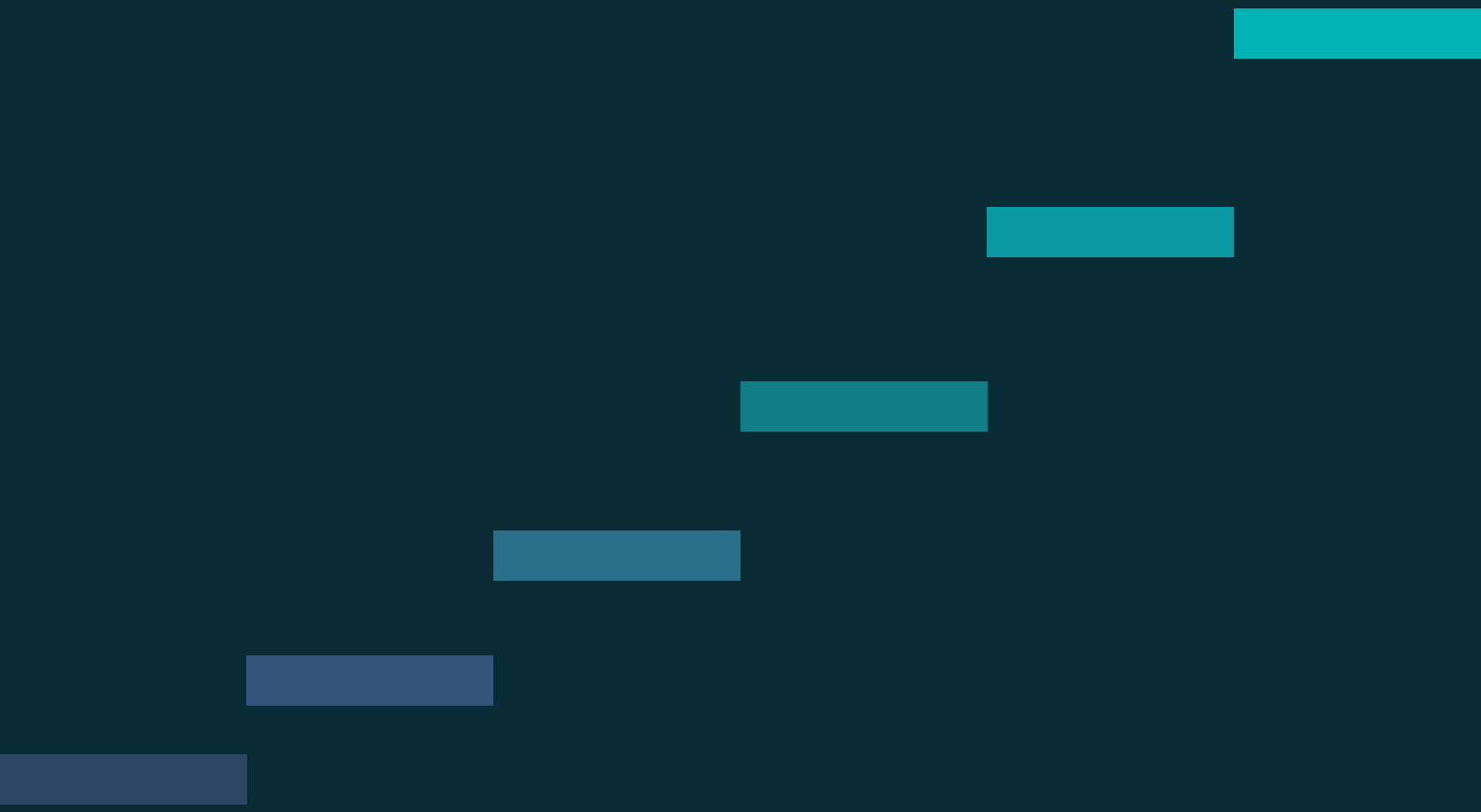
FIRST INDEPENDENT TEN-YEAR ANALYSIS

Are pharmaceutical companies making progress when it comes to global health?

MAY 2019



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The Access to Medicine Foundation is an independent non-profit organisation based in the Netherlands. It aims to advance access to medicine in low- and middle-income countries by stimulating and guiding the pharmaceutical industry to play a greater role in improving access to medicine. It has published the Access to Medicine Index every two years since 2008. In 2018, it published the first Antimicrobial Resistance Benchmark.

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First 10-year analysis of pharmaceutical company progress on global health

10-YEARS, 20 COMPANIES

- This report analyses ten years of data to assess whether pharmaceutical companies are doing more today for the 2 billion people worldwide who live without access to medicine.
- The data have been gathered since 2008 for the Access to Medicine Index, the most comprehensive, long-running independent survey of company behaviour on access to medicine.
- The 20 pharmaceutical companies evaluated in this report account for approximately 70% of global pharmaceutical revenues. Global pharmaceutical sales are expected to reach USD 1.06 trillion by 2022.[1] Emerging economies are expected to account for 25% of global spending on pharmaceuticals by 2020.[2]
- The findings identify which activities are increasing, where gaps remain, and where standard practice is improving. They cover strategy, R&D, pricing and licensing, among other areas.
- The report provides a springboard for discussions on how the progress to date can be expanded across the industry in order to achieve SDG 3 by 2030.

WHY NOW

In the era of modern medicine, many major milestones have been reached, from a near-eradication of polio globally to a reduction in new HIV infections by more than half since the peak of the HIV/AIDS crisis.[3] As the world works toward achieving the Sustainable Development Goals (SDGs) by 2030, continuing to expand access to medicine must be a top priority, particularly access for people living in low- and middle-income countries (LMICs), which together account for 83% of all people alive today.[4]

Action is needed from many quarters, including from national governments, civil society and the private sector. Pharmaceutical companies, as innovators and producers of medicines and vaccines, are key partners for advancing universal health coverage (UHC) and improving immunisation rates. They have a responsibility to develop real innovative treatments in priority areas and improve the availability of products to all people, regardless of socioeconomic standing.

SCOPE OF THE RESEARCH

This is the first independent ten-year report to assess how pharmaceutical companies are responding to calls to improve global health. It is based on data that have been collected, verified and analysed by the Access to Medicine Foundation. It covers 20 of the world's largest research-based pharmaceutical companies, which the Foundation has tracked since 2008.

This analysis covers: (a) areas where pharmaceutical companies have a clear role and responsibility to act; and (b) where action by pharmaceutical companies is critical for improving access to medicine. Much of the data were collated for the Access to Medicine Index, which evaluates the 20 companies in seven areas of behaviour: strategy and governance, conduct and compliance, R&D, pricing, licensing, capacity building and donations. The report assesses absolute progress and the changing level of industry engagement since 2008, examining the numbers of companies involved as well as key measures, such as the numbers of R&D projects or voluntary licences. The analyses go back as far as data permit, and no earlier than 2008.*

*See Appendix for more information on data sources and the methodology for comparative analyses.

AT A GLANCE

Are pharmaceutical companies making progress when it comes to global health?

Two billion people worldwide live on very low incomes without access to medicine or robust health systems.

The first Access to Medicine Index, published ten years ago, established a baseline measure of what 20 of the world's largest R&D-based pharmaceutical companies were doing to turn this situation around.

Data gathered since then show where progress has been made, and indicate where the main challenges lie for the next decade.

83% of all people alive today live in the 106 countries covered by this research.[2]

PHARMA COMPANIES ARE GRADUALLY CHANGING HOW THEY DO BUSINESS

Several pharmaceutical companies are now doing business in new, inclusive ways that aim to reach people on very low incomes. Plus, almost all companies now actively manage their progress toward access-to-medicine goals. Yet, only some companies are tackling the risks of unethical sales behaviour. Fewer companies consistently support international trade agreements (i.e., TRIPS flexibilities) designed to ensure the poorest people can benefit from medical innovation.

R&D PIPELINES GROW, PARTICULARLY FOR KEY DISEASES SUCH AS MALARIA, HIV/AIDS AND TUBERCULOSIS

R&D pipelines have grown markedly, due to an effective recipe for engaging pharmaceutical companies in specific R&D challenges. Plus, five companies now systematically plan, as part of the R&D process, to address access to successful projects. In general, R&D activity continues to track commercial opportunities; more medicines for profitable non-communicable diseases successfully left the pipeline than medicines for diseases of poverty.

USE OF ACCESS TACTICS INCREASES, BUT MANY PRODUCTS ARE NOT YET COVERED

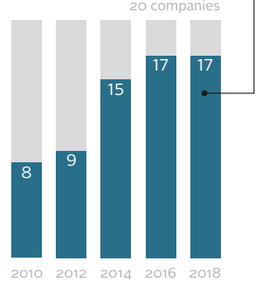
Pharmaceutical companies have three main tools for improving access to health products: pricing, licensing and donations. All three tools are being used more frequently than before and in pro-access ways. For example, access-oriented licensing has expanded steadily since 2010, and a complete suite of HIV/AIDS and hepatitis C treatments is now available via voluntary licensing. In the future, the use of these tools has potential to expand to many more products in additional countries, so more people can benefit.

In 2018, a few inclusive business models are running, with some being scaled up

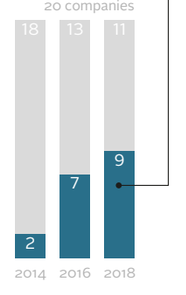
10 inclusive business models, run by 7 companies, with 8 models being scaled up.

12 best practices in capacity building, run by 6 companies.

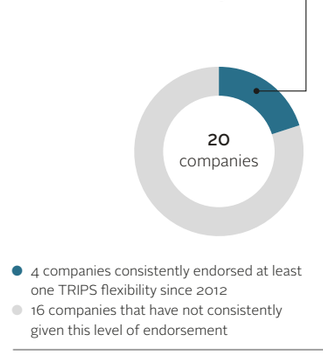
17 companies now set goals and targets related to access to medicine



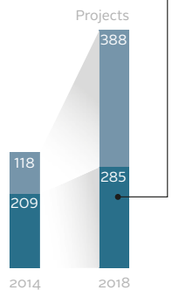
9 companies are now reforming incentives for sales agents by decoupling bonuses from sales incentives



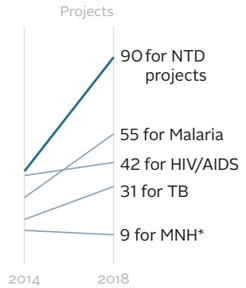
Only 4 companies have consistently endorsed at least one TRIPS flexibility since 2012



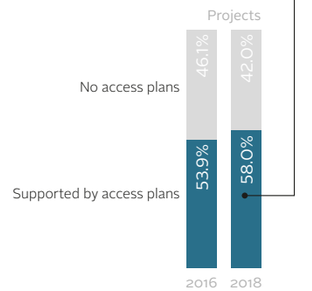
Pipeline for priority diseases has more than doubled since 2014. Now, 285 projects are in clinical development.



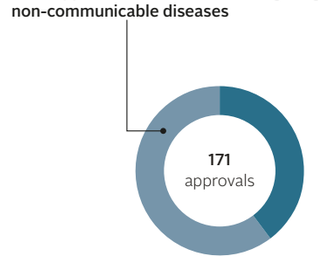
Pipelines for key diseases have grown, but not for maternal and neonatal health conditions



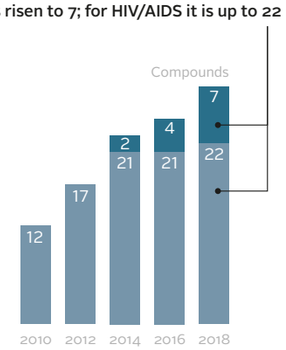
The coverage of access plans for late-stage R&D projects is largely unchanged



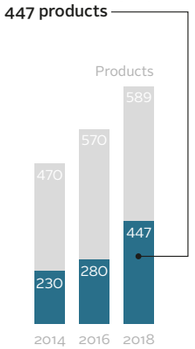
Since 2008, at least 171 new medicines have been approved. More than half targeting non-communicable diseases



The number of licensed compounds for hepatitis C has risen to 7; for HIV/AIDS it is up to 22

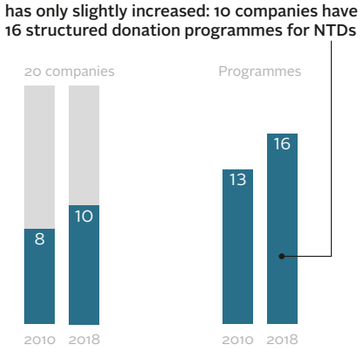


More products are now covered by equitable pricing strategies: 447 products



*Maternal & neonatal health conditions

No. of companies donating products for NTDs has only slightly increased: 10 companies have 16 structured donation programmes for NTDs



Interpreting the figures

The Access to Medicine Index has been published every two years since 2008. It covers seven areas of behaviour linked to access, including R&D, pricing, licensing, capacity building and donations. The analyses in this report go back as far as data permits within this timeframe. The parameters of all data sets have been controlled to ensure comparability over time.

SPRINGBOARD FOR DISCUSSION - KEY INSIGHTS

Access to medicine is increasingly seen as strategically important

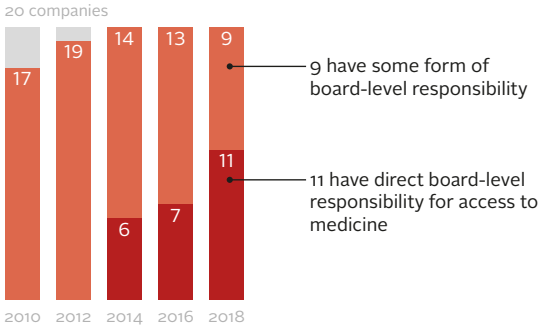
This report finds that access to medicine is widely recognised today by pharmaceutical companies as a strategic issue. Significantly, nearly all (17 out of 20) companies now have a strategy supported by goals and targets for addressing access to medicine. In 2010, eight companies had set access-related goals.

There are several reasons for this shift. Firstly, the dual burden of non-communicable and infectious diseases has emerged as an urgent issue impacting healthcare systems in LMICs. This is driving up long-term demand for healthcare products and creating additional commercial opportunities in LMICs for pharmaceutical companies. AstraZeneca and Sanofi, among other companies, generate approximately 30% of revenues from emerging markets.[5,6]

Secondly, pharmaceutical companies recognise that proactively addressing access is a way of managing the risks associated with public opinion, increased regulation (e.g., disclosure requirements) and compulsory licensing.

Thirdly, the social licence to operate for pharmaceutical companies – i.e., society's ongoing acceptance of a company's way of doing business – rests on addressing access to medicine for the people who need it, regardless of income. The public sector increasingly emphasises the need for better access to health products. Plus, changing societal values are also having an impact on the ability of pharmaceutical companies to attract, retain and motivate employees.

Figure 2. Since 2010, more company Boards now take direct responsibility for access to medicine

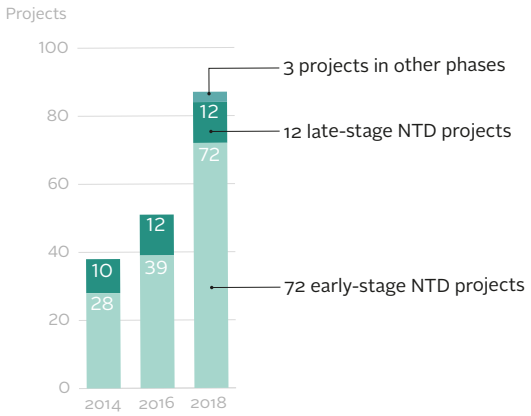


Sizeable leaps in companies' engagement observed in some areas of activity

In terms of companies' engagement levels, the greatest progress is in the level of response to neglected tropical diseases (NTDs), HIV/AIDS, malaria and tuberculosis. These diseases have been identified as the targets of urgently needed R&D and as access priorities for global health since before the scope of this study, when the groundwork for tackling access as a global issue was being laid – first by civil society, then by governments and donors. This groundwork focused on reducing the burdens of NTDs, HIV/AIDS, malaria and tuberculosis, as well as the scale of child and maternal mortality.

For example, the pipeline for high-burden and priority diseases has more than doubled since 2014. For NTDs, the number of companies contributing to the development of new medicines, diagnostics or other products has increased from nine to 15 since 2010, while the number of companies donating products for NTDs has increased from eight to ten. The number of donation programmes for NTDs has reached 16, up from 13 in 2010. Plus, nine companies that own (or have owned) patents for HIV/AIDS treatments have used intellectual property (IP) rights flexibly to facilitate generic supply in LMICs through voluntary licences or non-assert declarations. To date, IP rights have been used flexibly in this way for 29 compounds for two diseases: HIV/AIDS or hepatitis C. This includes first- and second-line treatments, pangenotypic regimens and other products on the World Health Organization's Model List of Essential Medicines (WHO EML).

Figure 24. Since 2014, early-stage pipeline for NTDs has more than doubled



Workable, scalable approaches for good practice now present in most areas of evaluation

In most areas of practice, there is now a workable, scalable approach for improving access to medicine that is being implemented by one or more companies, including in voluntary licensing and access planning during R&D.

Notably, since 2008, multiple companies have taken the step of pioneering good practice in critical areas. For example, Novartis is the first to publicly commit to establishing access plans for all innovative new medicines. Access plans can cover, for example, pricing, registration and supply. Merck KGaA became the first company to voluntarily disclose the status of patents, in 2014. GSK was an early adopter of tiered pricing, notably for vaccines, and has operated a tiered pricing approach for more than 20 years. Merck & Co., Inc. began its donation programmes for onchocerciasis in 1987.

Plus, seven companies are making efforts to develop and scale up commercial models that aim to include the poorest populations in their customer base. Several of these models focus on products for heart disease, diabetes and other non-communicable diseases (NCDs), which are on the rise globally. These models can complement pricing, licensing and donations initiatives to address the accessibility and affordability of health products for specific populations. Novartis, for example, has run its 'Healthy Family' programme since 2007, which includes health camps tailored to local health priorities and customs, focused on disease prevention, awareness and treatment, including essential medicines.

Companies are running and scaling up a range of inclusive business models

Novo Nordisk has worked with faith-based organisations in Kenya to limit price mark-ups and developed 'One-Stop Diabetes Support Centres' in Nigeria and Ghana.

Progress is concentrated among few companies, few diseases, few countries

Progress is clearly evident in other areas of practice, although generally confined to a few diseases or due to the actions of just a few companies. Without the long-term involvement of a more diverse group of pharmaceutical companies, radical improvements in access to medicine will be difficult to achieve – and even harder to sustain.

For example, in R&D, the 20 companies are now collectively developing more than twice as many medicines and other products needed by people living in LMICs as in 2014. Yet in 2018, five companies were found to be carrying out 63% of the most urgently needed R&D projects (GSK, Johnson & Johnson, Merck KGaA, Novartis and Sanofi). Further, the industry's engagement in such R&D is currently overwhelmingly focused on five high-burden and/or high-priority diseases: malaria, HIV/AIDS, tuberculosis, Chagas disease and leishmaniasis. Alongside closing the remaining innovation (R&D) gaps, a parallel challenge going forward is to ensure that new products are delivered efficiently to the different populations that need access.

In pricing, close to half (43%) of the products for the diseases and conditions in scope are now covered by an equitable pricing strategy (i.e., strategies that aim to address affordability). Only 18% of products with such strategies meet all of the quality criteria assessed.* These robust strategies are concentrated in just a few companies: the majority (53%) come from Boehringer Ingelheim, Gilead and Novartis.

Countries benefit from very different levels of attention, depending on the area of activity. Low-income countries (LICs) and Least Developed Countries (LDCs) are often the focus of least attention, particularly when looking at registration filings and pricing strategies. For example, in 2018, the Foundation reported that 13/46 of the sub-Saharan African countries in scope had zero registration filings for new products targeting diseases and conditions deemed access priorities in these countries.** These 13 countries are mainly LICs, and are home to more than 150 million people.[2] Even in countries such as Brazil, China and India, companies target their prices to suit the poorest population segments to only a limited extent. Capacity-building initiatives are generally more spread out, but the majority are still focused on middle-income and lower middle-income countries. For NTDs (the focus of most long-term structured donation programmes), donation programmes mirror patterns of disease distribution.

*Assessed by the Index, including whether strategies determine different prices for different populations within countries and use socioeconomic factors to determine prices.

**Priority countries are defined by the Foundation per disease. They identify countries with a greater need for access to products, based on disease burden, WHO data (2012), or IHME data (2015), and adjusted for multi-dimensional inequality (UNDP, 2012).

SPRINGBOARD FOR DISCUSSION - DRIVERS OF CHANGE

Three main factors are successful at driving pharmaceutical company engagement

The uptake of good practice is uneven, with different factors driving change. These can be commercial or regulatory; take the form of market-shaping or de-risking initiatives; or be clear priorities set by health organisations, donors and civil society, underpinned by public funding. Recent emphasis on sustainable investing over past years has also influenced company action. The Access to Medicine Index provides companies and their stakeholders with a yardstick by which to measure themselves against society's expectations and identifies best practices for companies to implement and improve upon.

Where there is a sizeable global market, the main driver for industry engagement is often commercial. This is likely the main reason NCDs such as diabetes consistently account for the larger pipelines. Research-based pharmaceutical companies generally view patent rights (and other related incentives such as data exclusivity) as a key incentive to innovate. IP rights can lead to constraints on supply and affordability. Under this model, patent owners must consciously choose to manage IP rights responsibly to balance commercial decisions that leave the needs of the poorest unaddressed.

Global health experts emphasise the need for expanding access to existing as well as new treatments for NCDs for people living in low- and middle-income countries. The current pharmaceutical industry model offers a far weaker incentive for companies to engage in these markets.

Where there is only a weak or no commercial market, but a high disease burden, the most effective current recipe for engaging the pharmaceutical industry is as follows:

1. Clear priorities endorsed by the international community of experts in global health. For companies, a clear and agreed-upon agenda lowers the barrier to engagement.
2. Publicly funded de-risking or market-shaping mechanisms, which enable resource sharing and reduce uncertainty.
3. Long-term and coordinated financial support from multiple donors, and a sustained investment in health from national governments, including to support healthy markets.

This recipe is currently being used for only a few diseases and conditions, such as NTDs, HIV/AIDS and child and maternal mortality. To cover the scale of the global disease burden, the prospect of long-term, well-funded and high-level political buy-in promises a wide range of committed partners from multiple sectors. Incentives are in place to stimulate companies to work in areas where global priorities are already clear.

For example, Priority Review Vouchers (PRVs) issued by the US FDA offer companies an accelerated product review process as a reward for developing products for neglected diseases. Advance market commitments and market-shaping mechanisms directly address the fragility and uncertainty of pharmaceutical markets for specific products or in certain geographic regions as a means of encouraging companies to enter markets and make products available. For example, pooled procurement mechanisms used by organisations such as Gavi, the Vaccine Alliance; the Pan American Health Organization (PAHO); and Unicef have helped to strengthen and provide security to the global vaccines market.

▸DRIVERS IN ACTION

For NTDs, WHO has played a pivotal role in coordinating and driving attention. The 2012 London Declaration on NTDs provided a platform for public commitment, engagement and sharing progress from the pharmaceutical sector. In 2012, 12 companies signed the London Declaration. Since then, the Foundation has noted more companies engaging in NTD donations and R&D. The Global Health Innovative Technology Fund (GHIT), supported by the Japanese government and organised with Astellas, Daiichi Sankyo, Eisai, Shionogi and Takeda, is another notable driver of R&D for prioritised diseases.

HIV/AIDS, malaria and tuberculosis have consistently had some of the largest pipelines of all communicable diseases examined. Combined, these diseases receive more than two thirds of total global neglected disease R&D funding[7] and they have been the strategic focus of multiple donors since the establishment of the Millennium Development Goals in 2000 and of the Global Fund to Fight AIDS, Tuberculosis and Malaria in 2002.

Product Development Partnerships (PDPs) have proven successful at re-engaging pharmaceutical companies with R&D for poverty-related diseases. In a 2016 paper, the Foundation identified nine benefits PDPs bring to efforts to ramp up access.[8] PDPs, such as the Medicines for Malaria Venture and the Drugs for Neglected Diseases initiative, primarily incentivise innovation for poverty-related diseases by facilitating financial risk-sharing across public and private sectors. There are currently no PDPs targeting NCDs.

New incentives are being developed for specific diseases or disease types. The Center for Epidemic Preparedness (CEPI) is addressing the risk of emerging infectious diseases such as Ebola and Zika. Greater attention is being paid by the international community to the challenge of NCDs. The 3rd UN High-Level Meeting on NCDs was held in September 2018. The World Health Assembly agreed a resolution on cancer in 2017. The majority of countries do now have a National Cancer Control Plan (NCCP).[9]

SPRINGBOARD FOR DISCUSSION – TOWARD 2030

Looking ahead to 2030: how to sustain and expand pharmaceutical company engagement

New engagement mechanisms and incentives, as well as action by pharmaceutical companies, have been heavily focused on NTDs, vaccines, HIV/AIDS, malaria and tuberculosis. Yet the scale of these developments does not match the scale of people's need for better access to medicine, particularly in LDCs and low-income groups in middle-income countries. Looking ahead to 2030, to the achievement of SDG 3 and as new priorities are set for global health, pharmaceutical company engagement must be sustained and expanded.

Progress at scale

The biggest challenge will be to make progress at scale and ensure different socioeconomic groups have access to healthcare. This includes addressing the cost of healthcare and prices for new medicines. Countries need support for their entire health systems as they work to establish universal health coverage (UHC). Initiatives run in silos, bringing additional stresses to those systems. For example, budgets and capacities are stretched by the need to assess, establish and maintain various initiatives.

One part of the solution will need to be the successful scale-up and replication, to more countries and diseases, of inclusive business models that explicitly aim to include people with low incomes in the customer base. Ten such models are currently running, including eight that have been scaled up since launch to reach more people. While this is encouraging, there is no blueprint yet for expanding these models to meet the level of need across different diseases and populations.

Prioritising non-communicable diseases

Starting in 2018, the UN and others increased their calls for action on NCDs, focusing on ensuring access to effective treatments such as those on the WHO Model List of Essential Medicines. Currently, companies are addressing access to NCD treatments via stand-alone initiatives to strengthen healthcare infrastructure. The triggers for greater involvement by the pharmaceutical sector in improving access to NCD products will be clear priorities and a way of coordinating and publicly tracking action.

For NCDs, it is important that access and affordability to existing treatments are improved, particularly for people who need life-long treatment. However, the markets for NCD treatments in many LMICs are limited by issues with healthcare infrastructure, access and affordability, among other factors. As a result, few new NCD products are being developed specifically with people in LMICs in mind. Many product gaps and delivery challenges remain, such as the availability of heat-stable or long-acting treatments and broader access to essential NCD treatments. Such gaps must be formally prioritised by the global health community.

Partnerships to strengthen health systems

New kinds of ambitious partnerships are needed that address countries' specific needs at the health system level, prioritising the availability and affordability of health products. These partnerships will need to be driven and owned by the public sector and be able to engage a diverse group of private sector companies. All partners must commit to working in a transparently ethical manner.

A core first task will be to jointly identify priorities, for example for underserved countries, as well as the roles and responsibilities of the different actors including pharmaceutical companies. For example, the role companies play in partnerships for healthcare delivery should match their core competencies and responsibilities: i.e., product innovation, supply (including manufacturing, production and delivery logistics), and fair pricing of health products.

Future investments in global health must be matched to these new kinds of partnerships by: expanding access to less affordable medicines; increasing both domestic and international financing; and increasing the diversity of financing sources. It is important that attention and funding does not shift away from current focuses until the goals that have already been set are actually achieved, including in the areas of HIV/AIDS, malaria, tuberculosis and vaccines. At the same time, pharmaceutical companies must make an internal cultural shift to be ready and able to dovetail their unique pipelines and portfolios with a systems-level approach. Signs of these shifts are already apparent in some companies.

A more diverse group of companies at the table

Although companies are taking action, and the industry has increased its involvement, the bulk of private sector engagement is being carried by just a few pharmaceutical companies. A retreat by just one of these companies could have a catastrophic effect on the progress made to date, not only for addressing R&D priorities, but also for increasing and sustaining the supply of products to the people who need them. As new priorities are set for global health, a more diverse group of companies must be brought to the table.

This report is a springboard for discussions on how improvements can be expanded across the pharmaceutical industry. Reaching the 2 billion people who still lack access to medicine worldwide is possible, provided we continue to build on what has already been achieved and are prepared to redraw and forge the path ahead.

10-year analysis: findings in detail

GOVERNANCE & STRATEGY

Companies increasingly view and manage access to medicine as a strategic issue

As pharmaceutical companies search for new commercial opportunities in low- and middle-income countries (LMICs), they have a responsibility to also increase access to their products for people on lower incomes. To achieve this balance, companies must view and manage access to medicine as a strategic issue. This section looks at the companies' strategies for improving access to medicine, and at how responsibility for delivering on them has changed.

ACCESS-TO-MEDICINE STRATEGY

What does a 'good' access strategy look like in 2018?

Having a strategy for improving access to medicine increases a company's chances of making long-term improvements in this area. The Foundation has evaluated whether companies have set measurable goals and targets for improving access, underpinned by a clear rationale, since 2010. Since 2014, it has also more directly assessed companies' access-to-medicine strategies. The Foundation has found improvement in both measures. The number of companies setting goals and targets related to access, and now also implementing clear, long-term strategies for improving access, has reached 17 (see Figure 1). AbbVie, Astellas and Daiichi Sankyo are the three exceptions. They engage in *ad hoc* approaches for increasing access.

There is no one-size-fits-all strategy for improving access to medicine. The Foundation identified several notable examples in 2018. One is from Novartis: the Novartis Access framework was implemented in 2015 and enables the company to tailor its approach for reaching different segments of low-income to middle-income populations, using a range of different access models. These include differential pricing, structured donation programmes and non-exclusive voluntary licensing. As another example, Johnson & Johnson uses an online scorecard to report on access management. This scorecard covers the company's access-to-medicine initiatives since 2016, listing goals, progress and other details, including quantitative and qualitative targets. The company publicly reports on its access-to-medicine outcomes and sets specific goals and measurable targets aligned with the United Nations Sustainable Development Goals (SDGs).

BOARD-LEVEL RESPONSIBILITY

Ongoing shift to direct board-level responsibility for access

The success of an access-to-medicine strategy is closely linked to how performance is measured, managed, motivated and rewarded. This includes appropriate governance and accountability structures. Since 2010, the Foundation has examined whether companies discuss access to medicine at the board level. Discussions were taking place at more than three quarters of companies in 2010, rising to all 20 companies by 2014. Since then, there has been a continuing shift from such indirect board-level responsibility to assigning direct responsibility to a named member of the board. In 2018, 11 companies were found to have board members that are directly responsible for how the company is addressing access to medicine (see Figure 2).

Figure 1. Compared to 2010, 17 companies now set goals and targets related to access to medicine

The chart shows the change, since 2010, in the number of companies with approaches for access to medicine underpinned by a clearly defined rationale, supported by measurable goals and targets.

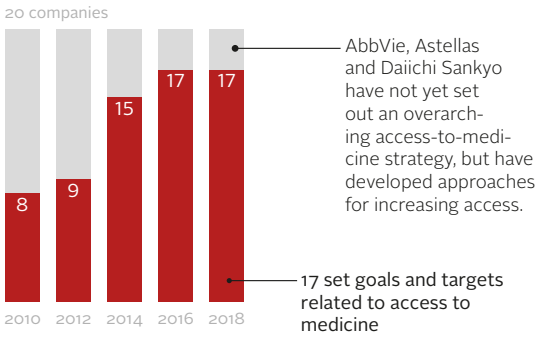
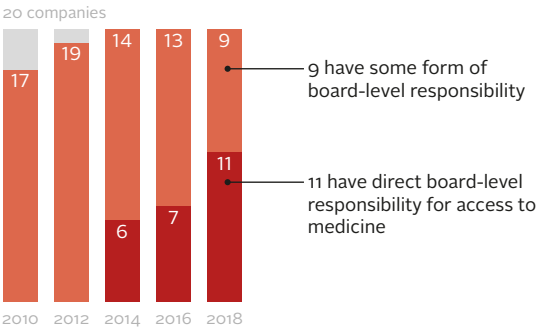


Figure 2. Since 2010, more company Boards now take direct responsibility for access to medicine

This chart shows how the number of companies that assign board-level responsibility for improving access to medicine has changed since 2010. By 2014, all companies discussed access at the board level in some form.



CONDUCT & COMPLIANCE

Misconduct continues, but companies are improving approaches for managing compliance

A combination of commercial incentives and weak regulatory systems can enable misconduct to take root and risk a negative impact on access to medicine. It is estimated that USD 455 billion was lost from global spending on global health in 2013 due to fraud, corruption or errors.[1] Wherever pharmaceutical companies operate, the Foundation expects them to uphold the same standards as in highly regulated countries and to take the initiative to expand policies and enforcement mechanisms to countries with weaker regulation. This section looks at evidence of breaches of laws or regulations relating to misconduct, as well as changes in how companies audit compliance with codes of conduct and incentivise good ethical conduct by sales agents.

CONDUCT

Addressing compliance

The Foundation has sought to track evidence of breaches of laws or regulations relating to marketing, corruption, bribery and lobbying in low- and middle-income countries (LMICs). It looks for information about fines and settlements reached under national laws and regulations, as well as about breaches of industry codes of conduct for good marketing practice (this does not include ongoing cases or allegations). Since 2014, the Foundation has identified 12 such confirmed breaches that occurred in LMICs, concerning multiple companies. Expert stakeholders have commented that the number is likely low when compared to such settlements in high-income countries because judicial and regulatory systems in many LMICs are weak, and misconduct is not reported, not investigated or not prosecuted. In fact, most of these breaches were identified and prosecuted through high-income country legislation, such as the UK Bribery Act (UKBA), and the Foreign Corrupt Practices Act (FCPA).

COMPLIANCE

Gradual shift away from sales-based incentives

Companies can implement a range of controls in order to mitigate the risk of corruption and unethical marketing. The Foundation has been examining how companies audit compliance with their codes of conduct and standards of behaviour since 2012. Since then, the number of companies conducting audits has increased steadily, reaching all 20 companies in 2016 (see Figure 3).

The Foundation has also noted an increase in the number of companies reporting that they are decoupling incentives for sales agents from sales targets. One common alternative is to reward technical knowledge rather than sales. By minimising the focus on sales volumes, there is less of a financial trigger for sales agents to behave unethically, e.g., by overselling. Nine companies, up from two in 2014, now have incentives that are no longer wholly linked to sales (see Figure 4). Roche and Takeda are the most recent companies to adopt non-sales-related targets for their sales personnel.

Roche has incorporated non-financial metrics relating to diversity, sustainability and the environment in its annual bonus plan. Takeda has implemented incentive programmes including incentives linked to technical and product knowledge.

All companies can reform their incentives for sales staff by deepening the shift away from using only sales volume and other sales-linked metrics as the basis for bonus calculations. The alternatives include using more long-term incentives and incentives linked to access objectives or service level. When it comes to auditing compliance, companies can work with external auditing agents and expand audits to include more countries and third parties. Taking a risk-based approach to auditing is also recommended (i.e., conducting audits where and when the risk of non-compliance is greater).

Figure 3. Compared to 2012, all companies now audit compliance with codes and standards

The chart compares how many companies per year demonstrate that they audit compliance with codes of conduct and standards of behaviour. The number of companies reporting that they conduct such audits has increased steadily since 2012. In 2018, all companies reported that they regularly audit compliance with codes of conduct and standards of behaviour.

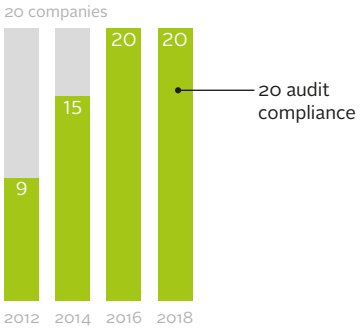
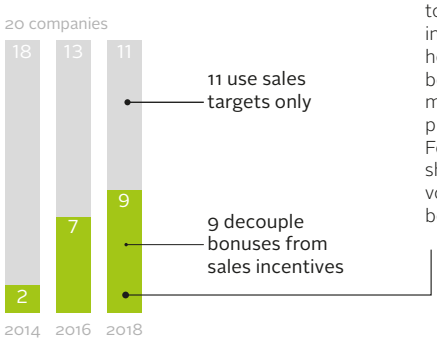


Figure 4. Since 2014, small increase in companies reforming incentives for sales agents

The chart compares, per year, how many companies are decoupling performance incentives from sales volumes for their sales agents.



Corruption may be linked to a misalignment of incentives,[2] including how sales staff earn their bonuses. It can also undermine rational prescribing practices. This is why the Foundation encourages a shift away from using sales volume as the basis for bonus calculations.

RESEARCH & DEVELOPMENT

R&D for high-burden diseases surges, with gradual increase in companies planning ahead to facilitate access

The Foundation regularly analyses pharmaceutical companies' R&D pipelines for specific diseases, conditions and pathogens. These comprise the most pressing access priorities for people living in low- and middle-income countries (LMICs), as defined by the Access to Medicine Foundation through consultation with experts working in global health. People in LMICs face more than 80% of the global burden of these diseases.[1]

This section examines how the number of R&D projects targeting these diseases and conditions has changed over time, the number of companies involved in the different R&D areas and whether companies are now more likely to plan ahead to facilitate access to successful R&D projects. This section also looks at which products have reached the market in the past decade.

R&D PIPELINE SIZE

R&D pipeline has doubled since 2014

Since 2014, a set of 47 diseases and conditions has consistently qualified for the Index analysis. These include: communicable diseases (infectious diseases), such as HIV/AIDS, malaria and tuberculosis; neglected tropical diseases (NTDs), including parasitic infections such as sleeping sickness (human African trypanosomiasis) and river blindness (onchocerciasis); non-communicable diseases (NCDs), such as diabetes mellitus, heart disease and stroke; as well as maternal and neonatal health conditions, such as maternal haemorrhage and preterm birth complications. The pipeline for this set of 47 diseases and conditions has more than doubled since 2014: from 327 projects to 673 (see Figure 5). The sharpest increase has been in the number of projects for NCDs (see page 18 for more information). If successful, products for NCDs have the greatest commercial potential.

In 2018, cancer and a number of additional communicable diseases were newly included in the Foundation's analysis. Cancer alone brought a further doubling of the pipeline, to 1,314 projects.

To break down this analysis further, the Foundation has pulled out changes in pipeline size for specific diseases and conditions since 2014: HIV/AIDS, malaria, tuberculosis, NTDs and maternal and neonatal health conditions (see Figure 6). Most of these pipelines have increased. Projects targeting maternal and neonatal health conditions have decreased marginally; some projects were discontinued, while others gained market approval (see Figure 6).

Notably, projects targeting NTDs have more than doubled, from 38 projects to 90. These projects have little commercial potential, as the people affected by these diseases generally live on very low incomes and/or have limited access to healthcare. The increase in NTD R&D can largely be attributed to efforts led by the World Health Organization (WHO) and product development partnerships (PDPs), such as the Drugs for Neglected Diseases initiative (DNDi), which have coordinated and driven attention for pharmaceutical R&D targeting NTDs (read more on page 24). The growth is mostly focused on three related diseases: leishmaniasis, Chagas disease and human African trypanosomiasis. Caused by related protozoan parasites, these three diseases have been the subject of focused attention from the global health community since at least 2009, when DNDi launched its Chagas Clinical Research Platform.[2] Many NTDs have seen sustained company activity over the years (see Figure 8).

Looking at these same diseases and conditions (as in Figure 6), there were generally more companies engaged in pharmaceutical R&D in 2018 than in previous years (see Figure 7). HIV/AIDS is an exception, with fewer companies that are engaging, and a growth in R&D projects. Some companies have left this space, while others, such as Gilead and GSK (working through ViiV Healthcare with Pfizer and Shionogi), have specialised.

There is a range of reasons why the number of companies engaging in R&D per disease may fluctuate. These include acquisitions and divestments, investigatory candidates yielding promising or poor results and new or discontinued partnerships.

Figure 5. Since 2014, the pipeline for high-burden and neglected diseases and conditions has more than doubled

The chart compares the number of R&D projects in company pipelines for 47 high-burden or neglected diseases and conditions in 2014 and 2018. The pipeline has more than doubled in size.

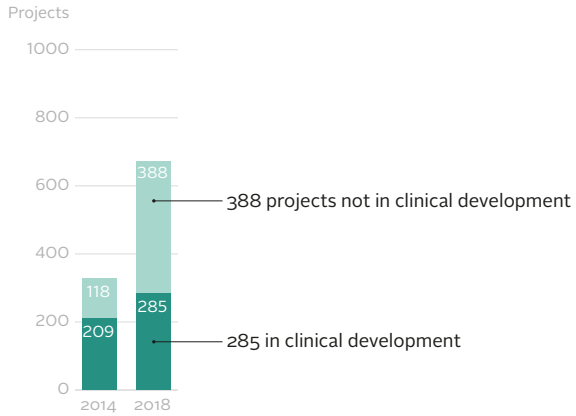


Figure 6. Since 2014, pipelines for key diseases have grown, but not for maternal and neonatal health conditions

The chart shows the change in pipeline size for key diseases or conditions between 2014 and 2018. The increase in R&D projects for NTDs is a response to increasing global attention coordinated by WHO.

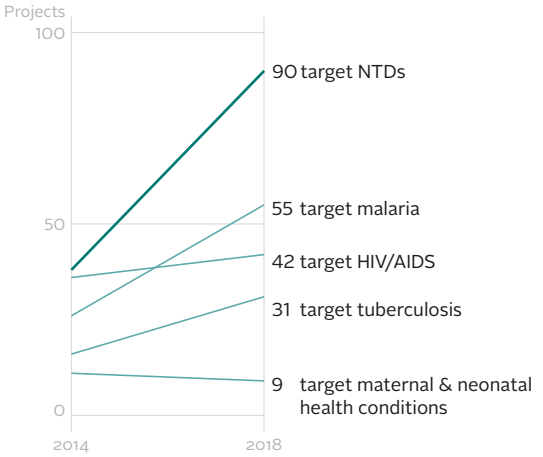


Figure 7. Compared to 2010, more companies are now involved in R&D for key diseases and areas

The chart shows the change in the number of companies engaged in R&D for key diseases or conditions between 2010 and 2018. Pipelines for maternal & neonatal health conditions were first comprehensively assessed in 2014. Across most areas, company engagement has increased. In HIV/AIDS, some companies have left while others have specialised.

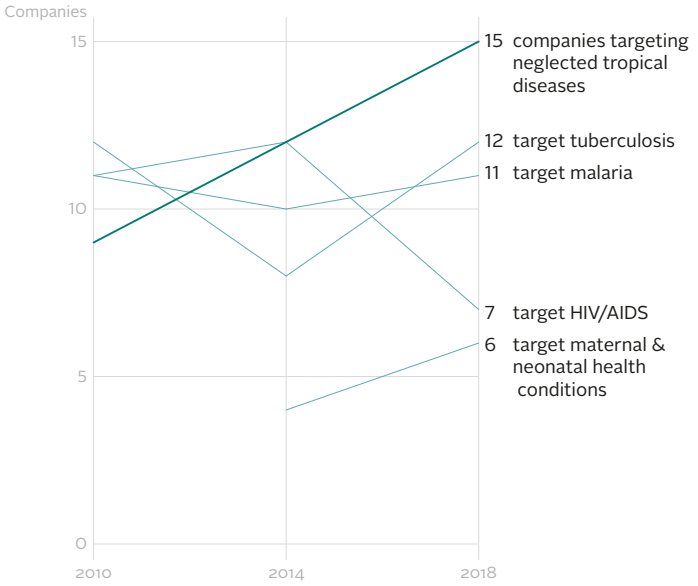
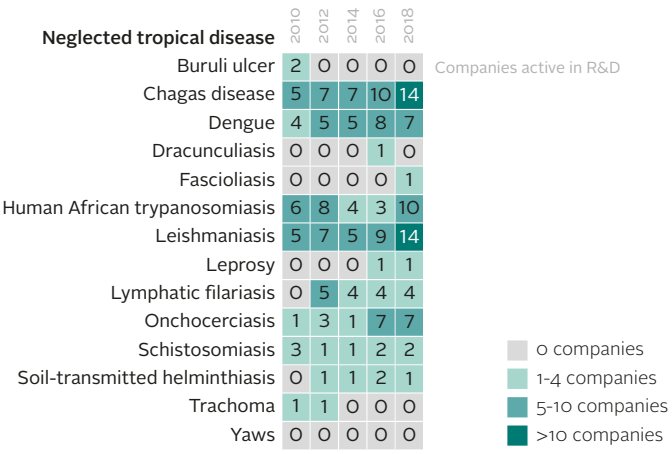


Figure 8. Since 2010, clear uptick in NTD R&D engagement for leishmaniasis, Chagas disease and HAT

The chart shows the change in the numbers of companies engaged in R&D for specific NTDs in scope since 2010. The strongest increases are in R&D for leishmaniasis, Chagas disease, onchocerciasis and human African trypanosomiasis (HAT), which have been prioritised by the global health community.



R&D FOR NCDS

High numbers of projects for non-communicable diseases

Most high-income countries offer healthy markets for new pharmaceutical products targeting NCDs such as heart disease, diabetes and respiratory conditions. R&D projects for NCDs have consistently accounted for the largest proportion of the R&D pipeline identified by the Index, despite the Index analysing similar numbers of NCDs and communicable diseases with each iteration. As noted earlier in this study, the R&D pipeline for the 47 diseases and conditions consistently in scope more than doubled between 2014 and 2018, with projects for NCDs accounting for more than half of this increase (57%). During the same period, the number of companies evaluated that engage in R&D for NCDs in scope since 2014 has remained stable: now at 18 companies out of 20 (see Figure 10). Almost all of the companies (19/20) are currently active in R&D for cancer care, and nearly three quarters (14) are active in R&D targeting diabetes (see figure 9). Of the 171 new medicine approvals identified since 2008, 60% (103) are for NCDs.

NCDs account for a rising burden of disease in most LMICs, a trend that is predicted to continue.[3] Experts in the global health community have emphasised the need for expanding access to existing and effective treatments for NCDs, especially those listed on the WHO EML. However, pharmaceutical companies have a responsibility to ensure that new NCD products can also be made available and accessible to these populations. However, low- and middle-income country (LMIC) markets are often viewed as less lucrative, due to the perception of regulatory challenges and reduced ability of patients in these countries to pay, for example. As a result, it is likely that new NCD products are not being routinely developed where R&D product gaps exist for those living in LMICs – for example, heat-stable formulations, additional oral oncology medicines and long-acting versions of treatments for chronic diseases.

There is evidence that some companies take the unique burden of NCDs for LMICs into account, considering the economic- and health-related consequences of these diseases in these countries. However, few provide evidence of detailed approaches to adapt or innovate NCD products specifically for those living in LMICs, leaving critical needs, such as for heat-stable medicines and vaccines, unaddressed.

PAEDIATRIC R&D

Small numbers of medicines being adapted for children

Many health products are not particularly well suited for treating children, for example, because they do not have a sufficiently low dosage, because they are difficult for children to swallow, or they were never tested in paediatric populations. Adapting medicines for children is a specific type of R&D. Particular needs for adaptive R&D were highlighted in 2006 when WHO identified serious gaps in research and several barriers to access, and indicated how to overcome them.[4] The number of medicines being developed or adapted for children by the companies in scope has remained relatively constant since at least 2014, with a small increase in pipeline size and few projects reaching the market. The total number of such projects currently in the pipeline is 29 (see Figure 11). In 2018, there were fewer companies engaged in this type of R&D than in 2014; just three companies (GSK, Johnson & Johnson and Sanofi) account for 21 out of 29 projects. The 29 paediatric medicines currently in the pipeline include: three new water-dispersible formulations for tuberculosis from Sanofi, which will be easier for children to swallow; four new paediatric indications of HIV/AIDS medicines from GSK; and a child-friendly formulation of the tuberculosis medicine bedaquiline (Sirturo®) from Johnson & Johnson.

PRIORITY R&D

R&D for priority product gaps increases; many gaps remain unaddressed

Diseases can have an effective cure available and still face product gaps – for example, the development of a single-dose oral treatment for syphilis would enable governments to bring this disease quickly under control during outbreaks. WHO and Policy Cures Research, an independent R&D-focused policy group, have published lists of the most urgently needed new products – here termed priority product gaps.[5-9]

The Foundation first examined R&D targeting priority product gaps in 2016. It looked at 22 diseases with 84 priority product gaps. It found companies taking action for 18/22 of these diseases and targeting 31/84 gaps, with 151 projects in total (see Figure 12). In 2018, looking at the same set of diseases and product gaps, the Foundation identified an additional 44 R&D projects (now 195 in total for 36/84 gaps).

These projects include diagnostics for schistosomiasis, medicines for the treatment of shigellosis and a number of vector control products. Most new projects since 2016 target leishmaniasis, malaria, Chagas disease, human African trypanosomiasis and tuberculosis. Product gaps that remain untargeted by the companies in scope include single-dose oral treatments for syphilis and preventive vaccines for NTDs such as Buruli ulcer and trachoma.

Figure 9. Since 2012, non-communicable diseases have remained as the focus of R&D engagement

The chart shows the numbers of companies engaged in pharmaceutical R&D for non-communicable diseases since 2012. For most diseases, the level of R&D engagement has remained fairly constant. The uptick in R&D for kidney diseases is likely because they affect large populations in high-income countries.

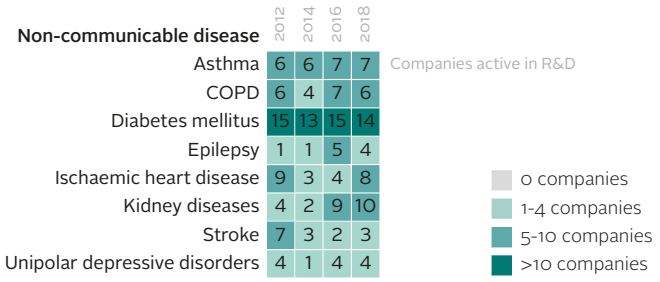


Figure 10. Since 2014, most companies have engaged in NCD research; R&D projects for NCDs have nearly tripled

The charts show how many companies engaged in R&D for 10 non-communicable diseases (NCDs) since 2014, as well as the corresponding number of R&D projects. The number of R&D projects has nearly tripled.

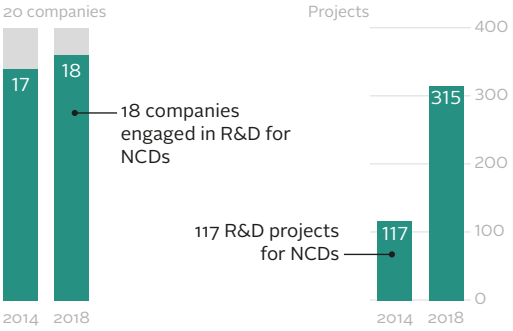


Figure 11. Since 2014, the number of medicines being developed or adapted for children remains low

The charts show the changing level of engagement by pharmaceutical companies in adapting medicines for children, as well as the number of projects. Although there are more medicines being adapted now than in 2014, the overall numbers remain low.

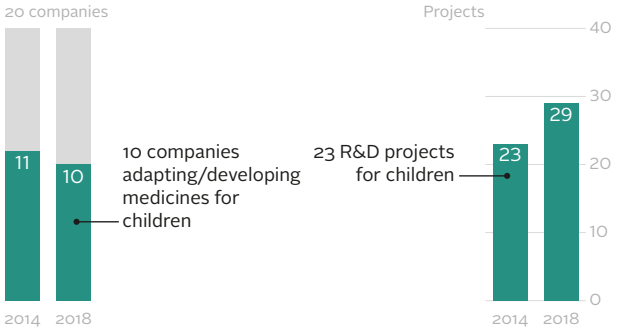
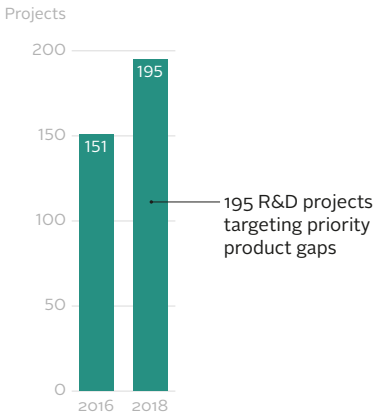


Figure 12. Since 2016, priority R&D has increased

The figure compares the number of R&D projects in 2016 and 2018 that target a set of 84 priority product gaps defined by WHO and Policy Cures Research. The number of projects has increased, now targeting 36 out of 84 gaps, but still leaving many unaddressed.



VACCINES R&D

Industry focuses on diseases common to high-income countries

Vaccines are important products in preventing the further spread of both communicable and neglected tropical diseases. However, the abundance of some infections such as pneumonia in both high-income countries and LMICs can play a critical role in shifting the industry's focus. Broadly, there has been little movement in or out of R&D for preventive vaccines among the companies in scope. In 2014, ten companies were developing at least one vaccine candidate, while in 2018, nine companies were involved in this space (see Figure 15). Similarly, there has been a slight reduction in the number of vaccine projects in the pipeline, from 86 in 2014 to 74 in 2018 (see Figure 15), when holding the disease scope constant from 2014 onward. Many diseases for which preventive vaccines have been identified as priority R&D product gaps have seen either a stagnation or consolidation of companies and/or projects between 2014 and 2018 (see Figures 13 and 14). Of note, GSK acquired Novartis' vaccine business in 2015, and has consistently been found to be developing a comparatively high number of R&D projects for urgently needed vaccines, along with Johnson & Johnson and Sanofi.

While HIV/AIDS, malaria and tuberculosis have been the subjects of intense scrutiny from global health organisations and funding, few companies have been active in developing vaccines for these diseases. This is in stark contrast to companies' efforts to develop vaccines for lower respiratory infections and meningitis, which tend to have promising market potential in high-income countries. Less lucrative diseases, in particular the NTDs and infections caused by drug-resistant bacteria, have received almost no attention in the last six years from companies in scope with regards to vaccines R&D, with the exception of dengue. Dengue vaccines are likely to have some commercial incentive because dengue is endemic in at least 100 countries, some of which have higher market potential.[10] Where there are R&D vaccine projects in other neglected areas, one or two companies are often responsible for sustaining this activity. For example, Eisai is the sole company developing a Chagas disease vaccine, and Takeda is the sole company developing a vaccine for chikungunya. Currently, GSK and Pfizer are actively developing Group B *Streptococcus* vaccines. A vaccine for these pathogens is urgently needed but does not yet exist.

ACCESS PLANS

Coverage of late-stage R&D projects with access plans remains constant

New medicines and other life-saving products must be made rapidly available to people who need them, wherever they live. This requires advance planning before new products are approved for sale. Access plans can include registration targets based on need, pricing commitments or licensing arrangements that will accelerate the speed at which products become accessible. The Foundation examines whether companies are planning ahead in this way, and what these access plans look like.

Over the past ten years, various initiatives have been established to engage pharmaceutical companies in R&D for global health, drawing on public and private funds to pool risks and share benefits. PDPs, for example, facilitate financial risk-sharing for R&D and systematically ensure access plans are developed early in product development.

In 2014, the Foundation looked at access plans for projects developed in partnership (40% of such R&D projects examined in 2014 were being developed through partnerships). It reported that 16% of all collaborative R&D projects were supported by access plans.

In 2016 and 2018, data were also collected on access plans for projects being carried out in-house. In 2018, the Foundation reported that close to a third of all projects are being developed with other organisations, and 16% of all projects have an access plan. When looking solely at late-stage R&D projects (from Phase II onwards) in 2018, just 19% of projects were found to be supported by access plans.

For late-stage communicable and NTD projects, the proportion of late-stage projects with access plans has not significantly increased since 2016 (see Figure 16). However, there has been a small rise in the number of collaborative projects targeting these disease types that also have access plans in place (from 33 to 37).

During this period, five companies have established new processes for considering access for all R&D projects for high-burden and neglected diseases (GSK, Johnson & Johnson, Merck KGaA, Novartis and Takeda). Novartis goes a step further, committing to developing access strategies for all new medicine launches including biosimilars.

GSK pioneered good practice in this area, starting in 2014 by systematically incorporating access plans into research contracts for projects targeting tuberculosis, malaria and NTDs that are developed at its Tres Cantos Open Laboratory Foundation (TCOLF) in Spain.

Figure 13. Since 2014, the number of companies developing vaccines for key diseases has remained consistently low

The chart shows the number of companies active in R&D to develop new vaccines for diseases that are designated as priorities. Since 2014, vaccines R&D for NTDs has remained limited.

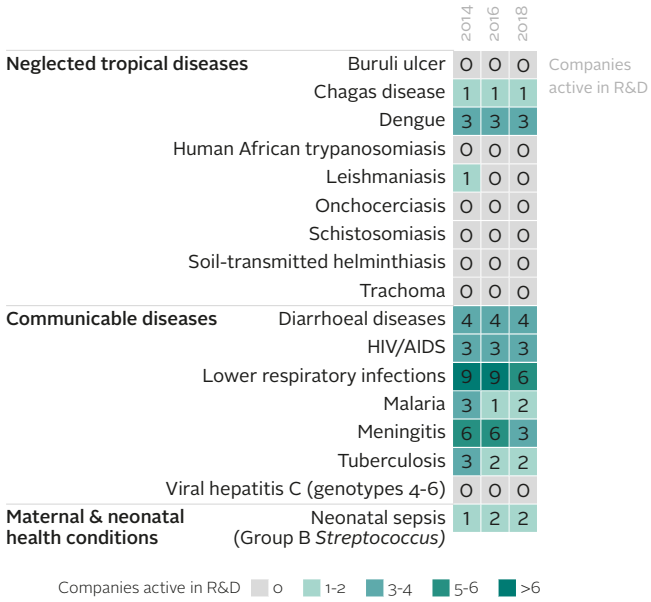


Figure 14. Since 2014, companies have focused efforts to develop new vaccines in a few diseases

The chart shows the number of vaccine R&D projects targeting diseases that are designated as priorities since 2014. This type of R&D is concentrated in lower respiratory infections, meningitis and diarrhoeal diseases.

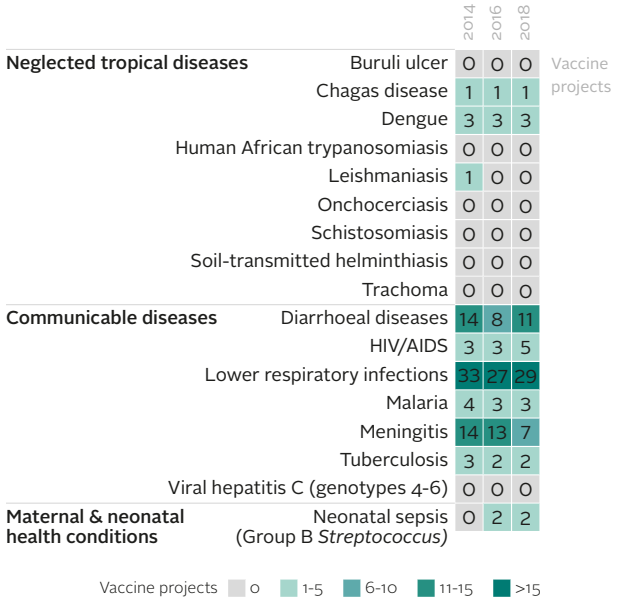


Figure 15. Since 2014, company engagement in vaccine R&D for diseases in scope has remained relatively constant

The charts compare how many companies are developing vaccines for diseases in scope and the number of corresponding R&D projects. Both measures have decreased slightly since 2014.

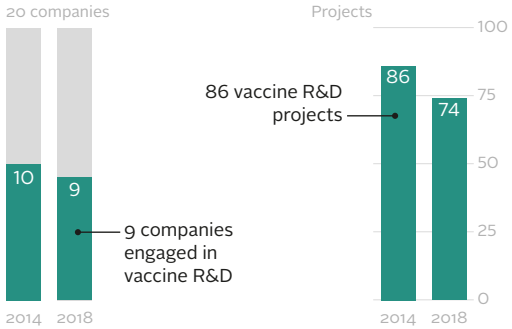
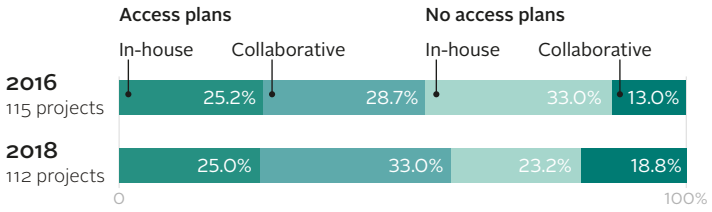


Figure 16. Since 2016, the coverage of access plans for late-stage projects is largely unchanged

The charts compare the percentages of late-stage R&D projects for communicable and neglected tropical diseases in scope with access plans in 2016 and 2018. They also show the proportion of projects being carried out through partnerships or in-house.



MARKET APPROVALS

At least 171 new medicines receive approval in past decade

The Foundation has examined new medicine approvals by the 20 companies for 76 of the 77 diseases, conditions and pathogens in scope examined in the 2018 Access to Medicine Index.* It was found that at least 171 new medicines received approval, mainly for NCDs (see Figure 17).

This analysis looked at new medicine approvals per applicant from the European Medicines Agency (EMA), US Food and Drug Administration (FDA), and Japan's Pharmaceuticals and Medical Devices Agency (PMDA) since 2008. Vaccines and diagnostics are not included, nor are biological agents, due to a lack of sufficient data.

The majority of new medicines (103) are for NCDs, mainly diabetes mellitus, cardiovascular conditions and chronic obstructive pulmonary disorder (COPD). Most of the remaining new medicine approvals target communicable diseases (62), mainly HIV/AIDS and viral hepatitis (see Figure 18). Very few are for maternal and neonatal health conditions or NTDs (five and one, respectively). The only NTD medicine to receive an approval since 2008 from the 20 companies was a chewable form of mebendazole (Vermox™ Chewable) developed by Johnson & Johnson to allow for easier administration to children. Notably, a new powder formulation of ritonavir (Norvir®, AbbVie, 2017) and dispersible artemether/lumefantrine (Coartem® Dispersible, Novartis, 2009), have also been approved since 2008, both also for children.

Recent approvals include new antiretrovirals for HIV/AIDS, such as dolutegravir/rilpivirine (Juluca®), developed in partnership by Johnson & Johnson and ViiV Healthcare, as well as glecaprevir/pibrentasvir (Mavyret™), a pangenotypic hepatitis C treatment developed by AbbVie. The 20 companies have received approval for at least 12 fixed-dose combination HIV/AIDS medicines from 2008 to 2018.

Out of the 20 companies, 19 have received one or more approvals for new medicines targeting diseases or conditions in scope (see Figure 19). The exception is Merck KGaA; it has gained approvals in this time period, but for diseases out of scope of this analysis, such as cancer and multiple sclerosis. Merck & Co., Inc. leads a group of seven companies that have had 12 or more medicines approved.

New medicines supported by access initiatives

Of the newly approved products analysed, at least 52 have an access initiative (i.e., an equitable pricing strategy, non-exclusive voluntary licence or structured donation programme). For example, Gilead's tenofovir disoproxil fumarate (Viread®) for HIV/AIDS has an equitable pricing strategy in 23 countries where pricing is considered a priority** and has a voluntary licence that covers 116 countries. Other examples are:

- Eisai's perampanel (Fycompa®) for epilepsy, which has equitable pricing strategies that include prices set for different population groups within a country (intra-country pricing).
- Johnson & Johnson's bedaquiline (Sirturo®) for tuberculosis, which has an equitable pricing strategy with per-country prices and a structured donation programme.
- Gilead's sofosbuvir (Sovaldi®) for hepatitis C, which has equitable pricing strategies that include intra-country pricing.

▸NEW MECHANISM TO ACCELERATE REGISTRATION

The European Medicines Agency, in cooperation with WHO, offers a pathway known as Article 58 that facilitates the approval of medicines and vaccines that are particularly needed by people living outside the EU. Some products that have been successfully submitted to this process include:

- RTS,S (Mosquirix™), a preventive vaccine for *P. falciparum* malaria developed by GSK in partnership with PATH's Malaria Vaccine Initiative, for use in children aged 6 weeks to 17 months.
- Chlorhexidine digluconate antiseptic gel (Umbipro™), developed by GSK in partnership with Save the Children for the prevention of umbilical cord infections in newborns.
- Oral fexinidazole, developed by Sanofi in partnership with DNDi as the first all-oral treatment for human African trypanosomiasis (see page 26).

▸WHAT IS LIKELY TO COME OUT OF THE PIPELINE NEXT?

At least 220 R&D projects from the 20 companies are in Phase III clinical development, or have been submitted for approval by a stringent regulatory authority, for 76 of the 77 diseases, conditions and pathogens examined in the 2018 Access to Medicine Index,* including, as of 6 May 2019:

- Two Phase III preventive vaccine candidates for Ebola: one each from Johnson & Johnson and Merck & Co., Inc.
- Cabotegravir/rilpivirine, a combination dual long-acting injectable being developed by ViiV Healthcare and Johnson & Johnson for the treatment of HIV, has been submitted for approval by the FDA.
- Oral semaglutide, being developed by Novo Nordisk for diabetes mellitus type 2. It belongs to a class of antidiabetic agents that are currently only available as injectables requiring refrigeration. Novo Nordisk has submitted this medicine for approval by the FDA.
- Heat-stable carbetocin, Ferring Pharmaceuticals' proprietary and investigational compound for the prevention of postpartum haemorrhage, is being developed to address heat-stability issues with the current first-line treatment oxytocin. Merck & Co., Inc. is collaborating with Ferring Pharmaceuticals and WHO through its Merck for Mothers Initiative to advance this compound and ensure affordability and sustainability. Ferring Pharmaceuticals is now seeking registrations for this medicine.
- An ultra-long-acting injectable form of paliperidone palmitate, in Phase III of clinical development by Johnson & Johnson, that could help patients living with schizophrenia through as few as two injections a year.
- Esketamine, an antidepressant with a new mechanism of action from Johnson & Johnson. Esketamine was approved by the FDA in March 2019 for the treatment of treatment-resistant depression in adults. Johnson & Johnson continues to investigate esketamine in treating major depression with imminent risk for suicide in adults and children.

*Cancer was excluded as the Index did not cover cancer products until 2018.

**Priority countries are disease-specific subsets of countries with a particular need for access to relevant products. See appendix.

Figure 17. Since 2008, at least 171 new medicines have received approval from the EMA, FDA and/or PMDA

Since 2008, the 20 companies evaluated have received approval from the EMA, FDA and/or PMDA for at least 171 new medicines for diseases and conditions that are especially important to public health in low- and middle-income countries. Most are for NCDs,* with very few for NTDs or maternal and neonatal health conditions.

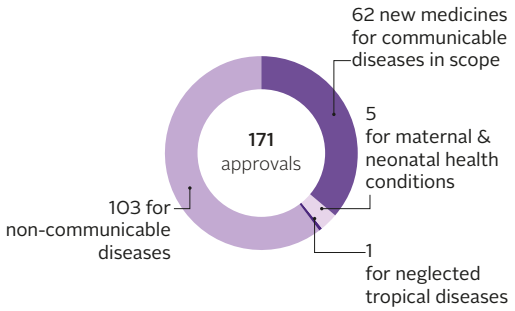


Figure 18. Since 2008, more medicines have been approved for diabetes mellitus and HIV/AIDS than other diseases

The figure shows the number of new medicines gaining EMA, FDA and/or PMDA market approval since 2008 per disease/condition. Nearly half target diabetes mellitus or HIV/AIDS.*

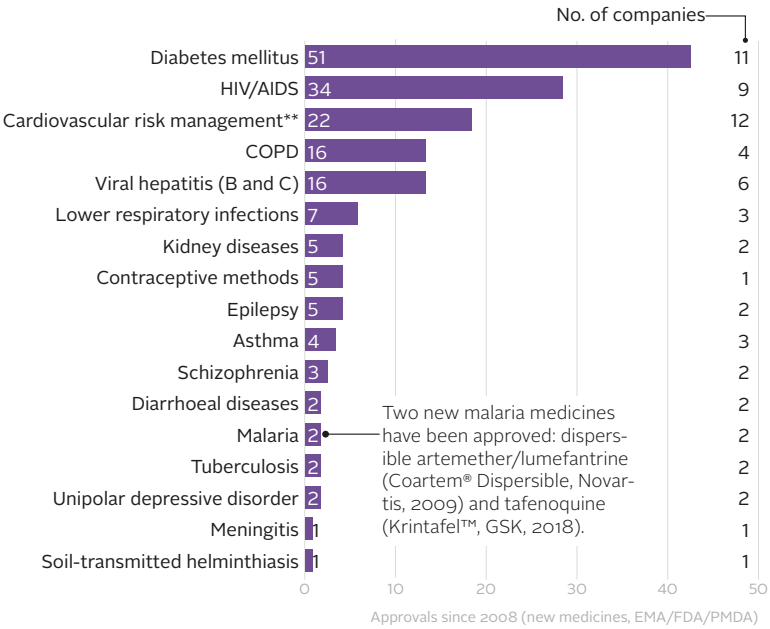
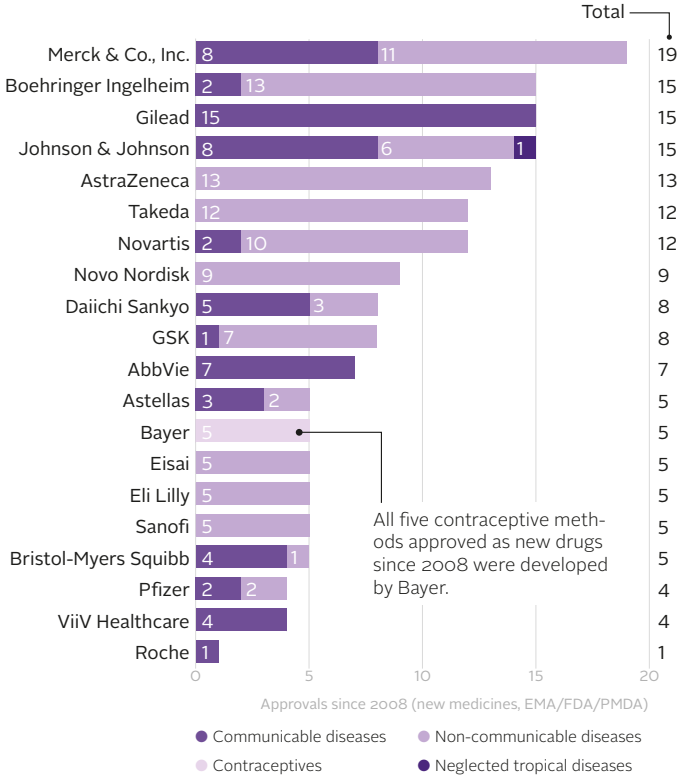


Figure 19. Since 2008, 19 companies have received approvals for at least 171 medicines for diseases and conditions in scope

The figure shows how many new medicines targeting diseases and conditions in scope* each company has received approvals for from the EMA, FDA and/or PMDA since 2008.



*Cancer was excluded as the Index did not cover cancer products until 2018.

**Cardiovascular risk management includes hypertensive heart disease, ischaemic heart disease and stroke.

ViiV Healthcare is a pharmaceutical company run in partnership by GSK, Pfizer and Shionogi (78.3%, 11.7% and 10% shareholders, respectively in 2018) that specialises in developing innovative treatments for HIV/AIDS.

NEGLECTED TROPICAL DISEASES

Significant uptick in engagement in R&D and donations for NTDs

The term 'neglected tropical diseases' (NTDs) was coined in 2003 to refer to a group of diseases that primarily affect people living in the world's poorest communities.[1] Many NTDs are caused by worms or other parasites, and they can lead to blindness, or disfiguring and painful swellings or ulcers. NTDs can keep children out of school and adults out of work and contribute to cycles of poverty.

The World Health Organization (WHO) has played a central and pivotal role in coordinating and driving attention toward NTDs, particularly since 2008. Before this, individual pharmaceutical companies (most notably Merck & Co., Inc.) were actively donating NTD treatments, while others were carrying out R&D, often through the Special Programme for Research and Training in Tropical Diseases (TDR), active since the 1980s and currently sponsored by UNICEF, UN Development Programme, World Bank and WHO. In 2012, WHO set global targets for controlling, eliminating and eradicating NTDs by 2020, published in its NTD Roadmap.[2] Inspired by the Roadmap, a broad range of partners including 14 pharmaceutical companies endorsed the 2012 London Declaration on NTDs, a multi-lateral public commitment to bringing ten NTDs under control by 2020.[3] Today, 20 diseases are categorised by WHO as being NTDs. This section examines how companies' engagement in donations and R&D for NTDs has increased since 2010.

DONATIONS

Marginally more companies now donate for NTDs

Since 2010, two additional companies have established structured donation programmes aimed at NTDs (see Figure 20). The number of structured donations programmes with products for NTDs has also slightly increased, from 13 to 16. In the majority of cases, all donation programmes for NTDs can be supported by commitments to continue donating until the diseases have been eradicated or eliminated. In 2012, 12 companies analysed by the Index signed the London Declaration on NTDs.

RESEARCH & DEVELOPMENT

Increase in company R&D activity for NTDs

NTDs predominantly affect people with little or no ability to pay for treatment. As a result, there is often little commercial incentive for pharmaceutical companies to develop new products. Nevertheless, in 2010, nine of the companies evaluated were working on at least one R&D project targeting an NTD in scope (see Figure 21). In 2018, fifteen companies were found to be developing projects for the 14 NTDs that have been in scope since 2010. Seven companies have newly started working on R&D for these NTDs since 2010, while one, Eli Lilly, has since stopped. Novo Nordisk, though not active in R&D for NTDs, donated a licence to its small molecule compound library to the National Center for Drug Screening (NCDS) in Shanghai, China in 2008 to identify new candidates for NTDs.

All four Japanese companies tracked by the Foundation (Astellas, Daiichi Sankyo, Eisai and Takeda) are now active in R&D for NTDs (see Figure 22). Eisai is the only Japanese company that was active in NTD research between the first Index in 2008 and the 2012 London Declaration on NTDs. Astellas and Takeda entered the field after this point. Daiichi Sankyo entered after 2014, following the formation of the Global Health Innovative Technology Fund (GHIT) in 2013. GHIT funds R&D for neglected diseases. All four of these Japanese companies are GHIT partners. At the 2016 Ise-Shima Summit, the G7 leaders committed to furthering R&D for NTDs, for example, by adopting policies to encourage product development and by promoting public-private partnerships such as GHIT.

Figure 20. Since 2010, the number of companies donating products for NTDs has only slightly increased

The chart shows how many companies were engaged in donations for NTDs before and after the 2012 London Declaration on NTDs. Since 2010, this number has only marginally increased. In 2018, six companies were found to have committed to donating medicines until eradication/elimination targets are met, for nine NTDs. Companies have been donating medicines for NTDs for many years. Some programmes go back as far as the 1980s.

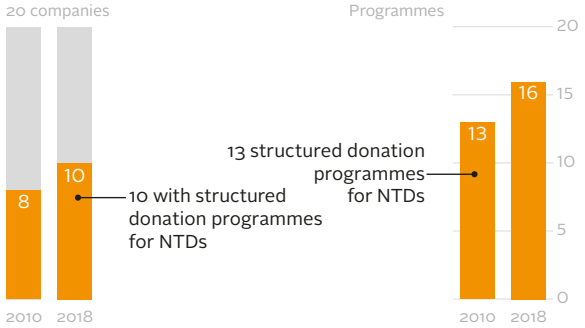


Figure 21. Since 2010, more companies are now engaged in R&D for NTDs

The chart compares how many companies were active in R&D for NTDs in 2010 with the number of companies active in 2018.

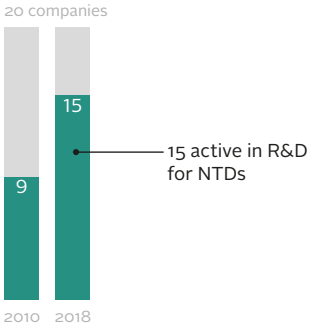
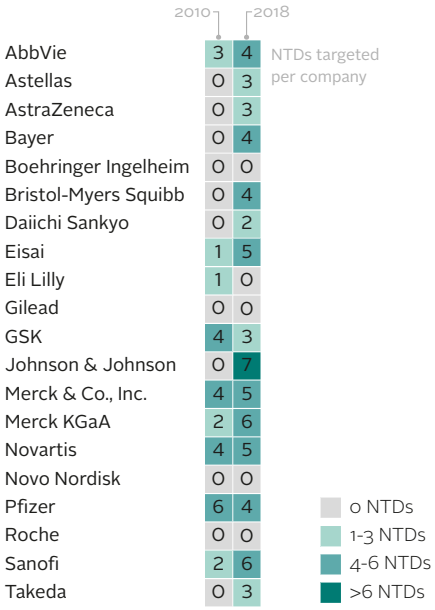


Figure 22. Since 2010, most companies active in NTD R&D have expanded to more diseases

The figure shows how many of the 14 NTDs defined in 2010 each company was targeting compared with 2018. More companies are now active in this space, and most companies have expanded their activity to more NTDs.



R&D pipeline for NTDs has doubled since 2014

The Foundation began examining pipelines in detail for NTDs in 2014. There are now more than twice as many NTD projects as in 2014, rising from 38 to 90 projects (see Figure 23). Since 2014, WHO has defined three additional diseases (scabies and other ectoparasites; mycetoma, chromoblastomycosis and other deep mycoses; and snakebite envenoming) as NTDs; only three out of the 90 projects target these more recently defined NTDs.

The number of projects in late stages of development targeting NTDs has grown slightly since 2014, while the number in early stages has more than doubled (see Figure 24). This increase in early stage R&D is encouraging, but due to the high failure rate of pharmaceutical R&D, many of these additional early-stage projects will likely not make it to clinical testing.

As noted on page 16, the increase in engagement for NTDs is centred on diseases that have been prioritised by the global health community. There are more companies involved in R&D for Chagas disease, leishmaniasis, onchocerciasis, lymphatic filariasis and human African trypanosomiasis than the other 15 NTDs. All five of these diseases were named priority targets in the 2012 London Declaration and have been the focus of the Drugs for Neglected Diseases initiative (DNDi). Since 2014, the majority of R&D projects for NTDs have involved an external partner, for example, through a PDP (see Figure 25).

Pipelines have been consistently empty for some NTDs since at least 2014: Buruli ulcer, dracunculiasis, trachoma and yaws. Dracunculiasis and yaws have relatively effective treatments available, and donation programmes are running. Buruli ulcer and trachoma also have effective treatments available, yet new products need to be developed, including vaccines and affordable, reliable diagnostics, as well as new medicines with shorter courses of treatment to improve effectiveness. For R&D, WHO and Policy Cures Research have published lists of the most urgently needed new products – termed priority product gaps – including for NTDs (see Appendix). As reported in the 2018 Access to Medicine Index, 27 gaps for NTDs (out of 41 in total) are currently not targeted by the companies in scope, with gaps for diagnostics getting the least attention overall. All companies are encouraged to assess how their R&D expertise, resources and IP assets can be applied in the global push to fight NTDs.

▸Which new NTD projects are moving close to the market?

SANOFI

Fexinidazole for the treatment of human African trypanosomiasis

This medicine received a positive opinion from the EMA in 2018 as the first complete oral treatment for human African trypanosomiasis (HAT, or sleeping sickness). It has since been registered in the Democratic Republic of Congo. It treats the strain of HAT known as g-HAT, which accounts for 97% of reported cases. Untreated, g-HAT is almost always fatal.[4] This promising new medicine had a success rate* of >90% in Phase II/III clinical trials.[5] It could replace the current first-line treatment for g-HAT, which must be administered intravenously by skilled medical professionals.

TAKEDA

Live-attenuated tetravalent dengue vaccine (DENVax)

Currently undergoing Phase III clinical testing, this could become the second dengue vaccine, after Sanofi's Dengvaxia®, to reach the market; it has already demonstrated immunogenicity against all four serotypes of dengue virus.[6] Treatment for dengue is currently limited to supportive care, with untreated cases of severe dengue leading to mortality rates of greater than 20%. There are as many as 390 million estimated dengue infections a year.[7]

BAYER

Fast-disintegrating nifurtimox (Lampit®) for treating Chagas disease in children

These fast-disintegrating tablets have been successfully tested in Phase I and Phase III studies in children and adults, making Chagas medication easier for all patients, especially young children, to use. It is expected to reach the market starting in 2020, with Bayer stating that it aims to register the product in endemic countries with high disease burdens and to apply for WHO prequalification. An estimated 6-7 million people worldwide are infected with *Trypanosoma cruzi*, the protozoan parasite responsible for Chagas disease.[8]

*Success rate was defined by the study's authors as patients being alive, having no evidence of trypanosomes in any body fluid, not requiring rescue medication and having a white blood cell count of 20 or fewer cells per microLitre of cerebrospinal fluid.

Figure 23. Since 2014, R&D projects for NTDs have more than doubled

The figure compares the numbers of R&D projects targeting NTDs since 2014. Since then, the number of projects has reached 90. Only three projects target a disease newly defined as an NTD since 2014 by WHO (new in scope).

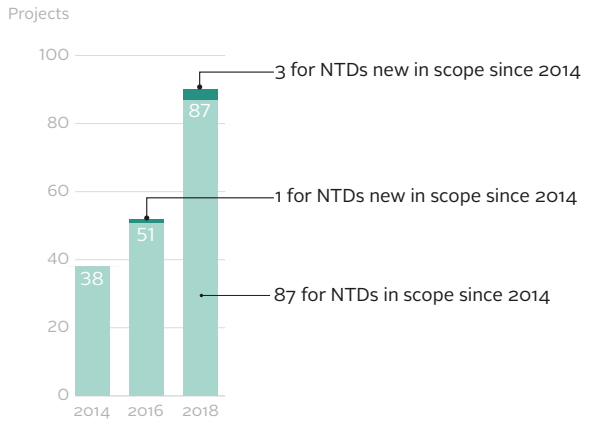


Figure 24. Since 2014, early-stage pipeline for NTDs has more than doubled

The figure shows the proportion of the NTD pipeline that is in either early or late stages of development each year. The proportion of projects in early stages has more than doubled.

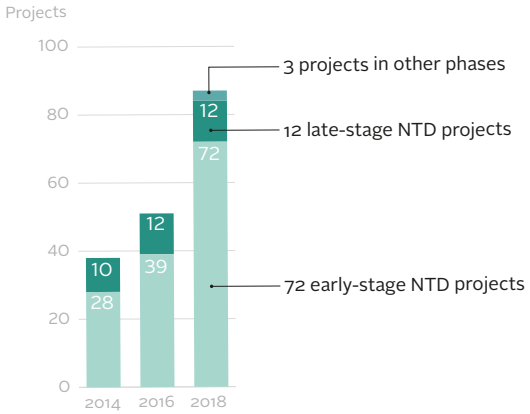
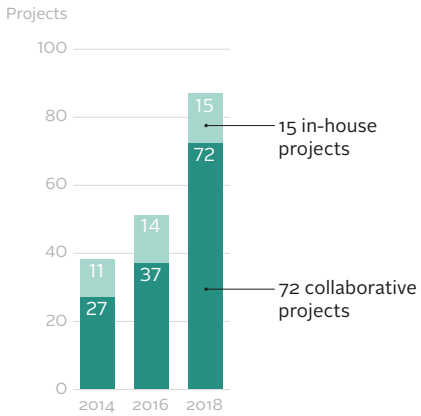


Figure 25. Since 2014, R&D for NTDs consistently driven by partnerships

The figure compares the numbers of NTD R&D projects each year that are being conducted in partnerships (i.e., are collaborative). Collaborative projects consistently account for the highest proportion. Projects that are being developed by more than one company are counted more than once.



ACCESS TO SPECIFIC PRODUCTS

Companies are only gradually increasing use of affordability strategies and voluntary licensing

Whether medicines, vaccines and other products reach the people who need them depends on the strategic choices companies make to support availability and affordability. The three main tools available to a pharmaceutical company for improving access to specific products are: equitable pricing strategies, voluntary licensing and product donations. This section looks at how companies' use of equitable pricing and licensing in low- and middle-income countries (LMICs) has changed over time (their use of donations in relation to neglected tropical diseases is summarised on page 24). This section also looks at three further areas of practice – registration filings, support for the Doha Declaration on the TRIPS Agreement and Public Health and patent transparency – as these practices act as key enablers for others, such as procurers and generic medicine manufacturers, to also improve access to specific products.

REGISTRATION FILINGS

Registration commitments become more specific

Registration is the first step to making a product available in a country. The Foundation has tracked how companies commit to filing to register new products in LMICs.

Between 2012 and 2014, 13 companies strengthened or expanded their commitments to registering products in LMICs. For example, Roche improved the timeframe within which it commits to registering its products, and Novartis provided a more specific commitment to registering products in countries in Africa.

Since 2014, the Foundation has also assessed the detail of companies' registration commitments, using three quality criteria (see Figure 26). It finds that companies' commitments to registering products are gradually getting more detailed; there is an upward trend in two out of the three areas, although still only small proportions of companies meet these quality criteria. Currently, only three companies (Gilead, GSK and Takeda) explicitly state that their commitments cover the majority of their products.

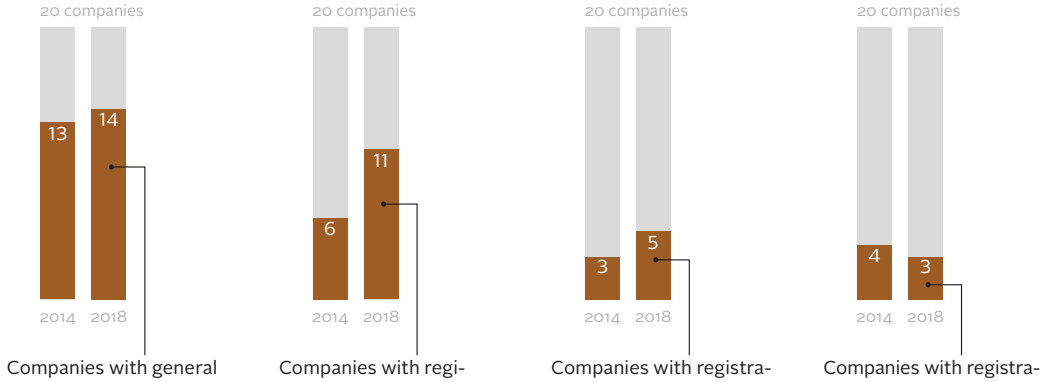
Registration in practice remains limited

While commitments are gradually strengthening, this has yet to translate into a significant change in registration practice. In 2014, the Foundation reported that 16 companies filed more than 50% of their products for registration in more than half of the 106 LMICs in scope. In 2016, the Foundation redefined its approach to assessing registration filings: to assess filings in countries designated as 'priorities' for specific diseases and conditions (these designations are based on factors such as disease burden and income inequality – an average of 13 countries are designated as priorities for each disease and condition). In 2016 and again in 2018, the Foundation found that less than a quarter of companies' newest products were being widely registered in priority countries (2016: 22% filed in >50% of priority countries, n=160; 2018: 21% filed in >50% of priority countries, n=187).

There are a variety of reasons why a company may not file a product for registration in a specific market. For example, companies may be deterred due to competing products already on the market, unclear local regulatory requirements or health authorities which lack specific capacities for processing registration dossiers. Political instability, conflict or economic sanctions can also play a role. The WHO prequalification system, WHO Collaborative Registration Procedure and the African Medicines Regulatory Harmonization (AMRH) programme are already providing support for registration. The newly created African Medicines Agency (AMA) may also help expedite the registration process across the continent.

Figure 26. Since 2014, commitments to registering products have gradually become more specific

The first chart shows the number of companies that have made general registration commitments, comparing 2014 and 2018. The three remaining charts each show how many companies have made commitments that meet one of the three quality criteria looked for in this analysis. There is some movement toward making more detailed commitments.



Companies with general commitments to registering products widely.

Companies with registration commitments that apply in at least one low-income or sub-Saharan African country.

Companies with registration commitments that include a pledge to register products within 12 months of first global launch.

Companies with registration commitments that apply to the majority of its portfolio.

▸KEY TERMS

Registration filings: where a product is filed for registration for sale in a country. Companies bear the primary responsibility to file for registration; without registration, the product cannot usually be imported, marketed or distributed.

Patent transparency: when a patent expires in a country. This makes clear which products are covered by patents in specific territories, giving guidance on, for example, where generic versions could potentially enter new markets.

Equitable pricing strategies: where affordability is taken into account by the pharmaceutical company when determining prices for different population segments.

Voluntary licensing agreements or non-assert declarations: licences give permission to generic medicine manufacturers to develop and manufacture versions of on-patent products under transparent and access-friendly terms. Non-assert declarations pledge not to enforce patents in certain territories or under certain conditions.

SUPPORT FOR TRIPS FLEXIBILITIES

Company support for the Doha Declaration remains conservative

Since at least 2012, companies have continued to take a conservative stance on the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) and the subsequent Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration). In that time, the level of endorsement has shifted among the companies, with some withdrawing public support and others newly supporting the Doha Declaration and at least one TRIPS flexibility. Some companies provide a limited degree of endorsement of the Doha Declaration, under specific restricted conditions. Four companies (Eisai, GSK, Johnson & Johnson and Merck KGaA) have consistently publicly supported the Doha Declaration and at least one TRIPS flexibility since 2012 (see Figure 27).

In 2018, half of the companies (10) evaluated do not publicly support the Doha Declaration and at least one TRIPS flexibility. AstraZeneca has set itself apart, acknowledging that countries are free to determine what constitutes a 'public health emergency'. Merck KGaA acknowledges that it is the right of countries – provided certain criteria are met, such as engagement with the patent rights-holder – to determine the grounds for issuing compulsory licences.

PATENT TRANSPARENCY

Sizeable leap in patent transparency supports procurement decisions

How pharmaceutical companies manage their IP impacts the availability and affordability of medicines, particularly in how they facilitate generic medicine manufacturers in bringing cheaper versions into new markets. Transparency about the patents companies hold is one element of a responsible IP strategy.

Broadly speaking, information about the status of patents should be available and accessible from country-level patent offices. However, this is often not the case in LMICs, where the capacities of regulatory systems can be constrained. As a result, a lack of certainty can arise about which patents are in force and where. Critically, this can have a detrimental effect on procurement decisions. Procurers may opt for lower-risk strategies that avoid the supply of generics to countries where patent status is ambiguous, potentially adding unnecessary costs. Conversely, patent transparency gives procurers greater confidence when procuring generic alternatives to patented products. The Foundation assesses whether companies disclose patent status, regardless of product type, checking for information such as patent number, expiry date and jurisdiction.

In recent years, the Foundation has seen a striking shift in the level of transparency about the patents pharmaceutical companies hold (see Figure 28). Merck KGaA was the first company to make such disclosures, in 2014. Today, 17 companies make some level of disclosure about the patents they hold.

LICENSING

Slow but steady increase in voluntary licensing

In 2018, the Foundation reported that the pharmaceutical industry continues to move slowly towards a more access-oriented approach to managing IP. In this context, 'access-oriented' refers to whether a company voluntarily licenses its products on terms that facilitate access, or uses other mechanisms to provide flexibility (i.e., non-assert declarations and non-filing or enforcement pledges).

The Foundation has found consistent growth since 2010 in the number of compounds covered by voluntary licences or non-assert declarations (when products that are no longer under patent are also included). In 2018, this had grown to 29 compounds (see Figure 29). In 2014, the first products for a disease other than HIV/AIDS were licensed (for hepatitis C treatments). Licensing today remains confined to these two diseases.

Since 2012, the Medicines Patent Pool (MPP) has become the main driving force behind quality, proactive voluntary licensing in the pharmaceutical industry (see Figure 30). The Foundation has consistently found that the transparency and flexibility of terms and conditions is highest when the MPP is involved. In 2018, seven companies were found to be involved in licensing activities: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, GSK, Johnson & Johnson and Merck & Co., Inc. Compared to 2012, only AbbVie is new to this group (Roche was in this group in 2012 but is no longer counted as the patent on its licensed product has since expired).

▶Which compounds are available for licensing?

Pro-access licences have been negotiated and applied to a complete suite of HIV/AIDS and hepatitis C medicines, including first- and second-line therapies and products on the WHO Model List of Essential Medicines (WHO EML). Through licences, all first-line WHO pangenotypic regimens for hepatitis C can now be made available in countries in scope through generic supply. Many licensed compounds were approved for use in the last 10 years. Novel patented products for HIV/AIDS and hepatitis C have been the primary candidates for the use of non-exclusive voluntary licences.

Figure 27. Since 2012, four companies have consistently publicly endorsed the Doha Declaration and at least one TRIPS flexibility

The chart shows the proportion of companies that have consistently publicly supported the Doha Declaration and at least one TRIPS flexibility since 2012. On average, ten companies have been found by each successive Index report to give this level of support, with the group of companies changing from year to year.

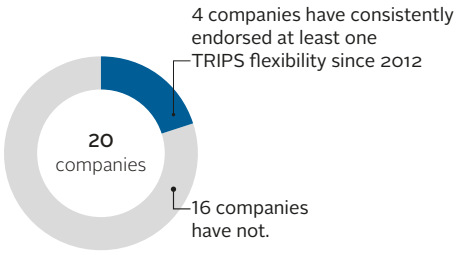
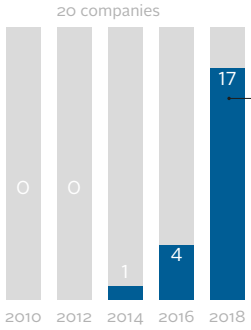


Figure 28. Since 2010, publicly disclosing patent information has become new industry standard

The chart shows how many companies publish at least some information about patent statuses. The first company to take this step was Merck KGaA, followed by AstraZeneca, Novo Nordisk and Gilead in 2016. By 2018, patent transparency could be said to have become standard practice.



16 companies disclose patent information through the Pat-INFORMED online database, an initiative coordinated between IFPMA and WIPO. AstraZeneca and Gilead self-publish patent information online.

Figure 29. Since 2010, number of licensed compounds has steadily increased

The chart shows, at two-year intervals, a cumulative total of the number of products that have been granted non-exclusive voluntary licence agreements or were subject to non-assert declarations. There has been a steady addition of new compounds since 2010 (when products now off patent are also counted).

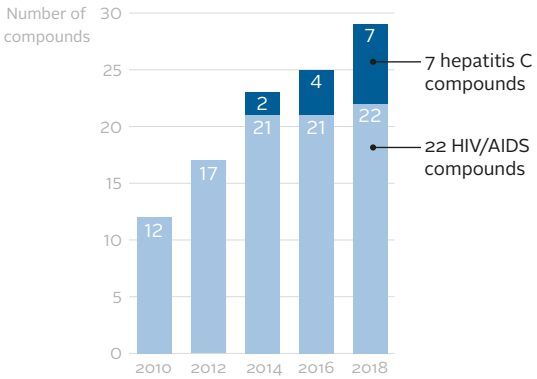


Figure 30. Compared to 2012, more companies are licensing medicines through the Medicines Patent Pool

The chart shows how many companies engage in voluntary licensing through the Medicines Patent Pool (MPP) in 2018 compared with in 2012. The MPP is now the main driving force for continued engagement, and is consistently associated with a push for more access-oriented licence terms.

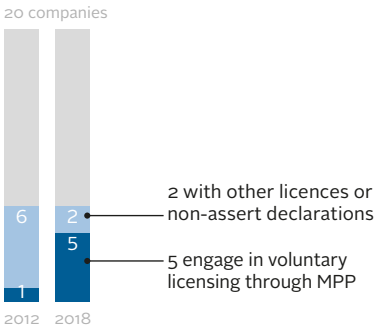


Table 1. Compounds currently with licences or non-assert declarations

The table shows the on-patent products with valid licences or non-assert declarations belonging to companies in scope. All compounds are used to treat either HIV/AIDS or hepatitis C. This table does not include licence agreements or declarations that have expired.

	Compound	Company	Disease	
LICENCES NEGOTIATED VIA MEDICINES PATENT POOL			HIV/AIDS	HCV
	Lopinavir, Ritonavir (adult and paediatric), Glecaprevir, Pibrentasvir	AbbVie	●	●
	Atazanavir, Daclatasvir	Bristol-Myers Squibb	●	●
	Cobicistat, Elvitegravir, Emtricitabine, Tenofovir Disoproxil Fumarate, Tenofovir Alafenamide, Bictegravir	Gilead	●	
	Abacavir, Dolutegravir (adult and paediatric)	GSK (ViiV)	●	
	Raltegravir (paediatric)	Merck & Co., Inc.	●	
NON-ASSERT DECLARATIONS				
	Nevirapine XR	Boehringer Ingelheim	●	
	Darunavir	Johnson & Johnson	●	
PRIVATELY AGREED LICENCES				
	Sofosbuvir, Ledipasvir, Velpatasvir, Voxilaprevir	Gilead		●
	Rilpivirine	Johnson & Johnson	●	

PRICING

Tackling inequity means tailoring strategies to specific communities

Whether a product is 'affordable' depends on who is paying – whether it is a patient and who that patient is, or whether it is another stakeholder in the local healthcare system. In LMICs, up to 70% of spending on medicines is made out of pocket.[1] Many people rely heavily on privately funded health services. Governments and insurance companies do not always cover the full cost of treatment. Even in middle-income countries (MICs), many millions of people living in poverty still face such issues.

Since at least 2014, almost all companies evaluated (18 out of 20) have been using equitable pricing strategies in some form. To qualify as 'equitable', a strategy cannot comprise discounting alone; strategies must include concrete steps for assessing the affordability of discounted prices.

The Index examines two types of equitable pricing strategies: inter-country strategies, where prices are set at the national level based on, e.g., GDP or GNI per capita; and intra-country strategies, where different prices are set within a country for different population segments, e.g., to reflect differences between the private and public sectors. Intra-country strategies are considered to be more sensitive to the ability to pay of a greater range of populations, especially when universal health coverage is not in place.

Increase in pricing strategies meeting key criteria

In 2014 and again in 2016, one third of products evaluated were covered by an equitable pricing strategy (see Figure 31). In 2018, this increased by 10% to 43% (447 out of 1,036 products).

More products are now meeting all of the criteria used by the Index to assess the depth of pricing strategies, increasing from 5% in 2016 to 18% in 2018 (see Figure 32). The Foundation began gathering data on these criteria in 2016.

This notable shift indicates that companies are beginning to think more strategically about how to improve affordability for people in LMICs. However, more progress is required to reach a higher proportion of products in scope of the Index, as 57% still lack any form of equitable pricing strategies.

To improve affordability, companies must take account of socioeconomic factors affecting the target population segments when setting prices, including disease burden, healthcare financing and healthcare infrastructure.

There are models of good practice for companies to adopt. In 2018, three companies provided evidence that they use specific tools when determining prices for different populations. For example, AstraZeneca assesses an individual's ability to pay based on a variety of socioeconomic factors in Brazil; Takeda has developed a tool for assessing people's ability to pay for products for Hodgkin's Lymphoma and inflammatory bowel disease in countries including the Philippines; and Novartis uses a framework to determine price segmentation and develop patient access programmes for countries in scope.

Figure 31. Compared to 2014, equitable pricing strategies are applied to more products

The chart shows the increasing use of equitable pricing strategies over time. The proportion of products with equitable pricing strategies has grown from 33% to 43% since 2014.

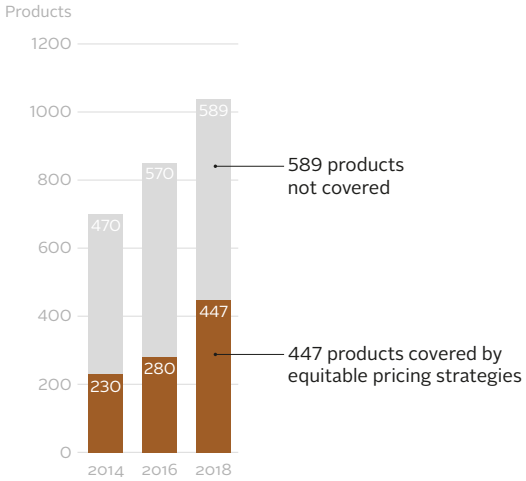
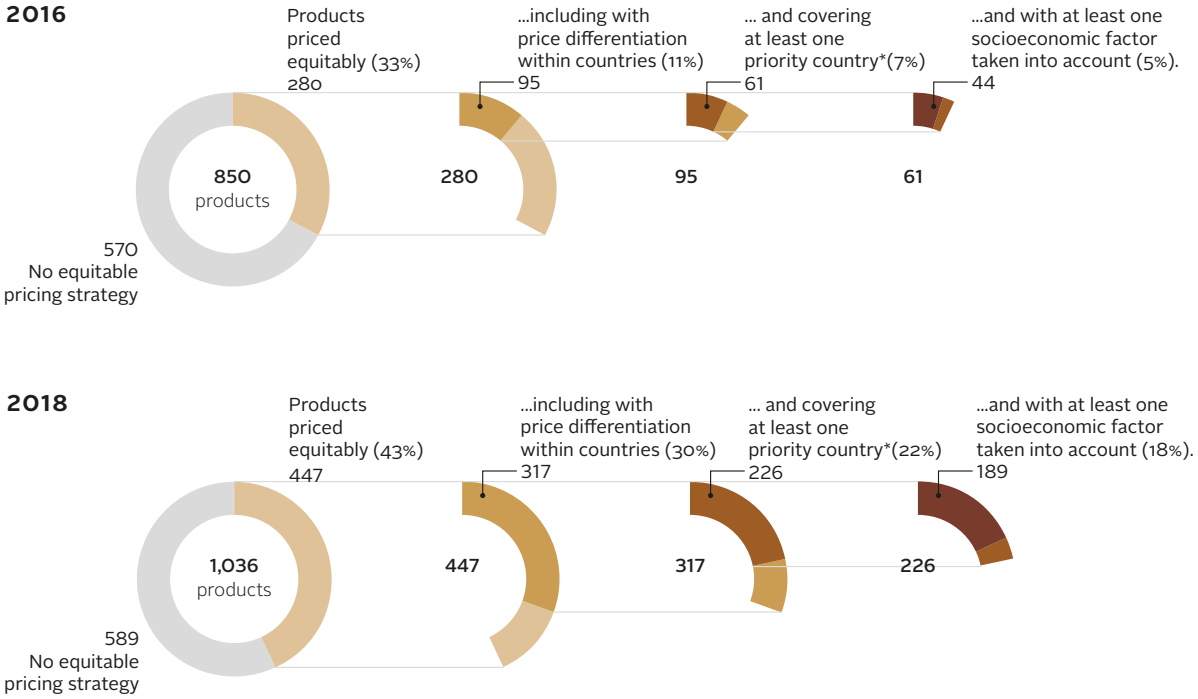


Figure 32. Since 2016, coverage of needs-based pricing strategies has remained limited

The top figure breaks down the coverage of equitable pricing strategies in 2016, showing how many products' strategies meet all key criteria looked for by the Foundation. The lower figure shows the same breakdown in 2018, when more products are attached to equitable pricing strategies, and more strategies meet all criteria, although 57% of all products examined still lack any form of equitable pricing strategies.



*Priority countries have been identified by the Foundation as having among the highest burdens for the disease in question, based on WHO data (2012), or IHME data (2015), and adjusted for multi-dimensional inequality (UNDP, 2012).

IN-COUNTRY ACCESS INITIATIVES

Companies are scaling up some on-the-ground activities

Hundreds of millions of people worldwide live on very low incomes, and have no access to the robust health systems needed in order for health products to be deployed, prescribed and administered efficiently. These people can neither afford nor access the medicines they need. This section looks at two ways in which pharmaceutical companies can directly address these barriers for specific populations and communities: inclusive business models and capacity building.

An 'inclusive' business model is one that explicitly aims to include people on very low incomes in its customer base. Inclusive models are either cost-neutral or, ideally, commercially sustainable. Such models can complement pricing, licensing and donations initiatives to address the accessibility and affordability of health products for specific populations.

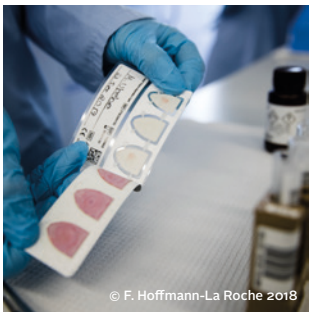
Capacity-building activities may include training for healthcare providers, such as nurses, or programmes to reduce stock-outs and other supply chain issues. Large pharmaceutical companies have the expertise and the capacity to strengthen local health systems, provided initiatives are carried out with appropriate partners. Companies' initiatives are expected to address local needs, have processes in place to avoid conflicts of interest, have clear goals and objectives, measure outcomes and/or impact and aim for sustainable models and long-term impact.

Over the past ten years, on-the-ground initiatives have evolved as global health priorities have shifted. There is now a greater emphasis on expanding access to essential medicines for NCDs and on strengthening in-country capacity to sustain this expansion. In some cases, companies are working to scale up existing projects deemed to be a success. However, in recent years, the global health community has identified a need for companies to report publicly on outcomes and to begin to measure the true impact of such projects. Impact measurement is now recognised as key for achieving broader and more rapid access. Some companies, such as Novartis and Novo Nordisk, publicly report on the results of their efforts and several others have recently made commitments to doing so.

INCLUSIVE BUSINESS MODELS

Use of inclusive business models appears to be expanding

The Foundation has identified inclusive business models since 2014, when it first evaluated innovative business models and captured six such models. The number of models has remained more or less constant since then, and in 2018, the Index identified five companies with six inclusive business models that had been scaled up or newly launched since the 2016 Index. Five of these are pre-existing models that are being expanded with the aim of reaching more people. These are encouraging signs that inclusive business models can be, and are, successful and sustained long-term. Table 1 sets out the ten inclusive business models identified by the Index since 2014 that are currently running. The longest-running models are Novartis' Health Family programme, which started in 2007, and Novo Nordisk's Base of the Pyramid programme, which started in 2010. Eight of these models have been scaled up since they first started.



Through GAP, Roche is expanding access to the plasma separation card for HIV viral load testing. GAP is being run with UNAIDS, the Clinton Health Access Initiative (CHAI), the President's Emergency Plan for AIDS relief (PEPFAR) and the Global Fund.

Eli Lilly's LEAP builds capacity of primary care physicians to manage patients' diabetes. The LEAP model provides training for primary care physicians in China to increase their confidence and skills in managing diabetes across all stages of the disease. The programme currently targets the middle class in China.

Table 2. Companies are running and scaling up a range of inclusive business models
The table sets out inclusive business models highlighted by the Index since 2014 that are either still running or being scaled up. In 2018, the Index identified five companies with six inclusive business models that had been scaled up or newly launched since the 2016 Index.

Company	Programme	Model	Scope or scale up since launch	Started in:
Eli Lilly	Lilly Expanding Access for People (LEAP)	Lilly Expanding Access for People (LEAP) builds capacity in diabetes care.	Scale up: to 14 provinces in China; from 13 in 2016	2015
GSK	Live Well	Live Well social enterprise model builds and supports local distributor networks.	Scale up: to 20 communities in Zambia, from four in 2016	2015
Merck & Co., Inc.	Programme Sambhav	The programme offers zero-interest, no-collateral loans for eligible patients with hepatitis C and a disease management option.	Runs in 11 cities in Punjab, India	2012
Merck KGaA	Suswastha*	Community-level meetings and educational health programmes run by healthcare professionals, as well as products based on needs in its target areas and with adapted price bands.	Scale up: to multiple communities across India in 2016	2013
	Curafa™	Curafa™ programme establishes local primary healthcare centres.	Runs in five counties in Kenya (new)	2018
Novartis	ComHIP	ComHIP programme enables people with hypertension to access diagnosis and care at the community level.	Scale up: to three districts in Ghana, from two in 2016	2015
	Healthy Family	Health camps focused on disease prevention, awareness and treatment, tailored to local health priorities and customs, including a wide range of essential medicines.	Scale up: to at least four countries (Cameroon, India, Kenya and Vietnam), from one, India, in 2007	2007
	Novartis Access	Novartis Access uses portfolio approach to address affordability for products for non-communicable diseases.	Scale up: to three additional countries (Pakistan, Rwanda and Uganda), from two in 2016 (Ethiopia and Kenya)	2015
Novo Nordisk	Base of the Pyramid	Project to improve diabetes care for the working poor by providing training to healthcare professionals, patient education to improve self-management, and addressing a stable, affordable supply of insulin.	Scale up: to five countries (Ghana, India, Kenya, Nigeria and Senegal) in 2013	2010
Roche	Global Access Program	Roche Global Access Program provides better access to diagnostic testing for HIV/AIDS in 82 countries.	Scale up: to 82 countries and more products for HIV/AIDS testing; and to hepatitis C testing	2015

*Since the acquisition of Merck KGaA's consumer health business by Procter & Gamble in 2018, Suswastha is no longer a Merck KGaA initiative.

FOCUS ON AFRICA

Capacity building and inclusive business models concentrated in sub-Saharan Africa

Seven of the ten inclusive business models are operating in one or more sub-Saharan African countries. These include models with a focus on enhancing early diagnosis, establishing primary healthcare centres, improving last mile supply chains and providing low cost medicines. These initiatives generally focus on one or a few countries, usually LMICs.

The Index first noted an increase in company interest and strategic initiatives in African countries in 2014: nine companies (AstraZeneca, Bayer, GSK, Merck and Co. Inc., Merck KGaA, Novartis, Novo Nordisk, Takeda and Sanofi) reported strategically tailoring or re-focusing their activities in sub-Saharan Africa. These activities included, for example, establishing new business units or strategies focused on the continent, strengthening companies' physical presence in Africa (by, e.g., setting up legal entities, local offices, subsidiaries or affiliates), expanding into more African countries, investing in local manufacturing capacity, engaging in new research partnerships or setting up new access programmes that target underserved populations and address local challenges.

African countries are also the focus of companies' efforts to build capacities in local healthcare systems and supply chains. These initiatives are diverse. As an example, Takeda works with the Kenyan Ministry of Health and other partners to ensure more people can access cancer care services. In Ghana, Merck KGaA is working with partners including the government to establish a new local vaccine manufacturing plant. Capacity building efforts are critical for advancing universal health coverage (UHC).

Companies generally invest in capacity building in markets where they have a strategic or commercial interest. In the 2018 Access to Medicine Index analysis (covering 106 countries, mainly LMICs, including 50 of the 54 countries in Africa), Kenya has the most capacity-building initiatives, followed by South Africa and then China. Overall, the Index identified and analysed 141 capacity building initiatives in African countries. The Index only analysed initiatives that meet local needs for specific capacities. Only one country in Africa in this analysis (Equatorial Guinea) has no initiative that qualified for analysis.

Novartis Healthy Family runs programmes in Cameroon, India, Kenya and Vietnam, with a focus on prevention, awareness and treatment. Programmes are tailored to local health priorities and customs and include a wide range of essential medicines.

A Senegalese healthworker checks stock levels as part of an initiative to improve stock management, part of the Merck & Co., Inc. 'Informed Push Model'. This model removes the burden of tracking and ordering inventory from pharmacies by using logistics operators to regularly deliver and track supplies to ensure sufficient stock.

With PATH (a global health NGO), Novo Nordisk implemented its No Empty Shelves project in 2014 to assess supply chain strengths and bottlenecks, as well as availability and affordability of essential medicines and technologies (EMTs). Data were collected in health facilities and pharmacies in Senegal to identify access barriers.

In Nampula, Mozambique, a healthworker uses GSK's mVacciNation mobile technology to improve patient-record keeping. GSK's mVacciNation programme started in Mozambique, where GSK tested whether mobile technologies can help increase childhood immunisation, in partnership with the Ministry of Health.

Table 3. Capacity building initiatives identified as best practices in 2018

The table sets out the capacity building initiatives identified in the 2018 Access to Medicine Index as best practices, each of which is currently running in at least one African country from the companies in scope. There are 12 initiatives from six companies, in three areas of capacity building. These best practices are typically initiatives that have been tested and proven, and some examples include initiatives that have been successfully scaled up from pilots.

Company	2018 Best Practice	Started in:	Currently active in:
R&D			
GSK	**Africa NCD Open Lab:** A notable number of collaborations with African institutions to assess, support and improve NCD research.	2014	Sub-Saharan Africa, including Cameroon, Ethiopia, Ghana, Kenya, Malawi, Mozambique, Nigeria, South Africa, Tanzania and Uganda
Johnson & Johnson	**Ugandan Academy for Health Innovation and Impact:** A public institute that supports the development of scientists in Africa and conducts its own research.	2015	Uganda
Takeda	**R&D AtM Employee Fellowship Program:** Employee fellowship programme that enters long-term engagements with selected NGOs.	2016	Haiti, Kenya and Tanzania
SUPPLY CHAIN			
GSK	**mVacciNation:** A successfully scaled-up mobile technology platform that tracks vaccine stock data in remote locations.	2012	Mozambique, Nigeria and Tanzania
Merck & Co., Inc.	**Informed Push Model:** Model removes the burden of tracking and ordering inventory from pharmacies by using logistics operators to regularly deliver and track supplies to ensure sufficient stock.	2013	Senegal
Novartis	**SMS for Life 2.0:** Enhanced mobile technology supply chain management system now utilising new technologies and expanding to countries and a wider range of products.	2009	Nigeria, Pakistan and Zambia
Novo Nordisk	**No Empty Shelves:** Partnership to assess supply chain strengths and bottlenecks, as well as availability and affordability of essential medicines and technologies (EMTs).	2014	Kenya and Senegal
Novo Nordisk	**The Base of the Pyramid (BoP):** Initiative to improve access to diabetes care reaches three new countries.	2012	Ghana, Kenya, Nigeria and Senegal
HEALTH SYSTEM STRENGTHENING			
GSK	**GSK and Save the Children partnership:** A wide range of projects through a global partnership with Save the Children, with the stated aim of helping one million children access needed medicine and vaccines.	2013	28 countries: Benin, Burkina Faso, Cambodia, Côte D'Ivoire, Dominican Republic, DRC, Ethiopia, Guatemala, Haiti, Honduras, India, Kenya, Liberia, Mali, Mexico, Myanmar, Niger, Nigeria, Senegal, Sierra Leone, South Africa, Sri Lanka, Sudan, Syria, Togo, Uganda, Vietnam and Yemen
Johnson & Johnson	**The New Horizons: Advancing Pediatric HIV Collaborative:** Collaborative initiative aimed at advancing paediatric HIV/AIDS care, particularly for those failing treatment.	2013	9 countries: Ethiopia, Kenya, Lesotho, Rwanda, South Africa, Swaziland, Uganda, Zambia and Zimbabwe. Additionally, in collaboration with Right to Care, Janssen, owned by parent company Johnson & Johnson, supported drug resistance workshops in Malawi (2016 and 2017), Mozambique (2016) and Nigeria (2018).
Merck & Co., Inc.	**Merck for Mothers/MSD for Mothers:** A USD 500 million, 10-year initiative to design scalable solutions to help end preventable maternal deaths.	2011	More than 30 countries, with a particularly strong focus on several countries in scope of the Index including Ethiopia, India, Mexico, Senegal, Tanzania, Uganda and Zambia.
Novartis	**Strengthening care at the community level:** *-Healthy Family* *-Community Health Educator Replication CHER II program* *-Health Express, Jian Kang Kuai Che (JKKC)* In the past 10 years, Novartis has run initiatives alongside government health ministries and local NGOs to ensure it tailors healthcare activities to local needs.	2007	Cameroon, Kenya, India and Vietnam (Healthy Family) Kenya (CHER II) China (Health Express , JKKC)

APPENDIX I

Methodology for this report

The Access to Medicine Index is the longest-running research programme at the Access to Medicine Foundation. The first Index was published in 2008. Since then, it has been published every two years as a relative ranking of twenty of the largest global research-based pharmaceutical companies, based on their policies and practices to improve access to medicine in low- and middle-income countries.

The Index methodology is developed through a process that systematically draws together the views of NGOs, governments, investors, the pharmaceutical industry and multi-lateral organisations to build a consensus, ratified by the Expert Review Committee for the Index, on how and where pharmaceutical companies can and should be improving access to medicine.

The findings of this longitudinal progress report incorporate the data collected across multiple iterations of the Access to Medicine Index by the Access to Medicine Foundation, using various methods to establish trends in access-to-medicine activities from the pharmaceutical industry over the past ten years. These methods, and their associated limitations, are detailed in this section. A more extensive detailing of how the Index assesses data and compares companies, and any associated limitations which may also apply to this study, can be found in the 2017 Access to Medicine Index Methodology and on pages 229 and 230 in Appendix IX of the 2018 Access to Medicine Index.[1,2]

Data availability

The quality of data obtained from companies varies, especially with regards to commercially sensitive data. Some data were provided under non-disclosure agreements (NDAs). Where data are provided under NDA, it is reported on in aggregate. If aggregate reporting is not possible, these data are excluded from the analysis. For example, the content of R&D contracts, early-stage research and investment information may be revealed more cautiously by companies. This variation can be an obstacle to finding and reporting reliable, industry-wide trends and specific relationships and conclusions in certain areas. In some areas, it was not possible to provide a more complete picture of the area of analysis due to these kinds of external constraints on the collection of data.

Where possible for each iteration of the Access to Medicine Index, data validation using external published sources was performed to verify company submissions. Additionally, companies were invited to fact check certain numbers and statements in this report (e.g., market approvals since 2008) prior to publication to ensure accuracy.

Identifying data points for longitudinal analysis

The framework of indicators the Index employs to assess companies was reviewed to identify data points that were measured across successive iterations of the Index without change. This produced a subset of consistent data points that would allow for longitudinal trend identification. Where data points were not measured across all iterations of the Index, the earliest available point of measurement possible was used. Where a narrower timeframe of comparison is used, this is indicated in the text. For example, engagement in neglected tropical diseases (NTDs) product donations has been measured since 2010, as has engagement in NTD research and development. Refinements in the analysis and evaluation of equitable pricing were made in 2014, and in 2016; progress and regress in this area can only be compared when taking these changes into account. An analysis of company internal control frameworks was introduced in 2018 and is therefore an example of a set of data points not included within this analysis, as progress or regress could not be shown over time.

Information used in the development of this progress report extends between the start of the period of analysis for the 2010 Index (January 2008) to the close of the period of analysis for the 2018 Index (May 2018). The 2010 and 2012 iterations of the Index were based on fiscal years. From the 2014 Index onwards, the period of analysis was fixed to 1 June of the year in which one Index was published to 31 May of the year in which the next Index was to be published (e.g., the period of analysis for the 2018 Access to Medicine Index extended from 1 June 2016 to 31 May 2018). An exception to this timeframe was for the analysis of new medicine approvals, for which approvals of new medicines by the European Medicines Agency (EMA), US Food and Drug Administration (FDA) and Japanese Pharmaceuticals and Medical Devices Agency (PMDA) were assessed between 1 January 2008 and 31 December 2018.

Maintaining the disease scope of the Index

The disease scope of the Index is updated every two years to reflect the evolving disease burdens and priorities unique to low- and middle-income countries (LMICs), then ratified by an Expert Review Committee comprised of a range of expert stakeholders. In 2008, the Access to Medicine Index primarily focused on NTDs as defined by WHO, expanding to include high-burden diseases including non-communicable diseases (NCDs) in 2010. The latest major addition to the disease scope was the inclusion of a group of cancers in the 2018 Access to Medicine Index.

To facilitate longitudinal trend analysis in this report, the disease scope was held constant when possible to allow for consistency in different analyses throughout the report, as indicated in the text. This is particularly of note in areas of the report that focus on the breadth and depth of company activity in certain disease areas (such as the R&D section), where the 2014 Access to Medicine Index disease scope was held constant for much of the analysis. Osteoarthritis, in scope in 2014, was removed from this analysis as this disease was excluded from the disease scope from 2016 onwards.

For this reason, the figures presented in this report often cannot be directly compared with analogous figures in the 2018 Access to Medicine Index, as they only include a subset of disease data. In general, trends were established using a fixed disease scope, as described in each section of the report. This scope varies between and within sections, but mainly, the 2014 disease scope was utilised in the R&D and NTDs sections of the report, and the 2018 disease

scope was utilised in the product deployment section of the report. However, some exceptions to this approach exist, as noted later in this methodology.

Specific approaches

Most of the analyses conducted for this report follow the previously mentioned approaches. This section includes specific approaches taken for some of the more complex data sets and the unique limitations related to these analyses.

Disease and country comparability in product deployment technical areas

Similar to how the disease scope has changed between iterations of the Index, the geographic scope has expanded or narrowed with each publication to best capture the countries where greater access to medicine is needed most. Some countries have moved into higher World Bank classifications over the timespan of the Index to date, while some upper middle-income countries have been added in more recent iterations of the Index as a reflection of high levels of socioeconomic inequality in these countries. Between the 2016 and 2018 iterations of the Index, for example, three countries (Georgia, Jamaica and Panama) were removed and two countries (Tonga and Tunisia) were newly included to reflect changes in inequality measurements and World Bank classifications.

The outputs analysed in the product deployment technical areas of this report relate to the geographical, disease, product and company scopes determined by the Expert Review Committee (ERC) during the methodology review process and as published in the 2017 Access to Medicine Index Methodology. For this analysis, the disease and country scopes were not held constant, as the product deployment technical areas measure the proportion of equitable pricing strategies across company portfolios over time. Even when removing newly in-scope products due to disease scope expansions from the analysis, the increase in the percentage of products with equitable pricing strategies remains notable. This analysis is thus intended to provide a more comprehensive picture of how companies are pricing products across a larger portfolio. This approach is also intended to maintain consistency with other Foundation publications in which the same charts are shown.

Analysis of compounds licensed

To accurately capture the net number of compounds licensed since 2010, the Foundation validated previously reported Index data points by reviewing external information pertaining to specific compounds retrieved from both the Medicines Patent Pool as well as the Research Handbook on Intellectual Property Licensing.[3,4] Individual compounds owned by companies in scope of the Index that have non-assert declarations or non-exclusive voluntary licences applied are included. Some companies may own the rights to products with multiple compounds, for example a double- or triple-combination therapy. In these cases, each individual compound is included in the analysis. The net number of compounds also includes those with patents or agreements that have since expired, even though those licences or agreements are no longer needed. These compounds are included for analysis to demonstrate the total instances of action from companies in scope of the Index since 2010.

Market approval analysis

For the purposes of assessing products developed by the 20 companies examined by the Index that have received market approval, the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (referred to as 'the Orange Book') and lists of approved products by the EMA and PMDA were utilised.[5-7] The contents of the Orange Book exclude vaccines and some therapeutic biological agents that can be found in the FDA Center for Drug Evaluation and Research's List of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (referred to as 'the Purple Book').[8]

Medicines that received an approval from one or more of these stringent regulatory authorities between 1 January 2008 and 31 December 2018 were included for analysis if they targeted a disease in scope: the diseases and conditions looked at by the 2018 Access to Medicine Index, with the exception of cancer. Cancer was excluded from the registration analysis to ensure that the overview of products brought to market by the 20 companies in scope since 2008 aligned closely to the Index disease scopes from previous cycles, and to aid comparison. The 2014 Index disease scope was predominantly used in the R&D analyses of this report.

For this analysis, only new medicines were included, and only new approvals for the four Japanese companies were referred to when examining PMDA approvals, as direct comparison between American/European and Japanese approvals before and during the period of analysis was not always possible. This analysis thus shows an incomplete portrayal of all new approvals in the past ten years but allows for the analysis and presentation of the trends for what information is available.

Additionally, the number of new market approvals that have access initiatives in place was limited by factors including incomplete information regarding equitable pricing strategies for older products, the analytical framework for which was substantially changed in the 2014 Index, and regarding what access initiatives were in place for some newer formulations of existing medicines. This led to the reporting of a more conservative value of new medicines with access initiatives from 2008 to 2018.

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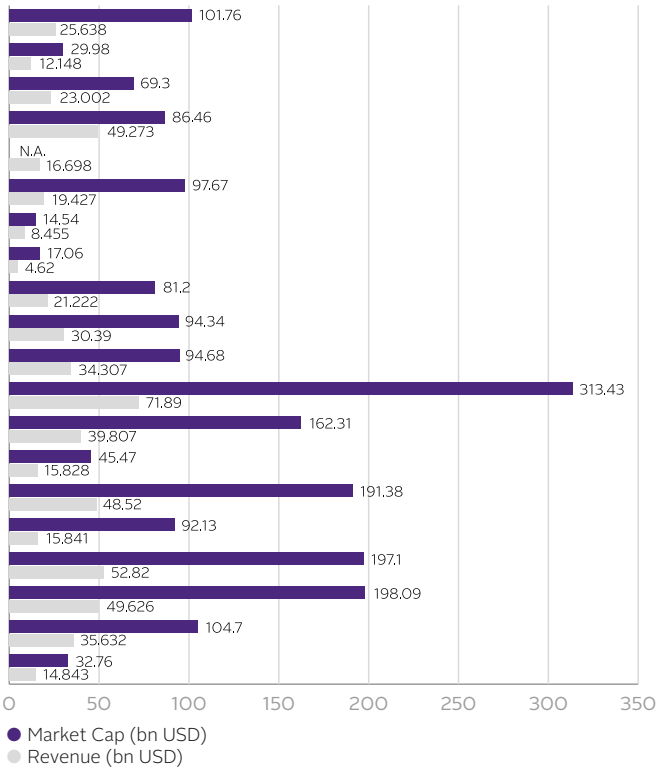
APPENDIX IV

Pharmaceutical companies in scope

The Access to Medicine Index assesses 20 of the world's largest research-based pharmaceutical companies on their policies and practices to improve access to medicine for people living in low- and middle-income countries. Considering their size, resources, pipelines, portfolios and global reach, these companies have a critical role to play in improving access to medicine. The Index has measured these companies for 12 years, meaning their performance can be tracked over time. Pharmaceutical companies that exclusively produce generic medicines remain excluded from the Index in 2018. The Access to Medicine Foundation recognises that generic companies play a significant role in access to medicine, particularly in low- and middle-income countries. Generic medicines marketed by the 20 research-based companies or any of their generic medicine subsidiaries in which they have more than 50% ownership are included for analysis.

Table 4. Market cap & revenue of companies listed in the 2018 Access to Medicine Index

Company	Ticker	Country	Market Cap (bn USD)	Revenue (bn USD)
AbbVie Inc.	ABBV	USA	101.76	25.638
Astellas Pharma Inc.	4503	JPN	29.98	12.148
AstraZeneca plc	AZN	GBR	69.3	23.002
Bayer AG	BAYN	DEU	86.46	49.273
Boehringer Ingelheim GmbH	N/A	DEU	N/A	16.698
Bristol-Myers Squibb Co.	BMY	USA	97.67	19.427
Daiichi Sankyo Co. Ltd.	4568	JPN	14.54	8.455
Eisai Co. Ltd.	4523	JPN	17.06	4.62
Eli Lilly & Co.	LLY	USA	81.2	21.222
Gilead Sciences Inc.	GILD	USA	94.34	30.39
GlaxoSmithKline plc	GSK	GBR	94.68	34.307
Johnson & Johnson	JNJ	USA	313.43	71.89
Merck & Co., Inc.	MRK	USA	162.31	39.807
Merck KGaA	MRK	DEU	45.47	15.828
Novartis AG	NOVN	CHE	191.38	48.52
Novo Nordisk A/S	NOVO B	DNK	92.13	15.841
Pfizer Inc.	PFE	USA	197.1	52.82
Roche Holding AG	ROG	CHE	198.09	49.626
Sanofi	SAN	FRA	104.7	35.632
Takeda Pharmaceutical Co. Ltd.	4502	JPN	32.76	14.843



*Source: Bloomberg terminal 2017
**Exchange rate 31 Dec 2016 vs USD, from oanda.com

APPENDIX V

Disease scope of the 2018 Access to Medicine Index

Diseases are included based on their global burden of disability-adjusted life years (DALYs)[1], other WHO classifications and the relevance of pharmaceutical interventions. Index diseases are defined according to the WHO International Classification of Diseases, 10th Revision (ICD-10) codes. The disease scope for the 2018 Index has expanded from 51 to 77 diseases, conditions and pathogens. Cancer is now in scope. 12 pathogens have been brought into the disease scope for the 2018 Index R&D analysis. These have been identified by the WHO priority pathogens list. Pathogens on this list are deemed by WHO as priority R&D targets for new and effective antibiotics active against the pathogens themselves and the diseases they cause. This WHO priority pathogens list does not define specific products needed. R&D projects targeting these pathogens are grouped under 'Other prioritised antibiotic-bacterial infections' in figures and tables. DALY burden and mortality data was collected from WHO's 2015 Global Health Estimates (GHE).

Table 5. Diseases, conditions and pathogens in scope of the 2018 Access to Medicine Index

NON-COMMUNICABLE DISEASES (14)	TOTAL DALYS (LICS & MICS)
Anxiety disorders	17,637,255
Asthma	22,489,628
Bipolar affective disorder	6,542,313
Cancer	DALY not applicable
Chronic obstructive pulmonary disease (COPD)	59,841,914
Diabetes mellitus	53,660,514
Epilepsy	12,610,507
Hypertensive heart disease	17,053,619
Ischaemic heart disease	137,803,915
Kidney diseases	30,361,404
Migraine	19,608,650
Schizophrenia	11,707,269
Stroke	113,999,836
Unipolar depressive disorders	40,359,896

COMMUNICABLE DISEASES* (21)	TOTAL DALYS (LICS & MICS)
Arenaviral haemorrhagic fevers (including Lassa fever)	N/A
Coronaviruses (including MERS-CoV and SARS-CoV)	N/A
Crimean-Congo haemorrhagic fever (CCHF)	N/A
Diarrhoeal diseases	83,764,595
Filoviral diseases (Ebola and Marburg)	N/A
Henipaviral diseases (including Nipah virus)	N/A
HIV/AIDS	59,213,043
Leptospirosis	N/A
Lower respiratory infections	131,150,237
Malaria	38,491,119
Measles	12,264,045
Meningitis**	22,781,461
Other prioritised antibiotic-resistant bacterial infections	N/A
Pertussis	5,950,007
Rheumatic fever	N/A
Rift Valley fever (RVF)	N/A
Severe fever with thrombocytopenia syndrome (SFTS)	N/A
Sexually transmitted infections (STIs)***	10,092,695
Tetanus	4,662,932
Tuberculosis	54,332,361
Viral hepatitis (B and C)†	24,703,328
Zika	N/A

NEGLECTED TROPICAL DISEASES (20)	TOTAL DALYS (LICS & MICS)
Buruli ulcer	DALY not available in GHE 2016
Chagas disease	191,781
Dengue and chikungunya	2,575,517
Dracunculiasis	DALY not available in GHE 2018
Echinococcosis	607,742
Food-borne trematodiases	DALY not available in GHE 2015
Human African trypanosomiasis	371,657
Leishmaniasis	1,346,249
Leprosy	484,820
Lymphatic filariasis	2,069,423
Mycetoma, chromoblastomycosis and other deep mycoses	DALY not available in GHE 2019
Onchocerciasis	1,135,571
Rabies	1,654,232
Scabies and other ectoparasites	DALY not available in GHE 2020
Schistosomiasis	3,478,062
Snakebite envenoming	DALY not available in GHE 2021
Soil transmitted helminthiasis	4,179,035
Taeniasis/cysticercosis	1,846,098
Trachoma	275,741
Yaws	DALY not available in GHE 2017

MATERNAL AND NEONATAL HEALTH CONDITIONS (10)	TOTAL MORTALITY (LICS & MICS)
Abortion	30,886
Birth asphyxia and birth trauma	726,826
Contraceptive methods	Mortality not applicable
Hypertensive disorders of pregnancy	46,270
Maternal haemorrhage	82,447
Maternal sepsis	17,399
Neonatal sepsis and infections	342,069
Obstructed labour	23,020
Other neonatal conditions	208,149
Preterm birth complications	768,639

Green text = newly in scope for the 2018 Index
Exclusions: none in 2018

* The 11 communicable diseases with the highest DALY burdens in countries in scope of the 2018 Index, plus 10 further diseases and 12 pathogens (grouped under 'other prioritised antibiotic-resistant bacterial infections') that have been identified as R&D priorities. Neglected tropical diseases, while also communicable, are highlighted separately throughout the Index.
** Projects targeting cryptococcal meningitis are included for the analysis of specified R&D priorities.
*** Includes chlamydia, genital herpes, gonorrhoea, syphilis and trichomoniasis.
† Includes acute hepatitis (B and C) and cirrhosis caused by hepatitis (B and C).

REFERENCE

1 World Health Organization. Global Health Estimates 2015: Disease burden by Cause, Age, Sex, by Country and by Region, 2000-2015. 2016. http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html

APPENDIX VI

Countries in scope of the 2018 Access to Medicine Index

The geographic scope for the 2018 Access to Medicine Index comprises 106 countries. All countries defined by the World Bank as low income or lower middle-income are included.[1] All countries defined by the UNDP as either low or medium human development are included.[2] This ensures that several central measures of human development (life expectancy, education and standard of living) are taken into account. All countries that receive a score of less than 0.6 on the UN Inequality-Adjusted Human Development Index are included.[2] This measure takes account of how health, education and income are distributed within each country. Finally, all Least Developed Countries (LDCs), as defined by the Committee for Development Policy of the UN Economic and Social Council (ECOSOC), are included.[3]

Table 6. Countries in scope of the 2018 Access to Medicine Index

Country	*Classification*
EAST ASIA & PACIFIC	
Cambodia	LMIC
China	HiHDI
Indonesia	LMIC
Kiribati	LMIC
Korea, Dem. People's Rep.	LIC
Lao PDR	LMIC
Micronesia, Fed. Sts.	LMIC
Mongolia	LMIC
Myanmar	LMIC
Papua New Guinea	LMIC
Philippines	LMIC
Samoa	LMIC
Solomon Islands	LMIC
Timor-Leste	LMIC
Thailand	HiHDI
■ Tonga	LMIC
Tuvalu	LDC
Vanuatu	LMIC
Vietnam	LMIC
EUROPE & CENTRAL ASIA	
Armenia	LMIC
Kosovo	LMIC
Kyrgyz Republic	LMIC
Moldova	LMIC
Tajikistan	LMIC
Turkmenistan	MHDC
Ukraine	LMIC
Uzbekistan	LMIC
LATIN AMERICA & CARIBBEAN	
Belize	HiHDI
Bolivia	LMIC
Brazil	HiHDI
Colombia	HiHDI
Dominican Republic	HiHDI
Ecuador	HiHDI
El Salvador	LMIC
Guatemala	LMIC
Guyana	MHDC
Haiti	LIC
Honduras	LMIC
Mexico	HiHDI
Nicaragua	LMIC
Paraguay	MHDC
Peru	HiHDI
Suriname	HiHDI
MIDDLE EAST & NORTH AFRICA	
Djibouti	LMIC
Egypt, Arab Rep.	LMIC
Iran	HiHDI
Iraq	MHDC
Morocco	LMIC
Palestine, State of/West Bank Gaza	LMIC
Syrian Arab Republic	LMIC
■ Tunisia	LMIC
Yemen, Rep.	LMIC
SOUTH ASIA	
Afghanistan	LIC
Bangladesh	LMIC
Bhutan	LMIC
India	LMIC
Maldives	HiHDI
Nepal	LIC
Pakistan	LMIC
Sri Lanka	LMIC
SUB-SAHARAN AFRICA	
Angola	LHDC
Benin	LIC
Botswana	MHDC
Burkina Faso	LIC
Burundi	LIC
Cabo Verde	LMIC
Cameroon	LMIC
Central African Republic	LIC
Chad	LIC
Comoros	LIC
Congo, Dem. Rep.	LIC
Congo, Rep.	LMIC
Côte d'Ivoire	LMIC
Equatorial Guinea	MHDC
Eritrea	LIC
Ethiopia	LIC
Gabon	MHDC
Gambia, The	LIC
Ghana	LMIC
Guinea	LIC
Guinea-Bissau	LIC
Kenya	LMIC
Lesotho	LMIC
Liberia	LIC
Madagascar	LIC
Malawi	LIC
Mali	LIC
Mauritania	LMIC
Mozambique	LIC
Namibia	MHDC
Niger	LIC
Nigeria	LMIC
Rwanda	LIC
São Tomé and Principe	LMIC
Senegal	LIC
Sierra Leone	LIC
Somalia	LIC
South Africa	MHDC
South Sudan	LIC
Sudan	LMIC
Swaziland	LMIC
Tanzania	LIC
Togo	LIC
Uganda	LIC
Zambia	LMIC
Zimbabwe	LIC

■ New inclusion

New inclusions: Tonga & Tunisia (LMICs)
Exclusions: Jamaica (HiHDI >0.6), Panama (HiHDI >0.6), & Georgia (UMIC)

CLASSIFICATION KEY

	Key	Data Source
LIC	Low-income country	World Bank
LMIC	Lower middle-income country	World Bank
LDC	Least Developed Country	ECOSOC (UN Economic and Social Council)
LHDC	Low Human Development	Country UNDP- UN Human Development Index (HDI)
MHDC	Medium Human Development Country	UNDP- UN Human Development Index (HDI)
HiHDI	High Human Development	
	Country with high inequality	UNDP- UN Human Development Index (HDI)

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2 UNDP. Human Development Index. http://hdr.undp.org/en/composite/HDI. Accessed April 30, 2017

3 LDCs at a Glance | Development Policy & Analysis Division. https://www.un.org/development/desa/dpad/least-developed-country-category/ldcs-at-a-glance.html. Accessed April 30, 2017.

Per disease, the set of priority countries includes five low-income countries (World Bank defined) in order to ensure the Index evaluates pricing strategies directed towards poorer countries.

Where data gaps exist, countries are automatically included. If a country has one of the highest DALY burdens for a disease, but its inequality coefficient is unknown or where DALY data for a country does not exist, it is included as a priority country. For example, for Kosovo and Tuvalu, no DALY data is available for any diseases in scope.

For diseases that were in scope in 2016, the priority countries are unchanged. For diseases that are newly in scope, the most current data (WHO, 2015; IHME, 2015; UNDP, 2015) has been used to determine the priority countries.

Iran, Islamic Rep.	Kenya	Kiribati	Korea, Dem. Rep.	Kosovo	Lao PDR	Liberia	Madagascar	Malawi	Maldives	Mali	Mauritania	Mexico	Micronesia, Fed. Sts.	Mozambique	Myanmar	Nepal	Niger	Nigeria	Pakistan	Papua New Guinea	Peru	Philippines	São Tomé & Principe	Senegal	Sierra Leone	Solomon Islands	Somalia	South Africa	South Sudan	Sri Lanka	Sudan	Suriname	Tanzania	Thailand	Timor Leste	Togo	Tonga	Tuvalu	Uganda	Vanuatu	Vietnam	Zambia	Zimbabwe	Disease/condition
																																											Non-communicable
				•												•			•													•				•						Anxiety disorders
				•											•	•		•														•				•	•					Asthma
			•	•												•		•														•				•	•					Bipolar affective disorder
•		•		•								•	•					•	•				•												•	•						Cancer (all except Kaposi Sarcoma)
	•	•		•				•					•	•				•					•					•	•						•	•	•			•	•	Cancer (Kaposi sarcoma)
			•	•												•			•													•				•						Chronic obstructive pulmonary disease
				•								•																				•				•	•					Diabetes mellitus
				•										•				•	•													•				•	•					Epilepsy
			•	•															•													•				•						Hypertensive heart disease
•			•	•												•			•													•				•						Ischaemic heart disease
				•										•				•	•													•				•	•					Kidney diseases
				•												•			•																	•						Migraine
			•	•														•													•				•	•					Schizophrenia
			•	•			•											•																		•						Stroke
				•															•																	•	•					Unipolar depressive disorders
																																											Communicable
			•	•										•				•									•					•				•	•					Chlamydia
				•														•	•												•					•	•					Diarrhoeal diseases
			•	•										•				•										•				•				•	•					Genital herpes
•				•										•				•	•									•		•							•					Gonorrhoea
				•				•					•	•				•								•	•					•		•			•	•	•				HIV/AIDS
				•													•	•	•																		•	•					Lower respiratory infections
				•													•	•																			•	•					Malaria
				•														•	•						•		•											•						Measles
				•						•								•																			•	•					Meningitis
				•														•	•																		•	•					Pertussis
				•														•																			•	•					Syphilis
				•														•	•								•										•						Tetanus
				•										•				•										•									•	•					Trichomoniasis
				•										•	•			•	•							•											•						Tuberculosis
			•	•						•						•		•																			•						Viral hepatitis B
			•	•												•		•	•										•								•	•					Viral hepatitis C
																																											Neglected tropical
	•	•				•		•				•						•		•	•			•	•				•	•		•				•		•					Buruli ulcer
				•								•																									•						Chagas disease
	•				•		•	•	•						•			•	•			•		•				•			•		•	•	•			•		•		•	Chikungunya
				•	•										•							•											•				•							Dengue
	•									•							•	•									•	•	•		•												Dracunculiasis
	•			•																											•						•	•					Human African trypanosomiasis
				•										•				•													•		•				•	•					Leishmaniases
				•			•							•	•	•		•																			•						Leprosy
				•			•			•				•				•														•		•				•	•					Lymphatic filariasis
											•	•					•							•				•				•												Mycetoma, chromoblastomycosis and other deep mycoses
				•		•												•											•	•		•						•						Onchocerciasis
				•													•	•	•									•				•						•						Rabies
			•	•											•	•			•														•					•	•					Scabies and other ectoparasites
	•			•			•							•				•													•	•					•						Schistosomiasis
												•				•		•	•			•																		•					Snakebite envenoming
																		•	•			•											•												Soil-transmitted helminthiases
				•										•				•														•					•	•					Trachoma
																				•						•								•	•			•						Yaws
																																											Maternal & neonatal
				•				•						•				•											•			•					•						Abortion
				•														•	•													•					•	•					Birth asphyxia and birth trauma
				•													•	•					•									•					•	•					Contraceptive methods
				•				•										•										•				•					•						Hypertensive disorders of pregnancy
				•													•	•										•				•					•						Maternal haemorrhage
				•				•		•								•										•				•					•						Maternal sepsis
				•						•							•	•	•												•						•						Neonatal sepsis and infections
				•			•											•										•		•		•					•						Obstructed labour
				•						•							•	•									•										•						Other neonatal conditions
				•						•								•	•													•					•						Prematurity and low birth weight

APPENDIX VII

Priority countries for the 2018 Access to Medicine Index

For each disease and condition in the scope of the 2018 Index, the Index has a defined list of 'priority countries'. These defined lists of countries are used for certain indicators in the Technical Area Pricing, Manufacturing & Distribution.

Priority countries have been identified as having one of the highest burdens for the disease in question, based on WHO data (2012), or IHME data (2015), and adjusted for multi-dimensional inequality (UNDP, 2012).

Table 7. Priority countries

This table shows the priority countries identified for each disease/condition – dots denote priority country status. Individual priority country lists exist for viral hepatitis (B and C) and the sexually transmitted infections included in the scope of the 2018 Index (chlamydia, genital herpes, gonorrhoea, syphilis and trichomoniasis). Countries in the scope of the 2018 Index that have not been designated as priority countries for any disease/condition are not included in this table.

For certain neglected tropical diseases and maternal and neonatal health conditions, where DALY data was not available, other criteria were used. Other criteria were also used to identify priority countries for cancer, to ensure alignment with the inclusion of cancer in the 2018 Index. Where DALY data was not used, Kosovo and Tuvalu are no longer listed as priority countries, unless identified based on the alternative criteria noted below.

Disease/condition	Afghanistan	Angola	Bangladesh	Benin	Bolivia	Brazil	Burkina Faso	Burundi	Cambodia	Cameroon	Central African Rep.	Chad	China	Colombia	Comoros	Congo, Dem. Rep.	Congo, Rep.	Côte d'Ivoire	Ecuador	Egypt, Arab Rep.	El Salvador	Equatorial Guinea	Ethiopia	Gabon	Ghana	Guatemala	Guinea	Haiti	Honduras	India	Indonesia
Non-communicable																															
Anxiety disorders	•		•			•							•			•							•						•	
Asthma			•			•							•			•							•						•	
Bipolar affective disorder						•							•			•							•						•	•
Cancer (all except Kaposi Sarcoma)			•			•							•							•									•	•
Cancer (Kaposi sarcoma)																							•							
Chronic obstructive pulmonary disease			•										•			•							•						•	•
Diabetes mellitus	•					•							•			•							•						•	•
Epilepsy													•			•							•						•	
Hypertensive heart disease	•					•							•			•							•						•	•
Ischaemic heart disease	•					•							•			•							•						•	
Kidney diseases			•										•			•							•						•	
Migraine	•		•			•	•						•			•							•						•	
Schizophrenia						•							•			•							•						•	•
Stroke	•					•							•			•							•						•	•
Unipolar depressive disorders	•					•							•			•							•						•	•
Communicable																															
Chlamydia													•			•							•						•	
Diarrhoeal diseases	•	•										•				•							•						•	
Genital herpes						•							•			•							•						•	•
Gonorrhoea	•															•				•			•						•	
HIV/AIDS																							•						•	
Lower respiratory infections	•															•							•						•	
Malaria		•					•					•				•													•	
Measles	•															•							•						•	
Meningitis		•										•				•							•						•	
Pertussis	•															•							•						•	
Syphilis		•										•				•							•						•	
Tetanus	•	•										•				•							•						•	
Trichomoniasis						•							•			•							•						•	
Tuberculosis	•		•													•							•						•	
Viral hepatitis B			•									•	•			•							•				•		•	•
Viral hepatitis C	•															•				•			•						•	•
Neglected tropical																															
Buruli ulcer		•		•		•	•			•	•		•			•	•	•				•		•	•		•			•
Chagas disease					•	•								•							•					•		•	•		
Chikungunya				•				•	•	•	•				•	•						•					•			•	•
Dengue						•			•							•							•					•		•	•
Dracunculiasis		•										•				•		•					•		•						
Human African trypanosomiasis											•	•				•											•				
Leishmaniases			•													•							•						•	
Leprosy						•							•	•		•							•						•	
Lymphatic filariasis																		•												•	•
Mycetoma, chromoblastomycosis and other deep mycoses																														•	
Onchocerciasis										•	•	•				•							•								
Rabies	•											•				•							•						•	
Scabies and other ectoparasites						•							•			•							•						•	•
Schistosomiasis																•							•							
Snakebite envenoming	•		•										•			•							•		•				•	•
Soil-transmitted helminthiases			•										•			•							•						•	•
Trachoma							•						•							•			•							
Yaws				•						•	•					•	•	•	•						•					•	•
Maternal & neonatal																															
Abortion													•			•							•							•	•
Birth asphyxia and birth trauma	•												•			•							•							•	
Contraceptive methods							•					•	•			•							•					•		•	•
Hypertensive disorders of pregnancy	•		•													•							•							•	•
Maternal haemorrhage	•															•							•							•	•
Maternal sepsis			•													•							•							•	•
Neonatal sepsis and infections	•		•													•							•							•	
Obstructed labour	•		•										•			•							•							•	•
Other neonatal conditions	•		•										•			•							•							•	•
Prematurity and low birth weight	•												•			•							•							•	

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