

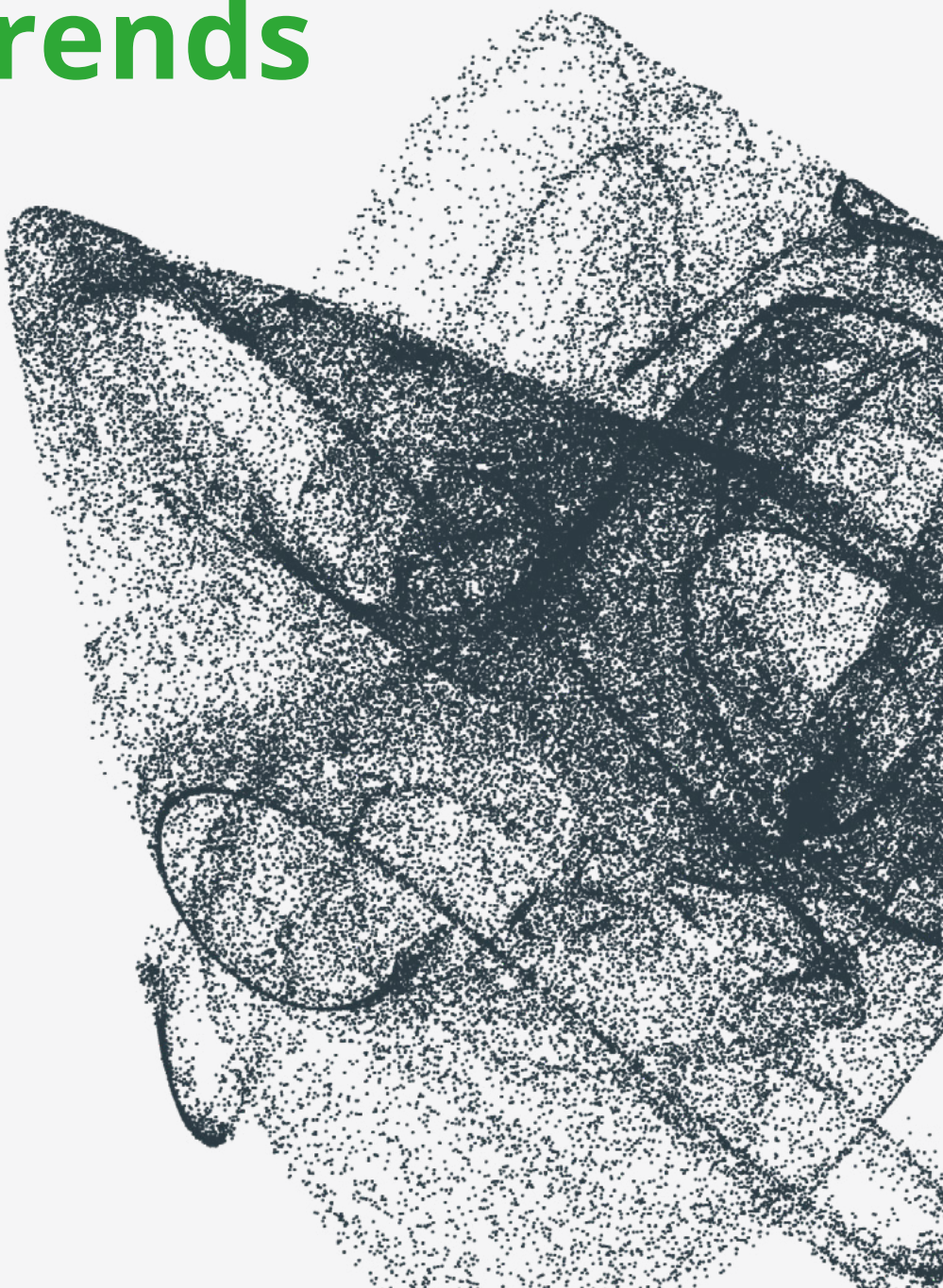


Global Medicine Spending and Usage Trends

OUTLOOK TO 2024



MARCH
2020



Introduction

The global use of medicines is one of the key influencers of global health and the practical ability to measure it in a timely and granular way provides a unique window on health systems across the world. Information about the amounts spent on which types of medicines provides an opportunity to compare countries and gain a better understanding of the current and future state of attempts to improve global health. In this, our ninth global forecast publication, we again bring forward insights to inform stakeholders globally.

There are significant variations in medicine use, spending, and health outcomes globally. This report provides unique and timely measures to inform an understanding of health and policy decisions that affect billions of people. It reviews trends in medicine use and spending from 2009 to 2019 and projections to 2024. For the first time this report includes use measures of days of therapy, essentially turning counts of pills, vials, patches, creams, etc., into normalized days of therapy using a standardized dosing assumption per product. Health policy researchers globally have been using this type of days of therapy measure from the World Health Organization for decades, but in piecemeal and often time-consuming efforts. In recent years, IQVIA databases have added some defined daily doses as a measure and this report is the first use of that data to help explain the global use of medicines. The practical benefit of interpreting drug shipment data as normalized days of therapy cannot be overstated. With volume metrics generally not discerning between doses that last a year or a month or an hour, and health systems adopting those forms differently, it has been impossible to determine like-for-like comparisons of use and cost.

This report also includes updated analyses of historic and forecast spending for key countries and regions, types of medicine products and seeks to explain the key drivers of growth.

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Global use of medicines

In 2019, patients globally received an estimated 1.8 trillion days of therapy, an average of 234 per person.

+ Overall, global use of medicine has increased at a 3% compound annual growth rate (CAGR) since 2014, slowing from a 4% rate seen 2009–2014.

+ The majority of medicine use is in pharmerging markets, which have large populations, but have per capita rates of use still markedly lower than in higher income countries.

+ Areas identified as global health priorities, such as diabetes and cardiovascular diseases, have seen significantly increased use of medicines.

Global medicine spending

Similar to medicine use, global medicine spending is projected to increase at 2–5% annually and exceed \$1.1 trillion in 2024.

+ Most developed and pharmerging markets will see slowing rates of growth in the next five years compared to the last five, with rates between 1–4% and 5–8%, respectively.

+ Pharmerging spending and growth are slowing as healthcare access expansions of the last decade begin to slow.

+ Developed markets are expected to see slowing brand growth despite increases in specialty medicine spending, as greater brand losses of exclusivity (LOE) offset higher new brand product spending, and price and volume growth both slow.

+ New brands will contribute \$165 billion in spending growth through 2024, up from \$126 billion in the past five years.

+ Brand LOEs are projected to have a \$139 billion negative impact on brand sales from 2020–2024, compared to the \$107 billion impact seen from 2014–2019.

+ Manufacturer net prices are expected to grow between 1% and -2% in the United States over the next five years, significantly below historic levels, while in other developed markets, net price declines of -2 to -5% are expected as a result of continued payer and government actions.

Overview

Implications and outlook

Key stakeholders in the global healthcare ecosystem will continue to face challenges as shifting dynamics will impact the price, access and availability of medicines.

- + Patients worldwide can expect greater access to medicines, especially for rare diseases and cancer, though they may come at a high cost to patients depending on their countries' healthcare payment and reimbursement systems.
- + Providers will have expanded treatment options, but will continue to be challenged to adjust to rapidly changing and progressively more complex guidelines. Cost will increasingly be a factor in provider decisions in some geographies.
- + Payers' approaches to managing overall cost growth trends will face challenges due to uncertainty around the prices and impact on spending of an increasing number of specialty, niche and rare disease medicines. Existing policies and negotiation strategies are not well-adapted to the difficult tradeoffs between limited healthcare budgets and supporting patient access to breakthrough, but often costly, medicines.
- + Manufacturers can expect lower financial returns through a combination of policies and payer negotiation strategies where new products will face greater scrutiny of pricing, market access and intensified competition with peers, and marketed products' net prices will decline.

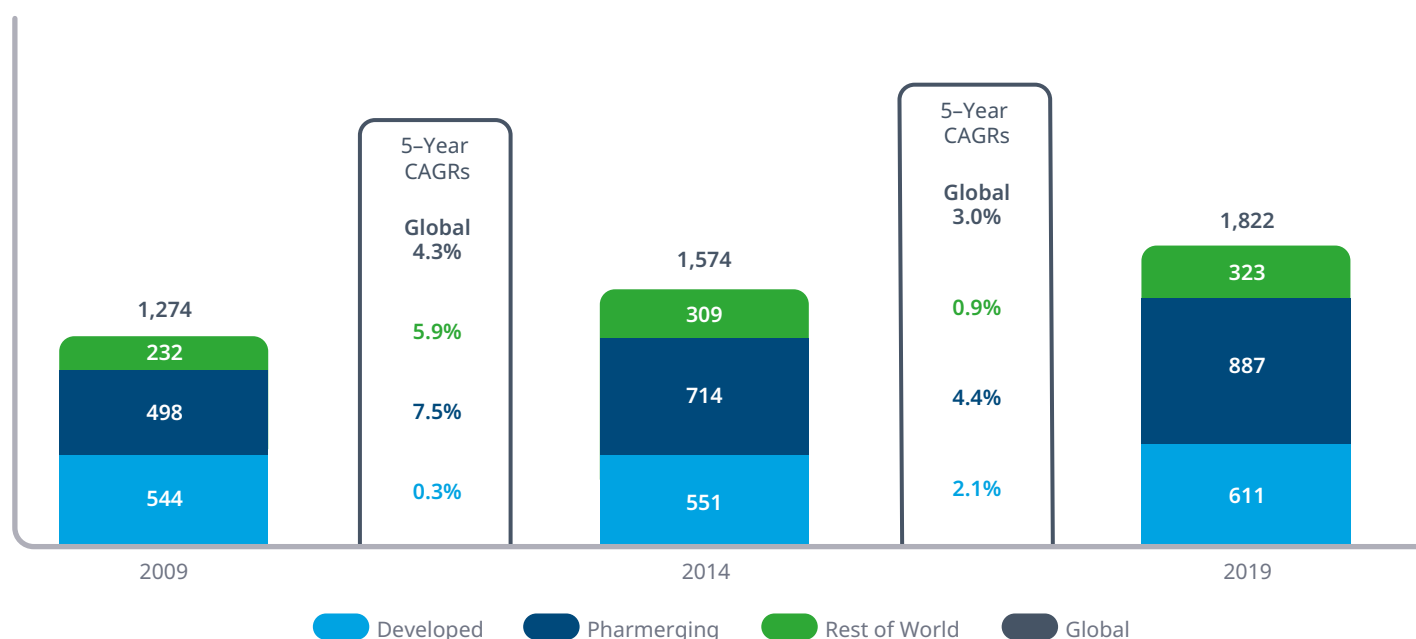
Global use of medicine

Overall global use of medicine has increased over the past ten years in areas of high priority, including the treatment of non-communicable diseases, which were responsible for 71% of deaths worldwide in 2016.¹ This rise demonstrates the value of medicines in addressing the needs of patients, prescribers and health systems around the world. Medicine consumption is closely tied to country income, though there is significant variation across countries with similar incomes. Given that the rate of increase in medicine use is currently outpacing population and economic growth, this indicates more patients are receiving treatment. This expansion has largely occurred in pharmerging markets, defined as countries with per capita income below \$30,000 per year and pharmaceutical spending growth above \$1 billion over five years (see Appendix). The use of medicine increased in the past ten years, however, the pace of growth in medicine use has slowed in the past five years across markets, in part due to declines or stagnation in economic growth compared to 2009–2014, and changing spending dynamics (see Exhibit 1).

To assess these changes in volume, a DDD (daily defined dose) metric was used to normalize use across countries, driving understanding of usage on a normalized days of therapy level. DDD consumption reached 1.8 trillion DDDs in 2019, a 16% increase over 2014, corresponding to a 3% compound annual growth rate (CAGR). Pharmerging markets saw the greatest CAGR of 4.4%, and accounted for 49% of DDD consumption (see Note on Defined Daily Doses).

The overall use of medicines is outpacing expected use and suggests there have been real improvements in the number of people receiving medicines.

Exhibit 1: Global Medicine Defined Daily Doses in Billions 2009–2019



Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Chart represents IQVIA Institute estimates of global defined daily doses (DDD). These estimates are based on IQVIA audited data and application of WHO-DDD factors in IQVIA MIDAS as well as additional DDD calculation assumptions developed by the IQVIA Institute (see Methodology).

DDD use in the top ten developed markets (see Appendix) account for 34% of total DDD use globally and grew at a 2.1% CAGR over the past five years. This is a notable change from 2009, when pharmerging and developed countries accounted for similar percentages of DDDs — 42% and 40% respectively — and 1.3 trillion DDDs were used worldwide. Additionally, from 2009–2014, the observed CAGR in DDDs was 4.3%. The decline in DDD growth in the past five years despite constant population growth,² signifies shifting dynamics in country segments. Pharmerging markets continue to show the greatest use and growth, but it is important to note this segment has also receded over the past five years.

National income is positively correlated with medicine use, with richer countries typically having higher rates of medicine use, shown as DDD per capita (see Exhibit 2). Given constant worldwide population growth and diminishing economic growth, the overall use of medicines is outpacing expected use and suggests there have been real improvements in the number of people receiving medicines. In this exhibit, and based on a separate regression analysis performed on the underlying DDD data, developed and pharmerging markets clearly cluster based on net national income per capita and DDD per capita.

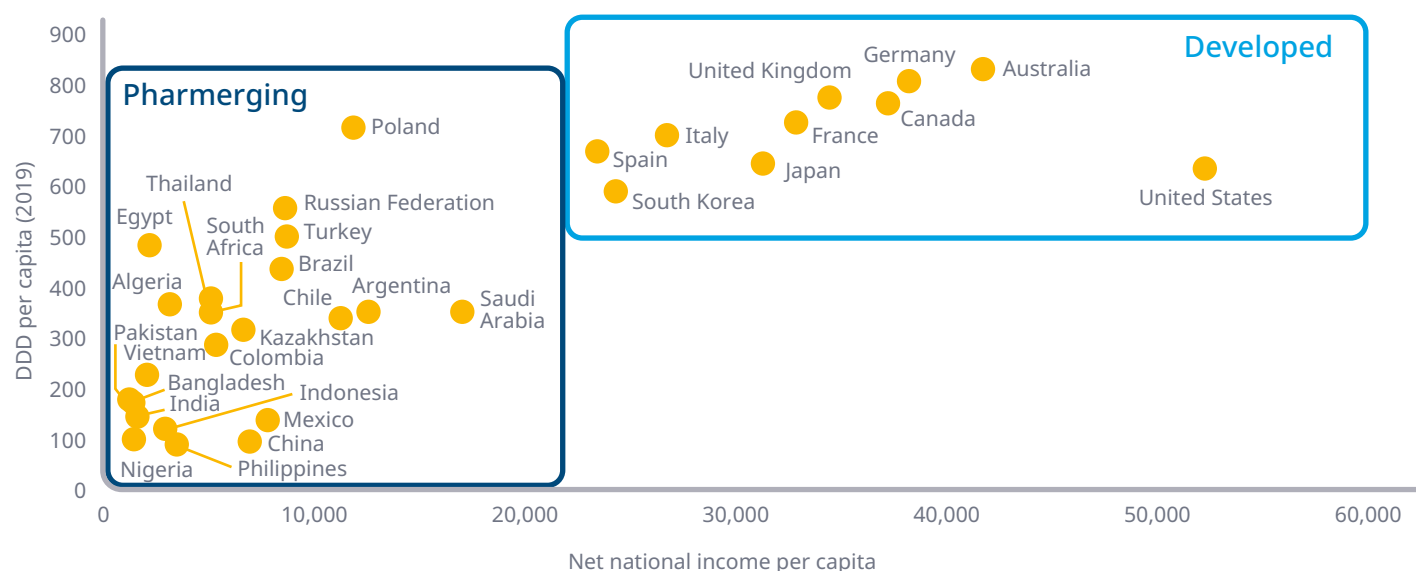
However, variations exist across countries and reflect each country’s internal dynamics and priorities. In developed markets, the average DDD per capita is 707, with the highest, 820, in Australia. Notably, among the top ten developed countries, the United States has the highest net national income per capita (\$51,000) and is ranked number nine in DDD per capita with a value of 440. EU5 countries and Japan rank above the United States in DDD per capita, though they have lower net national income per capita, reflecting the diversity in impacts of implemented healthcare systems and policies, including universal healthcare and the extent of patient cost-sharing.

The pace of growth in medicine use has slowed in the past five years across markets, in part due to declines or stagnation in economic growth... and changing spending dynamics.

NOTE ON DEFINED DAILY DOSES

To normalize the use of medicines that have varying intended doses, the World Health Organization (WHO) uses a method to arrive at defined daily dose (WHO-DDD). The WHO-DDD measure is intended to represent a standard day of therapy for a maintenance dose of a chronic therapy or a day of therapy for commonly used acute treatments. The WHO-DDD measure does not reflect actual treatment decisions and is not derived from distinct patients measured with anonymized data. The WHO guidance for calculating DDD is incomplete and the IQVIA Institute has developed additional factors using the same or highly similar concepts to estimate DDDs for over 63% of audited standard unit volume globally, an increase from the 55% already available in IQVIA datasets. These factors have then been used to estimate total DDDs in audited countries and then to further estimate DDDs in unaudited countries (see Methodology).

Exhibit 2: Defined Daily Doses (DDD) per Capita by GDP per Capita



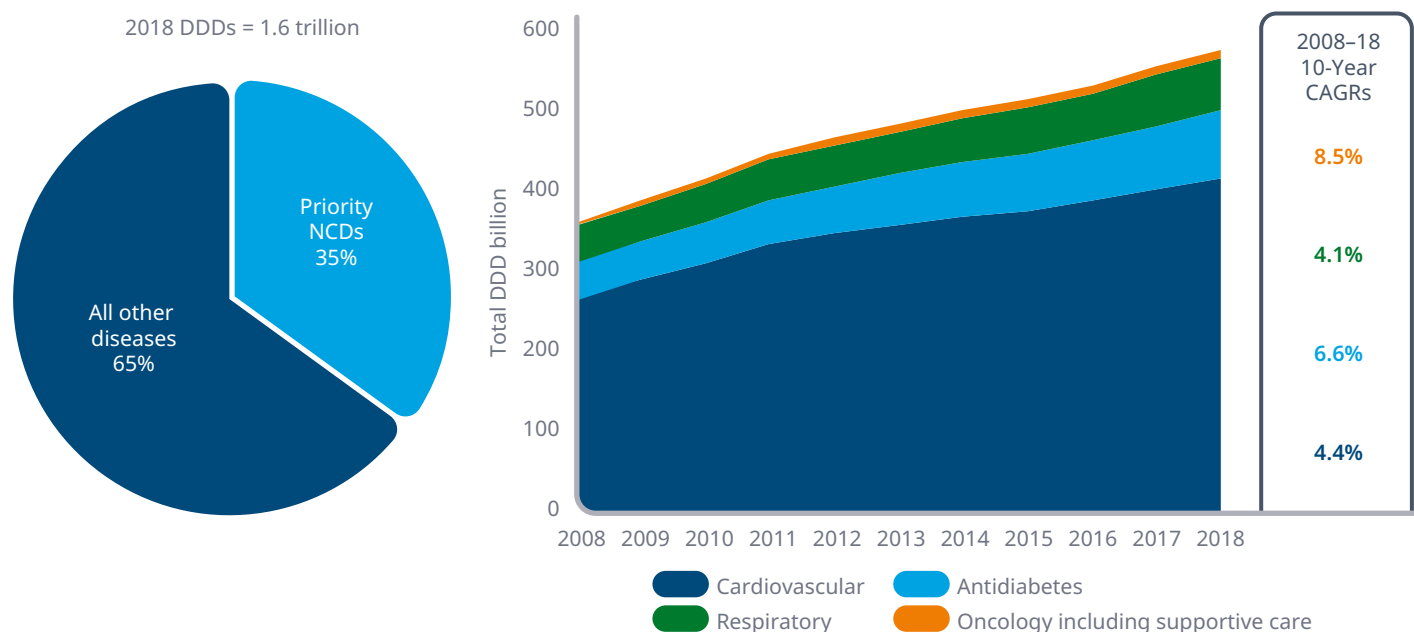
Source: IQVIA Institute, Jan 2020; The World Bank Sep 2019

Notes: DDD per capita has been projected for full year 2019 based on audited data through June 2019. Net National Income per capita has been based on the latest published World Bank Estimates which are updated to 2017. Info from <https://datacatalog.worldbank.org/public-licenses#cc-by>, accessed Jan 20, 2020.

In pharmerging markets, the range of DDD per capita is 93–712, with an average DDD per capita of 301. While pharmerging countries are responsible for most of the DDD volume growth, many pharmerging countries, such as India, China, and Mexico, have low DDD per capita, indicating greater access and/or availability is still needed to reach more patients. For countries falling within the \$8–10,000 net national income per capita, there is a six-fold difference in DDD per capita, suggesting factors other than finances affect use. There are several countries among these exhibiting high DDD per capita, including Poland (712), Russia (552), and Turkey (494). DDD per capita in these countries rival that in developed markets, likely indicating a priority on medicine spending in these countries, although it could also be driven by the health status of the population. Outside these key markets, which account for most industry revenues and global use of medicines, the rest of the world includes a mix of high- and low-income countries with a mix of trends. High-income countries like Luxembourg (not shown) more closely mimic developed countries.

The greater use and reach of medicines are in line with global health priorities for non-communicable diseases (NCDs) (see Exhibit 3). In 2018, priority NCDs represent 35% of global DDD volume, growing by a 4.7% CAGR since 2008. Therapy areas comprising most of the use include diabetes, respiratory, cardiovascular and cancer treatments and account for 71% of deaths worldwide. Over the past ten years, DDDs for these four priority diseases have increased by 200 billion, but growing at rates slower than overall use. Many of these priority NCDs can be managed with low cost medicines, allowing greater impact on DDD and overall health with lower spending. Overall, the use of these medications has increased, however, significant variability remains in the per capita of these medicines across countries, indicating additional strategies to further drive uptake of these important medicines can be implemented around the world. DDD use for ‘other diseases’ exhibits a slightly greater CAGR (5.8%) over the same period.

Exhibit 3: Audited Markets Medicine Use in DDDs by Therapy Types and Areas



Source: IQVIA MIDAS, Sep 2019; IQVIA Institute, Jan 2020

Notes: Analyses shown are for audited markets only, total DDDs estimated of 1.611 trillion in 2018, compared to an estimated 1.779 trillion including unaudited countries. Priority NCDs refer to medicines for non-communicable diseases where the WHO has identified them among their global health priorities.

While pharmerging countries are responsible for most of the DDD volume growth, many pharmerging countries, such as India, China, and Mexico, have low DDD per capita, indicating greater access and/or availability is still needed to reach more patients.

Global medicine spending

As seen with medicine use, global medicine spending is expected to grow more slowly, but projected to exceed \$1.1 trillion in the next five years. The rise in spending is partly due to increased use, but is also driven by changes in the specialty and innovative product composition of new brands reaching the market. Other factors, such as pricing pressures and brand losses of exclusivity offset rises in spending. With these dynamics, spending growth is projected to slow in the next five years.

Notably, dynamics will evolve differently in developed and pharmerging markets, especially as pharmerging markets are more volume-driven with lower brand use (see Appendix Exhibit 12). However, the same depressed pace of growth in medicine spending is expected.

GLOBAL MEDICINE SPENDING IN DEVELOPED AND PHARMERGING MARKETS

Global medicine spending growth is consistent with the increased global use of medicine and is expected to exceed \$1.1 trillion in 2024 (see Exhibit 4). Global spending has steadily increased from 2009–2019 with

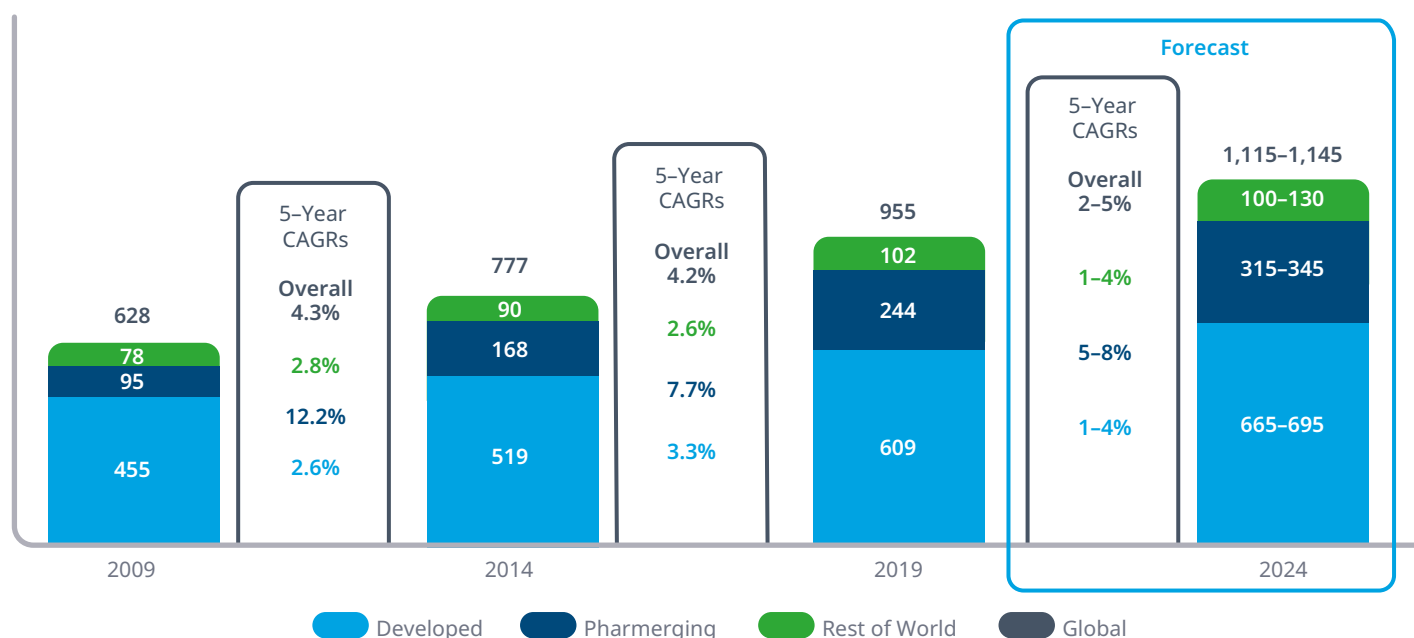
a 10-year CAGR of 4.2% (not shown) and spending reaching \$955 billion in 2019. This reflects a 23% jump from \$777 billion in 2014. This rise in spending is occurring despite discounts and rebates; net revenue for manufacturers is often much lower than spending at invoice prices. In this analysis, net market size in 2019 is \$295 billion lower than invoice spending, a difference expected to exceed \$400 billion by 2024 as the dynamics driving greater discounts and rebates — including payer negotiations and subsidies with coupons or cost assistance for patients — are expected to continue. Developed markets have been slightly steadier, with 2.6% and 3.3% CAGRs in net market size from 2009–2014 and 2014–2019, respectively. In 2019, this segment comprised 64% of spending and is expected to comprise 60–61% of spending in 2024. Pharmerging markets have seen the greatest growth, with a 12.2% CAGR from 2009–2014 and 7.7% CAGR from 2014–2019. In 2019, pharmerging markets comprised 26% of spending, which is expected to rise to 28–30% of spending in 2024. However, global growth is expected to moderate to 2–5% through 2024, as both developed and pharmerging markets exhibit comparable dynamics.

NOTE ON PRICING LEVELS

This analysis of medicine spending reports net market size, which is based on audited spending data net of publicly reported discounts and estimates of future off-invoice discounts and rebates (see Methodology). Invoice spending is based on prices reported in IQVIA audits of pharmaceutical spending that are, in general, reported at the invoice prices wholesalers charge to their customers including pharmacies and hospitals. In some countries, these prices are exclusive of discounts and rebates paid to governments, private insurers or the specific purchasers. In other countries, off-invoice discounts are illegal and do not occur. The mix of true prices and opaque pre-discounted prices means the invoice-level analyses in this report do not reflect the net market size. In countries where aggregate discounts and rebates are reported publicly, those have been included in the estimates. In other countries, estimates are based on expert interviews, while in the United States company-reported net sales have been compared to IQVIA audited data to inform the estimates (see Methodology).

Throughout this report unless explicitly noted, currency values for medicine are represented in nominal dollar values with exchange rates varying by period, while growth rates and ranking are represented in constant dollars with Q2 2019 exchange rates.

Exhibit 4: Global Medicine Net Market Size and Growth 2009–2024, Constant US\$Bn



Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Net Market Size after estimated off-invoice discounts and rebates, estimated at country level (see Methodology).

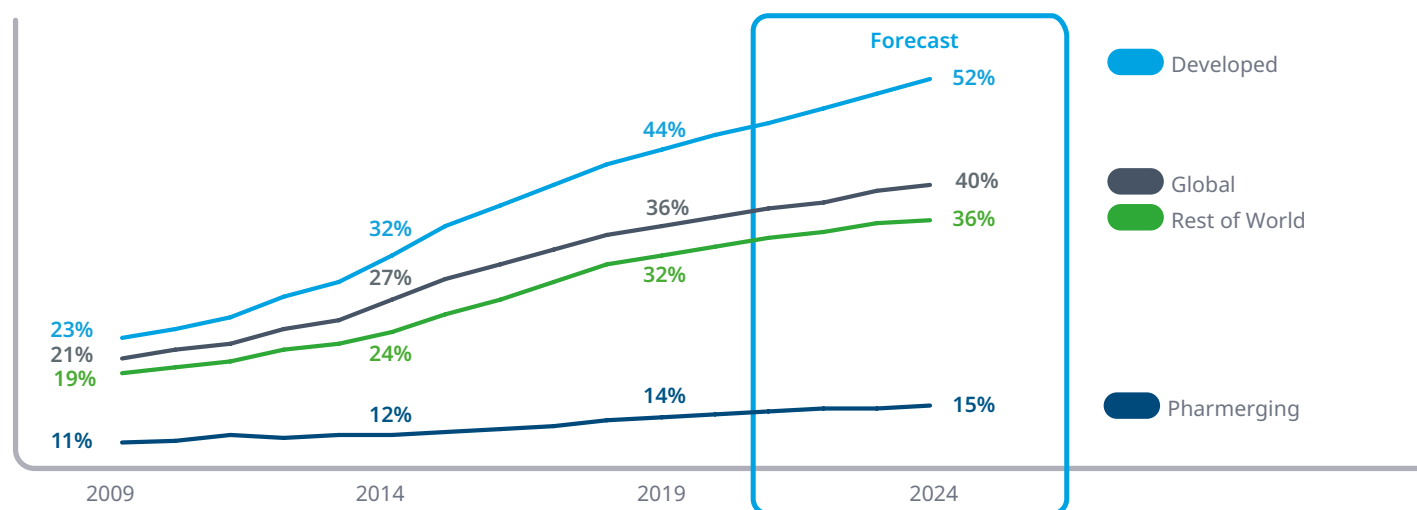
Developed markets are expected to see an average CAGR between 1–4% through 2024, below the historical 3.3% CAGR from 2014–2019 (see Exhibit 4). In these markets, medicine spending reached \$609 billion in 2019, with a slight increase in five-year CAGRs from 2.6% to 3.3%.

Pharmerging markets are expected to show the most growth with a 5–8% CAGR through 2024, albeit less than the 7.7% in the past five years (see Exhibit 4). Most pharmerging market growth has been driven by access expansions, leading to greater volume use and adoption of more novel therapies. These include specialty medicines, which are projected to contribute more to spending than in previous periods. However, most of the products used in these countries are non-original products (see Appendix Exhibit 12), which aids in keeping spending low despite expanding volume. As a result, projections suggest most countries will have slower growth than historical CAGRs.

SPECIALTY AND INNOVATIVE PRODUCTS' IMPACT ON SPENDING GROWTH

Adoption of specialty medicines (see Appendix) are driving spending increases and these products now account for 36% of spending globally. Specialty spending is projected to account for 40% of global spending in 2024 (see Exhibit 5). In developed markets, 44% of spending is on specialty products and is expected to reach 52% in 2024. While specialty spending growth remained largely constant at an 11% CAGR from 2014–2019, it is expected to lessen to 5–8 % by 2024. These products are often a focal point for payers in developed countries, although these medicines typically affect small patient populations and have only small volumes of use. New specialty products are increasingly in niche areas, including oncology and orphan drugs. The slowed growth of specialty spending in the projected period is, in part, due to brand losses of exclusivity (LOE) including biosimilars, which offset new product contributions. Historically, LOE impact was greater on traditional medicines rather than specialty products,

Exhibit 5: Global Medicines Specialty Share of Invoice Spending by Region



Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Specialty medicines are defined by IQVIA as drugs for chronic, complex or rare diseases which meet a majority of defined characteristics (see Methodology). Analysis shown is based on invoice price level, not reflecting rebates. Regions are based on country estimates including 219 countries in IQVIA Market Prognosis.

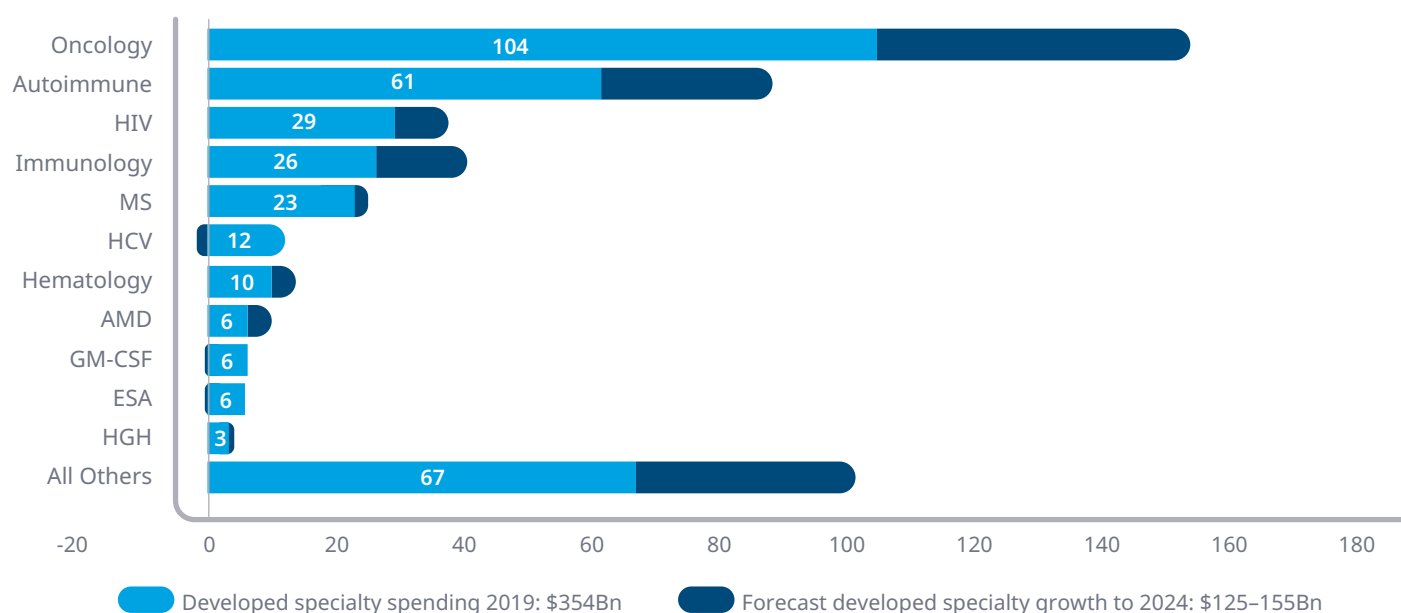
making this a notable shift in the 2024 projections. Additionally, price controls deriving from negotiations and reimbursements with innovative models such as outcomes-based contracts, have been implemented in developed countries to address the growing costs of specialty medicines. While several cell and gene therapies are poised to launch, their impact on spending through 2024 is not expected to be substantial.

In pharmerging markets, specialty medicines only account for 14% of spending and are expected to account for only 15% of spending in 2024. Specialty spending is expected to slow from an 11% CAGR from 2014–2019, to 7.5–10.5% through 2024. The small share of specialty is unsurprising, as pharmerging markets typically have significant patient out-of-pocket costs, delays in marketing of novel medicines compared to developed markets, limited reimbursement of specialty medicines, and disease morbidity differences. In the next five years, specialty spending in pharmerging markets is expected to rise by 1% of spending, much less than the 8% increase in

developed markets. The difference in specialty spending accounts for variable dynamics between developed and pharmerging countries; the more prevalent use of specialty products with higher price tags in developed markets is a contributor to their growth, while these products contribute less in pharmerging countries.

Specialty spending is projected to account for 40% of global spending in 2024... and is expected to reach 52% in 2024 in developed markets.

Exhibit 6: Specialty Invoice Spending by Therapy Area in Developed Markets, Constant US\$Bn



Source: IQVIA Therapy Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Leading specialty therapy areas and total others. All Others are classes with 2019 spending smaller than those shown. Analysis shown in constant US\$. Data is based on the eight developed markets available in IQVIA Therapy Prognosis (see Notes on Sources), does not include the developed markets Australia or South Korea.

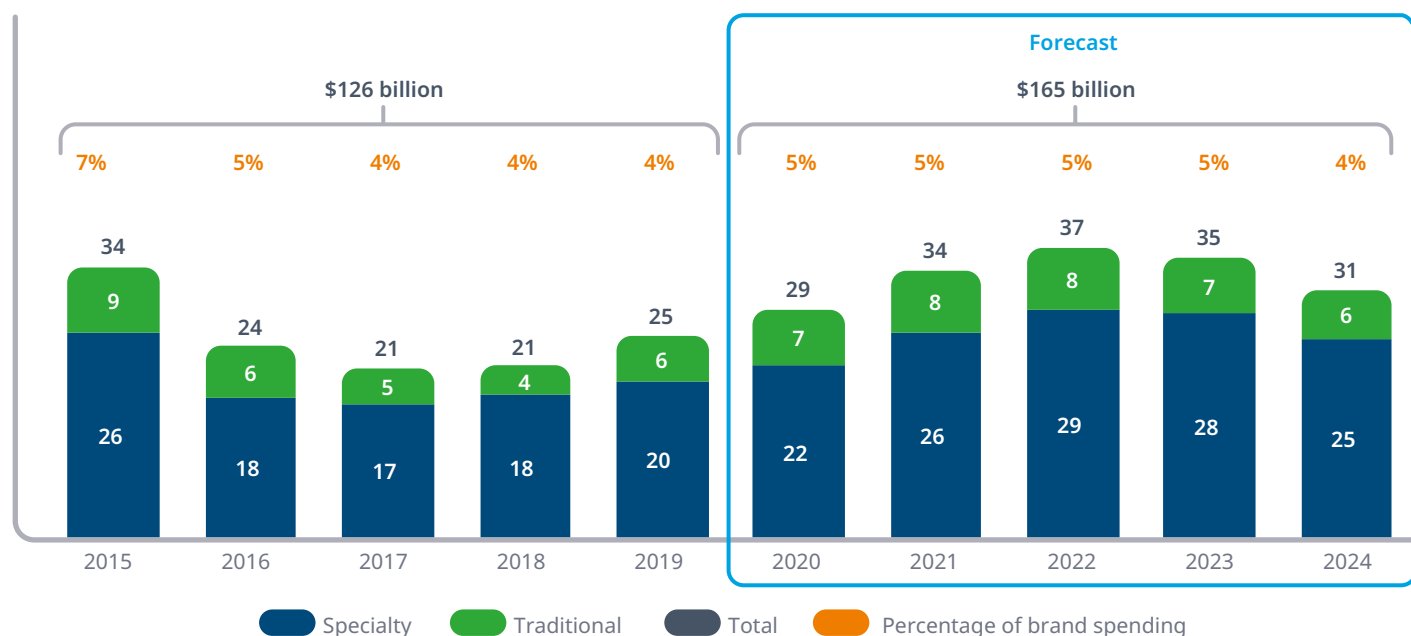
The adoption of innovative specialty products is driven by oncology and autoimmune therapies in both developed and pharmerging markets (see Exhibit 6). Developed markets spent a combined \$354 billion on specialty products in 2019, with 30% of that on oncology products.

Oncology spending is expected to remain the largest contributor to specialty spending, with a projected increase of 51% through 2024. Autoimmune therapy spending comprised 17% of spending in 2019, while HIV accounted for 8% of specialty products. Unlike HIV, spending on other viral diseases, especially HCV, have seen treatment volumes peak and are expected to have spending decreases through 2024. Similarly, GM-CSF and ESA treatments are also projected to have spending declines, due to the uptake of biosimilars.

Remaining specialty treatments are in smaller spending therapy areas, including many orphan drugs. Notably, pharmerging markets have a greater contribution from older immunology and blood coagulation therapies and less from autoimmune biologics. However, oncology spending is projected to nearly double by 2024, indicating some use of newer products.

While specialty spending in pharmerging markets is nearly 90% smaller in absolute terms than developed markets, the growth is substantial. It does not increase in share simply because traditional medicines will see comparably rapid growth. Pharmerging countries also have slower adoption of innovation, as well as higher use of non-original versions of some medicines at lower costs.

Exhibit 7: New Brands Invoice Spending Growth in Developed Markets, Constant US\$Bn



Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Jan 2020

Notes: Analysis shows the expected yearly growth from products less than two years after launch based on historic audited invoice level data and projections based on analyst consensus estimates. Total brand spending is used as the basis for calculating new percent of brand spending.

PRESSURES ON GLOBAL SPENDING

The observed and projected spending growth is slowing due to continued effects of pricing controls and increasing brand LOEs, and are offset by continued high numbers of new medicines. These three factors are described in greater detail below.

New products

New product growth is projected to contribute \$165 billion over the next five years, up from \$126 billion in the past five (see Exhibit 7). It also reflects the effects of market access and price controls in many markets that may contribute to slower growth. The IQVIA Institute estimates approximately 270 (~54 per year) new molecular entities (NMEs) are expected to be approved between 2020 and 2024, compared to 236 from 2015–2019, and 200 from 2010–2014, contributing to the rise in new brand spending. From 2015–2019, new brands comprised 4–7% of brand spending and are expected to consistently comprise 5% from 2020–2024. New brand spending growth is largely driven by

oncology, autoimmune, other immunology treatments and many other niche and orphan treatments. As a result, specialty spending is expected to comprise a greater proportion of new brand spending in 2024, reaching 78%, or \$130 billion of the projected \$165 billion spending in developed markets. New products spending growth is expected to be offset by declining price growth, particularly in the United States, and older products growing more slowly. The deceleration of spending growth in the face of rising specialty products and spending indicates countries and payers are succeeding at controlling price negotiations.

Projected spending growth is slowing due to continued effects of pricing controls and increasing brand LOEs.

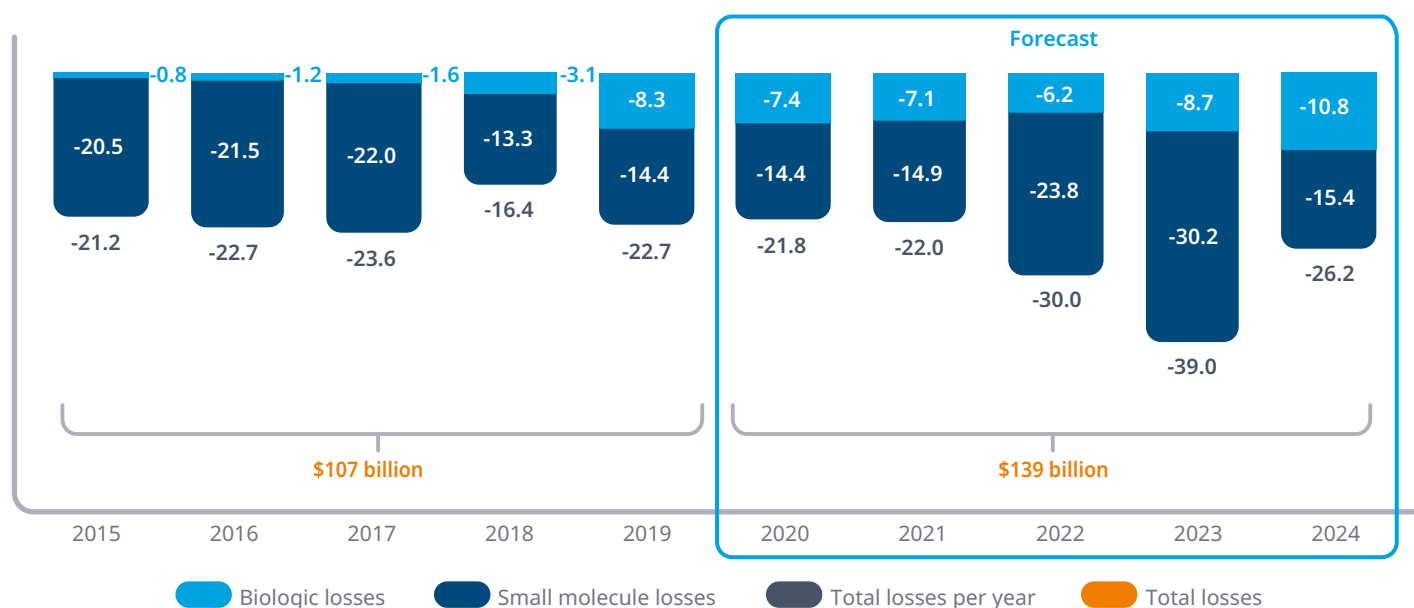
Impact of brand losses of exclusivity

Brand LOEs will result in \$139 billion less in brand sales at invoice-level in developed markets, an increase in LOE impact compared with the \$107 billion seen in the past five years (see Exhibit 8). The largest losses are projected in 2023, with an expected \$39 billion in losses in this year alone. Significant products contributing to brand LOEs in 2023 include sitagliptin (Januvia), adalimumab (Humira), liraglutide (Victoza), and lisdexamfetamine (Vyvanse) with combined projected losses of nearly \$15 billion. From 2020–2024, these products are predicted to generate losses of or greater than \$2.7 billion each. Importantly, the losses are not calculated at net prices, meaning losses could be slightly less when accounting for rebates, which are typically discontinued post-expiry. Additionally, some losses are offset by generic uptake and increased uptake overall, meaning payer savings could be less than the stated amounts. The timing of expiries and generic entry are particularly volatile and based on litigation and other factors.

Continued emergence of breakthrough therapies

With market dynamics shifting, including the rise in specialty products for smaller patient populations, the likelihood of breakthrough therapies coming to market that significantly impact patient care or provide a cure will increase, but are not expected to impact broad patient populations. After analysis of current pipelines (not shown), breakthrough therapies are not expected to escalate spending growth, as was observed with the advent of highly effective HCV treatments. In the period of 2014–2015, HCV treatments accounted for \$26.5 billion of new brand spending growth, nearly 30% of all new brand spending growth in developed markets in those two years. This impact on spending trends was unprecedented, and there is no clear pipeline therapy with similar characteristics expected to be commercially available in the next five years. While innovative gene therapies will reach the market shortly, the approvals and subsequent availability are expected to come gradually. As a result, in developed markets, novel payment infrastructure is already being explored to manage these high-cost therapies, potentially lessening their impact on spending growth.

Exhibit 8: Developed Markets Lower Brand Invoice Spending Due to Loss of Exclusivity, Constant US\$Bn



Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Jan 2020

Notes: Does not reflect offsetting spending increases from generic or biosimilar competitors. Losses in future periods are modeled based on expected pre-expiry growth for the brand and subsequent post-expiry loss of sales for the brands. The rates of loss are based on historic averages in each country and inclusive of adjustments for products with expiries in progress from historic periods where losses extend into the forecast periods. Historic period analyses are based on audited data. Expected loss of exclusivity dates are highly variable and can change due to outcomes of litigation, granting of new patents or changes in the expectation of launch of biosimilars. Information is current as of January 2020.

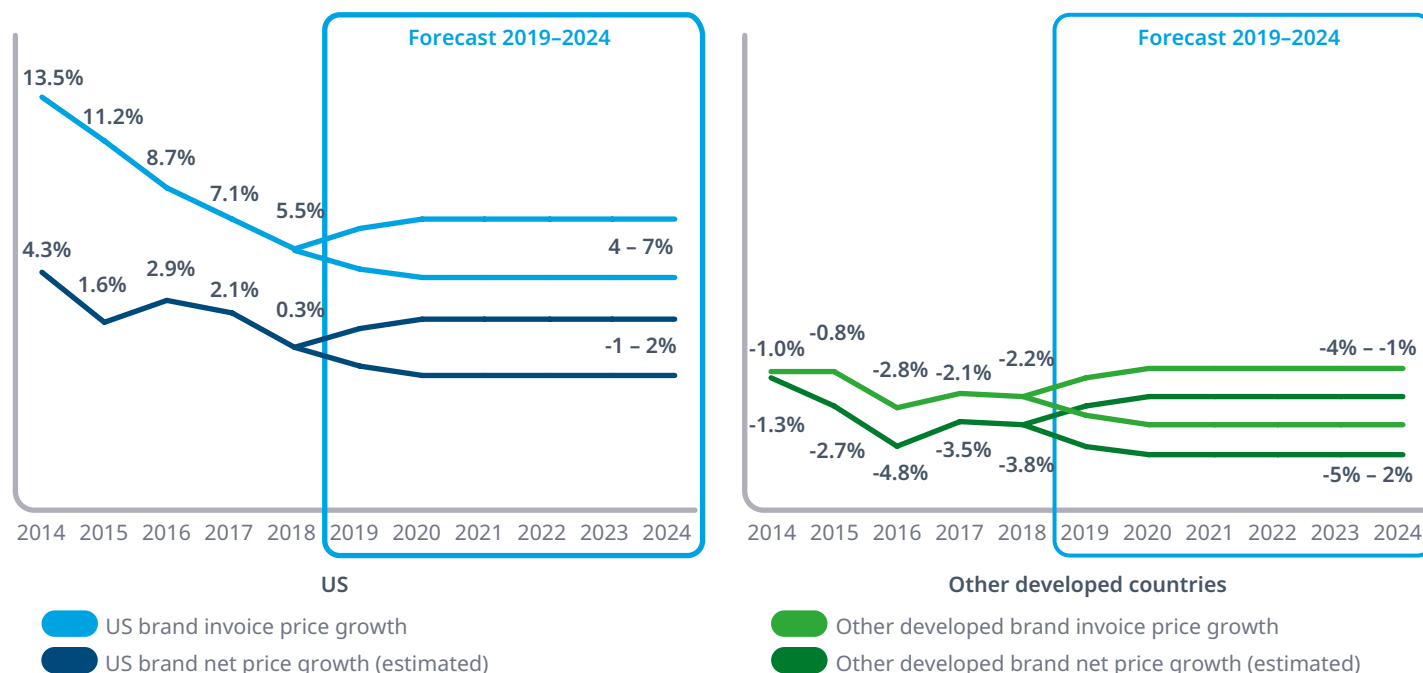
DECLINING PRICES

As a result of these pressures, growth due to price changes is expected to be lower than historical trends, including on a net-basis (see Exhibit 9). In the United States, brand prices have been increasing more slowly on an invoice basis over the past five years, slowing from 13.5% to 5.5%. They are expected to continue slowing, growing by 4–7% through 2024. The higher invoice price increases in earlier years were understood to be the result of several outlier products with more sizeable price increases on an invoice-basis but offset by larger rebates, and therefore, such increases are not present on a net-basis. Additionally, net prices in the United States also see slowing growth, from 4.3% in 2014 down to 0.3% in 2018, with growth expected in the range of -1–2% through 2024. The differences between invoice and net prices in the United States are influenced by a variety of factors, such as negotiated discounts and rebates, statutory fees and subsidies, and the use of consumer coupons. All of these reduce net prices and

contribute to the lower net trend. Generally, invoice price increases have been offset by greater discounts and rebates. In other developed countries, dynamics similar to historical periods are expected, with brand invoice growth projected to be -4 – -1%, or -5–2% on a net-basis. Increasingly negotiated discounts are being employed alongside direct setting of list prices with governments, resulting in smaller differences between invoice and net, but a broadly similar dynamic over time. Most developed countries do not allow prices to rise after a product launches and invoice price declines are typically the result of the government restructuring prices, which are further reduced on a net-basis by negotiations on specific products.

Growth due to price changes is expected to be lower than historical trends, including on a net-basis.

Exhibit 9: Developed Markets Protected Brands Invoice and Net Price Growth



Source: IQVIA MIDAS, IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Jan 2020

Notes: IQVIA Audited data in MIDAS is used to calculate price growth, and labeled here as 'invoice'. In most countries, prices reflect the transaction prices before the application of discounts and rebates. Estimated net price growth is based on IQVIA analysis to remove off-invoice discounts and rebates. For more details see Methodology. Analysis is based on full year 2018 inclusive of data for the US and input from experts in selected countries. Estimates are intended to represent a country average and Individual products or therapy areas or product types are understood to vary significantly.

Implications and outlook

Global medicine use and spending is increasing, albeit at a slower rate than historical periods, and spending is set to exceed \$1.1 trillion with increased normalized days of therapy. The complex dynamics at play in different markets have a significant impact on stakeholders across the healthcare ecosystem.

After careful assessment of these recent and current market dynamics, considering price controls, the number and magnitude of projected LOEs, policy and regulatory agendas and pipeline assessments, it is clear that each stakeholder in the global healthcare ecosystem will continue to face challenges as shifting dynamics impact price, access and availability. The following are some notable impacts for key stakeholders.

PATIENTS

Worldwide, patients can expect to see greater access to medicines. In developed markets,

- There will be more treatment options available for rare diseases and cancer, though they may come at a higher cost to patients in some countries.
- In the United States, where medicine costs have shifted to patients, it is likely this trend will continue, though this will be slightly offset by LOEs.

In pharmerging markets,

- Expanded access to treatment options will positively affect health outcomes due to the LOEs of specific products, along with further expansion of medicines spending.

PROVIDERS

In developed markets,

- Providers will continue to see expanded treatment options, new technologies, and innovative products with higher price tags targeting patients with critical unmet need.

- As a result, providers will be more exposed to additional administrative work burden for innovative payment strategies, such as outcomes or performance-based contracts.
- However, as well-known brands reach LOE, providers will be able to more easily and rapidly prescribe well-established medicines as they face less concern over patient affordability.

In pharmerging markets,

- Concerns over patient out-of-pocket costs will rise as specialty product access expands, and prescribing habits will likely shift.
- A sustainable infrastructure will need to be maintained and augmented to ensure expanded delivery of care to patients is possible.

PAYERS

Payers' budgets in 2024 will continue to be more challenged than today, as spending increases, and innovative medicines targeting rare diseases with critical unmet needs are brought to market. In developed markets,

- Payers will continue effective pricing and market access strategies, such as limiting launch prices and brand price increases after launch, as is done in many developed countries including the United States, and limiting access to new medicines through the use of health technology assessments or reimbursement through outcomes-based or other innovative contracts.
- Payers will need to adopt high-flexibility frameworks to maximize LOE savings while optimizing uptake, taking into account uncertainty in the costs of new specialty products for niche populations and potential biosimilar savings.

In pharmerging markets,

- Governments acting as payers or setting policy for payers will continue to work to enable greater access to novel and breakthrough therapies.

- Governments need to continue to balance the pace of spending growth with public and private ability to pay, enhancing their methods of improving access to basic healthcare and support for narrower populations with high-cost specialty drugs.
- Notable LOEs in the next five years will bring additional medicines to improve health outcomes as generics bring greater availability of medicines at lower cost and will expand access in these markets.

MANUFACTURERS

In developed markets,

- Pricing and market access controls will continue to affect uptake at launch for novel medicines and require evolving investments and efforts to achieve optimal usage of medicines.
- These pressures will be especially prevalent for me-too drugs, or those offering only incremental benefits over standard-of-care.
- Innovative products targeting niche patient populations or those with high unmet need present unique challenges in price-setting and achieving market access, as shifting thresholds of value evolve temporally in different countries.
- The next major cycle of LOEs in 2020–2024 brings another step in the shift from traditional large-volume therapies and will force another round of careful portfolio adjustments to fill the \$39 billion gap created in a single year.

In pharmerging markets,

- Multinational companies need to continue to adapt to local needs as they seek to offer value to these countries and compete with local or regional, and often generic, manufacturers.
- As growth continues to slow, many companies already invested in pharmerging markets will continue to derive financial returns, especially with the greater acceptance of specialty drugs, though fewer companies will move into these markets.

Appendix

DEFINITIONS

It is helpful to use a set of common definitions to fully understand the dynamics observed in medicine use and spending across the globe. For the purposes of this report, the following terms are used:

Developed markets are defined by IQVIA as ten countries with high incomes and with pharmaceutical spending greater than \$10 billion, namely the United States, Japan, Germany, France, Italy, Spain, United Kingdom, Canada, South Korea and Australia.

Pharmerging markets are defined as countries with per capita income below \$30,000 per year and five-year absolute growth in pharmaceutical spending greater than \$1 billion. These include Algeria, Argentina, Bangladesh, Brazil, Chile, China, Colombia, Egypt, India, Indonesia, Kazakhstan, Mexico, Nigeria, Pakistan, Philippines, Poland, Russia, Saudi Arabia, South Africa, Thailand, Turkey and Vietnam.

World Bank income bands such as High, Upper Middle, Lower Middle, and Low are based on World Bank methodologies. For current World Bank classifications see: <https://datahelpdesk.worldbank.org/knowledgebase/articles/906519>

Brand Losses of Exclusivity (LOE) are identified by IQVIA researchers noting the relevant patents or other protection for each product in each country. Exclusivity can be as a result of patents, market exclusivity, specific product approval types such as Orphan Drug Status, or extensions associated with patent delays or pediatric exclusivities. Losses of exclusivity generally result in the launch of a generic or biosimilar product, and lower brand sales as a result.

Specialty pharmaceuticals IQVIA defines specialty medicines as those that treat chronic, complex or rare diseases and have a minimum of four out of seven of the following additional characteristics:

- List price is in excess of \$6,000 per year
- Initiated/maintained by a specialist physician
- Requiring administration by another individual or healthcare professional (i.e., not self-administered)
- Requiring special handling in the supply chain (e.g., refrigerated, frozen, chemo precautions, biohazard)
- Requiring patient payment assistance
- Distributed through non-traditional channels (e.g., “specialty pharmacy”)
- Medication has significant side effects that require additional monitoring/counseling (including, but not limited to, REMS programs) and/or disease requires additional monitoring or therapy (e.g., monitoring of blood/cell counts to assess effectiveness/side effects of therapy).

The definition of specialty drugs often differs among stakeholders. For example, Centers for Medicare & Medicaid Services (CMS) defines specialty drugs only in the context of Part D (i.e., not Part B) and uses a dollar threshold; pharmacy benefit managers typically define specialty also based on cost; and pharmaceutical wholesalers consider specialty drugs to be those that require special handling due to low volume, cold-chain or other storage requirements, or are managed through separate organizational or delivery channels.

Exhibit 10: Global Invoice Spending and Growth in Selected Countries


































	2019 SPENDING US\$BN	2014-2019 CAGR	2024 SPENDING US\$BN	2020-2024 CAGR
Global	1,250.4	4.7%	1570-1600	3-6%
Developed	821.6	3.8%	985-1015	2-5%
United States	510.3	4.3%	605-635	3-6%
Japan	87	-0.2%	88-98	-3-0%
EU5	173.7	4.0%	210-240	3-6%
Germany	52.1	4.9%	65-75	4-7%
France	34.9	1.6%	38-42	0-3%
Italy	33.5	5.1%	41-45	3-6%
United Kingdom	28.7	4.5%	37-41	4-7%
Spain	24.5	4.0%	30-34	3-6%
Canada	22.5	4.6%	26-30	4-7%
South Korea	16.1	7.3%	21-25	5-8%
Australia	12.1	3.5%	13-17	3-6%
Pharmerging	357.7	7.0%	475-505	5-8%
China	141.6	6.7%	165-195	5-8%
Tier 2	71.2	9.4%	90-120	7-10%
Brazil	33.6	9.9%	45-49	6-9%
India	22	9.5%	31-35	8-11%
Russian Federation	15.6	8.4%	23-27	8-11%
Tier 3	145.1	6.2%	195-225	5-8%
Rest of the World	71	4.8%	85-95	2-5%

Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Spending in US\$Bn, CAGR = Compound Annual Growth Rate using Constant US\$ with Q2 2019 exchange rates

Appendix

Exhibit 11: Global Top 20 Countries Ranking and Invoice Spending Relative to United States

RANK	2014	% OF U.S.	RANK	2019	% OF U.S.	RANK	2024	% OF U.S.
1	United States	100.0%	1	United States	100.0%	1	United States	100.0%
2	 China	26.6%	2	China	27.9%	2	China	29.7%
3	 Japan	21.2%	3	Japan	16.9%	3	Japan	13.2%
4	Germany	10.6%	4	Germany	10.2%	4	Germany	10.3%
5	France	8.4%	5	France	6.8%	5	 Brazil	7.5%
6	Italy	6.4%	6	Italy	6.5%	6	Italy	6.4%
7	 United Kingdom	5.7%	7	 Brazil	6.3%	7	 France	5.9%
8	 Brazil	5.1%	8	 United Kingdom	5.6%	8	United Kingdom	5.7%
9	 Spain	4.7%	9	Spain	4.8%	9	 India	5.5%
10	 Canada	4.5%	10	Canada	4.3%	10	 Spain	4.7%
11	 India	3.4%	11	India	4.3%	11	 Canada	4.5%
12	 South Korea	3.0%	12	South Korea	3.1%	12	 Russian Fed.	4.1%
13	 Russian Fed.	2.7%	13	Russian Fed.	3.1%	13	 South Korea	3.4%
14	 Australia	2.6%	14	Australia	2.4%	14	 Argentina	3.0%
15	 Mexico	2.0%	15	Mexico	2.3%	15	Mexico	2.7%
16	 Argentina	1.8%	16	Saudi Arabia	1.7%	16	 Turkey	2.4%
17	 Saudi Arabia	1.8%	17	Poland	1.6%	17	 Australia	2.3%
18	 Poland	1.5%	18	 Turkey	1.5%	18	 Saudi Arabia	1.8%
19	 Belgium	1.4%	19	Belgium	1.3%	19	 Poland	1.6%
20	 Netherlands	1.3%	20	 Argentina	1.3%	20	 Egypt	1.6%

  Change in ranking over prior five years

Source: IQVIA Market Prognosis, Sep 2019; IQVIA Institute, Dec 2019

Notes: Rankings using Constant US\$ with Q2 2019 exchange rates, except Argentina using US\$

Exhibit 12: Global Medicine Invoice Spending Share and Growth by Region and Product Type

SPENDING 2019 US\$	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER	TOTAL US\$BN
Global	745.3	220.8	139.4	144.8	1,250.4
Developed	594.2	75.4	92.8	59.2	821.6
Pharmerging	82.0	115.4	36.7	70.6	304.7
Rest of World	69.2	30.0	9.9	15.0	124.1
2015–2019 CAGR	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER	TOTAL GROWTH
Global	6.1%	7.3%	2.5%	4.8%	5.7%
Developed	5.8%	7.0%	-0.1%	3.6%	5.0%
Pharmerging	9.9%	8.6%	11.0%	6.2%	8.6%
Rest of World	4.3%	3.7%	3.5%	3.2%	4.0%
SPENDING 2024 US\$	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER	TOTAL US\$BN
Global	58%	20%	11%	11%	1570–1600
Developed	71%	11%	11%	7%	985–1015
Pharmerging	28%	38%	12%	21%	475–505
Rest of World	56%	24%	8%	12%	85–95
2020–2024 CAGR	ORIGINAL BRANDS	NON-ORIGINAL BRANDS	UNBRANDED	OTHER	TOTAL GROWTH
Global	2–5%	4–7%	2–5%	2–5%	3–6%
Developed	1–4%	6–9%	1–4%	0–3%	2–5%
Pharmerging	6–9%	5–8%	6–9%	4–7%	5–8%
Rest of World	0–3%	-10– -7%	-1–2%	2–5%	-2–1%

Source: IQVIA Market Prognosis, Sep 2019; Innovation Insights, IQVIA Institute, Dec 2019

Notes: CAGR = Compound Annual Growth Rate

Spending in US\$ with historic and expected future exchange rates; CAGR in Constant US\$ with Q2 2019 exchange rates.

Other= OTC, Others and Vaccines

Methodologies

WHO-DDD

The World Health Organization (WHO) has developed a method of normalizing medicines of varying intended doses using a defined daily dose (WHO-DDD). The WHO-DDD measure is intended to represent a standard day of therapy for a maintenance dose of a chronic therapy. The WHO-DDD measure does not reflect actual treatment decisions and is not derived from distinct patients measured with anonymized data. The WHO-DDD guidance is provided online (see https://www.whocc.no/atc_ddd_index/) but does not include factors or guidance for all drug products. Distinct numeric factors are provided in relation to milligrams or international units (IU) depending on the medicine, or in terms of number of pills per day in the case of chronic medicines such as hypertension. Fixed dose combination products do not have WHO-DDDs directly provided by WHO but there are guiding principles suggested to calculate DDDs for these products. In reviewing the various areas of guidance, the IQVIA institute has developed factors using the same or highly similar concepts to represent over 99% of audited standard unit volume globally. These factors have then been used to further estimate DDD in unaudited countries. In unaudited countries, IQVIA Market Prognosis collates international trade data for the pharmaceutical sector. The IQVIA Institute has used audited data in geographically adjacent countries to infer various characteristics from this international trade data, including standard unit volumes. DDD in these countries has been estimated based on Standard Unit to DDD ratios in adjacent countries. Unaudited countries DDDs represent less than 5% of global estimated DDDs.

ESTIMATES OF NET MANUFACTURER REVENUE AND PRICES

IQVIA audits reflect invoice-based pricing derived from proprietary information gathered from wholesalers and company direct sales. While IQVIA invoice prices reflect supply-chain price concessions, they do not reflect the off-invoice discounts and rebates separately paid to insurers, or other price concessions paid to patients or other health system participants. In the U.S., estimated net prices and revenue are projected from a sample of large and mid-sized companies analyzed from 2011–2018, and projections of expected future changes to volume and prices to 2024. Branded products are included in the sample if their net sales amount is disclosed in financial filings with the Securities and Exchange Commission (SEC) and if the volume of sales captured in IQVIA audits is consistent with information provided directly by manufacturers in support of IQVIA proprietary datasets. Net prices are calculated by dividing publicly reported net sales values by volumes for the same products reported to IQVIA. Estimated brand net price growth for the total market is projected from the analysis sample to the total market. Net prices represent an estimate of the average manufacturer realized price, reflecting any reductions in net revenues due to off-invoice discounts, rebates, co-pay assistance or other price concessions, and do not necessarily reflect the net costs paid by insurers, the federal government or patients, which all vary significantly and independently. For generic companies, a sample of five large generic companies' generic portfolios were analyzed in aggregate consistent with their SEC filings, as specific generic product analyses are not possible. See *Medicine Use and Spending in the United States*, May 2019 for more details.

Notes on sources



This report is based on the IQVIA services detailed below.

IQVIA MIDAS® is a unique data platform for assessing worldwide healthcare markets. It integrates IQVIA national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and providing estimated product volumes, trends and market share through retail and non-retail channels. MIDAS data is updated monthly and retains 12 years of history.

IQVIA MARKET PROGNOSIS is a comprehensive, strategic market forecasting publication that provides decision makers with insights on the drivers and constraints of healthcare and pharmaceutical market growth. This includes political and economic developments, alongside dynamics in healthcare provision, cost containment, pricing and reimbursement, regulatory affairs and the operating environment for pharmaceutical companies. Market Prognosis contains economic forecasts from the Economist Intelligence Unit and delivers in-depth analysis at a global, regional and country level, and analyzes dynamics at distribution channel, market segment and therapy class level.

IQVIA THERAPY PROGNOSIS GLOBAL covers ATC3 level sales forecasts for major therapy areas in 14 key markets, 8 developed (United States, Japan, Germany, France, Italy, Spain, United Kingdom, and Canada) and 6 pharmerging (China, Brazil, Russia, India, Turkey and Mexico) and includes interactive modeling and event-based forecasts and comprehensive market summary.

ARK PATENT INTELLIGENCE is a database of biopharmaceutical patents or equivalents worldwide and including over 3,000 molecules. Research covers approved patent extensions in 52 countries, and covers all types of patents including product, process, method of use and others.

INNOVATION INSIGHTS is IQVIA's proprietary product classification system, categorizing products as original brands, non-original brands, unbranded, OTC or other on the basis of a selection of product attributes.

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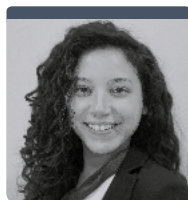
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Michael Kleinrock serves as research director for the IQVIA Institute for Human Data Science, setting the research agenda for the Institute, leading the development of reports and projects focused on the current and future role of human data science in healthcare in the United States and globally. Kleinrock leads the research development included in Institute reports published throughout the year. The research is focused on advancing the understanding of healthcare and the complex systems and markets around the world that deliver it. Throughout his tenure at IMS Health, which began in 1999, he has held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team, which is now the IQVIA Institute for Human Data Science. He holds a B.A. degree in History and Political Science from the University of Essex, Colchester, UK, and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, UK.



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About the Institute

The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry and payers.

Research Agenda

The research agenda for the Institute centers on 5 areas considered vital to contributing to the advancement of human health globally:

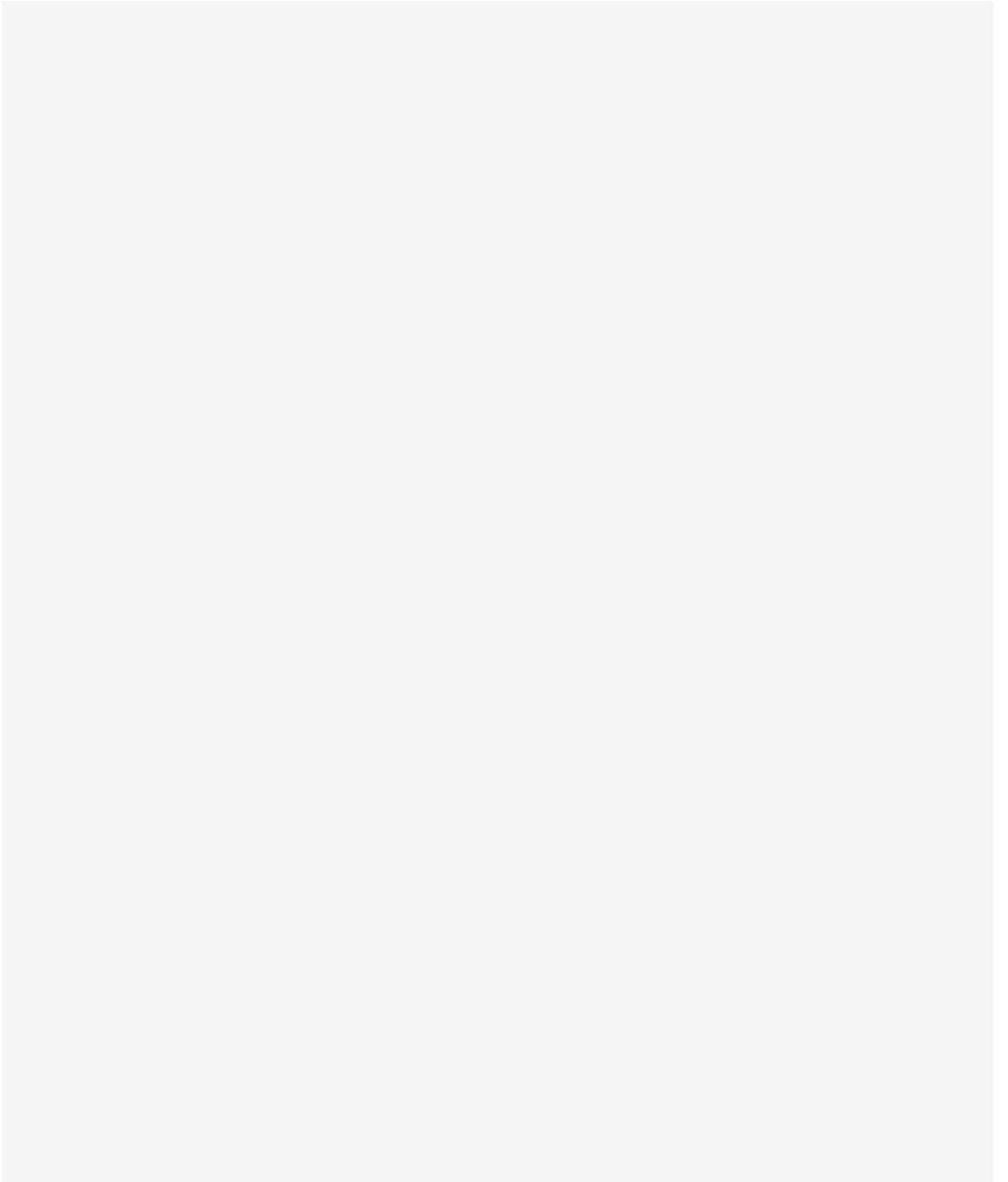
- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

Guiding Principles

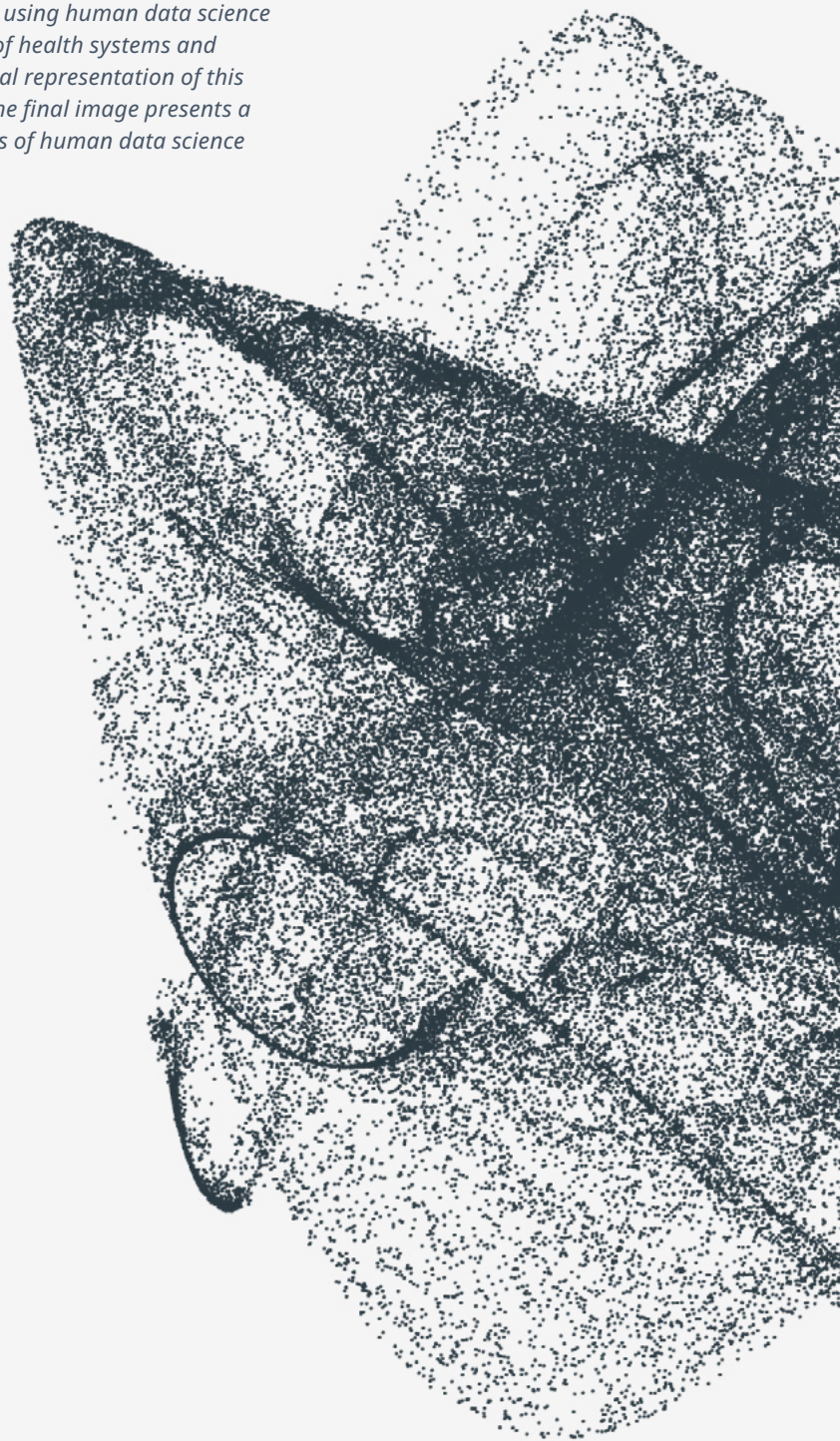
The Institute operates from a set of Guiding Principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.



The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.

The data on the cover for this Global Trends Report is derived from the core analytical files for the report. The data is global and includes medicine spending, defined daily doses and standard unit data, and the ratio of standard units to defined daily doses.



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