

Ten years in public health, 2007–2017: report by Dr Margaret Chan, Director-General, World Health Organization ISBN 978-92-4-151244-2

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By Dr Margaret Chan, Director-General, WHO

Ten years in public health 2007-2017 chronicles the evolution of global public health over the decade that I have served as Director-General at the World Health Organization.

This series of chapters evaluates successes, setbacks, and enduring challenges during my administration. They show what needs to be done when progress stalls or new threats emerge. The chapters show how WHO technical leadership can get multiple partners working together in tandem under coherent strategies. The importance of country leadership and community engagement is stressed repeatedly throughout the chapters.

Together we have made tremendous progress. Health and life expectancy have improved nearly everywhere. Millions of lives have been saved. The number of people dying from malaria and HIV has been cut in half. WHO efforts to stop TB saved 49 million lives since the start of this century. In 2015, the number of child deaths dropped below 6 million for the first time, a 50% decrease in annual deaths since 1990. Every day 19000 fewer children die. We are able to count these numbers because of the culture of measurement and accountability instilled in WHO.

The challenges facing health in the 21st century are unprecedented in their complexity and universal in their impact. Under the pressures of demographic ageing, rapid urbanization, and the globalized marketing of unhealthy products, chronic noncommunicable diseases have overtaken infectious diseases as the leading killers worldwide. Increased political attention to combat heart attacks and stroke, cancer, diabetes, and chronic respiratory diseases is welcome as a powerful way to improve longevity and healthy life expectancy. However, no country in the world has managed to turn its obesity epidemic around in all age groups. I personally welcome the political attention being given to women, their health needs, and their contributions to society. Investment in women and girls has a ripple effect. All of society wins in the end.

Lessons learned from the 2014 Ebola outbreak in West Africa catalysed the establishment of WHO's new Health Emergencies Programme, enabling a faster, more effective response to outbreaks and emergencies.

The R&D Blueprint, developed following the Ebola response, cuts the time needed to develop and manufacture new vaccines and other products from years to months, accelerating the



In a world facing considerable uncertainty, international health development is a unifying – and uplifting – force for the good of humanity.

development of countermeasures for diseases such as Zika virus. For example, in December 2016, WHO was able to announce that the Ebola vaccine conferred nearly 100% protection in clinical trials conducted in Guinea.

The chapters reveal another shared priority for WHO: fairness in access to care as an ethical imperative. No one should be denied access to life-saving or health-promoting interventions for unfair reasons, including those with economic or social causes. That principle is profoundly demonstrated in WHO's work on universal health coverage, which in the past decade has expanded from a focus on primary health care to the inclusion of UHC as a core element of the 2030 Agenda for Sustainable Development. Health has a central place in the global goals. Importantly, countries have committed to this powerful social equalizer. Universal health coverage reflects the spirit of the SDGs and is the ultimate expression of fairness, ensuring no one is left behind.

These chapters tell a powerful story of global challenges and how they have been overcome. In a world facing considerable uncertainty, international health development is a unifying – and uplifting – force for the good of humanity. I have been proud to witness this impressive spirit of collaboration and global solidarity.

Dr Margaret Chan, Director-General, WHO

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hree decades after the 1978 Health for All declaration, WHO called for a renewed focus on primary health care with the launch of the 2008 World Health Report. When countries sought guidance on financing health care, WHO commissioned a 2010 report on universal health coverage, a concept then pioneered as central to the Sustainable Development Goals and the ambition to leave no one behind.

The 1978 Declaration of Alma-Ata set out primary health care as the way to achieve health for all by the year 2000. It launched a revolutionary movement that did great good but eventually faltered, partly because it was so profoundly misunderstood. It was a radical attack on the medical establishment. It was a standoff between proponents of basic versus specialized care. It was hopelessly utopian; a selective approach, based on just a few inexpensive interventions that brought rapid results, had a better chance of success.

With its reliance on community health workers, it looked cheap: third-rate care for the Third World. For some countries, a declaration associated with a Soviet city raised suspicions that the call was a veiled attempt to push governments towards socialized medicine.

By the mid-1990s, a WHO review of changes in the development landscape bleakly concluded that the goal of health for all by 2000 would not be met. The emergence of HIV/AIDS, the related resurgence of tuberculosis, and an increase in malaria cases moved the focus of international public health away from broad-based programmes and towards the urgent management of high-mortality emergencies.

By the start of the 21st century, when the Millennium Development Goals were put forward as the overarching framework for development cooperation, the epidemics of AIDS, tuberculosis, and malaria were raging out of control. The yearly number of preventable maternal and childhood deaths had been stuck above 10 million for decades. Emergency action was needed.

The global health initiatives that were established to pursue the health-related goals eventually had a tremendous impact, readily measured in the number of interventions delivered, deaths averted and lives prolonged. All of these initiatives depended on well-functioning health systems to deliver medical commodities, yet rarely made the strengthening of health systems an explicit or funded objective. In many cases, weak public health infrastructures were simply



A revitalization of primary health care was put forward as the best - and most affordable way to get health systems back on track.

bypassed through the construction of parallel systems for the procurement and distribution of interventions, for laboratory services, and for budgeting, financing and reporting.

Some warning signals emerge

By 2005, some rumblings of discontent could be heard. Stalled progress towards the health-related MDGs forced a hard look at the results of decades of failure to invest in fundamental health infrastructures, services and staff. In the long term, powerful interventions and the money to purchase them could not buy better health outcomes in the absence of efficient systems for delivery.

The response to the AIDS epidemic, regarded as the most devastating of the three emergencies, was drawing staff away from broad government-funded health programmes, undermining their ability to provide essential services, including preventive care. With systems of financial protection in disarray, out-of-pocket payments for essential care were driving around 100 million people below the poverty line each year – a bitter irony at a time when the alleviation of poverty was the overarching MDG objective.

Opportunities for operational efficiency were being missed. Overlapping diseases were managed by separate initiatives. Single diseases were often managed by multiple initiatives, sometimes using different technical strategies. Duplication of efforts and fragmentation of services were frequent complaints. Some countries felt that their own national health priorities had been crowded out. Who actually owned these initiatives?

The burden on affected countries was heavy. Transaction costs were high. To satisfy donor requirements, some countries were required to issue yearly reports on as many as 600 health indicators. The need to make aid more effective became an urgent issue formally addressed in a series of high-level meetings and calls for major reforms.

Proposed changes took exclusive blame for ineffective aid away from recipient countries and made donor policies and practices equally responsible. Reforms called for greater harmonization of efforts, accountability for results, and alignment with national priorities, systems, and procedures in ways that helped build capacity. **Recipient countries made it clear: they wanted capacity, not charity.** Strengthened national capacity was the best exit strategy for development assistance.

The 2008 World Health Report: back to the basics

Against this background, WHO retrieved its brand name in 2007, when conferences in all six WHO regions unanimously called for a return to the principles and approaches of primary health care as the best way to organize health services. In that same year, the International Health Partnership was established to put the principles of effective aid into practice. The Partnership

encouraged wide support for a single national health strategy, a single monitoring and evaluation framework, and a strong emphasis on mutual partner accountability. It further encouraged the channelling of assistance through existing systems and structures as a way to build capacity.

Significant support for change came in 2008, when the World Health Report on *Primary health care – now more than ever* was published to mark the 30th anniversary of the Alma-Ata declaration. The report critically assessed the way that health care was organized, financed, and delivered in rich and poor countries alike, and found striking inequalities in access to care, health outcomes, and what people had to pay for care.

Data painted a disturbing picture of ailing health systems that had lost their focus on fair access to care, their ability to invest resources wisely, and their capacity to meet the needs and expectations of people. Fair access to care had particular resonance with lessons learned from the AIDS epidemic. With the advent of antiretroviral therapy, an ability to access medicines and services became equivalent to an ability to survive for many millions of people.

A revitalization of primary health care was put forward as the best – and most affordable – way to get health systems back on track. When countries at the same level of economic development were compared, those with health care organized around the tenets of primary health care produced a higher level of health for the same investment. In the largest sense, the report was a call to again put health equality on the international political agenda. A move towards universal health coverage was promoted as the core strategy for tackling inequalities.

The 2008 report of the Commission on the Social Determinants of Health increased the momentum for change with another set of arguments. Deeply concerned about the world's growing inequalities, the Commission found abundant evidence that the true upstream drivers of ill health come from factors in the social environment, like low incomes, little education, limited employment options, and poor living and working conditions.

The message was optimistic: social environments are shaped by policies, which makes them amenable to change. In the final analysis, the distribution of health within a population is a matter of fairness in the way economic and social policies are designed. In its traditional concern with prevention, public health had much to gain when the narrow biomedical approach to health was extended to include root causes of ill health that reside in non-health sectors. This was new thinking that viewed health as an outcome of social determinants and not merely the result of biomedical interventions.

Not surprisingly, the Commission championed primary health care as a model for a health system that acts on the underlying social determinants of health. Its emphasis on the need to extend prevention to non-health sectors was well-received at a time of growing alarm about the rise of chronic noncommunicable diseases.

Good timing in a very different world

This time around, the call to reorient health systems around primary health care resonated well with some stark and sharply defined concerns. An approach considered revolutionary three decades earlier had secured firm relevance in a very different world. Progress towards the health-related MDGs had stalled. Many attributed the poor progress, especially for maternal and child health, to weak health systems.

The evidence base was strong. Recommendations in the 2008 World Health Report could draw on 30 years of experience in the implementation of primary health care in a diverse range of countries. Rigorous studies confirmed the value of community participation, especially in contributing to sustained reductions in neonatal and maternal deaths. The contribution of community health workers was better defined, including the interventions they could best deliver and the tasks they could best perform. Moreover, evidence showed that this cadre of workers needed to be trained and paid. Several models for shorter durations of training provided an effective strategy for quickly scaling up the workforce.

Large studies coordinated by WHO demonstrated that increasing access to services would not reduce mortality in the absence of a firm emphasis on the quality of care. WHO and its partners no longer supported the training of traditional birth attendants as a route to better maternal health; research indicated that deaths would not go down until more women had access to skilled birth attendants and emergency obstetric care.

In addition, mounting evidence showed that programmes focused on delivering a single intervention, like vaccines, could be expanded to deliver others, thus operating as a stepping stone for building integrated health services. Research further showed that integration of common management functions, such as essential drugs, transport, supervision, and information, for all programmes could be another early step towards providing integrated and comprehensive care.

Simultaneously, the world economic order was abruptly shaken by the 2008 financial crisis, which proved highly contagious in a world of radically increased interdependence. It was also profoundly unfair: even countries that had taken few risks and managed their economies well were severely affected. As the crisis spread, the world economic outlook seemed to move from prosperity to austerity almost overnight.

That shock added to the crisis in health care, characterized by increasing demand, rising costs, and a return to hospital-based curative care. The austere economic outlook brought back some familiar risks. When money is tight, donors and parliamentarians want quick and measurable results, best delivered by a commodity-driven approach. The strengthening of health systems takes time and is notoriously difficult to measure. In a climate of deepening austerity, could the revived enthusiasm for primary health care be sustained?

A series of research papers published in *The Lancet* concluded that primary health care offered global health a lifeline and a renewed unity of purpose. It was increasingly viewed as the best way to reduce waste and improve efficiencies in service delivery, get the incentives for quality performance right, contain costs in well-off countries, and implement cost-effective interventions in low-resource settings.

The firm emphasis on fairness and social justice spoke to grave concerns about the world's growing inequalities, in income levels, opportunities, and health outcomes, as a source of social unrest and a potential security threat. The deep-seated focus on prevention and the long-standing call for multisectoral action attracted renewed interest as the best way to tackle the growing burden of chronic diseases.

In the midst of this positive reception, several proponents reminded health officials that universal health coverage, the foundational principle of primary health care, would be an even more powerful corrective strategy. That strategy took shape in 2010.

Universal health coverage: the ultimate expression of fairness

The 2010 World Health Report, on *Health system financing: the path to universal coverage*, argued for an even more fundamental reorientation of health systems. The report was commissioned by the WHO Director-General in response to a need, expressed by rich and poor countries alike, for practical guidance on ways to finance health care. The objective was to transform the evidence, gathered from studies in a diversity of settings, into a practical menu of options for raising sufficient resources and removing financial barriers to access, especially for the poor.

It gave policy makers a choice. At a time of rising costs, as populations age, chronic diseases increase, and new and more expensive treatments become available, countries should look first for opportunities to reduce waste and inefficiency instead of looking for ways to cut spending.

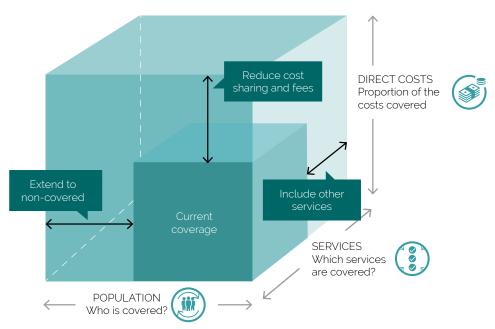
The report estimated that from 20% to 40% of all health spending was currently wasted and, in a key achievement, pointed to ten specific areas where better policies and practices could increase the impact of expenditures, sometimes dramatically. The overarching message was one of optimism. All countries, at all stages of development, could take immediate steps to move towards universal coverage. Countries that adopt the right policies can achieve vastly improved service coverage and protection against financial risk for any given level of expenditure.

The optimism was not overstated. If the call to revitalize primary health care was warmly welcomed, the response to the WHO push for universal coverage bordered on the sensational. Medical journals organized special issues devoted to exploring its potential and significance in the broader economic and political context. A commentary in *The Lancet* described the movement towards universal health coverage as a "great transition" that is "sweeping the globe, changing how health care is financed and how health systems are organized."

International conferences were held, and summits of health ministers added universal coverage to their agendas. Civil society organizations rallied, offering joint statements of support. Within two years, more than 70 countries, at all level of development, had requested WHO technical support in moving their health systems towards universal coverage. By that time, the 2010 World Health Report had been downloaded nearly 700 000 times.

In 2012, the United Nations General Assembly adopted a resolution that endorsed the goal of universal health coverage and gave it a high place on the development agenda. The resolution was sponsored by more than 90 countries, from every region of the world, and adopted by consensus. In a move described by some as "momentous", the resolution urged Member States to develop health systems that avoid significant direct payments at the point of care. As stated, mechanisms for pooling risk should be introduced to avoid catastrophic health expenditures that drive households into poverty.

The dimensions of the universal health coverage cube



Source: WHO

An approach that makes excellent economic sense

Further support came from leading economists. Jeffrey Sachs argued against the "lazy thinking" that continued to justify user fees as a protection against the overuse of health services. As he noted, for the very poor, no price is affordable. **Even nominal user fees can lead to massive exclusion of the poor from life-saving health services.** Significant progress against malaria began only after WHO policy called for the massive free distribution of insecticidal nets.

Nobel laureate Amartya Sen explained why universal health coverage was an "affordable dream", even for very poor countries. As he observed, **many poor countries have shown that basic**

health care for all can be provided at a remarkably good level at very low cost if society, including its political and intellectual leadership, shows high-level commitment.

Sen soundly refuted the common assumption that a poor country must first grow rich before it is able to meet the costs of health care for all. As he argued, health care is labour intensive everywhere. A poor country with low wages may have less money to spend on health, but it also needs to spend less to provide these labour-intensive services.

Finally. Sen explained how universal health coverage provides greater equality, but also much larger overall health gains since it manages the most easily curable diseases and the prevention of easily avoided illnesses that are otherwise left out when the system relies on out-of-pocket payments.

In September 2015, on the eve of the United Nations General Assembly that would adopt the 2030 Agenda for Sustainable Development, leading economists from 44 countries called on global policy makers to prioritize a pro-poor pathway to universal health coverage as an essential pillar of development. As they noted, "Health systems oriented towards universal health coverage, immensely valuable in their own right, produce an array of benefits: in times of crisis, they mitigate the effect of shocks on communities; in times of calm, they foster more cohesive societies and productive economies."

Firmly on the agenda

The inclusion of a target for universal health coverage in the 2030 Agenda for Sustainable Development articulates the very spirit of the agenda's transformational ambition: leave no one behind. It is the unifying platform for delivering on all other health targets. It is the ultimate expression of fairness and one of the greatest social equalizers among all policy options. It contributes to social cohesion and stability – assets in every country.

The WHO Director-General's statement, that "universal health coverage is the single most powerful concept that public health has to offer", looks increasingly accurate. At a time when policies in so many sectors are actually increasing social inequalities, it is especially gratifying to see health lead the world towards greater fairness in ways that matter to each and every person on this planet.



early 2 billion people have no access to basic medicines, causing a cascade of preventable misery and suffering. Since the landmark agreement on the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, WHO and its partners have launched a number of initiatives that are making market forces serve the poor. The WHO prequalification programme is now firmly established as a mechanism for improving access to safe, effective and quality-assured products.

WHO has struggled to improve access to medicines throughout its nearly 70-year history. and rightly so. Good health is impossible without access to pharmaceutical products. Universal health coverage depends on the availability of quality-assured affordable health technologies in sufficient quantities.

Lack of access to medicines causes a cascade of misery and suffering, from no relief for the excruciating pain of a child's earache, to women who bleed to death during childbirth, to deaths from diseases that are easily and inexpensively prevented or cured. Lack of access to medicines is one inequality that can be measured by a starkly visible yardstick: numbers of preventable deaths.

Efforts to improve access to medicines are driven by a compelling ethical imperative. People should not be denied access to life-saving or health-promoting interventions for unfair reasons. including those with economic or social causes. Millions of yearly childhood deaths from diseases that could have been prevented or cured by existing medical products would be unthinkable in a fair and just world.

The world is neither. An estimated two billion people have no access to essential medicines, effectively shutting them off from the benefits of advances in modern science and medicine.

A complex - and vexing - problem

In recent years, the need for uninterrupted supplies of medicines has become more urgent. The importance of preventing stockouts has been underscored by the advent of antiretroviral therapy for HIV, the long duration of treatment for multidrug-resistant tuberculosis, the ability



When prices are so low they preclude profits, companies leave the market.

of artemisinin-combination therapies to prevent malaria deaths if administered quickly, and the need for life-long treatment of chronic conditions such as hepatitis B infection and diabetes.

Lack of access to medicines is one of the most complex – and vexing – problems that stand in the way of better health. The agenda for improving access is exceptionally broad. Affordability is the cornerstone of access, but many other factors also determine whether people get the medicines they need.

Gaps in local health systems and infrastructures hamper the delivery of medicines to millions of people. Access also depends on procurement practices, tax and tariff policies, mark-ups along the supply chain, and the strength of national drug regulatory authorities. Apart from being affordable and of good quality, medicines must also be safe; a system for pharmacovigilance needs to be in place. Secure supply chain management is likewise needed to protect populations from substandard or falsified medical products.

International conventions for the control of narcotic drugs can be another barrier to access. They place a dual obligation on governments: to prevent abuse, diversion and trafficking, but also to ensure the availability of controlled substances for medical and scientific purposes. Many controlled substances play a critical role in medical care, for the relief of pain, for example, or use in anaesthesia, surgery, and the treatment of mental disorders. Unfortunately, the obligation to prevent abuse has received far more attention than the obligation to ensure availability for medical care. WHO estimates that 80% of the world's population lives in countries with zero or very little access to controlled medicines for relieving moderate to severe pain.

Efforts to improve access are complicated by a number of economic issues. Affordability matters for households and health budgets. WHO estimates that up to 90% of the population in low- and middle-income countries purchases medicines through out-of-pocket payments. If a household is forced to sell an asset, like the family cow, or take its children out of school, this payment can be the final nail in the coffin that buries the family in intergenerational poverty. This is the pathology of poverty when no forms of social protection, such as those provided by universal health coverage, are available and even low-cost generic products are a heavy financial burden.

For health budgets, staff costs usually absorb the biggest share of resources, with the costs of drug procurement following closely behind. The part of the budget devoted to medicines varies significantly according to a country's level of economic development. Medicines account for 20% to 60% of health spending in low- and middle-income countries, compared with 18% in countries belonging to the Organization for Economic Co-operation and Development.

One of the most daunting economic issues comes from the fact that the research-based pharmaceutical industry is a business, and a big one. Multinational pharmaceutical companies, concentrated in North America, Europe and Japan, are powerful economic operators. Economic power readily translates into political power. When ways to improve access are negotiated at WHO, a familiar polarizing tension surfaces. Which side should be given primacy, economic interests or public health concerns?

As many have argued, letting commercial interests override health interests would lead to even greater inequalities in access to medicines, with disastrous life-and-death consequences. At the same time, the pharmaceutical industry is a business, not a charity. **When prices are so**

low they preclude profits, companies leave the market – and leave a hole in the availability of quality products, as happened with anti-snakebite venom.

Economic factors shape another pressing public health concern. Many diseases mainly prevalent in poor populations have no medical countermeasures whatsoever, or only old and ineffective ones. In other cases, access suffers from the lack of products adapted to perform well in resource-constrained settings with a tropical climate.

The patent system, with its market-driven R&D incentives, has historically failed to invest in new products for poor populations with virtually no purchasing power, resulting in a paucity of R&D driven by the unique health needs of the poor. Apart from having few new products that address their priority diseases, the poor are punished in a second way: the common practice of recouping the costs of R&D through high prices protected by patents means that those who cannot pay high prices do without.

Recent shifts in the poverty map introduces another set of problems. An estimated 70% of the world's poor now live in middle-income countries which are losing their eligibility for support from mechanisms like the Global Fund to Fight AIDS, Tuberculosis and Malaria and Gavi, the Vaccine Alliance. Will governments step in to make up for the shortfall in access to medicines and vaccines? If not, vast numbers of poor people living in countries that are rapidly getting rich will be left to fend for themselves.

Keeping substandard and falsified products out of the supply chain

WHO has recently stepped up its efforts to combat yet another threat to the life-saving and health-promoting power of medicines: the health harms caused by substandard and falsified medical products. These products flood the markets in countries with weak drug regulatory authorities, or circumvent regulatory controls through sales via the internet. The complex web that characterizes the global production and distribution of pharmaceutical products, including a long and convoluted supply chain, places all countries at risk. **Products that enjoy lucrative commercial markets are particularly susceptible to falsification**, as are badly needed medicines and vaccines that are in short supply. Substandard and falsified medicines not only steal income from consumers who pay for products that have little or no medical value. They cause harm by not resolving a medical problem and have sometimes caused hundreds of deaths, especially when the products contain toxic ingredients.

The WHO Global Surveillance and Monitoring System for Substandard and Falsified Medicines was launched in West Africa in July 2013. Since then, more than 400 regulatory personnel from 126 countries have been trained to use this system for the rapid reporting of substandard or falsified products. Reports from national regulatory personnel are immediately uploaded to a secure WHO website. If investigation confirms harm to health, WHO responds within 24 hours, providing coordination and technical support in the event of an emergency.

When warranted, WHO issues a global Medical Product Alert to warn countries and populations of the existence of a dangerous medical product. The alerts, which include photographs of falsified products, also encourage increased vigilance and regulatory action to protect populations and supply chains. In the past two years, alerts were issued for falsified yellow fever vaccines, hepatitis C medicine, meningitis vaccines, anti-malaria medicines, and treatments for epilepsy. Information gathered by the surveillance and monitoring system can have broader policy implications. For example, many anti-malaria tablets, sold at street markets in endemic countries, contain no active pharmaceutical ingredients at all.

Building on previous innovations

In 1977, on the eve of the Alma-Ata conference on primary health care, WHO issued its first Model List of Essential Medicines as the Organization's signature contribution to rational drug procurement. The concept that a limited number of inexpensive medicines could meet the priority health needs of a country's population was considered revolutionary at the time. Historically, the model lists gave priority to effective medicines that offer clear clinical benefits, while also paying attention to their costs and impact on health budgets. That position changed in the 1990s with the advent of expensive yet highly effective antiretroviral therapies for HIV.

It changed again in 2015, after new medicines came on the market that transformed hepatitis C from a barely manageable condition to one that could be safely and easily cured by all-oral treatment options. Those new direct-acting antivirals created an unprecedented dilemma for public health: the arrival of breakthrough drugs with tremendous potential to treat millions of patients with a potentially deadly liver infection, but at a price considered unaffordable, even in high-income countries.

The 2015 list also included 16 drugs, including some with high prices, which can increase survival times for common cancers, such as breast cancer, or can successfully cure up to 90% of patients with rare cancers, such as leukaemia and lymphoma. The list further included second-line drugs for the treatment of multidrug-resistant tuberculosis.

WHO anticipated that including these sometimes extremely expensive medicines in the list would stimulate efforts to get prices down through policies such as tiered pricing, voluntary and compulsory licensing, pooled procurement, and bulk purchasing. WHO was specifically asked to help countries negotiate lower prices and to rapidly introduce prequalified generic formulations, especially for the hepatitis C antivirals. In several countries, prices dropped significantly for hepatitis C antivirals, but less so for the newly listed cancer drugs. Of the options available, WHO prequalification of generic products held considerable promise as a proven way to increase affordable access.

The concept of essential health technologies evolved further in 2017, when the Expert Committee on the Selection and Use of Essential Medicines approved the establishment of a complementary Model List of Essential Diagnostics. For essential medicines, inclusion in the model list was often necessary before large funders, like ministries of health, funding agencies, and insurers, would invest in large-scale procurement of a given medicine. The establishment of a list of essential

diagnostics is expected to perform a similar role in guiding rational procurement decisions and improving population access to tests that will have the biggest impact on their health.

Introduced in 2001, the WHO Prequalification Programme was equally revolutionary. The programme responded to an urgent need. Generic manufacturers, largely concentrated in India, were producing large quantities of low-cost treatments for HIV, tuberculosis, and malaria, but those products were coming on the market without authorization from a stringent regulatory authority. The WHO programme stepped in to meet the need for stringent assessment by sending expert teams to inspect manufacturing facilities and ensure compliance with WHO Good Manufacturing Practices and testing to see if the quality and efficacy of generic products matched those of patented originator products.

The programme clearly satisfied an urgent and unmet need at a time when the three epidemics were still rapidly expanding. It eventually extended its remit to include the prequalification of active pharmaceutical ingredients and drug-testing laboratories. Today, the WHO "prequalified" stamp of approval means that medicines and vaccines are considered safe, effective and of high quality, and thus recommended for bulk purchase.

After years of stepwise improvements urged by WHO, China's National Regulatory Authority was assessed as fully functional for the regulation of vaccines in 2011, when WHO certified that the authority's oversight of vaccine quality met rigorous international standards. That assessment paved the way for the prequalification of individual vaccines, and opened the door to exports from the country that had the largest vaccine manufacturing capacity in the world.

The first vaccine made in China, for Japanese encephalitis, was prequalified by WHO in 2013. The vaccine was not only less expensive than vaccines already on the market, it was also a better product. The vaccine is easier to administer, being effective after a single dose, and can be safely given to infants, greatly simplifying the logistics of vaccine delivery and cutting costs even further. The prequalification of this vaccine by WHO was welcomed as a true game-changer for a disease that is the leading viral cause of disability in Asia. Japanese encephalitis kills or causes neurological disabilities in 70% of those infected.

In February 2017, WHO assessed India's National Regulatory Authority as fully functional, reporting 100% compliance with a roadmap, set out by WHO in 2012, for strengthening the national authority. That seal of approval is expected to go a long way towards securing international confidence in medical products manufactured in India, often referred to as the "pharmacy of the world".

The programme's major contribution to the availability of life-saving medical products is now widely recognized. The initiative deserves much credit for the fact that more than 18 million people living with HIV in low- and middle-income countries have seen their lives turned around by access to antiretroviral therapy. It has had other successes as well. By allowing smaller manufacturers producing quality products to compete on an equal footing with multinational companies, it has increased supplies, improved their predictability, and used competition to get prices down, sometimes dramatically.

Less well-known is the programme's contribution to capacity building. It conducts in-country training programmes, lets regulators in developing countries learn from mature regulatory authorities, and uses expert inspections as an additional training and corrective tool. The programme

also operates a system of rotational fellowships at WHO for hands-on learning. In these ways, WHO helps countries move towards self-sufficiency in their regulatory capacity, also when serving the domestic market.

Partnerships: another route to new products

Public-private partnerships are the most visible manifestation of the power of collaboration to promote R&D for diseases that predominantly affect the poor. Products developed through these partnerships nearly always have clear and transparent strategies to ensure access, providing the best examples of specific features that can ensure broad and affordable coverage. Some of these partnerships have been remarkably successful.

The Meningitis Vaccine Project, coordinated by WHO and PATH with substantial funding from the Bill and Melinda Gates Foundation, successfully developed a new conjugate vaccine for use in Africa's meningitis belt. It is arguably the best illustration of the ability of public-private partnerships to attract broad-based collaboration, and the best demonstration of the unique benefits of doing so.

A consortium of academics and scientists developed the vaccine. Technology was transferred from the US and the Netherlands to the Serum Institute of India, which agreed to manufacture the vaccine at the target price of 50 cents per dose. African scientists contributed to the design of study protocols and conducted the clinical trials. Canada assisted the Indian National Authority in regulatory approval, and WHO pre-qualified the vaccine using accelerated procedures.

The vaccine, developed in record time at one-tenth the cost of a typical new vaccine, was tailor-made for an African need, priced for Africa, and developed with hands-on support from African scientists. For once, Africa was the first to receive a product that was the best that the world, working together, could offer.

The impact has been significant. Since the vaccine's launch at the end of 2010, more than 230 million people in 16 countries in Africa's meningitis belt have been vaccinated against meningococcal meningitis serogroup A, with support from Gavi and the Bill and Melinda Gates Foundation. Given the added impact of herd immunity, the recurring outbreaks of meningitis A that devastated 26 African countries for decades have now been virtually eliminated.

Following the Ebola outbreak in West Africa, WHO convened a series of expert consultations to develop a blueprint for the expedited development and regulatory approval of new medical countermeasures during public health emergencies. By setting up collaborative models, standardized protocols for clinical trials, and pathways for accelerated regulatory approval in advance, the blueprint aimed to cut the time needed to develop and manufacture candidate products from years to months. One of these consultations led to the establishment of the Coalition for Epidemic Preparedness Innovations, announced in January 2017 with initial funding of nearly \$500 million. The Coalition was further guided by a new WHO list of priority pathogens that have the potential to cause severe epidemics yet have no vaccines to slow their spread.

The Coalition is building a new system to advance the development of safe, effective and affordable vaccines, ensuring that price is not a barrier to access for populations most in need – a vital insurance policy against the growing threat from emerging and re-emerging diseases. Three diseases from the WHO list of priority pathogens have been initially targeted: Lassa fever, Nipah virus disease, and the Middle-East Respiratory Syndrome, or MERS. The Coalition is pursuing a proactive ("just in case") and accelerated ("just-in-time)" vaccine development strategy for epidemic threats that moves vaccine candidates through late preclinical studies to proof of concept and safety in humans before epidemics begin, so that larger effectiveness trials can begin swiftly during an outbreak and small stockpiles are ready for potential emergency use. The strategy is also building technical platforms and institutional capacities that can be rapidly deployed against new and unknown pathogens.

The Global Antibiotic Research and Development Partnership is another new initiative established to develop and deliver new antibiotic treatments with prices fixed to be sustainably affordable. Initiated in May 2016 as a collaborative project between WHO and the Drugs for Neglected Diseases initiative, the antibiotic R&D partnership responds to the call in WHO's Global Action Plan on Antimicrobial Resistance for public-private partnerships designed to develop new antimicrobial agents and diagnostics. The partnership is supported by initial seed funding and pledges of \$5.33 million from the governments of Germany, the Netherlands, South Africa, Switzerland and the UK as well as from the medical charity Médecins Sans Frontières.

A Scientific Advisory Group is overseeing the portfolio of priority R&D projects. Initial priorities include a new first-line antibiotic for the treatment of neonatal sepsis and a new second-line treatment for managing infants with drug-resistant infections. Antimicrobial resistance is a major factor determining clinical unresponsiveness to treatment and rapid evolution of infections to sepsis and septic shock. WHO estimates that around 214 000 yearly neonatal deaths due to sepsis worldwide can be attributed to resistant pathogens. A second initial project aims to recover data, trial results and assets from R&D projects that were abandoned as large pharmaceutical companies closed down their work on antibiotics. The partnership views this project as a bridging measure aimed at recovering urgently needed replacement products while the search for new classes of antibiotics is being pursued. A third project will give urgent attention to new antibiotics to treat gonorrhoea, a widespread disease that may soon become untreatable as it develops resistance to all existing classes of antibiotics.

High ambitions enter a highly contentious area

While all of these initiatives are doing great good, they address only pieces of a much bigger – and deep-seated – problem: the way the patent system operates to preferentially stimulate innovation for wealthy markets, establish a 20-year minimum monopoly on high prices, and leave the poor – and their vast health needs – abandoned by the wayside. A 2002 WHO document expressed the situation well: "A significant proportion of the world's population, especially in developing countries, has yet to derive much benefit from innovations that are commonplace elsewhere."

WHO's approach to access issues became far more ambitious in 2006, when the WHO Commission on Intellectual Property, Innovation and Public Health issued its report. The Commission concluded that, while governments bear much responsibility, WHO must take the lead in promoting more sustainable funding mechanisms to stimulate innovation in cases where intellectual property acts as a barrier to access to medicines.

In line with that conclusion, the report urged WHO to "develop a global plan of action to secure enhanced and sustainable funding for developing and making accessible products to address diseases that disproportionately affect developing countries." WHO Member States promptly acted on that advice.

Two years later, after tense and sometimes heated negotiations, the World Health Assembly approved the Organization's first Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property, an achievement immediately hailed as a milestone. WHO had taken a daring step into the potential minefield of the patent regime, with major implications.

As one of its strengths, the strategy and action plan tackled the need for innovation and affordable access simultaneously. The resulting text did indeed contain some breakthrough proposals. It raised the prospect of managing intellectual property in a more responsible manner that maximized needs-driven innovation and promoted access to affordable medical products. It called for exploration of new incentive schemes that would delink the costs of R&D from the price of medical products. Financial prizes for R&D milestones or bringing a product to market were put forward as one way of doing so.

And it scolded, drawing attention to the practice, often embedded in trade agreements, of stipulating more extensive intellectual property protection than required by the World Trade Organization's Agreement on Trade-related Aspects of Intellectual Property Rights – the so-called TRIPS-plus measures. Commonly used measures include extending the term of a patent longer than the 20-year minimum, introducing provisions that limit the use of compulsory licenses, and requiring data exclusivity, which blocks market entry by generic manufacturers. WHO was unquestionably taking a stand in contentious territory.

With an agreed strategy and action plan in hand, the next step was to finance its implementation. As requested, WHO appointed expert working groups to explore innovative proposals for financing and coordinating R&D. The report of the Consultative expert working group, issued in 2012, critically and systematically assessed 15 proposals for financing R&D and recommended five as best meeting its established criteria: a binding R&D convention or framework, pooled funds, direct grants to companies, milestone prizes and end prizes, and patent pools.

While the experts believed the time was right to initiate negotiations for a binding convention, Member States disagreed. By 2012, the impact of the 2008 financial crisis was being felt almost universally. The proposal to negotiate a binding convention did not resonate well in a climate of austerity. Governments were reluctant to accept any new instrument that committed them to substantial and sustained financial support.

During discussions of the report in subsequent sessions of the World Health Assembly, WHO was asked to pursue several recommendations: to establish an R&D observatory, to appoint an expert committee to advise on R&D priorities and means of coordination, to elaborate a mechanism

for the voluntary pooled funding of R&D, and to conduct demonstration projects for designated diseases of the poor. The latter initiative was crippled by a significant funding gap.

The proposal to negotiate a binding R&D convention was revived in 2016, when the UN Secretary-General's *High-level panel on access to medicines* issued its report. That report also drew attention to the fact that many countries were not using fully the flexibilities under the TRIPS Agreement, for reasons ranging from capacity constraints to undue political and economic pressure from states and corporations. As the report noted, "Political and economic pressure placed on governments to forgo the use of TRIPS flexibilities violates the integrity and legitimacy of the system of legal rights and duties created by the TRIPS Agreement, as reaffirmed by the Doha Declaration."

WHO works closely with the World Trade Organization, the World Intellectual Property Organization, and other UN agencies to support the unimpeded use of measures that can improve access, such as local production, giving least-developed countries a transition period, implementing patentability criteria that reward only genuinely innovative discoveries, and compulsory licensing. On request, WHO provides direct technical support to countries that intend to make use of these flexibilities.

Improving industry behaviours

By entering what had long been forbidden territory and publicly asking some hard questions, WHO opened up opportunities for others to act in novel ways.

The Access to Medicine Index, launched in 2008 and published every two years since, holds the world's 20 leading research-based pharmaceutical companies accountable for making their products more accessible in low- and middle-income countries. The index gives particular attention to problematic industry behaviours identified in the WHO global strategy and action plan. WHO experts serve on the review committee and technical subcommittees.

Under public scrutiny, the behaviour of the pharmaceutical industry has progressively improved in some, though not all, ways. The 2016 index shows that intellectual property can indeed be managed in a more responsible way. Access-oriented approaches to intellectual property management include responsible patenting policies, transparency about existing patents, and a willingness to engage in non-exclusive voluntary licensing. On the negative side, the index exposed continued lobbying for TRIPS-plus measures and legislation, the breaching of laws or codes relating to corruption and unethical marketing, and several blatant instances of company misconduct. On balance, though, the situation is improving. Many of the problems addressed in the WHO global strategy and action plan have captured industry's attention and stimulated remedial action.

The 2016 Access to Medicines Index gave high marks to companies that have negotiated licenses for antiretrovirals and hepatitis C medicines through the Medicines Patent Pool. The Medicines Patent Pool was set up in 2010 to improve access to antiretroviral therapy in low- and middle-income countries, with a remit later expanded to include hepatitis C and tuberculosis treatments.

It is sponsored and fully funded by UNITAID, a drug purchasing facility that draws substantial and sustainable funding from a levy on airline tickets. Patent pools were recommended in the WHO global strategy and action plan and strongly endorsed by the expert groups on the innovative financing of R&D.

Since the first company joined the pool in 2012, it has operated as an independent driver of access-oriented licensing in the pharmaceutical industry. It is transparent as well as effective. Companies that engage with the patent pool are obliged to disclose information about their patents, which the pool then makes public. Data exclusivity waivers are included in all agreements. Through the patent pool mechanism, licensing by patent holders has accelerated, with broader geographical coverage, greater competition, and improved terms and conditions, enabling more robust competition.

The patent pool works well because it offers something for everyone. Patent holders are rewarded with fair royalties that accumulate as low-priced generics bring a surge in demand. Generic manufacturers benefit from the vastly simplified procedure of dealing with a single negotiating body, plus the ability to enter the market before patents expire. They further benefit from the waiving of data exclusivity and the market clarity that comes when details about patents are made publicly accessible.

Innovation is facilitated by making it possible to produce fixed-dose combinations using medicines from different patent holders. Paediatric formulations are encouraged by an obligatory waiving of all royalties on all paediatric medicines. As companies have licensed their best-inclass medicines to the patent pool, patients benefit from widespread geographical access to affordable quality-assured medicines that are the best the world has to offer.

A model for fair pricing

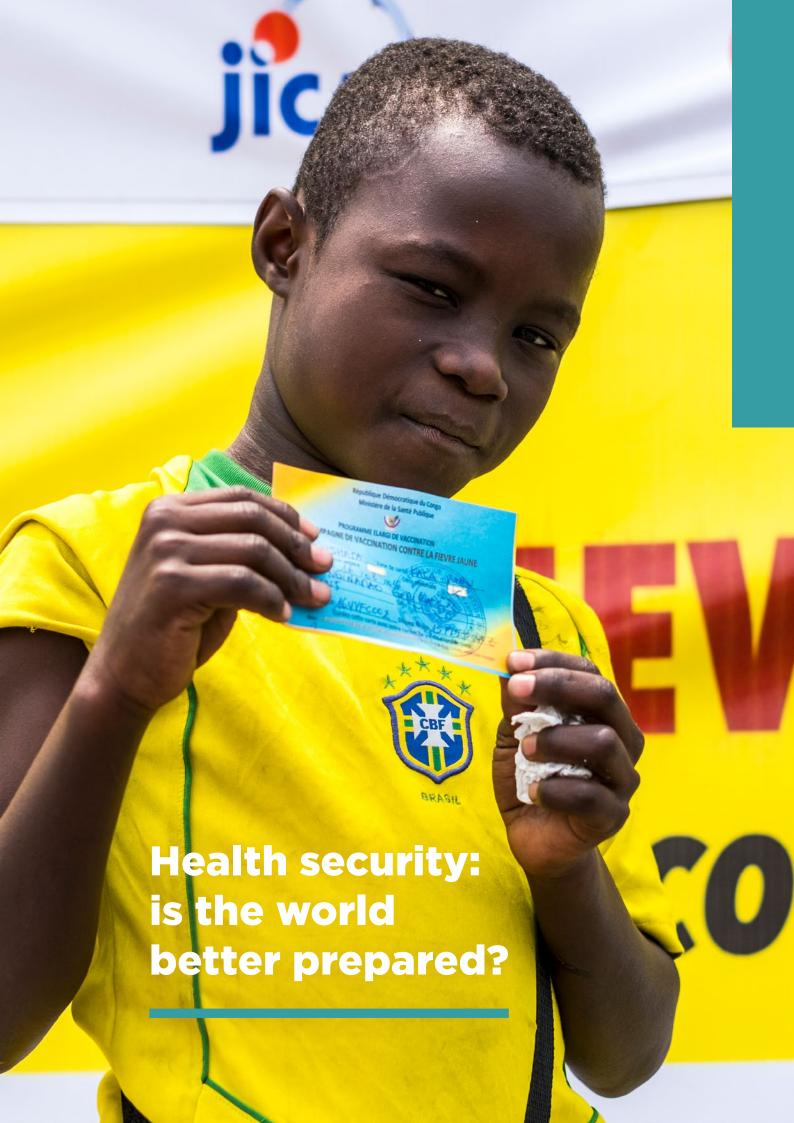
WHO is providing a platform to discuss the fair pricing of pharmaceutical products. The issue of fair pricing is framed by two extremes: prices so high they are unaffordable, even in the world's richest countries, and prices so low they drive high-quality manufacturers out of the market, leading to drug shortages. The SDG target for universal health coverage depends on finding ways to tackle both extremes. The overarching objective is to find a model for fair pricing that makes essential medicines available in sustainable quantities at prices that are sustainably affordable for patients, third party payers, and health system budgets.

The extremely high prices charged for newly approved drugs for the treatment of cancer and hepatitis C are indicative of a trend in which new medicines are nearly always more expensive. For some new drugs approved for various cancer indications, the high prices have not always been justified by studies of their therapeutic advantages over existing medicines. In addition, prices for older off-patent products can increase astronomically when a new company gains a monopoly on the market. Recent controversies in the United States – the overnight 5000% increase in the price of pyrimethamine and the price increase for epinephrine auto-injection devices – are the most egregious manifestations of this second trend.

In late November 2016, WHO convened an informal group of experts from governments, international organizations, research institutes and academia to gather advice on the full range of issues that determine whether the prices charged for pharmaceutical products are fair. The advisory group was also asked to identify issues that will need further exploration during a May 2017 Fair Pricing Forum being co-hosted by WHO and the government of the Netherlands.

The ultimate aim, the experts agreed, should be a price that assures new medicines are affordable to all patients and health systems, allows for an acceptable profit margin, also as a stimulus for further innovation, and assures a stable supply of generic medicines. In working towards a model for fair pricing, the experts identified a number of priority issues and information gaps, including the need for market transparency in prices actually being paid in different settings, the true costs of R&D for new product development, the costs of manufacturing a product, and the range of profit margins that result.

The group looked with some scepticism at industry's common argument that rising prices reflect the escalating costs of R&D and found some evidence that prices are fixed according to what the market will bear. Although the report of the advisory group demonstrated that a range of factors influence medicine prices, it confirmed that more transparency around production and R&D costs would move the discussion forward during the Fair Pricing Forum in May 2017.



A disease outbreak best demonstrates the acute need for a guardian of health. Lessons learned from the West Africa Ebola outbreak in 2014 catalyzed the creation of a new Health Emergencies Programme, enabling a faster, more effective response to outbreaks and emergencies. WHO helps countries implement the International Health Regulations and guides R&D collaboration to develop new vaccines and treatments for epidemic-prone diseases. The response to subsequent outbreaks of Zika and yellow fever has improved but more work is needed to ensure that the world is better prepared to handle the next epidemic.

Managing the global regime for controlling the international spread of infectious diseases is a central and historical responsibility of WHO. The *International Health Regulations*, administered by WHO, provide the legal instrument for doing so. These regulations are the only internationally-agreed set of rules governing the timely and effective response to outbreaks and other health emergencies that may spread beyond the borders of an affected country. Yet fewer than a third of WHO Member States meet the minimum requirements for core capacities needed to implement the IHR. This is the situation nearly ten years after the regulations entered into force.

At the same time, the factors that govern global health security extend well beyond the mandate of WHO and its capacity to respond. Much responsibility falls to countries. In line with IHR provisions, affected countries need to report unusual disease events promptly and openly. When they do so, other countries need to stop punishing them by imposing unjustified restrictions on travel and trade. A promise of financial and technical support is a powerful incentive for early reporting, but is often impeded by an inadequate response from the international community. As abundant experience shows, prompt and transparent reporting is compromised when the certainty of economic damage outweighs the prospect of financial and technical support.

Implementation of the IHR requires that countries move out of the sanctuary of national sovereignty in the interest of the common good. For example, countries must be willing to issue visas for foreign emergency responders, let them investigate, and grant them full and unfettered access to data and records. Countries and airlines must agree to send patient samples to WHO collaborating centres with designated expertise in the handling and analysis of dangerous or



Countries with well-functioning and inclusive health systems are more likely to catch an outbreak early when the chances of rapid containment are best.

unusual pathogens. Many WHO-led responses to outbreaks have been delayed or encumbered when countries exercise their sovereign right to refuse international collaboration, regarding it as unwelcome interference with national affairs.

Above all, to prevent another devastating event like the Ebola outbreak in West Africa, countries need resilient and inclusive health systems that extend to rural areas, a sensitive early warning system coupled with rapid response capacity, and informed and engaged communities that trust their government and the health services it provides. Countries also need access to effective and affordable vaccines, diagnostics and treatments (when these exist), outstanding laboratory and logistics capacity, and safe and abundant treatment facilities, properly staffed and equipped.

The world has a long way to go before reaching such a level of preparedness. An estimated 400 million people have no access whatsoever to even the most basic health services. WHO has identified nine severe pathogens that have epidemic potential but no or inadequate medical countermeasures – another glaring gap in the world's collective preparedness.

Fortunately, recent G7 summits and a growing body of research see a strong mutually-reinforcing compatibility between the goals of universal health coverage and global health security. Countries with well-functioning and inclusive health systems are more likely to catch an outbreak early when the chances of rapid containment are best. Countries with strong health systems are better prepared to cope with the added demands on health services and staff that outbreaks and other health emergencies inevitably bring. Recent history has many examples of fragile health systems pushed to the brink of collapse, often by comparatively mild outbreaks. Finally, the commitment to fairness and protection against financial ruin, embodied in universal health coverage, can inspire the public confidence and trust that underpin compliance with recommended control measures.

Ebola: WHO must change the way it works

The Ebola outbreak in West Africa was the largest, most severe, and most complex in the nearly four-decade history of this disease. WHO was too slow to recognize that the first Ebola outbreak in West Africa would behave very differently than the previous 17 outbreaks that occurred in equatorial Africa since 1976. Even the largest of these outbreaks, which were mostly confined to rural areas, was contained within 5 months.

In Guinea, where the outbreak began in late 2013, the virus circulated, undetected and undeterred, for three months. By the time the causative agent was identified in March 2014, the virus had already reached hospitals in crowded urban areas. Subsequent spread to Sierra Leone and Liberia overwhelmed fragile health systems within little more than a month, especially after the virus entered the capital cities. As cases began increasing exponentially, WHO introduced rapid course corrections and dramatically scaled up its response.

Other countries in West Africa, namely Nigeria, Mali and Senegal, fared much better. As their surveillance systems were on high alert and response capacity was in place, they were able to hold their outbreaks to just a single or a handful of cases. Likewise, during the simultaneous

but unrelated outbreak in the Democratic Republic of Congo, caused by the same Zaire virus, health officials, facing their seventh Ebola outbreak, were able to contain the disease within less than two months.

The unprecedented scale and duration of the West African outbreak prompted a large number of critical assessments, largely focused on the role of WHO and shortcomings in the Organization's performance. All assessments made specific recommendations for WHO reform, often calling for similar changes. These recommendations shaped the design of a new health emergencies programme, which extended WHO functions from largely normative and standard-setting work to an operational role within countries experiencing an emergency.

First tests for early reforms

Many early reforms were put to the test in 2015, when Zika made its first appearance in the Americas and raised the alarming possibility that a mosquito bite during pregnancy could cause severe neurological abnormalities in newborns. Innovations, such as the introduction of an event management system and a clear pathway for command-and-control, coupled with the early declaration of a public health emergency of international concern, supported a level of WHO performance that has been generally praised for its speed and strategic focus.

2016 saw a second major test, when Angola and the Democratic Republic of Congo confirmed outbreaks of yellow fever in their capital cities, marking the largest and most ominous African outbreaks of this disease experienced in four decades. Travellers and foreign workers carried the virus to Kenya and China, despite requirements for yellow fever vaccination certificates for travellers set out in the IHR. A market in fake vaccination certificates quickly sprung up.

Those outbreaks demonstrated what can happen when migrants from rural areas and workers from mining and construction sites carry the virus into urban areas with powder-keg conditions: dense populations of non-immune people, heavy infestations with mosquitoes exquisitely adapted to urban life, and the flimsy infrastructures that make mosquito control nearly impossible.

The world has had a safe, low-cost vaccine that confers life-long protection against yellow fever since 1937. Despite this advantage, the response faced a crippling initial shortage of vaccines, which WHO and the experts that advise the agency were eventually able to address. The result was the largest emergency vaccination campaign against yellow fever ever undertaken in sub-Saharan Africa. A crisis was averted. The resurgence of the yellow fever threat and the inadequacy of the vaccine supply were again illustrated in March 2017, when WHO despatched 3.5 million doses from its emergency stockpile to support Brazil's response to its expanding of yellow fever outbreak.

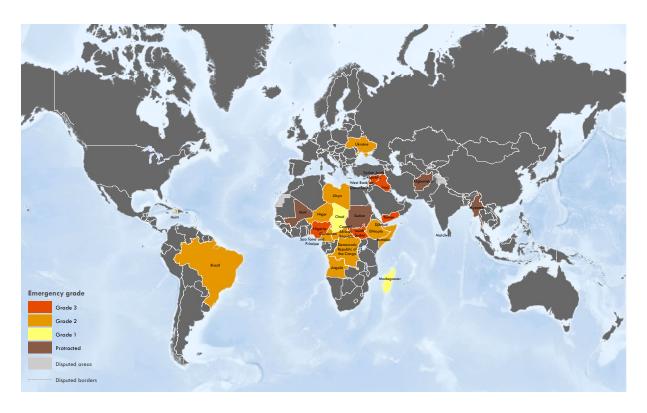
A new emergencies programme is launched

The WHO emergencies programme, launched in August 2016, is playing a central role in coordinating a number of activities with partners. **Early warning and rapid detection systems are being strengthened in vulnerable countries**, and procedures are in place to activate established mechanisms for coordinating the emergency response to outbreaks of infectious diseases and humanitarian crises.

A formal process of quality control for the training and verification of emergency medical teams is strengthening the global health emergency workforce, offering vetted surge capacity during outbreaks and bringing order to a situation historically prone to chaos. The teams verified and registered by WHO are qualified and fully self-sufficient, responsible for bringing their own equipment and supplies – another requirement that relieves the pressure on local health systems and officials.

Member States, at all levels of economic development, are prioritizing peer-reviewed assessments of their core capacities to implement the IHR. A major concern is the lack of assured financial and technical assistance to fill the gaps identified during these assessments.

Graded Countries and Protracted Emergencies (April 2017)



Source: WHO

New models and tools

The January 2017 Executive Board confirmed that the Pandemic Influenza Preparedness Framework, set up in 2011 after years of negotiations, works as a bold and innovative preparedness tool that puts virus sharing and benefit sharing on the same footing. At that time, the Framework had secured guaranteed access to around 350 million doses of influenza vaccines as they roll off the production line during the next pandemic. Partnership contributions from industry, amounting to more than \$110 million, have been largely invested to build surveillance, laboratory, regulatory and other capacities in developing countries.

This is one successful model for better – and fair – preparedness, and there are other encouraging signs. The WHO R&D Blueprint, developed in response to lessons learned during the Ebola outbreak, has been immediately applied to expedite the development of new medical products for Zika virus disease. It aims to cut the time needed to develop and manufacture candidate products from years to months. In December 2016, WHO published final clinical trial results demonstrating that the new Ebola vaccine confers nearly 100% protection.

As announced in January 2017, a \$500 million Coalition for Epidemic Preparedness Innovations, which draws on the R&D Blueprint and the WHO list of nine priority pathogens, holds great promise for developing vaccines ahead of epidemics. Initially focused on Lassa fever, Nipah virus and the MERS coronavirus, the Coalition will need far more funds to develop vaccines for the remaining high-risk pathogens with epidemic potential.

Four famines: the worst crisis since 1945

WHO has also become more directly operational during humanitarian crises. Working through ministries of health, WHO coordinates the work of partners and conducts rapid assessments of needs, delivers large quantities of medical supplies, and operates mobile laboratories and clinics.

The scale of needs is unprecedented. On 11 March 2017, the UN humanitarian coordinator informed the Security Council that more than 20 million people were at risk of starvation and famine across four countries in Africa and the Middle East: north-eastern Nigeria, Somalia, South Sudan and Yemen. The situation was described as the world's worst humanitarian crisis since 1945.

In all four countries, already fragile hand-to-mouth survival has been crushed by the deadly combination of drought and fierce fighting. Drought caused farmers to abandon their fields and families to flee as livestock died off and water supplies dried up. The threat from fighting keeps people displaced by drought constantly on the move. Between starvation and death nearly always lies disease. Severe undernutrition compromises immune functions. Diseases that a well-nourished body can ward off turn fatal. Displaced people living in crowded unsanitary camps are vulnerable to outbreak of multiple diseases.

In South Sudan, where nearly three years of conflict have left the health system in tatters, life expectancy has dropped to 55 years and health needs have risen exponentially. In February 2017, the UN declared a famine in parts of the country and warned that almost half of the total population was in need of urgent food assistance. Given the strict criteria used, **the declaration of a famine means that people are already dying from starvation.** Together with the Ministry of Health, WHO coordinates the work of 35 partners, sounding alerts to hot spots and investigating dozens of disease outbreaks, including a cholera outbreak confirmed in July 2016. In 2016, three million children were vaccinated against polio and more than 200 000 against measles. A nation-wide vaccination campaign against cholera began in April 2017.

In Somalia, the greatest concern is the ongoing cholera outbreak fuelled by a severe drought that has, as elsewhere, forced people to consume contaminated water. Since the start of 2017, 22 000 cholera cases have been reported, representing a nearly five-fold increase over the previous year. To contain the rapidly spreading outbreak, Gavi, the Vaccine Alliance, delivered nearly a million doses of oral cholera vaccine; 450 00 people received their first dose in mid-March 2017. The vaccines are being administered by the government with support from WHO and UNICEF. A recent investigation of 12 cholera treatment centres and units found that none had adequate water and sanitation facilities. While WHO has delivered badly needed emergency medical supplies and equipment to the hardest-hit areas, more will be needed if the number of cases continues to rise.

The eight-year conflict in north-eastern Nigeria led to a deepening humanitarian crisis, displacing farmers from their land and leaving a massive food shortage in its wake. Despite the challenging security situation, WHO and its partners have targeted 8.2 million people across the region, including nearly six million in north-eastern Nigeria, for emergency health assistance. Borno is the most severely affected state, with 35% of health facilities destroyed and another 30% damaged. Childhood mortality is off the charts. WHO has deployed 35 mobile teams to the most remote and insecure parts of the state, where travel on poor roads requires a military escort. Apart from offering general health care, these teams have provided treatment for malaria, the biggest killer in the severely undernourished population. Given the precarious immunization status resulting in the emergence of new polio cases, WHO supported vaccination campaigns which protected nearly three million children from measles and more than 1.8 million from polio. In March 2017, Borno State reported its first Lassa fever outbreak since the disease was first detected 48 years ago, again illustrating the vulnerability created when health systems collapse.

In its 2017 response plan for Yemen, WHO and its partners will be providing targeted assistance to 10.4 million people living in the country's most vulnerable districts. The focus is on the health needs of young children, pregnant and lactating women, people injured in the conflict, and patients with chronic diseases. In 2016, WHO and its partners received financial support to sustain the functionality of more than 400 health facilities in 145 districts. Essential medicines and supplies, also for surgery and acute care, were delivered to support the health needs of more than 3 million people. WHO also established 26 centres for cholera treatment and expanded an electronic early warning system for outbreaks from 440 sites in 2015 to nearly 2000 sites the following year. As further operational support, WHO delivered more than two million litres of fuel to keep hospital generators and ambulances running. In April 2017, WHO announced that nearly five million children in the war-torn country had been vaccinated against measles and polio in a nation-wide campaign that took two months and required more than 5000 rented vehicles.

On the frontlines: a unique chain of care

The WHO response to health needs in the embattled city of Mosul, Iraq, which began in November 2016, has provided the most dramatic demonstration of the impact of reforms on WHO performance in emergencies. WHO country staff watched the situation closely and spotted the biggest health needs immediately: injuries from bullets, shrapnel, suicide bombings and shelling. Civilians were caught up in the brutal fighting, stepping on landmines, fleeing frontlines and being crushed in buildings booby-trapped with explosives. Civilians were also being deliberately shot by snipers as they sought safety.

Staff decided that a chain of trauma care was urgently needed to save lives. Three key things needed to be put in place quickly. Stabilization points no further than 10 minutes from the frontline would get patients stable enough to travel, and code them by critical level from red to green. Field hospitals a few minutes away would perform emergency surgical interventions, then prepare patients for another ambulance ride. Finally, a set of well-equipped tertiary facilities – ideally all in the same province to keep transport times short – would provide the necessary care.

At the urgent request of the Ministry of Health, WHO rapidly set up two field hospitals, with a third expected to open in the spring of 2017 and a fourth one planned. In addition, WHO helped rebuild and reopen two general hospitals in the vicinity that had been partially destroyed during the fighting. WHO also supported the laboratory screening of blood supplies for transfusions, airlifted 47 ambulances, stocked facilities with essential surgical and other supplies, paid some doctors when government funds ran low, and equipped one hospital to respond to potential further emergencies caused by the use of chemical weapons. In this way, a well-functioning chain of care encircled the fighting, with patients moving along the chain from the frontlines to tertiary hospitals within 60 minutes – the so-called "golden hour" when critical trauma care saves lives

As a first-time innovation, the chain of care is all the more remarkable as it unfolded amid some of the most intense fighting Iraq has experienced in several years. As the humanitarian coordinator for the UN mission in Iraq told Devex, the media platform for the global development community, "It's been exceptional leadership from WHO." As the Devex report further noted, the Iraqi work makes a strong case for a frontline role for WHO in emergencies. Interviews with aid groups, donors, doctors and patients in Mosul confirmed that the chain of referral is working well. In Mosul, WHO's new leadership role as an innovator and implementing agency benefitted from generous funding from the European Commission and the UN Central Emergency Response Fund.

The worst-case scenario: coming soon?

The Ebola outbreak in West Africa was a large, long, deadly and frightening human tragedy. But Ebola, which requires close physical contact to spread, causes severe and highly visible

illness when patients are most contagious, and does not spread easily via international air travel, is not a worst-case scenario.

Adequate global health security means being prepared for a severe disease that spreads via the airborne route, or can be transmitted during the incubation period when infected people look and feel well enough to travel.

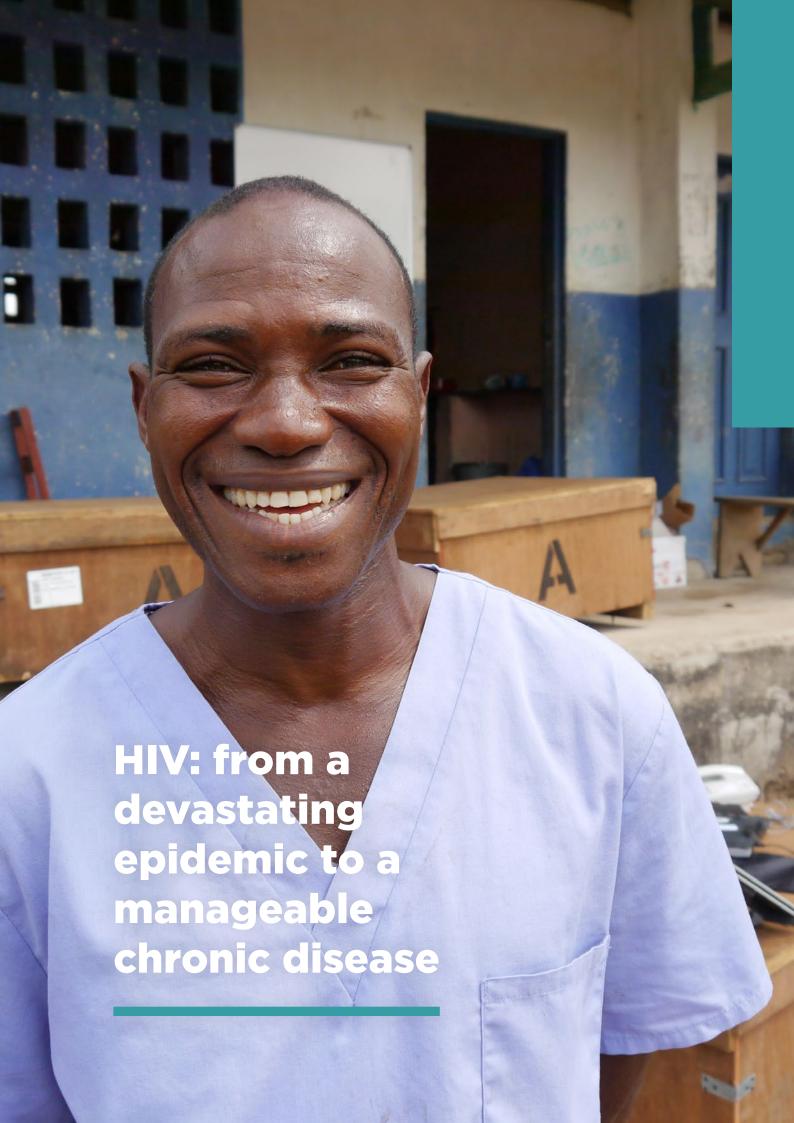
Constant mutation and adaptation are the survival mechanisms of the microbial world. There will always be surprises. The outbreaks of Ebola, Zika and urban yellow fever show how changes in the way humanity inhabits the planet have given the volatile microbial world multiple new opportunities to exploit.

These are opportunities created by rapid unplanned urbanization that leaves people crowded together in slums and shantytowns poorly served by water supplies and sanitation, people living in close proximity to animals (including camels, birds and pigs), incursions (for adventure, economic gain or food) into previously uninhabited jungles and rainforests, the industrialization of food production, the overuse of antimicrobials and phenomenal increases in international travel and trade. None of these trends can be easily reversed.

In addition, the climate is changing. Unusual weather patterns are reflected in unusual patterns in the distribution of wild animals and disease vectors. Dengue has exploited these opportunities to become the most important mosquito-borne viral disease in the world.

The three outbreaks also show how older diseases can behave in dangerously unfamiliar ways when they invade new territory or enter an urban environment with poor infrastructure. Weak public health systems, especially for the early detection of unusual pathogens, the concentration of most health resources in cities and the demise of programmes for mosquito control leave the world highly vulnerable to the next microbial surprise.

The world is better prepared, but not at all well enough.



n the decade since the United Nations declared HIV an unprecedented human catastrophe, the AIDS response has underscored the ethical imperative of fair access to medicine. WHO's standard-setting work helped make prevention and treatment more accessible, safe, effective and efficient, and encouraged integrating HIV services into existing health systems. WHO has prequalified more than 250 products for HIV-related conditions. New targets aim to prevent 1.6 million new infections and 600 000 deaths per year, ending AIDS as a public health threat by 2030.

HIV, with its long incubation period, its multiple modes of often intimate transmission, and its defiance of monumental efforts to develop a vaccine and a definitive cure, is one of the most complex, the most challenging and arguably the most devastating of all infectious diseases that humanity has ever had to face.

In 2015, the global HIV epidemic claimed fewer lives than at any point in almost two decades, and fewer people became newly infected with HIV than in any year since 1991. The fact that the MDG target of halting and reversing the spread of HIV was met nine months ahead of schedule is a stunning achievement.

The HIV response changed the face of public health in profound ways, opening new options for dealing with multiple other health problems. Treatments can be found. Prices can plummet. Funds can be secured. High-impact services can be delivered in resource-constrained settings. Attitudes can change. Communities can be mobilized to take action. With sufficient will, commitment and resources, a bleak and depressing situation can be turned into one that offers hope.

Above all, the AIDS response underscored the ethical imperative - the life-and-death significance - of fair access to the best quality-assured medicines and diagnostics on offer, to all in need.

How this happened, including WHO's specific role, deserves analysis. Recent achievements look all the more remarkable when viewed against the situation a decade ago. A look at these achievements also yields one of the best examples of how WHO's standard-setting work and direct support to countries translates into lives saved and suffering averted.



By 2017, WHO estimated that more than 18 million poor people now had access to antiretroviral therapy.

An "unprecedented human catastrophe"

In 2002, WHO launched its "3 by 5" initiative with the goal of extending coverage with antiretroviral therapy to 3 million people in the developing world by the year 2005. The initiative, with "kickstart" funding from the Canadian government, stimulated a remarkable expansion of treatment programmes supported by generous funding in countries, most notably from the Global Fund and the United States President's Emergency Plan for AIDS Relief. Despite this rapid expansion of treatment, international efforts were still running behind the epidemic. By 2005, more people were receiving treatment but many more were becoming newly infected. Efforts to get ahead of the epidemic needed to broaden the approach to include prevention and care as well as the delivery of treatments. The focus shifted from universal access to HIV treatment to universal access to HIV prevention, treatment and care.

The Political Declaration on HIV/AIDS, adopted by the United Nations General Assembly in 2006, described the epidemic as an "unprecedented human catastrophe" that posed "one of the most formidable challenges to the development, progress, and stability of our respective societies and the world at large".

The list of concerns was long. The epidemic was still expanding. Women were particularly affected, accounting for the majority of people infected with HIV in sub-Saharan Africa. HIV was disproportionately affecting the young. Rates of infection in children and adults under the age of 25 years were rising, accounting for nearly half of all new infections. Previously agreed targets for improving access to prevention, treatment, care and support were not being met. **Poverty was one factor fuelling the epidemic, but so were gender inequities, gender-based violence and the sexual exploitation of women and girls.** In other regions, vulnerable and marginalized populations were those most affected, with epidemics among men who have sex with men, sex workers, transgender people, people who inject drugs, and prisoners.

In short, urgent and exceptional action was required at all levels to curb the devastating effects of the epidemic. The declaration stressed in particular the need to scale up significantly towards the goal of universal access to comprehensive prevention programmes, treatment, care and support by 2010. Universal access meant reaching everyone in need, including those living on the margins of society and beyond the reach of health services.

In 2007, an estimated 33.2 million people were living with HIV, of whom 22.5 million were in sub-Saharan Africa, where AIDS was by far the leading cause of death. The year saw 2.5 million new HIV infections and 2.1 million deaths globally. Nearly 300 000 children under the age of 15 years were infected, and more than 12 million children in sub-Saharan Africa had lost one or both parents to AIDS.

At the end of 2007, nearly 3 million people in resource-constrained settings were receiving antiretroviral therapy, representing a jump of 1 million people compared with the previous year. Though the increase was encouraging, therapy was still reaching only 12% of those infected and only the sickest were considered eligible for treatment. A mere 20% of people with HIV were aware of their infection status, and prevention services were not reaching the majority of those at greatest risk. The world was still running behind a devastating epidemic.

The search for new preventive tools continued. In 2005, studies reported that male circumcision could lower the risk of HIV acquisition by men in sub-Saharan Africa. Subsequent research confirmed even better news: male circumcision could cut the risk of acquiring HIV by more than half. Acting on this evidence, WHO promoted voluntary medical male circumcision as a new preventive tool with good results. Between 2008 and 2015, nearly 12 million men underwent voluntary circumcision in 14 priority countries in eastern and southern Africa.

The power of reliable data

By 2007, the HIV response had significantly contributed to better health information systems, enabling some of the best global and country-level monitoring of any major health condition. WHO and UNAIDS produced detailed annual reports on changing HIV epidemics, their social determinants, and the responses in individual countries and globally. Evidence was emerging about what worked best to reduce HIV risks, to shrink the gaps in service coverage, to step up access to life-prolonging therapy, and to reduce the number of new infections and deaths. Evidence further revealed the vibrant role that community networks and civil society initiatives played in getting services closer to people, providing home-based care, and calling loudly for better coverage with more affordable drugs.

Better data revealed additional statistics with significant programmatic implications. **Preventive interventions were not reaching girls and young women.** Newer data showed that, in sub-Saharan Africa, girls and young women accounted for more than 70% of all young people infected with HIV. In terms of awareness of their HIV status, more women were being tested, but men were being missed.

At the 17th International AIDS Conference held in Mexico City in 2008, WHO launched a package of priority interventions designed to help low- and middle-income countries move towards universal access to HIV prevention, treatment, care, and support. The package captured what the global AIDS response needed to deliver to reach this goal.

Using mathematical modelling, WHO scientists estimated that universal and annual voluntary testing, followed by immediate antiretroviral therapy – regardless of the clinical stage or CD4 count – could reduce new HIV infections by 95% within ten years. But that was an aspirational calculation in the realm of "ifs". Such a dramatic shift in the approach to control would need better and cheaper drugs plus the persuasive power of a breakthrough. That, too, would come.

While some asked whether the world could treat its way out of the epidemic, others argued that renewed and intensified efforts in HIV prevention would be needed to push the epidemic into an irreversible decline. As history would prove, an epidemic as widespread, entrenched, and difficult as HIV needed both.

Dramatic leaps in treatment access

Significant court rulings in Brazil and India, aided by vocal civil society groups, opened the market for low-cost generic antiretroviral medicines. The WHO prequalification programme rigorously assessed their safety and efficacy compared with originator products, adding an important layer of quality control. The programme also kept close watch over quality standards, removed products from its list when standards slipped and updated the list, in line with WHO treatment guidelines, as safer and more effective medicines came on the market. Confidence in the quality of low-cost generics, prequalified by WHO, increased.

As the volume of low-priced generics grew, funding initiatives, like the Global Fund, PEPFAR and the Clinton Health Access Initiative, could reach significantly more people with available funds. UNITAID kicked in, first as a drug-purchasing facility and later to support innovations such as fixed-dose combination drugs, which improve patient adherence, and badly needed paediatric formulations This support also shaped market dynamics to increase access to more affordable medicines and diagnostics. That role accelerated in 2010 when UNITAID established the Medicines Patent Pool. Together, all these initiatives contributed to a 100-fold drop in the price of antiretroviral therapy and vastly increased supplies, triggering the fastest scale up of a life-saving intervention in history.

The public health approach pushed by WHO fuelled the drive to constantly streamline and simplify recommended strategic options and technical advice. WHO also worked to ensure that the quality of services and programmes, even in very poor countries, was not compromised by cost constraints and achieved outcomes comparable to those in well-off countries. WHO took a leading role in monitoring the effectiveness and safety of recommended drugs. When evidence emerged that certain drugs showed unacceptable adverse effects, WHO moved rapidly to change treatment recommendations and call for their withdrawal.

In a most encouraging trend, evidence was emerging that adults with HIV on long-term combination therapy could reach a life expectancy comparable with that in the general population. In poor communities, what had once been a death sentence was transformed into a disease that could be managed like other chronic conditions. To capitalize on these encouraging trends, countries asked WHO to provide more detailed policy advice and operational guidance.

The threat of HIV epidemics stimulated major investments in HIV research, ranging from basic and clinical research through to implementation research and findings from the social sciences. Never before had public health benefitted from such a rapid evolution of medical science and its practical application, from better understanding of the immune system, to the development of new drugs and diagnostics, to the identification of the health behaviours and social determinants that were driving the epidemics. WHO was well-positioned to tap the best scientific data, clinical evidence and experiences from country programmes, and then translate these data into practical technical guidance adapted to resource-constrained settings. When breakthroughs occurred, which were many and frequent, WHO convened expert consultations to interpret the results and gather advice on how to reflect their significance in revised guidelines for countries.

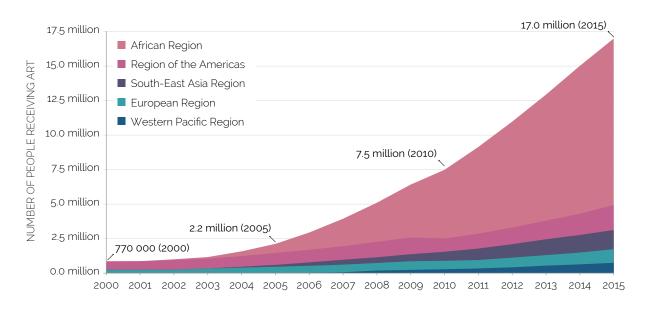
Universal access: edging closer

As prospects for a massive scale up of treatment brightened, AIDS began to lose its status as an "exceptional" disease requiring a unique strategic approach that set it apart from other diseases. HIV could now be managed within the existing health system. The move towards a more normalized approach was formally recognized by a World Health Assembly resolution, adopted in May 2010, that called for the integration of HIV services with existing health services, including those for maternal, neonatal, and child health, reproductive and sexual health, tuberculosis, and harm reduction programmes for people who inject drugs. That resolution was followed by WHO's global health sector strategy on HIV 2011-2016, approved in 2011.

In June 2010, WHO introduced a new treatment framework – a five-pronged programmatic approach aimed at making antiretroviral therapy more accessible, safe, effective and efficient. As a contribution to efficiency gains, the framework introduced concepts of radical simplification, standardization and cost reduction while also acknowledging the gains that come from community engagement in providing testing and treatment.

The treatment framework relied on simplified, less toxic drug regimens which could maintain therapeutic efficacy with minimal clinical monitoring. The recommended drug regimens also carried high barriers to the development of drug resistance. Asking patients to take only one pill a day – a combination of three different drugs – was a further simplification designed to improve patient adherence. WHO scientists estimated that implementation of the treatment framework could prevent 15.5 million new infections over the coming five years.

Estimated numbers of people receiving antiretroviral therapy globally and by WHO Region and percentage coverage globally, 2000-2015



Source: WHO

Breakthrough: the true power of antiretroviral therapy

In 2011, three decades after the first reports of AIDS were published, a groundbreaking trial, conducted by the US National Institutes of Health, showed that antiretroviral therapy also contributes to HIV prevention. In discordant couples, where one partner had HIV and the other did not, treatment of the person with HIV resulted in a 96% reduction in transmission to the partner. Those results were hailed as a true game-changer that would drive a revolution in the approach to prevention. At that time, sexual transmission accounted for about 80% of new infections. That breakthrough also changed the vocabulary, from references to the devastating AIDS epidemic to talk about HIV as a preventable and treatable infection.

The fact that treatment could double as prevention had two additional positive effects. First, it provided a powerful incentive for people to be tested and immediately started on therapy. Second, it changed the public face of the disease. The stigma of contagion associated with an HIV positive status lost much of its sting.

By 2012, the situation looked even more encouraging. An estimated 9.4 million people had access to antiretroviral therapy. Funding was stable, with a large share coming from domestic sources. The HIV response had pushed life-saving health services to reach formerly excluded communities, advancing efforts to achieve universal health coverage. In 2013, WHO took the next big step towards simplification by issuing its first consolidated guidelines on the strategic use of antiretroviral therapy for both prevention and treatment. The consolidated guidelines contained recommendations on what drugs to give, but also on how to deliver services to reach a maximum number of people.

At the same time, studies demonstrated people who are not infected yet face an exposure risk could block acquisition of HIV by taking antiretroviral drugs prior to exposure. In 2012, WHO made its first recommendation on using such pre-exposure prophylaxis of HIV infection as an effective additional approach to HIV prevention.

A tipping point is reached

In 2013, the epidemic reached its tipping point. For the first time in the decades-long history of this disease, the number of people newly started on antiretroviral therapy in 2013 surpassed the number of new infections. That epidemiological breakthrough was facilitated by advances on multiple fronts.

WHO recommended diversifying HIV testing approaches, including provider-initiated and community-based testing services, as a way to increase the number of people aware of their HIV status and thus able to reap the benefits of early antiretroviral therapy. More evidence emerged on the effectiveness of pre-exposure prophylaxis in different populations. Studies conducted by WHO and supported by UNITAID produced compelling evidence that pre-exposure prophylaxis

was both effective and acceptable in key populations. In 2015, WHO recommended its use in all population at a substantial risk of HIV infection.

The decision to integrate HIV services with maternal, child health, reproductive and sexual health services was reaping additional benefits. In 2016, Armenia, Belarus, the Republic of Moldova, and Thailand joined Cuba as countries where the elimination of mother-to-child transmission of HIV had been validated by WHO. Belarus, the Republic of Moldova and Thailand were also validated as having eliminated mother-to-child transmission of syphilis. Cuba was the first country to achieve both milestones in 2015. In the African region, several countries with very high levels of maternal testing and treatment are currently approaching the elimination targets. Their prospects of success have been boosted by earlier diagnosis of HIV in pregnant and breast-feeding women.

Data also improved. WHO provided capacity-building support to 80 countries to enhance the collection and analysis of surveillance and programme data to measure programme performance and impact along the continuum of HIV services. That work benefitted from close collaboration with the US President's Emergency Plan for AIDS Relief, the US Centers for Disease Control and Prevention, and the Bill and Melinda Gates Foundation.

In May 2016, the World Health Assembly adopted the Global Health Sector Strategy on HIV for 2016–2017, together with global strategies on viral hepatitis and sexually transmitted infections. These three strategies used a common framework of universal health coverage. The HIV strategy, driven by the goal of eventually eliminating the infection as a public health problem, aimed to steer the HIV response in a new direction. It emphasized the importance of embedding the HIV response in the broader public health agenda as a contribution to the target set out in the 2030 Agenda for Sustainable Development. The strategy underscored the need for countries to define an essential set of HIV interventions and services to be included in national health benefit packages, funded through national health budgets. The strategy also highlighted the need to adapt HIV services and ensure sustainable financing so that all people can access the HIV services they need without experiencing financial hardship.

"Treat all": ultimate simplification, ultimate fairness

The Global Health Sector Strategy adopted the UNAIDS "90-90-90" targets for 2020 – 90% of people with HIV knowing their HIV status, 90% of those diagnosed with HIV receiving antiretroviral therapy, and 90% of people on antiretroviral therapy achieving viral suppression. In June 2016, WHO launched its "treat all" consolidated guidelines on the use of antiretroviral therapy for treating and preventing HIV infection. The guidelines hit the ground running. Close to 80 low-and middle-income countries had already adopted "treat all" policies or planned to do so within the year – a critical step towards achieving the 90-90-90 targets. WHO worked closely with ministries of health to ensure the rapid translation of the new recommendations into national policy and implementation plans.

The consolidated guidelines removed all limitations on eligibility for therapy among people living with HIV. The recommendations made all populations and groups with HIV, including pregnant

women and children, eligible for treatment. Prospects for reaching universal access improved considerably. As another contribution to simplified treatment programmes, WHO recommended the same once-per-day combination pill for all adults living with HIV, including those with tuberculosis, hepatitis and other co-infections. The recommendations were ambitious in their expected impact, yet simplified in their approach, firmly rooted in evidence, and driven by an ethical imperative.

The recommendations aimed to improve the quality of HIV treatment and to bring the world closer to the universal health coverage ideals of integrated services, community-centred and community-led health care approaches, and shared responsibility for effective programme delivery.

The treat-all recommendations marked major improvements for programmes but most especially for people, including pregnant women. Previous recommendations in 2013 called for lifelong antiretroviral therapy for all pregnant and breastfeeding women with HIV to prevent HIV transmission to babies but also to take care of women's health. The 2016 guidelines reinforced these recommendations and promoted a life-course approach to HIV prevention and treatment, consistent with the 'Born Free, Stay Free and AIDS Free' framework. That framework aimed to strengthen efforts to eliminate mother-to-child transmission of HIV, scale-up paediatric treatment, prevent new HIV infections among adolescent girls, and provide treatment to adolescent girls and women.

Compared with the extraordinary increase in access to treatment, uptake of HIV testing was disappointingly sluggish. In 2015, around 40% of people infected with HIV globally were still not aware of their status and were still missing out on the enormous benefits of treatment. In guidelines issued near the end of 2016, WHO promoted the simplified new diagnostic tests that enabled people to test themselves for HIV, with results available in 20 minutes or less. Doing so was a way to both get more people started on treatment and further normalize the epidemic by reducing stigma and discrimination.

The phenomenal expansion of HIV programmes poses its own set of challenges. The large number of people now being treated makes it essential to maintain the quality of services, to ensure the most efficient use of resources, to achieve the best treatment outcomes, and to prevent the emergence of HIV drug resistance. In July 2017, WHO will launch the first Global Action Plan on HIV Drug Resistance. The plan sets out guidance that can help countries prevent and, if necessary, manage the emergence of HIV drug resistance, a risk that could threaten the remarkable gains made over the past 15 years. The plan aims to position HIV drug resistance within the broader WHO framework of tackling antimicrobial resistance.

Unstoppable momentum

The momentum is set to continue. By the end of 2016, WHO had prequalified more than 250 finished pharmaceutical products for treating HIV-related conditions, 29 active pharmaceutical ingredients, and two male circumcision devices. Since 2013, more than 100 countries have drawn on WHO technical support to develop concept notes for their Global Fund grant applications. The quality of funding applications improved, resulting in grants totalling \$2 billion for country HIV programmes.

By 2017, WHO estimated that more than 18 million poor people now had access to antiretroviral therapy. In a remarkable achievement for a global health initiative, treatment coverage in eastern and southern Africa surpassed the global average.

Further expanding access to treatment is now at the heart of new "fast track" treatment targets for 2020, with the aim of ending the AIDS epidemic as a public health threat by 2030. WHO estimates that meeting the fast-track targets could prevent 1.6 million new infections and 600,000 deaths per year.

Inspired by past achievements, optimism is great that sufficient momentum can be built to push the HIV epidemic into an irreversible decline, though the road ahead is not an easy one. The encouraging global outlook conceals the many countries with a major HIV burden yet low treatment coverage. Stark inequalities mar the landscape of service access. Stigma stifles the health-seeking behaviour of marginalized groups. The yearly number of new infections, stuck at more than 2 million, is way too high for a disease that can be prevented as well as treated. In some places, the number of new cases shows a stubborn upward trend.

The fact that HIV claimed more than a million lives in 2015 is a sobering reminder of the struggle ahead. The availability of affordable and highly effective medicines makes that figure stand out even more as an ethically compelling reason to do more.



nergized in 2007 by a call for malaria eradication, the world united around a new agenda to control and eliminate this ancient scourge. WHO-driven policies led to massive coverage with free or subsidized insecticide-treated nets. As malaria ceased to be the main cause of fever in African children, WHO recommended treatment only after diagnostic confirmation. Malaria deaths dropped 62% from 2000 to 2015, and WHO set an ambitious global technical strategy for malaria through 2030, drawing on the advice of more than 400 experts from 70 countries.

In 1969, the World Health Assembly adopted a carefully worded resolution that effectively ended the Global Malaria Eradication Programme launched in 1955. While long-term plans for malaria eradication were kept on the table, the resolution frankly admitted the failures and setbacks encountered during implementation of the global eradication strategy and shifted the responsibility for moving forward to national public health organizations. The campaign succeeded in eliminating malaria from many parts of the world, but no major gains were made in sub-Saharan Africa, the historical heartland of this disease. The goal of defeating malaria was replaced by the more realistic ambition of holding the disease at bay. In Africa, the malaria situation deteriorated to the point that its only positive feature was stability: things could hardly get any worse.

Interest in malaria control revived in 1992, when the government of the Netherlands hosted a ministerial conference on malaria, co-sponsored by WHO. The conference, attended by senior health leaders from 65 countries, aimed to map out plans for a renewed assault on malaria that acted on lessons from the past. Participants at the conference regarded the fight against malaria as a fight against poverty that demanded better coverage with essential health services. In Africa, WHO estimated that malaria killed one out of every 20 children in rural areas before their fifth birthday and was the most prevalent illness in young adults, sapping productivity and eroding prospects for development. The conference adopted a World Declaration on the Control of Malaria, which was endorsed by the World Health Assembly the following year.

The window of political will and financial resources began to open when WHO established the Roll Back Malaria partnership in 1998, with the goal of cutting malaria deaths in half by 2010.



By 2004, the malaria burden was still expanding as the biggest obstacle to development in a large number of countries, especially in sub-Saharan Africa.

The window opened even wider in 2000, when targets for turning the malaria epidemic around were included in the Millennium Development Goals. However, midway into Roll Back Malaria's drive, signs were clear that its targets would be missed by a longshot.

By 2004, the malaria burden was still expanding as the biggest obstacle to development in a large number of countries, especially in sub-Saharan Africa. In that part of the world, only 2% of children were sleeping under an insecticide treated net. Though childhood deaths from other causes were declining, deaths from malaria were rising.

Malaria parasites had again exercised their uncanny ability to develop resistance to virtually any single chemotherapeutic agent administered on a large scale. Drug-resistant strains of *Plasmodium falciparum*, which causes the most lethal form of the disease, had swept through the African continent, rendering the first-line treatment, chloroquine, nearly useless. The newer artemisinin-combination therapies were highly effective but, at twenty times the price of older drugs, were beyond the reach of most national control programmes. Despite the renewal of ambitious targets, the overall situation looked bleak.

By 2006, the numbers were large, round, and deeply familiar: 3 billion people at risk in 109 malarious countries and territories and around 266 million cases annually, leading to nearly 750 000 deaths.

Unrealistic goals?

In October 2007, malaria experts were stunned when, at a malaria forum in Seattle, Washington, Bill and Melinda Gates uttered a forbidden word in back-to-back speeches calling for the eradication of malaria. The WHO Director-General stepped up to support that goal, further fanning the shockwaves. Reactions were sharply divided. Some cautioned against setting unrealistic goals that were doomed to crash and burn in the absence of new breakthrough tools, most notably a vaccine.

Others pointed to recent reductions in malaria cases and deaths of 50% and even higher in a handful of African countries with small populations and excellent coverage with available interventions. That, they said, was evidence of what could be achieved with existing tools. They argued for elimination goals in groups of neighbouring countries that could gradually shrink the malaria map. As they further argued, more ambitious coverage targets could bring a more ambitious R&D agenda in their wake, especially if supported by the deep pockets of the Bill and Melinda Gates Foundation. Contrary to the expectations of many, that was precisely what began to happen.

A move towards more ambitious coverage turned out to be the preferred way forward for governments in endemic countries, WHO, and the many international partners joining the malaria assault. The will to tackle malaria now had a focused goal: a massive scale up of existing interventions, and most especially, of coverage with insecticide treated nets. In 2008, the UN Secretary-General called for universal access to malaria interventions.

As malaria in Africa affects the poorest of the poor, often living beyond the reach of formal health services, efforts to scale up coverage began with a paucity of reliable data to pinpoint hotspots, assess the effectiveness of different interventions, and establish benchmarks for measuring progress. Nonetheless, some tantalizing evidence was beginning to emerge.

In 2008, WHO recommended that insecticide treated nets be distributed at heavily subsidized prices or no cost to users and on a massive scale. That recommendation ended a long debate. One side argued that the best route to sustainable supplies was through local manufacturing, with nets sold at a subsidized price. Besides, as the argument went, people tended to value and use correctly items for which they had to pay. The other side argued that, for people mired in poverty, no price – however low – was affordable. Nets must be distributed at no cost.

WHO's recommendation for massive free distribution of nets coincided with two welcome trends. First, more and more African heads of state were taking charge of the malaria response, sometimes leading to an elimination effort in groups of neighbouring countries. Second, the money was rolling in. International funding commitments for malaria control increased from around \$300 million in 2004 to \$1.7 billion in 2009, largely from such sources as the Global Fund, the World Bank Booster Programme, the US President's Malaria Initiative, and other agencies.

But national and international efforts still had a very long way to go. As set out in the 2008 *World Malaria Report*, surveys showed that supplies of insecticidal nets were sufficient to protect only around 26% of people in 37 African countries. Even worse, only 3% of children with fever were being treated with artemisinin-combination therapy.

The impact of policy coherence

With massive scale up of coverage with free insecticidal nets now an agreed programmatic goal, the dam broke. Within a year, sufficient insecticidal nets had been delivered to protect nearly 580 million Africans. An estimated 75 million Africans living in high transmission zones were further protected by indoor residual spraying. The trend continued. WHO estimated that the number of nets procured in just the two years between 2008 and 2010 was sufficient to protect 73% of the 800 million people considered at risk.

Access to diagnostic tests was also rapidly growing, especially following the advent of rapid tests that could quickly detect malaria right down to the community level. To direct this rapid growth towards the selection of quality-assured products, WHO established a testing programme in 2008 to determine the comparative reliability of new tests coming on the market. A detailed checklist to aid procurement was also introduced to add another layer of quality control. Again, the results were impressive. At the turn of the century, fewer than 5% of suspected malaria cases reported in Africa were confirmed by a diagnostic test. By 2010, the worldwide figure had grown to 76%, with the largest increase in sub-Saharan Africa.

By 2010, the situation had improved so much that WHO could issue a new policy recommendation: treatment should be given to suspected malaria cases only after a diagnostic test had confirmed infection. That policy change had three dimensions. First, by ending the blanket administration

of artemisinin-combination therapy to every child with a fever, WHO hoped to reduce selective pressure on the parasite and thus delay the development of resistance. Second, excluding malaria in children with fever would increase the prospect of prompt and effective treatment for the many other common diseases that killed young children in Africa. Finally, the recommendation was made feasible by some very good news: most cases of childhood fever, even in Africa, were no longer caused by malaria.

The impact of all these improvements was dramatic. By 2010, reductions in malaria cases of more than 50% were being reported in 43 of the 99 countries with ongoing transmission, with downward trends recorded in an additional 8 countries. The epidemic's iron brake on African development that had stubbornly persisted for centuries was losing its grip.

WHO strengthened its policy-making architecture even further. In 2010, WHO initiated an extensive review of its policy-making process for malaria control and elimination. The aim was to establish a more rigorous, efficient, and transparent process that would allow for timely responses to the ongoing challenges faced by national malaria programmes.

Following the recommendations of an external advisory group, a Malaria Policy Advisory Committee was established in 2011 to provide independent advice to WHO on all policy areas related to malaria control and elimination. This strengthened policy-setting architecture repositioned WHO as the credible international public health authority on malaria policy, guidance, and technical support in malaria-endemic countries.

Since establishment of the new architecture, WHO has issued more than 15 policy recommendations on issues ranging from the use of seasonal malaria chemoprevention in the Sahel sub-region in Africa, to advice on how to estimate the longevity of insecticidal nets, to a warning about the risks of scaling back vector control in areas where transmission has been reduced.

The Malaria Eradication Research Agenda: malERA

By 2010, the world had embraced an ambitious plan for scaling up malaria control that progressed towards country-by-country and regional elimination, with the ultimate goal of global eradication. A meeting was held in Washington, DC to refine a research agenda to underpin the eradication goal. Participants agreed on a multi-pronged approach that included health systems, operational research, and monitoring and evaluation in addition to the basic and applied sciences. A false assumption that the epidemiology and pathophysiology of malaria were fully understood contributed to the failure of the first eradication effort. Scientists were determined to get things right this second time around.

The meeting was attended by the WHO Director-General, who had argued for more aggressive malaria control since the start of her administration. In her remarks at the close of the weeklong event, Dr Chan thanked participants for putting so much smart science in the service of a disease that affects the very poor, but reminded them that **no single technical breakthrough** in any single area would be sufficient to eradicate a disease as complex and tenacious as malaria. Even a highly effective vaccine, she said, would need to be supported by the

simultaneous use of drugs, vector control, and good monitoring and evaluation delivered by well-performing health systems.

Good will - and innovation - kick in

Public health is replete with good will and a creative desire to innovate, especially when doing so might change a situation where a child was dying from malaria every second of every day.

In 2008, the UN Secretary-General appointed Ray Chambers, an American business entrepreneur, philanthropist, and humanitarian, as his first Special Envoy for Malaria. Articulate and compelling, Mr Chambers undertook his role with passion, contributing to the visibility of malaria, understanding of its impact, and above all the need for funding. Also in 2008, at the request of its Member States, WHO launched the first of what would become annual World Malaria Days as awareness-building events.

Part of that awareness was a keen appreciation of the need for new tools. Several public-private partnerships were established to develop new products for malaria control, including the Medicines for Malaria Venture, the Malaria Vaccine Initiative, the Innovative Vector Control Consortium, and a malaria project supported by the Foundation for Innovative New Diagnostics, which aims to develop high-quality affordable diagnostic tests for diseases of the poor.

But one existing tool also needed innovation to maximize its impact. Though increases in coverage with insecticidal nets were nothing less than spectacular, access to artemisinin-combination therapies remained disappointingly low in most African countries. In 11 of 13 countries surveyed in 2009, fewer than 15% of children with fever were treated with these superior life-saving medicines. Data from that same year further showed that countries were receiving less than half of needed treatments. Annual joint tenders issued by WHO and UNICEF for multi-source generic treatments meeting international quality standards led to more quality products on the market, but supplies were still inadequate and prices were still too high for most national control programmes.

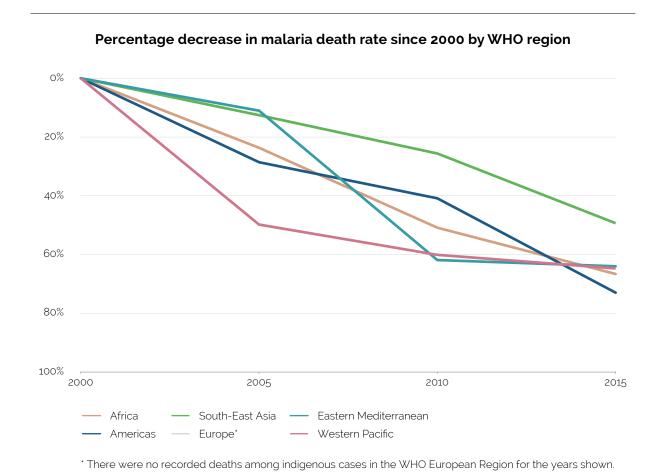
Apart from high prices, the barriers to better access were numerous and difficult to break down. Procurement required exceptionally long lead times. Artemisinin and its derivatives are manufactured from the leaves of the sweet wormwood, or *Artemisia annua*, plant. Cultivation, extraction, processing, and manufacturing of the final product require at least 18 months. Manufacturing and quality control are especially complex operations. The raw plant materials vary greatly in quality; impurities must also be removed. Artemisinin and its derivatives are chemically unstable, a characteristic that accounts for their superior antimalarial activity but adds to the challenge of manufacturing a consistently high-quality product. Finished products can deteriorate easily, creating special demands for packaging and storage.

Additional problems were market-related. The supply of treatments was highly fragmented, with a huge and lucrative market in the private sector, typically beyond the control of national regulatory authorities. The high price of medicines lured the producers of counterfeit products and cheaper monotherapies to flood the market, raising deep concern that these products

would hasten the development of drug resistance. The long lead time from cultivation to finished products contributed to a notoriously unstable supply chain, with supplies and their prices fluctuating wildly in what has been called a "bullwhip effect". A year of oversupply was typically followed by a year of dire shortages with a high risk of stock outs. The uncertainty of future demand gave pharmaceutical companies little incentive to expand production.

One solution came in 2010 with publication of the *WHO guide to good procurement practices* for artemisinin-based antimalarial medicines. Through its concise 16-step checklist, the manual covered all aspects of the procurement cycle, from selecting the best products, through defining product specifications and inviting tenders, to post-shipment quality control and the detection of variations.

In improving access to both diagnostic tests and medicines, the WHO prequalification programme played a decisive role, especially given the very low demand for antimalarial medicines and diagnostic tests in countries with stringent regulatory authorities. The situation improved significantly. The number of manufacturers of quality-assured artemisinin-combination therapies grew from a single company in 2006 to nine prequalified generic manufacturers in 2013. Together, they produced 22 prequalified patient-friendly fixed-dose combinations and two prequalified paediatric formulations.



Source: WHO

Community-directed delivery of interventions

In addition to insecticidal nets, WHO recommended three preventive interventions for use in parts of Africa with high transmission of *Plasmodium falciparum* malaria. One policy recommendation covered the use of sulfadoxine-pyrimethamine for the intermittent preventive treatment of pregnant women. A second covered the preventive treatment of infants. In 2012, WHO recommended the seasonal chemoprevention of malaria in areas with highly seasonal malaria transmission as an additional approach to control. Implementation of the recommendations required more frequent contact with health services, which is always a problem for diseases that predominantly affect the rural poor. For example, the recommendation for the preventive treatment of pregnant women required that drugs be administered at each of four antenatal care visits.

To improve access to treatment, the Special Programme for Research and Training in Tropical Diseases, or TDR, had a tailor-made solution based on scientific understanding of why good drugs, good diagnostics, and good preventive strategies fail to have a proportionate impact on tropical diseases in poor countries. In 2009, TDR published the results of a three-year multicentre experimental study designed to test whether community-directed distribution, which had successfully delivered ivermectin to 75 million rural Africans at risk of onchocerciasis, could also distribute other priority interventions, including insecticidal nets and medicines for the home-based management of malaria. When malaria interventions were delivered using the community-directed strategy, coverage with both nets and treatments more than doubled, at lower costs than with conventional delivery systems. The results further showed that 77% of children in the seven study sites received artemisinin-combination therapy within 24 hours following the onset of fever.

Moving forward, the approach holds great promise as a platform for the integrated delivery of services, aligned with the core principles of primary health care and the ambition of reaching universal coverage.

The best news yet: 6.8 million lives saved

The way so many partners and innovative approaches kicked in to break down the barriers to everhigher coverage was emblematic of an initiative that looked destined for unprecedented success.

By 2013, 79 of the 88 endemic countries had adopted artemisinin-combination therapies as the first-line treatment for *Plasmodium falciparum*. The purchasing of treatments increased dramatically, from 11 million treatment courses in 2005 to nearly 400 million in 2013. At that time, generic treatments accounted for 73% of purchases by UNITAID, a drug-purchasing facility that draws substantial and sustainable resources from a levy on airline tickets.

Another milestone was reached in 2013. For the first time, the number of diagnostic tests supplied to Africa for use in the public sector exceeded the number of treatments administered. The test-

before-treat strategy was clearly working to conserve treatments and hopefully prolong their effective market life.

In terms of net distribution, 2014 was the strongest year ever, with more than 189 million nets delivered to countries in sub-Saharan Africa, bringing the total number of nets delivered to that region since 2012 to 402 million. Not surprisingly, deaths from malaria in sub-Saharan Africa dropped by 54% compared with the situation in 2000.

In 2014, WHO estimated that 670 million fewer cases and 4.3 million fewer deaths occurred between 2001 and 2013 globally than would have occurred had the incidence and mortality rates seen in 2000 remained unchanged. Another new estimate was equally compelling: from 2000 to 2014, reductions in malaria cases in sub-Saharan Africa saved countries an estimated \$900 million – money that would otherwise have gone to malaria case management. Mosquito nets contributed to the largest savings, followed by artemisinin-based combination therapies and indoor residual spraying.

But the 2016 World Malaria Report brought the best news yet. Data in the report showed – beyond any shadow of a doubt – that the MDG target for halting and beginning to reverse the incidence of malaria had been met. Between 2000 and 2015, the rate of new malaria cases declined globally by an estimated 41%. Over the same period, the global malaria death rate fell by 62%. Equally important, an increasing number of countries had moved towards malaria elimination. Between 2000 and 2015, six countries were certified by WHO as malaria free. An additional 11 countries met the criteria of zero indigenous cases for three years or more and were awaiting official certification of malaria-free status by WHO. All previously endemic countries that eliminated malaria prevented reestablishment of the disease. Elimination is considered especially important in areas of South-East Asia with low malaria incidence but high rates of drug resistance.

By 2016, WHO could revise its estimates upward: **between 2001 and 2015**, a **cumulative total of 6.8 million lives were saved** due to reductions in malaria mortality, which is testimony to the commitment of governments supported by the efforts of multiple partners on multiple fronts – an enormous victory for families, communities and countries.

In May 2015, the World Health Assembly approved WHO's *Global technical strategy for malaria 2016–2030*, a 15-year blueprint for all countries working to control and eliminate malaria. The strategy set ambitious but attainable targets for 2030, including reducing malaria case incidence and death rates by at least 90%, eliminating malaria in at least 35 countries, and preventing the reintroduction of malaria in all countries that are malaria free.

The global technical strategy marked the first malaria strategy endorsed by the World Health Assembly since 1993. It resulted from the collective effort of more than 400 malaria experts from 70 countries and consultations in seven regions. In June 2015, the Global Malaria Programme was restructured to better respond to the challenges outlined in the global technical strategy.

With the target of reducing malaria cases and deaths by at least 90%, the world is clearly moving into an era that wants to see no child die from a mosquito bite anymore. The malaria experience supports one further conclusion: investment in health development works.

In 2016, WHO announced a significant breakthrough. The world's first malaria vaccine, approved by the European Medicines Agency the previous year, is set to be piloted in three countries in sub-Saharan Africa beginning in 2018. The vaccine, known as RTS,S, has been shown to provide partial protection against malaria in young children. It will be evaluated as a potential complement to the existing package of WHO-recommended malaria preventive, diagnostic, and treatment measures. The benefits of the vaccine are expected to be greatest in areas with high transmission of *Plasmodium falciparum* malaria and associated high child mortality.

Though the eradication of malaria remains the ultimate goal for WHO, endemic countries, and their multiple partners, the way ahead is not an easy one for a disease as complex and tenacious as malaria. The burden, though diminished, remains huge. Worldwide, malaria caused 212 million new cases and 429 000 deaths in 2015. In Africa, an estimated 43% of people at risk of malaria do not have access to the core WHO-recommended vector control tools, namely insecticide treated nets and indoor residual spraying. Significant coverage gaps undermine the effectiveness of WHO recommendations for the protection of the two most vulnerable groups: pregnant women and infants.

The fear of further spread of resistance to artemisinin continues to haunt control programmes. The resistance of mosquitoes to insecticides is another significant worry. Since 2010, 60 countries have reported mosquito resistance to at least one class of insecticides used in nets and indoor spraying. Of these, 50 reported resistance to two or more classes of insecticides.

These and other challenges will need to be addressed in the same spirit of determination, ingenuity, and global solidarity that has brought so much progress – and saved so many millions of lives – in the recent past.



he fight against tuberculosis faced two challenges in 2007: co-infection with HIV and the emergence of drug resistant strains made the disease more deadly. WHO and its partners have pursued a culture of measurement and innovation, leading to more effective and affordable diagnostic tests, firm policies for their appropriate use, and several new treatments in the pipeline. In May 2014, WHO launched an ambitious strategy to end TB by 2035, and is elevating the TB fight from the technical to the highest political levels.

During the first five decades of its history, WHO gave TB control widely varying degrees of priority, first swinging up, then down, then dramatically up again in line with the evolving epidemiology of this disease. In 1948, the newly established agency singled out malaria, TB and sexually transmitted diseases, especially syphilis, as epidemics requiring urgent international attention. The discovery of streptomycin in 1944, shown to have striking therapeutic efficacy, meant that it was widely available by 1948. The availability of two new TB drugs, isoniazid and pyrazinamide, in the early 1950s, followed by the discovery of rifampicin some 20 years later, transformed TB from a major killer to a disease that could be easily and cheaply cured, at least in affluent nations.

In the developing world, a series of research studies, supported by WHO and the governments of India and the United Kingdom, laid the foundation for a radical integration of TB control into general health services. Patients were treated in homes instead of segregated in specialized hospital wards. Doctors diagnosed cases based on respiratory symptoms alone. The mobile radiography units – long the symbol of TB control in poor countries – were dismantled. As treatment courses were long, TB control borrowed from the success of the leprosy programme and recommended that patients be directly observed as they took their daily medicines, thus improving adherence.

The tuberculosis epidemic was held at bay, but just barely. The incidence of new cases declined in middle-income countries, but at half the rate seen in wealthy nations.



In July 2011, WHO issued its first-ever negative policy recommendation to tackle diagnostic practices that were both dangerous for TB control and wasting resources in the millions of dollars.

By the 1980s, tuberculosis had lost its status as a top international priority at WHO and elsewhere. Research dwindled. Medical journals that had been exclusively devoted to tuberculosis were rebranded as journals covering respiratory diseases. International conferences on tuberculosis diminished in frequency and then stopped altogether. At WHO, only two TB experts were kept on its headquarters staff. TB dropped to the status of a largely forgotten disease. In reality, though, its power to resurge was merely waiting in the wings. That neglect changed dramatically in 1993, when WHO took the unprecedented step of declaring the epidemic a global emergency. The agency had good reasons to do so.

Two major crises

In 2007, when Dr Margaret Chan took office, WHO estimated that 13.7 million people were living with active tuberculosis, including 9.3 million new cases. TB killed an estimated 1.8 million people that year, making it one of the world's biggest infectious killers. Tuberculosis control faced two major crises. First, the emergence and then explosive spread of the HIV epidemic was accompanied by sharp increases in TB morbidity and mortality. As immunodeficiency spread, more of the roughly two billion people who harmlessly harbour *Mycobacterium tuberculosis* as a latent infection developed overt disease. **The two epidemics converged to deliver an especially deadly blow, most notably in sub-Saharan Africa.**

Second, strains of the bacterium resistant to multiple drugs emerged, making multidrug-resistant tuberculosis, or MDR-TB, a formidable new threat. Second-line drugs were toxic, difficult to administer, in short supply, and at least 100 times more costly. Whereas treatment of drug-susceptible TB took six months, the time needed to treat MDR-TB was 20 months or more. Even with the best treatment and supportive care available, fewer than 50% of patients could be cured. The threat was global. In wealthy countries, drug-resistant strains showed how quickly they could exploit populations made vulnerable by poverty, illness, social marginalization, or lack of access to basic health care. In the US, MDR-TB gained its first foothold in the homeless populations living on the streets and sidewalks of New York City.

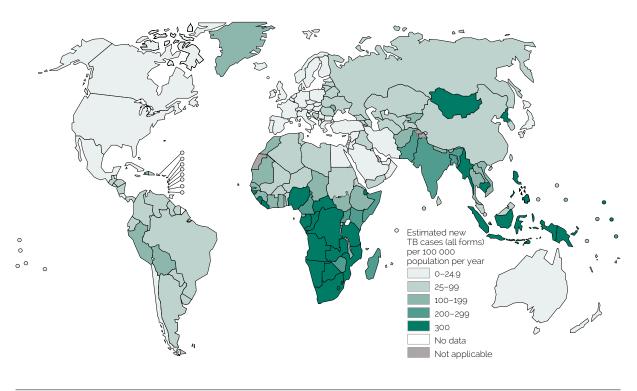
Moreover, TB experts were still reeling from the results of an investigation of an especially severe TB outbreak at Tugela Ferry Hospital located in a rural and desperately poor district in South Africa. The results of that investigation, published in 2006, found 221 patients with MDR-TB. Of these, 53 were infected with a strain that was resistant to the two most powerful classes of first-line drugs but also to at least two of the six most powerful classes of second-line drugs. All 53 patients were co-infected with HIV. Working together, WHO and the US Centers for Disease Control and Prevention defined the newly detected form of this disease as "extensively drug-resistant TB", or XDR-TB.

Extensively drug-resistant TB was extreme in every sense. It was extremely lethal. Of the 53 patients with XDR-TB, all but one died, with an average survival time of only 16 days following diagnostic confirmation. While some infections had been acquired in the community, the vast majority of infections moved from person to person in the hospital setting. That made the emergence of

XDR-TB extremely alarming, as few hospitals in sub-Saharan Africa were equipped to prevent the spread of infection; many had no reliable supplies of electricity or clean running water.

The news quickly got worse. A retrospective investigation, jointly undertaken by WHO and CDC, of samples stored in an international network of specialized TB laboratories confirmed that XDR-TB had already spread well beyond the African continent. By the end of 2014, XDR-TB had been reported in 105 countries, with the highest incidence in Belarus, Georgia, Latvia and Lithuania.

Estimated new tuberculosis cases in 2015



Source: WHO

A problem-solving culture of innovation

In dealing with these dramatic new threats, WHO and its partners had much to build on. In 2006, a new Stop TB Strategy was launched by WHO following intensive exploration and discussion with the managers of TB control programmes in high-burden countries and their partners, including technical agencies and donors. At that time, broad adoption of the WHO DOTS strategy, or directly-observed treatment, short course, had produced remarkable progress in TB control for nearly a decade. The new strategy was designed to pursue DOTS expansion while adding

five new lines of action judged essential for meeting the MDG TB target. Ways to tackle TB/HIV co-infection and MDR-TB were included together with strategies for strengthening health systems, engaging all care providers in the private and public sectors, empowering people and communities, and promoting targeted research. To support the new strategy, WHO issued a fully costed Global Plan to Stop TB 2006–2015.

WHO had already established a culture of innovation. The Stop TB Partnership, hosted and housed at WHO, demonstrated a remarkable ability to solve problems through the creation of innovative new facilities and mechanisms, including the establishment of a dedicated global drug facility. By procuring drugs at competitive prices and consistently ensuring that their quality met WHO's stringent standards, the global drug facility brought order to a market previously characterized by chaos.

To address the many problems raised by the emergence of MDR-TB, WHO established a Green Light Committee in 2000 to ensure the supply of second-line drugs, oversee the proper and rational use of drugs, and make them more affordable. Before releasing second-line drugs, the committee rigorously reviewed country proposals to ensure that their use would not further promote drug resistance. That requirement had the additional advantage of transferring high-level expertise in drug management from WHO to national control programmes. The Global Fund backed the initiative by issuing a requirement that all funds for the purchase of second-line drugs must be approved by the Green Light Committee.

Policy breakthroughs

In 2008, WHO and UNAIDS introduced the "3 I's" strategy for addressing the management of HIV/TB co-infection. Intensified case finding was the first prong of the strategy. Even in an era with widespread access to antiretroviral therapy, too many people living with HIV died because of undiagnosed TB co-infection. WHO recommended that all people living with HIV should be screened for their TB status with a clinical algorithm at each clinical encounter. In the second prong of the strategy, WHO recommended that people infected with HIV, but proven to not have TB, should be given isoniazid preventive therapy for at least six months as part of a comprehensive package of HIV care. That recommendation was strengthened by evidence that the effects of isoniazid preventive therapy augmented the effects of antiretroviral therapy in reducing the incidence of TB. As people with HIV are exceptionally vulnerable to the risk of nosocomial TB transmission, the third prong set out measures for infection control that should be strictly implemented in all facilities providing HIV care.

In July 2011, WHO issued its first-ever negative policy recommendation to tackle diagnostic practices that were both dangerous for TB control and wasting resources in the millions of dollars. WHO urged countries to ban the use of inaccurate and unapproved commercial blood tests to diagnose active tuberculosis. Before making that recommendation, WHO meticulously gathered and verified compelling evidence that these serological tests were inconsistent, imprecise, and put patients' lives at risk. The many false-positive results delivered by these tests meant that patients took toxic medicines for months, for no reason. False-negative results meant that

people received no treatment and took no precautions to prevent infecting others, a particularly dangerous failure for an airborne disease that readily spreads via a cough or a sneeze.

WHO estimated that more than a million of these inaccurate blood tests were carried out each year, often at great costs to patients, who paid up to \$30 per test. At that time, the marketing of blood tests for TB was targeted at countries with weak regulatory control of diagnostics, where perverse market incentives were allowed to override the welfare of patients. In short, a multimillion dollar business was selling substandard tests with unreliable results.

That negative policy recommendation had a rapid and welcome impact. In June 2012, India's Ministry of Health and Family Welfare banned the manufacture, sale, distribution and use of the tests throughout the country. The government decree directly attributed that decision to a "negative policy statement issued by WHO that commercial serodiagnostic tests provide inconsistent and imprecise findings."

A breakthrough in testing technology

When the emergence and spread of HIV brought TB roaring back, the tools for coping with the surge in cases were antiquated. Sputum microscopy, quick and cheap but tedious and prone to human error, had been the principal diagnostic test for more than a century. Growing the bacterium in culture was the highly accurate diagnostic "gold standard" but could take up to two months to get results. Drugs for treating drug-susceptible TB dated back to the 1950s and 1970s, with nothing new since. Needless to say, no ready-made diagnostic tools were on hand to manage the formidable new challenges of MDR-TB and XDR-TB.

In 2009, case-finding and testing were still missing nearly 40% of suspected TB cases. The prevalence of MDR-TB had increased to an estimated half a million cases, of whom fewer than 7% were diagnosed and, of those diagnosed, only one in five received treatment. Nearly two million people were still dying of TB each year, mainly from drug-susceptible forms of the disease that could have been easily and cheaply cured.

In the autumn of 2010, a breakthrough looked eminent. The Foundation for Innovative New Diagnostics, or FIND, in partnership with the Cepheid corporation and the University of Medicine and Dentistry of New Jersey, had developed a new molecular platform for the diagnosis of TB using the Xpert MTB-RIF machine, or Xpert. Many – though not all – hailed the new technology as having the potential to revolutionize TB testing.

With its compact and sleek table-top design that looked like an espresso machine, the Xpert machine had much to offer. Fully automated, it was easy to use and posed no biosafety hazards for staff. Large-scale testing and demonstration projects in India and South Africa showed high sensitivity and specificity in the detection of both drug-susceptible TB and MDR-TB. As a major advantage, the test produced results in less than two hours instead of weeks or months. That speed greatly increased the prospects of successful case management: patients waiting for test results could be immediately started on the right treatment.

However, as sceptical critics noted, operation of the machine required a steady and reliable supply of electricity. The machine needed yearly maintenance and calibration and performed best under controlled conditions of temperature and humidity – luxuries in most facilities providing care in high-burden countries. Moreover, with all its advantages, Xpert came on the market at a prohibitively steep price. The initial market price of different testing machines ranged from \$17 000 to \$62 000. The cost of the disposable test cartridges, with their short shelf lives and huge demands for storage space and waste disposal, ranged from \$17 to \$120 – equivalent to the entire annual per capita health expenditure in most high-burden countries.

In September 2010, FIND submitted its dossier of trial results to WHO for evaluation. In December 2010, WHO formally endorsed the use of the new molecular assay. WHO recommended Xpert as the first-choice test for presumptive TB in people living with HIV or suffering from severe disease, and in individuals with presumptive MDR-TB. That endorsement by WHO was the seal of approval needed to change the situation dramatically. What followed demonstrated the power of WHO to get multiple partners working in concert to take an innovation forward in a massive, structured, phase-wise campaign, precisely targeted at hot spots in greatest need and gathering further evidence along the way.

FIND leveraged its investment by directly negotiating price reductions with the manufacturer; reduced prices were offered to nearly 150 purchasers in low- and middle-income countries. The US government, UNITAID, and the Bill and Melinda Gates Foundation provided upfront payment of \$11 million to the manufacturer to reduce unit prices further. The price of cartridges dropped from \$17 to under \$10.

In 2013, UNITAID and WHO started the largest rollout of Xpert ever, with UNITAID investing nearly \$26 million to purchase more than 220 Xpert machines and 1.4 million cartridges for 21 countries in Africa, Eastern Europe, and Asia. Through the concerted and determined efforts of multiple partners, high-burden countries were indeed being equipped with a revolutionary new tool for detecting difficult forms of TB.

Other new diagnostic options were also gaining recognition. As part of its programme for the testing of new technologies, WHO evaluated molecular line probe assays for the rapid screening of patients at risk of MDR-TB and issued policy recommendations on their use. WHO also evaluated the use of loop-mediated isothermal amplification (TB-LAMP), a manual assay that required less than one hour to perform and could be read with the naked eye under ultraviolet light. Nonetheless, the ideal of an inexpensive point-of-care diagnostic test that matched the simplicity and accuracy of HIV antibody tests and required no electricity remained elusive.

New drugs push WHO into a novel role

For the first time in more than 40 years, a novel class of TB drugs with a novel mechanism of action, bedaquiline, was granted accelerated approval by the US Food and Drug Administration in December 2012. That approval, which was based on late phase II clinical data, created a unique dilemma for WHO. As the new drug was so desperately needed for the treatment of MDR-TB, the risk was great that countries would start using it in ways that would contribute to the rapid

development of resistance – causing the world to lose its first new TB chemotherapeutic drug in more than four decades. The lack of phase III trial data on safety and efficacy created another worry: would early use of the drug actually do more harm to patients than good?

These concerns pushed WHO into the novel role of translating available data into guidelines and advice aimed at protecting both patient welfare and the lifetime of the drug. The following year. WHO issued its interim guidance for the inclusion of bedaquiline in the combination therapy of MDR-TB in accordance with existing WHO guidelines for the programmatic management of drug-resistant TB. The guidance set out requirements for patient selection, informed consent, drug administration, monitoring of efficacy, and pharmacovigilance to detect and manage adverse drug reactions and potential interactions with other drugs.

In 2014, WHO performed a similar evaluation of a second novel class of drugs with a novel mechanism of action, delamanid, still in phase III trials but granted conditional approval by the European Medicines Agency in April 2014. WHO interim guidance, published the same year, stipulated the specific conditions and safeguards that must be in place before programmes use delamanid to treat adults with MDR-TB.

In 2015, five anti-TB drugs, including bedaquiline and delamanid, were added to the WHO Model List of Essential Medicines. Four of the newly listed drugs were recommended by WHO for use in the treatment of MDR-TB and XDR-TB. The fifth drug, rifapentine, was indicated for the preventive treatment of latent TB in people living with HIV. The inclusion of these TB drugs in the Model List is expected to stimulate the interest of drug manufacturers to invest more in the development of new anti-TB medicines.

Also in 2016, WHO announced good news for the control of MDR-TB. A new DNA-based test was available that could identify genetic mutations in MDR-TB in just 24 to 48 hours, down from the three months previously required. In addition, WHO announced a new and shorter treatment regimen that allowed MDR patients to complete treatment in half the time and at nearly half the cost. Such innovative steps forward supported the feasibility of new goals.

The ultimate ambition: end TB

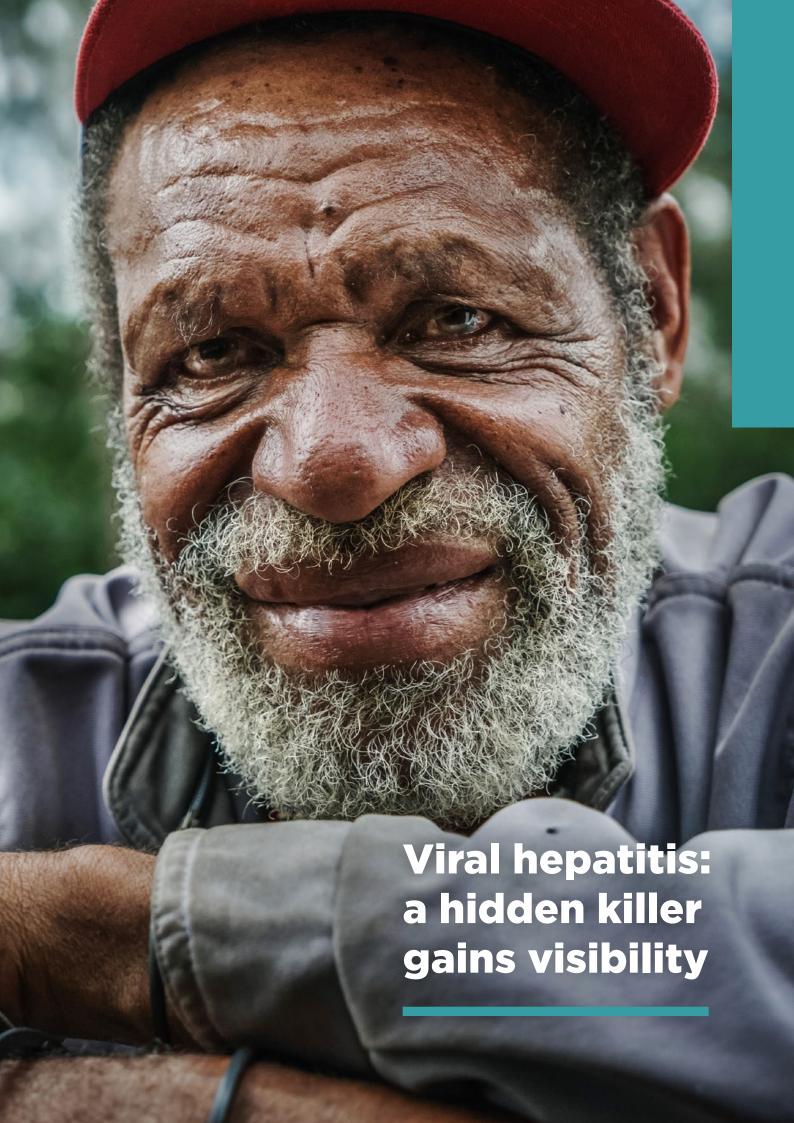
In May 2014, the World Health Assembly approved WHO's ambitious new strategy to end the tuberculosis epidemic by 2035. The strategy, with its three indicators and milestones at five-year intervals, had a visionary goal: zero TB deaths, zero TB disease, and zero TB suffering. Three pillars provided the foundation for this visionary goal: integrated patient-centred TB care and prevention, bold policies and supportive systems, and intensified research and innovation. Though ambitious even for an optimistic organization like WHO, the wisdom of aiming high for TB was being firmly endorsed by external economic evaluations.

In January 2015, *The Economist* news magazine published a report on "The economics of optimism", which ranked the benefit per dollar invested in various development initiatives. Reducing tuberculosis ranked first among health development initiatives, showing a return of \$43 on every investment dollar. As *The Economist* noted, the prominence given to TB was a "no-

brainer". The ranking drew on the work of the Copenhagen Consensus Center, an initiative which commissioned some 60 teams of economists, plus representatives from the UN, civil society, and business communities, to rank the sustainable development targets that would produce the most "phenomenal" value for money. The TB target was one. As the Copenhagen Center noted, "The economic case, put simply, is that TB treatment is low cost and highly effective, and on average may give an individual around 20 years of additional life."

As a further endorsement, the related *Nobel laureates guide to the smartest targets for the world 2016–2030*, issued in 2015, pared the 169 targets in the 2030 Agenda for Sustainable Development down to just 19. The nine people-related targets included the reduction in tuberculosis deaths by 90%. As the guide noted, concentrating on this select list of 19 targets could triple the benefits for the world's poorest.

The new End TB Strategy has another solid reason for its hope. In 2016, WHO estimated that, since the start of the century, efforts to stop TB had saved some 49 million lives. To secure high-level commitment to do even more, WHO will be holding its *First ministerial conference on ending tuberculosis in the sustainable development era* in November 2017 in Moscow, Russian Federation. As requested in a resolution of the UN General Assembly, a high-level meeting on the fight against tuberculosis will be held in 2018. **The momentum to end TB is already building at the highest political level.**



s the epidemics of HIV, malaria and tuberculosis receded, viral hepatitis became more visible as a leading killer worldwide. Many hard-won lessons from the HIV experience provided a head start for a targeted approach to a disease situation that mirrors the early years of HIV. For example, while it took nearly a decade to get the price of antiretroviral therapy down, prices for the new hepatitis C cures plummeted within two years.

As huge gains were made in reducing the impact of HIV, another long-neglected epidemic became more visible: the devastating and complex health problems caused by viral hepatitis infections. No longer overshadowed, hepatitis moved into the spotlight as one of the leading killers worldwide. WHO estimates that, in 2015, infections with hepatitis B and C virus – the two out of five hepatitis viruses responsible for the greatest burden of disease – caused 1.34 million deaths worldwide, compared with 1.1 million deaths from HIV in that same year, 1.4 million deaths from tuberculosis, and 438 000 deaths from malaria. Whereas the HIV, TB, and malaria epidemics have peaked and are now in decline, morbidity and mortality from viral hepatitis are on the rise. WHO estimates that deaths from hepatitis have risen by 22% since 2000. Unless more people with chronic infections are diagnosed and treated, the number of deaths caused by viral hepatitis will continue to increase.

The burden of viral hepatitis

Hepatitis B and C are bloodborne infections, with significant transmission of hepatitis B occurring in early life and of hepatitis C occurring through unsafe injections, including injection drug use, and medical procedures. Transmission through sexual contact occurs, though less commonly. The resulting disease burden is enormous and felt worldwide. WHO estimates that, in 2015, 257 million people were living with chronic hepatitis B infection, and 71 million with chronic hepatitis C infection. The hepatitis B epidemic affects parts of Africa and the Western Pacific most severely, while the hepatitis C epidemic is more evenly distributed worldwide. An estimated 67% of people who inject drugs have been infected with the hepatitis C virus. The Eastern Mediterranean and European regions have the highest reported prevalence of hepatitis C infection. Among the 36.7 million people living with HIV in 2015, an estimated 2.7 million had chronic hepatitis B infection and 2.3 million had been infected with hepatitis C.



The burden of liver cancer is particularly heavy in the developing world.

Chronic infection from the viruses can severely damage the liver, leading to cirrhosis and hepatocellular cancer. **The burden of liver cancer is particularly heavy in the developing world.** In sub-Saharan Africa, for example, liver cancer is the most common cancer among men and the third most common cancer in women.

Clinical management: the outlook is improving

Although infections with both B and C hepatitis viruses can be prevented and treated, doing so encounters some challenges. Diagnosis is problematic. As chronic hepatitis infections can cause no symptoms and remain silent for decades, many people are unaware of their infection and do not seek treatment until the disease has progressed to severe – often irreversible – liver damage. Medical care is demanding. In wealthy countries, patients with hepatitis B and C infections are treated by highly trained specialists, such as hepatologists, gastroenterologists, and infectious-disease experts. Expanding care in countries with fewer resources calls for simplified and standardized protocols that extend clinical competence to non-specialized health professionals. WHO experiences with HIV show that such a transfer of competence is entirely feasible.

The recent development of highly effective medicines has revolutionized the treatment of chronic hepatitis C infections. The new oral direct-acting antivirals are well-tolerated and can achieve cure rates above 95%. However, with initial launch prices in the US of between \$66,000 and \$84,000 per patient per treatment course, the drugs were prohibitively expensive everywhere. Low-cost and effective medicines are available to treat hepatitis B infection, but most patients require lifelong treatment. The price of tenofovir, for example, has recently dropped to as little as \$48 per person per year. However, costs mount for any drug that needs to be taken for a lifetime.

The hepatitis B vaccine: an early win for prevention

A safe and effective vaccine that prevents hepatitis B infection has been available since 1981. As mother-to-child transmission is an important route of infection, WHO recommends a three-dose immunization schedule with the first dose administered within 24 hours following birth. This is particularly important, as infection acquired at birth is more likely to result in chronic infection and subsequent liver disease. Introduction of the vaccine into routine childhood immunization programmes brought an early win in the hepatitis response. The world will reap major benefits from the current emergence of hepatitis B-free generations. WHO estimates that, in 2015, 84% of the world's young children were reached with three doses of hepatitis B vaccine. The success achieved with the scaling up of immunization has helped to reduce hepatitis B infection in children, though more infants need to receive a first dose of the vaccine within 24 hours of birth. In Africa, for example, only 10% of newborns are covered with the birth dose.

Much more needs to be done to prevent hepatitis B and C infections in the general population. WHO recommends a comprehensive preventive approach that includes assurance of safe blood products, safe injection practices, preferably through the expanded use of self-destructing disposable syringes, comprehensive harm reduction services for people who inject drugs, and the promotion of safe sex. The political declaration agreed at the 2016 UN General Assembly Special Session on the World Drug Problem includes WHO recommendations for harm reduction as a way to protect the health of people who inject drugs. However, implementation of the WHO harm reduction package in countries remains patchy and insufficient.

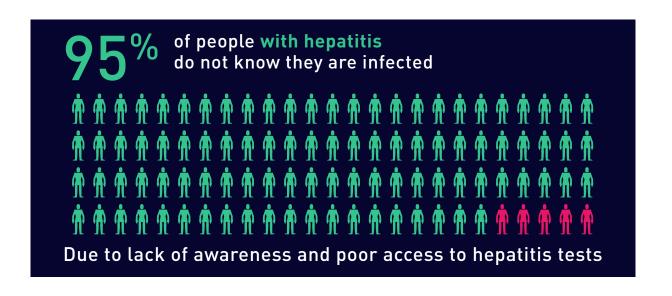
Current challenges – like the early years of AIDS

In many ways, efforts to prevent and control viral hepatitis face challenges that mirror the early years of the AIDS epidemic, when public awareness and the determination to act were just beginning to build. Stigma and discrimination associated with hepatitis infection are high, as is the tendency of the disease to disproportionally affect marginalized populations. The groups at highest risk for hepatitis C infection are similar to those for HIV: men who have sex with men, sex workers, injecting drug users, and prisoners. As with HIV, viral hepatitis can be transmitted from mother to child. Both the HIV and the hepatitis epidemics require special attention to the safety of the blood supply.

The fact that chronic infection with viral hepatitis can remain silent for decades mimics the long incubation period for HIV infection, with all the challenges this means for early diagnosis and treatment as a strategy for preventing further spread. As with the early years of HIV, demanding requirements for diagnostic testing and clinical management raise questions about whether hepatitis can be effectively treated in resource-constrained settings. Finally, as was the case when the first antiretroviral medicines were licensed, the costs of hepatitis treatments are way too high, giving fair access to treatment a compelling moral imperative. **People should not be denied access to life-saving interventions for unfair reasons, including those with economic or social causes.**

Though hepatitis B and C are old diseases, they have been ignored for so long that the gaps in data and knowledge – like the paucity of reliable data from seroprevalence studies and the lack of country-specific data on the prevalence of liver cirrhosis and hepatocellular cancer – are what might be expected for a newly emerging disease. These gaps in knowledge make it difficult for health officials in high-burden countries to persuade their governments to make viral hepatitis a priority, in terms of policy and also for funding. At the same time, because the hepatitis epidemics are global in their impact, affecting rich countries as well as very poor ones, the incentives for the pharmaceutical industry to develop new products are high. A rich and promising set of new tools has been developed over the past few years. The job now, as in the early years with AIDS, is to push for lower prices and simplified diagnostics through a range of proven strategies that can shape market forces to serve the poor. Progress is being made. Over the past three years, WHO has prequalified three new diagnostic tests for hepatitis, including the first rapid test for detecting hepatitis C.

The similarities between the HIV and viral hepatitis epidemics are important in that they give efforts to control viral hepatitis a head start. Many hard-won lessons from the HIV experience provide a firm foundation for accelerated – and aggressive – action to get the hepatitis burden down. The pace of progress for hepatitis is indeed accelerated. While it took nearly a decade to get the price of antiretroviral treatments down, prices for hepatitis C treatments have plummeted in many countries over just the past two years.



Source: WHO

WHO reports: an eye-opener

Over the years, WHO governing bodies had addressed viral hepatitis, but nearly always as just one component of a much larger health problem. Beginning in 1992, hepatitis B was discussed at World Health Assemblies under agenda items on immunization, cancer prevention, and the protection of health care workers from the risk of infections. Some approaches to prevention were also discussed under agenda items on blood safety and safe injection practices.

Viral hepatitis first appeared as a stand-alone item on the agenda of the World Health Assembly in 2010. The WHO report for that session on the disease and its burden, and the many opportunities for prevention and control that were being missed, was an eye-opener for Member States. It led to the adoption of WHO's first resolution on viral hepatitis, marking the dawning of a new era of awareness about the magnitude of the disease burden and the need for urgent action on multiple fronts. The resolution also led the WHO Director-General to establish the Organization's first global viral hepatitis programme.

In response to growing concern and welcome pressure from active civil society groups, WHO issued a framework for hepatitis prevention and control in 2012. The framework aligned recommended actions around four strategic objectives: to raise awareness, promote partnerships, and mobilize resources, to gather data and evidence as policy support, to prevent transmission, and to improve screening, care, and treatment. Given several similar challenges facing the HIV and hepatitis epidemics and opportunities for synergistic responses, the Director-General placed management of the new programme under the WHO Department of HIV in late 2013.

Viral hepatitis returned to the agenda of the World Health Assembly in 2014, this time with a report that mapped out the many barriers to prevention and control. That report gave viral hepatitis the status of a serious but under-recognized global public health problem. Whereas hepatitis B vaccination programmes had expanded as primary prevention, diagnosis and management of existing cases were demanding, with most countries providing only limited clinical care to those who could afford it. **Treatment and care needed a public health approach that could extend the benefits more equitably**. Many countries lacked the human resources and sophisticated medical infrastructure needed to provide treatment. The road ahead would not be easy.

The 2030 Agenda for Sustainable Development, adopted in September 2015, included a target that called on the public health community to "combat hepatitis" but gave no endpoint for an expected result. Civil society organizations were instrumental in persuading WHO Member States to respond far more ambitiously, urging them to aim for elimination. Already in 2014, Member States asked WHO to explore the feasibility of eliminating the epidemic of viral hepatitis as a public health threat. In many ways, such a sweeping ambition made sense technically. Hepatitis C has no animal host or ecological reservoir of infection, and both diseases have proven tools for prevention and treatment. The ambition also looked appropriate for a disease that had moved out of obscurity to rank among the leading killers worldwide. Nonetheless, the obstacles to success were immense.

WHO's first global strategy on viral hepatitis

In 2016, the World Health Assembly approved the Organization's first-ever Global Health Sector Strategy on Viral Hepatitis, covering the five years from 2016 to 2021. As another first, the strategy set global targets for reducing hepatitis infections and deaths and expanding coverage with preventive, testing, and treatment services. As with the response to the HIV epidemic, the strategy adopted a public health approach that gives priority to the prevention of infection and disease, the promotion of health, and the prolongation of life among the population as a whole. It aims to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized interventions and services that can be readily taken to scale and decentralized, including in resource-constrained settings.

As few high-burden countries have national hepatitis strategies, plans, and budgets, the strategy gives particular attention to the development of surveillance systems that can gather the data needed to leverage political commitment. Such data further allow the strategic targeting of high-impact interventions to match the distinct features of local epidemics. The strategy proposes a

set of six core interventions and services to end the epidemic: hepatitis B vaccination, prevention of mother-to-child transmission of hepatitis B, prevention in health care settings through injection and blood safety, harm reduction for people who inject drugs, hepatitis testing, and treatment and care for those with chronic infections.

In April 2017, WHO issued its first *Global Viral Hepatitis Report*, which sets out the first WHO-validated baseline data for monitoring progress and highlights examples of countries that have taken action to implement the strategy.

Making hepatitis C treatments affordable

Work to reduce the prices of the new direct-acting antivirals that can cure hepatitis C is already bringing dramatic results for some populations in a number of countries. Mechanisms being used include licensing agreements that stimulate competition among generic manufacturers, local production, price negotiations with the originator company, and use of a game-changing Medicines Patent Pool. The Medicines Patent Pool, which relies on products prequalified by WHO, was set up in 2010 to improve access to antiretroviral therapy in low- and middle-income countries. Its remit was later expanded to include hepatitis C and tuberculosis treatments. It is sponsored and fully funded by UNITAID, a drug purchasing facility that draws substantial and sustainable funding from a levy on airline tickets.

In October 2016, WHO announced that more than one million people living in low- and middle-income countries had been treated with the revolutionary hepatitis C curative medicines since their introduction two years earlier. The announcement coincided with the release of a WHO report *on Access to Hepatitis C Treatment: Focus on Overcoming Barriers*. The report provides comprehensive data on levels of access, prices charged in different countries, and the situation with patents and registration of the medicines.

The report demonstrated the burden of unmet needs but also introduced transparency to the market, allowing price comparisons across countries. For example, costs per patient per treatment course range from \$9,400 in Brazil to \$79,900 in Romania. Egypt, which has the world's largest hepatitis C burden, has also had the greatest success in getting prices down, from \$900 in 2014 to less than \$200 in 2016. Elsewhere, high costs have led to treatment rationing in some countries, including in the European Union, where price reductions are insufficient to allow national health budgets to cover all in need of treatment. However, several countries, including Australia, France, and Georgia, are now providing hepatitis C treatment through their public health budgets.

Inclusion of the new hepatitis C medicines in the 2015 WHO *Model List of Essential Medicines* is another step that is expected to further stimulate efforts to get prices down. To achieve the targets set out in the global health sector strategy for viral hepatitis, WHO estimates that 80% of patients with hepatitis C will need to be treated.

As happened with antiretroviral treatments for HIV, several civil society organizations, including Médecins Sans Frontières, have simultaneously filed patent challenges against the originator company in an effort to remove affordability barriers, improve access, and end the need to ration medicines. Opposition of this nature has already led to the revoking of patents in China and Ukraine; decisions are pending in other countries, including Argentina, Brazil, India, the Russian Federation, and Thailand.

Again, efforts to control viral hepatitis are benefitting from the hard-won lessons of the AIDS response. To date, the number of countries that have secured hepatitis C medicines at affordable prices is much too low for a disease that affects some 71 million people. The world needs to show more outrage over a situation in which the high price of medicines denies so many millions a cure for a disease that is highly stigmatized and so often fatal.



he poorest of the poor have suffered from deadly, painful and disfiguring tropical diseases since ancient times, but the battle against neglected tropical diseases is now being won. Since 2007, WHO has helped streamline delivery of donated drugs and stimulate the development of new ones. In the London Declaration of 2012, leading pharmaceutical companies agreed to donate billions of dollars' worth of drugs through 2020, guided by a technical strategy devised and managed by WHO. This bold collaboration is providing close to a billion people per year with access to free treatment and helping to put several of these tropical diseases on the path to elimination.

Though medically diverse, the neglected tropical diseases (NTDs) form a group because all are strongly associated with poverty, all flourish in impoverished environments, and all thrive best in tropical areas, where they tend to overlap. Most are ancient diseases that have plagued humanity for centuries. They blind, maim, disfigure, and debilitate their victims, causing untold misery that anchors populations in poverty.

Once widely prevalent, many of these diseases gradually disappeared from large parts of the world as economies developed and living conditions and hygiene improved. Today, the neglected tropical diseases have their hotbeds in the places left furthest behind by socioeconomic progress, where substandard housing, lack of access to safe water and sanitation, chronic hunger, filthy environments, and abundant insects and other vectors contribute to their efficient transmission. In the recent past, the need for control has been hidden from the international community as the diseases themselves rarely travel beyond such deeply impoverished settings.

The situation has changed dramatically over the past ten years, making the control of these diseases one of the best rags-to-riches success stories in modern public health. With more than one billion people affected, efforts to control these diseases are a pro-poor initiative on a massive scale - in effect, a frontal assault on a root cause of poverty. Stepped-up control is based on a deliberate decision not to wait for these diseases to gradually disappear as living conditions improve, but to strike aggressively using a population-wide preventive approach.



Today, the neglected tropical diseases have their hotbeds in the places left furthest behind by socioeconomic progress.

The appeal of viewing the neglected tropical diseases in this way has been compelling for several groups, most notably the pharmaceutical industry. When the first NTD global partners meeting was convened by WHO in 2007, industry was present with commitments to donate large quantities of effective high-quality medicines to suppress common tropical parasitic and bacterial infections. That commitment opened the way for mass drug administration to at-risk populations with the goal of reducing the human reservoir of parasites and pathogens, eventually resulting in the interruption of transmission.

With large quantities of safe, effective, and free drugs on offer, the goal of immediately expanding access emerged as a moral imperative. It also threw down the gauntlet: if the world cannot deliver high-quality free drugs to those in desperate need, how will it manage to solve much more complex problems?

Several overarching principles and assumptions underpinned the design and implementation of control programmes. First, as the people in greatest need are the poorest of the poor, interventions – no matter how low the price – are unaffordable and must be made available free-of-charge. Drug donations are the only option.

Second, as most at-risk people live beyond the reach of effective health systems, interventions must be simple, safe enough to be administered by non-health staff, and undemanding, ideally requiring only once-yearly contact with the health services.

Third, diseases that are concentrated in very poor populations carry few market incentives for R&D. Many treatments are old and some have toxic side-effects that can be deadly. The job here is to move forward fast with what already exists while clamouring for better products, using field experience to define the ideal product profile, right down to the price.

Finally, ignorance is the first battle that must be fought in the war against extreme poverty. As these diseases are so deeply dreaded by affected populations, community engagement has huge potential to generate grassroots demand for treatment and reduce the stigma that so often rips away social opportunities, especially for women.

Many of these treatments produce tangible results that communities can readily understand. A person who takes a pill and then expels large numbers of worms provides highly visual evidence of cause and effect. Watching the crippling, stigmatizing signs of leprosy disappear in a community or seeing ugly skin conditions and bloody urine vanish provides powerful proof that physical pain, deformities, and emotional misery are not the inevitable companions of poverty. Instead, they can be deliberately and definitively ended. Hope is a precious gift for the extremely poor.

A streamlined integrated approach

As subsequent research would show, drugs for preventive chemotherapy, when distributed according to WHO guidelines, raise no safety issues when administered on a massive scale. Many are effective after a single once-yearly pill, and several can be administered by non-

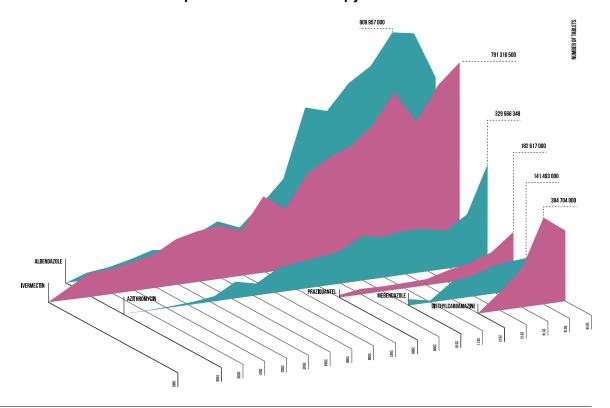
health staff. For praziquantel for schistosomiasis, for example, a simple "dose pole" lets teachers deliver the right dose to schoolchildren according to their height. Research made two additional contributions: some pills provide protection against several diseases, and several pills can be safely taken together, further simplifying control programmes in the many areas where neglected tropical diseases overlap.

Those findings paved the way for simplified and streamlined approaches that reduced costs and logistical demands on countries. WHO technical guidance for an integrated approach was just one of many operational innovations. **As the diseases frequently overlap, delivery systems for one have been used by others.** Some programmes ride piggy-back on existing systems to deliver childhood immunization, bednets for malaria, nutrition supplements like vitamin A, and school meals provided by the World Food Programme.

In another boost to control, research pioneered by the Special Programme for Research and Training in Tropical diseases (TDR) showed that community-directed treatment can revolutionize the reach and sustainability of delivery systems: communities themselves take on the responsibility for inclusive drug delivery, supervised by the health services.

Funding followed feasibility. In 2008, the US Agency for International Development pledged \$350 million for NTD control. In 2011, the UK's Department for International Development pledged to increase its funding for NTD control from \$78 million to \$383 million over the next four years.

Donated medicines for preventive chemotherapy of NTDs (number of tablets)



Source: WHO

A watershed event

The event that most decisively rebranded NTD control occurred in January 2012, when Bill Gates, the WHO Director-General, the CEOs of major pharmaceutical companies, senior government officials from endemic and donor countries, and representatives of academic institutions and civil society gathered in London at a meeting entitled "Uniting to combat NTDs: ending the neglect and reaching the 2020 goals". The 2020 goals, set for a core group of diseases targeted for eradication, elimination, or accelerated control, were spelled out in a WHO roadmap launched before the event.

The London meeting was a landmark in public health cooperation, setting an ambitious agenda for the next decade. It marked a massive expansion of support, including a donation of \$363 million by the Bill and Melinda Gates Foundation. In the outcome document, the London Declaration, twelve of the world's biggest pharmaceutical companies collectively committed to extend their donations through 2020 to help meet the control and elimination goals set by WHO. Some of these donations are open-ended – "for as long as needed" – and most are made through WHO. The value of donated medicines has been estimated at from \$2 billion to \$3 billion yearly.

The NTDs, so long starved for resources, were getting rich. Equally important was support from foundations and funding agencies, including the Drugs for Neglected Diseases initiative, to promote basic and applied research for the development of new treatments and diagnostic tests. For many diseases, new products are desperately needed.

The most difficult diseases: success against all odds

Unlike diseases amenable to preventive chemotherapy, African sleeping sickness, Buruli ulcer, Chagas disease, and leishmaniasis have been identified by WHO as requiring innovative and intensified disease management. All of these diseases have poorly understood burdens, lack optimal control tools, receive insufficient R&D investment, and affect the poorest of the poor. For decades, their control faced extremely complex challenges. Left untreated, severe permanent disabilities can develop. Fatality rates for sleeping sickness, Chagas disease, and leishmaniasis are the highest of all the neglected tropical diseases. The signs of early illness, when the prospects of treatment are best, are subtle and non-specific. Most poor people will not seek treatment until symptoms become severe. Active screening for cases is required, but difficult to carry out in remote areas.

For a long time, the only treatment options were old, dangerous, and extremely painful. Treatment required specialized care, including extended stays in hospitals, and diagnostic support from well-equipped laboratories. However, this situation has begun to change with the advent of new technical tools, supported by an increasing number of public-private partnerships for product development, which brings the best science to bear on the most neglected diseases. Thanks to these new tools, even these diseases are being beaten back as part of a comprehensive assault on the neglected tropical diseases.

Significant recent progress includes the development of rapid and reliable diagnostic tests, suitable for use in resource-constrained settings, for visceral leishmaniasis, sleeping sickness, and Chagas disease. Research shows that a single dose of the antifungal medication, amphotericin B liposomal (AmBisome), cures up to 96% of cases of visceral leishmaniasis that would otherwise be fatal. For African sleeping sickness, a new treatment combination therapy, nifurtimox-eflornithine, was added to the WHO Model List of Essential Medicines in 2009. Studies have shown that this combination therapy is a highly effective treatment option for one form of second-stage disease.

Attacked on multiple fronts, the burden of sleeping sickness has been reduced from more than 37 000 new cases in 1999 to well under 3 000 cases in 2015, representing the lowest yearly number since reliable records began.

Antibiotic therapy has revolutionized the management of Buruli ulcer, and WHO and its partners have guaranteed an uninterrupted supply of antibiotics to affected countries to ensure that all patients receive free treatment. However, progress remains constrained by the lack of a reliable diagnostic test suitable for use in the field.

In 2007, the control strategy for Chagas disease was scaled up. Donated drugs were secured, the screening of at-risk populations was improved, transmission through blood transfusion and organ transplants was systematically prevented, and new diagnostic tests were introduced.

The emergency response to outbreaks of leishmaniasis has been strengthened. For example, in South Sudan, more than 36 000 cases were treated from 2009 to 2014 with a low case fatality rate. In the Syrian Arab Republic, where the distinctive skin lesions became known as the "Aleppo ulcer", more than 200 000 cases have been treated over the past three years.

In 2015, the target for the elimination of visceral leishmaniasis was achieved in 82% of sub-districts in India, in 97% of sub-districts in Bangladesh, and in 100% of districts in Nepal. Those countries have adopted single-dose AmBisome as the first-line treatment; WHO supplies the medicines donated by the pharmaceutical industry.

Following an intense seven-year campaign based on active case finding and intramuscular injections of penicillin, India eliminated yaws. The last case occurred in 2003, ending a disease that had plagued the country for centuries. Prospects for elimination of the disease elsewhere were considerably increased in 2012, when researchers showed that a single dose of azithromycin, a well-known and safe antibiotic, cures yaws in the same way as intramuscular injections of penicillin. That breakthrough shifted the control strategy to mass drug administration aimed at reaching all people in endemic areas with a single pill. The prospects for yaws elimination in the remaining 13 endemic countries look much brighter as a result.

All of these achievements have benefitted from collaboration with the pharmaceutical industry. Apart from donating supplies of drugs, participating companies provide funds for drug delivery within countries. Drug donations are made to WHO. **WHO** is in charge of distributing the medicines, in line with its own technical strategy, for which it has sole responsibility.

Rapid impact interventions: spectacular progress

For diseases with rapid impact interventions, progress has been spectacular. For example, supplies of praziquantel for schistosomiasis control are now sufficient to blanket every school in sub-Saharan Africa. Donations of praziquantel, albendazole, and ivermectin are being distributed as a rapid-impact package to control schistosomiasis, soil-transmitted helminths, and lymphatic filariasis. Ivermectin, a drug that earned its co-discoverers the 2015 Nobel Prize in Medicine, has already freed 18 million West African children from the risk of blindness and is now being used to shrink the map of onchocerciasis even further. Donations of ivermectin presently amount to about 270 million treatments each year.

Trachoma, the world's leading infectious cause of preventable blindness, is strongly associated with flies and filth in conditions of extreme poverty. Donations of the antibacterial agent azithromycin are a cornerstone in the WHO four-pronged SAFE strategy to eliminate blinding trachoma (surgery for those with trichiasis, antibiotic treatment to clear conjunctival infection, and facial cleanliness and environmental improvement to reduce transmission). To date, Oman, Morocco, and Mexico have been validated by WHO as having eliminated trachoma as a public health problem.

Success in Morocco followed several decades of community-based interventions and surveillance, supported by government-sponsored training of medical and nursing staff, including training in surgical skills. Beginning in the mid-1990s, all four components of the SAFE strategy were fully implemented. Antibiotic coverage exceeded 80% in each treatment round in each affected province. Beyond demonstrating that the SAFE strategy worked, the initiative brought multiple other benefits to the country's poorest communities. Household access to potable water increased from less than 20% in 1990 to more than 90% in 2007. A rural electrification system delivered power to more than 2 million households. Simultaneously, extreme poverty virtually vanished.

The incidence of guinea-worm disease, slated for eradication, has been reduced from an estimated 3.5 million cases in 1986 to just 25 cases in 2016. In that year, only three countries reported cases: Chad, Ethiopia, and South Sudan. However, the surprising finding, first in Chad, that dogs can serve as a second mammalian host is likely to delay achievement of the eradication goal, though not derail it. The eradication of guinea-worm disease will mark the first time an infectious disease was vanquished by community engagement and behavioural change, without support from a vaccine or treatment.

The success of these various partnerships makes an additional important point. When all partners work according to an agreed technical strategy, devised and overseen by WHO, the Organization can collaborate with the pharmaceutical industry at no cost to its integrity.

Of the core diseases targeted for eradication, elimination, or accelerated control, lymphatic filariasis is racing fastest towards the finish line. Several external reviews of the programme show strong progress towards the goal of eliminating this disease by within the next few years.

Since WHO established the global programme to eliminate lymphatic filariasis in 2000, mass drug administration and other interventions are estimated to have prevented 97 million cases, averting more than \$100 billion in economic losses. A cumulative total of 6.2 billion treatments have

been delivered, covering more than 820 million people with at least one treatment course. To date, WHO has validated the elimination of lymphatic filariasis in ten countries as diverse as China, Cambodia, and Sri Lanka. An additional 12 countries have been able to stop mass drug administration and are now in a surveillance phase.

Haiti, with its well-recognized resource constraints, provides an especially remarkable example. In 2012, the country scaled up mass drug administration to reach all endemic areas. Since then, Haiti has been able to stop treatment in nearly 43% of endemic areas, while extending treatment to 4.2 million people in the remaining targeted areas.

The momentum continues to build. In sub-Saharan Africa, an unprecedented effort to map NTDs has pinpointed areas of endemicity, allowing a much more targeted approach to mass drug administration and the surveillance needed to oversee its impact on disease transmission. An extended special project for the elimination of neglected tropical diseases in Africa was launched in 2016

The stunning success over the past ten years has provoked an intriguing question: can poverty be treated with pills? Not entirely. To make a true dent in extreme poverty, the current frontal assault on the neglected tropical diseases must be combined with the broader attack on the social, environmental, and economic determinants of health called for in the 2030 Agenda for Sustainable Development. Targets set for water supply, sanitation, nutrition, and housing will likely have the largest long-term impact.

On current trends, though, many of these ancient diseases may well be brought to their knees before the 2030 deadline arrives.



accines prevented at least 10 million deaths between 2010 and 2015, and many millions more lives were protected from illness. The global push to end polio has reached its final stages, with just 3 remaining countries still working to eradicate this debilitating disease. The ambitious Global Vaccine Action Plan to reach everyone with vaccines by 2020 started strong but is falling behind. WHO challenges all health leaders to make immunization one of the biggest success stories of modern medicine.

Vaccines have been one of the biggest success stories of modern medicine. WHO estimates that at least 10 million deaths were prevented between 2010 and 2015 thanks to vaccinations delivered around the world. Many millions more lives were protected from the suffering and disability associated with diseases such as pneumonia, diarrhoea, whooping cough, measles, and polio. Successful immunization programmes also enable national priorities, like education and economic development, to take hold.

Such success builds on a long history of research and innovation, with discovery science producing new product breakthroughs and delivery science carving out ways to reach universal vaccine coverage.

The Expanded Programme on Immunization was born out of success at a time of tremendous optimism about the game-changing potential of vaccines. The Programme was established in 1974 as the world moved closer to smallpox eradication. Confidence was high that, with international commitment and cooperation, other vaccine-preventable diseases could be conquered. The 1979 certification of smallpox eradication was taken as proof of the power of vaccines to permanently improve the world.

In the decades since, the Expanded Programme on Immunization has remained true to its privileged birthright. It numbers among the most successful of all public health programmes. Since its inception, the Programme has been a pathfinder for universal coverage. In 1974, only 5% of the world's children were protected from the six killer diseases targeted by the



We have few opportunities to change the world for the better in a permanent way. If we don't meet this virus with an immediate surge of commitment, the virus may win.

Programme. Today, that figure is 86%, with some developing countries reaching more than 95% immunization coverage.

In the era of sustainable development, immunization programmes have matured to the point that they can now serve as a model and a platform for delivering other priority public health interventions. This broadened role has been amply demonstrated by the global initiative to eradicate polio.

Polio eradication: from deep trouble to likely triumph

In 2007, the initiative to eradicate polio was in deep trouble. As stakeholders gathered in Geneva for an urgent meeting, they faced a situation characterized by the highest number of polio cases reported in more than six years. Though the virus was endemic in only four countries, Afghanistan, India, Nigeria, and Pakistan, travellers from Nigeria and India had seeded outbreaks in an additional nine countries.

A strategy was in place, with clear guidance for the rapid detection of circulating poliovirus, the conduct of large-scale rounds of immunization using a type-specific monovalent oral vaccine, and the maintenance of highly sensitive surveillance. Still, progress was too slow.

The eradication effort in Nigeria faced a host of complex operational challenges, including vaccine refusals, especially in some northern states. But India was considered the most formidable challenge, given the country's vast size, dense and mobile population, high birth cohort, and poor living conditions, all favouring high and efficient virus transmission. At the end of 2006, the country reported a 10-fold increase in new cases compared with the previous year. New evidence made some question whether eradication in India could ever succeed in the absence of dramatic improvements in sanitation and hygiene.

The spearheading partners and donors were tired. Staff, including tens of thousands of community volunteers, were demoralized. The initiative faced a funding shortfall of \$575 million for 2007–2008. As the WHO Director-General told the meeting, "We have few opportunities to change the world for the better in a permanent way. If we don't meet this virus with an immediate surge of commitment, the virus may win."

Stakeholders rallied behind that call. WHO, Rotary International, the US Centers for Disease Control and Prevention, UNICEF, and the Bill and Melinda Gates Foundation renewed their commitment. The money was found. The Director-General visited the heads of state in endemic countries to secure high-level political commitment. The initiative struggled on.

By 2009, however, the world's largest-ever global health initiative had clearly stalled. The strategies that had so effectively reduced polio incidence by more than 99% worldwide were not powerful enough to eradicate the disease in its last stubborn strongholds. New approaches would have to be found.

That same year, work began to develop a bivalent oral polio vaccine that could simultaneously target the two remaining serotypes in a single dose. The decision to do so was made at the start of the year. Evaluation, clinical trials, licensing, and production took place in record time. The new vaccine was introduced in Afghanistan in December, then rolled out programme-wide in early 2010.

Another important innovation came in 2010, when WHO established the Independent Monitoring Board of the Global Polio Eradication Initiative. The Board's hard-hitting, straight-talking reports, issued twice yearly, took management to task at every level of the initiative, from donors, to international partners, to country operations. Finger-pointing was the norm. If a national eradication programme was "riddled with dysfunction", the Board said so. It also demanded solutions, and harped when change came too slow. As the eradication machinery got better, the Board urged it to get great.

Emergency operations centres were established. Vaccination overage increased as did the accuracy of monitoring and reporting. National programmes shifted from counting the number of children covered to counting those that were missed.

The introduction of health camps – outreach services that provide basic health care, including simple diagnostics and medicines – helped allay suspicions that a singular and intense focus on polio must serve some sinister purpose. The co-delivery of free check-ups and medicines expanded the initiative's contribution to include the treatment of common community ailments, like worm infections, scabies, anaemia, vitamin deficiencies, gastric pain, fevers, and diarrhoeal disease and malaria. Pakistan alone set up nearly 2000 health camps dotting underserved areas in remote and destitute districts. The initiative's call to "reach every child" now meant reaching entire communities with basic health care.

In 2012, polio eradication was put on an emergency footing. The Independent Monitoring Board had requested consideration of a resolution to "declare the persistence of polio a global health emergency". The World Health Assembly acted on that request and adopted a resolution that declared the completion of poliovirus eradication "a programmatic emergency for global public health". The resolution also urged countries with ongoing transmission to declare such transmission "a national public health emergency". On its part, WHO was asked to rapidly develop a comprehensive polio eradication and endgame strategy. This was done in a plan covering the period 2013–2018.

The breakthroughs began. On 11 February 2014, India proved that there is no such thing as impossible. That date marked three years since the country's last case of wild poliovirus. WHO declared that the territory of one of the world's most densely populated countries was now free of a virus that had killed and crippled children for centuries. Many thought that day would never come: the virus was too firmly entrenched in India and the barriers to eradication were too great. The country's dedicated leadership and determined vaccination teams proved them wrong.

In July 2014, Nigeria – a country that had, over the years, re-infected 26 polio-free countries – reached what looked like its last case. The euphoria of finding no new cases continued for two years, but then dissipated in the second half of 2016, when four new cases were confirmed in Borno State, an area rendered virtually inaccessible by insurgency and a devastating humanitarian

crisis. Genetic analysis indicated that the poliovirus had been circulating undetected for several years. Though the setback caused dismay, it redoubled the country's determination to rid itself of poliovirus once and for all.

To secure the impressive gains, WHO convened in 2014 the first of several Emergency Committees, set up under the International Health Regulations, to look at ways to prevent the international spread of wild poliovirus. The Committee declared that doing so was a Public Health Emergency of International Concern, and recommended vaccination, prior to international travel, of all residents and long-term visitors in countries that were exporting wild poliovirus.

The global eradication of wild poliovirus type 2 was declared in September 2015. The Polio eradication and endgame strategic plan 2013–2018 called on countries to introduce at least one dose of inactivated polio vaccine into routine immunization schedules, strengthen routine immunization, and withdraw oral polio vaccine in a phased manner. In line with this plan, another major step forward occurred during the spring of 2016. During a short two-week period in April, 155 countries successfully switched from trivalent to bivalent oral polio vaccine, marking the largest coordinated vaccine withdrawal in history.

The primary purpose of introducing inactivated polio vaccine was to ensure that new birth cohorts had some protection against the type 2 poliovirus, either wild or vaccine-derived, hence mitigating the potential consequences of any re-emergence of type 2 poliovirus following the switch. Introducing at least one dose of inactivated polio vaccine would also boost immunity against poliovirus types 1 and 3, likely hastening their eradication.

In 2017, the eradication programme found itself in the extraordinary position of being closer to its goal than at any time in history. By early April, Afghanistan had reported three cases of wild poliovirus and Pakistan had reported two. Nigeria had not yet detected a case. To safeguard achievements, more than 190 000 polio vaccinators in 13 countries across West and Central Africa began a week-long campaign in late March 2017 to immunize more than 116 million children. The synchronized coast-to-coast vaccination campaign, one of the largest of its kind ever implemented in Africa, is part of urgent measures to permanently stop polio on the continent.

But being on the brink of triumph is not enough. The job will be done only when the entire world has been certified polio-free. The magnitude of that victory will no doubt boost world confidence in the power of public health – and vaccines – to build a better world.

The vast infrastructure and finely-tuned machinery needed to take the world this far are another asset that will continue to bring benefits as part of the initiative's legacy. This capacity was best demonstrated in July 2014, when a traveller from Liberia brought the Ebola virus to the sprawling city of Lagos, Nigeria. At that time, the country had put together one of the world's most innovative eradication campaigns, using cutting-edge technologies to ensure that no child was missed.

Health officials immediately repurposed polio technologies and infrastructures to conduct real-time Ebola case-finding and contact-tracing. World-class epidemiological detective work eventually linked every single one of the country's 19 confirmed cases back to direct or indirect contact with the July air traveller from Liberia. By October 2014, WHO could declare the Ebola outbreak in Nigeria over.

The Decade of Vaccines and the Global Vaccine Action Plan

In 2001, Gavi, the Vaccine Alliance, supported by a large grant from the Bill and Melinda Gates Foundation, was launched to reinvigorate the drive to protect children from vaccine-preventable diseases. The Alliance was founded on the principle of fairness. Poverty, or the place where a child was born, should not determine access to life-saving vaccines, including the newer and more expensive ones. **Every child deserves the best that science can offer.** The Alliance was also a tribute to the power of innovation to move the human condition a big step forward. A world that could put a computer in every home could surely put vaccines in every child.

By 2007, Gavi and its partners, including WHO, had revitalized immunization as a strategy for averting millions of childhood deaths each year. The new rotavirus and pneumonococal vaccines raised hope that diarrhoea and respiratory infections – the two biggest childhood killers – could be more routinely prevented.

In 2010, the Decade of Vaccines was launched at the World Economic Forum as an effort, supported by multiple stakeholders, to extend the full benefits of immunization to all by 2020. To support this goal, the World Health Assembly approved the ambitious Global Vaccine Action Plan in 2012 as the framework for delivering universal access to vaccines.

The Vaccine Action Plan has been described as "one of the largest and most ambitious public health initiatives ever launched". It set new targets for the decade, defined their indicators, proposed six strategic objectives and the actions needed to achieve them, and provided an initial estimate of resource requirements and return on investment.

As a contribution to measurement and accountability, WHO's Strategic Advisory Group of Experts (SAGE) on immunization has issued annual progress reports on implementation of the plan. The 2016 report provides a careful analysis of progress and challenges at the midpoint in the decade. Despite some bright spots in global immunization efforts, the overall picture is sobering.

On the bright side, more children are being immunized worldwide than ever before, with the highest level of routine coverage in history. **Indigenous measles and rubella have been eliminated from the Americas, and maternal and neonatal tetanus has been eliminated in South-East Asia**.

Since 2010, 99 low- and middle-income countries have introduced one or more new or underutilized vaccines, exceeding the target set out in the action plan. While data are not yet available to quantify the associated impact on child health, the steep decline in morbidity and mortality from pneumonia and diarrheal disease recorded in some countries that introduced the pneumococcal and rotavirus vaccines suggests that the contribution will be substantial.

At the same time, sustainability is an issue of growing concern. Even very poor countries have used domestic resources to support free immunization services as a public good. As more countries progress to middle-income status, they lose their eligibility for financing from GAVI, raising questions about whether introduction of the newer and more expensive vaccines can be fully financed from domestic budgets.

The success of the polio eradication initiative raises additional long-term concerns. For example, the 2016 outbreaks of urban yellow fever in Angola and the Democratic Republic of Congo prompted the largest emergency vaccination campaign ever undertaken in Africa. A crisis was averted, partly because countries could draw on the experience, massive infrastructure, and human resources of polio programmes already in place.

On the R&D front, substantial progress was recorded in developing vaccines for HIV, malaria, dengue, and tuberculosis. However, that progress underscores the urgent need to expand clinical trial capacity and strengthen the procedures used by national regulatory authorities to evaluate and license vaccines and technologies in the developing world. These needs are being addressed by two WHO initiatives: the African vaccine regulatory forum and a network of vaccine regulators from developing countries.

New platform delivery technologies are also being developed to make vaccines easier to safely store, transport, deliver, and administer. These technologies, once tested, licensed, and deployed at scale, will have a powerful impact on health and well-being around the world. They will enable many countries to expand immunization to reach even the most remote and vulnerable populations.

Yet, as the SAGE assessment revealed, progress towards other key targets has been sluggish and is woefully inadequate to meet the soaring ambitions of the action plan. Halfway through the decade, global targets set for maternal and neonatal tetanus, measles, and rubella, all slated for elimination, were missed by a long shot. Although more infants than ever before are receiving the critical third dose of diphtheria-tetanus-pertussis vaccine, global coverage of these basic vaccines has increased by only 1% since 2010, putting one of the plan's most important targets seriously off track. In 2015, 68 countries fell short of the target to achieve at least 90% national coverage with the third dose. Some 26 countries reported no change in coverage levels and 25 countries reported a net decrease.

The SAGE experts commended the 16 countries that made good progress, especially in reaching vulnerable and marginalized populations. Their success confirms that progress on immunization can be achieved with strong domestic leadership, smart and sustained investments, and effective accountability mechanisms. Some countries with the highest number of unvaccinated children made the most progress, including the Democratic Republic of Congo, Ethiopia, and India. While these countries did not meet the target, all are moving in the right direction.

The long-standing problem of poor quality data persists, impairing the identification of populations that are being missed and the design of targeted corrective strategies. **Replacing guesswork with solid data can bring surprises.** After improving the accuracy of its immunization data, Mexico found that immunization coverage was actually 10% lower than previously thought. By making pockets of missed people visible, Mexico was able to make them a priority for remedial action.

Success stories in individual countries brighten the sobering picture considerably. Beginning in 2010, India made new investments in health systems, replacing and repairing cold chain equipment, training and accrediting thousands of social health activist workers, and using micro-planning to support immunization. These improvements and the intensification of services through special campaigns resulted in coverage jumping from 79% to 87%. In numbers, that meant two million more children received vaccination services in 2015 than in 2010.

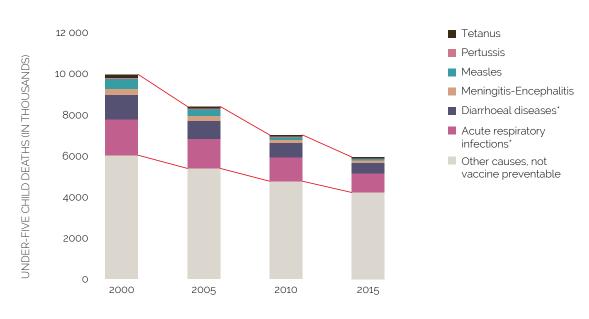
Chad used the "Reaching every community" strategy to achieve hard-won coverage gains that rose from 39% to 55%, proving that progress is feasible in any determined country. Like Mexico, Uganda took risks to change systems and improve outcomes for the better even if the payoff is yet to come.

The assessment also revealed a general failure to appreciate the broader value-added benefits that a well-performing immunization programme brings to overall health care. When systems for vaccine procurement and delivery operate as a fully integrated component of a health system, they can drive the move towards universal health coverage.

Moreover, immunization has become a fundamental strategy for achieving more recent health priorities, from preventing liver and cervical cancer – the biggest causes of cancer in the developing world – through hepatitis B and human papilloma virus vaccines, to curbing antimicrobial resistance, to providing a platform for improving antenatal and newborn care and meeting the long-neglected needs of adolescents.

WHO is now challenging international and national health leaders to make immunization not only one of the biggest success stories of modern medicine, but the greatest success story ever. Technically, this is entirely feasible. Full implementation of the Global Vaccine Action Plan remains the best route for doing so. In a world where vast social inequalities create unrest and disturbing instability, the game-changing power of universal coverage with safe, protective, and cost-effective vaccines deserves a much higher profile.

Vaccines have been key contributors to the global reduction in under-five mortality since 2000



Source: WHO

Pandemic preparedness: increasing the supply of influenza vaccines

The wave of human infections with the H7Ng avian influenza virus that began in China in September 2016 has again raised alarm about the threat of a pending influenza pandemic. The Pandemic Influenza Preparedness Framework has worked in innovative ways to prepare the world for such an event. As an additional capacity-building measure, WHO established a Global Action Plan for Influenza Vaccines in 2006 to address the projected serious shortfall of vaccine supplies during the next pandemic. The plan, which was intended to operate for a decade, set out a three-pronged preparedness strategy: improve the use of seasonal vaccines, increase vaccine production capacity, especially in the developing world, and promote R&D for better vaccines and vaccine production technologies.

Its achievements have been significant. Studies over the past 10 years, documenting the burden of seasonal influenza, have encouraged 115 countries to put in place national policies for increasing the use of seasonal influenza vaccines, up from only 74 in 2006. Making good use of seasonal influenza vaccines not only protects health. It also provides the market incentive needed to increase production capacity and builds the delivery infrastructure that will be critically important during a pandemic.

In 2006, WHO estimated that global pandemic vaccine manufacturing capacity was around 1.5 billion doses per year, with all capacity concentrated in a few wealthy countries. A decade later, that capacity has more than quadrupled to reach 6.4 billion doses. An innovative technology transfer initiative brought the funding and technical support needed to establish 14 vaccine manufacturers in developing countries. Six of these countries have licensed locally produced influenza vaccines, of which three have been prequalified by WHO. Other countries are making steady progress towards this goal.

WHO has further worked to strengthen expertise in the national regulatory authorities of all 14 countries. Here, too, progress has been substantial. In 2006, only four of these countries had a functional regulatory authority. Now ten do. This progress highlights the synergy between the Global Action Plan for Influenza Vaccines and the Pandemic Influenza Preparedness Framework, which has an investment stream for strengthening the capacity of national regulatory authorities.

Vaccines and their production technologies also improved. Numerous advances include adjuvanted pandemic vaccines that permit dose-sparing and conserve the use of antigen, live attenuated vaccines with improved production efficiency and significant operational advantages, tetravalent vaccines with broader strain coverage, and tissue-culture and recombinant vaccines that avoid the need for huge quantities of eggs in the production process and can thus be produced more quickly and efficiently. However, the ideal product – a universal vaccine that protects, year after year, against both circulating seasonal strains and a pandemic strain – remains elusive.

Nonetheless, all of these improvements have left the world vastly better prepared to respond quickly, and with benefits fairly shared, when the next influenza pandemic inevitably comes.

A vaccine stockpile with a huge impact

As WHO further demonstrated, even something so seemingly simple as a stockpile of vaccines can have an outsized impact on outbreak response while also improving many of the factors that influence access to vaccines.

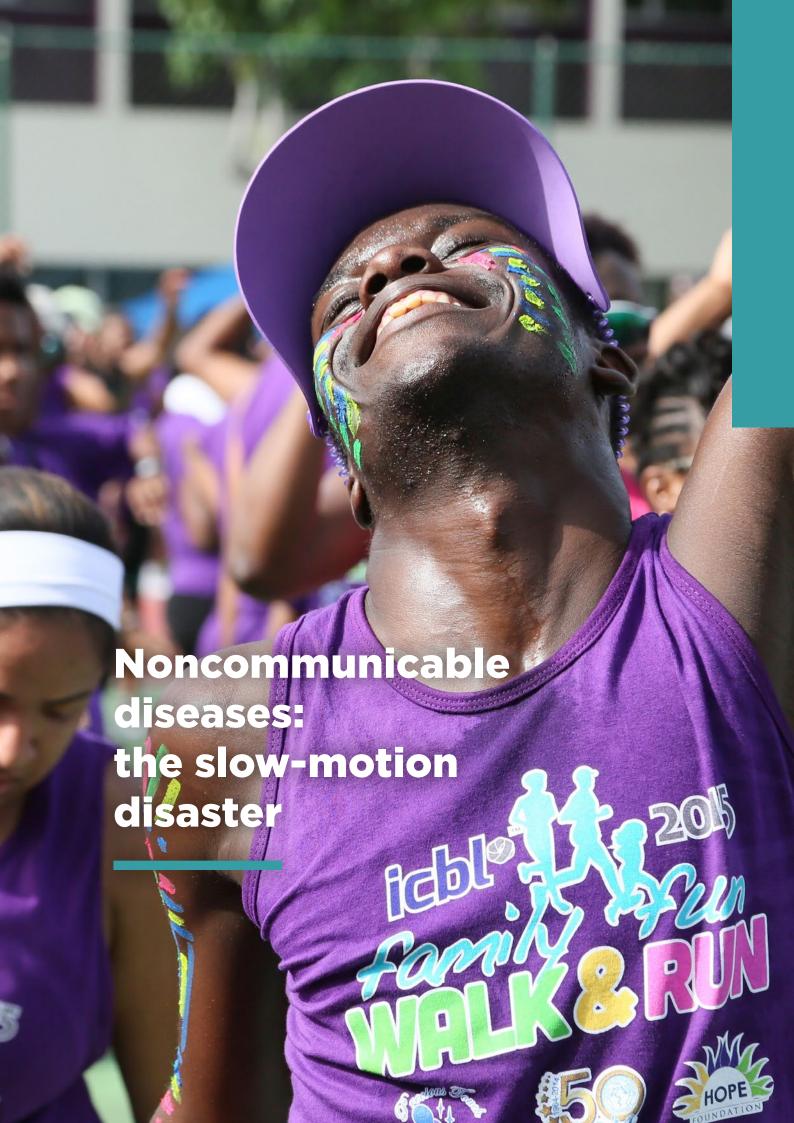
In 2013, WHO created a stockpile of oral cholera vaccines in response to a critical situation. Cholera epidemics were raging, yet the use of vaccines was low and manufacturers had little incentive to increase supplies. In establishing the stockpile, WHO made a commitment to buy and use 2 million doses a year in order to facilitate the availability of vaccine to underserved populations.

Although the cholera vaccine stockpile is essentially a vaccine access, procurement and distribution mechanism, it has generated multiple health benefits well beyond saving lives. It improved reporting. In public health, the promise of assistance is one of the strongest incentives to report epidemic-prone diseases immediately and transparently. As long experience shows, the temptation to cover up a cholera outbreak is great, given the potential impact on trade and tourism.

The stockpile improved access to oral cholera vaccine and therefore the capacities of emergency response, especially in the context of humanitarian crises, such as the ones currently being experienced in South Sudan and Somalia. Following receipt of a request by the International Coordinating Group, vaccines are due to arrive in the country within a maximum of 10 days. It also increased supplies. Three producers have now been prequalified by WHO, with vaccine supply set to triple in 2017. These vastly increased supplies have opened the first opportunity for large scale campaigns in "hot spots" with repeated outbreaks.

In addition, the stockpile decreased costs as more producers entered the market, and generated additional data on vaccine safety, effectiveness, and impact, thus strengthening the case for further investment.

In short, a seemingly simple thing, like the setting up of a stockpile, has transformed a vicious cycle of low demand, low production, high price, and inequitable distribution to a virtuous cycle of increased demand, increased production, reduced price, and greater equity of access. WHO regards a stockpile of rabies vaccine as a logical next step to follow.



f all the major health threats to emerge, none has challenged the very foundations of public health so profoundly as the rise of chronic noncommunicable diseases. Heart disease, cancer, diabetes, and chronic respiratory diseases, once linked only to affluent societies, are now global, and the poor suffer the most. These diseases share four risk factors: tobacco use, the harmful use of alcohol, unhealthy diets, and physical inactivity. All four lie in non-health sectors, requiring collaboration across all of government and all of society to combat them.

At the turn of the century, chronic noncommunicable diseases were not widely recognized as a barrier to development and were not included in the Millennium Development Goals. In terms of gaining attention and financial support, these diseases were overshadowed by the devastating epidemics of HIV, tuberculosis, and malaria and the large number of maternal and childhood deaths. In 2010, only US\$ 18.2 million in development assistance was devoted to NCD prevention and control, amounting to just 0.8 % of total aid for health.

Much of WHO's work in the earliest years of the decade involved collecting the data and making the arguments that would elevate NCDs on the global health and development agendas. On their part, countries - especially those with emerging economies - used the WHO STEPwise approach to gather standardized data on the true burden of these diseases. Those efforts culminated in 2011, when the UN General Assembly held a high-level meeting on NCDs and adopted a farreaching Political Declaration.

The Political Declaration acknowledged that the threat of NCDs constitutes one of the major challenges for development in the 21st century, undermining social and economic progress throughout the world, and made WHO the principal agency for leading the global response. Several relevant WHO resolutions and regional initiatives were cited as providing a framework for stepped-up action on multiple fronts. WHO was specifically asked to prepare recommendations for a set of voluntary global targets. Despite the existence of low-cost, feasible, and high-impact interventions, WHO's so-called "best buys", the Political Declaration recognized the complexity of these diseases, the challenges facing prevention and control, and the need for a whole-ofgovernment and whole-of-society approach.



High blood pressure, or hypertension, is the leading risk factor for heart disease and stroke.

So began a period of intense demands for WHO leadership and expectations for guidance that would deliver a measurable impact. The number of initiatives under WHO leadership soon grew to reflect the magnitude of the challenges, the breadth of the issues that needed to be addressed, and the large number of partners with something unique to contribute.

In 2013, the World Health Assembly adopted a comprehensive global monitoring framework for NCDs, with nine voluntary targets and 25 indicators. The Health Assembly also approved the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020, which provided a roadmap and menu of options for taking coordinated and coherent action to attain the targets. For each of the global targets and indicators, WHO issued an array of practical tools to facilitate implementation in countries, often adapted to regional settings. Of central importance was the STEPwise guide to the development, implementation and monitoring of national multisectoral action plans.

That same year, a UN Inter-Agency Task Force on the Prevention and Control of Noncommunicable Diseases was established by the UN Secretary-General and placed under the leadership of WHO to coordinate the engagement of UN agencies. The Task Force built on the work of the Ad Hoc Inter-Agency Task Force on Tobacco Control as another problem requiring collaboration from multiple non-health agencies. In 2014, the WHO Member States established the Global Coordination Mechanism on the prevention and control of NCDs to coordinate the engagement of nongovernmental organizations, philanthropies, business associations and academic institutions around coherent policy objectives, while also protecting public health and the integrity of WHO from potential conflicts of interest. In 2016, ECOSOC encouraged members of the Task Force to provide support to countries in reflecting the new NCD-related targets in the 2030 Agenda for Sustainable Development in their national responses.

However, as one country after another – whether rich or poor – struggled to make progress, many obstacles emerged. The complexity of the task ahead, concealed by so many years of inadequate attention, became readily apparent.

The most democratic of all diseases

Of all the major health threats to emerge since the start of this century, none has challenged the very foundations of public health so profoundly as the rise of chronic noncommunicable diseases. The prevalence of heart disease, cancer, diabetes, and chronic respiratory diseases, once considered the close companions of affluent societies, is now global, with the heaviest burden concentrated in low- and middle-income countries.

These are among the most democratic of all diseases, affecting populations at every income level in every country, but the poor suffer the most. In wealthy countries, where these diseases have been a research priority for nearly a century, high-income groups benefit from a range of treatments for lowering blood pressure, cholesterol and glucose levels, managing diabetes, and relieving the symptoms of chronic respiratory diseases. The use of sophisticated interventions, usually requiring specialized treatment in hospitals, has improved survival rates for heart disease and cancer significantly. Populations in wealthy countries also benefit from screening programmes

designed to detect the diseases early when the prospects of successful treatment are greatest. In these countries, low-income groups with poor access to health services and poor financial protection bear the heaviest burden of premature mortality.

In most emerging economies, risk factors first appear in wealthier groups who can afford to abandon traditional lifestyles and dietary patterns. In the typical pattern, risk factors – and the diseases they cause – then settle into poorer groups, who tend to smoke the most, consume the most alcohol, and eat the most cheap and convenient junk food. These groups also tend to seek health care only when a disease has progressed to severe symptoms that can no longer be ignored. In developing countries, for example, the vast majority of cancer patients are diagnosed so late that the only treatment option is pain relief. WHO estimates that, for various reasons, some 80% of the world's population lacks adequate access to the medications needed for palliative care.

The trends are deadly, carry crippling economic costs, and cannot be easily reversed under the unique conditions of the 21st century. Health in all regions is being shaped by the same forces: demographic ageing, rapid urbanization, and the globalized marketing of unhealthy products. Under the pressure of these forces, chronic noncommunicable diseases have overtaken infectious diseases as the leading killers worldwide. In terms of its significance for health development, this shift in the disease burden has profound implications, as it challenges the very way socioeconomic progress is defined.

Beginning in the 19th century, improvements in hygiene, living conditions and nutrition were followed by vast improvements in health status and life-expectancy. These improvements aided the control of infectious diseases, totally vanquishing many major killers from modern societies. Today, the tables are turned. Instead of diseases vanishing as living conditions improve, socioeconomic progress is actually creating the conditions that favour the rise of chronic diseases. Economic growth, modernization, and urbanization have opened wide the entry point for the globalized marketing of health-harming products and the spread of unhealthy lifestyles. The world has 800 million chronically hungry people, but it also has countries where more than 70% of the adult population is overweight or obese.

The disease burden and its implications

WHO estimates that noncommunicable diseases kill 40 million people each year, accounting for 70% of all deaths worldwide. The yearly number of deaths includes 15 million people who died between the ages of 30 and 70 years. The majority of these premature deaths could have been prevented or delayed. Among the premature deaths, 85% occurred in developing countries, including 41% in lower-middle-income countries where the probability of dying from a chronic disease between the ages of 30 and 70 years is up to four times higher than in wealthy countries.

The implications for health systems and the care they provide are profound, calling for a change in the mindset of public health. The traditional approach to health that relies on the biomedical model, focused on the cure of individual diseases, is inadequate. The essential emphasis on prevention requires a greater reliance on the social and life sciences. Though better care is

needed everywhere, it is increasingly unaffordable – again everywhere. In several countries, the management of diabetes alone absorbs up to a third of the entire health budget. The average cost of newly approved treatments for various cancer indications is \$120,000 per person per year, suggesting that advanced cancer treatment is becoming unaffordable for even the richest countries in the world. A study conducted by the World Economic Forum estimated that, under a "business as usual" scenario, low- and middle-income countries could lose \$500 billion per year over the period 2011–2025 due to NCD morbidity and mortality, amounting to roughly 4% of average GDP.

These high costs, in turn, have four implications. First, they underscore the ethical imperative of fairness in access to life-saving and health-promoting interventions. Second, they make the need for systems of social protection more sharply obvious. For example, in parts of sub-Saharan Africa, people with diabetes living in rural areas can spend up to 60% of total household income on insulin. Third, they make prevention the cornerstone of the global response. Finally, they make it clear that **no country in the world can hope to "spend its way out" of the NCD crisis by investing in treatment services alone.**

The greatest challenge arguably falls on the way health systems are designed and services are delivered. Most health systems were built to manage brief episodes of acute illness, in which the patient either survives or dies, and are ill-equipped, staffed and budgeted to manage the demand for long-term or even life-long care. The health workforce, too, is inadequate in numbers and training, as was acknowledged in 2016 with the launch of the report of the High-Level Commission on Health Employment and Economic Growth.

Prevention faces two main barriers. First, most doctors worldwide are trained to diagnose, treat, and cure diseases, but not to prevent them. Incentive schemes in many health care settings reflect that emphasis. Second, the risk factors for these diseases – tobacco use, the harmful use of alcohol, unhealthy diets, and physical inactivity – lie in non-health sectors and are strongly influenced by the behaviours of powerful economic operators.

To address the underlying determinants of health, public health has long relied on collaboration with friendly sister sectors, like education, nutrition, housing, and water supply and sanitation. Tackling the forces that drive the marketing of health-harming products is far more complex and contentious, but it can be done.

Noncommunicable diseases are a slow-motion disaster, as many take decades to develop overt signs of disease. However, predisposing risk factors are known to start early in life, calling for a life-course approach to prevention and control. WHO has internationally agreed guidelines for managing all four diseases, especially when detected early. Most medicines needed for treatment are included in the WHO Model Lists of Essential Medicines, and many of these medicines are low-cost generics.

The approaches needed to combat such a monumental and broad-based challenge are numerous – from considering the implications of trade and foreign investment agreements to legislative and fiscal measures that enforce population-wide prevention, from community engagement and a life-course approach to people-centred health services that focus on integrated care instead of individual diseases, from finding ways to shape the behaviours of powerful economic operators to persuading municipal authorities to create safe playgrounds and spaces for pedestrians and cyclists.

These demands have shaped the direction WHO and health ministries have taken when calling for health system reforms. Of all the diseases under the WHO mandate, few others depend so heavily on health systems organized around the principles of primary health care and oriented towards universal coverage.

Shared risks but different needs

Though they share risk factors and approaches to prevention, each of the four principal noncommunicable diseases has its distinct epidemiological profile and distinct set of needs for both prevention and treatment. Even if preventive interventions were perfectly implemented, clinical cases of all four diseases will continue to burden health systems and societies.

Cardiovascular disease. WHO estimates that 17.5 million people die each year from cardiovascular disease, accounting for around 31% of all deaths worldwide and making this disease the world's biggest killer. Some 80% of these deaths are caused by heart attacks and stroke. High blood pressure, or hypertension, is the leading risk factor for heart disease and stroke, and accounts for more than 12% of total deaths from cardiovascular disease. A large proportion of heart attacks and stroke can be prevented by controlling major risk factors through lifestyle interventions and pharmacological treatment when indicated. In 2013, WHO issued a *Global brief on hypertension* and, to raise public awareness, made the monitoring of blood pressure the theme for World Health Day. The new Global Hearts Initiative, launched by WHO, the US Centers for Disease Control and Prevention, and other partners in 2016, includes a SHAKE technical component aimed at helping countries devise population-wide policies to reduce salt intake.

Cancer. WHO estimates that 14.1 million new cases of cancer and 8.2 million cancer-related deaths occurred worldwide in 2012. Of these deaths, 4.3 million were premature, with 75% occurring in low- and middle-income countries. Based on current knowledge, **between one third and one half of all cancers are potentially preventable.** In addition to the risk factors shared by NCDs, the risk of cancer increases with exposure to indoor and outdoor air pollution, radiation, environmental chemicals, and occupational exposures. Tobacco use directly contributes to about 22% of global cancer deaths. In less developed countries, cancer-causing infections are a major risk factor, responsible for more than 20% of cancer deaths. Vaccines are currently available for two common oncogenic infectious agents, namely human papillomavirus, which causes cervical cancer, and hepatitis B virus, which causes liver cancer. In less developed regions, WHO's International Agency for Research on Cancer ranks liver cancer as the second most common cause of cancer deaths and cervical cancer as the seventh most common cause.

The discrepancies for cancer outcomes between wealthy and poorer countries are stark. For childhood acute lymphoblastic leukaemia, a highly treatable cancer, the five-year survival rate in poorer countries is less than 20% compared with 90% in select high-income countries. In poorer countries, late diagnosis of cancer is common, with many patients presenting for care only when the disease has reached an advanced or metastatic stage. Limited access to diagnostic services, including pathology, is likewise common. In 2014, the World Health Assembly adopted

its first resolution on the Strengthening of palliative care as a component of comprehensive care throughout the life course.

The costs of interventions, new medicines and sophisticated procedures and technologies are becoming unaffordable, even for the world's wealthiest countries. The 2015 WHO Model List of Essential Medicines includes 16 low- and high-cost drugs which can increase survival times for common cancers, such as breast cancer, or can successfully cure up to 90% of patients with rare cancers, such as leukaemia and lymphoma. Different strategies have been used by countries and companies to address high prices, including measures to foster generic competitions, price regulation, use of voluntary licenses, and use of flexibilities set out in the World Trade Organization's TRIPS agreement. Unaffordable high prices for essential medicines are a legitimate justification for countries to foster price regulation or ultimately issue compulsory licenses.

Diabetes. In 2016, who issued its first *Global report on diabetes*, underscoring the enormous scale of a crisis. The report estimated that **the number of adults living with diabetes has almost quadrupled since 1980**, moving from 108 million in 1980 to 422 million in 2014. More than half of these people are unaware of their disease status and even more receive no treatment. The global prevalence of diabetes in the adult population has also increased, nearly doubling from 4.7% in 1980 to 8.5% in 2014. Like population-wide obesity, its precursor, diabetes is increasing most markedly in the cities of low- and middle-income countries. Most people are affected by type 2 diabetes – once known as adult-onset diabetes, but no longer, as so many adolescents and children are now affected.

Each year, diabetes causes around 1.5 million deaths. High blood glucose contributes to an additional 2.2 million deaths, largely by increasing the risk of cardiovascular disease. That means 3.7 million yearly deaths related to high glucose levels. Of these deaths, 42% occur prematurely, before the age of 70 years.

The Asia-Pacific region is generally considered the epicentre of the diabetes crisis. In these countries, people develop the disease earlier, get sicker, and die sooner than their counterparts in wealthier countries. Some researchers are investigating whether a genetic predisposition may be at work. Others are looking at factors in the environment that could amplify a genetic risk or operate on their own to explain this unique epidemiological pattern. Evidence is mounting that bodies programmed during gestation and early childhood to survive on low energy intake are metabolically challenged when confronted with even modest increases in calorie intake. Some researchers believe this may be one reason why people in India and China develop diabetes about a decade earlier than people of European origin and can do so following only a small weight gain.

In some of Asia's most populous countries, a generation that grew up in rural poverty, with too little to eat and jobs involving hard manual labour, now lives in urban high-rise apartments, with sedentary jobs, low-cost cars, and food environments loaded with cheap and convenient calories. Partly as a result of these changes, millions of people lifted out of poverty to join the booming middle class now find themselves trapped in the misery of diabetes and all its costly complications.

Chronic respiratory diseases. Chronic respiratory diseases are diseases of the airways and other structures of the lung. Some of the most common are chronic obstructive pulmonary disease,

asthma, occupational lung disease, and pulmonary hypertension. WHO estimates that 235 million people, especially children, suffer from asthma. Chronic obstructive pulmonary disease kills around three million people each year, with more than 90% of these deaths occurring in poorer countries. In addition to tobacco smoke, other risk factors include air pollution, exposure to occupational chemicals and dusts, and frequent lower respiratory tract infections. Although this group of diseases cannot be cured, various forms of treatment that help dilate major air passages and improve shortness of breath can control symptoms and improve the quality of life. Worldwide, most chronic respiratory diseases are under-diagnosed and under-treated. Access to essential medications in many countries is poor. In 2007, WHO published a comprehensive approach to Global surveillance, prevention and control of chronic respiratory diseases.

The four risk factors: root causes in non-health sectors

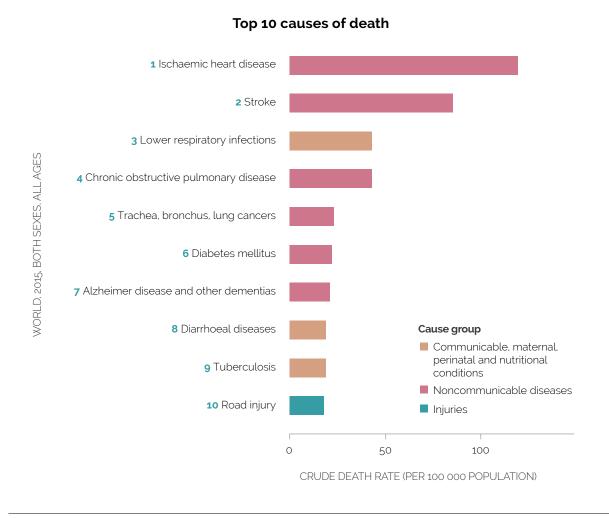
The highest-burden noncommunicable diseases share the same four risk factors. All lie in non-health sectors, which makes the control of these diseases one of the most powerful examples of the need for multisectoral collaboration that takes a whole-of-government and whole-of-society approach.

Tobacco use. Smoking is the second leading risk factor for early death and disability worldwide. More than 1.1 billion people, or one in five adults, currently smoke tobacco, leading to around 7.2 million deaths each year. Moreover, global tobacco use exerts an extraordinary toll on the world's economy. In 2017, the US National Cancer Institute and WHO jointly estimated that tobacco use causes more than \$1.4 trillion in health care costs and lost productivity annually.

As shown in internal company documents, the tobacco industry has long regarded WHO as its biggest enemy, a distinction the WHO Director-General has worn as a badge of honour. Full implementation of the WHO Framework Convention on Tobacco Control is the most powerful way to reduce the huge harms to health caused by tobacco. To support the implementation of the treaty on the ground, WHO introduced MPOWER – a set of six measures, aligned with the treaty, which help countries reduce the demand for tobacco, using methods that are high-impact but also practical and low-cost.

Progress in adopting MPOWER measures demonstrates countries' commitment to tobacco control. In 2007, only 1 in 10 people living in low- and middle-income countries were protected by at least one MPOWER measure at the highest level of achievement. Seven years later, with the support of many partners including Bloomberg Philanthropies, this level of protection is enjoyed by nearly 1 in 3 people in those countries.

Time and again, increasing taxes on tobacco products to raise retail prices has been proven to be the most effective and efficient of the best-buy demand-reduction measures to reduce tobacco use. Unfortunately, it is also the least widely implemented measure. Despite all the positive progress made, raising tobacco taxes lags behind implementation of the other MPOWER measures. In 2014, only 10% of the world's population was covered by taxes that amount to more than 75% of the retail price. The big picture, however, is promising: countries are moving in the right direction on all MPOWER measures, with great progress made on some.



Source: WHO

A substantial factor in lack of progress in implementing tobacco control is interference by the tobacco industry. A large body of evidence demonstrates that tobacco companies use a wide range of tactics to interfere with tobacco control. Such strategies include direct and indirect political lobbying and campaign contributions, financing of research, attempting to affect the course of regulatory and policy machinery, and engaging in social responsibility initiatives as part of public relations campaigns.

Most recently, the way the industry opposes tobacco control measures has been clearly on display in their response to the introduction of tobacco plain packaging. Tobacco industry opposition to this policy has been long-standing. In 1993, tobacco companies formed an industry wide "plain packs group" to oppose plain packaging laws. Today, the experience in countries introducing plain packaging suggests that tobacco companies will go above and beyond their typical opposition to tobacco control measures by undertaking a massive opposition campaign to plain packaging through lobbying and litigation. Industry opposition focuses on questioning established evidence, the supposed unintended consequences, and arguments about paternalism. Tobacco companies argue that plain packaging will increase illicit trade,

push prices down, and create confusion for retailers. These claims are not supported by the evidence and are contradicted by Australia's experience.

In 2012, Australia became the first country to fully implement plain packaging of all tobacco products. Australia faced a number of legal challenges to this legislation. A domestic Constitutional challenge brought by the tobacco industry was dismissed by the High Court of Australia. Philip Morris also used the investor-state dispute settlement mechanism in a bilateral investment treaty between Australia and China (Hong Kong Special Administrative Region) to seek compensation for losses it claimed were caused by plain packaging, including expropriation of its intellectual property. In December 2015, this claim was dismissed for lack of jurisdiction. The disputes at the World Trade Organization over Australia's tobacco plain packaging measure remain ongoing.

By the end of May 2017, tobacco plain packaging will be fully implemented in France and the UK. Both countries have also faced domestic legal challenges to their legislation; in each instance the claims were dismissed by domestic courts. Ireland, Hungary, New Zealand, Norway, Slovenia and Thailand have passed plain packaging legislation. Other countries are at an advanced stage of the policy development process or have the policy under active consideration. In 2016, World No Tobacco Day focused on tobacco plain packaging, and WHO expects that interest in tobacco plain packaging will continue to grow among its Member States.

Other recent legal victories have also been significant. In 2016, the European Court of Justice upheld the European Union's 2014 Tobacco Products Directive, which implements a number of provisions in the WHO Framework Convention on Tobacco Control. Also in 2016, after six years of litigation, Uruguay was successful in defending a claim for compensation brought by Philip Morris under the investor-state dispute settlement mechanism in a bilateral investment treaty. The claim challenged the introduction of large graphic health warnings and a single presentation requirement restricting the number of brand variants available on the market. In dismissing the claim, the Tribunal hearing the arbitration also ordered Philip Morris pay Uruguay \$7 million towards the country's legal costs.

The progress made in implementing tobacco control measures – despite powerful industry opposition – may offer some lessons for other areas of public health that face opposition to policy initiatives from powerful corporate interests.

The harmful use of alcohol. The harmful use of alcohol causes immense damage to health and societies and imposes a heavy burden on health systems and health budgets. Alcohol can be a killer. WHO estimates that the harmful use of alcohol is responsible for around 3.3 million deaths worldwide each year. Alcohol can kill slowly, as it gradually contributes to diseases like cirrhosis of the liver and cancer at several sites. Harmful drinking is also a major risk factor for cardiovascular disease.

Alcohol can kill quickly, sometimes instantly, when it contributes to road traffic crashes, injuries, poisoning, violence, violent crime, and suicide. Alcohol use can lead to the development of alcohol dependence and a range of neuropsychiatric disorders. Through various mechanisms, it increases the risks of infectious diseases, like tuberculosis and HIV, and has a negative impact on their treatment outcomes. Alcohol consumption during pregnancy can cause permanent physical and mental damage to the developing fetus resulting in a range of health conditions known as Fetal Alcohol Spectrum Disorders.

Preventive action is deeply desired by many governments, many civil society organizations, and many millions of people around the world who have seen lives, families, careers, and communities devastated or destroyed by the harmful use of alcohol. Like many other societal problems, the harmful use of alcohol has multiple dimensions and contributing factors that extend well beyond the health sector. Depending on the national context, efforts to protect populations from the harmful use of alcohol can require support from fiscal policies, trade policies, the judicial system, law enforcement, and government ministries responsible for youth, road safety, consumer affairs, and commerce.

All countries wishing to introduce or strengthen alcohol policies have a powerful instrument to assist them: the Global Strategy to Reduce the Harmful Use of Alcohol, approved by the World Health Assembly in 2010. The strategy sets out a menu of policy options and supporting interventions that each country can draw on to craft effective and affordable policies that match distinct national problems and priorities, as expressed in distinct cultural and religious contexts. The strategy was developed during wide-ranging negotiations and consultations that lasted nearly three years. Its unanimous endorsement was a landmark for public health, WHO, and governments concerned about the harm that alcohol consumption can cause.

The menu of options is organized around ten areas recommended for targeted action, ranging from community action, to responses within health services, to a number of regulatory measures. Regulatory measures are particularly effective in preventing deaths and injuries from drink-driving, constraining the availability of alcohol, and reducing the impact of marketing, especially on young people. Ways of countering the problems of illicit alcohol and home-made brews are also covered.

Increasing the price of alcoholic beverages is one of the most effective preventive interventions. Unfortunately, alcohol consumption is expanding in precisely those countries that lack the regulatory and enforcement capacities to protect their populations. The WHO Global Information System on Alcohol and Health, integrated with the Global Health Observatory, provides regularly updated information on alcohol consumption, its health consequences, and policy responses at global, regional and country levels.

On the positive side, the research that supports the strategy shows that strong alcohol policies work. A reduction in the density of stores selling alcohol has been shown, over time, to reduce rates of child maltreatment and drink-driving. Having fewer outlets has also been linked to fewer traffic crashes and pedestrian injuries. Restrictions on the times when alcohol is available have an impact. In one city in Australia, late-night assaults declined by nearly 40% when closing hours for alcohol purchase were turned back modestly. In a city in Brazil with one of the highest murder rates in the country, the introduction of restrictions on alcohol availability was followed by a 44% decline in murders.

In short, national alcohol policies are needed, desired, entirely feasible, and highly effective. They are also feared and fought by the alcohol industry. In 2013, the WHO Director-General made a public statement following the unmasking of efforts by an industry-sponsored group to shape alcohol policies in four developing countries. She articulated two red lines that industry must never cross: **industry cannot sit at the table or have a voice when WHO defines its standards and preventive strategies**, and it cannot supplant government's role in formulating policies for alcohol control.

In the view of WHO and many others, the formulation of alcohol policies is the sole prerogative of national health officials and regulatory authorities. Policies shaped by industry consistently fail to include those measures proven by the evidence and endorsed by WHO to have the greatest impact.

Unhealthy diets. In the second half of the previous century, the world's food system began to concentrate almost exclusively on increasing the production and reducing the cost of food. Food production became industrialized. Food processing became a science engineered to produce almost irresistibly tasty foods that were also cheap and convenient. Ways were developed to grow vegetables without soil. Confined animal feeding operations sprung up to meet the demand for cheap meat and dairy products, with well-documented consequences for the environment, human health, animal welfare, and the economies of rural areas.

Many large middle-income countries adopted factory farming models from North America and Europe to meet the growing consumer demand for meat that nearly always follows new prosperity. For example China now has mega-factory farms capable of producing more than a million pigs each year. While consolidating meat production undoubtedly improves food safety, it is environmentally unsustainable. Moreover, it comes at a time when WHO and other health agencies are advising populations to reduce meat consumption as part of an overall healthy diet.

For all these reasons, much food production is now divorced from its primary purpose of providing the nutrients that sustain human life in good health. Following a series of high-profile mergers and acquisitions, agribusiness is now operated by just a handful of large multinational corporations that control the food chain, from seeds, feed, and chemicals, to production, processing, marketing, and distribution.

Population-wide overweight and obesity are the signal that bad trouble is on its way, especially given the strong links between obesity and overweight and diabetes, heart disease, and cancer at several sites. However, progress is being made. In 2010, the World Health Assembly approved a set of recommendations on the marketing of foods and beverages high in sugar, salt, and fats to children. In 2013, the Codex Alimentarius Commission, jointly administered by FAO and WHO, harmonized the disclosure of total sugars, sodium, and saturated fatty acids in its international guidelines for food labelling.

In 2014, Mexico – which has one of the world's highest burdens of obesity and associated diabetes – became the first country to introduce a tax on sugar-sweetened beverages. Studies showed that soda sales fell by 5.5% in 2014 compared with the year before, and by 9.6% in 2015, again compared with 2013. The largest reductions were recorded in the poorest population groups.

Also in 2014, the WHO Director-General established the WHO Commission on Ending Childhood Obesity. One of the strongest recommendations in the Commission's 2016 report calls on governments to implement an effective tax on sugar-sweetened beverages. The Commission's report further urged governments to accept their responsibility to protect children, including a responsibility to take action without considering the impact on producers of unhealthy foods and beverages. The oft-heard argument that lifestyle behaviours are a matter of personal choice does has limited application to children. An implementation plan for taking the Commission's work forward will be considered by the 2017 World Health Assembly.

In 2015. WHO issued new guidelines for free sugars, recommending that they account for less than 10% of total energy intake. A further reduction to less than 5% of total energy intake was recommended to bring additional health benefits. The higher profile given to sugar prompted South Africa, with its obesity epidemic, and the Philippines, where 97% of six-year-olds have tooth decay, to seek WHO guidance in drafting appropriate legislation to tax sugar-sweetened beverages. These countries will join US cities, like Philadelphia in Pennsylvania, Cook County in Illinois, and Berkley, San Francisco, Oakland, and Albany in California, which are already taxing soda.

In the view of the WHO Director-General, the widespread occurrence of obesity and diabetes throughout a population is not a failure of individual willpower to resist fats and sweets or exercise more. It is a failure to make bold political choices that take on powerful economic operators, like the food and soda industries. If governments understand this duty, the fight against obesity and diabetes can be won. The interests of the public must be prioritized over those of corporations.

Physical inactivity. Regular and adequate levels of physical activity reduce the risk of hypertension, coronary heart disease, stroke, diabetes, and some cancers, including breast and colon cancer. Physical activity also reduces the risk of falls and hip or vertebral fractures and is fundamental to energy balance and weight control. In addition to its role in preventing these conditions, evidence shows that physical activity can reduce depression and help maintain functional abilities in ageing populations.

Despite these well-documented contributions to good health, overall levels of physical activity have declined in nearly all countries and remain a neglected dimension of prevention and intervention, especially in low- and middle-income countries. **Globally, around 23% of adults and 81% of adolescents do not meet WHO recommended levels of physical activity.** Low or decreasing levels of physical activity often coincide with a high or rising gross national product. In high-income countries, 26% of men and 35% of women were insufficiently physically active, as compared to 12% of men and 24% of women in low-income countries.

The drop in physical activity is partly due to inaction during leisure time, sedentary behaviour on the job and at home, and an increase in the use of "passive" modes of transportation. Other factors associated with urbanization and modernization include high levels of urban air pollution which discourage outdoor activity, the failure of authorities in rapidly growing cities to provide playgrounds and walking and cycling lanes, and the increasing amount of leisure time spent behind the screens of TVs, computers, and hand-held devices.

In 2010, WHO issued its first *Global recommendations on physical activity for health*. The recommendations set out the frequency, duration, intensity, type, and total amount of physical activity needed to prevent noncommunicable diseases in three age groups: 5–17 years, 18–64 years, and 65 years and older. For all age groups, recommended levels of daily or weekly activity are considered essential to improve cardiorespiratory and muscle fitness, bone health, and mental health and to reduce the risks of stroke, hypertension, obesity-related diabetes, and breast and colon cancer. For the oldest age group, recommendations are further intended to improve balance, reduce falls, and maintain cognitive abilities.

In 2013, the WHO Global NCD Action Plan for the Prevention and Control of NCDs established the target of a 10% relative reduction in the prevalence of insufficient physical activity by 2025. In 2016, the WHO Commission on Ending Childhood Obesity called for the implementation of comprehensive programmes that promote physical activity and reduce sedentary behaviours in children and adolescents. In January 2017, the Executive Board asked WHO to develop a Global Action Plan on Physical Activity to be considered by the World Health Assembly in 2018.

Democratizing the benefits of clinical care

With the burden of premature mortality overwhelmingly concentrated in poor settings and experiences elsewhere showing the dramatic impact of risk reduction and clinical care, WHO sought a way to translate at least some of this success into clinical protocols and technical guidelines suitable for use in low-resource settings. In doing so, WHO adopted the public health approach that worked so well to extend high-quality care for HIV and tuberculosis, achieving expanded coverage and good results despite limited resources. Central to this approach was the use of evidence – accumulated over decades in wealthy settings – to standardize and simplify the demands on health systems and staff. Such an effort deliberately countered the assumption that poor people living in poor places will inevitably receive poor care or no care at all.

The quest to democratize the benefits of clinical care culminated in 2013, when WHO published its *Package of essential noncommunicable disease interventions for primary health care in low-resource settings*, which became known as WHO PEN. The package includes clinical protocols and technical guidelines covering the questions to ask and the step-by-step actions to follow to screen for breast and cervical cancer, manage the symptoms of asthma and chronic obstructive pulmonary disease, and get people with high blood pressure and high glucose and cholesterol levels on treatment. The PEN approach recognizes that multiple factors work together to increase risks and need to be managed in an integrated way. A protocol on counselling for behaviour change is also included.

PEN uses a simplified approach that relies on just a few technical tools and a core list of essential medicines that can have a high impact, even without the backup of laboratory services. For example, the package makes good use of simple colour-coded wall charts, co-developed by WHO and the International Society of Hypertension, which help predict the 10-year risk of a fatal heart attack or stroke looking at a limited set of risk factors in 14 specific epidemiological settings. By using the wall charts and other simple non-invasive measures, countries can stratify populations according to the level of risk and manage those at highest risk using low-cost generic drugs.

A major strength of the package is its evaluation and ranking of the evidence used to support recommendations, especially as most studies of effective interventions had been conducted in affluent countries and some scepticism existed about whether certain medicines could be safely administered and tests accurately performed in low-resource settings. By setting out the evidence, WHO also set the stage for developing simple algorithms, adapted to the local situation, for the training of primary health care staff. The package also includes evidence-

based recommendations for self-care for cardiovascular disease, diabetes, and chronic respiratory diseases.

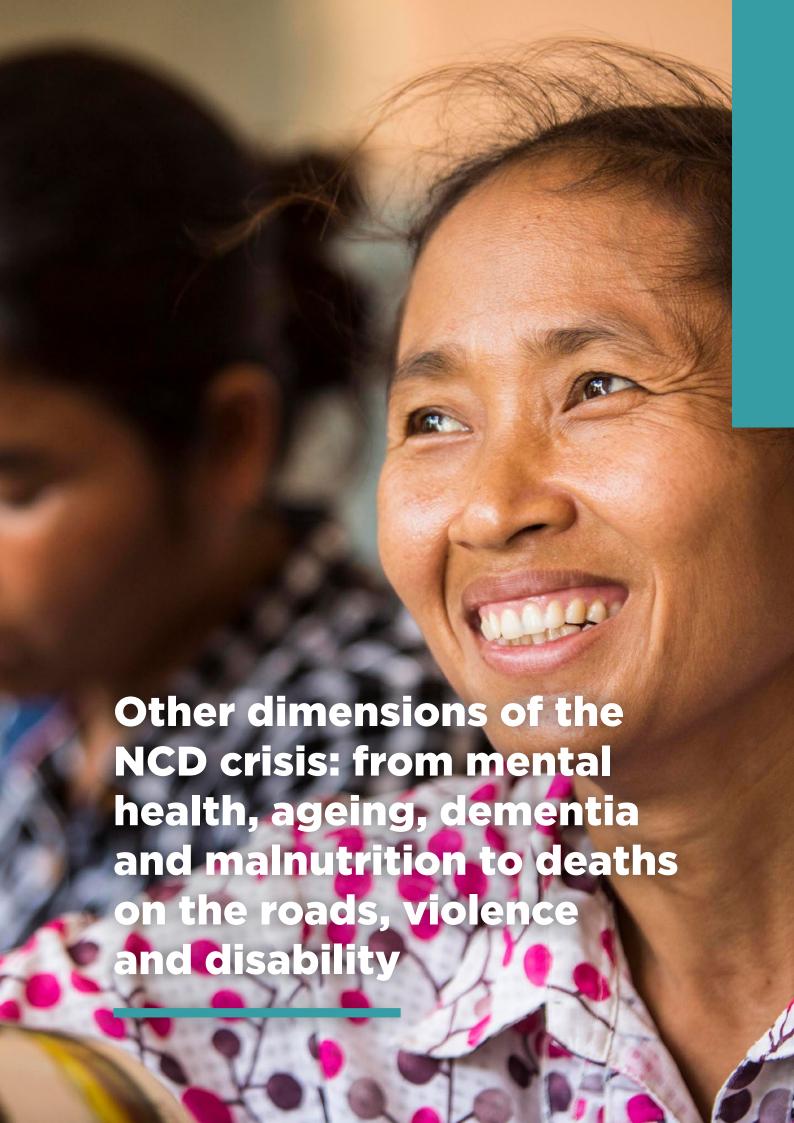
WHO PEN obviously met an urgent need, as it stimulated a flurry of pilot studies that tested the protocols with consistently good results, especially in reducing the risks for heart attacks and stroke and improving the management of diabetes and hypertension. In 2016, the World Hypertension League recommended implementation of WHO PEN in low-resource settings as a cost-effective and equitable means to control hypertension and other risk factors. The endorsement further argued that implementation of WHO PEN could strengthen the efficiency and equity of the health system as a whole.

The principles and approaches of WHO PEN took another step forward in 2016, when WHO, the US CDC, and other partners launched the Global Hearts Initiative aimed at scaling up measures, known to have the greatest life-saving impact, under the constraints typically found in developing countries. The initiative represents an unprecedented effort of wealthy countries that have substantially reduced deaths from cardiovascular disease to adapt lessons from their success to settings with far fewer resources.

The initiative has three technical packages focused on tobacco control, reduced salt consumption, and the prevention of heart attacks and stroke in primary health care. The heart package systematically addresses barriers to care and uses a protocol-driven approach to simplify and standardize the integrated management of risk factors. It further provides a monitoring framework for the PEN initiative.

A high profile on the development agenda

Taken together, these events, initiatives, targets, and achievements show that **the world is now wide-awake to the threat from noncommunicable diseases** – no longer sleep-walking towards a disaster as it was at the start of the century. The control of noncommunicable diseases is now more broadly recognized as one of the most powerful ways to improve longevity and healthy life expectancy. The inclusion of an ambitious target for reducing premature deaths from noncommunicable diseases in the 2030 Agenda for Sustainable Development formalizes the elevated place of these diseases on the international development agenda.



HO has included several new dimensions to the crisis of noncommunicable diseases (NCDs) by drawing attention to conditions that impact the health and safety of all people. This year's focus on depression builds awareness of mental health. Healthy ageing is a key priority, including assisting those who battle dementia. The fight against malnutrition now includes the opposite extreme of obesity. Road deaths, the biggest killer of people aged 15-29, are targeted, as is support for people with disabilities and those suffering violence, especially women and children.

Health problems caused by mental and neurological disorders, unsafe roads, violence, disability, malnutrition in its two extreme forms, and the ageing of the world's population add considerably to the burden of noncommunicable diseases (NCDs). As highlighted on World Health Day 2017, depression is the leading cause of ill health and disability worldwide. According to the latest estimates from WHO, more than 300 million people are now living with depression, an increase of more than 18% between 2005 and 2015. Lack of support for people with mental disorders, coupled with a fear of stigma, prevent many from accessing the treatment they need to live healthy and productive lives. In addition, more than one billion people worldwide experience significant disability, and up to one billion children are exposed to violence each year.

Demographic ageing is now a universal trend, with populations ageing fastest in low- and middle-income countries. By the middle of this century, the population of people aged 65 and older will outnumber children for the first time in history. "Ageism" – based on outmoded stereotypes of the ageing process – is another barrier that blocks access to the many interventions that contribute to healthy ageing. Changes in the world's dietary patterns now mean that severe undernutrition, which stunts and wastes young children, often exists side-by-side with overnutrition, leading to overweight, obesity, and a host of chronic health problems. In a positive trend, the number of deaths and injuries caused by road traffic crashes – though still much too high – has not increased as expected given the continuing rise of more and more vehicles on the world's roads.



The world did not have a comprehensive and affordable plan for coping with the tidal wave of dementia that is engulfing rich and poor countries alike.

Mental health: from the shadows into the spotlight

Mental health received unprecedented attention over the past decade, moving truly "out of the shadows". This work culminated in the World Health Day 2017 campaign on depression, which is a one-year campaign aimed at ensuring that more people with depression, in all countries, seek and get help.

The decade began with a ground-breaking series on Global Mental Health published in the *Lancet* in 2007, with WHO staff as contributing authors. Noting that mental health disorders remain both neglected and deeply stigmatized across societies, papers highlighted the scale of the problem and the treatment gap, and set out some eye-opening statistics: in some parts of the developing world, nearly 80% of people with mental health disorders receive no treatment whatsoever.

In 2008, WHO developed the mental health Global Action Programme (mhGAP) aimed at scaling up care for mental, neurological, and substance use disorders. That work culminated in 2010, when WHO published its *mhGAP Intervention Guide*. The guide covered the most prevalent mental, neurological, and substance use disorders and set out an inventory of effective interventions, often simple and inexpensive, for each. Most importantly, it showed how these disorders could be managed by health personnel with no specialized training in primary health care settings.

In preparing the guide, WHO used some of the world's best experts to demystify and simplify their specialized knowledge, transferring vast competence into non-specialist hands. The result was a world of expertise translated into less than 100 pages of clinical wisdom and succinct practical advice. The emphasis was firmly placed on interventions that can be undertaken by busy doctors, nurses, and medical assistants working, with limited resources, at first- and second-level facilities. With publication of the guide, no country in the world could be excused for not taking action.

To address the long neglect of mental health at the policy level, WHO launched its landmark *Mental health and development report* in 2010. The report argued that people with mental health conditions were a vulnerable group that continued to be marginalized in terms of development aid and government attention. It made a strong case for addressing the needs of this vulnerable group through the integration of mental health interventions into broader strategies for poverty reduction and development.

In 2013, the World Health Assembly adopted its first mental health plan, the Comprehensive Mental Health Action Plan 2013–2020. The action plan and accompanying resolution – a first in the history of WHO – formally made mental health a priority in the agendas of WHO and its Member States. They further expressed the commitment of countries to work towards the achievement of several ambitious targets. The negotiations leading up to adoption of the action plan were lengthy, not because of contentious issues but because Member States were so determined to craft a resolution with enough substance to end the long neglect of mental health needs worldwide. That action definitively moved mental health out of the shadows and into the spotlight. Work done by the mhGAP programme continues as a driving force.

The action plan gave particular attention to the stigma, discrimination, and gross human rights violations that people with mental health conditions continue to face. In the view of WHO, the mental health of people cannot improve if their rights are violated in the very places that are expected to provide treatment and care. In 2012, WHO issued its Quality-Rights Tool Kit, which provides countries with practical guidance and tools for assessing and improving compliance with human rights standards in mental health and social care facilities. The tool kit aims to put an end to past neglect and abuses while also ensuring high-quality services.

In 2013, WHO used another entry point to strengthen mental health services: humanitarian emergencies and the severe mental health and psychosocial needs they create. *Building back better: sustainable mental health care after emergencies* used experiences from ten crisis-affected countries to show how concern about immediate mental health needs during an emergency can be channelled to build high-quality and sustainable mental health services for the future. The report provided detailed accounts of how mental health reform was accomplished under challenging circumstances, emphasizing common barriers and how they were overcome. The report provided convincing evidence that building back better is possible, no matter how weak the existing mental health system or how challenging the emergency situation.

Substance abuse: strengthening the health system response

In April 2016, the WHO Director-General addressed the UN General Assembly Special Session on the World Drug Problem, arguing that the response to the drug problem needed a strong public health focus. Her messages were straightforward and uplifting. Drug use can be prevented. Drug use disorders can be treated. Drug dependence that contributes to crime can be effectively addressed by public health interventions. People with drug dependence can be helped and retuned to productive roles in society.

She asked participants to remember the people: the people wishing to be free from drugs who get no help from the health or social services, the people forced into crime or prostitution to pay for their addiction, and the millions whose injecting drug use adds HIV or hepatitis to their misery. WHO promotes a comprehensive package of interventions, including harm reduction measures, to help these people.

During the decade, collaboration between WHO and the UN Office on Drugs and Crime on health-related issues of the world drug problem has been strengthened significantly, culminating in the signing of a Memorandum of Understanding for expanded collaboration in 2017. WHO brings to this collaboration its focus on normative guidance, research, and health system and technical tools on identification and management of opioid dependence, alcohol, and drug-use and substance-use disorders during pregnancy, the prevention and treatment of HIV and hepatitis among injecting drug users, brief interventions for substance use in health care settings, and community management of opioid overdose.

In March 2017, the WHO Director-General addressed the 60th anniversary session of the Commission on Narcotic Drugs. As she noted, the ultimate objective of drug control policies is to save lives; WHO urges that public health policies be based on the medical and scientific evidence, and not on emotions or ideology.

Dementia: the world gears up to tackle a devastating disease

Of all mental disorders, dementia is among the most devastating, costly, deeply dreaded, and poorly understood by both populations and the medical profession. An estimated 47.5 million people are currently living with dementia. On current trends, WHO estimates that the number of dementia cases will nearly double every 20 years. About 60% of the disease burden falls on low- and middle-income countries, which are experiencing the most rapid acceleration of demographic ageing and have the least capacity to cope, medically, socially, and economically. In many developing countries, modernization and high population mobility have unravelled the extended family networks that traditionally cared for the elderly.

Worldwide, most care for dementia takes place in family homes. This care is immensely challenging, physically, psychologically, and financially. People with dementia need services and support, as do their carers. At the personal level, the costs of care can be catastrophic, especially as they are often paid for out-of-pocket. The wages of informal carers are sacrificed when they give up their jobs to provide the full-time care that people with advanced dementia nearly always need. In such situations, the lifetime savings of people with dementia and their carers can be lost.

The alarming trends, in numbers affected and the soaring costs of associated care, will only get worse in the absence of effective preventive strategies and better technical tools, especially for treatment. The R&D incentives to develop new medicines are potent given the burden of dementia in high-income countries. However, after a series of repeated and costly failures, pharmaceutical companies began to retreat from the search for a dementia cure. Many research projects were postponed or shelved because of the high technical and financial risks of failure.

In the second decade of this century, **the world** had plans for dealing with a nuclear accident, cleaning up chemical spills, mitigating natural disasters, and responding to an influenza pandemic. But it **did not have a comprehensive and affordable plan for coping with the tidal wave of dementia that is engulfing rich and poor countries alike.**

That situation began to change in a series of watershed events. In 2012, WHO and Alzheimer's Disease International jointly issued a report that explained why dementia must be treated as a global public health priority. The report also set out the many things that can be done to improve the lives of people with dementia and support their carers. With dementia now established as a public health priority, the UK convened a G8 Dementia Summit in London in 2013. The summit was a ground-breaking event. The deliberations expressed a strong sense of urgency to catch up with a runaway human tragedy and set out powerful proposals for doing so. Acting together.

G8 countries aimed to transform the approach to dementia, which was often summarized in four words: "Nothing can be done."

The summit – and its proposals – took a dramatically different approach. High-level leadership and commitment can defeat dementia through a three-pronged approach that steps up research for new interventions, finds ways to improve the quality of life and care, and does more to support carers and families. Participants gave particular attention to the policies and incentives needed to accelerate research and discovery by creating a more attractive environment for innovation. A better bridge between research conducted in publicly-funded academic institutes and research undertaken by industry was considered essential. In one of its most significant achievements, the summit articulated the bold ambition of doubling funding for dementia research and finding a cure or disease-modifying therapy by 2025.

To take the agenda forward, WHO convened the first Ministerial Conference on Global Action against Dementia in 2015. That event showed how a sense of urgency can inspire invention. Presentations explored ways to break through some long-standing barriers to rapid product development. Proposals looked at ways to streamline, simplify, and harmonize regulatory approval and formally coordinate research undertaken by industry with research conducted in publicly-funded academic institutions. The conference also reviewed an inventory of existing options for jump-starting innovation when market forces fail. In addition, strategies were proposed to improve the delivery of care as a way of immediately cushioning dementia's impact on health systems and families. Above all, the conference continued the spirit of collective social responsibility that emerged during the London summit: political leadership must step in to take up the slack when market forces fail to deliver new tools for a burden of this magnitude.

A WHO Global action plan on the public health response to dementia is on the agenda for the World Health Assembly in 2017. The action plan draws on cross-cutting principles, such as the human rights of people with dementia and the empowerment and engagement of people with dementia and their carers. One area for strategic action is specifically focused on dementia awareness and "friendliness" based on an important new premise: increasing public awareness, acceptance, and understanding of the diseases can enable people with dementia to maintain their participation in social life and maximize their autonomy.

Healthy ageing: creating age-friendly societies

Demographic ageing is a universal trend, affecting countries at all levels of development in every region of the world. By the middle of this century, the population of people aged 65 and older will outnumber children for the first time in history. Populations are ageing fastest in low- and middle-income countries. A transition towards an older society that took more than a century in Europe is now taking place in less than 25 years in countries like Brazil, China, and Thailand. In an unprecedented trend, most people can now expect to live into their 60s and beyond, and health systems everywhere are unprepared to meet the needs of the growing number of people living longer lives.

The implications for governments are huge. These older populations are a significant human and social resource, but they will also present challenges, especially when the demands of a disease like dementia are factored in. The most crucial determinant of where the balance lies between the opportunities and risks of demographic aging is the health of these older populations.

To truly liberate the potential of these older populations, health professionals need to think of health in older age as more than just the absence of disease. Most people over the age of 65 experience multiple coexisting chronic health conditions. However, when these conditions are managed effectively, older people can still enjoy good health. With this goal in mind, WHO has developed a new narrative for healthy ageing that is framed around the functioning of the older person.

This approach is articulated in the first *World report on ageing and health* released by WHO in 2015. That report moved the health needs of the elderly from the back burner at WHO to the full heat of attention and recommended actions. Apart from charting global trends, the report reached a number of conclusions that promise to reshape thinking about the ageing process and its implications for health. As the foundation for its recommendations, the report looks at what the latest evidence has to say about the ageing process, noting that many common perceptions about older people are based on outdated stereotypes. As these misperceptions are among the most pervasive barriers to maintaining the health and independence of older people, the report soundly refutes them with the facts.

As the evidence shows, the loss of capacity and ability associated with ageing is only loosely related to a person's chronological age. Some people in their eighties retain the robust health of a twenty-year-old, while others require significant care and support at much younger ages. As the report makes clear, there is no "typical" older person. This diversity in the capacities and health needs of older people is not random, but rooted in events throughout the life course that can often be modified, underscoring the importance of a life-course approach to healthy ageing. Moreover, contrary to common assumptions, ageing has far less influence on health care expenditures than other factors, including the high costs of new medical technologies.

Guided by the evidence, the report aims to move the debate about the most appropriate public health response to population ageing into new – and much broader – territory. The overarching message is optimistic: with the right policies in place, population ageing can be viewed as a rich new opportunity for both individuals and societies. The resulting framework for taking action offers a menu of concrete steps that can be adapted for use in countries at all levels of economic development.

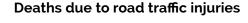
Throughout the report, examples of experiences in different countries are used to illustrate how specific problems can be addressed through innovative solutions. Practical examples show how health systems can be better aligned with the needs of older people and how fair and sustainable systems for long-term care can be built in every country. The report further illustrates what is meant by age-friendly environments and explains how the many knowledge gaps that plague understanding of healthy ageing can be filled.

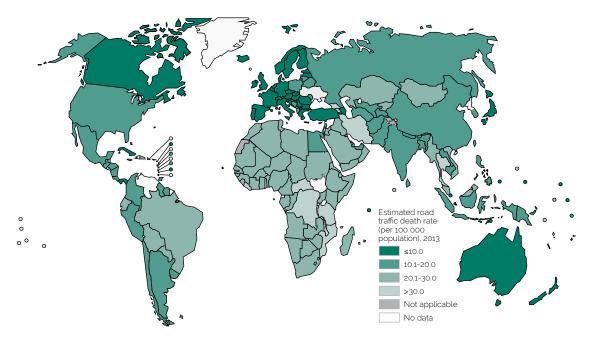
The report provided the foundation for the WHO Global Strategy and Action Plan on Ageing and Health, which was adopted by the World Health Assembly in 2016. The plan has two complementary goals. First, where sufficient evidence exists, it proposes action to maximize

functional ability. Second, it describes what can be done to fill evidence gaps and establish the partnerships needed to support a Decade of Healthy Ageing from 2020–2030. The strategy also asks countries to realign health systems to match the needs of older populations, to develop age-friendly environments, and to lay the foundations for systems of long-term care.

Combating ageism is another central objective: unless ageism is tackled and fundamental misconceptions about older people are changed, the capacity to seize innovative opportunities to foster healthy ageing will be limited. The strategy was subsequently endorsed by the 2016 G7 summit meeting in Ise-Shima, Japan, in its Vision for Global Health, which specifically called for implementation of the strategy, with adaptation to suit national contexts in all countries.

These major steps forward build on other significant work undertaken by WHO over the past 10 years. This work includes the WHO Global Network for Age-Friendly Cities and Communities which, by 2017, had become a movement embracing more than 400 cities and communities and 11 affiliated programmes that together cover 146 million people. All these municipalities aspire to becoming better places in which to age, whether it be through providing better access to transportation, lifelong learning and social support or through initiatives to foster links between generations and overcome isolation.





Nutrition: ending all forms of malnutrition

The prevalence of malnutrition as a public health problem is characterized by the two extremes of undernutrition and overnutrition. Traditional determinants of undernutrition persist while newer drivers of overweight and obesity split the nutrition profile. WHO estimates that nearly 160 million young children are stunted and 50 million are wasted. Deprived of essential nutrients so early in life, many of these children will suffer life-long health consequences. The four countries in Africa and the Middle East currently on the brink of famine constitute a humanitarian crisis on a scale not seen since the end of World War II.

In addition, more than two billion people suffer from micronutrient deficiencies, leading to complications ranging from poor pregnancy outcomes, to the impaired cognitive development of infants and young children, to blindness. At the same time, nearly an equal number of people are obese or overweight. Since 1980, WHO estimates that the prevalence of obesity has nearly doubled in every region, with the fastest increases recorded in low- and middle-income countries. These countries often face a double burden of malnutrition, with undernutrition occurring side-by-side with overweight and obesity in the same communities and families across the life-course. WHO estimates that, in 2015, more than 1.9 billion adults worldwide were overweight and more than 600 million were obese. In the same year, around 42 million children under the age of five were obese or overweight.

WHO has long contributed to the technical foundations for sound nutrition policies by recommending a range of acceptable daily intakes of micronutrients, with the minimum intake needed to prevent deficiency diseases and the upper intake needed to prevent chronic diet-related diseases. WHO has also contributed to the safety of the food supply through a long-standing series of reports that have set acceptable daily intakes for several hundred food additives, contaminants, and veterinary drug and pesticide residues in food. Risk assessments on a number of foodborne pathogens have likewise been undertaken by WHO. These evaluations and assessments contribute to the work of the joint FAO/WHO Codex Alimentarius Commission, which has been setting international standards for food safety and quality and providing information for consumers since 1963.

WHO's role in leading the global response to malnutrition assumed a higher profile in 2012, when the World Health Assembly adopted a *Comprehensive Implementation plan on maternal, infant and young child nutrition*. The plan charted the way forward to 2025 with six global nutrition targets. The *Global action plan for the prevention and control of noncommunicable diseases,* adopted in 2013, included two diet-related targets to be reached by 2025: to achieve a 30% relative reduction in mean population intake of salt, and to halt the rise in overweight and obesity. The Global Monitoring Framework for NCDs also includes indicators on saturated fatty acids, *trans*-fatty acids, fruits and vegetables, and policies to reduce marketing to children.

Another pivotal point occurred in 2014 when FAO and WHO jointly convened the Second International Conference on Nutrition in Rome, Italy. The conference achieved consensus on the multiple challenges of malnutrition, including obesity and overweight, a vision on the way forward, and commitments to undertake specific actions. Two outcome documents were adopted: the Rome Declaration on Nutrition and a corresponding Framework for Action, which

recommends a set of policy options and strategies to promote diversified, safe, and healthy diets at all stages of life.

In 2015, the 2030 Agenda for Sustainable Goals set a bold goal of ending hunger, including targets for ending all forms of malnutrition and ensuring sustainable food production. The sense of urgency communicated in the Rome documents prompted the UN to launch a Decade of Action on Nutrition starting in July 2016. Nutrition had truly arrived on the international development agenda, with WHO and FAO given the leadership role in coordinating the response. The pressure was on as never before to implement the decade's specific, measurable, achievable, relevant, and time-found policies – the so-called SMART policies.

The determinants of malnutrition are multiple and extremely complex. Action to end malnutrition in all its forms – from hunger and disease associated with micronutrient deficiencies, to obesity and overweight as risk factors for diabetes, cardiovascular disease, and cancer at several sites – will require a movement that engages all of society, from consumer groups to businesses, and from those who negotiate trade agreements to multinational corporations.

All of these groups must also be engaged in ensuring that food, as it moves from the farm to the plate, is kept safe. WHO estimates that unsafe food – contaminated with bacteria, viruses, parasites, or chemical substances – causes more than 200 diseases. Food safety is inextricably linked to nutrition and food security. Unsafe food creates a vicious cycle of disease and poor nutrition, especially in infants, young children, the elderly, and people with underlying conditions. WHO estimates that foodborne diseases cause 600 million illnesses and 420 000 deaths every year. In 2015, WHO devoted World Health Day to food safety, asking both producers and consumers to be aware of the many common errors that can turn a meal into the start of a foodborne disease.

Road safety: 1.25 million predictable and preventable deaths

Unsafe roads cause significant premature deaths and disabilities that place a heavy burden on health systems, both for trauma care and long-term rehabilitation. The fact that the overwhelming majority of traffic deaths and injuries are predictable and preventable provides a powerful incentive to act. As the causes of traffic crashes are so numerous, preventing them requires collaboration with other sectors, such as those responsible for municipal infrastructure, transport systems, road engineering, education, vehicle registration and safety, trauma care, and far-reaching legislation and law enforcement.

In 2009, the Russian Federation hosted the first Global Ministerial Conference on Road Safety in Moscow to give the issue a higher profile on the international agenda. That conference led the following year to the adoption of a UN General Assembly resolution which proclaimed 2011–2020 as the Decade of Action for Road Safety, with WHO appointed to serve as the decade's secretariat. To track trends and monitor progress, WHO issued its second *Global status report on road safety* in 2013. In 2015, as the midpoint in the decade approached, WHO issued an

updated global status report which became the centrepiece for the Second Global High-level Conference on Road Safety held the same year in Brazil.

The WHO report showed that the toll of road traffic crashes, as measured by the number of deaths and injuries, had not increased as expected given the continuing rise in the number of vehicles on the world's roads. However, the numbers were still far too high. The report estimated that road traffic crashes were claiming 1.25 million lives each year. Strategies put in place since the first ministerial conference were saving some lives, but the pace of progress was too slow.

Data in the report raised concern on several levels. The risk of dying on the roads was strongly associated with a country's level of economic development. Low- and middle-income countries accounted for 90% of road traffic deaths, despite having just 54% of the world's vehicles. Europe had the lowest death rates. Africa had the highest. In a particularly alarming statistic, the report showed that road traffic crashes are the number one killer of people in the age group of 15 to 29 years. The report targeted additional vulnerable groups for action. Motorcyclists accounted for 23% of all road traffic deaths, pedestrians for 22%, and cyclists for 4%. As noted, the large proportion of pedestrian deaths called for more planning on how vehicles and people can safety share roads.

All of these initiatives and reports, with the support of many partners including Bloomberg Philanthropies, helped secure a firm place for road safety on the 2030 Agenda for Sustainable Development. The importance of road safety is explicitly recognized in two targets, one each under the goals for health and for cities: first, by 2020, to halve the number of global deaths and injuries from road traffic crashes, and second, to provide access to safe, affordable, accessible, and sustainable transport systems for all, notably by expanding public transport. The two targets provide a rallying point to stimulate further commitment and action. While ambitious, both targets are feasible. The epidemic of deaths and injuries on the road is a crisis made by people. Solutions are known and backed by abundant evidence.

The business case for improved road safety is readily made. Changing road user behaviour through adopting and enforcing good laws cuts road deaths. Evidence shows that laws reduce risks associated with speed and drink-driving. Laws also increase the use of established preventive measures, like seatbelts, motorcycle helmets, and child restraints. Vehicle technology exists to increase safety. These safety technologies need to be included in vehicles sold in both rich countries and poorer parts of the world.

Many affordable road improvements, such as footpaths, safety barriers, bicycle lanes, and paved shoulders, save lives. Moreover, footpaths or sidewalks and bicycle lanes encourage physical activity, which is an especially important health asset in urban environments. The SDG targets ask the international community to do two things: first, to work together to create a world free of high-risk roads, vehicles and behaviours, and second, to ensure that the benefits of safe mobility are evenly shared.

Violence prevention: an opportunity and responsibility

Interpersonal violence includes child maltreatment, youth violence, intimate partner violence, sexual violence, and elder abuse. Over the past decade, violence has moved from the margins of the development agenda to the centre. Violence prevention features strongly in three of the 2030 Agenda for Sustainable Development targets: ending violence against women; ending violence against children, and significantly reducing deaths due to all forms of violence. This shift in the attention given to violence has been driven by dramatic improvements in the ability to measure its prevalence and consequences, and rapid expansion of the scientific evidence base for what works best for prevention.

WHO first marshalled the scientific evidence for what works to prevent violence in the 2002 World report on violence and health. At that time, data on the national prevalence of different types of violence were lacking in many countries. Since then, considerable work on national data collection and scores of country surveys have led to much improved documentation on most types of violence. For example, many countries have conducted surveys to assess the extent of violence against children. At the global level, recent data show that up to one billion children worldwide are exposed to violence each year. As a result, and over the course of their lifetime, these children are at greater risk of mental illness and anxiety disorders, chronic diseases such as heart disease, diabetes and cancer, infectious diseases such as HIV, and social problems such as crime and drug abuse.

Similarly for violence against women, a surge of national surveys has helped put the problem in stark relief. Globally, WHO now estimates that around one in three women worldwide have experienced physical or sexual violence by an intimate partner at some point in their lives, leading in many instances to a similarly lifelong set of health and social consequences as those faced by children. More information than ever before has emerged about violence against older people, with elder abuse affecting one in six adults over 60 years of age worldwide – some 141 million people. Homicide is now also somewhat better documented: of the estimated 470,000 homicides each year, males account for more than 80% of all cases, and nearly half involve firearms.

In order to disseminate the evidence base on violence prevention, in 2007 WHO established an interactive online resource known as the *Violence Prevention Evidence Base*. The resource has shown steady, year-on-year increases in the number of published scientific studies of intervention effectiveness, and as of 2016 included 653 such studies, each one a compelling confirmation that violence is preventable. Geographically, sub-Saharan Africa has emerged as one of the most prominent growth points in the evidence base, especially as it concerns interventions to address violence against children and against women. In 2016, this evidence was sufficient for WHO and nine partner agencies to launch *INSPIRE: Seven strategies for ending violence against children*, a first-ever global technical package of evidence-based interventions that point the way to deeper and more effective engagement in violence prevention everywhere.

To take stock of how these advances work at country level, WHO published in 2014 the first *Global status report on violence prevention*, offering a snapshot of violence prevention initiatives in 133 countries. The report generated several headline findings: countries are beginning to

invest in prevention programmes and policies; laws related to violence prevention are critical and exist in most countries, but their enforcement remains inadequate; and the availability of services for victims of violence varies markedly, with services to protect and support victims in place in just over half of countries.

The report's findings were widely taken up in various planning and policy processes. Importantly, these included the processes leading to the May 2014 World Health Assembly resolution on strengthening the role of the health system in addressing violence, which called for WHO to develop a global plan of action for addressing the problem. This initiative culminated in the May 2016 World Health Assembly's adoption of a resolution endorsing the plan of action. The plan addresses interpersonal violence in all its forms, has special sections on violence against children and violence against women, and emphasizes the importance of both prevention and victim service provision.

Far from walking the violence prevention path alone, WHO is in good company with strong partners from multiple sectors. Since 2004, the Violence Prevention Alliance has continued to strengthen its network of connections with partners from criminal justice, criminology, education, and social work. Launched in 2016, the Global Partnership to End Violence Against Children is spearheading efforts to support countries in their actions to achieve the SDG target on ending violence against children, with WHO represented on its Board and Executive Committee. Moreover, as a founding partner of the Sexual Violence Research Initiative, WHO continues to commit its expertise and convening powers to this critical endeavour.

The world has an opportunity and a responsibility to prevent violence. Doing so will have a positive impact on a broad range of health, social, and economic challenges. Violence can be prevented if the global community acts now, acts wisely, and acts together.

Disability: a public health challenge

Almost a decade ago WHO embarked on an endeavour to compile the most up-to-date information on the extent of disability around the world, and the obstacles faced by people living with disabilities. The result of this effort was the 2011 *World report on disability*, produced in collaboration with the World Bank, which found more than one billion people in the world experience significant disability.

People with disabilities have generally poorer health, lower education achievements, fewer economic opportunities, and higher rates of poverty. These disadvantages are largely due to the lack of services available to them and the many obstacles they face in their everyday lives, difficulties that are exacerbated in less-advantaged communities. The World report on disability describes the best available evidence about what works to overcome barriers to health care, to promote rehabilitation, education, employment, and support services, and to create the environments which will enable people with disabilities to flourish. The report ends with a concrete set of recommended actions for governments and their partners which continue to be a guiding influence in setting the global agenda for disability.

WHO's role in leading the public health disability agenda was also strengthened by the adoption of a global disability action plan 2014–2021. Through the implementation of this action plan, WHO supports Member States to take action across a number of the recommendations laid out in the *World report*. Follow-up technical tools have also been provided to guide the implementation of these recommendations. For example, WHO issued the Model Disability Survey which supports improved national data collection on disability, allowing countries to estimate the extent of disability using a standardized and internationally comparable methodology. This tool has been implemented in several countries and continues to be rolled out globally.

As the discussion regarding the post-2015 development agenda gained momentum, the international community turned to the evidence and recommendations of the *World report* to make the case for the inclusion of disability into the development agenda. In September 2013, the United Nations General Assembly convened a High-level Meeting on Disability and Development at the level of Heads of State and Government, with the overarching theme "The way forward: a disability inclusive development agenda towards 2015 and beyond." This meeting was the first step towards the inclusion of disability into the Sustainable Development Goals.

The global disability action plan also recommends strengthening rehabilitation services and assistive technologies around the world. The Global Cooperation on Assistive Technologies was launched in 2014, and a list of priority assistive products for country implementation was launched at the World Health Assembly in 2016. In February 2017, WHO launched the initiative *Rehabilitation 2030: a call for action* to raise awareness about the need to strengthen health systems to provide rehabilitation services, with the aim of progressively achieving universal health coverage in the context of the SDG agenda.

Global efforts to address disability have been accompanied by an internal initiative to make WHO itself more disability friendly. This initiative includes ensuring equal employment opportunities for people with disabilities, making WHO offices wheelchair accessible, and issuing health information products in a variety of formats that are accessible to people living with disabilities.



A fter decades of stagnation, political will to cut the number of needless deaths of mothers and children emerged in 2010 with the United Nation's US\$ 40 billion Every Woman Every Child initiative. Dramatic progress came from better data collection, more births in health facilities, better nutrition and vaccines against diarrhoea and pneumonia, the biggest child killers. A revised global strategy views the focus on maternal, newborn, child and adolescent health as an entry point for increasing universal health coverage.

In 1985, *The Lancet* published a pivotal, thought-proving commentary that riveted attention on a neglected tragedy: maternal mortality. "Where is the M in MCH?" the authors asked. The article opened with the WHO estimate that complications of pregnancy, unsafe abortions and childbirth were killing at least half a million women in developing countries every year. Left out of that calculation were many more poor adolescents and women who suffered life-long complications from unsafe abortions and deliveries.

In part, the article attracted so much attention because it challenged the widespread assumption that most maternal deaths could be prevented by detecting at-risk women during antenatal care and screening. As pointed out, a sizeable proportion of serious complications occur among women with no recognizable risk. When those complications occur, the authors stressed, most life-saving interventions require emergency obstetric care in hospital facilities staffed with highly trained doctors, midwives and nurses. A reliance on traditional birth attendants would not save those lives.

In other words, an agenda that aimed to get the death rate down needed to be an agenda that improved access to essential health services, including emergency obstetric care and facility-based birth with skilled attendants. Citing the excellent maternal health care provided in Cuba and China, the authors concluded that lack of political will to face the problem was the biggest reason why a tragedy on this scale continued.

In the published debate that followed, some authors questioned whether MCH really needed an M at all. The better focus was on women, and this needed to be a focus on the health of girls and women throughout the life course. Though women's reproductive functions made them vulnerable to health problems, an exclusive focus on these functions reduced the status



Births, deaths, and causes of death were not registered, leaving countries and their partners working in the dark. of women to vessels for procreation. Both the health needs of women and their contributions to society were much, much broader.

All of these concerns were eventually reflected in formal WHO policies and strategies.

The situation in 2007: dire prospects for progress

In 2007, WHO, UNICEF and the UN Population Fund issued new country-specific estimates for maternal mortality. Though 22 years had passed, the "neglected tragedy" looked no better than in 1985. The estimated number of maternal deaths stubbornly stood at 536 000 worldwide, with developing countries accounting for 99% of those deaths. In sub-Saharan Africa, around 900 women died during pregnancy and childbirth per 100 000 live births. In wealthy countries, that figure dropped 100-fold to just 9. The statistics were the starkest in all of public health. For example, the adult lifetime risk of dying during pregnancy and childbirth in Niger was 1 in 7. In Ireland, it was 1 in 48 000.

As the new estimates showed, maternal mortality had decreased at an average of less than 1% annually between 1990 and 2005, far below the 5.5% decline needed to achieve the fifth MDG. The decline in sub-Saharan Africa was the lowest, estimated at 0.1%.

The news for child mortality was better, but just barely. In 2006, the annual number of children dying before their fifth birthday fell to 9.7 million, marking the first time that yearly childhood deaths dropped below 10 million since records began. Though the slight decline was welcome, the millions and millions of deaths from largely preventable causes looked outrageous six years into the MDG era.

On its part, WHO recommended a life-course approach to the health of both women and children, ranked the leading causes of morbidity and mortality, and identified the interventions that were likely to have the biggest life-saving impact. WHO developed norms, tools, clinical standards, protocols and guidelines in areas ranging from antenatal care and the management of sexually transmitted infections, to the treatment of maternal peripartum infections and a simple colour-coded tool for the detection of anaemia, to human rights and contraception, optimal nutrition for girls and women, and appropriate feeding practices for infants. WHO also made a major effort to improve access to sexual and reproductive health services offering a wide choice of modern family planning options, and issued safe abortion guidance for use in countries where abortions are legally permitted.

But efforts to reduce both maternal and childhood mortality shared two major challenges. First, the quality of country-specific data was abysmal. Some 85 countries, representing 60% of the world population, had no reliable systems for civil registration and vital statistics. **Births, deaths, and causes of death were not registered, leaving countries and their partners working in the dark.** In 2008, countries with medically certified vital registration accounted for only 4% of the 8.8 million childhood deaths estimated for that year.

Second, efforts to reduce maternal and child mortality had no single commodity, like antiretroviral therapy for HIV, cocktails of inexpensive drugs for tuberculosis, or insecticidal nets for malaria, that could be scaled up to have a dramatic impact on morbidity and mortality. Widely-used childhood vaccines were highly effective in protecting children from leading infectious killers, averting up to 3 million deaths each year, but that still left nearly 9 million yearly deaths occurring from largely preventable causes. As WHO argued, maternal and childhood deaths would not go down until access to quality health services improved. For maternal health, evidence was mounting that even the vastly improved access to services that followed the elimination of user fees would have little impact on deaths and "near misses" in the absence of high-quality standards of care

Everyone agreed that, as economies grew and living conditions improved, many of the conditions – like undernutrition and especially anaemia, poor water supply and little sanitation, dirty environments, and dirty indoor air – that made women and children so vulnerable to early death would gradually get better. But that would take decades. No one wanted to wait.

In line with the culture of measurement and accountability that drove the MDG era, those dismal figures halfway to the 2015 deadline provoked the international community to take aggressive action on multiple fronts. Several new partnerships, initiatives and strategies were launched and operational by 2010. The results over the next five years would be dramatic.

A new global strategy puts accountability on the map

At the UN General Assembly in 2010, the Secretary-General launched a new global strategy for women's and children's health, which became known as the Every Woman Every Child initiative. That high-profile event initially attracted commitments of \$40 billion in funds for the five-year period leading to 2015. Full implementation of the strategy was expected to save the lives of 16 million children, prevent 33 million unwanted pregnancies, end stunting in 88 million children, and protect 120 million children from pneumonia by 2015. The political will, so tragically missing in 1985, had arrived. The strategy was almost immediately backed by the findings of a UN Commission that identified 13 life-saving commodities for women and children that were vastly underutilized. The Commission estimated that wide and proper use of these 13 commodities alone could save the lives of at least 6 million women and children.

The new strategy was shaped by the expertise and practical experiences of WHO and members of the Partnership for Maternal, Newborn and Child Health, which coordinated the work of more than 80 agencies, country programmes, civil society initiatives, academic groups, and donors. WHO was asked to lead the strategy's implementation. In an unprecedented step, WHO was further asked to convene a Commission on Information and Accountability for Women's and Children's Health. The Commission's objective was to develop a framework for ensuring that promises of resources for women's and children's health were kept and that results were measured. The Commission was established in December 2010 and delivered its final report in May 2011.

Members of the Commission agreed on 10 recommendations, with related indicators, to help ensure that the \$40 billion pledged to support the global strategy were spent in the most effective way, and that both donors and recipients were held accountable. The report linked accountability for resources to the results, outcomes, and impacts they produce, and to the capacity of recipient countries to measures those results. The Commission also called for the establishment of an independent Expert Review Group to issue critical annual reports on implementation of the strategy and its impact.

The appointment of an independent Expert Review Group joined the Independent Monitoring Board of the Global Polio Eradication Initiative as "firsts" for global health. Their emphasis on measurement and accountability reshaped the design of global health strategies and action plans at WHO to consistently include accountability frameworks. Highly innovative initiatives, like the Pandemic Influenza Preparedness Framework, also appointed independent expert monitoring boards to assess impact and recommend strategic course corrections. Measurement and accountability formally moved into the mainstream as part of the definition of a well-conceived strategy designed to produce results.

However, accountability means counting. As the first reports of the independent Expert Review Group made clear, reliable measurement was greatly impeded by the absence of systems for civil registration and vital statistics in the vast majority of high-burden countries. As long as countries lacked the capacity to measure results, progress would be impaired, especially at a time of financial austerity when parliamentarians in donor countries needed to show that investments in health development brought results.

Improving information systems

Improving information systems became the next objective, spearheaded by the government of Canada with its G8 Muskoka Initiative in 2010. That initiative, which secured commitments of more than \$7.3 billion in funding over the next five years, put information and accountability firmly on the agenda of plans for improving maternal and child health. As health officials increasingly recognized, the information collected in a well-performing system for civil registration and vital statistics saved lives but also provided proof of legal identity. Having that legal identity facilitated access to essential social services, including health and education.

The international community had much to build on. Country-specific estimates of maternal and child mortality had been steadily improving since 2004, when WHO, UNICEF and the World Bank launched two interagency groups to produce yearly estimates of maternal and child mortality. The interagency groups used a standardized methodology that brought consistency and greater precision to what had been widely varying estimates separately issued by the three agencies. Membership of the interagency group was later expanded to include the UN Population Division and several national and academic institutes devoted to the improvement of statistical data. Over the years, the modelling approach was refined to optimize the use of diverse country-specific data sources and provide more precise estimates of uncertainty. The two annual estimates of maternal and child mortality became the foundation for other

annual reports, including UNICEF's *The State of the World's Children*, the World Bank's *World Development Indicators*, and WHO's *World Health Statistics*.

The estimates from the interagency groups also informed the annual reports, starting in 2005, of the Countdown to 2015 for Maternal, Newborn and Child Survival initiative, which became the principal instrument for monitoring and accountability in the 75 countries that bear 99% of the burden of maternal and child mortality. Drawing on the expertise of more than 40 participating institutions and agencies, including WHO, Countdown gave measurement a strong technical component, with a standardized methodology that brought confidence in the data and facilitated reliable country comparisons and charting of trends.

Countdown's annual reports assessed coverage with specific life-saving interventions and gave particular attention to health systems and financing as the two main drivers of coverage. With their focus on the situation in individual countries, the reports showed how building on existing systems for monitoring and reporting was the best way to achieve realistic and sustainable improvements.

In 2010, the heads of WHO and seven other agencies working in global health issued a call to improve health data in response to demands for evidence of results and accountability. The agency heads called for a shift away from the current focus on defining indicators and reporting requirements towards building the capacity of information systems within countries. They also noted that systems for civil registration and vital statistics had shown virtually no improvements over the past several decades.

At the time, maternal mortality estimates were based on statistical models, which increase global awareness of the problem, but do not provide information needed for a targeted and timely response. To improve the situation, WHO built on the established methodology for conducting maternal death reviews to put forward a comparatively new approach, Maternal Death Surveillance and Response, based on the premise that **each maternal death has a story to tell and, if properly investigated, can yield data on ways to prevent future deaths among women in similar circumstances.** The emphasis was firmly placed on taking action in a continuous cycle of investigation, learning, and introducing improvements. Using the approach, investigation leads to identification of the barriers women faced, the resources available, and the care they received, benchmarked against standards of best practice where available. Apart from supporting progressive improvements in the prevention of maternal deaths, the approach made health professionals accountable for ongoing self-assessment.

WHO also issued guides showing how ICD-10, the standard coding tool, could be used to accurately capture and classify the causes of perinatal and maternal deaths.

Women: delivering far more than babies

In 2010, a new initiative, Scaling Up Nutrition, was launched following publication of a policy paper and framework for action in the *Food and Nutrition Bulletin*. The framework for action drew on broad consensus among UN, multilateral and bilateral development agencies, foundations,

developing countries, civil society organizations, researchers, and the private sector. WHO promptly endorsed the policy paper and called for its wide support. More than 80 institutions responded to that call, and the SUN movement was born.

The SUN movement focused on scientific evidence that **nutrient intake during the first 1000 days of life – from pregnancy to two years of age – was a window of opportunity when good nutrition would have the highest impact** in reducing nutrition-related deaths and disease and avoiding irreversible harm to the child. The movement also aimed to correct a situation in which nutrition frequently appeared as an afterthought in development priorities, both within countries and at the international policy level.

By 2010, concern about the stalled progress for MDGs four and five had created a more favourable context for scaling up nutrition as a set of interventions with demonstrated life-saving potential. The movement became operational in 2012, offering a unique focus on country ownership, structured sharing of best practices among participating countries, and networks of agencies offering external assistance. When countries join the SUN movement, they commit to develop and cost a national nutrition plan and to establish a multi-stakeholder platform and budget line for nutrition. As the initiative evolved, it offered guidance on coherent multisectoral policies backed, where appropriate, by laws, and strategies for raising domestic resources and working with the business community.

In line with WHO advice and global nutrition targets approved in 2012, the SUN platform for action focused on the delivery of a limited number of affordable and feasible interventions backed by solid evidence of their impact. A package of just 13 interventions was put forward in the categories of good nutrition practices, like breastfeeding and hand hygiene, the provision of vitamin supplements to children and their mothers, population-wide approaches, like salt iodization and iron fortification of staple foods, and therapeutic feeding for severely undernourished children, including the use of ready-to-use therapeutic foods. Even with only 50% coverage with these interventions, estimates showed that 500 000 young lives could be saved each year.

By 2016, 57 developing countries had joined the SUN movement. Between 2012 and 2016, the worldwide number of stunted children dropped by 9 million. SUN-supported monitoring recorded the most dramatic reductions in Bangladesh, Nepal, Lesotho, and El Salvador.

In 2016, at the Women Deliver Conference in Copenhagen, Denmark, SUN launched a series of case studies showing how the empowerment of women and girls can build a sisterhood of success for food security. Doing so was considered another essential line of action. In developing countries, women farmers were responsible for 60% to 80% of food production. However, their rights and socioeconomic status were rarely equal to those of men. As the case studies showed, when women farmers were empowered, they were not only more productive, but as the main source of food for their children, they gave future generations a better start in life.

The first Women Deliver conference, held in 2007, brought together nearly 2000 advocates, researchers, policy makers and global leaders from 115 countries. It put the world on notice: the deaths of more than half a million women each year in pregnancy and childbirth would no longer be tolerated. The evidence and arguments presented during the conference brought new ammunition to the case for investing in maternal and newborn health. Subsequent conferences,

held at three-year intervals, rapidly increased the visibility of these issues and the impact of the many new initiatives that grew out of the meetings.

The 2016 conference drew nearly 6000 participants from 169 countries and was covered by more than 500 journalists. That conference had a simple but powerful message: sustainable development is possible only when girls and women are healthy and thriving. Investment in women and girls has a ripple effect. All of society wins in the end.

Scaling up new vaccines

Over a 20-year period, several new vaccines had been licensed for use in children, including vaccines that protect against *pneumococcus* and rotavirus infections, leading causes of childhood deaths from pneumonia and diarrhoea. Though prequalified by WHO, the vaccines were initially not being utilized in developing countries where the vast majority of deaths from pneumonia and diarrhoea occur. Historically, new vaccines have taken from 10 to 15 years to gradually trickle into the immunization programmes of developing countries. Again, no one wanted to wait. Everyone looked to WHO for guidance.

WHO issues authoritative position papers on vaccines, published in its *Weekly Epidemiological Record*, when new data on safety, efficacy, benefits or dosing schedules emerge, especially from studies conducted in resource-constrained settings, or when new products are licensed. These position papers shape Gavi policies and are also widely used by the managers of immunization programmes everywhere, but especially in the developing world, to align their strategies with the latest technical evidence and recommendations from WHO. In preparing the position papers, WHO scientists draw heavily on the Strategic Advisory Group of Experts on immunization.

The introduction of the new rotavirus vaccines in wealthy countries rapidly cut in half the number of hospital admissions of children with acute gastroenteritis. However, high rates of undernutrition and co-infections with other enteric pathogens raised doubts about whether similar positive outcomes could be expected in developing parts of Africa and South Asia. In its first position paper on rotavirus vaccines, issued in 2007, WHO was not prepared to recommend the inclusion of rotavirus vaccines in the national immunization programmes of these countries.

That position changed following the completion of studies in developing countries where sanitation was poor, mortality from diarrhoeal disease was high, and maternal infections with HIV were widespread. In 2013, a new position paper on rotavirus vaccines was issued in response to additional evidence on vaccines, their safety, and the duration of protection. WHO recommended that rotavirus vaccines should be included in all national immunization programmes and considered a priority, particularly in countries in Africa and South Asia with high mortality associated with gastroenteritis caused by rotavirus infection. In those countries, WHO further recommended that vaccination be part of a comprehensive package of prevention and treatment interventions.

Similar procedures were followed in 2012 when WHO issued a position paper on the new pneumococcal conjugate vaccines, protective against 10 and 13 common serotypes of *Streptococcus*

pneumoniae. The position paper concluded that the new conjugate vaccines were safe and efficacious and represented significant progress in the fight against pneumococcal morbidity and mortality, especially in the developing world. WHO therefore recommended the inclusion of the vaccines in childhood immunization programmes worldwide. In developing countries, WHO recommended that vaccination be viewed as complementary to the use of other measures to control pneumonia.

A cornerstone objective of Gavi is to accelerate the introduction of new vaccines. By 2015, 19 countries had added rotavirus vaccines to their routine immunization schedules with GAVI support. By the end of 2015, more than 36 million children had been immunized with the vaccines. Beginning in 2010, GAVI supported rollout of the new pneumococcal vaccines in more than 50 countries. By the end of 2015, WHO estimated that nearly 80 million children had been protected. Thanks to these efforts, children in the world's poorest countries were receiving the world's best vaccines simultaneously with children in rich countries.

Introduction of the new vaccines was a show of solidarity and a willingness to innovate.

Through the mechanism of an advance market commitment, the governments of Italy, the United Kingdom, Canada, the Russian Federation, and Norway, further supported by the Bill and Melinda Gates Foundation, contributed \$1.5 billion to stimulate manufacturing of the pneumococcal conjugate vaccines for the developing country market. The mechanism was innovative but the signal was straightforward: if companies invest in expanded manufacturing capacity, the money will be there to purchase the products. The advance market commitment mechanism brought a substantial reduction in the price of the pneumococcal vaccines for use in the poorest countries. It also encouraged new manufacturers, including those in developing countries, to invest in the development of vaccines, potentially contributing to further price reductions in the long term.

Higher ambitions: building on success

With all these initiatives working in concert through WHO coordination, childhood deaths began to decline dramatically, with the fastest declines recorded in sub-Saharan Africa. Maternal mortality finally broke free of the historical half-a-million yearly figure, though the decline was still too slow to meet the MDG targets. As so often happens in public health, when deaths from one set of causes begin to recede, they reveal another set of deadly problems hidden beneath. This proved true for neonatal mortality.

In 2012, WHO published *Born too soon: the global action report on preterm birth.* The groundbreaking report set out the first-ever national, regional and global estimates of preterm birth. It demonstrated the extent to which preterm birth was on the rise in most countries, ranking as the second leading cause of death globally for young children, after pneumonia. The report made addressing preterm birth an urgent priority for reaching MDG four. To encourage targeted action, the report argued that rapid change is possible and identified the priority interventions that could contribute most substantially to reductions in preterm births, especially in low-resource settings. The *Every newborn action plan to end preventable deaths* followed in 2014.

Other ambitious goals followed research that allowed simplified approaches to the leading childhood killers. In 2013, WHO and UNICEF issued an integrated global action plan for *Ending preventable child deaths from pneumonia and diarrhoea by 2025.* The plan responded to some dire statistics. **Together, pneumonia and diarrhoea accounted for nearly 30% of all childhood deaths, amounting to the loss of two million young lives every year.** Though effective interventions were available for prevention and treatment, only 60% of children with suspected pneumonia received appropriate care. Even fewer were being reached with lifesaving treatments: only 31% of children with suspected pneumonia received antibiotics and only 35% with diarrhoea received oral rehydration salts.

The integrated strategy for ending both diseases made perfect sense. Since the determinants largely overlap, preventive strategies and platforms for delivery could be shared. Maximum benefits would come when effective interventions for both were promoted together. Previous groundbreaking research supported by WHO and USAID had shown that antibiotics for the treatment of pneumonia could be safely and effectively delivered in homes. Apart from the advantage of easy access, home-based treatment of pneumonia spared sick children from the risk of exposure to other pathogens in crowded hospital wards.

Other neglected problems moved into the spotlight. In 2014, WHO issued its first report fully focused on the health needs of the world's one billion adolescents. Health for the world's adolescents: a second chance in the second decade provided a state-of-the-art assessment of health status and unmet needs of people in the age group of 10–19 years. Issued as a dynamic, multimedia online report, it explained why adolescents need their own set of interventions, distinct from those designed for children and adults. The report's evidence and arguments were later included when the Global strategy for women's and children's health was revised.

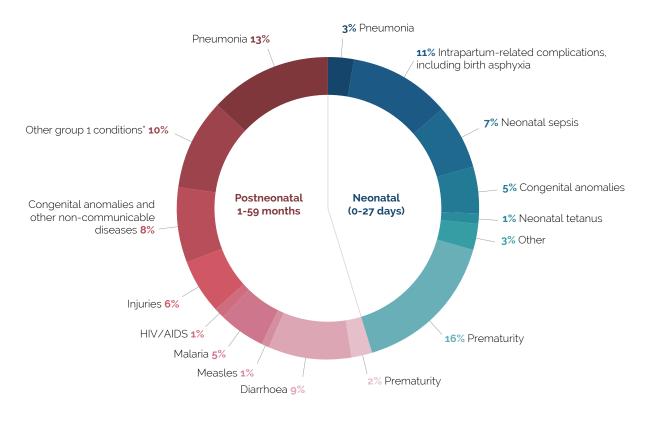
An indicator of fairness

As measurement improved for both maternal and child mortality, the data found additional uses, especially as an indicator of fairness in access to care. As addressing the social determinants of health and progress towards universal coverage emerged as priorities for global health, systems for detecting where inequalities exist and monitoring changes over time became essential instruments for health system reform and a tool for accountable public policies. Improvements in equitable care for women and children were regarded as powerful indicators of overall equality within societies.

In 2013, WHO issued a handbook on health inequality monitoring to enable countries to better monitor and evaluate their progress and performance with a high degree of accountability and transparency. The handbook was followed in 2015 with a report on the status of inequality in reproductive, maternal, newborn and child health. Using 22 indicators, the report profiled the status of inequality within and across countries, with data disaggregated by four dimensions of inequality: economic status, education, rural or urban residence and sex of the child. Where possible, the report tracked changes in health outcomes for population subgroups over time. It showed how a dedicated focus on inequality can compel targeted corrective action that gets to the heart of trouble spots concealed by national averages. For example, the proportion of births

attended by skilled health personnel differed by up to 80% between the richest and poorest subgroups. The use of modern contraceptives was at least twice as high among women with a secondary education or higher as among women with no education. For childhood mortality, deaths in rural areas exceeded those in urban areas by 16 child deaths per 1000 live births.

Causes of deaths among children under 5 years, 2015



Source: WHO

*Group 1 conditions are communicable diseases, maternal, perinatal and nutritional conditions.

What explains the success?

While the leading causes of maternal and child mortality have long been known, less data were available to explain why some countries at the same level of economic development have achieved superior results or what strategies were used to accelerate progress. In an effort to extract every possible lesson from the dramatic declines in mortality, WHO, the Partnership for Maternal, Newborn and Child Health, the World Bank, and several academic institutes looked at how ten of the world's poorest countries achieved outstanding success in reducing maternal and child mortality. The ten case studies were published in *Success factors for women's and*

children's health, a 2014 report which includes statistical and econometric analyses of data from 142 low- and middle-income countries over two decades, and policy reviews in the ten "fast-track" countries.

As demonstrated, the best results were obtained through investments in high-impact interventions such as quality care at birth, immunization, and family planning, combined with investments that target fundamental drivers of preventable mortality in other sectors, including education, nutrition, women's political and economic participation, and access to clean water, sanitation, and modern energy.

19 000 fewer deaths each day

As low-cost generic antiretroviral treatments for HIV became widely available, further progress in reducing maternal and childhood mortality came from the large number of countries that launched initiatives to eliminate mother-to-child transmission of HIV and followed WHO recommendations to "treat all", including pregnant women. The Medicines Patent Pool brought paediatric formulations of HIV treatment onto the market, extending the benefits of these medicines to more children. Significant drops in childhood deaths from malaria further contributed to the dramatic decline. Although the MDG goals for reducing maternal and childhood mortality were missed at the global level, the final Countdown report in 2015 recorded impressive progress.

The yearly number of maternal deaths dropped to around 289 000, with deaths still caused by conditions that could have been prevented through the provision of quality antenatal, delivery and postnatal care. Between 1990 and 2015, childhood mortality dropped by 53%. **Estimates for 2015 indicated 5.9 million childhood deaths that year, compared with 10.8 million in 2000.** This reduction means that 19 000 fewer children are dying each and every day.

The causes of childhood deaths showed a striking shift. In 2000, the leading causes of the 10.8 million deaths were neonatal conditions (33%), diarrhoea (22%), pneumonia (21%), malaria (9%) and AIDS (3%). In 2015, the leading causes of the 5.9 million deaths were preterm birth complications and other neonatal causes (45%), pneumonia (16%), diarrhoea (9%), malaria (5%), and AIDS (1%), strongly suggesting that scaled up coverage with interventions had a major impact. The sharp acceleration of declines in child mortality further suggested that even greater progress can be expected in the coming years. As the report noted, the growing concentration of deaths in the newborn period and the improved understanding about the causes of newborn deaths have sparked the scaling up of long-existing interventions and the development of new ones.

In Countdown countries, suboptimal nutrition, including fetal growth restriction, stunting, wasting and deficiencies of vitamin A and zinc along with suboptimum breastfeeding, were cited as an underlying cause of 45% of all childhood deaths, reinforcing the importance of initiatives like Scaling Up Nutrition. The collection of high-quality country data showed real progress. For example, the number of countries with information about postnatal care visits for babies increased from five during the period 2000–2006 to 35 by 2014. Against these positive trends, Countdown noted extreme inequalities, within and between countries, in coverage with life-saving interventions. Immunization was the notable exception, with coverage rates consistently reaching or exceeding 85% in most Countdown countries.

As an instrument for accountability, Countdown also tracked resource flows. Official development assistance surged after the MDG summit in 2000. Trends from 2003 to 2012 showed a tripling of development assistance to maternal, newborn, and child health, from \$2 billion to \$6 billion. Resource flows then slowed under the lingering effects of the 2008 financial crisis.

A \$12 billion head start for the future

In July 2015, the UN, the World Bank Group and the governments of Canada, Norway and the USA launched the Global Financing Facility to support the revised Every Woman Every Child strategy, drawing an initial US\$ 12 billion in financial commitments. The Facility was designed to act as a pathfinder in a new era of financing for development by pioneering a model that shifts away from a principal reliance on official development assistance to an approach that combines external support, domestic financing and innovative sources for resource mobilization in a value-added way. The overarching objective is to build long-term domestic financing as the principal route to fiscal sustainability.

Building on the approach used by the International Health Partnership Plus, the Facility uses a financing platform that is country-driven and country-owned. Countries develop their own roadmap for improving the health of women and children, and their own financing. implementation and accountability frameworks. The frameworks, in turn, operate to harmonize funding from multiple initiatives, align joined-up funds around a single investment case, and simplify coordination.

The Facility has been hailed as a visionary leap forward for financing health development in the era of the 2030 Agenda for Sustainable Development. It views the focus on maternal, newborn and child health as an entry point for moving towards universal health coverage with people-centred integrated services that follow a life-course approach and offer a continuum of care. Its emphasis on capacity building is reflected in the principle of building on what is already working in the country, underscoring another key lesson from the Countdown monitoring reports. In other words, existing health systems and infrastructures must be strengthened through the way financial support is channelled, and not circumvented by the creation of parallel systems run by development partners.

Finally, the Facility recognizes that the broad determinants of women's and children's health require multisectoral collaboration to improve education, nutrition, water supply, sanitation, and gender equality – health determinants that all have targets under the Sustainable Development Goals.

Moving forward: supremely ambitious targets

In 2012, encouraged by the substantial reduction in mortality for young children, the international community, spearheaded by the governments of Ethiopia, India and the USA, in collaboration with WHO, UNICEF and others, put forward a vision of ending preventable child deaths. That vision was later echoed in new targets for maternal mortality. Preparatory work for revising the maternal health component of the global strategy included a series of technical consultations convened

by WHO. After broad discussions that tapped the views of country programme managers, scientists, donors and other partner agencies, consensus was reached on the bold vision of ending preventable maternal mortality. Based on five years of remarkable progress, the vision was considered both realistic and feasible.

The resulting report on *Strategies toward ending preventable maternal mortality* set out the conviction that a "grand convergence" is within reach, in which the highest levels of maternal death can be reduced to rates now observed in the best-performing middle-income countries. Doing so required a firm emphasis on the ability to count every maternal and newborn death, equality in the provision of both quality clinical care and the reduction of risk factors in the wider social environment, and an understanding that maternal mortality is not solely a health and development issue, but also a sign of discrimination against women.

The strategy was further adjusted to address the "obstetric transition", in which the primary causes of maternal death shift towards indirect causes as fertility and mortality decline. It called for a shift from an approach focused on emergency care for a minority of women to care focused on wellness for all. To help set realistic targets in line with each country's unique situation, the strategy proposed a methodology for tracking progress based on the achievement of milestone values adjusted to reflect the country's initial burden of maternal mortality as the starting point.

When the UN General Assembly approved the 2030 Agenda for Sustainable Development in September 2015, the updated Global Strategy for Women's, Children's and Adolescents' health was simultaneously launched as a showcase platform for implementation of the Agenda's ambitious targets and goals. Because the determinants of women's and children's health are so broad, the updated Global Strategy translated the holistic approach of the SDGs into a series of precise actions, ranging over multiple sectors and supported by an accountability framework, designed to meet the targets set for ending preventable deaths of newborns and young children and substantially reducing maternal mortality. Other targets that called for ending discrimination and violence against women and girls reflected areas where WHO studies had brought international attention to the related health harms, including the 2013 report of *Global and regional estimates of violence against women* and its subsequent health systems strategy for addressing interpersonal violence.

The strategy is supremely ambitious: the world has all the knowledge and technology needed to end preventable deaths among all women, children, and adolescents and to greatly improve their health and well-being. allowing them to realize their full human potential as a cornerstone of development. The effects of doing so will ripple throughout societies, contributing substantially to a more prosperous and sustainable future for all.

After a decade of sluggish then dramatic progress, women and children now have an agenda which makes their health needs a high priority and looks after them in a comprehensive and sustainable way. The political will to address the tragedy of millions of avoidable deaths each year has now fully arrived.



lobal defences against universal transboundary threats to health, like climate 🗾 change, air pollution and antimicrobial resistance, depend on WHO's role as a guardian of public health. This role involves tracking rapidly evolving threats, quantifying the harm to health, and sounding the alarm. WHO also works to raise political awareness and extend advice on the best protective strategies for safeguarding public health. In these - as in many other areas - protective strategies require collaboration with multiple non-health sectors.

Climate change: a climate treaty is also a health treaty

Climate change is the defining issue for the 21st century. Climate variables affect the air people breathe, the water they drink, the food they eat, and even where they are able to live. Extreme weather events are becoming the norm and records are constantly being broken, with the past three years ranking as the hottest since records began.

For infectious diseases, climate change is a threat multiplier. It takes existing threats – whether from a cholera outbreak, the spread of Zika to new geographical areas, or the severe malnutrition that accompanies drought - and enhances them. The risks are familiar but their impact is amplified in frequency and severity. A changing climate can expand the distribution of infectious diseases, especially those transmitted by mosquitoes and other vectors, and invite the emergence of others. The emergence of Nipah virus and Hanta virus as human pathogens has been traced to extreme weather events that forced animal hosts to leave their ecological niches and invade human settlements.

In the historic 2015 Paris Agreement on Climate Change, countries made important commitments to cut greenhouse gas emissions and scale up adaptation to climate change. But more needs to be done. As many have noted, the world is recklessly late in agreeing to take action.



WHO estimates that climate change is already causing tens of thousands of deaths every year.

The stakes are high. WHO estimates that climate change is already causing tens of thousands of deaths every year. These deaths arise from more frequent epidemics of diseases like cholera, the vastly expanded geographical distribution of diseases like dengue, and deaths that follow extreme weather events, like heatwaves and floods.

Experts predict that, by 2030, climate change will be causing an additional 250 000 deaths each year from malaria, diarrhoeal disease, heat stress and undernutrition alone. The heaviest burden will fall on children, women and the poor, widening already unacceptable gaps in health outcomes.

The health sector has critical evidence, and persuasive arguments, to compel actions that can limit the adverse consequences of climate change. The Paris agreement is not just a treaty for saving the planet from severe, pervasive, and irreversible damage. It is also a significant public health treaty, with a huge potential to save lives worldwide.

If commitments are supported by actions on a sufficient scale, efforts to combat climate change will produce an environment with cleaner air, more abundant and safer freshwater and food, and healthier populations. Existing strategies that work well to combat climate change also bring important health gains. Investments in low-carbon development, clean renewable energy, and greater climate resilience are investments in better health.

Implementing and enforcing higher standards for vehicle emissions and engine efficiency can reduce emissions of short-lived climate pollutants, like black carbon and methane. Doing so could save around 2.4 million lives a year by 2030 and reduce global warming by about half a degree Celsius by 2050. Researchers have estimated that reform of global energy subsidies could reduce carbon dioxide emissions by more than 20%, cut premature air pollution deaths by more than half, and raise government revenues by nearly \$3 trillion. Measures such as earlywarning systems for heatwaves and the protection of water, sanitation, and hygiene services against floods and droughts strengthen the resilience of health systems to withstand the shocks of climate change. Doing so safeguards recent progress against climate-sensitive diseases.

In 2015, WHO, in collaboration with the secretariat of the UN Framework Convention on Climate Change and other partners, launched the first set of climate change and health country profiles. The aim is to empower ministers of health and other decision-makers to include health in climate negotiations. Profiles provide a snapshot of up-to-date information about current and future impacts of climate change on human health, and current policy responses in individual countries. They also illustrate, within the country context, the health benefits that arise from actions to mitigate climate change, like shifting to cleaner energy sources, using public transport, and promoting walking and cycling.

Minimizing adverse effects on public health has been part of the Framework Convention on Climate Change's objectives since the first agreement in 1992. However, further efforts are needed to fully exploit the opportunity to protect the planet's most valuable resource, its people. A ruined planet cannot sustain human lives in good health

Air pollution: the most deadly form of environmental degradation

WHO estimates that outdoor and indoor air pollution kill 6.5 million people yearly, making polluted air the most deadly consequence of environmental degradation. Air pollution is one of the most pernicious threats to health because it is so pervasive. No one can escape it. Everyone has to breathe. When breathing becomes deadly, entire cities become a hazard to health.

Though cities are a principal concern, air pollution easily travels hundreds of kilometres beyond cities to endanger health in surrounding areas. Parts of densely-populated Asia are nearly completely shrouded year-round by a lingering haze of polluted air.

A common misperception is that health damage comes from the kind of heavy pollution that people can see and feel, stinging their eyes or making them cough. However, the biggest risk to health is not during episodes of peak, acute pollution, when governments may advise people, including schoolchildren, to stay home or recommend that people avoid exercising outdoors. What causes the greatest health damage is long-term exposure to pollutants in the air that exceed the safe limits established by WHO. Again, people cannot escape dangerously polluted air, but they cannot always see it either.

Abundant evidence shows that exposure to air pollution, either indoors or outdoors, is a significant cause of respiratory disease, including lung cancer. Air pollution, with its multiple toxic compounds, penetrates deep into the lungs, but it also penetrates the bloodstream, causing inflammation and a gradual narrowing of the arteries, similar to the well-known damage caused by tobacco smoke. WHO estimates that more than one-third of all deaths from stroke, lung cancer, and chronic lung disease are associated with exposure to air pollution.

In the developing world, exposure to indoor air pollution, linked to the use of cheap and dirty fuels for cooking, heating and lighting, is the principal cause of chronic lung disease in women and of pneumonia in young children. This form of exposure contributes to nearly 4.3 million deaths each year. Poverty is the root cause. Less well known is damage to the heart caused by exposure to air pollution. Recent evidence shows how air pollution narrows the blood vessels, contributing to a quarter of fatal heart attacks. The rise in global asthma prevalence, recorded over the past decade, has been linked to increasingly widespread air pollution.

When asked what causes outdoor air pollution, most people will cite the burning of fossil fuels, too many cars, diesel trucks spewing foul exhaust, or the continuing use of coal-fired energy plants. However, the actual causes vary considerably around the world. In parts of the developing world, a principal cause of outdoor air pollution in the burning of wastes and garbage. Agricultural practices, like slash-and-burn tactics, are another major source. This is why the first step for prevention is to identify the sources and then tackle them in a focused way. WHO's country- and city-specific monitoring data reveal the worst hot spots. As global data show, **only one person in ten lives in a city that complies with WHO's safe limits for air quality.**

In response to these challenges, WHO and its partners have launched a Breathe-life campaign which alerts the public to what is regarded as a largely invisible killer. Apart from educating

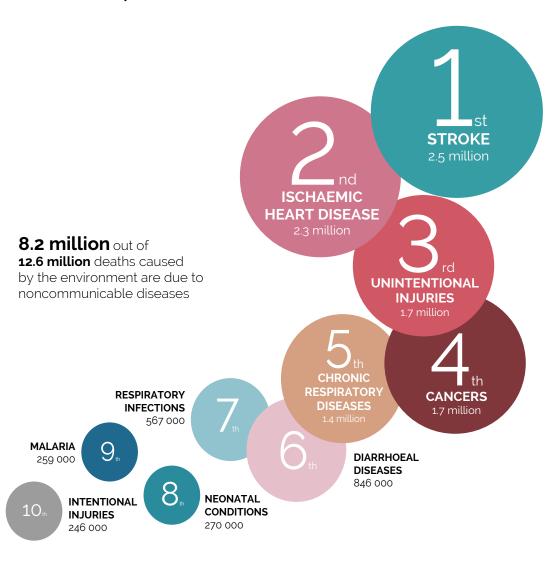
the public, the campaign encourages the sharing of data and solutions between cities, better monitoring of pollution levels, and better communications when the situation becomes dangerous. In many countries, the media play a major role in alerting the public when air pollution levels surpass WHO's acceptable limits. Such alerts, in turn, can put pressure on governments to take corrective action.

One of the strongest economic incentives to clean up the air comes when foreign investment firms decide to leave a country because they do not want their employees, and especially their children, to be exposed to harmful air pollution. Threatened departures of investment firms generally get the government's attention and can compel corrective action.

The best solutions, like a shift to cleaner energy and re-engineering cities to encourage walking and cycling and to promote the use of public transportation, take time and cost money. Some more immediate solutions include passing legislation that prohibits the use of slash-and-burn tactics in agriculture and stops the open incineration of wastes. Other strategies for mitigating urban air pollution include energy-efficient buildings, good waste management, and strong emission controls on industrial smokestacks. Several cities, especially in Latin America, have cut air pollution by improving systems for public transport, adding green spaces, and creating paths that invite walking and cycling

Combining short-term and long-term measures is a good way to move forward. For example, China, a country that still depends heavily on coal as an energy source, is investing billions of dollars in converting the entire country to the use of cleaner energy sources. A more immediate measure is to move coal-fired energy plants from cities into less densely-populated areas.

Children are especially vulnerable to the harm caused by air pollution. Damage from exposure to air pollution starts in the womb. Children born to exposed mothers show lower birth weights and are especially vulnerable to pneumonia. In 2017, WHO released a report documenting the disproportionate impact that environmental factors, including air pollution, have on children. The report identifies respiratory diseases, including pneumonia, as the biggest single cause of childhood deaths. Respiratory diseases in children are strongly linked to exposure to both outdoor and indoor air pollution.



Top 10 causes of death from the environment

Source: WHO

Antimicrobial resistance: now a political priority

Antimicrobial resistance is one of the most complex global health challenges, threatening to reverse the substantial progress against infectious diseases made since the golden era of antibiotic discovery during the second half of the previous century. These "miracles of modern medicine", and their tremendous gains for health, have long been taken for granted. The world largely ignored repeated WHO warnings that some antibiotics are losing effectiveness after

decades of overuse and underuse in human medicine and food production. As WHO reports show, antimicrobial resistance is on the rise in every region of the world.

With few replacement products in the pipeline, the world is moving towards a post-antibiotic era in which common infectious will once again kill. If current trends continue, sophisticated interventions, like organ transplantation, joint replacements, cancer chemotherapy, and care of pre-term infants, will become more difficult or even too dangerous to undertake.

Already, the emergence and spread of drug resistance has made common illnesses, like bacterial pneumonia, post-operative infections, certain cancers, and the world's biggest infectious killers, namely HIV, tuberculosis, and malaria, increasingly difficult and costly to treat. The tuberculosis experience, in particular, shows how easily drug-resistant strains can pass directly from one person to another and how well they can travel internationally. Second- and third-choice antibiotics are more costly, more toxic, need longer durations of treatment, and may require administration in intensive care units.

Superbugs haunt hospitals and intensive care units all around the world. Gonorrhoea is now resistant to multiple classes of drugs. An epidemic of multidrug-resistant typhoid fever has been rolling across parts of Africa and Asia. Worsening antimicrobial resistance could have serious public health, economic, and social consequences around the world. The World Bank has warned that antimicrobial resistance could cause as much damage to the economy as the 2008 financial crisis.

Antimicrobial resistance can be tackled only through a concerted global effort, led by heads of state and global institutions, and through coordinated action by the health and agricultural sectors, in partnership with the food industry, campaign groups, and community organizations. Incentives need to be found to encourage the development of replacement products. The pharmaceutical industry is reluctant to invest in costly antibacterial discovery. The return on investment is poor, as antibiotics are taken for a short time, cure their target disease, and can fail – especially when misused – after a brief market life.

Consumers have to stop demanding antibiotics when they have a viral infection, like a cold or influenza. Doctors have to stop prescribing them in appropriately. The medical profession needs better diagnostic tests, so that antibiotics are prescribed only on the basis of a firm diagnosis. More vaccines are needed to prevent infections in the first place.

The food industry needs to reduce its massive use of antibiotics, at sub-therapeutic doses, as growth promoters. Specific antibiotics, listed by WHO as critically important for human medicine, should not be used in animal husbandry or agriculture. Consumers should make antibiotic-free meat their preferred choice. Governments need closely aligned policies on the responsible use of medicines in human and animal health, and new standards for antibiotic use in food production. All of these actions are urgently needed.

Political awareness of the need for urgent action is now high. The 2015 World Health Assembly adopted a global action plan which sets out a series of strategic objectives. The action plan, developed in close collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE), recognizes that a crisis of this magnitude requires an effective One Health approach involving coordination among many

sectors at national and international levels. In 2016, the UN General Assembly held its first high-level meeting on antimicrobial resistance and adopted a far-reaching political declaration. The issue has also been on the agendas of recent G7 and G20 summits.

More than 100 countries have completed, or are about to complete, their national multisectoral action plans. WHO has established a global antimicrobial resistance surveillance system to track which drug-resistant pathogens are posing the greatest challenge. In May 2016, the Drugs for Neglected Diseases initiative and WHO launched a global research and development partnership to develop new antibiotics and promote their responsible use.

In August 2016, WHO updated its guidelines for the prevention and treatment of three common sexually transmitted infections – chlamydia, gonorrhoea, and syphilis. Based on a review and analysis of national guidelines and prescribing practices for 20 common syndromes, WHO is revising the antibiotics included in the WHO model life of essential medicines. The Organization has also rolled out a global awareness-raising campaign targeting policy-makers, health and agriculture workers, and consumers.

For HIV, the drug regimens recommended by WHO carry high barriers to the development of drug resistance. However, with 18 million people currently receiving antiretroviral therapy, the emergence of more widespread levels of drug resistance is expected to occur. In July 2017, WHO will launch the first Global Action Plan on HIV Drug Resistance. The plan sets out guidance that can help countries prevent and, if necessary, manage the emergence of HIV drug resistance, a risk that could threaten the remarkable gains made over the past 15 years. The malaria situation is already precarious, as parasites are developing resistance to artemisinin-combination therapies and mosquitoes are showing resistance to the most commonly used insecticides. However, the biggest current threat comes from resistant strains of tuberculosis. WHO estimates that nearly half a million cases of multi-drug resistant tuberculosis occur each year. Extensively drug-resistant TB has now been reported by more than 100 countries.

To scale up activities, governments can build on existing regulatory frameworks, surveillance systems, laboratory and infection control infrastructure, and human resources that are already in place to manage drug resistance in medicines for HIV, tuberculosis, and malaria. Diagnostic tools, logistics, and technologies for sharing data can be used to link programmes at the country level. Most supranational tuberculosis reference laboratories have already confirmed they could expand susceptibility testing for other pathogens, should funding be made available.

An ad-hoc interagency coordination group is being established by the UN Secretary-General in consultation with WHO, FAO and OIE. In 2017, **WHO issued a list of the 12 most important antibiotic-resistant bacteria, in addition to** *Mycobacterium tuberculosis*, requiring urgent R&D.

WHO is preparing proposals for a global development and stewardship framework to support the development, control, distribution, and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines, and other interventions. In another welcome trend, several large fast-food chains have announced plans to source their meat, especially poultry, from farms that do not use antibiotics critically important in human medicine as growth promoters in animals. Such changes are a welcome consequence of the high level of political concern that crystalized during the 2016 UN meeting on antimicrobial resistance.

This report is available on WHO's website www.who.int/publications/10-year-review/en/

