVANCES IN DIGITAL HEALTH INNOVATION, INCLUDING AI-ENABLED TOOLS, ALLOW PUBLIC AND PRIVATE SECTOR STAKEHOLDERS TO USE THIS TECHNOLOGY TO IMPROVE HEALTHCARE DELIVERY AND OUTCOMES AND DRIVE SUPPORTIVE POLICY EFFORTS.

Digital innovation continues to rapidly transform healthcare while, at the same time, raising several policy challenges, including privacy, security, data sharing and interoperability, transparency, safety and effectiveness, and equity. These challenges are global, requiring multistakeholder collaboration. The pandemic has increased the demand for digital health and AI-enabled tools and, correspondingly, the urgency in developing policy solutions.

In the coming year, we expect to see continued emphasis by health sector stakeholders worldwide on addressing these challenges, with the goal of safely, effectively, and equitably scaling health digitization.

VIRTUAL CARE WILL BE INCREASINGLY IMPORTANT IN HEALTHCARE DELIVERY

Worldwide innovation in virtual care, including remote patient monitoring tools and telehealth platforms, will continue to augment patient care for an expanding spectrum of clinical applications.

The pandemic has sharply increased this trend. In some countries, including the United States, policymakers have made temporary or permanent changes to regulations that impact the use of such tools in order to expand access. These changes have been supported by efforts to expand the enabling

infrastructure for adoption.

Post-pandemic, policymakers are likely to focus on evolving existing laws and regulations to support continued use and adoption by providers and patients. In some countries, this will involve developing a new legal structure to support use of digital technologies, creating opportunities to leverage best practices and improve global regulatory harmonization. We see virtual care being a critical tool for expanded access to care in remote areas worldwide.

MORE RULES WILL BE APPLIED TO DATA USAGE

Given the importance of health data to patient care, governments and businesses will continue to work to determine how to simultaneously improve access to and protect health data.

In many countries, patients have a

ARTIFICIAL INTELLIGENCE/DIGITAL HEALTH

right to access their health data. In the United States, this long-standing patient right has been strengthened by recent interoperability regulations, which strive to make it easier for patients to access their health data electronically and for providers to access and use such data to optimize patient care. The expansion of individual data rights in many countries, along with greater portability of health data, will drive new waves of innovation that make use of that data. This will likely prompt regulators to increasingly scrutinize the use of health data in consumer applications.

Meanwhile, there is increased attention to the value of using real-world data (RWD) to support regulatory approvals. RWD is often leveraged in U.S. regulatory approval processes, and other governments, including in the Asia-Pacific region, have begun to explore RWD policies.

The EU's General Data Protection Regulation (GDPR) has formed a basis upon which many governments have developed their own privacy rules. In the U.S., most new privacy laws carve out health data subject to HIPAA, but also may cover health data in mobile apps that are not covered by HIPAA. Policymakers are likely to focus on striking a balance between access to data and privacy and security protection for the same data.

AI GUIDANCE WILL COME INTO SHARPER FOCUS

Many stakeholders have developed high-level ethical principles for AI systems. Many such initiatives center on accountability, bias, and transparency. This "soft law" approach is likely to

be "hardened" as new regulations are implemented.

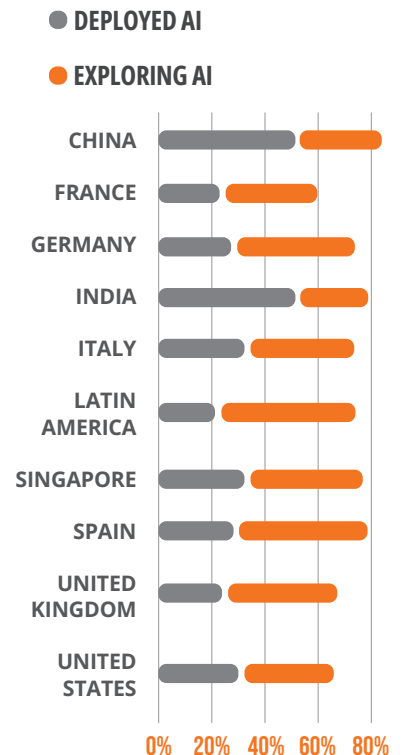
For example, the European Commission's proposed Artificial Intelligence Act (EU AI Act), which takes a risk-based approach, would have broad implications for AI-enabled health tools, especially if they are considered "high-risk." Since the Act is novel, it may enjoy a "first-mover effect" akin to GDPR, in which other governments pass similar regulations.

Key activities are occurring elsewhere in the world. Effective March 1, China has implemented rules governing algorithms with key functions in the digital economy, including those that set prices and recommend and filter content. Singapore's Infocomm Media Development Authority's Model AI Governance Framework—the first of its kind in Asia—provides actionable guidance to businesses on AI ethics and governance issues across sectors, with the goal of promoting understanding and trust.

Governments have also begun to issue national strategies to develop their domestic AI industries, which often include financial commitments, such as recent investments in Chile and India. These developments provide potential opportunities for industry to partner with governments as they develop their economies' AI capabilities.

Finally, strategies focused on AI and healthcare are likely to receive further attention. For example, collaboration between regulators in the U.S., UK, and Canada on the guiding principles for the use of AI and machine learning in medical devices is a key example of ongoing harmonization efforts. Potential future implementation activities relating to the GMLP principles will be important for stakeholders to monitor.

AI ADOPTION RATES AROUND THE WORLD



Almost one-third of IT professionals worldwide say their firms are using AI technology and almost half say their companies are exploring it.

The top drivers of AI adoption in organizations are:

1. Advances in AI that make it more accessible (46%)
2. Business needs (46%)
3. Changing business needs due to COVID-19 (44%)

Source: From *Roadblock to Scale: The Global Sprint Towards AI*. IBM, 2021



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