50 YEARS OF GLOBAL HEALTH PROGRESS

IFPMA

SustainAbility

CONTENTS

FOREWORDS

IAN READ, PFIZER CHAIRMAN & CEO, IFPMA PRESIDENT

A desire for quality healthcare is something that unites all of us because a healthy society is essential to ongoing global development. It creates stronger families and communities, enables more productive and innovative workforces, and supports economic growth. That's why patients and their needs have been the IFPMA's 'north star' for the last 50 years, and why they will continue to guide our efforts and allocation of resources into the future.

During my 40 years in the pharmaceutical industry, I have been inspired by the monumental advancements that have fundamentally altered the healthcare landscape. Today we benefit from incredible medicines and vaccines that have:

- turned fatal illnesses like HIV/AIDs into chronic conditions;
- slowed disease progression for rheumatoid arthritis;
- cured a disease such as hepatitis C;
- helped to prevent previously widespread childhood illnesses such as rotavirus, chicken pox and pneumococcal disease;
- reduced mortality rates for cardiovascular and diabetes patients around the world, and;
- revolutionized the care for some cancer patients with personalized therapies that have improved outcomes and extended life.

While the pharmaceutical industry has been instrumental to this progress, none of it would have been accomplished without partnership. From patient advocates to our biotech and academic partners to local governments who help ensure access on the ground, innovation is only as good as the partnership that supports it.

Last year I was incredibly proud to help launch Access Accelerated, a first-of-its-kind collaboration led by more than 20 pharmaceutical companies, IFPMA, the World Bank and the Union of International Cancer Control that is focused on improving access to treatment and care for non-communicable diseases in low- and middle-income countries. We must continue to lean in to these types of endeavors that help ensure the life-changing therapies we work so hard to develop reach those who need them most.

The next 50 years promises to deliver an even more exciting era of medical discovery. With more than 7,000 medicines in development around the world, we see the potential for additional breakthroughs and cures that will transform millions of lives. As we continue on this journey, we must continue to build trust around the vital role we play in improving global health. This is an obligation that I embrace, and I know IFPMA will continue to lead us in this effort for years to come.

THOMAS CUENI, IFPMA DIRECTOR GENERAL

Health is vital for societal well-being and progress. While we may despair at health threats in the headlines – dementia, antimicrobial resistance, pandemics – the truth is that we have lived through 50 years of health progress.

The research-based biopharmaceutical industry has played its part in a network of research institutes, government departments and donor organizations not only to deliver prevention and treatment, but to strengthen health systems and to make universal health coverage a possibility.

Like any wave of progress, there are setbacks and mistakes have been made. One of the greatest was in 1998 when 39 companies sued the South African government to stop legislation facilitating import of lower priced medicines. The lawsuit became a symbol of industry's insensitivity to the plight of patients in sub-Saharan Africa.[1] Profit, via patents and prices, were understood to be barriers to treatment until the parties reached a then-revolutionary settlement. The court case led to major soul-searching among pharmaceutical companies and resulted in government and industry working together to find solutions for the epidemic — a precursor to the norm today.

From suing Nelson Mandela to becoming an active partner in delivering global health solutions, the industry has evolved and learned. This needs to continue. We need to safeguard the progress made. And we have to do even more.

We need to do more to reach all patients, regardless of economic circumstances. Investment in health infrastructure, the ways services are delivered and the role of prevention must be part of the dialogue. Today, more than half the world's population have to pay for their medicines out of pocket.[2] Improving access for these people requires navigating a complex value chain. For example, there are often mark-ups along the supply chain that make essential diabetes treatments unaffordable for many.[3]

Progress will be hampered as long as universal health coverage is not in place. We worry about the cost of treatment – and prevention – but rarely tally the cost of *not* treating.

To do better, go further and faster we'll need partnerships, of all kinds. More dialogue is a must, and that we welcome.

As we live longer, the diseases of ageing raise a new set of questions. Climate change and conflict require new ways of thinking about disease transmission and delivering care. And antimicrobial resistance poses a real threat to global health security.

The last 50 years has seen companies move to greater global accountability. The next 50 will be about further delivering on our purpose: putting patients first to deliver better health for everyone, everywhere.

REFLECTING ON 50 YEARS OF GLOBAL HEALTH PROGRESS

IN 1968...

...THE THREATS OF SMALLPOX AND MALARIA WERE TOP OF MIND FOR THE PUBLIC HEALTH COMMUNITY. The 21st World Health Assembly brought public health actors together in Buenos Aires to explore the cooperation with other organizations needed to tackle these challenges. Thanks to global immunization campaigns, smallpox, one of the most devastating diseases facing humanity, was eradicated in 1980. Malaria, despite the rate of new cases falling by over a third between 2000 and 2015,[4] remains one of the world's biggest killers. Elimination remains high on global public health agenda.

...STUDIES OF CANCER IN NONHUMAN PRIMATES PROVIDED COMPELLING NEW EVIDENCE FOR THE EXISTENCE OF A HUMAN CANCER VIRUS.[5] Fifty years later, experts' understanding of the biology of cancer, and how to diagnose and treat it, has advanced considerably. Cancer is now known to be a group of over 100 different and complex diseases, all involving the uncontrolled division of the body's cells.[6] Cutting-edge research is giving rise to new treatments in the field of immunotherapy, which harnesses the immune system to fight cancer from within.[7] Improved understanding of cancer-related genes means that doctors can use personalized medicine to target the specific mutation that's driving the cancer.[8]

HEALTH ENABLES HUMAN DEVELOPMENT AND PROSPERITY

THE LAST 50 YEARS HAVE SEEN AN INCREASED RECOGNITION THAT ACCESS TO HEALTH IS A RIGHT.”

Mariângela Simão,
Assistant Director-General for Access to Medicines, Vaccines and Pharmaceuticals, World Health Organization

Health is a most basic and essential asset not limited to any one agenda. Poor health can limit opportunity and prevent the living of a full and rewarding life.

Disease reinforces and worsens poverty. By some estimates, from 2011-2025, the cumulative lost output in low- and middle-income countries (LMICs) from non-communicable diseases (NCDs) was more than USD 7 trillion, making a powerful economic case for effective prevention and intervention strategies.[9]

Individuals, communities, nations, and the global community benefit from good health. Whether living free of disease through prevention programs, vaccines, treatments and cures, or enjoying better quality of life living with and managing diseases, health is the basis upon which successful, flourishing, and sustainable societies develop. For instance, malaria eradication campaigns in Uganda are associated with long-term improved education and livelihoods.[10] AIDS treatment, care and prevention has resulted in increased employment in sub-Saharan Africa.[11]

Health progress drives prosperity, wellbeing, enhanced livelihoods, economic development, and equality.

SOCIAL IMPACTS OF IMPROVED HEALTH:

A MALARIA FREE AFRICA WOULD MEAN...

POVERTY REDUCTION
25% MORE INCOME FOR HOUSEHOLDS

LABOUR PRODUCTIVITY
MORE PEOPLE IN PAID WORK

ECONOMIC GROWTH
1.3% ECONOMIC GROWTH (TOURISM, AGRICULTURE)

MORE CHILDREN IN EDUCATION
15% LESS SCHOOL ABSENTEEISM

BETTER SCHOOL PERFORMANCE
60% INCREASE IN SCHOOLCHILDREN LEARNING ABILITY

THE CONTRIBUTION OF THE R&D-BASED BIO-PHARMACEUTICAL INDUSTRY TO GLOBAL HEALTH PROGRESS

The International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) was created in 1968 with a mission to bring the research & development (R&D)-based biopharmaceutical industry and the health community together to tackle global health challenges. Fifty years since, significant global health progress has been made.

The R&D-based biopharmaceutical industry (the industry) develops and provides medicines and vaccines that improve the lives of patients worldwide. It has played a unique and important part in delivering better health for millions of people across the world.

Innovation is crucial, and the industry has contributed significantly to understanding health challenges and developing solutions, investing USD 159 billion in R&D in 2017.[12] The industry has learned that global health is about much more than medicines and vaccines – it requires building and supporting strong health systems, developing public health education, and strengthening standards and regulations. For innovations to reach the people who need them, broader progress is needed, such as improved diagnostic capabilities and better-informed healthcare providers. Partnership, alongside innovation, is crucial to deliver on progress.

This report seeks to tell **seven stories of progress over 50 years**. Stories that showcase advances, partnership, and challenges, and demonstrate not only unfinished business, but also hope for the future. At the start of each story of progress, the reader will find a personal story about how lives have been transformed, using the lens of individual lives to represent the progress made and imagine the future. These are illustrative only.

- **VACCINES:** Saving, protecting and enhancing lives
- **HIV/AIDS:** Overcoming one of the worst human pandemics
- **NEGLECTED TROPICAL DISEASE, MALARIA AND TUBERCULOSIS:** Thinking beyond traditional models
- **CANCER:** Persisting in research and innovation to deliver better patient outcomes
- **CARDIOVASCULAR DISEASE:** Innovating for longer and better lives
- **DIABETES:** Improving quality of life through management of a complex disease
- **HEPATITIS C:** Discovery to cure in 25 years

Future trends are also explored, what’s on the horizon and well beyond it.

A UNITED HEALTH ECOSYSTEM

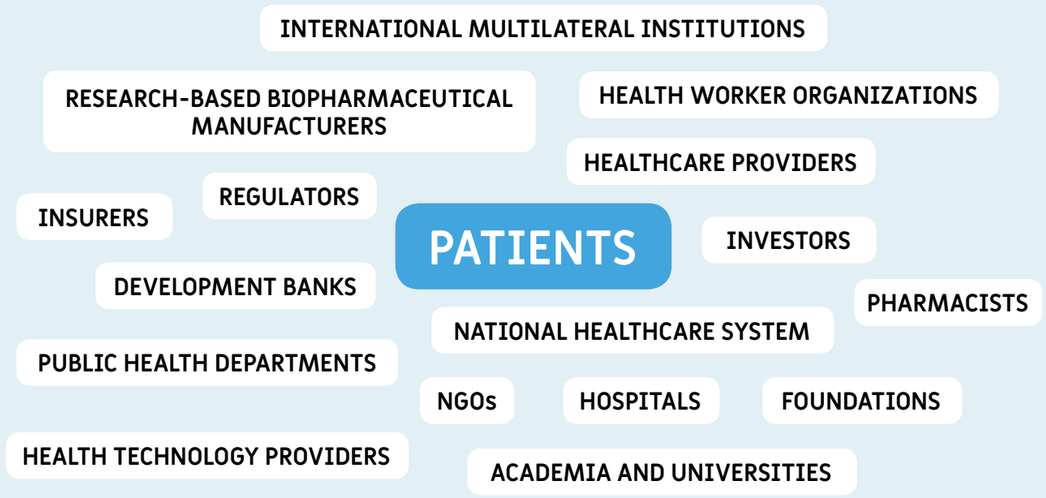
Global health progress relies on all actors sitting around the table: activists, governments, technical groups and industry.

David Heymann,
Professor, Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine

Be it controlling NCDs, precision medicine for cancer or eliminating Neglected Tropical Diseases (NTDs), health progress has been made possible by researchers in academia and in industry understanding diseases and developing vaccines and medicines, regulators incentivizing bringing of drugs to market, NGOs and foundations developing programs to deliver medicines, financial institutions defining innovative funding mechanisms, and healthcare providers training health workers. All are connected by the drive to understand and respond to the needs of the patient.

The cycle of care, from prevention to treatment to quality of life and cure, is both complex and highly personal. Health is impacted by a range of factors: from security to sanitation, and from geography to genetics. The research-based biopharmaceutical industry has played its part by bringing life-saving and life-prolonging medicines and vaccines to individuals, improving both personal and public health outcomes. Together, industry and others have reimagined how medicines make the journey from lab to patient.

The industry's contribution to global health challenges has evolved over 50 years – enabled by a strong ethical code of practice. The way companies innovate and partner with others has delivered numerous health benefits to individuals and societies.



BUILDING TRUST

The importance of ethics and safety is reflected in the highly regulated nature of the industry. In the early 20th century the industry was dubbed 'the ethical drug industry', in reference to the safety and efficacy requirements to which R&D-based biopharmaceutical manufacturers adhere when bringing products to market.[13] Today, ethics refers to much broader values and principles.

Fairness, honesty, respect, and care are foundational to the success of the industry, to broader global health progress and to patient outcomes. Progress requires an environment that encourages risk-taking, exploration and innovation, which is made possible through trust built upon proactive ethics.

IFPMA's mission is based on the establishment and promotion of ethical principles for the industry. The seeds of a shared ethos were planted in 1981, when the first IFPMA Code of Practice was created as the foundation for global self-regulation.[14] Updated and revised over the decades, the code set the rules-based compliance framework for clinical research and transparency, fees for services, support for continuing medical education, training, interactions with patient organizations and physicians, and many other areas. Many local and regional associations rely on the IFPMA code and guidance for their own codes of conduct.

Progress was punctuated by other major global milestones: In 1988, the World Health Organization (WHO) published its *Ethical Criteria for Medicinal Drug Promotion*;[15] in 1996, the first WHO International Summit of National Bioethics Commissions was held;[16] in 2012, the Mexico City Principles for Voluntary Codes of Business Ethics in the Biopharmaceutical Sector were endorsed by Asia-Pacific Economic Cooperation heads of state, establishing a comprehensive ethical and integrity framework for the industry.

The current version of the IFPMA Code of Practice expands the scope beyond marketing practices to cover all interactions with healthcare professionals, medical institutions and patient organizations. Revision of the Code is ongoing. The revised Code (effective January 2019) will be more principles-based and incorporate an expanded understanding of ethics and business integrity.

The industry and partners continue to engage with emerging ethical challenges presented by collaborative public health programs, including privacy, autonomy, and equity. For example, the 2017 WHO *Guidance on Ethical Issues in Public Health* in set out the first international framework for government, health workers, NGOs, and the private sector to navigate these challenges.[17]

TRANSFORM AND INNOVATE

Researching, developing, manufacturing, and improving medicines and vaccines is at the heart of the industry's contribution to health.

R&D – and improving the underlying understanding of diseases – is essential. This has helped to take medicine from treatment based on controlling symptoms to understanding diseases and causation, enabling more nuanced, targeted, and systematic approaches across treatment, prevention, and care. For example, advances in understanding the complex genetic, environment and lifestyle causes of cardiovascular disease, and the effects of statins and anti-hypertensive drugs, has paved the way for better and more effective treatment. Fifty years ago, doctors had few tools to fight cancer, but through incremental advances and occasional breakthroughs, many cancers that were once uniformly fatal are now generally treatable.

Every treatment or vaccine over the last 50 years has roots in the scientific advances and breakthroughs made by others before. Industry tirelessly seeks out new discoveries. Each vaccine or medicine takes years to develop and billions of dollars in investment,[18] with just one in 5,000 drug candidates making it all the way from drug discovery to market.[19] The development of a malaria vaccine is proving to be more than a 30-year quest.[20]

Over the last 50 years, biotherapeutics (therapies derived from living organisms) have become an integral part of modern medicine. Insulin was one of the first medicines produced using biotechnological methods, and biotechnology is now used for diseases including cancer, rheumatoid arthritis, heart disease and multiple sclerosis. The

> *Intellectual property exists to encourage innovation and creativity, which stimulate improvements in our quality of life, spur economic growth and address the radical challenges we confront such as climate change, clean energy, food security and health.*
>
> **Francis Gurry,**
> Director, World Intellectual Property Organization[25]

introduction of recombinant human erythropoietin into clinical practice in the 1980s was a major breakthrough in the treatment of the anemia of patients with chronic kidney disease.[21] Understanding of biologics is crucial to the emerging practice of gene therapy, whereby disease is treated or prevented through the addition or modification of DNA. Decades in the making - first tested on humans in 1990, and informed by the completion of the Human Genome Project in 1993 - gene therapy enables a deeper, personalized and more precise approach to health. For example, gene therapy is used to treat particular types of cancers by targeting specific cell mutations as well as curing sickle cell disease by modifying stem cells.[22]

Intellectual property (IP) protection, typically granted in the form of patents and data exclusivity, incentivizes investments to make advances and enables companies to re-invest in their R&D capability. IP is a critical element of the innovation ecosystem, alongside a science-based regulatory system and appropriate rewards and incentives. IP can also help to create certainty in the overall business climate to usher in future overall investments (including beyond the R&D-based biopharmaceutical industry). This competitive research model has delivered many successes in previous decades,[23] with industry and partners continuing to learn how to operate more effectively and collaborate.[24] IP has also contributed to the creation of the generics manufacturing industry, enabling the R&D-based companies to focus on just that, R&D. IP has given the industry the necessary confidence to invest in markets, accelerate the adoption of technology, and increase patient access to a wider choice of medicines.

PARTNER AND ENGAGE

In 1968, actors of a given health system operated in siloes. Since then, new approaches and more creative partnerships have emerged – whether delivering healthcare more efficiently, effectively conducting research, or strengthening the capacity of healthcare systems.[26]

In recognition of the complementarity of their research objectives and interests – and to an extent the limits to public funding for research – there has been an upsurge in academic-industrial collaboration.[27] Combined, their unique contributions lead to greater insights and innovation. Some partnerships rely on close collaboration, such as research to jointly explore the new frontier of immunotherapy or conducting advanced clinical trials requiring tight partnership between doctors, patients, and R&D-based pharmaceutical manufacturers.[28]

Other collaborations adopt more radical approaches to improve patient outcomes. For instance, 2000 saw the launch of Gavi, the vaccine alliance, a public–private partnership committed to increasing access to immunization in poor countries.[29] In 2002, The Global Fund was developed as a unique financing partnership between governments, civil society, companies and people affected by the diseases they seek to end: AIDS, TB and malaria.[30] The London Declaration on Neglected Tropical Diseases

> If countries invest in making progress towards universal health coverage, they lay the foundation for progress towards ending poverty, improving gender equality, decent work and economic growth, and more.
>
> **Tedros Adhanom Ghebreyesus,** Director General, WHO[35]

agreed in 2012, the largest mass drug administration in history, commits companies as well as WHO, foundations, and others to work cooperatively to maintain and expand drug donation programs to meet demand through 2020.[31] Access Accelerated, founded in 2017, brings together 23 biopharmaceutical companies, teaming up with the World Bank, Union of International Cancer Control (UICC), and Boston University to demonstrate that significant progress can be made in addressing the NCD epidemic through cooperative action.[32]

Partnerships are crucial to improving patient access through strengthening health systems: 90% of 'essential' medicines are generics, and yet not all reach patients.[33] Without access to prevention support and quality health services, global health progress will be uneven. Achieving universal health coverage (UHC) means ensuring all people receive essential health care without risking financial hardship.

Achieving UHC is one of the targets under the Sustainable Development Goals (SDGs). Partnerships contribute to this by training healthcare workers, building infrastructure such as testing facilities, and delivering education to schools and community organizations to promote prevention. For instance, UHC2030 brings together diverse stakeholders to advocate for political commitment, strengthen dialogue and facilitate knowledge sharing in order to strengthen health systems.[34]

These close partnerships could hardly have been imagined in previous decades.

Faces of progress...

Progress is often depicted in terms of blockbuster headlines and global statistics. But it is important to recognize the people behind the headlines: patients, researchers, doctors, health workers who have contributed to progress, often overcoming huge odds to do so. Consider the tenacity of researchers such as Dr Joe Cohen, who worked as part of a team for almost three decades to develop the first malaria vaccine,[36] and Maysoun Shomali, who has dedicated 20 years of her career to developing therapies for breast cancers resistant to other treatments.[37]

50 YEARS OF GLOBAL HEALTH PROGRESS

TRANSFORM AND INNOVATE

PARTNER AND ENGAGE

1968: Studies of cancer in nonhuman primates provided compelling new evidence that the Epstein-Barr virus, discovered four years earlier, can lead to cancer in humans.[38]

1971: Measles, mumps and rubella (MMR) vaccine approved, providing protection against three highly infectious illnesses at the same time, via one shot.[39]

1974: Expanded Programme on Immunization (EPI) established to develop and expand immunization programs, initially targeting diphtheria, whooping cough, tetanus, measles, poliomyelitis, and tuberculosis, towards the goal of providing universal immunization for all children by 1990.[40]

1977: The first angiotensin-converting-enzyme (ACE) inhibitor developed for the treatment of hypertension, is discovered.[41]

1978: First synthetic 'human' insulin produced, the first human protein to be manufactured through biotechnology, enabling patients to avoid the allergic reactions that insulin from cattle and pigs could cause.[42]

1980: Worldwide vaccination programs result in the eradication of smallpox, a contagious virus with no known cure which killed an estimated 300-500 million people in the 20th century.[43]

1981: First IFPMA Code of Practice developed as the foundation for industry's global self-regulation, setting ethical and professional standards.[44]

1985: First manufactured insulin pen launched, offering greater ease of use and accuracy for patients versus the vial-and-syringe method of insulin delivery.[45]

1987: The first antiretroviral (ARV) drug is approved by the US FDA as treatment for HIV, beginning a new era of highly active ARV treatment.[46]

1987: Ivermectin developed for parasitic infections in animals and it is later found an effective treatment for river blindness and lymphatic filariasis in humans, two debilitating diseases which affect the world's poorest populations.[47]

1987: First statin approved, a key step in reducing cardiovascular disease.[48]

1988: WHO publishes Ethical Criteria for Medicinal Drug Promotion, the first frame of reference for judging proper behavior in drug promotion.[49]

1988: Establishment of the Global Polio Eradication Initiative, which has contributed to the 99.9% reduction in global incidence of polio.[50]

1989: Biotechnology scientists identify the previously unidentified virus Hepatitis C, which is now known to affect about 2% of the world's population.[51]

1996: A new class of combined antiretroviral treatment, HAART, is developed, leading to a 50% drop in the number of AIDS-related deaths in the U.S. and Europe in three years.[52]

2000: Adoption of the Millennium Development Goals (MDGs), a blueprint for meeting the needs of the world's poorest with a focus on child mortality, maternal health, HIV/AIDS, malaria, and other diseases.[53]

2000: Launch of Gavi, the Vaccine Alliance, a public–private global health partnership committed to increasing access to immunization in poor countries.[54]

2006: Human papilloma virus (HPV) vaccine approved, which protects from cervical cancer, a common cancer among women under 35.[55]

2011: Approval of direct-acting antivirals (DAAs), called protease inhibitors, which, combined with interferon and ribavirin, improve cure rates among patients with the most common hepatitis C genotype to 70%.[56]

2012: Signing of the London Declaration on Neglected Tropical Diseases: 14 billion treatments pledged and commitment to control, eliminate or eradicate 10 debilitating NTDs responsible for more than 90% of the global neglected diseases burden by 2020.[57]

2012: First approval of a TB drug in 40 years, bedaquiline, unique in that it interferes with the enzyme required by bacteria to replicate.[58]

2014: Development of CAR-T cell therapies - programmed T cells aim to hunt, bind to, and eliminate cancer cells.[59]

2015: Sustainable Development Goals (SDGs) adopted by world leaders, setting out a global sustainable development agenda which emphasizes collaboration across countries, actors, and sectors for a wide array of development outcomes, health and wellbeing prime among them.[60]

2017: Launch of Access Accelerated with 23 global biopharmaceutical companies, the World Bank, the Union of International Cancer Control (UICC), and Boston University to combat NCDs globally.[61]

2018: RTS,S malaria vaccine introduced in pilot immunization programs in three African countries – Kenya, Malawi, and Ghana.[62]

BUILDING ON SUCCESSES AND SETBACKS

Progress is rarely a steady, straight line. Innovation tends to be messy, unpredictable, and risky.

For instance, ivermectin was originally developed as a veterinary drug and was subsequently found to be ideal for combatting two of the world's most devastating NTDs, river blindness and lymphatic filariasis in humans. The pneumococcal disease conjugate vaccine from 1977 that protects against pneumonia was found to be unsuccessful in children. Decades of development finally brought the breakthrough PCV7 vaccine licensed in 2000.

Demographic shifts are altering disease burden and complicating progress: movement of people from rural to urban areas and the growth of the middle class is associated with reductions in infectious diseases, maternal and child illness, and malnutrition while more young and middle-aged adults are suffering and dying from NCDs.[63]

Persistence and perseverance across the ecosystem have underpinned progress. The industry, like all actors in global health, has needed to play the long game, and breakthroughs have resulted from the work of many. For example, tackling the global HIV/AIDS epidemic has relied on resolution to innovate and iteratively improve antiretroviral treatments, as well as diligent research towards a vaccine.

Mistakes have been made. The industry has learned from these in order to move forward. This includes the thalidomide tragedy in the 1960s, which resulted in more structured drug regulations and the development of applications of the drug for treatment of leprosy and certain cancers.[64]

The arc of progress since 1968 is evident when considering patient safety and medicine quality – for instance, the raising of standards through post-marketing safety surveillance (pharmacovigilance). The number of national pharmacovigilance centers has increased from just 10 in 1968 to 67 by 2002,[65] and legislation has been passed in many geographies to ensure safe monitoring of medicines.[66] Approaches to pharmacovigilance have evolved from reacting to negative drug responses to proactively addressing product safety throughout the clinical development process, before and after approval. Recent product recalls emphasize the need for regulators and companies to continue pharmacovigilance efforts through the generation and capture of quality data, improved tools for analysis, and consistent communication of benefits and risks.[67]

Advancing patient safety relies on combatting substandard and falsified products, which damage patients and entire health systems.[68] Vulnerable communities are most affected, with one in 10 medical products circulating in LMICs being substandard or falsified.[69] Industry, multilaterals, and governments work to combat substandard and falsified products through regulation and governance, building tools and technical capacity to enforce quality standards in the manufacturing supply chain. For example, R&D-based pharmaceutical manufacturers are teaming up with organizations offering mobile-based medicine verification schemes for consumers.[70]

Patient safety and medicine quality must keep up with the evolution and globalization of pharmaceutical supply chains, whereby products are manufactured, packaged, and assembled in different countries, online pharmacies are growing rapidly, and new business models have increasing operational complexity.

LOOKING AHEAD:

IN PURSUIT OF CONTINUED, ACCELERATED PROGRESS

IN TACKLING THE HEALTH CARE CHALLENGES OF THE DEVELOPING WORLD, WE NEED TO LEAVE OUR OWN 'COMFORT ZONE' AND COLLABORATE WITH OTHERS, BE IT IN ENGAGING ON HEALTH SYSTEMS REFORM OR IN PARTNERSHIPS TO BRING MEDICINES TO PEOPLE IN RESOURCE-CONSTRAINED SETTINGS.”

Thomas Cueni,
Director General, IFPMA[73]

This 50 year milestone is as much an opportunity to look ahead as it is to reflect back on progress. Whatever the future may bring – as we live longer lives, as technology advances, and the world changes in ways we can only partially understand (see ‘Present to Future’ section) – the world depends on improved global health to continue to promote prosperity and enable human progress.

The SDGs, launched in 2015, give greater visibility of the role of the private sector in a shared societal agenda and emphasize the importance of collaboration across countries, actors, and sectors for a wider array of development outcomes - health and wellbeing prime among them. Meeting the highly ambitious 17 goals and 169 targets by 2030 will require further scientific breakthroughs and strategic innovations.[71]

Health underpins the common view of the future we want, as articulated in the SDG agenda for 2030, not only SDG 3 for good health and wellbeing. The R&D-based biopharmaceutical industry is no stranger to multi-stakeholder partnership and looks forward to continuing to deliver positive outcomes in collaboration.[72]

1 NO POVERTY — PRIORITIZING THE **HEALTH NEEDS** OF THE POOR

2 ZERO HUNGER — ADDRESSING THE CAUSES AND CONSEQUENCES OF ALL FORMS OF **MALNUTRITION**

3 GOOD HEALTH AND WELL-BEING — ENSURE **HEALTHY LIVES** AND PROMOTE **WELL-BEING** FOR ALL AT ALL AGES

4 QUALITY EDUCATION — SUPPORTING HIGH-QUALITY EDUCATION FOR ALL TO IMPROVE **HEALTH AND EQUALITY**

5 GENDER EQUALITY — FIGHTING GENDER INEQUITIES, INCLUDING **VIOLENCE AGAINST WOMEN**

6 CLEAN WATER AND SANITATION — **PREVENTING DISEASE** THROUGH SAFE WATER AND SANITATION FOR ALL

7 AFFORDABLE AND CLEAN ENERGY — PROMOTING SUSTAINABLE ENERGY FOR **HEALTHY HOMES** AND LIVES

8 DECENT WORK AND ECONOMIC GROWTH — PROMOTING **HEALTH EMPLOYMENT** AS A DRIVER OF INCLUSIVE ECONOMIC GROWTH

9 INDUSTRY, INNOVATION AND INFRASTRUCTURE — PROMOTING NATIONAL R&D CAPACITY AND MANUFACTURING OF AFFORDABLE ESSENTIAL **MEDICAL PRODUCTS**

10 REDUCED INEQUALITIES — ENSURING EQUITABLE **ACCESS TO HEALTH SERVICES** THROUGH UNIVERSAL HEALTH COVERAGE BASED ON STRONGER PRIMARY CARE

11 SUSTAINABLE CITIES AND COMMUNITIES — FOSTERING **HEALTHIER CITIES** THROUGH URBAN PLANNING FOR CLEANER AIR AND SAFER AND MORE ACTIVE LIVING

12 RESPONSIBLE CONSUMPTION AND PRODUCTION — PROMOTING **RESPONSIBLE CONSUMPTION OF MEDICINES** TO COMBAT ANTIBIOTIC RESISTANCE

13 CLIMATE ACTION — **PROTECTING HEALTH** FROM CLIMATE RISKS, AND PROMOTING HEALTH THROUGH LOW-CARBON DEVELOPMENT

14 LIFE BELOW WATER — SUPPORTING THE RESTORATION OF FISH STOCKS TO IMPROVE SAFE AND DIVERSIFIED **HEALTHY DIETS**

15 LIFE ON LAND — PROMOTING HEALTH AND PREVENTING DISEASE THROUGH **HEALTHY NATURAL ENVIRONMENTS**

16 PEACE, JUSTICE AND STRONG INSTITUTIONS — EMPOWERING STRONG LOCAL INSTITUTIONS TO DEVELOP, IMPLEMENT, MONITOR AND ACCOUNT FOR AMBITIONS NATIONAL **SDG RESPONSES**

17 PARTNERSHIPS FOR THE GOALS — MOBILIZING PARTNERS TO MONITOR AND ATTAIN THE **HEALTH-RELATED SDGS**

Based on WHO's 'Health in the SDG era' graphic

UNIVERSAL HEALTH COVERAGE: THE FOUNDATION FOR PROGRESS

In the 21st century people's expectations everywhere for their health are increasingly equal, and as such, UHC is an investment that allows each citizen access to good quality services without financial compromise.”

Tim Evans,
World Bank Group

At the core of SDG 3 is the powerful concept of universal health coverage (UHC): that patients, wherever they live, should be able to receive the quality health services they need without suffering financial hardship.

Following a coordinated effort by the global health community in 2016, there is now a global agreement on how progress towards UHC will be measured. The success of any health initiative depends on achieving UHC.

Likewise, there is increasing recognition that strong, sound, financially sustainable health systems generate a healthier and more productive society. One that can access education and gain skills, enabling their participation in a dynamic global economy. Health, in this sense, brings wealth.

UHC is also an opportunity for the R&D-based biopharmaceutical industry to redouble its strong commitment to invest in it. Such investment can be multifaceted:

- By discovering new medicines and vaccines to prevent and treat diseases;
- By fostering innovation across the continuum of medical education, prevention, treatment and care, including expanding patient access to quality medicines and vaccines through innovative solutions;
- By sharing its expertise and experience in technology solutions, training of health care workers, human resources management, logistics and supply chain management, health literacy, media and communications; and
- By participating in multi-sectoral partnerships that encompass actors working on the environment, transportation, information and communications, and education to support countries to strengthen health systems, create innovative finance models and build the bodies of evidence that will be crucial to implementing UHC.

Thanks to global efforts and a collective push, major progress on health service coverage can be seen, especially in Africa.

Developing more public-private collaborations will enable healthcare companies to deliver products and services more efficiently, and can accelerate progress towards reaching UHC.

STORIES OF PROGRESS:

VACCINES

Saving, protecting and enhancing lives

TRANSFORMING LIVES

Present Day...

SARA RECEIVES VACCINATIONS

As a young child, Sara receives routine vaccinations: polio, meningitis, rotavirus, hepatitis A, hepatitis B, pneumonia, TDAP (typhoid, diphtheria and pertussis), MMR (measles, mumps and rubella), BCG, yellow fever, and Hib. She receives the HPV vaccine when she is 11.

Fifty years ago...

In 1968, Sara would have received far fewer vaccines: smallpox, polio, measles, mumps and DTP (for diphtheria, tetanus and pertussis).

In the future...

Sara hopes her children and grandchildren will benefit from hoped-for vaccines to protect them from malaria and HIV/AIDS.

In 1796, Edward Jenner carried out what would become one of the most famous medical experiments when he vaccinated James Phipps against smallpox. Today, vaccines are viewed as one of the most effective and cost efficient medical technologies ever developed,[74] resulting in the control, elimination or near elimination of numerous infectious diseases.

Immunization saves between two and three million children's lives per year.[75] The continuing development of vaccine science and growing partnerships for delivery have enabled the benefits of immunization to be realized across the globe, dramatically decreasing the spread of infectious disease and supporting efforts to achieve global health security. However, one in five children still miss out on routine life-saving immunization.[76]

50 YEARS OF VACCINES

"The eradication of smallpox uniquely combined product innovation, process innovation and policy innovation – with an unprecedented level of stakeholder collaboration."

Mariângela Simão,
WHO

Research and development is, and always has been, at the heart of immunization success. Germ theory – the identification of organisms that cause disease - has been central to vaccine advances in the second half of the 20th century,[77] with the development of the first vaccines for smallpox, diphtheria, tetanus, anthrax, cholera, plague, typhoid, TB, and polio.

As vaccine science continued to develop during the 20th century, improvements in cell culture technologies welcomed in a second golden age of vaccines. Scientific innovations at this time led to the creation of vaccines for measles, mumps, rubella, hepatitis A and B, chicken pox, pneumonia, and influenza. Notable is the work of Maurice Hilleman, who developed over 40 vaccines and eight of the 14 routinely recommended today.[78] Hilleman is credited with saving more lives than any other medical scientist in the 20th century across his career.

Innovation also led to improved vaccine delivery technologies which have helped reduce the global infectious disease burden. For example, advances in vaccine thermostability has reduced the need for refrigeration and increased access to vaccines globally.[79] Development of delivery techniques such as microneedles and intradermal devices has enhanced vaccine effectiveness and make it easier for health workers to administer immunizations. Combination vaccines have been developed to reduce the number of shots a child needs while maintaining the same level of protection, such as the MMR combination vaccine licensed in 1971.[80]

In the 50 years since IFPMA was founded, smallpox has been eradicated and polio nearly so across most of the world. Great strides have been made in reducing measles infections. To date, vaccines have been developed to prevent 26 diseases, including more recently developed vaccines for hepatitis B, hepatitis A, HPV and meningococcal group B.[81] IFPMA members have been at the forefront of science to achieve these developments.

KEY MILESTONES

1971: Measles, Mumps and Rubella vaccine approved, providing protection against three highly infectious illnesses at the same time, via one shot.[82]

1974: The Expanded Programme on Immunization is established to develop and expand immunization programs, initially targeting diphtheria, whooping cough, tetanus, measles, poliomyelitis, and TB, towards the goal of providing universal immunization for all children by 1990.[83]

1980: Worldwide vaccination programs result in the eradication of smallpox, a contagious virus with no known cure, which killed an estimated 300-500 million people in the 20th century.[84]

1986: Hepatitis B recombinant vaccine is licensed.[85]

1988: Establishment of the Global Polio Eradication Initiative, which has contributed to the 99.9% reduction in global incidence of polio.[86]

1995: Hepatitis A vaccine is licensed.[87]

2000: Launch of Gavi, the Vaccine Alliance, a public–private global health partnership committed to increasing access to immunization in poor countries.[88]

2000: Pneumococcal conjugate vaccine PCV7 is licensed, tackling one of the biggest killers of children under five – pneumonia. This breakthrough vaccine improves earlier versions that did not generate consistent immunity in children.[89]

2006: HPV vaccine approved in the US, providing protection from cervical cancer, a common cancer among women under 35.[90]

2006: Approval of vaccine for rotavirus, the most common cause of diarrheal disease among infants and young children.[91]

2012: Global Vaccine Action Plan adopted by World Health Assembly as a roadmap to prevent millions of deaths by 2020 through equitable access to vaccines.[92]

2015: First dengue vaccine licenses obtained.[93]

2015: RTS,S vaccine became the first vaccine candidate to get approved for use against malaria.[94]

2016: Americas region is the first region in the world to be declared measles-free.[95]

2017: The Coalition for Epidemic Preparedness Innovations launched to finance and coordinate the development of new vaccines to prevent and contain infectious disease epidemics and contribute to global health security.[96]

ACHIEVING ERADICATION OF POLIO

The development of polio vaccines and the effort put into eradicating the disease shows how innovations and partnerships can come together to eliminate a disease across much of the world.

Polio is caused by a virus that reproduces in the gut from where it can spread to the nervous system. In the pre-vaccine era, when poliovirus was the leading cause of permanent disability in children, almost all children became infected by poliovirus, with one in 200 susceptible individuals developing the paralyzing poliomyelitis.[97]

With effective vaccines available, health policymakers began to look at eradicating polio.[98] In 1974, the World Health Assembly recommended the oral polio vaccine (OPV) as the vaccine of choice.[99] In 1985, Rotary International launched their PolioPlus program financially supporting the public health ambition to rid the world of polio.[100] In 1988 the 41st World Health Assembly adopted a resolution for the worldwide eradication of polio.[101] The Global Polio Eradication Initiative (GPEI) brought national governments, WHO, Rotary International, the US Centers for Disease Control and Prevention, UNICEF and a number of key partners such as the Bill & Melinda Gates Foundation (BMGF) together.[102] Industry contribution, led by Sanofi Pasteur providing almost 10 billion doses of OPV worldwide, including more than six billion doses to UNICEF, has proven to be instrumental in taking polio to the brink of eradication. Since GPEI was launched, the number of polio cases has fallen by over 99.9%.[103] In 1994, the Americas were certified polio-free, followed by the WHO Western Pacific Region in 2000, the WHO European Region in 2002, and the WHO South-East Asia region in 2014.[104] Poliovirus transmission levels are currently at the lowest point in history and eradication is a realistic expectation.[105]

The infrastructure introduced to enable mass immunization has broader impacts in strengthening delivery of health services. For example, in Nigeria medicines for malaria are being delivered on a mass scale as part of the infrastructure for delivering the polio vaccine.[106] Evolving and strengthening this infrastructure can support access to a wider range of medicines and vaccinations.

A SHIFT TO LIFE COURSE VACCINATION - HUMAN PAPILLOMA VIRUS VACCINE

A more recent example of vaccine development is the development of the first ever vaccine targeting cancer. The WHO defines the preventative, life-course approach as one that aims at increasing effectiveness of interventions throughout a person's life. It addresses the causes and not the consequences of ill health at all stages of life.

As NCDs such as cancer, diabetes and Alzheimer's disease become epidemic in the ageing populations of both the developed and developing world, research is looking at vaccines, which have previously been mainly seen as a solution to infectious diseases for children. This perception can be damaging: In the US, more adults die of vaccine preventable illnesses than children. Innovation in the industry is shifting to life-course vaccines to target people's needs throughout their life as and when they need them. A life-course approach to immunization can help reduce disease burden, relieve pressure on caregivers and allow older populations to not only benefit from the preventative power of vaccines, but remain active members of the community.

The HPV vaccine provides the first great example of a shift in research and development towards life-course vaccines. In 1976, Harald zur Hausen made the connection between cervical cancers and infection with HPV (work for which he shared a Nobel Prize in Medicine in 2008).[107] It is estimated that cervical cancer affects more than 500,000 women each year, 80% of whom live in the developing world.[108] Screening programs have been effective in early stage diagnosis to catch and treat cervical cancer, but they have been less widely implemented in LMICs than in developed economies. The HPV vaccine is ideally given to boys and girls at a young age to prevent cancer. In 2006, a quadrivalent (four-strain) vaccine was licensed followed by a bivalent (two-strain) vaccine for girls in 2007 and in 2014 a nine-strain HPV vaccine was approved. The impact of immunization on cervical and other HPV-related cancers will be evident in the next decades – but a marked decrease in HPV infections, precancerous lesions and genital warts is already dramatic in the vaccinated populations.[109]

IMMUNIZATION FOR ALL

Today, vaccines are a key part of the ambition for UHC and the UN SDGs to help end poverty, protect the planet, and ensure prosperity for all. Vaccines offer the opportunity of truly global and equitable healthcare.

The resurgence of measles in some parts of the world today serves as a reminder of the potential impacts of infectious diseases, which are easily preventable with vaccines.[110]

Immunization not only saves lives and improves health, it also unlocks the potential of the community. A vaccinated community is healthier, stronger, and more productive. Vaccination reduces the global burden of infectious disease; not only by protecting vaccinated individuals, but by indirectly protecting unvaccinated individuals through community protection or 'herd protection'.[111]

However, without successful immunization programs and collaborations, the benefits of vaccine innovation will not be fully realized. The new programmatic approach to developing the recent dengue and malaria vaccines shows that, more than ever before, industry needs to work hand-in-hand with governments, civil society, and global health policymakers to enable the benefits of vaccination to extend to all. Several landmark initiatives demonstrate the potential for such collaboration and impact, including:

- The Expanded Programme on Immunization initiated by the WHO in 1974 with the goal of making vaccines available to all children.[112]
- The founding of Gavi in 2000 by the BMGF, the World Bank, WHO, UNICEF and vaccine manufacturers including Sanofi Pasteur, Pfizer, MSD, GSK, Novartis and Janssen.[113]
- The creation of the Developing Countries Vaccine Manufacturers Network in 2000 with the aim of protecting all people against infectious diseases by increasing the quality and affordability of vaccines for all.[114]
- The Global Vaccine Action Plan's Decade of Vaccines, 2011-2020, endorsed by 194 member states with the aim of delivering universal access to immunization regardless of where children were born, who they are or where they live.[115]
- The Humanitarian Mechanism, launched in 2017 by WHO, UNICEF, Médecins Sans Frontières and Save the Children, to enhance access to vaccinations for traditionally 'left behind' populations such as refugees and displaced people.[116]

FUTURE INNOVATION

> *Investment in vaccines is critical to address AMR. Vaccines can prevent illness and death and eliminate the need for the use of antimicrobials in the first place.*
>
> **David Heymann,**
> London School of Hygiene and Tropical Medicine

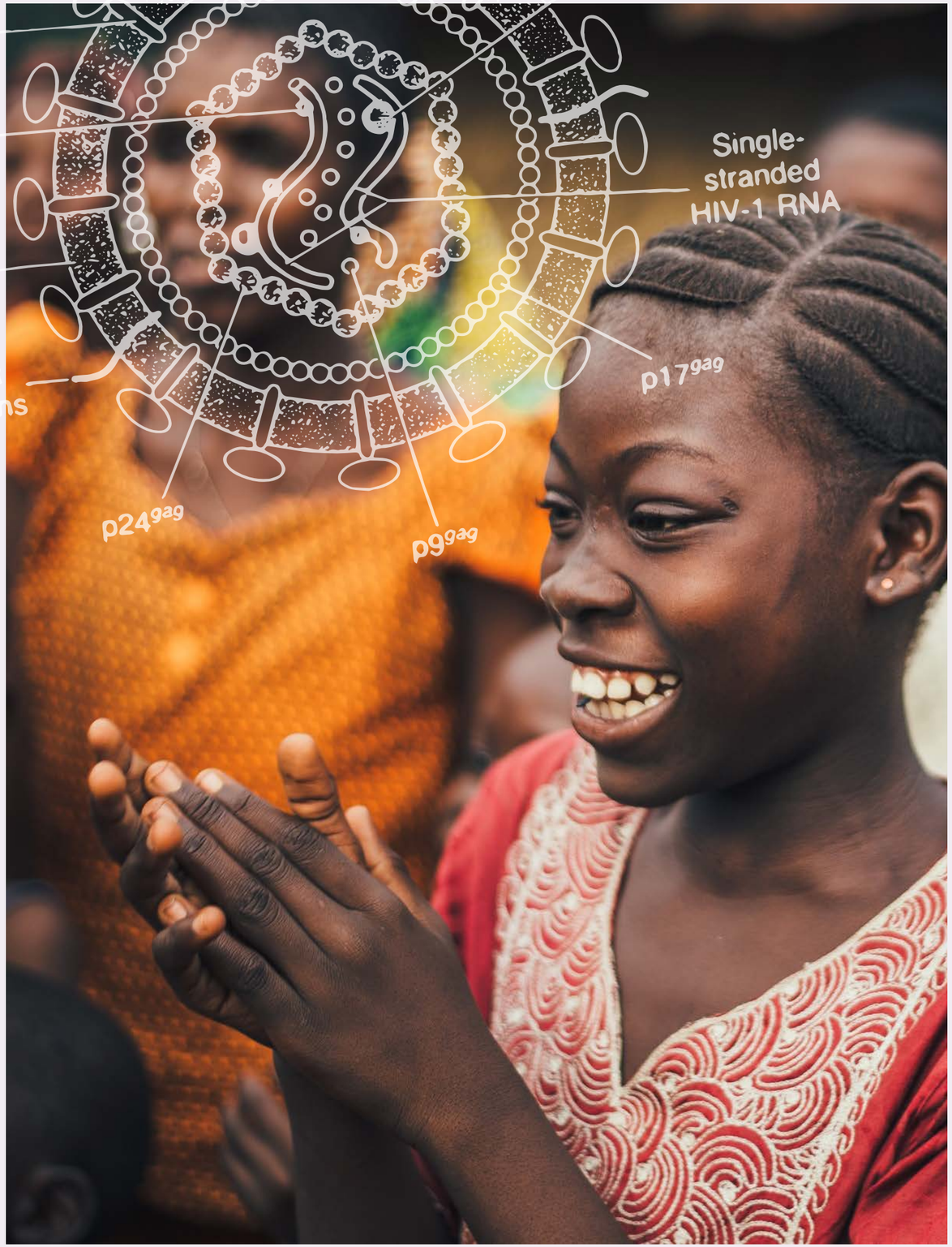
Industry is committed to driving vaccine innovation to help achieve global health security, prevent unnecessary disease and to address challenges presented by ageing populations. Together, vaccine development and immunization programs can strive to eliminate, contain, and prevent infectious diseases and NCDs.

The next phase of innovation will be driven by a greater understanding of pathogens and immune responses as well as data and technology-led developments in research.

Smarter technologies will also play a big role in the development of vaccines in the future. For example, vaccines that utilize messenger RNA (mRNA) are developing quickly. They work by providing instructions to our cells to make whatever we need to prevent disease, including antibodies. mRNA vaccines offer prompt and flexible design, cost-optimized production, and safer administration.[117] Other projects are underway to bring vaccine adjuvants – which can improve vaccine efficacy by aiding its effect on the immune system – to market.[118] Today there are 264 vaccines in the pipeline in the US alone, including a mix of life-course and infectious disease vaccines.[119]

Vaccines can also play a vital role in the fight against AMR, reducing infections and limiting their transition, enabling less reliance on antibiotics as well as reducing the inappropriate use of antibiotics for viral infections.

Vaccines remain the safest, most effective, and cost-effective medical technology ever developed. They are deployed globally to all, regardless of gender or location. Global vaccination programs have introduced key infrastructure to improve broader access to medicines in the developing world. Vaccines also offer alternative solutions to life-course diseases and an ageing population.



STORIES OF PROGRESS:

HIV/AIDS

Overcoming one of the worst human pandemics

TRANSFORMING LIVES

Present Day...

ZAIN'S HIV/AIDS STORY

Zain was diagnosed, is able to manage his illness and can expect a near normal lifespan, thanks to starting combined antiretroviral (ARV) treatment early in the course of the infection. He now takes a one-a-day pill.

Thirty years ago...

In 1988, Zain would have had a life expectancy of just one year from diagnosis and would not have had access to combined ARV treatment.

In the future...

Zain hopes a vaccine will prevent people like him being infected with HIV and halt the spread of AIDS.

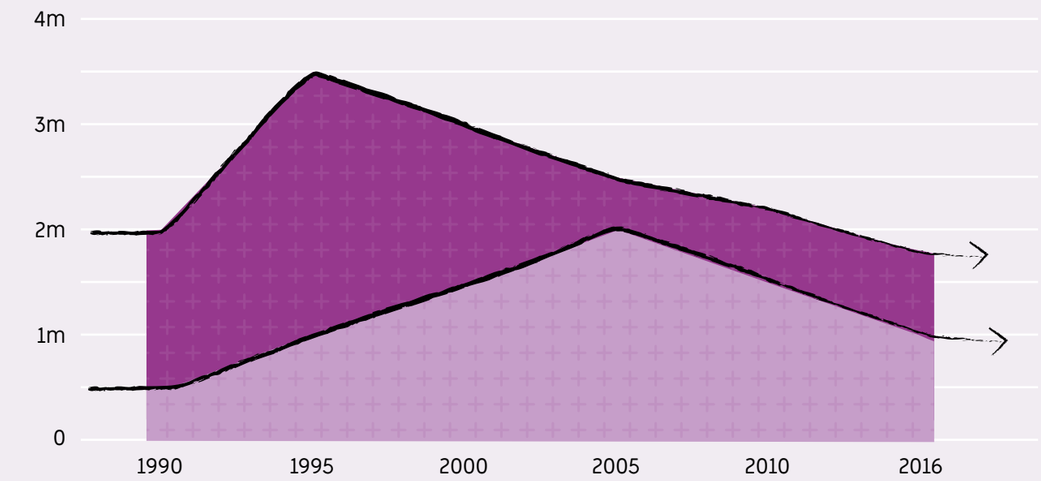
It has been 36 years since the world was first introduced to the term AIDS. With the first reported cases of HIV/AIDS (human Immunodeficiency virus / acquired immune deficiency syndrome) in the 1980s, the world faced a new and unknown virus.

The epidemic was defined by fear and death as HIV infection rates and AIDS-related deaths grew throughout the 1980s and 1990s.[120] As the global response ramped up, thanks to scientific advances and programs targeting those in need, 2005 marked a turning point as the number of AIDS related deaths peaked.[121] Although patients in developed countries have access to treatment and can expect near-normal lifespans, HIV/AIDS remains a particularly heavy burden in sub-Saharan Africa, where it is the leading cause of death for adults.[122]

Breakthrough innovations, notably antiretroviral (ARV) therapy, have had significant impact on confronting the epidemic and enabling those infected with HIV to live long and healthy lives. Equally important have been partnerships to deliver access to treatment, care, and education to those most affected around the world.

Patients diagnosed with AIDS in 1990 could expect to live only months, during which time they would be likely to contract a number of other infections. Today, an HIV infected patient who receives ARV therapy may expect to live a normal lifespan.[123] In fact, the HIV/AIDS death rate has dropped by 85% since 1991.[124]

The global response delivering improved patient outcomes for those with HIV/AIDS has also strengthened healthcare systems and access more broadly, with knock-on effects of improving gender equality.



AIDS RELATED DEATHS PER YEAR

NEW HIV INFECTIONS PER YEAR[125]

KEY MILESTONES

The HIV/AIDS epidemic is defined by scientific breakthroughs as well as transformative partnerships and initiatives that controlled the epidemic through generations:

1982: The term AIDS is first used; tracking of disease begins in US.[126]

1984: The retrovirus that causes AIDS is identified.[127]

1987: The first antiretroviral (ARV) drug, azidothymidine, is approved by the FDA as treatment for HIV.[128]

1996: 1996: Combined multi-drug ARV treatment is introduced, changing the course of the HIV epidemic.[129]

1996: The Joint UN Programme on HIV and AIDS (UNAIDS) is established, serving as the main advocate for accelerated global action on the epidemic.[130]

2001: UN Declaration of Commitment on HIV/AIDS calls for the respect of human rights of people living with HIV.[131]

2002: The Global Fund to fight AIDS, Tuberculosis and Malaria (The Global Fund) is set up, a public-private partnership to attract resources to fund prevention and treatment in resources limited settings.[132]

2002: FDA approval of the first rapid home-use HIV testing kit providing results in twenty minutes.[133]

2003: Launch of The President's Emergency Plan for AIDS Relief, a US government initiative to address the global HIV/AIDS epidemic.[134]

2003: Approval of new anti-HIV drug, enfuvirtide or T-20, the first in a new class of drugs designed to prevent entry of the virus into human cells.[135]

2006: The first one-a-day pill to treat HIV is approved in the US.[136]

2010: Medicines Patent Pool is founded, the first voluntary licensing and patent pooling mechanism in public health, aiming to improve access to affordable and appropriate HIV, hepatitis C and TB medicines.[137]

2012: The first medication to protect those who do not have HIV from infection, called pre-exposure prophylaxis, is approved.[138]

2015: UNAIDS announces that the MDG target of 15 million people on life-saving HIV treatment by 2015 has been met 9 months ahead of schedule.[139]

2015: Launch of the SDGs, which include a target to end the AIDS epidemic by 2030.[140]

R&D AND INNOVATION: FROM DEATH SENTENCE TO LIFETIME TREATMENT FOR PATIENTS

THE HIV/AIDS CRISIS TRIGGERED A LEVEL OF GLOBAL SOLIDARITY THAT HAD NOT BEEN SEEN BEFORE. WE MUST GARNER THE SAME SUPPORT FOR NON-COMMUNICABLE DISEASES.”

Mariângela Simão,
WHO

Advances in R&D have transformed HIV from an untreatable and almost uniformly fatal virus into a manageable, chronic condition. These innovations have extended the lives of millions of people living with HIV. In the 30-plus years since the discovery of the HIV virus, more than 30 medicines have been approved to treat the HIV infection. Over time, medicines have improved in tolerability, efficacy, and convenience for patients.

A major breakthrough was the development of ARV therapy, which works by preventing HIV from multiplying, reducing the viral load in the body and allowing the immune system to keep it in check. The first generation of these therapies was developed in the mid 1980s by Burroughs-Wellcome (now GSK) in collaboration with the National Cancer Institute.[141] Azidothymidine was the first ARV drug to be approved by the US FDA as treatment for HIV.[142]

Since then, research has improved both understanding of the disease and its evolution, simplifying the medication mechanism for patients.[143]

As understanding of the disease and the effects of ARV on patients grew, a ‘combination therapy’ approach emerged as far more effective than any single drug treatment. So-called ‘cocktail’ approaches work by combining drugs in different sequences. The adoption of HAART (highly active antiretroviral therapy) in 1996 inaugurated a new era in HIV treatment.[144] The combination approach was quickly incorporated into clinical practice and has since become the default therapeutic approach.

Preventing transmission from mother to child also has huge implications for halting the spread of HIV/AIDS and is another key focus area for R&D. Increased understanding of ARV therapies allowed the use of treatment on pregnant mothers. Through increased understanding of ARV therapies it was found that HIV positive mothers adhering to ARV for several weeks or months before birth could eliminate the risk of transmission to the baby through pregnancy, birth, and breastfeeding.[145]

A key challenge has been enhancing access to, and funding for treatment in resource-scarce communities, including many of the geographies worst affected by the virus. The development of less costly care regimens has allowed the extension of effective treatment. For example, NNRTIs (non-nucleoside reverse transcriptase inhibitors) now provide a lower cost option for LMICs and facilitated treatment expansion efforts.[146]

Newer classes of drugs include integrase inhibitors, today a recommended first-line treatment in many cases, which work by preventing the virus from incorporating its DNA into the host genome.[147]

PARTNERSHIPS ADDRESS THE FULL LIFECYCLE OF HIV/AIDS, DELIVERING CARE TO THOSE WHO NEED IT MOST

RESEARCH COLLABORATION

Partnerships have played a crucial role in supporting R&D advances for the treatment of HIV/AIDS, bringing together academia, governments, and industry. The National Cooperative Drug Discovery Group Programme for the Treatment of AIDS (NCDDG-AIDS) is a collaboration platform established early in the epidemic. The AIDS Clinical Trial Group (ACTG) supports clinical trials and laboratory studies in order to set standards of care for HIV infection.[148]

TREATMENT FOR VULNERABLE GROUPS

A key challenge has been the development of pediatric ARV formulations. Initiatives like the Pediatric HIV treatment Initiative (PHTI), The Global Accelerator for Pediatric formulations (GAP-f) and the Collaborative Initiative for Pediatric HIV Education and Research (Cipher) aim to close the treatment gap between adults and children.

In 2011, the Global Plan to eliminate new HIV infections among children by 2015 was launched by organizations convened by the President’s Emergency Plan for AIDS Relief and The Joint UN Programme on HIV and AIDS (UNAIDS).[149] As part of this, companies pledged funding for programs to ensure access to treatment for pregnant women and maternal and family planning health services. Pledges included Johnson & Johnson at USD 15 million,[150] and more recently AstraZeneca with USD 10 million over five years to cover HIV/AIDS.[151] The number of children acquiring HIV infection declined from 360,000 in 2009[152] to 160,000 in 2016.[153]

Mother to child transmission is preventable and has been virtually eliminated in the developed world.[154] Saving Mothers Giving Life[155] - a public-private partnership between USAID, MSD, and others - makes strategic investments to reduce deaths of mothers with HIV. The International Partnerships for Microbicides, a partnership between civil society, research-based pharmaceutical manufacturers, and research centers develops HIV prevention products and other sexual and reproductive health technologies for women with a focus on microbicides.[156] Other public-private partnerships include between ViiV Healthcare and the Pediatric European Network for the Treatment of AIDS, which develops treatment strategies for children living with HIV including project EPIICAL, a predictive in vitro platform to treat HIV-infected children, as well as those to support research and build research and healthcare capacity in pediatrics HIV with the Clinton Health Access Initiative, Amfar TREAT Asia and the International AIDS Society.[157]

People practicing intravenous drug use (IDU) remain disproportionately affected by HIV, accounting for one in 10 new HIV infections worldwide.[158] Harm reduction strategies target IDU by focusing on explicit and peer-based education about the risk of HIV from sharing injecting equipment, needle syringe programs, drug treatment (especially opiate substitution treatment), and community development.

PARTNERING FOR DELIVERY

Diagnosis is as important to effective HIV/AIDS treatment as medicines. Currently, only 60% of people with HIV know their status.[159] AmpliCare, a public-private partnership

between Roche, the Clinton Foundation, USAID, and UNICEF aims to address barriers that prevent early diagnosis of infants with a focus on sub-Saharan Africa.[160] Roche has redesigned its tests, developed a novel methodology for gathering and transporting blood samples, as well as introducing SMS technology for test results. This has resulted in expanded access to diagnosis in the remotest areas, where over six million infants have been tested for HIV.

Despite the breakthroughs in treatment, by 2000, less than one million of the 34 million people living with HIV/AIDS[161] were accessing ARV therapy.[162] In particular, many in developing countries were left behind as treatments were not accessible.

In 2000, UNAIDS, WHO, Boehringer Ingelheim, BMS, Roche, GSK and MSD announced a plan to improve access to treatment – the Accelerating Access Initiative (AAI). The program, which concluded in 2012, applied preferential pricing to ARVs, opening the door to a new future of access to ARV medicines in developing countries and laying the foundation for future access to medicine initiatives.[163]

Many companies have made commitments reflecting the need for affordable treatment options for the most affected countries. One mechanism to improve access to ARVs is voluntary licensing agreements whereby the patent holder grants a voluntary license over product patents in certain countries to generic manufacturers, which enables them to develop, manufacture and sell generic versions of the licensed product(s) in resource-limited settings. GSK gave the first voluntary license in 2001 for Retrovir, Epivir and Combivir in South Africa. Within a year there was a significant increase in supply and reductions in ARV prices in the developing world. The scope and approach to voluntary licensing agreements has continued to evolve – both directly between patent-holding companies and generic manufacturers, and through the UN-backed Medicines Patent Pool – and remains a key approach in improving access to ARVs. ViiV Healthcare's voluntary licensing approach, for example, enables accelerated access to the innovative new HIV treatment, dolutegravir, across all LMICs, least developed and Sub-Saharan African countries.[1]

Access to treatment grew in the 2000s. By 2006, 28% of those in need in sub-Saharan Africa received treatment, compared to just 2% in 2003;[164] 2007 saw a 54% increase in the number of people in LMICs receiving ARV therapy.[165] There is a need for continued progress in access for LMICs, alongside interventions in prevention, diagnosis and broader health system strengthening.

STRENGTHENING HEALTH SYSTEMS

Caring for those living with HIV/AIDS extends beyond provision of treatment. Since 1999, the 'Secure the Future' initiative run by the Bristol Myers Squibb Foundation has supported those living with HIV/AIDS in sub-Saharan Africa, with particular focus on women and children and the links between cervical cancer and HIV.[166] The Foundation has invested USD 181 million to date, partnering with governments and NGOs to build comprehensive care models through investments at a community level to support outreach, home based care, and psycho-social support.

UNAIDS highlights the connection between HIV/AIDS responses and human rights.[167] Education plays a crucial role in the fight against HIV and AIDS and stigma against those living with it. It also promotes awareness of how to protect from AIDS, encourages people to get tested and reduces discrimination against HIV-positive people. GSK and ViiV Healthcare's Positive Action programs tackle societal barriers to addressing the global HIV epidemic such as stigma and discrimination, gaps in education and sexual health services. The programs support community-based organizations and NGOs to focus on populations worst affected by HIV such as women and girls, adolescents, men who have sex with men, transgender people, incarcerated individuals, sex-workers, and intravenous drug users.[168]

Botswana is an example where public-private partnerships have improved health system capacity for treatment and prevention in a country with one of the highest adult prevalence rates in the world. In 2000, MSD joined with BMGF and the government of Botswana to form the African Comprehensive HIV/AIDS Partnerships (ACHAP). ACHAP developed a comprehensive approach to increase prevention and treatment of HIV/AIDS and care for those infected in support of the government of Botswana's response to the epidemic. The MSD Foundation and BMGF committed to support ACHAP with USD 106.5 million. In addition, MSD donated its antiretroviral medicines to Botswana's national ARV treatment program for the duration of the partnership. Botswana was among the first countries in sub-Saharan Africa to reach universal access to treatment for HIV.[1]

Building on this progress, in 2016, ViiV announced an agreement to supply its latest HIV medicine to support the government of Botswana's national Treat All program, which aims to ensure people living with HIV in the country get tested and receive treatment.

2030: THE END OF THE AIDS EPIDEMIC?

Ending the AIDS epidemic by 2030, as set out in SDG target 3.3, will only be achieved with innovation and multi-sector partnerships.[169]

Despite the array of effective HIV prevention tools such as male and female condoms, pre-exposure prophylaxis, voluntary male circumcision, and behavior change interventions (e.g. the use of clean needles), 1.8 million people became newly infected with HIV in 2016.[170]

UNAIDS outlines the priority challenges for the next decade in their ambitious 90-90-90 targets for 2020:[171]

90%
of all people living with HIV know their HIV status

90%
of all people diagnosed with HIV infection receive sustained ARV therapy

90%
of all people receiving ARV therapy will have viral suppression

To get there, many look to industry and partners for additional pre-exposure options, a cure or vaccine, and support closing the gap in treatment.

THE SEARCH FOR A CURE

While current treatments enable patients to live longer lives, the search for a cure continues. Researchers have successfully lowered levels of the virus to undetectable levels in certain children for a period of time,[172] though there has not yet been a confirmed case of an infant totally cured. AIDS researchers continue to improve our understanding of how interventions can best impact infant immune system responses to HIV. Many R&D eradication efforts focus on 'flushing' the HIV virus out of latently infected cells, which are often seen as the major barrier to cure. This so called 'shock and kill' technique works by 'waking up' inactive cells, forcing them to produce new virus particles that are susceptible to current antiretroviral drugs. Several techniques for this are in development with research ongoing into cytokine therapy, valproic acid, and histone deacetylase inhibitors.[173]

VACCINE DEVELOPMENT

The development of a vaccine holds promise but has proven elusive due to the genetic diversity of the virus and its ability to rapidly mutate.[174] The International AIDS Vaccine Initiative brings together public and private actors to research, design and develop vaccine candidates.[175] Researchers are optimistic that a vaccine will be found in our lifetime. For example, Johnson & Johnson is working to develop a mosaic-based vaccine is yielding encouraging results from clinical studies and is progressing to the next phase of clinical development.[176]

CLOSING THE FUNDING GAP

Of the 37 million people globally living with HIV, 21 million have access to ARV therapy – and more year-on-year. Yet, millions still lack access to therapy, many in LMICs. It is estimated that just 12 million of the 25 million living with HIV/AIDS in Africa receive ARV therapy.[177] UNAIDS estimates the funding gap for HIV in LMICs over the 2015 to 2020 period stands at USD 26 billion, and it looks to public and private partners to ensure the gains in R&D innovation do not exclude those in need of existing or older treatments.[178] Individual R&D-based pharmaceutical manufacturers – through licensing, pricing initiatives and various partnerships – continue to seek to improve access for LMICs, alongside critically needed interventions in prevention, diagnosis and broader health system strengthening. Only a holistic approach will ensure critical treatments are available to all people in need.

STORIES OF PROGRESS:

NEGLECTED TROPICAL DISEASES, MALARIA AND TUBERCULOSIS

Thinking beyond traditional models

TRANSFORMING LIVES

Present Day...

NISHA'S EXPERIENCE WITH LYMPHATIC FILARIASIS, A NEGLECTED TROPICAL DISEASE

Nisha receives treatment for the disease through donations received as part of the London Declaration.

Twenty years ago...

In 1998, Nisha might not have had access to treatment and would have lived with this debilitating disease all of her life.

In the future...

Nisha hopes that partnerships will continue to provide access to treatment for everyone suffering from lymphatic filariasis (LF), enabling it to be eradicated globally.

NTDs, malaria, and TB carry significant social and economic burdens, despite the fact that many of these diseases can be effectively controlled, and in many cases, eliminated. Because these diseases disproportionately affect vulnerable people, mainly in LMICs, they do not receive the same level of attention as other diseases.

These diseases worsen and reinforce poverty, persisting in populations with limited access to adequate sanitation or medical care and in close contact with infectious vectors and domestic animals and livestock.

Women, children, and HIV/AIDS sufferers are most likely to be infected by NTDs. Women are particularly likely to be affected due to gendered roles which expose them to transmission, such as caring for sick children, cleaning of materials likely to carry infection, or collecting water.[179] The majority of malaria deaths are in children under five and one million children catch TB each year. Sick children miss out on school, illness reduces families' earnings, and diseases are a huge burden on already fragile healthcare systems.

INNOVATIVE RESEARCH MODELS

A central challenge for this group of diseases is the lack of competitive markets for vaccines and medicines in the LMICs where the diseases are most prevalent. In spite of these challenges, R&D-based biopharmaceutical companies are working to accelerate the elimination or control of these diseases through the discovery of new treatments and interventions through innovative mechanisms, including product development partnerships (PDPs), IP sharing and open innovation, and programs to expand access in endemic countries.

Companies foster R&D by sharing IP assets, compound libraries, access to research facilities, hosting scientists and providing training. Additionally, the private sector has transferred technology and built technical expertise to develop, manufacture, register and distribute products. The Tres Cantos Open Lab Foundation allows independent researchers to access GSK facilities, resources, and expertise to advance research into TB, malaria and kinetoplastid infections.[180] Similarly, the Novartis Institute for Tropical Disease is a collaborative research centre, where academic institutions such as the University of Singapore and non-profits such as the TB Alliance work together with Novartis scientists to develop new therapies.[181] WIPO Re:Search is a global consortium of over 100 companies, academia, research centers, non-profits and government agencies that facilitates sharing of know-how, technologies, and bridge research gaps.[182] To date, 95 research collaborations have been established through WIPO Re:Search by BIO Ventures for Global Health.[183]

Innovative collaborations have tremendous potential to advance progress towards new drugs and diagnostics addressing neglected diseases. 90% of NTD related programs in which IFPMA members are active are collaborative efforts which involve over 50 organizations, including universities, NGOs, and public and private sector institutes.[184]

An innovative public-private partnership

The first of its kind in Japan, the Global Health Innovative Technology (GHIT) Fund, is a partnership between the BMGF, the Japanese government, pharmaceutical companies, the Wellcome Trust and UNDP.[185] The fund invests and manages a portfolio of development partnerships, mobilizing Japanese and international pharmaceutical companies and academic organizations to get new medicines, vaccines, and diagnostic tools to people afflicted by NTDs.

PARTNERING FOR DELIVERY

In many cases, methods to prevent, diagnose and treat these diseases are known. Much harder, yet equally essential to eradication, is ensuring access to interventions. This is where innovative partnerships are important.

Many R&D-based pharmaceutical companies have committed to drug donations until diseases are eliminated. The progress realized through these global donation efforts demonstrates the power of strategic collaboration in reducing the impact of NTDs on health and society.

Partnerships and collaborative efforts such as The London Declaration on Neglected Tropical Diseases (The London Declaration), USAID Neglected Tropical Diseases Programme, Medicines for Malaria Venture (MMV) and the Stop TB Partnership bring together public, private, and civil society actors to improve access to treatments, capacity building and policy advocacy. These are essential to end these diseases.

The success of drug distribution campaigns relies on an integrated treatment approach. In the past, many countries conducted separate treatment campaigns for individual diseases. Now, many programs provide treatments for several diseases at the same time. For example, a national program can treat all children in a region for intestinal worms, onchocerciasis and LF in a single school visit. These large-scale campaigns also offer an opportunity to reach people with other health interventions and can support country progress towards stronger health systems and UHC.[186]

NEGLECTED TROPICAL DISEASES

KEY MILESTONES

1971: Benznidazole introduced for the treatment of Chagas disease.[187]

1975: Development of albendazole for treatment of parasitic worm infections including cysticercosis.[188]

1986: Approval of clofazimine to treat leprosy, a key constituent of multidrug therapy (MDT) alongside rifampicin and dapsone.[189]

1987: Development of ivermectin (also known as Mectizan®) for parasitic infections in animals and finds it can be used to treat river blindness in humans and LF. Established the Mectizan® Donation Programme to provide ivermectin to all who needed it, for as long as needed.[190]

1998: Azithromycin begins to be prevalently used as a first-line response for eliminating blinding trachoma.[191]

2003: The term 'neglected tropical diseases' is coined by Peter Hotez and colleagues to counterbalance the attention given to HIV/AIDS, TB and malaria.[192]

2007: First Global Partners' Meeting on NTDs held at WHO headquarters in Geneva, bringing together over 200 public and private institutions dedicated to contributing their time, efforts, and resources to control neglected tropical diseases.[193]

2009–13: USAID launches Neglected Tropical Diseases Initiative committing USD 350 million to deliver integrated NTD treatment to 300 million people in Africa, Asia, and Latin America.[194]

2012: WHO NTD Roadmap sets targets and milestones to control, prevent, eliminate, and eradicate NTDs.[195]

2012: The London Declaration on Neglected Tropical Diseases (The London Declaration): 14 billion treatments pledged and commitment to control, eliminate or eradicate 10 debilitating NTDs responsible for more than 90% of the burden by 2020.[196]

2013: Development of high-quality diethylcarbamazine citrate tablets for treatment of LF, with a formulation suitable for worldwide distribution.[197]

2015: The number of people requiring treatment and care for neglected tropical diseases falls 21% since 2010, to 1.6 billion people.[198]

2016: Approval of new child-friendly chewable tablet formulation for children infected by intestinal worms (soil-transmitted helminthiasis).[199]

2017: Clinical trial results show efficacy and safety of fexinidazole, the first oral monotherapy for Human African Trypanosomiasis, which could avoid the need for lumbar puncture and for systematic hospitalization of patients.[200]

2017: NTD Summit (Geneva): half-way to The London Declaration, which has been awarded the title of 'biggest donation' ever by Guinness World Records.[201]

UPDATED 2017

WHO LIST OF
NEGLECTED TROPICAL DISEASES

HELMINTH

Dracunculiasis (guinea-worm disease)
Echinococcosis
Foodborne trematodiases
Lymphatic filariasis
Onchocerciasis (river blindness)
Schistosomiasis
Soil-transmitted helminthiases
Taeniasis/Cysticercosis

BACTERIA

Buruli Ulcer
Leprosy (Hansen's disease)
Trachoma
Yaws (Endemic treponematoses)

VIRUSES

Dengue and Chikungunya
Rabies

PROTOZA

Chagas Disease
Human African trypanosomiasis (sleeping sickness)
Leishmaniasis

ADDED IN 2017

Mycetoma, chromoblastomycosis and other deep mycoses
Scabies and other ectoparasites
Snakebite envenoming

> *"The breakthrough global collaborative effort to control river blindness responded to the links between disease and rural development and for the first time recognized health as an investment with a positive return."*
>
> **Tim Evans,**
> World Bank Group

One in seven people suffer from an NTD,[202] with the vast majority of cases in LMICs where parasites, bacteria and viruses thrive in subtropical climates. NTDs are painful and can blind, disfigure, and cause severe and permanent disabilities. Disfiguring NTDs such as Buruli ulcer, yaws, and leprosy are frequently associated with stigma, increasing the burden of disease.

Progress has been made in eradicating NTDs with the elimination of some diseases in certain geographies. A notable milestone was the discovery that ivermectin for parasitic infections could be used to treat river blindness and lymphatic filariasis (LF) in humans. There was no market as those infected were too poor to pay, so MSD made an open-ended commitment to give away as much of the drug as necessary until river blindness is eliminated.[203] Similar commitments followed. In 2017 the Japanese pharmaceutical company Eisai renewed its pledge to donate diethylcarbamazine until the global elimination of LF is achieved.[204] GSK has donated eight billion tablets of albendazole to date to prevent LF and control intestinal worms and has also pledged to donate albendazole to every country that needs it until LF is eliminated. Lymphatic filariasis transmission has now been eliminated in 11 countries including China, Costa Rica, Egypt, South Korea, Sri Lanka, and Thailand.[205]

The Drugs for Neglected Diseases Initiative (DNDi) works in partnership with industry, research institutions and the public sector on the most neglected diseases. This includes Human African Trypanosomiasis (HAT), leishmaniosis and Chagas disease, which fall outside the scope of market-driven R&D.[206] USAID Neglected Tropical Diseases Programme delivers integrated NTD treatment to 300 million people in Africa, Asia and Latin America and reached two billion treatments by 2016.[207]

In addition to the donations by MSD, GSK and Eisai, a number of other programs focus on the elimination of particular NTDs:

- **Bayer** works with WHO to tackle Chagas disease and African Sleeping Sickness, both of which are completely curable in the early stages with drugs.[208]
- **Pfizer** partners with the International Trachoma Initiative - an independent NGO dedicated to eliminating trachoma - to donate antibiotics and work with agencies to implement the WHO recommended SAFE (Surgery, Antibiotics, Facial Cleanliness, and Environmental improvements) strategy for trachoma control.[209]
- **Merck KGaA** works to fight schistosomiasis in Africa through its 'One Merck for Schistosomiasis' program, which includes the development of a pediatric formulation of praziquantel via a consortium of partners to treat children younger than 6 years old and the development of innovative schistosomiasis diagnostics in association with the current efforts of the BMGF.[210]
- **Johnson & Johnson** co-founded Children Without Worms to tackle soil-transmitted helminthiases through interventions including mass drug treatment and preventative chemotherapy.[211]
- **Sanofi** has initiated partnerships to address HAT including with the WHO to donate existing drugs and with DNDi to develop a new oral treatment.
- **Novartis**, through partnering with WHO, has committed to deliver Multi Drug Therapy for leprosy to 1.3 million people by 2020.[212]

More and more countries are eliminating these diseases. River blindness and Chagas disease have been eliminated from several countries in the Americas.[213] Morocco, Cambodia and the Lao People's Democratic Republic have eliminated trachoma as a public health problem.[214] In 2015, India was the first country to be declared yaws-free.[215]

Progress has been enabled by the large-scale donation of medicines. In 2015, nearly a billion people received donated treatments for at least one NTD.[216] The London Declaration is a flagship partnership for driving control or elimination of NTDs. The industry is delivering on its promise of 14 billion donated treatments (USD 7 billion worth of medicine) over 10 years. Millions of health workers and community volunteers have been trained, strengthening health systems in the poorest communities to ensure appropriate treatment and care. The London Declaration has been awarded the title of 'biggest donation' ever by Guinness World Records (April 2017). By 2020, nearly USD 18 billion worth of medicines will have been distributed, the largest medicine donation the world has ever seen.

Preventative chemotherapy is one of the interventions deployed by the WHO, involving administering six medicines in seven different combinations, to combat at least five NTDs. Since the integrated approach began in 2008, 14 previously endemic countries have been declared free of at least one NTD that is receptive to preventive chemotherapy.[217]

MALARIA

KEY MILESTONES

1972: Chinese scientist Tu Youyou discovers artemisinin, a cornerstone of malaria treatment.

1979: Clinical trials of artemisinin published.[218]

1985: First large-scale trials of insecticide treated nets.[219]

1992: The RTS,S malaria vaccine enters clinical trials.[220]

1998: Launch of the Roll Back Malaria Partnership.[221]

1999: The Medicines for Malaria Venture launched to develop antimalarials for the most vulnerable populations.[222]

2000: The UN General Assembly adopts the MDGs, setting a target to halt and begin reversing malaria incidence by 2015.[223]

2001: The first artemisinin-based combination therapy (ACT) is brought to the global market.[224]

2002: Launch of The Global Fund, the world's largest financier of anti-AIDS, TB, and malaria programs.[225]

2008: Launch of Global Malaria Action Plan, the first comprehensive blueprint for global malaria control and elimination.[226]

2009: Launch of the first high-quality ACT formulated especially for children.[227]

2015: The RTS,S vaccine is the first malaria vaccine candidate to receive positive scientific opinion from the European Medicines Agency (EMA).[228]

2015: WHO reports that since 2010, 60 countries have reported mosquito resistance to at least one insecticide class and of these, 50 reported resistance to two or more insecticide classes.[229]

2017: Regulatory application submitted for tafenoquine, the first new medicine for the radical cure (prevention of relapse) of *P vivax* malaria in patients aged 16 and older in more than 60 years.[230]

2018: RTS,S vaccine introduced in pilot immunization programs in three African countries – Kenya, Malawi, and Ghana.[231]

HISTORY HAS SHOWN THAT WITH MALARIA THERE IS NO STANDING STILL—WE MOVE FORWARD OR RISK RESURGENCE.

Bill Gates,
Bill and Melinda Gates Foundation[241]

Malaria is caused by parasites transmitted from the bites of infected mosquitoes. Malaria costs the African economy more than USD 12 billion every year.[232] In countries with high malaria rates, economic growth is slowed by 1.3%.[233] Malaria control is increasingly recognized as an important tool for poverty reduction - households in Africa lose up to 25% of their income to the disease.

Between 2000 and 2015, the rate of new cases of malaria fell by 37% globally.[234] Since 2000, eight countries have eliminated malaria and many others have reduced transmission to low levels.[235] However, malaria remains one of the world's biggest killers.

Treatments have helped reduce malaria deaths. The current WHO-recommended first-line treatment for malaria, artemisinin, was discovered in in 1972 by Tu Youyou, a Chinese scientist who was awarded a Nobel Prize in 2015 for her discovery. Artemisinin is particularly effective when combined with other medicines in artemisinin-based combination therapy (ACT), which the standard treatment for malaria today. Novartis started producing it in the late 1990s and began marketing it in the 2000s. Alongside the discovery of novel treatments, continuous investment in R&D is needed for new pediatric formulations given that children and pregnant women are most at risk of contracting malaria. In 2009, Novartis, in partnership with The Medicines for Malaria Venture (MMV), launched the first dispersible ACT formulated for babies and children.[236] New drugs to treat and prevent malaria in children are in development by the likes of Merck KGaA, who leverage the screening of compound libraries to identify new candidates.[237]

MMV is one of the most well-known PDPs, launched in 1999 to develop antimalarials for vulnerable populations. In 2008, MMV in partnership with Sanofi and DNDi, launched the first anti-malarial drug resulting from a public-private partnership: a fixed-dose combination of artesunate and amodiaquine which enables better adherence to treatment and reduces the risk of resistance by avoiding selective use of a specific component.[238] MMV also works with GSK to develop tafenoquine to cure relapsing P. vivax malaria, submitted for regulatory approval in both the US and Australia in 2017. If approved, tafenoquine would be the first new medicine for the prevention of relapse of *P vivax* malaria in more than 60 years.[239]

Control of malaria will be significantly aided by the development of a vaccine. After more than 30 years of research, GSK, along with partners Programme for Appropriate Technology in Health, Malaria Vaccine Initiative and the BMGF, is close to bringing a vaccine to endemic countries. RTS,S is the first, and to date, only vaccine to show partial protection against malaria among young children. The vaccine is being made available from 2018 through routine immunization programs to young children in Ghana, Kenya and Malawi.[240]

The industry recognizes that the elimination of malaria requires action in a number of different areas, not just treatments and vaccines but increasing access to antimalarials, equipping hospitals, supporting improved sanitation, training of health workers, and the strengthening of health systems. Ensuring access to vector control tools such as bed nets is fundamental to reducing cases of malaria. RBM is a global platform for coordinated action, with 500 members including the private sector, NGOs, community organizations, foundations, and research institutions. So far 70 campaigns distributed free treated bed-nets to all households in areas with malaria since 2000.

The disease does not stand still. Antimalarial resistance is a real and growing threat to hard won progress. For the first time in 10 years, global malaria cases are no longer falling, driven in part by drug resistance.[242] New funding mechanisms and tools such as advanced mosquito surveillance using genetic sequencing will be needed to ensure the world does not see a resurgence of the disease.

TUBERCULOSIS

KEY MILESTONES

1970: First outbreak of drug-resistant TB in the US.

1993: WHO declares TB 'a global emergency' with deaths from TB higher than any previous year.

2002: Launch of Global Fund to fight HIV/AIDS, TB, and Malaria.

2005: The number of deaths annually from TB peaks worldwide at 2 million.

2010: Launch of the Gene Xpert molecular test for TB,[243] a rapid test which is endorsed by WHO and hailed as a major breakthrough.

2012: The first approval of a TB drug in 40 years, bedaquiline, unique in that it interferes with the enzyme required by bacteria to replicate.[244]

2014: Approval of delamanid, for active multidrug resistant TB, which is added to the WHO's essential medicines list.[245]

2015: WHO launches the 'End TB' strategy with the goal of ending the TB epidemic by 2035.[246]

2018: (March) Delhi TB Summit; (September) First ever UN High-level meeting on TB in New York City.

Although TB has long been preventable and curable. it is the ninth leading cause of death worldwide and the biggest infectious killer, above HIV.[247] In 2015, 10.4 million cases (one million children) and 1.8 million deaths (170,000 children, not including those with HIV) occurred from TB.[248] LICs and LMICs see 95% of TB deaths.[249]

An estimated 53 million lives have been saved through TB diagnosis and treatment between 2000 and 2016.[250] Drugs included in first-line TB treatments were developed more than 30 years ago. Current treatments for multi-drug TB require patients to take multiple antibiotics for nine to 24 months or longer, are complicated to administer, and have significant adverse effects. Many patients stop their drugs before the bacteria have been destroyed, which can further encourage drug resistance. Shortening treatment regimens is a priority.

The inadequacy of current diagnosis has challenged efforts to contain the spread of TB and forms a core component of the WHO's End TB strategy. Janssen, a company of Johnson & Johnson, has partnered with the non-profit FIND to increase access to molecular diagnostics tools for TB case detection and multi-drug resistant TB (MDR-TB) diagnosis.[251]

Drug resistance is another growing threat. Each year, there are roughly half a million new cases of MDR-TB, many of them transmissible. Breakthroughs by Johnson & Johnson and Otsuka have recently emerged: two new medicines (bedaquiline and delamanid) have been approved for the treatment of MDR-TB under programmatic conditions in numerous countries, with both added to the WHO's Essential Medicines List. A priority is getting these new treatments to patients by broadening sustainable and responsible access.

PRE-COMPETITIVE COLLABORATION

The **TB Drug Accelerator** is an effective example of pre-competitive collaboration and resource sharing, through which the expertise of partner organizations is leveraged to speed the development of medicines. The TB Drug Accelerator, launched in August 2012, is a BMGF sponsored discovery consortium of nine pharmaceutical companies (GSK, AbbVie, AstraZeneca, Bayer, Eisai, Eli Lilly, MSD, Sanofi, and J&J) and major academic organizations to speed up discovery and development of novel compounds against TB. Through early-stage TB research collaboration, it aims to develop five new pre-clinical drug candidates with treatment-shortening potential within five years, and proof-of-concept for a one-month three-drug regimen within 10 years. Members have opened up access to TB compound libraries to enable collaborative screening and data sharing. The TB Drug Accelerator aligns asset progression across portfolios so that members work to accelerate the most deserving discovery programs, regardless of where the drug originated, to avoid duplication. Coordinating previously siloed research teams and sharing knowledge of fundamental biology, screening capability and drug discovery resources has led to faster development timelines.

Other resource sharing programs include Eli Lilly's technology transfer program, which began in 2003 to provide R&D-based pharmaceutical manufacturers in MDR-TB 'hot spots' (China, India, Russia and South Africa) with trademarks, technology and know-how.[252] The BIO Ventures for Global Health partnership hub which brokered discussions between the Centre for World Health & Medicine (CHWM) and GSK, both work on methionine aminopeptidases (MetAP) as a drug target for TB. GSK tests identifying inhibitors of MetAP had disappointed and CWHM consequently placed its MetAP inhibitor on hold to avoid repeating experiments, saving money and time.[253] The PreDICT-TB Consortium, a public-private consortium, is working to overcome the barrier of inaccurate prediction of clinical effectiveness by currently available laboratory methods in order to speed up the identification of the most effective combination of new drugs.

THE PATH TO ERADICATION

"There a number of new medicines and diagnostics in the pipeline, which may change the perspective for these neglected tropical diseases and hopefully allow us to go further towards eliminating or near eliminating these diseases by 2030."

Dirk Engels,
Director of Neglected Tropical Diseases, WHO[258]

Despite progress, much remains to be done to meet SDG target 3.3 to end epidemics of TB, malaria and NTDs by 2030. The challenge consists of two missions: delivering health services for prevention and those living with diseases and eliminating transmission by addressing resistance and vaccine development.

Neglected diseases thrive in areas that lack adequate sanitation. About 2.4 billion people do not have access to adequate washing facilities. Hygiene can reduce transmission of the bacterial infection that causes trachoma. Breeding sites for mosquitoes are reduced through improved water management, limiting transmission of mosquito borne diseases. Protecting freshwater resources can prevent transmission of schistosomiasis. Improving access to water, sanitation, and hygiene (WASH) will be crucial to combat NTDs, as set out in the WHO's strategy in 2015.[254]

Climate change, growing megacities, and conflict present a challenge to meeting control and elimination targets. Overcrowding and poor hygiene and sanitation facilitate the spread of diseases. It is expected that climate change will increase the malaria burden in several regions of the world, particularly densely populated tropical highlands. An increase in NTD cases (including dengue fever and Chagas disease) in southern Europe is likely due to changing climate. Given the projected growth in the size of the world's population by 2030, more people will be living in areas at risk of neglected diseases, putting further strain on overstretched health systems and program budgets. War and refugee zones can increase exposure and susceptibility to infection. New approaches must deliver interventions in less time, provide flexible funding, and empower communities to administer care when external support is unavailable.

These diseases are not restricted to LMICs; many are found among the poor living in G20 nations. Estimates suggest that 12 million people in the US live with at least one poverty-related neglected or emerging disease.[255] NTDs can only be eradicated if all in wealthier nations receive the treatment and care they need.

Comorbidity also remains a challenge. HIV patients are at greater risk of TB and malaria. The risk of death in co-infected individuals is twice that of HIV infected individuals without TB.[256] There is a need to find new and improved treatments and interventions to tackle this joint disease burden.

Tackling sub-standard drugs and vaccines development remain critical to addressing drug resistance, given that antimalarials and antibiotics are the most commonly reported sub-standard or falsified products.[257] These medicines are at best ineffective, and at worst, can result in death. They also contribute to AMR and drug-resistant infections and reduce patient confidence. Drug resistance presents a major challenge to eradicating TB and malaria. The need for ongoing innovation and a robust pipeline for treatment will become more urgent as strains become resistant to traditional treatments.

STORIES OF PROGRESS:

CANCER

Persisting in research and innovation to deliver better patient outcomes

TRANSFORMING LIVES

Present Day...

JANE'S BREAST CANCER JOURNEY

Jane discovers a lump in her breast and is diagnosed with breast cancer. The tumor is removed, followed by a course of chemotherapy, after which she undergoes hormone therapy to reduce the risk of it returning.

Fifty years ago...

In 1968, Jane would have undergone a radical mastectomy, surgically removing the entire breast and much of the underlying musculature, and her cancer would still have a high likelihood of returning.

In the future...

Jane hopes that targeted therapies will be developed that can defeat all hard-to-treat and metastatic cancers. Immuno-oncology therapies offer hope that people's own immune systems can destroy all types of cancer cells, preserving healthy cells.

Cancer is not a single disease but a group of over 100 diseases,[259] each one incredibly complicated. Treatment is a complex process with many stages, varying in each patient and from one type of cancer to another. This complexity calls for many more specializations within diagnostics, surgery, radiotherapy and beyond than other disease areas. Early detection is often the difference between life and death.

In the past 50 years understanding of cancer has advanced considerably, and treatments are far more effective, and less punishing. From 1991 to 2015, nearly 2.4 million cancer deaths were averted in the US alone,[260] primarily as a result of new and innovative therapies. Some cancers that were once terminal in every case are now generally treatable. In 1968, a child with acute lymphoblastic leukemia (ALL) had a diagnosis that was almost uniformly fatal. Today's best treatments provide cure rates approaching 90% for ALL.

These gains have been hard won. Fifty years ago, doctors had few tools to treat cancer, success was limited and interventions often difficult for patients to endure. The development of successful treatments for cancer has followed our understanding of the biology of the disease, attained through incremental advances and occasional moments of great insight.

The fight, however, is far from over: cancer remains the second leading cause of death globally. There has been tremendous progress in some areas, but there is also huge disparity in results depending on the type of cancer, and by geography. Approximately 70% of deaths from cancer occur in LMICs,[261] where many of the improved outcomes seen in well-resourced settings have not carried over. With around one-third of deaths from cancer due to the five leading behavioral and dietary risks,[262] cancer prevention remains one of the key priorities for public health.

KEY MILESTONES

1968: Studies of cancer in nonhuman primates provided compelling new evidence that the Epstein-Barr virus, discovered four years earlier, can lead to cancer in humans.[263]

1971: Discovery of tamoxifen for breast cancer.[264]

1971: The hypothesis that tumor growth is angiogenesis dependent (the physiological process through which new blood vessels form from pre-existing vessels) and that inhibition of angiogenesis could be therapeutic, is first proposed.

1975: Technique for producing monoclonal antibodies[265] is developed. MABs help the immune system to attack cancer. Many different MABs are available today to treat cancer, with more in clinical trials.

1981: Trials organized by Bernard Fisher, a Pennsylvania surgeon, show that removing just the tumor and not the whole breast works equally well for early breast cancer.[266]

1983: The first study demonstrates the function of a cancer-causing gene, the sis oncogene.[267]

1984: Harald zur Hausen[268] discovered HPV16 and HPV18 responsible for approximately 70% of cervical cancers.

1998: Trastuzumab, a monoclonal antibody drug aimed at hormone-sensitive breast cancer, is licensed.[269]

2003: Completion of the human genome project, turning point in cancer research.[270]

2006: HPV Vaccine licensed in the US.[271]

2011: The FDA approves the first medicine, ipilimumab, using a new treatment approach which harnesses the body's own immune system to fight cancer, called immunotherapy or immuno-oncology.[172]

2013: Research reveals 80 new genetic variations that increase the risk of breast, ovarian and prostate cancers.[173]

2014: Development of CAR-T cell therapies - programmed T cells aim to hunt, bind to, and eliminate cancer cells that have a specific antigen on their surface - such as CD19.[274]

2015: Approval of oncolytic viral therapy for the treatment of advanced melanoma, talimogen laherparepvec. The treatment is directly injected into melanoma tumors.[275]

2017: The FDA approves pembrolizumab, a checkpoint immunotherapy against all advanced solid tumor types regardless of the site of the tumor. Pembrolizumab blocks a protective mechanism of cancer cells and allows the immune system to destroy those cancer cells.[276]

EARLY TREATMENTS WERE INCREDIBLY HARSH, AND RARELY EFFECTIVE

The discovery that specific toxic chemicals administered in combination can treat certain cancers ranks as one of the greatest innovations in modern medicine. Childhood leukemia, testicular cancer, and Hodgkin's disease – previously fatal – are now generally curable through chemotherapy. Advances in surgical procedures and radiotherapy were also remarkable and often life-saving.

The approach of using chemotherapy to kill cancer cells – which unavoidably also kills non-cancerous cells – had severe side effects. Many patients did not survive this aggressive treatment, and some found that chemotherapy itself could cause cancer. This approach dominated the 1960s and 1970s.

By the 1970s, breast cancer was among the leading causes of death among American women.[277] The radical mastectomy – an extreme surgery removing the breast, lymph nodes and musculature – was pioneered at the turn of the 20th century.[278] This was based on the flawed understanding that cancer spread outwardly in a concentric fashion from a central point, making surgery a primary means of saving life.

In 1971, the US embarked on a 'war on cancer' beginning an era of huge investment in cancer research. Limited understanding of the disease meant that research was based on trial and error, and progress was slow. Scientists were deeply divided over competing theories. Treatments lacked an understanding of the underlying mechanism of cancer, and inflicted damage while saving some lives. Ultimately, patients demanded less punishing and more effective treatments.

ADVANCING OUR UNDERSTANDING OF THE DISEASE

The focus of research in the 1970s was on finding treatments without much more than a basic understanding of the disease.[279] There were three competing theories about what causes normal cells to turn cancerous: viruses, chemicals in the environmental, and our genes.[280] Each had evidence behind it, but without an understanding of carcinogenesis, researchers were divided.

As the field of microbiology advanced significantly, oncogenes and tumor suppressive genes were discovered in a major breakthrough: genes in our bodies that cause normal cellular growth, but if disrupted, can lead to cancer.[281] With a better grasp of the metastatic process, cancers such as breast cancer began to be understood as systemic, rather than local. Enough was known about cancer to move beyond trial and error, and a new era of targeted therapies could be envisioned.

And the need for more effective treatments was more urgent than ever. By 1986, there had been great strides in the understanding of the disease, but few new treatments.[282] The fact that people were simply living longer, combined with diet and lifestyle factors such as smoking, meant that mortality from cancer was growing. Governments and health institutions began to focus on prevention.

FROM A DEEPER UNDERSTANDING TO IMPROVED PATIENT OUTCOMES

By 1985, a clinical trial examining the effectiveness of the radical mastectomy found favor for the much less extreme lumpectomy.[283] With an understanding of the metastatic process, chemotherapy, and systemic drugs such as tamoxifen were found to be effective in combination with surgery. These advances, along with improved diagnosis and detection methods, greatly benefited patients, bringing the five-year survival rate in the US up from 75% in 1975 to over 90% today.[284]

Oncologists started to use their newly acquired understanding of oncogenes and of monoclonal antibodies to develop targeted treatments. Monoclonal antibodies are custom-designed antibodies that can target a given substance or cell type. They are a class of 'large molecule' drugs, much more complex than traditional small molecule drugs and can interact with more challenging targets. In the 1980s, scientists identified a potential antitumor target, CD20, for non-Hodgkin lymphoma. Monoclonal antibody rituximab was developed to specifically bind to CD20 and eliminate the cancerous cells. This led to the development of more than a dozen new monoclonal antibody cancer treatments, not least among them, trastuzumab, which blocks a particular oncogene and can affect the growth of breast cancer.[285] Trastuzumab, in combination with chemotherapy, increased breast cancer survival rates by 37% with virtually no additional side effects, a significant achievement in the history of cancer medicine.[286]

In 1973, geneticist Janet Rowley identified the specific genetic mutation in Chronic Myelogenous Leukemia (CML): effectively, the cells at the ends of two different chromosomes switched places.[287] In the 1990s, Ciba-Geigy invented a drug that seemed to wipe out CML cells.[288] In 1998 the results were out: imatinib was a huge breakthrough and would later help increase the five-year survival rate for people with CML from 31% in 1993 to 66% between 2006 and 2012.[289]

> *Understanding of the human genome has great potential to tailor-make medications and is enabling major steps forward in drug and vaccine development.*
>
> **David Heymann,**
> London School of Hygiene and Tropical Medicine

Another huge breakthrough was the discovery in 1984 by Harald zur Hausen that two strains of HPV were responsible for approximately 70% of cervical cancers, winning him the Nobel Prize.[290] This led to the development of the HPV vaccine, which has the potential to virtually wipe out cervical cancer through vaccination.

The discovery of oncogene-based treatments like trastuzumab and imatinib, along with the completion of the Human Genome Project in 2003, contributed to a growing optimism for a new era of targeted cancer treatments. But with the launch of the Cancer Genome Atlas in 2005, it became clear that the cancer genome is much more complex than originally thought.

As scientists and companies began to pursue drugs targeted at specific genes, the struggle was to find molecules that could target a single gene perfectly without causing toxicity to the patient. And there was a new problem: many of the new drugs that had been developed stopped working in patients after a matter of months. Researchers soon understood why: when cells become cancerous, they also become 100 times more likely to genetically mutate than regular cells.[291]

Through DNA and genome mapping, researchers are advancing our understanding of the specific mutations that are important to target. It is now understood that there are around 200 genes in breast and colorectal cancers alone that exist and operate under specific pathways, and that those pathways themselves can be disrupted.[292] With the cost of genetic sequencing plummeting, it may be possible to treat each cancer patient with a personalized combination of drugs.

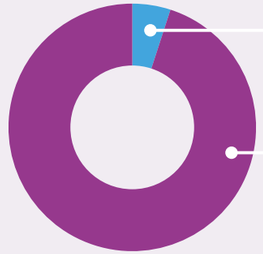
Despite these advances, the vast majority of cancers today are still primarily treated with chemotherapy. Survival rates, and rates of cure, are much improved, particularly for early stage breast, colon, and prostate cancer. Several approaches have been developed which improve the activity and reduce the side effects experienced by patients undergoing chemotherapy.[293]

ENHANCING ACCESS TO CANCER TREATMENT

IN MANY CASES, WHERE YOU WERE BORN AND WHO YOU WERE BORN TO STILL DECIDES WHETHER YOU WILL HAVE ACCESS TO CANCER TREATMENT OR NOT.

Mariângela Simão,
WHO

GLOBAL COST OF CANCER[294]



5% annual sales of cancer medicines by top 40 pharma companies 2010 (USD 55.3 bn)

95% annual economic cost of cancer 2010 (USD 1.16trn)

Cancer treatment is costly, which relates to the complexity of the disease: clinical research for new cancer medicines takes an average of 1.5 years longer than treatments for other disease areas.[295] But improving access to cancer treatment does not have to require significant increases in costs. Countries with similar levels of cancer spend currently have very different survival rates for the same types of cancer.[296]

Improving cancer treatment, and access to treatment, requires a holistic approach in which all key stakeholders are encouraged to work together and address cancer from prevention through to treatment and palliative care.[297] Better treatment and improved survival means people are able to return to work and play an active role in society and the economy. It also enables people beyond working age to live longer, more active and fulfilling lives.[298] A study in the UK showed that GBP 15 billion of public spending on cancer research since the 1970s had resulted in GBP 124 billion worth of health benefits to the public.[299]

The inequalities of access are felt most keenly in developing countries, where population ageing, unplanned urbanization, and the uptake of unhealthy lifestyles means that cancer and other NCDs are on the rise. A lack of capacity for prevention, public education, screening, and early detection, diagnosis, and treatment, means that the response to this public health issue is limited.[300]

In tackling health care challenges of the developing world, collaboration with others holds enormous promise. For example, Access Accelerated brings together 23 global R&D-based biopharmaceutical companies, teaming up with the World Bank, the UICC, and Boston University in an effort to demonstrate that significant progress can be made addressing NCDs through cooperative action.[301] In 2006, Sanofi set up the My Child Matters program to fight childhood cancer which, through 55 projects in 42 countries, has contributed to train 20,000 healthcare professionals and treat over 75,000 children.[302]

In a landmark for cancer on the global health agenda, the 2017 WHO Cancer Resolution reaffirms cancer control as a critical health and development priority.[303] This is an opportunity for national governments to use the momentum of the Resolution's adoption to drive action on cancer and seek new and effective partnerships.

GROWING OPTIMISM FOR A NEW ERA IN CANCER TREATMENTS

Today, a new era in medicine is revolutionizing how we diagnose, treat, and hopefully one day cure the many diseases that make up cancer. The biopharmaceutical pipeline has never been more promising with 79% of medicines in development for cancer having the potential to be first in class treatments, introducing entirely new ways to treat disease. More than 70% of cancer medicines in the pipeline also have the potential to be personalized medicines.[304]

Promising areas of cancer research

- **Poly ADP ribose polymerase (PARP) inhibitors**, initially approved for ovarian cancer, and more recently for breast cancer, are continuing to be explored in trials for other types cancer. PARP inhibitors interrupt cancer's hyperactive DNA repair systems, thus allowing tumors to be crippled and die.
- **Immuno-Oncology (IO)** seeks to reprogram the body's natural immune system to attack cancer. The first generation of IO drugs, called checkpoint inhibitors, are poised to become the standard of care across multiple tumor types in advanced disease, and are already being followed with other immune-activating agents.
- **Oncolytic viral therapies** zero in on cancer cells, replicate, and cause them to rupture. They have been recognized as a promising new treatment, with the potential to be a standard therapeutic option for all cancer patients.[305]
- The gene editing technology **CRISPR/Cas9** allows researchers to manipulate cancer cell function. The first clinical trial involving CRISPR, a family of DNA sequences in bacteria and archaea, started in 2016. Today there are over 20 human trials underway. One of these trials will feature the first-ever attempt to edit cells inside the body, with the aim of targeting and destroying the genes of HPV that cause tumor growth.[306]

The latest and most exciting development in our search for a cure for cancer is in the growing field of immunotherapy or immuno-oncology. These therapies enlist and strengthen the power of a patient's immune system to attack tumors.[307] The class of immunotherapies called PD-1 inhibitors have already achieved FDA approval in a range of other cancers, including certain types of melanoma, non-small cell lung cancer, renal cell carcinoma, bladder cancer, head and neck cancer, liver cancer and classic Hodgkin's lymphoma.[308]

Another immunotherapy approach called adoptive cell transfer (ACT) collects and uses a patients' own immune cells to treat their cancer. One of the more advanced forms of ACT is CAR T-cell therapy. CAR-T cell therapy employs the use of T-cells, which play a critical role in orchestrating the immune response and killing cells infected by pathogens. With the potential for this treatment to be effective against a wide variety of aggressive cancers, expectations and hopes are running high.

STORIES OF PROGRESS:

CARDIOVASCULAR DISEASE

Innovating for longer and better lives

TRANSFORMING LIVES

Present Day...

AKASH'S HEART DISEASE

Akash discovers he is at high risk of heart disease and manages his condition with cholesterol-lowering and anti-hypertensive drugs, while trying to limit the lifestyle factors that raise his risk.

Forty years ago...

In 1968, Akash may not have been diagnosed in time to take action. Experiencing a heart attack, he would have been resuscitated with a poor understanding of the role of blood clots, and no statins, would have been treated with painkillers and monitored for abnormal heart rhythms. He then would have taken beta blockers, with the high risk of another cardiac event remaining.

In the future...

Akash hopes that digital technologies and improved understanding of biomarkers will help him to monitor his disease more closely. If he does suffer a heart attack, he hopes his heart can be fully repaired with stem cell therapy. He hopes risk factors are more readily identified and people are empowered to choose healthy diets and lifestyles.

Cardiovascular disease (CVD) includes all the diseases of the heart and circulation including coronary heart disease, angina, heart attack, congenital heart disease and stroke.[309]

CVD was long considered an inevitable, though unfortunate, part of getting older. In the last 50 years, understanding of the interplay of various genetic, environmental and lifestyle factors have advanced considerably along with the available range of preventive medicines. While these medicines have had tremendous success saving and extending lives, CVD remains the leading cause of death worldwide today.

KEY MILESTONES

1969: First clinical implantation of a total artificial heart.[310]

1970s: Mounting evidence of the role of the major CVD risk factors (diet and blood lipids, blood pressure, and smoking) led to intensified practical approaches to prevention.[311]

1971: Aspirin's mechanism of action in its prevention of clotting was made clear, paving the way for its use as a cornerstone in antiplatelet therapy.[312]

1977: The first angiotensin-converting-enzyme inhibitor developed for the treatment of hypertension, is discovered.[313]

1982: The WHO Expert Report on Prevention of Coronary Heart Disease attempted to reduce the antagonistic aspects and emphasized complementary roles of the medical high-risk approach and the population-public health strategy of prevention.[314]

1987: The first statin, a drug lowering cholesterol in the blood, approved.[315]

1991: The first in a new class of drugs, P2Y12 receptor antagonists, is approved. P2Y12 receptor antagonists are antiplatelet agents that have been shown to significantly reduce the risk of cardiovascular events.

1999: Lifetime risk at age 40 years of developing coronary heart disease is found to be one in two for men and one in three for women.[316]

2001: High-normal blood pressure is found to be associated with an increased risk of CVD, emphasizing the need to determine whether lowering high-normal blood pressure can reduce the risk of CVD.[317]

2004: Serum aldosterone levels are found to predict future risk of hypertension in non-hypertensive individuals.[318]

2011: Death rate from heart disease dropped 46% since 1991, thanks in part to innovative new medicines.[319]

2011: pCMV-vegf165 is registered by The Human Stem Cells Institute in Russia as a first-in-class gene therapy drug for treatment of peripheral artery disease, including the advanced stage of critical limb ischemia.[320]

2013: World Heart Federation board adopts the United Nations and World Health Organization targets for CVD, launching the 25 x 25 campaign to reduce premature death from CVD by 25% by 2025.[321]

2015: A new class of drugs, PCSK9 inhibitors are approved. PCSK9 inhibitors are monoclonal antibodies and have been shown to dramatically lower LDL cholesterol levels when combined with a statin.[322]

2017: There are 1,400 plus products in the global CVD pipeline, of which 320 are first-in-class products that act on a novel molecular target.[323]

FROM UNDERSTANDING TO MANAGING RISK

The field of study in CVD has made use of, and in many ways pioneered, long-term epidemiological studies. Observing participants in detail over a long period led to an understanding that a healthy diet, not being overweight or obese, not smoking, and regular exercise are all important in maintaining good heart health.[324] Indeed, one of the oldest and most successful cohort studies, the Framingham Heart Study, is the origin of the term 'risk factor'.

With improved understanding of the risk factors for CVD, trials could be designed to determine whether these factors are causal. Lowering cholesterol with drugs, particularly in the Lipid Research Centers Primary Prevention Trial of the 1980s and later statin trials, demonstrated its role in atherosclerosis and paved the way for lipid modification as a medical and public health prevention strategy.[325]

In the 1970s, the first cholesterol-lowering agent was identified by a team lead by Akira Endo. While never marketed due to adverse side effects in clinical trials, it caught the attention of MSD who would go on to identify and market lovastatin in 1987. Since then, the effect of statins on lowering cholesterol and preventing CVD has been demonstrated in numerous studies. Synthetic statins were subsequently developed, including atorvastatin, at one point the world's best-selling medication.[326] They have extended the lives of millions of people at risk of heart attack and stroke, with minimal management: one pill a day, with limited to no side effects.[327] Statins remain the most widely prescribed class of medications today.

It was also found that anti-hypertensive drugs could reduce the risk of heart attack and stroke. This cemented the role of high blood pressure in CVD and confirmed the pursuit of hypertension control as an effective health intervention.[328]

In parallel to the discovery and introduction of preventive statins and anti-hypertensives, effective surgical approaches have been developed and refined. Drugs that prevent clotting and stop immune systems from rejecting transplanted organs have played a major role in improving the effectiveness of these operations. Almost all patients who receive an organ transplant must take immunosuppressant drugs.[329]

CARDIOVASCULAR DISEASE TODAY: IMPROVING ACCESS THROUGH PARTNERSHIPS AND GENERIC MEDICINES

There has been measurable global progress in the prevention of CVD. So why does CVD remain the number one cause of death worldwide? In part, because people live longer. Controlling for age, the CVD death rate has declined in all high-income and some middle-income countries since 1990, although this decline has now stalled for many regions of the world.[330] At the same time, incidence and mortality due to CVD has risen steadily in the developing world. Over three-quarters of CVD deaths take place in LMICs.[331]

Improving access to generic medications, which typically cost significantly less than their brand-name counterparts,[332] is one strategy available for addressing unmet health needs. With increasing availability and use, generic drugs account for almost 90% of all prescriptions in the US[333]. Generic hypertensive and cholesterol medications

Investment in R&D for NCDs is crucial. Diseases such as hypertension no longer affect only developed countries, they are becoming more and more relevant in low income and low to middle income countries.

Mariângela Simão,
WHO

saved the US health care system almost USD 60 billion in 2016.[334] Improving access to medicines must also be balanced with the need for investment in innovation, made possible by the patent system, as the R&D-driven biopharmaceutical industry is expected to develop the drugs of the future.[335]

Population-wide interventions such as reducing tobacco and alcohol consumption and promoting improved diets and regular exercise have been effective in many countries and can be implemented in poorer communities. These strategies have been highlighted by organizations such as the WHO as a primary means to reduce the burden of CVD.[336] Secondary prevention involves treatments with medication, after which surgery may be required.

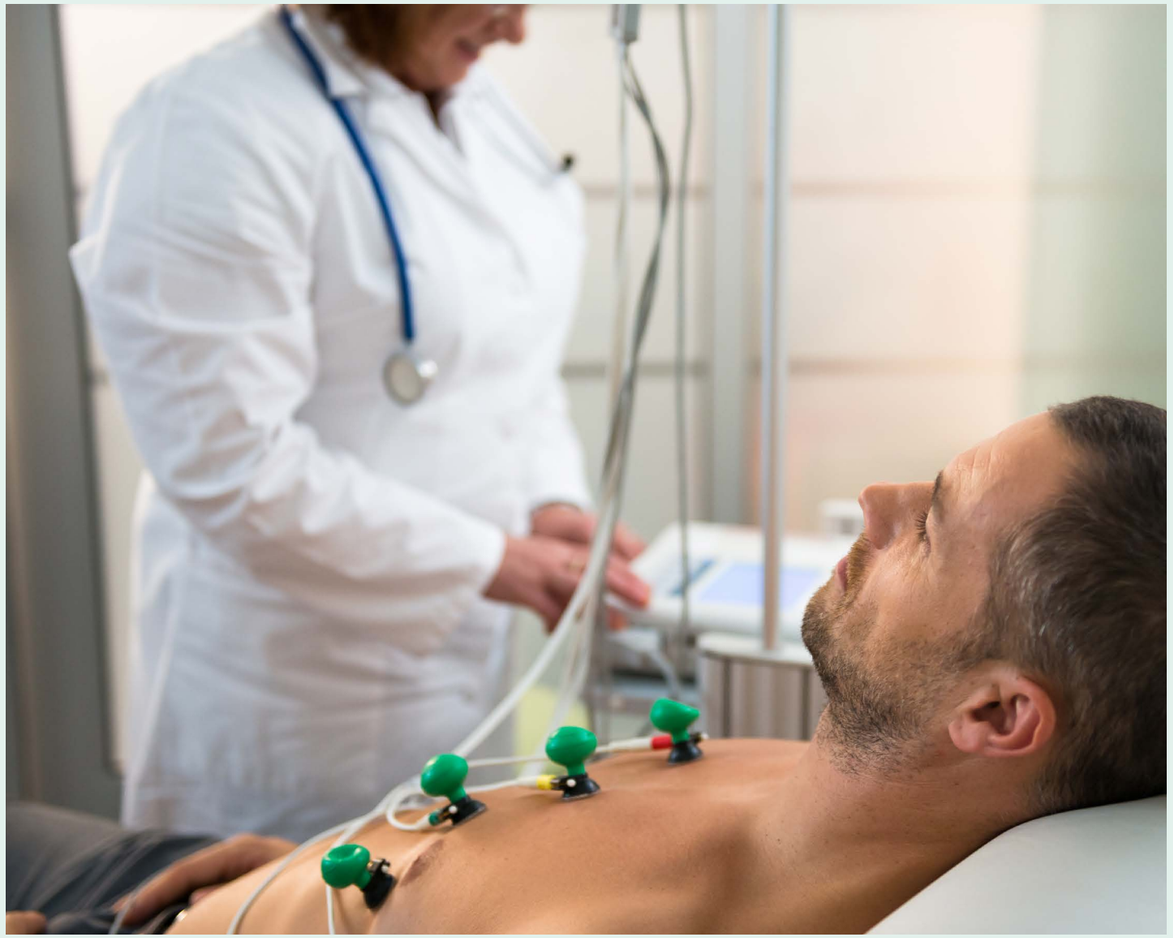
Finally, joint program and company-led access initiatives are helping to address access challenges. AstraZeneca's Healthy Heart Africa is designed in consultation and collaboration with non-governmental and community-based organizations, international organizations, health experts and governments to support local health systems by increasing awareness of the symptoms and risks of hypertension and by offering education, screening, treatment and control.[337] It aims to improve access to hypertension care and sells branded AstraZeneca medicines that are part of the program in a no-profit/no-loss business model.[338] Since its launch in 2014 in Kenya, and 2016 in Ethiopia, it has conducted 5.7 million blood pressure screenings, trained over 5,000 healthcare workers, activated 675 healthcare facilitates and identified over one million people living with high blood pressure.

Pfizer also collaborates with the international non-profit Population Services International to improve the diagnosis and treatment of hypertension, a condition that can often lead to stroke and impacts one-quarter of all adults in Myanmar and Vietnam as a leading cause of mortality. Its Healthy Communities program also provides hypertension management to underserved communities by aiming to screen more than 500,000 people and train up to 400 healthcare workers in 360 private sector health facilities.[339]

EMERGING SOLUTIONS: FROM LENGTH OF LIFE TO QUALITY OF LIFE

Although accounting for more than 30% of global deaths,[340] CVD research has stalled. The R&D of new cardiovascular medicines represents less than 10% of global R&D spending.[341] There are many reasons for this, among them, the high regulatory bar, which demands 'hard' endpoints like reducing death and heart attack.[342] The successes in the history of innovation in CVD also makes it hard to demonstrate a meaningful benefit over existing medicines.[343] But there are promising signs this may be about to change.

Companies are looking to the successes in other areas of medicine, such as oncology, which has improved patient outcomes through precision medicine. Precision medicine allows doctors and researchers to predict more accurately which treatment and prevention strategies will work in which patients, considering their genes, environment, and lifestyle.[344] The first hypertension gene was discovered in 1998,



and while the role of genes in CVD is not well understood, it is a very promising area of research. A precision medicine approach also means looking at biomarkers – the naturally occurring molecules, genes, or characteristics that signal particular diseases and specific pathological or physiological processes. Tracking these in a patient means that treatment can be adjusted according to their real-time development.[345]

Improved rates of CVD survival bring new challenges. The number of people surviving a heart attack, or two or three heart attacks, has increased and there are many more people now living with very badly damaged hearts.[346] These people are living with heart failure, which occurs when the heart is weakened and cannot pump enough blood to meet the body's needs. Despite available drugs which improve the lives of people with heart failure, it remains a debilitating condition, often significantly reducing quality of life.[347] But recent advances have shown that certain cells in the heart play a role in its repair, so-called progenitor cells. This opens up possibilities to help damaged hearts repair themselves to restore full function.[348]

The next big phase of genetics will be informatics, bringing together masses of data and trying to understand how hundreds of small genetic differences combine to put people at risk of a particular disease.

Peter Weissberg,
former Medical Director,
British Heart Foundation[357]

CVD patients are considered an at-risk population for developing serious complications from the flu, and studies have shown that influenza is associated with an increase of heart attacks and stroke. This means that those with heart disease or who have had a stroke need to take steps to fight the flu, and as recommended by the Centers for Disease Control and Prevention (CDC), should get a flu vaccine.[349]

Irregular heart beat (atrial fibrillation) is the most common cardiac arrhythmia. The majority of patients have non-valvular atrial fibrillation (NVAF) and the risk of stroke is five times higher in this patient population. For decades, the standard of care for NVAF required routine blood testing and frequent dose adjustments. While a risk of bleeding is associated with all oral anticoagulants, novel versions that now exist offer potential advantages over previous treatments, including fewer drug interactions and fixed doses, without the need for routine blood testing.[350]

Researchers are targeting inflammatory pathways to prevent cardiovascular events where there is a sudden drop in blood flow to the heart. An anti-inflammatory medicine in development inhibits certain enzymes associated with the inflammation that occurs in the blood vessels during and immediately following an acute coronary syndrome event.[351]

CVD research stands to benefit from sophisticated data-led advances that can bring to light insights from large-outcome trials that would otherwise remain hidden. Take, for example, the Novartis CANTOS trial which observed 10,000 patients over six years, showing that targeting inflammation in heart attack survivors reduces CVD risk.[352] Similar approaches are being explored in genetics, combining huge amounts of data to uncover how small genetic differences combine to put people at risk of a particular disease.[353] By linking population outcomes to specific genes, Amgen's deCODE discovered a gene associated with a 34% lower risk of coronary artery disease.[354]

The establishment of large, quality patient registries has fueled large-scale real-world evidence generation, helping inform clinical debate as well as payer and regulatory decision-making. CVD-REAL is a recent example, a study of more than 700,000 patients with type-2 diabetes from registries spanning North America, Europe, Asia Pacific, and the Middle East, looking at the use of diabetes drugs and their impact on critical cardiovascular outcomes. This research reflects a growing understanding of links between cardiovascular disease and conditions such as kidney disease and diabetes, and their common underlying mechanisms.

And finally, there is huge potential for digital technologies to revolutionize prevention and care. Companies are collaborating with payers and other stakeholders to develop algorithms that can predict risk and drive early intervention.[355] Big data, sensors and artificial intelligence open up the possibility of precise, real-time monitoring of patients – a whole new world for CVD.[356]

STORIES OF PROGRESS:

DIABETES

Improving quality of life through management of a complex disease

TRANSFORMING LIVES

Present Day...

HARU'S LIFE WITH DIABETES

Haru lives comfortably with type 2 diabetes and manages his condition through an insulin pump and medication to control blood glucose.

Forty years ago...

In 1978, Haru's condition would have meant more complicated treatment. He would have used traditional syringes and animal insulin, without a mechanism for monitoring blood glucose levels himself.

In the future...

Haru hopes that people with diabetes will access cell treatment to restore the normal pancreas function. He wants to ensure his children have a healthier, lower risk lifestyle and can prevent diabetes with physical exercise and good nutrition.

One in 11 adults have diabetes, which represents 425 million patients globally.[358] Together with cardiovascular diseases, cancers and chronic respiratory diseases, diabetes is one of the world's four major NCDs, and one of the only chronic diseases that continues to increase in prevalence. It refers to a group of disorders whereby the body is unable to regulate blood sugar. It is a lifelong illness that requires complex, delicate management of glycemic control and targeted prevention of long-term complications.

Today, diabetes is categorized as Type 1 or Type 2. Patients with Type 1 diabetes (often called insulin-dependent diabetes) are unable to produce insulin in the pancreas due to an auto-immune disease. Patients with Type 2 diabetes (often called adult-onset diabetes), have lost their ability to produce insulin and often develop the disease in adulthood as a result of excessive body weight and insufficient exercise.

Type 2 diabetes has been distinguished from Type 1 since the 1970s. Rates of Type 2 diabetes have risen rapidly, driven largely by lifestyle factors including growing obesity rates. Because sophisticated laboratory tests are required to distinguish between Type 1 and Type 2 diabetes, separate global estimates of diabetes are challenging,[359] but estimates suggest that Type 2 diabetes accounts for 90-95% of cases worldwide.[360] Although Type 1 diabetes is not preventable, patients can avoid complications through proper diagnosis and treatment to regulate blood sugar. In contrast, Type 2 diabetes can be prevented and reversed through targeted lifestyle interventions.

Poorly managed diabetes can lead to serious complications for patients, including heart attack, stroke, blindness, amputation, kidney failure - and early death. Patients with weak or compromised immune systems as a result of diabetes are three times higher risk of developing TB. By some estimates, only about 6% of patients will live free of diabetes-related complications.[361]

Since 1980, age-standardized diabetes prevalence has more than doubled in men and increased by 60% in women worldwide with millions dying from diabetes or higher-than-optimal blood glucose.[362] The global economic burden of diabetes and its associated complications was estimated to be USD 1.3 trillion in 2015, or 1.8% of gross domestic product.[363] Two thirds of these costs were direct medical costs (USD 857 billion) and one third were indirect costs, such as lost productivity. Diabetes, therefore, is not only a worldwide health issue because of its effect on mortality, morbidity, and quality of life, it also has a significant impact on national economies. With global diabetes rates on the rise, the economic burden is expected to increase USD 2.2 trillion by the year 2030.[364]

Rates of diabetes are growing in LMICs, with nearly 80% of people with diabetes living there.[365] Improving economic status and associated rise in poor diets and lack of exercise, drives the incidences of diabetes to unprecedentedly high levels and creates a mounting health challenge.

Patients can now live with diabetes and manage its symptoms, but not everyone is diagnosed and treated.

KEY MILESTONES

1973: Invention of the first wearable insulin infusion pump.[366]

1978: Synthetic 'human' insulin is produced using recombinant DNA techniques, the first human protein by to be manufactured through biotechnology.[367]

1982: Regulatory and marketing approval for human insulin, was granted in the UK and the US, made possible through cooperative efforts between physicians and scientists working in research institutions, universities, hospitals, and the pharmaceutical industry.[368]

1985: Launch of the first manufactured insulin pen.[369]

1989: St Vincent Declaration: WHO and International Diabetes Federation effort for multi-stakeholder agreement on goals for the care of people with diabetes.[370]

1990s: Development of multiple anti-diabetic medicines to improve blood glucose control, including oral antidiabetic agents such as Alpha-glucosidase inhibitor, meglitinides and thiazolidinediones.[371]

2000: Insulin glargine, a first long-acting human recombinant insulin, is launched.[372]

2002: World Diabetes Foundation founded, a leading funding mechanism dedicated to preventing and treating diabetes in developing countries, which has provided USD 137 million in funding to date.[373]

2005: The approval of the first GLP-1 receptor agonist therapy, exenatide, which lowers blood sugar in Type 2 diabetics.

2011: WHO issues new guidelines recommending HbA1C as a diabetes screening tool which offers greater stability by monitoring glucose levels over several months.[374]

2012: The first SGLT-2 inhibitor, dapagliflozin, is approved, which reduces blood sugar and demonstrates cardiovascular benefits.

2013: University of Cambridge develops an artificial pancreas that pairs the technology of an insulin pump with a continuous glucose monitor.[375]

2014: Inhalable insulin is approved by the FDA, facilitating fast-acting pre-measured insulin.[376]

2015: Launch of the SDGs, including the target to reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being by 2030.

50 YEARS OF INNOVATION TO IMPROVE DISEASE MANAGEMENT

The therapies that have been developed over the last couple of decades for the treatment of diabetes...the progress has been terrific. There have been major changes in the kinds of insulin that one can take, in terms of how quickly they may act or insulin that lasts for a whole day to give 24 hour coverage.

William Chin,
Chief Medical Officer, Frequency Therapeutics[381]

The quality of life of people with diabetes has changed considerably since 1968 thanks to evolution in types of insulin, mechanisms for delivering it, as well as tools to monitor and more accurately control blood glucose levels. Since the development of synthetic human insulin as the primary treatment for diabetes, innovation has made insulin easier to use, faster acting, and longer lasting. Treatment has transformed diabetes into a disease that patients can live with. Side effects and long-term complications have been reduced, and the choice of treatments for patients expanded. Appropriate treatment, close monitoring and behavioral changes can delay or prevent its progression.

The first insulin pen was introduced in 1985. It improved patient ease of use and adherence. Accuracy of treatment led to reduced diabetes care costs, compared with using a vial and syringe. Pens can now record the date, time, and amount of previous doses so that patients and healthcare providers can see exactly how much insulin the patient last took and when. Improvements in insulin pumps have also improved the quality of life of patients. Features include the ability to connect wirelessly to a blood glucose meter or under-the-skin sensors which monitor and regulate insulin semi continuously. A new trend in the design of insulin pumps is the tubing-free patch pump that adheres directly to the skin.

There are currently hundreds of medicines to manage diabetes being developed that could further improve insulin delivery.[377] For instance, researchers are exploring a slow-dissolving molecule which could keep insulin in a patient's body for over two weeks. If successful, it has the potential to replace daily shots altogether. Similarly, a once-a-week natural hormone could effectively regulate blood sugar, as might modulating genes responsible for insulin sensitization. A cream has also been developed.[378]

In addition to insulin, people with diabetes often rely on multiple other anti-diabetic drugs to adequately control blood glucose. Metformin is a popular first-line oral anti-diabetic drug (OAD) developed in the 1920s and understood to treat Type 2 diabetes from the 1970s.[379] However, because diabetes is progressive, first-line treatments like metformin may eventually fail to control sugar levels, meaning second-line, and eventually third or fourth-line therapies may be required. Many new classes of OADs have been developed over the past decades. For example, dipeptidyl peptidase-4 inhibitors (DPP4), first discovered in 1967, lowers sugar levels in novel ways which means it can be used in combination with other medication. The introduction of second-generation sulfonylurea agents, which are more potent than first-generation agents, allowed patients to take smaller and less frequent doses per day.[380] Most recently, the approval of the novel sodium-glucose cotransporter 2 (SGLT-2) inhibitors, have proven to significantly reduce blood sugar and blood pressure while also leading to weight loss and important cardiovascular benefits. There have been advances in injectable drugs also. Glucagon-like peptide-1 (GLP-1) receptor agonists such as exenatide, a synthetic version of a protein found in the saliva of a species of the Gila monster, help to lower blood sugar levels in people with Type 2 diabetes.

The progressive nature of the disease underscores the need for innovative medications with improved efficacy to provide additional therapeutic benefit and lower risks for certain complications in diabetic patients.

Identifying diabetes early is key to effective treatment, and approaches have evolved for earlier and more precise diagnosis for patients. The traditional diagnostic method of testing of blood glucose, a fasting plasma glucose (FPG) test, is a relatively inexpensive 'finger-prick' for patients. However, this test fails to diagnose approximately 30% of previously undiagnosed diabetes.[382] The oral glucose tolerance test is more sensitive and substantial, able to detect specific types of prediabetes which FPG cannot. Random plasma glucose tests can be more convenient for patients as they are completed without fasting in advance. Some blood tests can complement basic tests by looking specifically for antibodies, which might be a sign of Type 1 diabetes. In 2011, WHO issued new guidelines recommending a diabetes screening tool that offers greater stability by monitoring glucose levels over several months.[383] Many non-invasive tests have been developed which measure glucose without the need to draw blood,[384] and recently, researchers have attempted to use patient saliva as a non-invasive method test.[385]

COLLABORATIONS TARGET RISK FACTORS

Helping people lead healthy lifestyles is a means to reversing the rise in diabetes. Type 2 diabetes is largely preventable through healthy diet and regular physical activity. Actions to prevent diabetes are most effective before birth and in early childhood.

Sanofi's Diabetes in Schools partnership in Turkey has been effective at enhancing early diagnosis of Type 1 diabetes in school age children, as well as in raising awareness among children and teachers of childhood obesity and the importance of healthy eating habits in preventing diabetes. IFPMA works with the International Federation of Red Cross and Red Crescent Societies in the promotion of '4 Healthy Habits': healthy eating, moderate consumption of alcohol, physical activity and not smoking.[386]

A focus on prevention, screening, early diagnosis and managing hyperglycemia in pregnancy is critical to reducing maternal, perinatal, and neonatal mortality. Not to mention, preventing diabetes in the next generation. Novo Nordisk's program Changing Diabetes® in Pregnancy focuses on the link between gestational diabetes and maternal and new-born health through capacity building, screening of pregnant women and awareness-raising. It partners with local health authorities and global partners such as the International Federation of Gynecology and Obstetrics, Women Deliver, and Management Sciences for Jhpiego.[387]

Many partnerships use new technologies to promote healthy behaviors. For example, IFPMA partner with International Telecommunications Union's Be He@lthy Be Mobile initiative on the mDiabetes program which uses SMS technology to promote prevention and control of diabetes.[388] The program has reached 8.5 million people in India, over 200,000 people in Egypt and over 150,000 people in Senegal, with

quantitative evaluation of the program demonstrating a positive influence on the intervention group.

Urbanization is also a lens for addressing diabetes risk factors. The Cities Changing Diabetes program launched in 2014 by three global partners (Steno Diabetes Centre Copenhagen, University College London, and Novo Nordisk) accelerates the global fight against urban diabetes. Today, the program features local partnerships in 10 cities[389] to address the social factors and cultural determinants[390] that can increase vulnerability of Type 2 diabetes among certain people living in cities.

BETTER HEALTH SYSTEMS KEY TO IMPROVED DIAGNOSIS AND CARE

Keeping up with such programs enables us as upcoming physicians to be able to treat our patients according to the most recent developments.”

Cheryl Tikolo,
medical student on the Merck Capacity Advancement Programme[392]

Improved health infrastructure enables awareness raising, early diagnosis and better care management. Nearly one in two people that have diabetes are undiagnosed. In many cases, they are unaware they have the disease, which can result in complications and early death.[391]

Trained health care workers and sophisticated laboratory tests are usually required to diagnose and manage the disease. Education is crucial to creating a health workforce which can effectively care for patients with diabetes. The Capacity Advancement Programme, led by Merck KGaA in partnership with ministries of health, universities, and local diabetes associations across five African countries, focuses on strengthening health systems to enable more effective prevention, diagnosis, and management of diabetes. The program expects to have trained over 50,000 by the end of 2018. Students are equipped with understanding of the most recent advancements in diabetes, allowing patients to benefit from the latest knowledge and techniques.

The growth of Type 2 diabetes in poor regions can only be tackled by context-specific interventions. Eli Lilly and Company, through the Lilly Global Health Partnership,[393] specifically tackles rising diabetes in countries of Brazil, China, India, Mexico, South Africa, and the US. The partnership works with governments and local partners to bring care closer to primary level and improve health outcomes by tackling key pain points in the cascade of care, with the ultimate ambition of increasing early detection, intervention, and treatment.[394]

Targeting serious and specific diabetes-related risks is also where industry and others are active. For instance, one frequently encountered complication of diabetes is neuropathy, particularly affecting the feet. Sanofi works to prevent diabetes amputations through early intervention strategies as part of its Diabetes Africa Foot Initiative.

In Type 2 diabetes, prevention, early detection, early control, and early access to the right interventions can deliver significant improvements in patient outcomes. AstraZeneca takes a unique look at youth and primary prevention. 70% of premature deaths from the most common non-communicable diseases, of which diabetes is one, can be linked to risk behaviors that started in youth.[395] Through its Young Health Programme, AstraZeneca has reached more than 2.25 million youth with health information on the importance of physical activity, healthy eating and avoiding tobacco use.[396]

The lack of access to affordable insulin also remains a key impediment to successful treatment and management. Novo Nordisk’s Access to Insulin Commitment[397] since 2001 (updated in 2017) means the company supplies human insulin in least developed countries and other low-income countries at a price that does not exceed 20% of the average realized price for Europe, the US, Canada, and Japan. Others, such as Novartis through Novartis Access – also commit to differential pricing in LMICs to widen the availability of treatments.[398]

Affordably priced insulin and generic treatment often does not reach patients in LMICs due to lack of healthcare financing, weak supply chains, and health care infrastructure. Ultimately, reducing rates of diabetes and reaching patients with care will rely upon improved health systems and infrastructure.[399]

FUTURE FOCUS ON DISEASE MANAGEMENT AND TENTATIVE STEPS TOWARDS A CURE

The WHO projects that diabetes will be the seventh leading cause of death in 2030, with an expected increase of 205 million additional cases by 2035 if appropriate action is not taken. Huge strides have been made in managing the disease and improving quality of life. The ultimate goal of all efforts must be to improve outcomes of patients through vaccines and ultimately, a cure.

Research into the development of an artificial pancreas brings the world one step closer to a developing a cure. The University of Cambridge developed an artificial pancreas in 2013 that pairs the technology of an insulin pump with a continuous glucose monitor. Described as ‘a bridge to a cure’, it delivers both insulin and glucagon every five minutes as required, connecting via Bluetooth to a smartphone app to calculate the required doses needed.[400]

R&D has also been strongly focused on cell therapy, injecting or inserting living cells into a patient to take over the function of the faulty cells. This brings the hope of potentially restoring the normal function of the pancreas, reducing the need for insulin therapy to only the most severe cases.

Preventing Type 1 diabetes is another area of interest, specifically immunotherapy. A patient’s own immune system can be re-educated not to attack beta cells, potentially delaying the clinical onset of the disease.[401]

STORIES OF PROGRESS:

HEPATITIS C

Discovery to cure in 25 years

TRANSFORMING LIVES

Present Day...

TASMEEN AND HEPATITIS C

Tasmeen receives combination therapy over 12 weeks and is cured of hepatitis C.

Thirty years ago...

In 1988, Tasmeen would not have been diagnosed. The disease was not fully understood, no treatment options were available, and she could have developed liver cancer as a result of the virus.

In the future...

Tasmeen hopes hepatitis C will be eliminated through improved diagnosis and access to treatment.

Hepatitis C is a viral, blood-borne disease that progresses slowly over time. If left untreated, it can cause life-threatening damage to the liver. An estimated 71 million people have chronic hepatitis C infection with almost 400,000 deaths each year.[402] The hepatitis C virus (HCV) is the leading cause of liver cancer and the main reason for liver transplantation.

Prior to the identification of HCV in 1989, so little was known about the virus that it was simply called *non-A, non-B hepatitis*. Since identification, effective treatments have been relatively rapidly developed. Compared to the first-ever HCV treatment approved in 1991, in which a patient faced cure rates of around 6%, drugs today have more than a 95% success rate over short treatment courses.[403] That makes HCV the fastest viral disease ever to be identified and cured. It remains the only chronic viral illness that can be completely cured, allowing millions of people to regain their health and live full and productive lives.

Of those living with HCV, only 20% know that they are infected.[404] Due to the blood-borne nature of the disease, many of those infected with HCV have contracted the disease through drug use. They tend to be the hardest to reach with the least access to care. But injecting drugs is not the only route to infection, and that misperception creates a stigma that keeps people from being screened. With a cure available, the barriers for eliminating HCV now lie in diagnosing those infected and increasing access to life-saving treatments.

KEY MILESTONES

1989: Biotechnology scientists who partnered with the CDC identified and officially named the virus hepatitis C. Prior to that, it was associated with blood transfusions, but was called non-A, non-B hepatitis because the virus could not be identified.[405]

1991: The first treatment for hepatitis C was approved by the FDA, an injectable drug called interferon which provides cure rates of about 6%.[406]

1998: The FDA approves the first-ever interferon and ribavirin combination treatment improving cure rates to 29% in patients with certain genotypes.[407]

2007: Despite progress, US deaths from hepatitis C surpass those from HIV at almost 5 per 100,000.[408] For some, hepatitis C is a short-term illness, but for 70%–85% of those infected, it becomes a long-term, chronic infection.[409]

2010: World Hepatitis Day established by WHO.[410]

2011: Direct-acting antivirals (DAAs) approved - called protease inhibitors, combined with 24-48 weeks of pegylated interferon and ribavirin improve cure rates among patients with genotype 1 to 70%, (duration 23-48 weeks).[411]

2013: The FDA approves new DAAs.[412] One regimen produced an overall cure rate of 90% in as little as 12 weeks with greatly reduced side effects. Cure rates now range between 80-90% in just 12-24 weeks and for some patients (genotypes 2-3).

2013: Rapid point-of-care diagnostic HCV antibody test approved by FDA.

2014: 25 years after discovery, combination therapies approved (sofusbuvir and ledipasvir) and have treatments of eight to 12 weeks, with a 94-96% cure rate.

2015: 90% of patients with most common form of disease can expect to be cured in as little as eight weeks with new therapies; compared to cure rates of 41% over 48 weeks with severe side effects for the same patients just over a decade ago.

2016: Sofosbuvir/velpatasvir developed as the first drug therapy to treat all hepatitis C genotypes in tablet form.[413]

2016: NOhep,[414] a global movement uniting governments, medical professionals, patients, and the hepatitis community to eliminate viral hepatitis by 2030 established.

2016: Number of people receiving treatment for hepatitis C rose 33% since 2015, from approximately one million to 1.5 million people.[415]

2017: FDA approved a daily combination pill of glecaprevir and pibrentasvir providing an eight week treatment for all genotypes (1-6).[416]

2018: 75 more drugs are in clinical development in the US with elimination a prospect. [417]

INNOVATING AGAINST A SILENT KILLER

IMAGINE TAKING AN INJECTION AND A PILL THAT MADE YOU FEEL – EVERY DAY – WORSE THAN YOU EVER FELT FROM THE INFECTION THAT WAS BEING TREATED.”

Alexea Gaffney-Adams,
MD, infectious disease specialist[427]

Hepatitis C is dubbed ‘the silent killer’ as it typically progresses without symptoms, often leaving patients unaware they are infected until their condition is very serious. HCV damages the liver slowly over many years, often moving from inflammation to scarring (fibrosis) to permanent, irreversible scarring (cirrhosis). As liver damage increases, symptoms eventually include jaundice, joint pain, fever, fatigue, nausea, and loss of appetite, among others.[418]

Once a patient has cirrhosis, the liver is unable to heal itself, and this condition can rarely be reversed. For those with end-stage liver disease, treatment is more focused on preventing further damage in an effort to avoid complications, including liver cancer, liver transplantation, and premature death. Hepatitis C has also been associated with other serious conditions, including diabetes, kidney disease, and depression.[419]

In 1987, scientists working at Chiron Corporation, later acquired by Novartis, partnered with the CDC. Using a novel molecular cloning approach, they officially identified and named the virus hepatitis C in 1989.[420]

Screenings to detect HCV in blood supplies were quickly developed, as blood transfusions were, and remain, the main route of transmission in the developing world.[421] This dramatically reduced new infections, along with prevention and infection control measures designed to curb the spread of HCV. Scientists were also newly able to estimate the prevalence of HCV, leading to its recognition as a major global health issue. In some regions today, up to 2% of the population is infected with HCV.[422]

Identifying the HCV molecular structure and genetic makeup enabled specific treatments to be developed. The genetic diversity of the virus, combined with patients’ weak immune response to infection, ruled out an effective vaccine.[423] Instead, researchers focused on combatting the infection by producing a sustained viral response to clear it completely from the patients’ blood.

Interferon was the first, and for a time, the only treatment for hepatitis C.[424] An interferon is a protein produced by the body’s immune system in response to an infection. Treatment involved injecting large doses of interferons to help the body target infected cells for destruction. Side effects were debilitating, and many patients dropped out of what was a very long course of treatment.

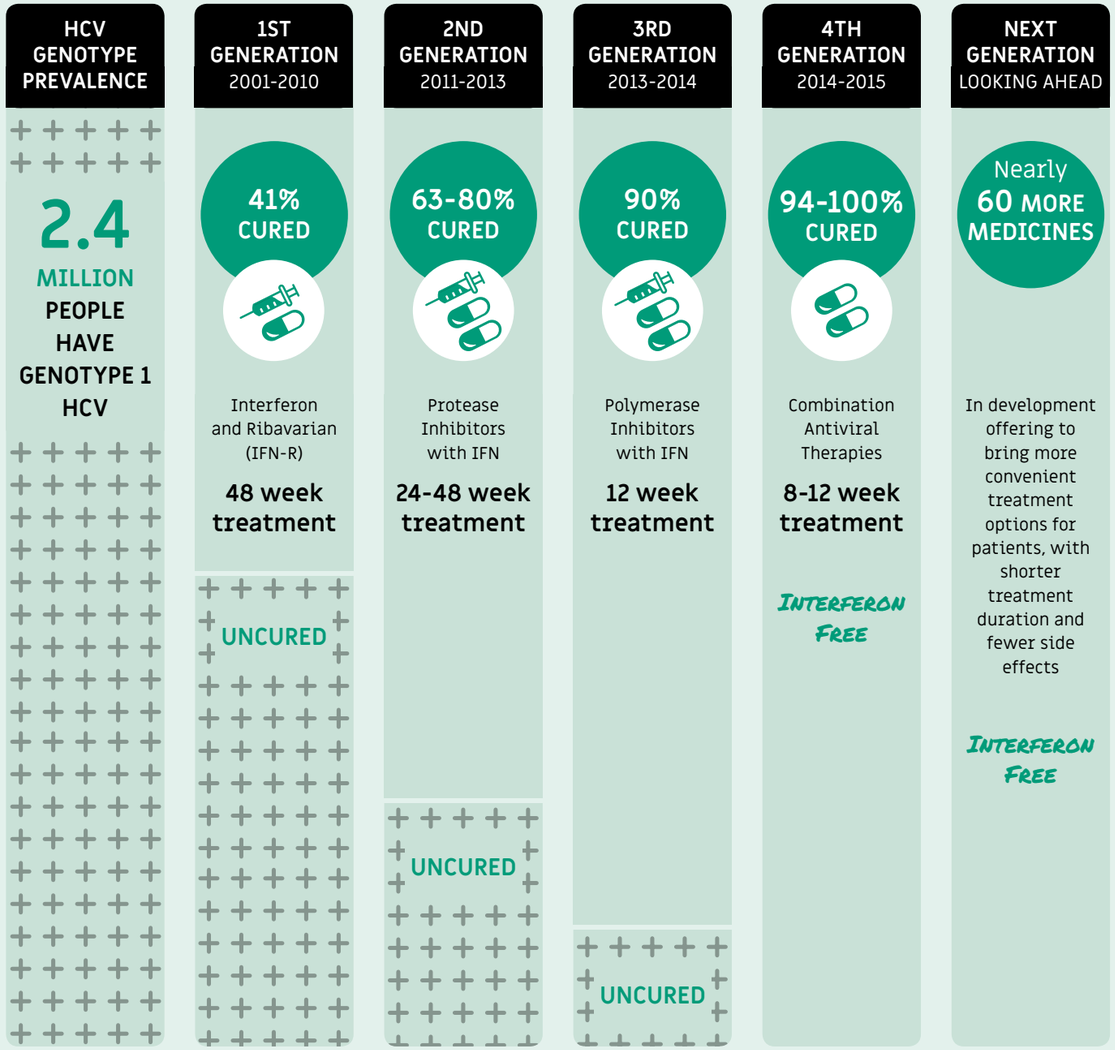
It was also a largely ineffective treatment, with cure rates of about only 6%.[425]

Step-by-step, scientists began to understand the virus’ life cycle and how it replicates itself in people. By 2010, there was considerable interest from the industry, with multiple drugs in development. And lessons were learned from HIV and the potential of protease inhibitors to block the virus from replicating.[426]

While 77 investigational medicines failed in clinical trials over 1998-2014 – they were either too toxic to the patient, or not effective enough – they laid the groundwork for

12 approved medicines over the same period.[428] In a landmark moment, a new class of medicines called direct acting antivirals was introduced in 2011. Through experiments in combination therapy, these medicines today can cure more than 90% of people in an eight to 12 week regimen, without the debilitating side effects of older treatments.[429]

DIAGNOSIS AND ACCESS



Based on graphic from innovation.org

As of 2015, only 7% of the 71 million people with chronic hepatitis C had access to treatment that cures within three months.[430] In part, this is due to lack of access to testing in many parts of the world; the vast majority of those affected by hepatitis C live in LMICs where testing facilities are not available. Combined with the absence of symptoms for some 80%, up to 57 million people today are unaware they are living with the disease.[431]

For many of those that are diagnosed, healthcare payers may not cover the cost of innovative treatment. While characterized by some as initially expensive, these breakthrough and life-saving treatments are, in fact, both highly cost effective and transformative for patient lives. They improve quality of life, prevent the development of liver cancer, and costly and difficult liver transplants.

Comparisons are often drawn between the hepatitis C epidemic and HIV in the late 1990s. Both involve the global spread of an under-diagnosed disease that carries significant stigma, hardship, and cause life-long illness and death. Industry developed highly innovative and effective products to radically curb both global epidemics and transform people's lives.[432] In both cases, rapid development of access pricing and voluntary licensing initiatives increased access in the developing world, shortly after launch of the drugs in the developed world. Competition in the market brought about second and third generation drugs, and delivered both lower prices and newer, more effective and convenient regimens.[433] Moreover, prices paid in developed markets have provided the economic incentive for the development of new, innovative medicines. Through recourse to differential pricing, these innovative medicines can be brought to patients in need in the developing world, while maintaining the economic incentive for R&D provided by the developed world markets. Tackling the burden of HCV, however, has been hindered by a lack of large-scale global donor funding to expand treatment, unlike HIV.

While barriers exist to broad access, particularly in LMICs, where a lack of financing and awareness has hindered national programs, many countries have succeeded in making treatment more widely available. Individual companies have implemented initiatives to enable countries in the developing world to access lower cost DAAs, including differential pricing and voluntary licensing to generic manufacturers to facilitate scale up of national treatment programs. In Rwanda, despite facing many challenges as a low-income country, the government has developed a national treatment program and is seeing rapid progress.[434]

TOWARDS ELIMINATION BY 2030

There is widespread support, and optimism, for the WHO commitment to eliminate viral hepatitis (B and C) by 2030. Collaborative efforts and active policy and pricing discussions are underway. Multi-stakeholder platforms such as NoHEP, launched by the World Hepatitis Alliance in 2016, includes civil society and multilateral organizations to help fill gaps in screening.[435] Quick Start – a new program run by the Clinton Health Access Initiative, Duke Health and AmeriCares with the support of Bristol-Myers Squibb, Hetero, Mylan and Roche – is looking to cure 25,000 hepatitis C patients in Africa and Southeast Asia through better access to new drugs. The Medicines Patent Pool – a UN-backed public health organization working to increase access to HIV, hepatitis C and tuberculosis treatments in LMICs – is working with generic partners to speed the development and distribution of new HCV treatments that can eliminate the virus through a short course of oral therapy in regions with a high HCV burden.[436]

A primary challenge is identifying those infected. Collaboration is needed across organizations that work with at-risk individuals, the public health sector, and the R&D-based biopharmaceutical industry. With hundreds of millions of at risk individuals that should be screened and tested for HCV infection, future diagnostic approaches that are affordable, provide results in a single visit, and inform the choice of treatment regimen will be a huge asset in the fight against HCV.[437]

Lastly, despite being a ‘master virus’ for which it was once thought there was no chance of a vaccine, there are now a number of candidates in development. An affordable, effective vaccine might just be the most powerful tool for defeating HCV.[438]

Tackling these global health challenges is hard. Despite different perspectives, we must be united in our belief that our decisions must ultimately benefit the patient.

Mariângela Simão,
WHO

Growing rates of NCDs, increasingly powerful patient data and technology, a global population living healthier and longer lives - what does the next 50 years hold? What new challenges will industry and other actors need to respond to? What could achieving just one of the SDG targets – UHC – make possible?

By 2068, the world and state of health is set to look radically different – from demographics, to the spread of diseases and players in the ecosystem.

DEMOGRAPHICS

Demographics are likely to change dramatically with ageing societies, migration, and growth of urbanization and middle-class lifestyles.

DISEASES

The diseases that burden us are evolving as generations become free from infectious diseases such as TB and AIDS, and the threats of NCDs and AMR grow.

HEALTH ECOSYSTEM

The health ecosystem could be transformed as innovative partnerships grow to become the new normal, emerging players such as health technology companies become more established, and patients take more control over their health.

Looking ahead, the more we know, the more "unknowns" are revealed, making the future of global health – or any field – difficult to predict and leaving more questions than answers.[439] In this ever-changing landscape, collaboration and dialogue will be essential to engage with emerging issues and address associated challenges.

This chapter explores just some of the opportunities and risks for global health over the next five decades. Recognizing these issues cannot be tackled in silos, it is offered in the spirit of collaboration and dialogue. The research-based biopharmaceutical industry looks forward to continuing to engage with the global health community to respond to these risks and opportunities together.

HEALTH SECURITY

How can the world prepare?

The global community must recognize that health security presents a clear risk for all nations – it cannot be addressed solely by philanthropic endeavors.

David Heymann,
London School of Hygiene and Tropical Medicine

This year marks the 100th anniversary of the great influenza pandemic, which killed between 50 and 100 million people, and happens to be one of the worst flu years in recent history.[440] Despite advances in understanding and the development and use of vaccines, concern with flu looms large in public consciousness. Combined with unpredictable outbreaks of infectious diseases – Ebola and Zika in recent memory – global health security is top of mind.

WHAT CAN BE LEARNED FROM THESE PANDEMICS TO BETTER PREPARE?

SEVERE ACUTE RESPIRATORY SYNDROME (SARS)	EBOLA	ZIKA
Within weeks the virus spread from China to 37 countries through air travel in 2002, infecting 8,000 people worldwide and killing 800.	The 2014-15 outbreak in West Africa left 11,000 dead from over 28,000 cases.	Two years after the peak epidemic in Central and South America, the world is still understanding the full impact of its damaging effects, such as microcephaly.

DISEASE X REPRESENTS THE KNOWLEDGE THAT A SERIOUS INTERNATIONAL EPIDEMIC COULD BE CAUSED BY A PATHOGEN CURRENTLY UNKNOWN TO CAUSE HUMAN DISEASE.

– WHO[447]

With more than a billion people travelling outside their country every year, it is extremely easy for viruses to spread.[441] An infectious disease in one location can – in as little as 36 hours – pose a global threat.[442] This year WHO added a hypothetical virus, 'Disease X', to its list of priority diseases, encouraging the global health community to build resilience and capacity to tackle all threats – not just predictable ones.[443]

Beyond direct effects on health, global disease outbreaks have significant economic impact. This includes direct costs to sufferers and communities, aversion costs as people seek to avoid exposure, as well as broader costs in a connected global economy. The World Bank estimated that, in 2015, Ebola caused a potential GDP loss of more than USD 1.6 billion in the three most affected countries, and more than USD 500 million across the rest of the African continent. Studies estimating the cost of future health security threats suggest that drug resistant infections could cost USD 100 trillion between now and 2050, with the annual death toll reaching 10 million over that period.[444]

AMR poses an increasingly formidable threat to global health security, too. Common infections are becoming resistant to antimicrobial medicines, causing an estimated 700,000 deaths each year.[445] In 2016, 490,000 new cases of multi-drug resistant tuberculosis emerged, and AMR is starting to complicate the fights against HIV and malaria.[446] Without efforts to tackle misuse of antimicrobials in people and animals, and improve infection control and sanitation, superbugs have the potential to reverse the gains made from modern medicine.

HOW CAN HEALTH SYSTEMS BECOME AGILE AND READY TO RESPOND WHEN HEATH SECURITY THREATS ARISE?

There are emerging opportunities in programs and partnerships being piloted right now.

- The **2014-15 Ebola outbreak** uniquely united actors including Gavi and MSD to fast-track projects that would otherwise take decades, although development has recently slowed as the outbreak and its associated urgency wanes.
- The **Coalition for Epidemic Preparedness Innovations**, a public-private consortium developed in the wake of the Ebola crisis aims to take a more proactive approach to avoid potential epidemics by accelerating development of safe and affordable vaccines.[448]
- The **Global Supply Network for Pandemic Preparedness and Response** focuses on supply chain and logistics improvements to help the world's ability to effectively respond to pandemics.[449]
- Partnerships such as the **AMR Industry Alliance**, including different life science sectors including R&D-based pharmaceutical companies, diagnostics, generics, and SME/biotechnology companies, will be crucial to curbing antimicrobial resistance.

CLIMATE CHANGE

The greatest health need of this century?

From exposing larger numbers of people to heatwaves to increasing the risk of infectious disease, climate change is already having profound effects on human health. Acting as a disease amplifier, climate change augments existing threats such as the spread of Zika to new geographies or severe malnutrition that accompanies drought.[450] By 2030, some suggest that climate change will cause an additional 250,000 deaths each year from malaria, diarrheal disease, heat stress, and undernutrition alone.[451]

Climate change also closely links to air pollution, with the extraction and burning of fossil fuels being major sources of pollutants and CO2 emissions. Air pollutants were responsible for nine million premature deaths in 2015 – representing 16% of all deaths worldwide and three times more than AIDS, TB, and malaria combined.[452]

Environmental pollution is a clear risk factor contributing to acute and chronic respiratory disease, with children particularly at risk. In 2012, ambient air pollution was responsible for three million deaths worldwide, and 169,250 child deaths under five.[453] In many high-income countries, chronic obstructive pulmonary disease is already the cause of the lengthiest hospital stays.[454]

Without collective action, we can expect more of the same. According to WHO, the Paris Climate Agreement is as much a public health treaty as it is a framework for saving the planet from irreversible damage.

CLIMATE CHANGE ISN'T JUST HURTING THE PLANET – IT'S A PUBLIC HEALTH EMERGENCY.

Christiana Figueres,
Former Executive Secretary, United Nations Framework Convention on Climate Change[458]

WHAT INTERVENTIONS ARE NEEDED TO RESPOND TO THE HEALTH CHALLENGE OF CLIMATE CHANGE?

Some solutions are offered in work already underway.

→ Several biologics are in development that target a cure for **respiratory disease**.[455]

→ The **Smart Health Facilities Initiative** and **Smart Hospitals Toolkit** is being implemented through the Pan American Health Organization in the Caribbean with the aim of supporting governments of selected countries to assess and prioritize vulnerability reduction investments in their health facilities.[456]

→ In high-income countries, the **CDC's Changing Climate program** identifies the US populations most vulnerable to impacts, predicts future trends, creates systems to detect and respond to emerging health threats, and designs programs to manage health risks now and in the future.[457]

DEMOGRAPHIC AND DISEASE SHIFTS

How will connected challenges manifest?

Populations and societies are aging. By 2030, there will be more people over the age of 60 than under the age of 10. It will happen much earlier in some countries.[459] Myriad advances over the last 50 years have extended human lifespans through efforts to preserve, improve and regenerate bodies and minds for better and longer lives.

Ageing societies present a host of questions regarding the sustainability of our healthcare systems. How can the system support individuals to plan for healthcare expenses as they live longer, empower communities to care for older relatives, and enable governments to support people who are retired from work and require additional healthcare?

Changing lifestyles are also impacting the way people live their lives and their healthcare needs. Accelerated urbanization and growing middle classes are linked to lifestyle changes such as more sedentary behavior, reduction in exercise, increase in unhealthy diets, tobacco, and alcohol consumption. Estimates suggest 65% of the population will be middle class by 2030, which could have profound impacts on the health challenges facing the world.[460]

The interplay between these two demographic shifts manifests in unexpected ways. Interestingly, for the first time in decades, in some high-income countries young people are not expected to live as long as their parents, due to unhealthy lifestyles.[461] NCDs are also disproportionately high in developing countries – where health systems have evolved to cope with infectious diseases, which was the primary disease burden.[462]

> *Thanks to unparalleled success in improving child survival over the last few decades, we are dealing more and more with a set of illnesses that are a function of increased survival such as NCDs and mental illness.*
>
> **Tim Evans,**
> World Bank Group

AGE-RELATED DISEASE

Currently, age-related diseases are responsible for 100,000 deaths per day and billions are spent around the world in attempts to slow ageing.[463] The most common neurodegenerative disorder is Alzheimer's dementia, which makes up 13% of the global burden of disease. The prevalence of dementia is forecast to increase in every region of the world, affecting 131.5 million people in 2050.[464] But despite costing the global economy USD 818 billion in 2015, research has made little progress and treatments target the symptoms rather than the disease.[465] A study in 2014 reported Alzheimer's drug candidates to have one of the highest failure rates of any disease area – 99.6%, compared with 81% for cancer.[466]

What, then, does the future hold? Despite the challenges, some scientists anticipate a huge impact through delaying onset and progression of the disease to reduce the number of people reaching a severe stage.[467] Driven by recent drug trial successes, some researchers are even optimistic that treatment and prevention methods will be available in the next decade.[468] For example, recent studies have linked certain gene proteins with greater risk of developing cognitive impairments later in life.[469]

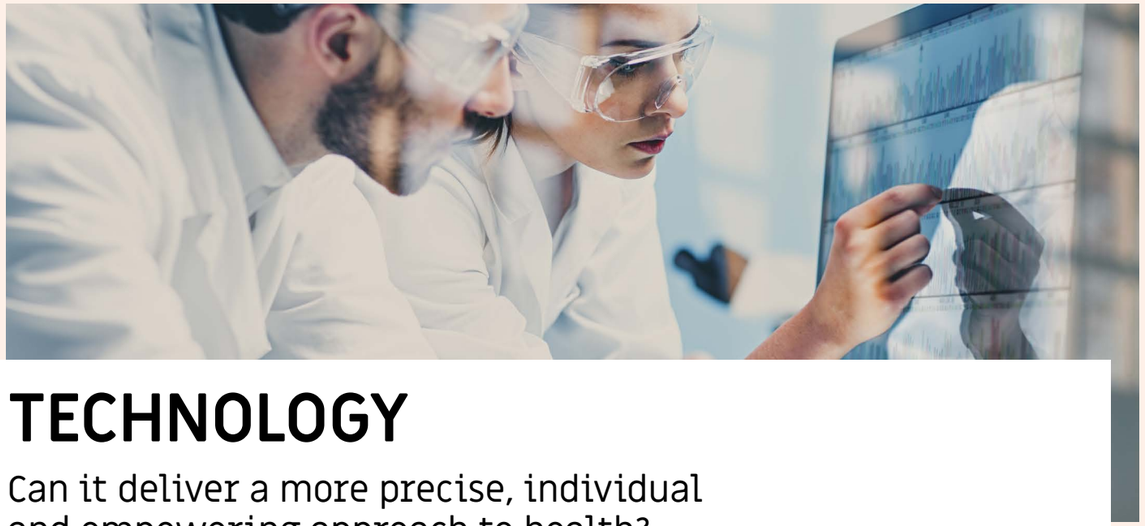
Looking even further ahead, will people be able to delay, or even escape, the process of ageing?[470] Philosophers may have once pursued eternal youth, but researchers now believe there are areas worth investigating, making regenerative therapies a priority for some research centers.

THE RISE OF NCDS

Today, NCDs kill more than 40 million people each year and it is estimated that they will cost the global economy more than USD 47 trillion in lost productivity by 2030.[471] In every country, health systems are struggling to respond to the growing needs of patients with NCDs. As the world ages, this is only going to get worse, disproportionately so in poor and impoverished populations.

NCDs do not only afflict maturing or aging populations. They are appearing in younger and younger populations, driven by lifestyle factors and modifiable risk behaviors: tobacco use, the harmful use of alcohol, physical inactivity, and unhealthy diets. In 2017, The Lancet reported a 10-fold increase in obesity levels among adolescents over the past four decades.[472]

How might we mitigate disease severity or delay onset? Many point to the need to invest in prevention, particularly focusing on young people. With more than 70% of the most common NCDs linked to behaviors that start in adolescence, it is an opportunity to shift the trajectory of disease. More than 80% of adults in the US first started smoking in their teens and there is strong evidence that shows if you are obese in your teens, you are more likely to be obese as an adult.



TECHNOLOGY

Can it deliver a more precise, individual and empowering approach to health?

Innovation in technology continues to influence society, and healthcare can expect both opportunities and challenges.

GENETICS AND PRECISION MEDICINE

Sixty years since the structure of DNA was discovered, understanding of the role of genes in health and disease has advanced enormously, alongside technologies that identify the genetic make-up of individuals.[473] These advances could shift the healthcare model from treatment based on generalizeddemographics to precision medicine, which matches patients with drugs targeting specific genetic drivers. Leading pharmaceutical companies have doubled investment in precision medicine in the last five years and a further increase is expected in the next five.[474] This would mean oncologists could use genetic tests to identify which treatments a tumor is likely to respond to, sparing patients from receiving treatment that may do more harm than good.[475] In 2017, for the first time, the US FDA approved a cancer treatment based on a common biomarker rather than the location in the body where the tumor originated.[476]

An emerging debate, likely to continue as precision medicine becomes widespread, concerns the market dynamics of genome medicines such as gene editing and gene therapy, which offer the promise of a 'one shot cure'. How might business models need to change as advances move the industry from a focus on disease and treatment to prevention and cures?[477]

> *Machine learning is mature enough to start accurately predicting medical events—such as whether patients will be hospitalized, how long they will stay, and whether their health is deteriorating despite treatments.*
>
> **Katherine Chou,**
> Google Brain team[490]

WEARABLE AND MOBILE DEVICES

Wearable devices are becoming a part of everyday life for some, collecting real-time data on biological and environmental changes.[478] Some 20 billion devices are already connected to the internet, expected to grow to 50 trillion by 2045.[479] How will having 20,000 times more digital information in 2025 than there is today impact health?[480] People will be more aware of their health than ever, able to measure signs such as heart rate or body mass index as well as be reminded about interventions such as taking insulin or increasing movement. This could increase treatment adherence and efficacy, and spur more personalized treatment. Privacy and trust, already challenged, will be vital to ensure patient data is not exposed to unnecessary risk or discrimination.[481]

Connected devices can also transform healthcare in lower resource settings. Mobile phones and mHealth solutions can extend care, new payment models, and health-related information to remote areas as well as monitor health services and consumption of vaccines and medicines.[482]

With wearables that may track symptoms, the pace of consumer engagement might accelerate. Social networks are poised to enable powerful customer engagement, allowing patients and health actors to interact in new ways. Information might be shared and disseminated through peer-to-peer support networks such as PatientsLikeMe and HealthUnlocked. How will consumer demand for transparent, convenient, and high-quality care grows challenge business models? Companies that offer meaningful and highly personalized solutions will succeed in this environment.[485]

ARTIFICIAL INTELLIGENCE (AI) AND SMART ROBOTS

When applied to data collected through connected devices, AI could benefit healthcare through increased productivity and improved product quality.[486] AI enabled machines could also perform administrative and clinical functions such as medical imaging, risk analysis and diagnosing health conditions. Deep learning could identify patterns in large data sets, revealing new linkages between genes and disease more rapidly than its human counterparts.[487] Some estimate that clinical health AI applications could save the US healthcare economy USD 150 billion annually by 2026.[488] Recognizing significant opportunities presented by AI, actors across the health ecosystem must also assess the appropriate roles of technology and establish standards to manage what to delegate to machines.[489]

COMMITMENT TO **FUTURE PROGRESS**

People are collectively healthier, living longer and better lives than 50 years ago.

Whatever the future may bring, the world depends on improved global health to continue to promote prosperity and enable human progress.

The R&D-based biopharmaceutical industry remains committed to innovate and partner to deliver better health for everyone, everywhere. Its unique role in bringing about the discovery of and access to life-saving and life-enhancing medicines and vaccines matters as greatly now as 50 years ago – or 50 years down the line.

Industry will continue to learn and evolve, appreciating now more than 50 years ago the power of partnership with actors across the health ecosystem. Patient needs – and the 2030 agenda set by the SDGs – unite those actors. Together they will seek to drive efforts that are sustainable in the long-term and integrated into broader health system strengthening.

IFPMA and its members are active in more than 300 global health partnerships in global health – from training tomorrow's scientists, to innovating to deliver access for underserved communities. Just a few of these collaborations underway shaping our shared future include:

- **Access Accelerated** is an industry-led partnership focused on improving care for NCDs in low-income and LMICs, starting with cancer and diabetes.[491]
- The **AMR Industry Alliance** is comprised of life sciences industry companies and associations. The partnership unites efforts to combat antimicrobial resistance through R&D, stewardship, access, and manufacturing.[492]
- **Patent Information Initiative for Medicines** (Pat-INFORMED) promotes the accessibility of patent information for health agencies tasked with procurement of medicines to be able to make more informed, smarter decisions.[493]
- With the **Centre on Global Health Security** at Chatham House and the **Global Health Centre** at the Graduate Institute, industry sponsors the **African Global Health Leaders Fellowship**, supporting the development of the next generation of public health leaders in Africa.[494]

For the last half century, IFPMA has served as an advocate for practices and policies that have spurred major health gains. It will continue to convene the industry and other actors, renewed in its commitment to future global health progress.

IFPMA

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