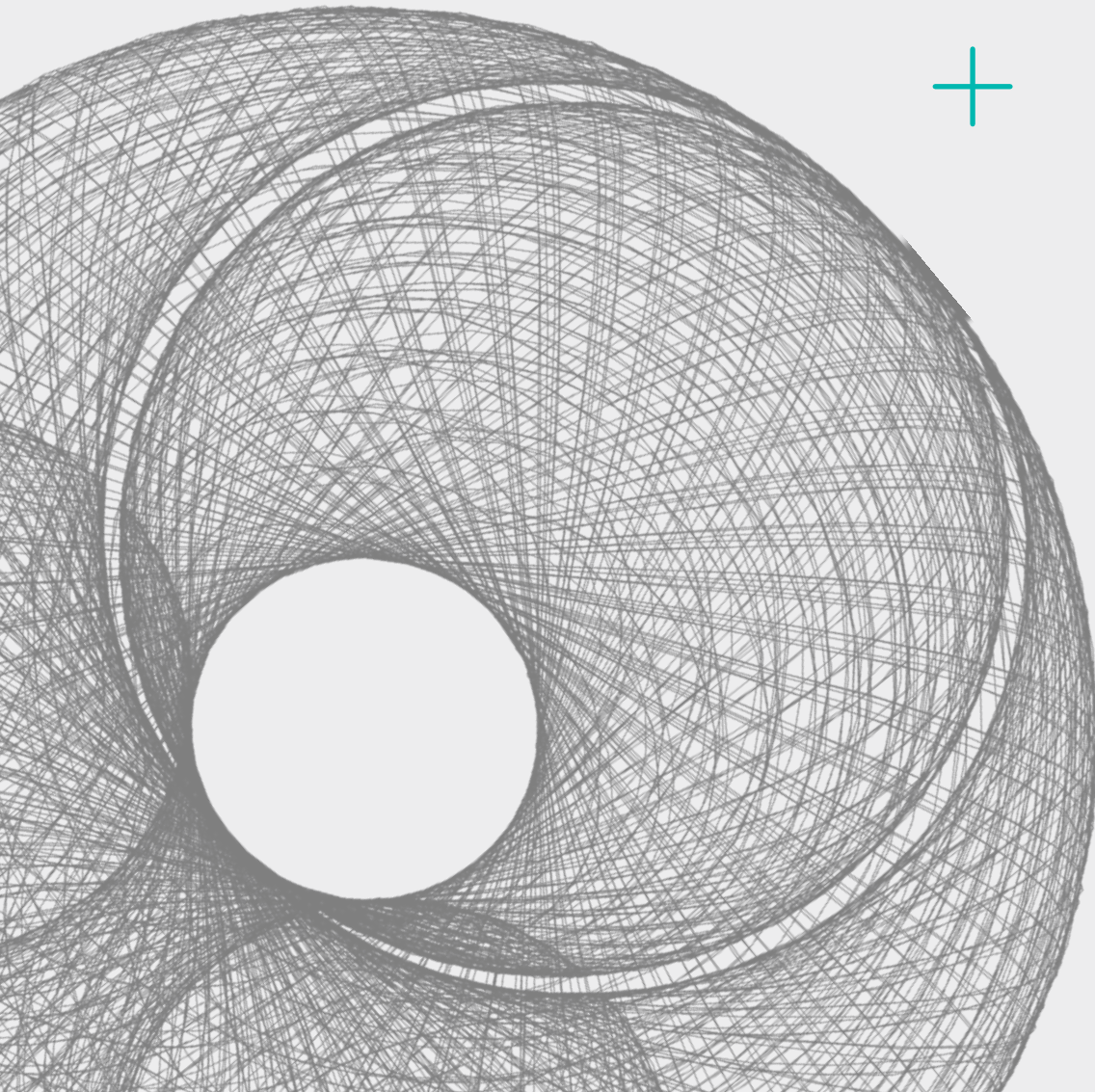




# The Use of Medicines in the U.S. 2023

USAGE AND SPENDING TRENDS AND OUTLOOK TO 2027



APRIL  
**2023**

# Introduction

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As we look back on 2022, the third year of the COVID-19 pandemic, we see areas of greater clarity around the utilization of health services, medicine use, and spending trends, while in other areas — including the impact of the most consequential healthcare reform in more than a decade — greater uncertainty appears to be on the horizon. The U.S. healthcare system remains fragmented, opaque and often dysfunctional, despite the rallying efforts of the pandemic years.

Evidence-based research and dissemination of findings remain a key foundation to advance our collective understanding and interpretation of events, and to take actions that will shape the future for all stakeholders. This annual trend report is intended to contribute to that understanding.

Areas of focus in this year's report range from looking at health system utilization and its recovery from the pandemic, to how medicine usage patterns have shifted, the complex nature of drug pricing, and the impact of out-of-pocket costs on patients.

While forecasting in this environment is not for the faint of heart, we have laid out our view of the drivers of change in medicine spending over the next five years. This includes the impact of biosimilar introductions affecting the single biggest selling drug in the U.S., and our assessment of the consequences of policy changes already legislated but still unclear and which will take effect in the coming years.

This study was produced independently by the IQVIA Institute for Human Data Science as a public service, without industry or government funding. The contributions to this report of Mohit Agarwal, Shahnveer Alam, Allen Campbell, Ruthy Glass, Luke Greenwalt, Urvashi Porwal, Abhinandan Sarmah and many others at IQVIA are gratefully acknowledged.

## Find Out More

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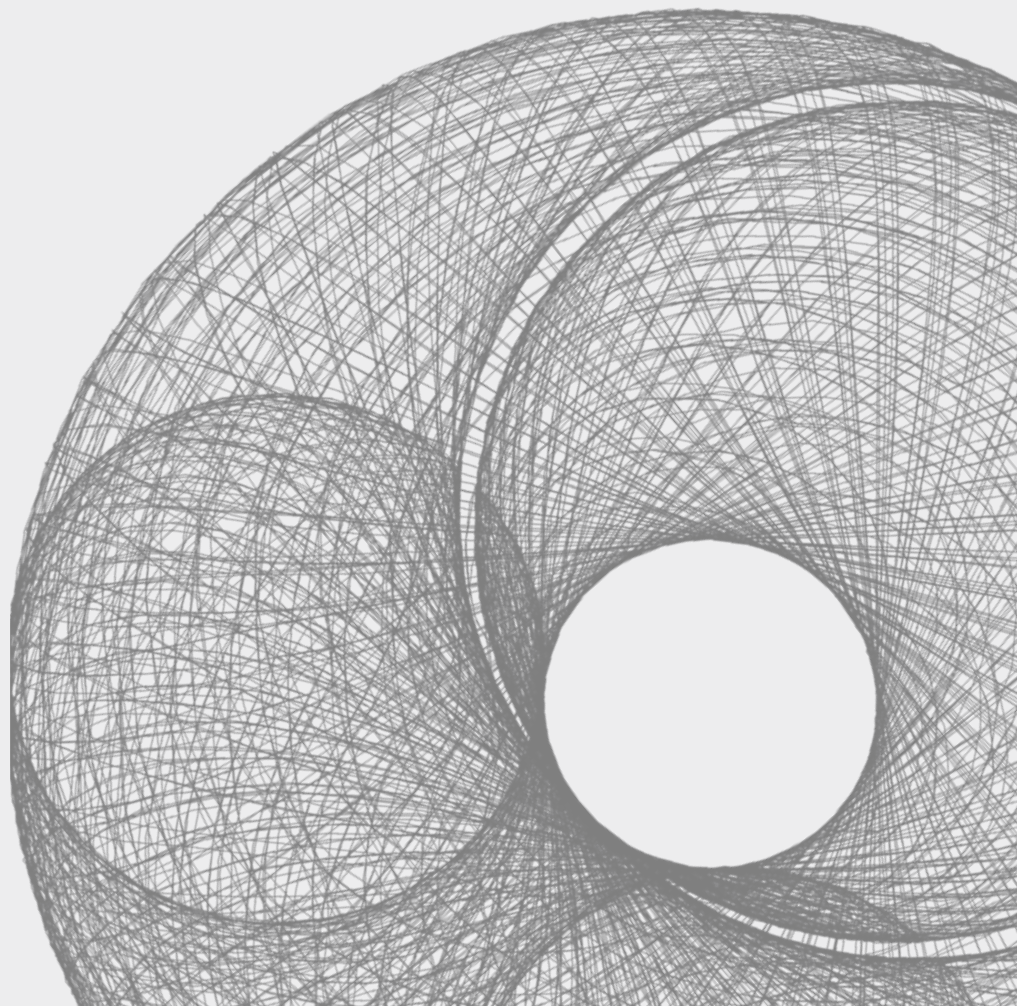
## MURRAY AITKEN

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# Overview

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The U.S. health system exhibited strong growth in medicine use and spending in 2022, while how patients engage with the health system and medicine utilization has shifted. The complex nature of how medicines are paid for and the changing policy environment raise important questions around medicine spending and patient out-of-pocket costs in the coming years.

## HEALTH SERVICES UTILIZATION

The IQVIA Health Services Utilization Index — which tracks patients visits, screening and diagnostic tests, elective procedures, and new prescriptions — has recovered to 100% of pre-COVID-19 levels in Q4 2022 while utilization has shifted in key indicators, with increased visits and new prescriptions but decreased elective procedures and screening and diagnostic tests. Telehealth visits have fallen to 5% of total visits in 2022, down from the peak of 26% seen early during the pandemic, but much higher than the pre-pandemic level of <1% and suggesting a fundamental shift in healthcare delivery.

Acute new prescriptions were elevated late in 2022 due to the severe respiratory illness season, including increased levels of flu, COVID-19, and respiratory syncytial virus circulating in the U.S. The current flu season peaked earlier than prior years and cases were 14% higher than the three-season average through early

March. Due to increased concern over the impact of flu, flu vaccinations remain 20% above historic levels. Other pediatric vaccinations remain below pre-pandemic levels while adult vaccinations have returned to normal, with shifts in the types of vaccines received and the setting where vaccines are administered.

## MEDICINE USE

Medicine use reached 242.6 billion days of therapy in 2022, growing 2.6%. Biosimilars have provided increased patient access to medicines, accounting for 25% of total volume of the molecules with biosimilars on the market, although there is wide variation in uptake across molecules, reflecting differences in strategies adopted by originator and biosimilar manufacturers, payer and PBM decisions, as well as clinician and patient preferences.

In retail drug usage, dispensed prescriptions reached 6.7 billion in 2022 with growth at 3.6% exceeding pre-pandemic levels. Within this growth are notable areas of utilization in 2022, including ADHD medicines, mental health prescriptions for girls under 19, antibacterials and newer diabetes therapies also used to treat obesity. Lower levels of utilization were recorded in 2022 for prescription opioids — where levels are now lower than in 2000 — and long-acting birth control.

## MEDICINE SPENDING AND GROWTH DRIVERS

Spending on medicines — at net manufacturer prices — reached \$429Bn in 2022, growing 5.3% including the continued contribution of COVID-19 vaccines and therapeutics. Spending at list prices grew at 7.4% over the past five years, but payers' spending grew at 4.5% and patients' costs grew at 1.4%. Spending at list prices has increased faster than all-payer net spending but far slower than 340B institutions, as negotiated discounts and rebates to payers and providers increase in competitive markets and 340B organizations account for a larger share of medicine use.

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***Spending on medicines — at net manufacturer prices — reached \$429Bn in 2022, growing 5.3% including the continued contribution of COVID-19 vaccines and therapeutics.***

Specialty medicines now account for 51% of spending, up from 32% in 2012, driven by growth in immunology and oncology, though the contributions of COVID-19 vaccines and oral therapeutics have lifted the share of spending on traditional medicines in the last two years.

Total drug spending at estimated net manufacturer prices increased by \$103Bn over the past five years, primarily driven by new products and brand volume. Volume growth has been driven by immunology, oncology, COVID-19 and diabetes. Losses of exclusivity for biologics and introduction of biosimilars has increased dramatically in the past three years, offsetting increased spending on new products, with brand sales of those products dropping by \$33Bn over the past five years compared to \$4Bn over the prior five years and reflecting a growing role for biosimilars. Increases in list prices of protected brands have fallen to a low of 3.7% in 2022, while net prices were unchanged on average, marking the fifth consecutive year with net price increases of less than 1%.

### **PATIENT OUT-OF-POCKET COSTS**

Patient out-of-pocket costs rose \$3Bn in 2022 to \$82Bn and remain a significant burden for a relatively small part of the population even as average costs per prescription are flat or declining. Without the nearly \$19Bn in manufacturer copay assistance in 2022, out-of-pocket costs would have exceeded \$100Bn. Medicare aggregate out-of-pocket costs have risen over the past five years, with population and volume increases accounting for most of the increase offset by price reductions.

Overall, 7% of patients reach annual out-of-pocket costs above \$500 compared to 15% in Medicare, with commercially insured patients having lower costs due to benefit designs and use of co-pay coupons or vouchers. Annual out-of-pocket caps in Medicare Part D passed in the Inflation Reduction Act could save 1 million patients \$1,700 on average. Due in part to high costs, patients starting new therapy abandoned 94Mn prescriptions at

pharmacies in 2022 with increasing frequency as out-of-pocket costs rise and abandonment over 40% for prescriptions over \$125.

Insulin costs continue to decline but patient payments above \$35 are more common for these drugs than in the overall market. Over 20% of insulin prescriptions carry an out-of-pocket cost above \$35 and with policy changes under the Inflation Reduction Act and manufacturer price reductions, patients could have saved \$561Mn in 2022 with costs capped at \$35.

### **OUTLOOK TO 2027**

Use and spending on medicines in the U.S. will return to pre-pandemic growth projections by 2024 but new pressures on net growth from new pricing policies will impact later years. Spending on medicines is forecast to be unchanged over the next five years with growth expected between -2 to 1%, remaining similar to current levels of spending at \$429Bn. This outlook reflects structural market dynamics, complex usage patterns, and competition, as well as the effects of new policies and legislation.

Over 250 new drugs are expected to launch within the next five years and contribute over \$100Bn in new spending. Policy changes, competition between manufacturers, and payer pressure are expected to ensure net prices of protected brands decline over the next five years and list price growth remains low. Biosimilar introductions and uptake are expected to save the U.S. healthcare system over \$180Bn over the next five years, though uncertainties remain around pricing and uptake.

Oncology, neurology, and obesity will drive the most growth in spending during the forecast period, and next-generation biotherapeutics may reach \$12Bn in annual sales by 2027, though significant scientific and commercial uncertainty exists in this fast-evolving area.

## Health services utilization

- The Health Services Utilization Index has recovered to 100% of pre-COVID-19 levels in Q4 2022 while utilization has shifted in key indicators, with increased visits and new prescriptions but decreased elective procedures and screening and diagnostic tests.
  - The Health Services Utilization Index indicates the U.S. has a cumulative lower level of utilization of 8% compared to pre-COVID-19 levels, which may embed a mix of concerning gaps in prevention, diagnosis and treatment and disengagement from care, and some avoided interactions from decreased routine illness such as flu.
  - Telehealth visits have fallen to 5% of total visits in 2022, down from the peak of 26% seen early during the pandemic, but much higher than the pre-pandemic level of <1% and suggesting a fundamental shift in healthcare delivery.
- New prescriptions for chronic therapies remain below pre-pandemic levels while chronic continuing were not disrupted, with acute new prescriptions elevated late in 2022 due to the severe respiratory illness season.
  - The current flu season peaked earlier than in prior years and cases are 14% higher than the three-season average through early March. Flu vaccinations remain 20% above historic levels.
  - Pediatric vaccinations remain below pre-pandemic levels while adult vaccinations have returned to normal, with shifts in the types of vaccines received and the setting where vaccines are administered.

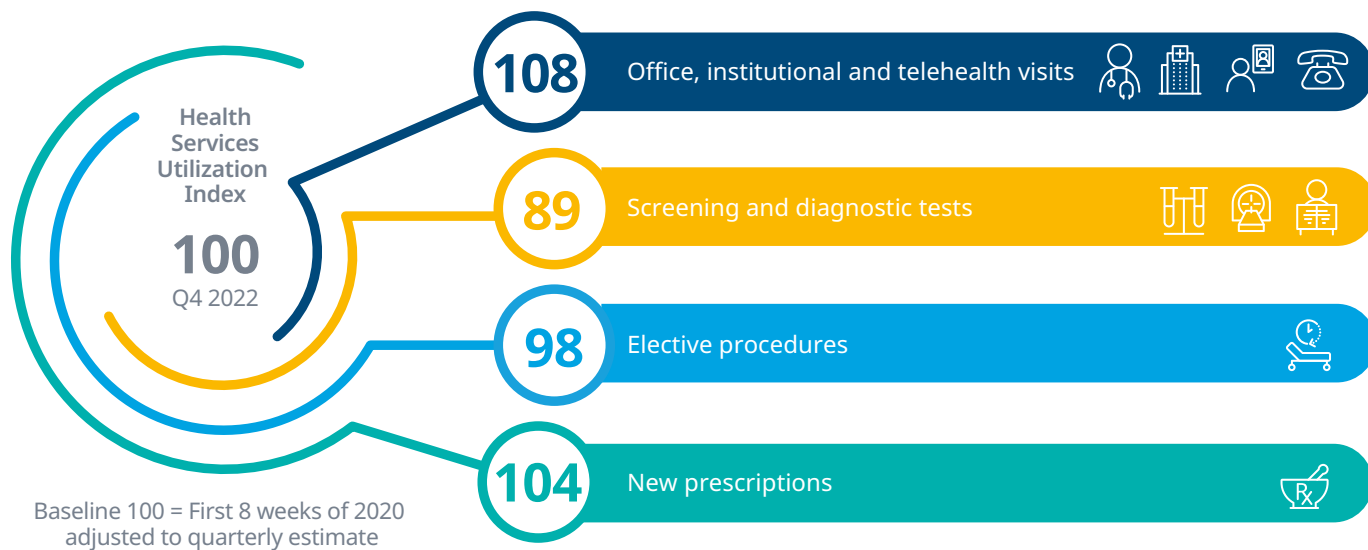


*Overall healthcare utilization has returned to pre-pandemic levels with utilization varied across individual indicators. However, the U.S. healthcare system had a cumulative 8% lower level of utilization across the pandemic compared to pre-COVID-19 levels.*



# The Health Services Utilization Index indicates the U.S. is operating at pre-COVID-19 levels with shifts in utilization

Exhibit 1: Overview of Health Services Utilization Index



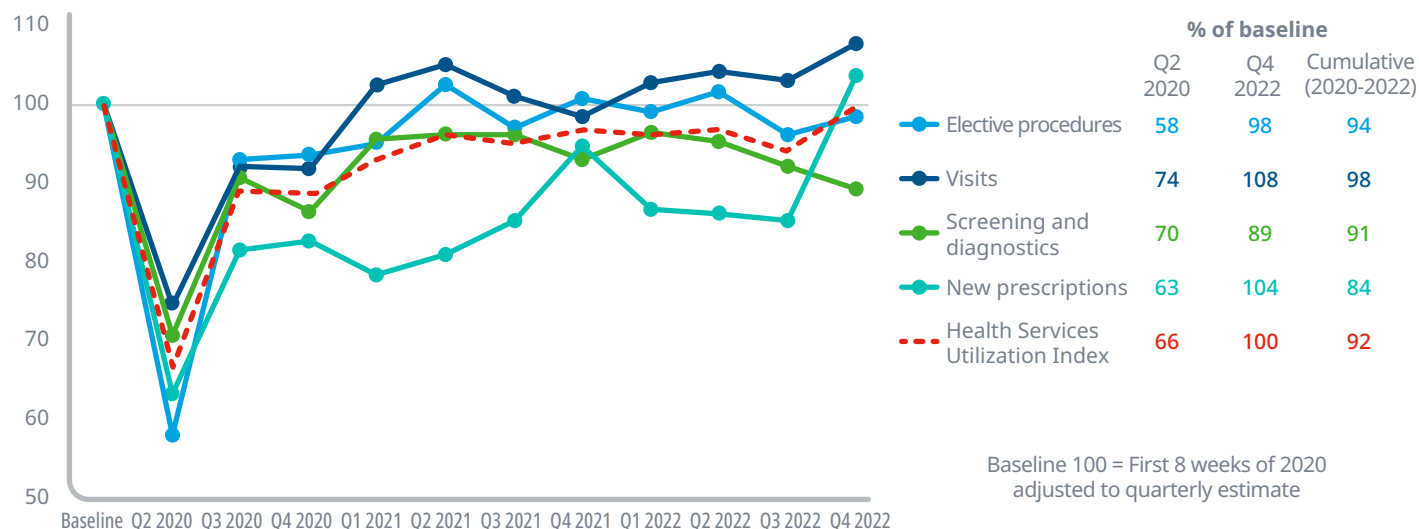
Source: IQVIA Institute; IQVIA Medical Claims Data; LAAD Prescription data, week ending 12/30/2022.

- The return to a pre-pandemic level of utilization in the health system is critical to ensuring all Americans — including those who have not been infected by the virus SARS-CoV-2 — receive the preventive and treatment services they need.
- A Health Services Utilization Index has been created and includes four essential components of a health system and measures their utilization against a base period of the eight-week average from January 4 to February 28, 2020.
- The four index components are equally weighted, and for each component a score of 100 or higher indicates a return to baseline levels, including elective procedures, doctor visits (face-to-face — office, hospital or clinic — or via telehealth), diagnostic lab tests, and new brand or generic prescriptions filled.
- By fourth quarter of 2022, with COVID-19 cases significantly lower than in prior years and many Americans returning to pre-pandemic activities, the overall utilization index recovered to 100, indicating a return to baseline, with both visits and new prescriptions above baseline but diagnostic tests and elective procedures 11% and 2% below baseline, respectively.

Notes: Each component of the index compares the difference between actual values per week and baseline average for the eight weeks from January 4 to February 28. New prescriptions excludes COVID-19 vaccines and therapeutics.

# The Health Services Utilization Index recovered to 100 in Q4 2022 from increased office visits and flu vaccines while other indicators lag

Exhibit 2: Health Services Utilization Index and component metrics percentage of 2020 baseline



Source: IQVIA Institute; IQVIA Medical Claims Data; LAAD Prescription data, week ending 12/30/2022

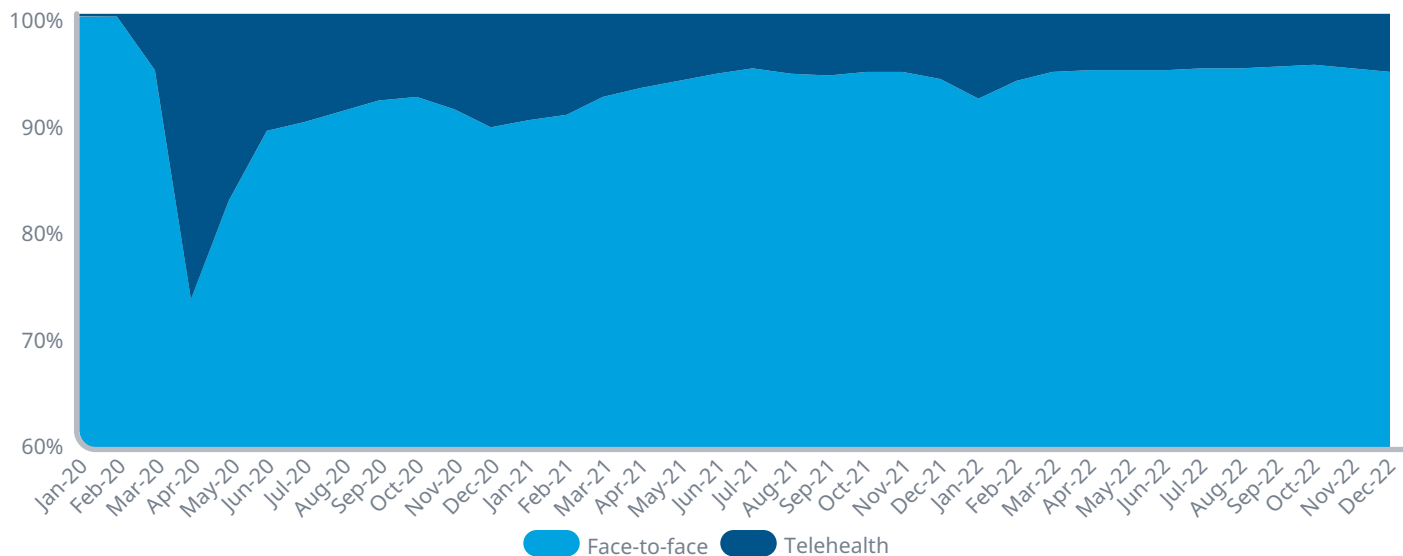
- The cumulative Health Services Utilization Index across the pandemic (Q2 2020-Q4 2022) remains at 92 despite a recovery in recent quarters to pre-pandemic levels, indicating both concerning gaps in preventive and treatment services that have yet to be addressed and avoided interactions with the healthcare system due to declines in routine illnesses (e.g., flu).
- Doctor visits — including face-to-face and telehealth — were the least impacted during the pandemic and have remained above pre-pandemic levels since early 2021, however the cumulative index remains 2% below baseline.
- Screening and diagnostic tests have remained below baseline throughout the pandemic and declined throughout 2022, likely driven by the declining use of COVID-19 testing in medical settings as testing decreased and at-home testing became more accessible.
- Elective procedures were the most heavily impacted early in the pandemic but returned to baseline in 2021 and have remained at or near baseline since; however, the cumulative index is heavily impacted by the early pandemic decline and remains 6% below baseline.
- Until Q4 2022, new prescriptions remained below baseline throughout the pandemic, with a cumulative index 16% below baseline. A bump in new prescriptions in Q4 2022 was driven by high levels of flu vaccination; without this factor, new prescriptions would be 7% below baseline.

Notes: Each component of the index compares the difference between actual values per week and baseline average for the eight weeks from January 4 to February 28. New prescriptions excludes COVID-19 vaccines and therapeutics.



## Telehealth visits accounted for 5% of visits in 2022, down from 26% in April 2020 but up from <1% pre-pandemic

Exhibit 3: Share of visits face-to-face vs. telehealth, 2020–2022

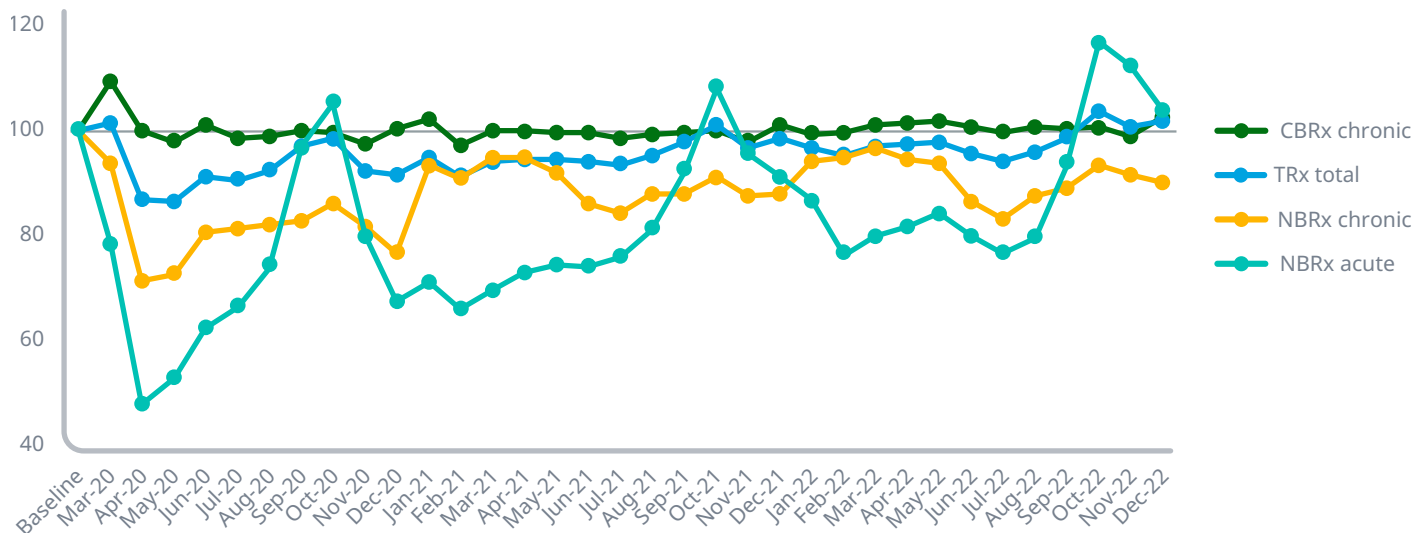


Source: IQVIA National Medical and Treatment Audit, Dec 2022.

- Early in the pandemic, the rapid adoption of telehealth offset some of the declines in doctor visits during lockdowns and requirements in hospitals and medical practices.
- Telehealth visits accounted for less than 1% of visits prior to the pandemic, rose to 26% in April 2020 at the height of the pandemic, and declined to 5% over the last half of 2022.
- Slight increases in the use of telehealth can be seen during times of increased COVID-19 activity (i.e., December 2020, January 2022) as phone or video visits, particularly for those suspected of having COVID-19, can be used to reduce the spread of the virus.<sup>1</sup>
- As of the end of 2022, 43 states required commercial insurers to reimburse for telehealth, although only 24 states have laws addressing payment parity between face-to-face and telehealth visits.<sup>2</sup>
- As the COVID-19 Public Health Emergency is set to come to an end in 2023, some of the flexibilities for telehealth allowed under the emergency will expire. The ability to prescribe medications via telehealth was broad throughout the pandemic, however the Drug Enforcement Administration recently proposed permanent rules for telehealth prescribing of controlled substances, which would require at least one in-person visit for controlled substance prescriptions.<sup>3</sup>

## New prescriptions for chronic therapies remain below pre-pandemic levels while chronic continuing were not disrupted

Exhibit 4: Dispensed new and continuing prescriptions by therapy type as a percent of 2020 baseline by month



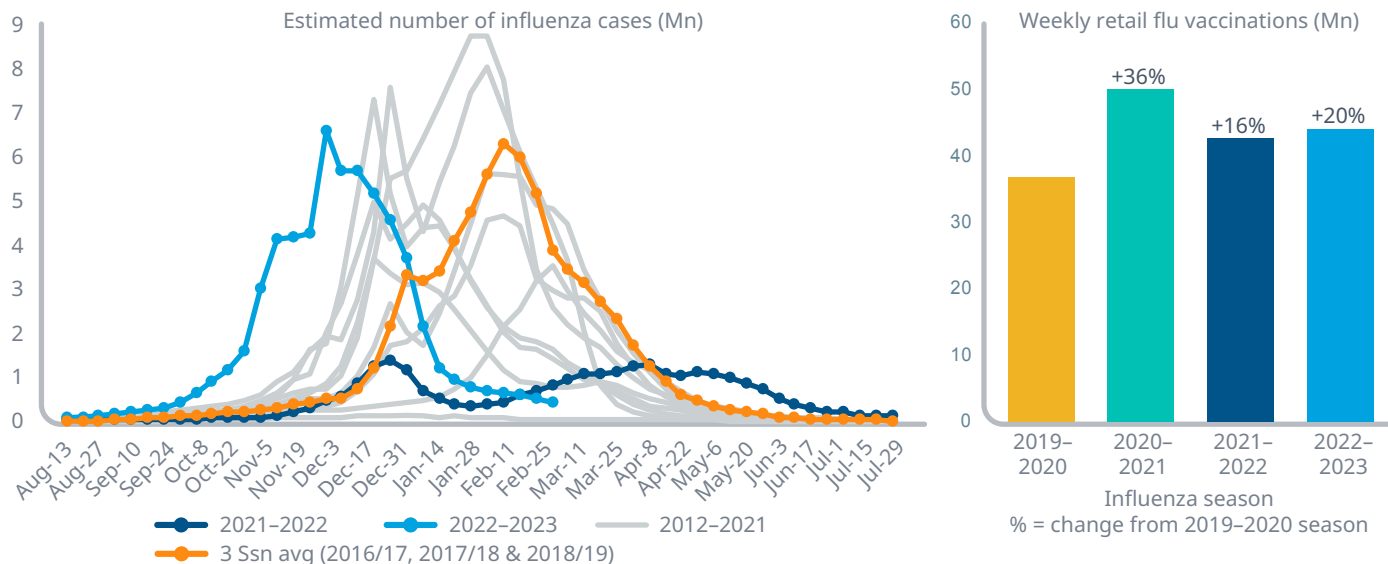
Source: IQVIA National Prescription Audit: New to Brand, Jan 2023.

- New to brand prescriptions (NBRx) are those where the patient is new to the medicine in the past year, and these were significantly below baseline for chronic prescriptions.
- Acute prescriptions have been significantly disrupted throughout the pandemic with the exception of flu vaccines in the fall months, predominantly because patients didn't require them due to reductions in risk factors from masking, social distancing, stay-at-home orders, and other public health controls. A significant respiratory illness season late in 2022 resulted in an increase in acute prescriptions above baseline.
- Chronic continuing prescriptions have remained relatively stable since March 2020 when a significant amount of stockpiling occurred as COVID-19 began to spread across the U.S.
- If adjusted for seasonality and compared to historic 2018/2019 prescription levels, both acute and chronic new prescriptions were above historic levels throughout 2022, suggesting January-February 2020 had unusually high levels of medicine use.

Notes: Average monthly difference between actual values per week and baseline average for the eight weeks from January 4 to February 28 are plotted. Prescriptions are unadjusted. New to Brand (NBRx) prescriptions are those where the patient had no prescription of the medicine in the prior year and includes naïve patients as well as those who switch from another drug or add a new drug to their existing regimens. Continuing prescriptions (CBRx) are those where the patient has filled a prescription of the same medicine in the past year and can include gaps in dispensing. Chronic is determined as whether the medicine is generally intended to be prescribed for more than 180-days, and acute are all other medicines. Chronic and acute are not specific patient or prescription attributes and do not reflect the potential for some medicines to be used on a long-term basis against recommendations. Excludes OTC and COVID-19 vaccines and therapeutics.

# The current flu season peaked earlier than prior years and cases are 14% higher than three-season average through early March

Exhibit 5: Estimated number of U.S. influenza cases and total retail flu vaccinations



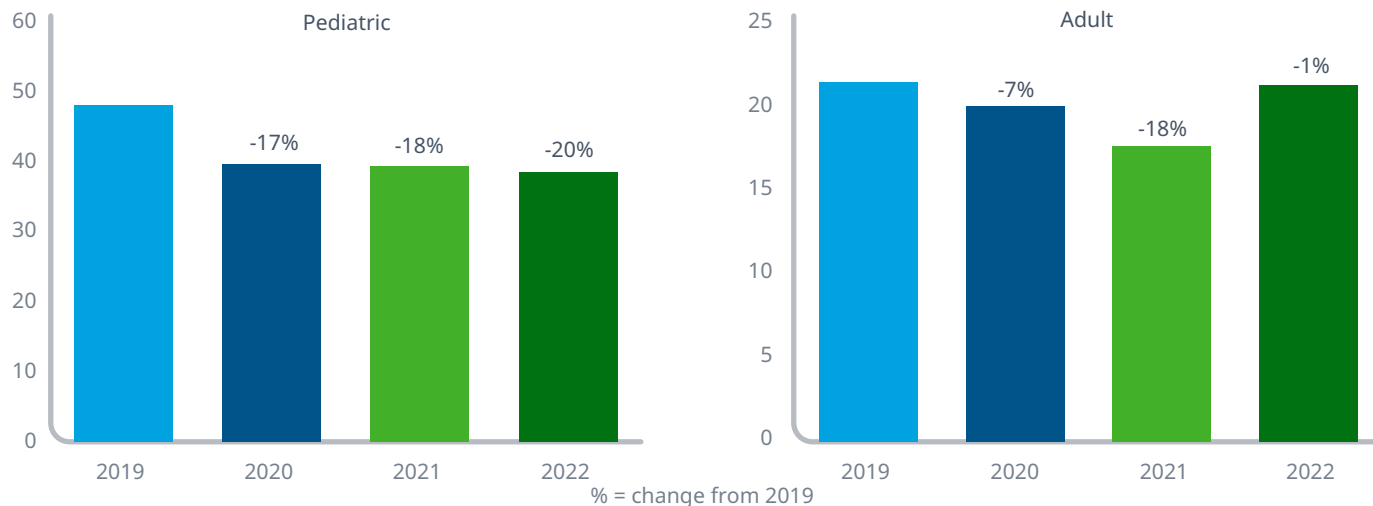
Source: IQVIA Consumer Health FAN, week ending 3/11/2023; IQVIA RxInsight, IQVIA Institute, Mar 2023.

- During the COVID-19 pandemic, public health measures such as social distancing and masking significantly reduced the levels of influenza in the U.S.<sup>4</sup>, with the estimated number of influenza cases in the 2020-2021 and 2021-2022 seasons being 94% and 60% below the historic three-season average, respectively.
- As Americans largely returned to pre-pandemic activities in 2022 and social distancing and masking became less frequent, influenza cases rose rapidly in October and November and were seven times historic levels through the end of December, with the Centers for Disease Control and Prevention (CDC) issuing a health advisory in early November to alert the nation to a concerning early rise in respiratory viruses as influenza, COVID-19, and respiratory syncytial virus (RSV) strained healthcare systems.<sup>5</sup>
- Influenza cases rapidly dropped in January 2023 as Americans took measures to protect themselves, including vaccination; however, cumulative seasonal influenza cases through early March 2023 remained 14% above historic levels.
- Influenza vaccinations continued to be higher than pre-pandemic levels with vaccinations reaching 44Mn Americans in the 2022-2023 season up 20% from the 2019-2020 season but down 12% from the peak vaccinations seen in the 2020-2021 season.

Notes: IQVIA's FAN (Flu/Cold/Respiratory Activity Notification Program) modeling draws on a combination of diagnostics information from office-based medical claims, prescription claims from retail pharmacies, and deliveries of over-the-counter medications to establish estimates of diagnosed and treated populations. Flu vaccinations captured in IQVIA RxInsight are based on transactions processed through pharmacy dispensing systems in chain and independent pharmacies, food stores and mass merchants.

## Pediatric vaccinations remain below pre-pandemic levels while adult vaccinations have returned to near historic levels

Exhibit 6: Number of vaccines given annually for selected vaccines by age group (Mn), 2019–2022



Source: IQVIA National Sales Perspective, Dec 2022; IQVIA Institute, Mar 2023.

- Adult and pediatric vaccines shown here on average represent 79% of all vaccine (excluding influenza and COVID-19 vaccines) volume in the U.S., with the other 21% of volume composed of vaccines approved across age groups and travel vaccines.
- Annual pediatric vaccines have continued to decline throughout the pandemic, with 2020 17% below, 2021 18% below, and 2022 20% below 2019 levels, while the pediatric population has declined 1% during the pandemic through 2021.<sup>6</sup> Coinciding with this drop in vaccination is a 12% increase in the share of Americans who believe parents should be able to choose not to vaccinate their children.<sup>7</sup>
- Adult vaccinations in 2022 remained near pre-pandemic levels due to increased levels of pneumococcal vaccination, offset by decreased levels of shingles and HPV vaccination.
- The Public Readiness and Emergency Preparedness (PREP) Act expanded the role of pharmacists and interns in vaccine administration during the COVID-19 pandemic. Pharmacies play an important role in vaccination, particularly in adults (e.g., shingles, pneumococcal vaccines).<sup>8</sup>

Notes: Pediatric vaccines include vaccines for haemophilus influenzae type b (Hib), hepatitis A, hepatitis B, poliovirus, pneumococcal (Pneumovax 13 only), rotavirus and the combo vaccines for measles-mumps-rubella (M-M-R), DTaP/hepatitis B/polio and DTaP/Poliovirus/Hib/Hepatitis B Vaccine. Adult vaccines include vaccines for HPV, shingles, and pneumococcal (Pneumovax 23, Prevnar 20 and Vaxneuvance only). Adult and pediatric vaccines all retail and non-retail. List and age group based on a review of CDC's U.S. Vaccine's webpage: <https://www.cdc.gov/vaccines/terms/usvaccines.html> and the FDA label for vaccines not included on CDC's list.



## Medicine use

- Use of medicines by days of therapy grew by 2.6% to 242.6 billion in 2022, down from 4.7% growth in 2021.
- In non-retail drug usage, long-term care usage remains below 2019 levels due to disproportionate impacts of the pandemic on these settings and has recovered the least of non-retail sites of care.
- In retail drug usage, dispensed prescriptions reached 6.7 billion in 2022 while growth at 3.6% exceeds pre-pandemic levels.
- Changes in the share of prescriptions by method of payment were driven by changes in both usage and enrollment.
- Biosimilars launched to date account for 25% of competitive molecule volume with wide variation in uptake across molecules.
- Most therapy areas continued to grow in adjusted prescription volumes in 2022, with a severe respiratory illness season contributing to strong growth in infectious disease and anti-bacterial prescriptions.
- Use of antibacterials grew 6.8% in 2022 to 2.4 billion days of therapy but remains below pre-pandemic levels, with use in children increasing rapidly in the second half of 2022.
- Use of ADHD medicines grew 11% over the last five years, with women 20–64 now accounting for one-third of prescriptions.
- Mental health prescriptions have increased since 2019 with girls under 19 seeing a 33% increase in use.
- Newer diabetes therapies have seen significant growth with GLP-1 agonist use rising across both diabetes and obesity late in 2022.
- Per capita prescription opioid use continues to decline to levels seen in 2000, however overdose deaths continue to rise.
- Contraception use peaked in 2017 and has been declining over the last five years, driven by lower use of long-acting birth control.

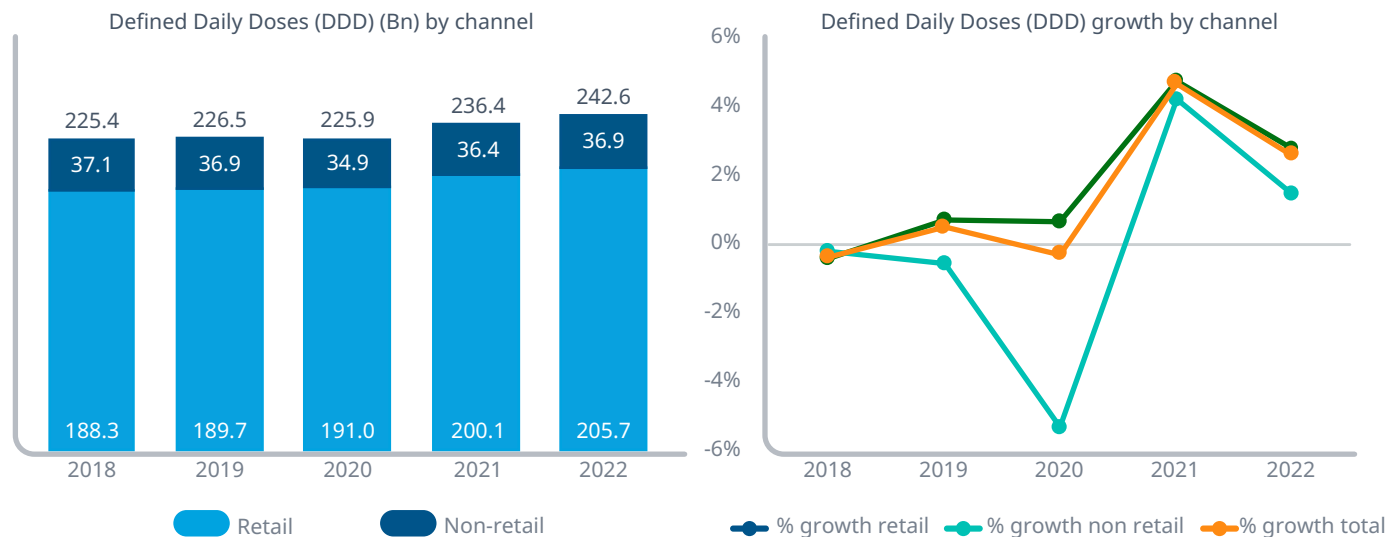
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*Medicine use continues to grow but with patterns reflecting a new normal in a post-COVID world.*

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# Growth in days of therapy across retail and non-retail has slowed in 2022 following a strong rebound in 2021

Exhibit 7: U.S. Defined Daily Doses (DDD) trend and growth by channel, 2018–2022



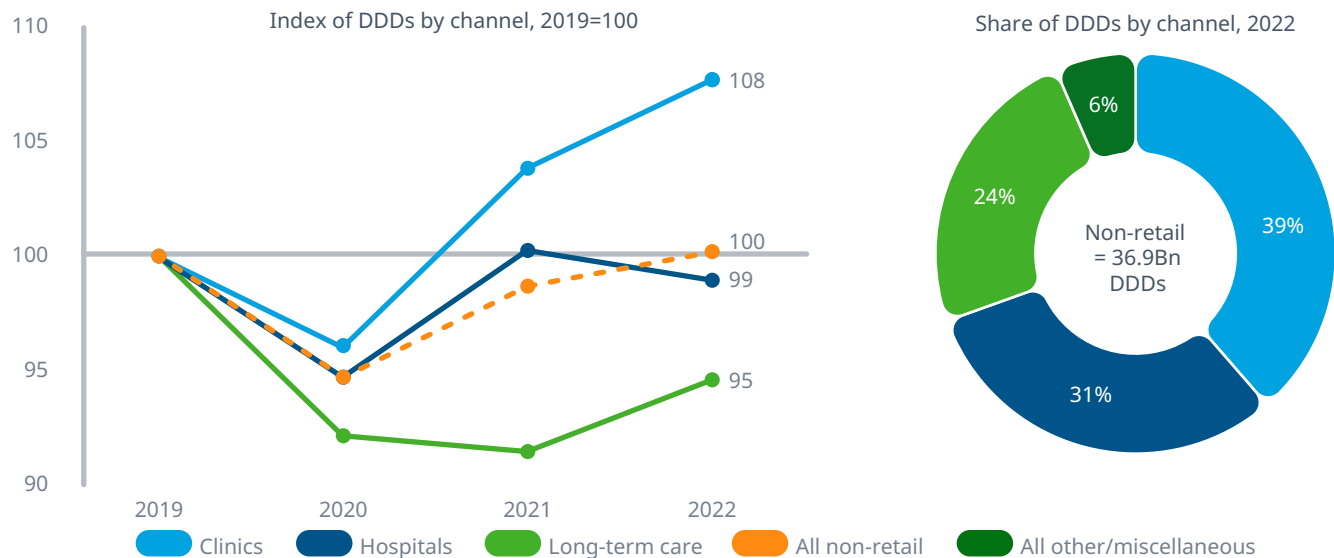
Source: IQVIA National Sales Perspective, Dec 2022; IQVIA Institute, Feb 2023.

- The use of medicines in the U.S. — based on defined daily doses — has grown 7.2% over the last five years to nearly 243 billion days of therapy in both retail and non-retail settings in 2022.
- Retail drugs currently represent 85% of medicine use in the U.S., with only 15% of use in non-retail settings, which has been declining since 2018.
- The use of drugs dispensed from retail pharmacies has continued to grow at a rate of 1.7% annually, on average, reaching 205.7 billion days of therapy in 2022.
- Drugs in non-retail settings, such as hospitals and long-term care, were significantly impacted by the pandemic, with days of therapy contracting 5.3% in 2020, but recovering to pre-pandemic levels in 2022.
- The non-retail downturn and muted recovery reflect how care in these settings was impacted due to lockdowns and healthcare setting requirements.

Notes: Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology). Excludes COVID-19 vaccines and therapeutics.

# Long-term care drove declines in non-retail medicine use since 2019, while hospitals and clinics have recovered after disruptions

Exhibit 8: U.S. Non-retail Defined Daily Doses (DDD) indexed to 2019 values and share by channel



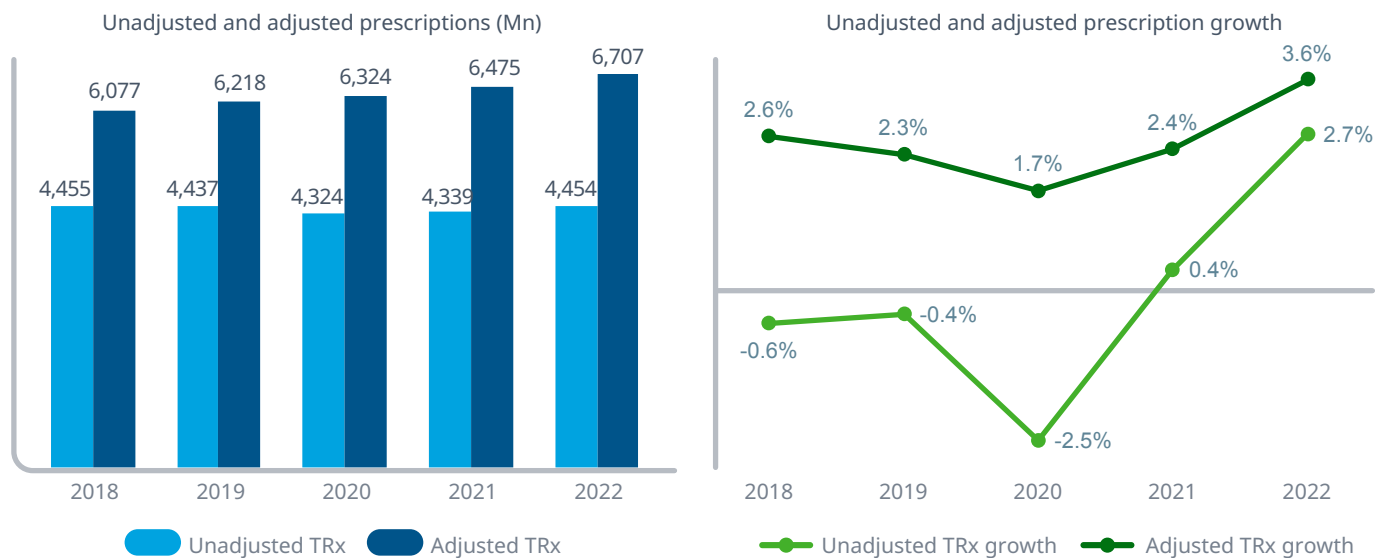
Source: IQVIA National Sales Perspective, Dec 2022; IQVIA Institute, Feb 2023.

- Non-retail medicine use has seen significant impacts over the last three years, returning to baseline pre-pandemic use in 2022 following a 5% decline in the first year of the pandemic.
- Despite a return to baseline, non-retail medicine use has shifted as usage in clinics, which was least impacted by the pandemic, is now 8% above baseline levels and usage in long-term care, which declined 8% early in the pandemic, remains 5% below baseline.
- This decline is driven by declines in use in long-term care facilities, which declined 7.3% in 2020 and an additional 0.7% in 2021, having significant impact on overall non-retail usage, given long-term care accounts for 28% of non-retail days of therapy.
- Patient utilization of long-term care facilities declined during the pandemic, likely due to concerns about high levels of COVID-19 cases and deaths in these settings.<sup>9</sup>
- Clinics and hospitals represent 70% of non-retail medicine use and have recovered from disruptions in medicine use in 2020, offsetting declines in other non-retail settings.
- Other non-retail settings such as prisons, universities, and home health, account for just 6% of non-retail medicine use, and these settings have had varying impacts on medicine use due to the pandemic, with home health seeing an 18% increase in usage since 2019 as patients received care at home to avoid contracting or transmitting COVID-19 in medical settings.

Notes: Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology). Hospitals includes non-federal hospitals and federal facilities. All other/miscellaneous includes home health, HMO, prisons, universities and all other non-retail not separately defined. Excludes COVID-19 vaccines and therapeutics.

# Dispensed prescriptions reached 6.7Bn in 2022, with 3.6% growth compared to 2021

Exhibit 9: Unadjusted and adjusted dispensed prescriptions (Mn) and growth, 2018–2022



Source: IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023.

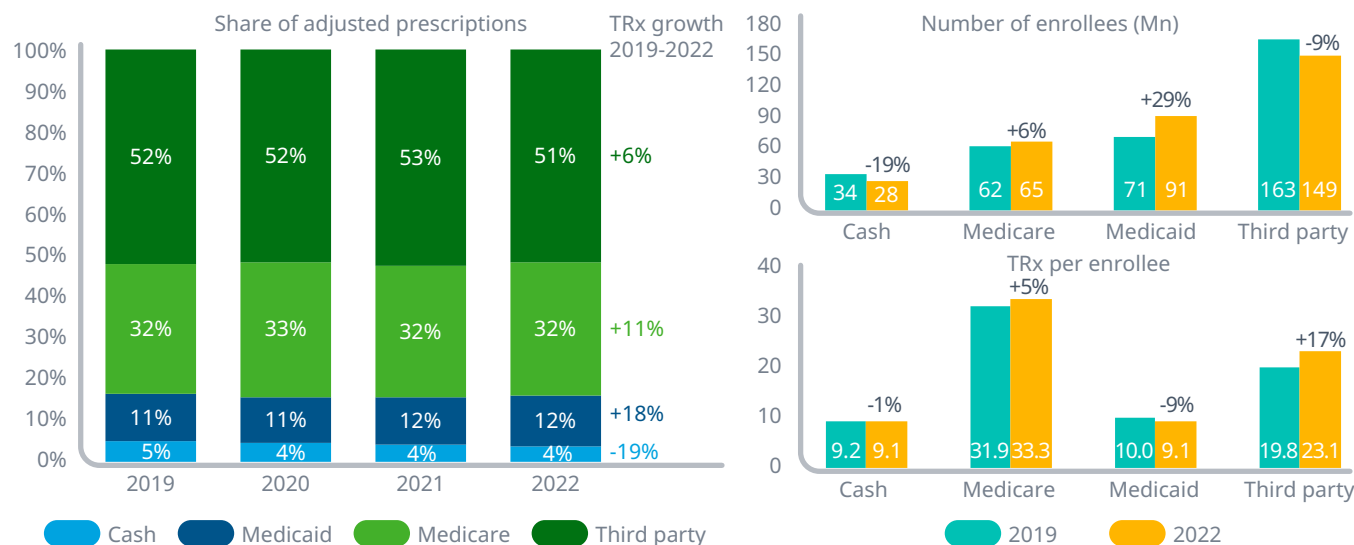
- Total prescriptions — adjusted for prescription length — reached 6.7 billion in 2022, up from 6.1 billion in 2018.
- In total, dispensed prescriptions increased 3.6% in 2022 and had minimal impacts on growth throughout the pandemic.
- The increasing importance of 90-day prescriptions is evident as the rate of growth without adjustment for prescription length was -0.1% on average over the last five years, but 2.5% after adjustment with 1.1 billion 90-day prescriptions in 2022.
- Mail prescriptions, which had been declining prior to the pandemic, have increased 7% from 2019.
- In 2022, 50% of all prescriptions were dispensed in 90-day amounts, up from 40% in 2018. This increasing utilization of 90-day prescriptions could lead to higher adherence to chronic medications as patients have been shown to be more adherent with 90-day prescriptions compared to 30-day.<sup>10</sup>
- The share of prescriptions dispensed as 90-day varies across channel, with 89% of mail prescriptions dispensed in 90-day amounts compared to 49% of retail pharmacy prescriptions. The 90-day share of retail pharmacy prescriptions has increased 12% over the last five years while mail has remained relatively stable.

Notes: Adjusted prescription counts are adjusted for length of prescriptions and re-aggregated (see methodology). Includes prescriptions dispensed in retail, mail, and long-term care settings. Excludes COVID-19 vaccines and therapeutics.



# Medicaid scripts per enrollee have declined 9% since 2019 while enrollment has grown 29%

Exhibit 10: Adjusted dispensed prescriptions by method of payment, 2019–2022



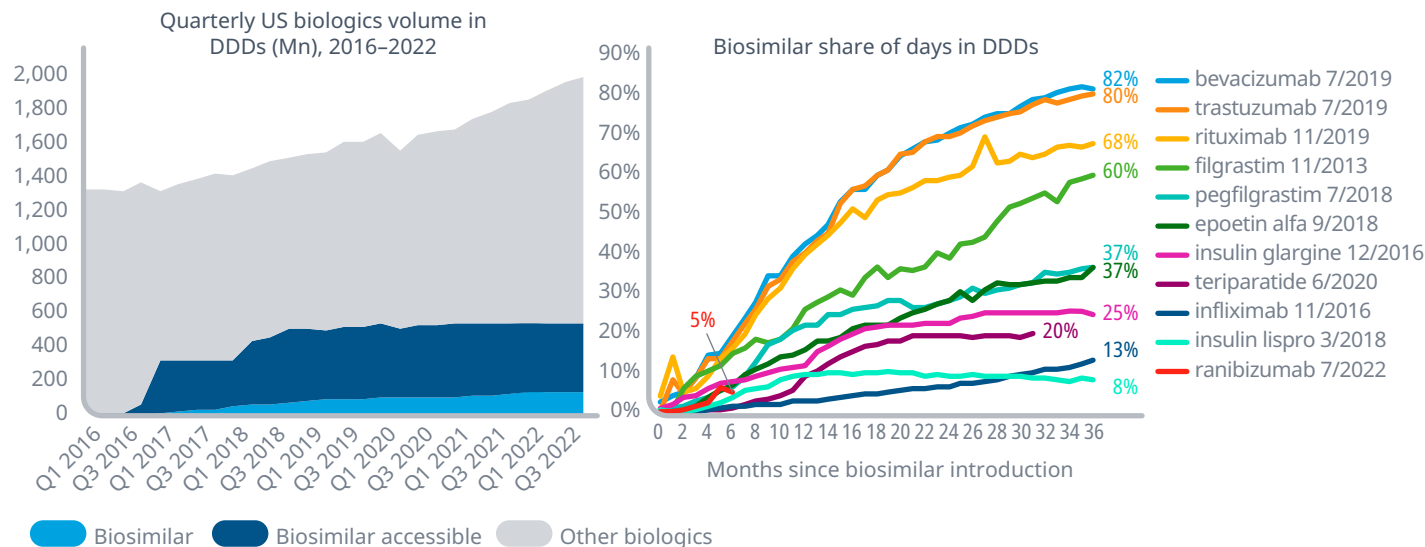
Source: IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023; Centers for Medicare & Medicaid Services, Oct 2022.

- The pandemic caused significant shifts in insurance coverage, with third-party enrollment declining 6% over the prior three years likely due to job loss and an aging population becoming eligible for Medicare. Commercial prescriptions, which account for 51% of prescriptions, have increased 17% per enrollee over the last three years.
- While the uninsured population in the U.S. has declined from 10.3% in 2019 to 8.3% in 2022,<sup>11</sup> people paying cash have been filling fewer prescriptions, with similar rates of decline in cash prescriptions and the uninsured population, leading to a less than 1% decline in per capita prescription usage.
- As the U.S. population continues to age, Medicare enrollment has climbed 6% since 2019 and 17% since 2016; medicine use also grew 11% throughout the pandemic, resulting in a 5% increase per enrollee over the last three years.
- Medicaid enrollment has increased 29% since 2019, or by 120 million people, due to economic disruption and Medicaid policy changes tied to pandemic relief legislation. Starting in April 2023, states may again begin disenrolling Medicaid enrollees — previously restricted by the COVID-19 public health emergency — which could result in 5 to 14 million people losing coverage.<sup>12</sup>
- Despite this growing population of Medicaid beneficiaries, Medicaid’s prescriptions have only grown 18% since 2019, resulting in a declining number of prescriptions per enrollee.

Notes: Enrollment numbers based on Medicare and Medicaid enrollment statistics from the Centers for Medicare and Medicaid Services and uninsured statistics from the Centers for Disease Control and Prevention. Excludes COVID-19 vaccines and therapeutics.

# Biosimilars launched to date account for 25% of competitive molecule volume with wide variation in uptake across molecules

Exhibit 11: Biologics volume and biosimilar share by molecule in Defined Daily Doses (DDDs)



Source: Biosimilars in the United States 2023–2027: Competition, Savings, and Sustainability. January 2023. Report by the IQVIA Institute for Human Data Science.

- The first biosimilar approved under the abbreviated pathway established by the Biologics Price Competition and Innovation Act launched in the U.S. in 2015, while some non-original biologics have been approved through other pathways both before and since.
- Currently, biosimilars represent 7% of total biologic volume with an additional 20% of volume accessible to biosimilars (i.e., originator medicines for which a biosimilar is on the market). Beginning in 2023, an additional 4% of volume is expected to become accessible as immunology drugs adalimumab, ustekinumab, and tocilizumab face biosimilar competition.<sup>13</sup>
- In molecules for which biosimilars are available, biosimilars represent 25% of volume, up from 14% in 2018 as biosimilars have become more widely accepted.
- In the first three years of launch, biosimilar uptake varies widely across molecules, from 8% of volume in insulin lispro to 82% of volume in bevacizumab, with several factors influencing uptake, including distribution method and reimbursement.<sup>13</sup>
- Biosimilar introduction frequently results in higher utilization of a molecule as lower costs — across both biosimilars and originators — offer increased access to patients.<sup>13</sup>

Notes: Biologics market volume excludes COVID-19 vaccines and therapeutics. Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology).

# Notable shifts in medicine use occurred across therapy areas in the U.S. in recent years

Exhibit 12: Notable trends in medicine use in 2022




## Antibiotic use and rising antimicrobial resistance

- **2.4Bn antibiotic days of therapy** in 2022 down 7% from pre-pandemic.
- Use in **children and older adults up 8%** in Q4 2022 from historic seasonal levels.

- **ADHD medicine** use **grew 11%** over the last 5 years to over 3Bn days of therapy in 2022.
- **Women aged 20–64** now **account for 33%** of prescriptions, up from 27% in 2018.

## Stimulant use and related shortages






## Mental health in young people

- **Mental health prescriptions** reached **567Mn** in 2022 up 9% since 2019.
- Mental health prescriptions in **girls under 19 up 33%** since pre-pandemic to 17Mn in 2022.

- **Over 500k GLP-1 agonist** new prescriptions across diabetes and obesity in February 2023, **up 152%** compared to prior year.

## Rising use of novel obesity drugs

## Combatting the opioid overdose epidemic

- Per capita prescription **opioid use down 64%** since the peak in 2011.
- Opioid overdose **deaths up 253%** since 2011.

- **Contraception use down 6%** in 2022 with **100Mn fewer** days of therapy.
- **Lower use of long-acting** birth control, such as IUDs and injectables.

## Concerning gaps in women's health

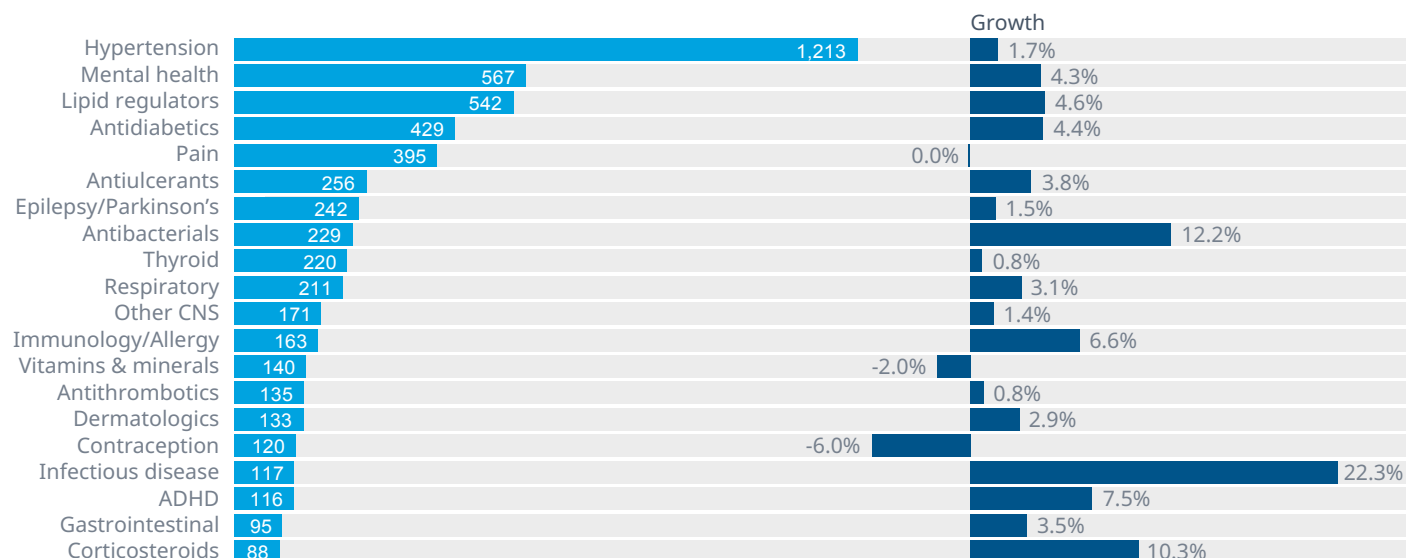


Source: IQVIA Institute, Apr 2023.

Notes:XXXXXXXXXXXXXXXXXX

## Most therapy areas grew in 2022, with a severe respiratory illness season impacting infectious disease and antibacterials

Exhibit 13: Adjusted dispensed prescriptions 2022 (Mn) and % growth from 2021



Source: IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023.

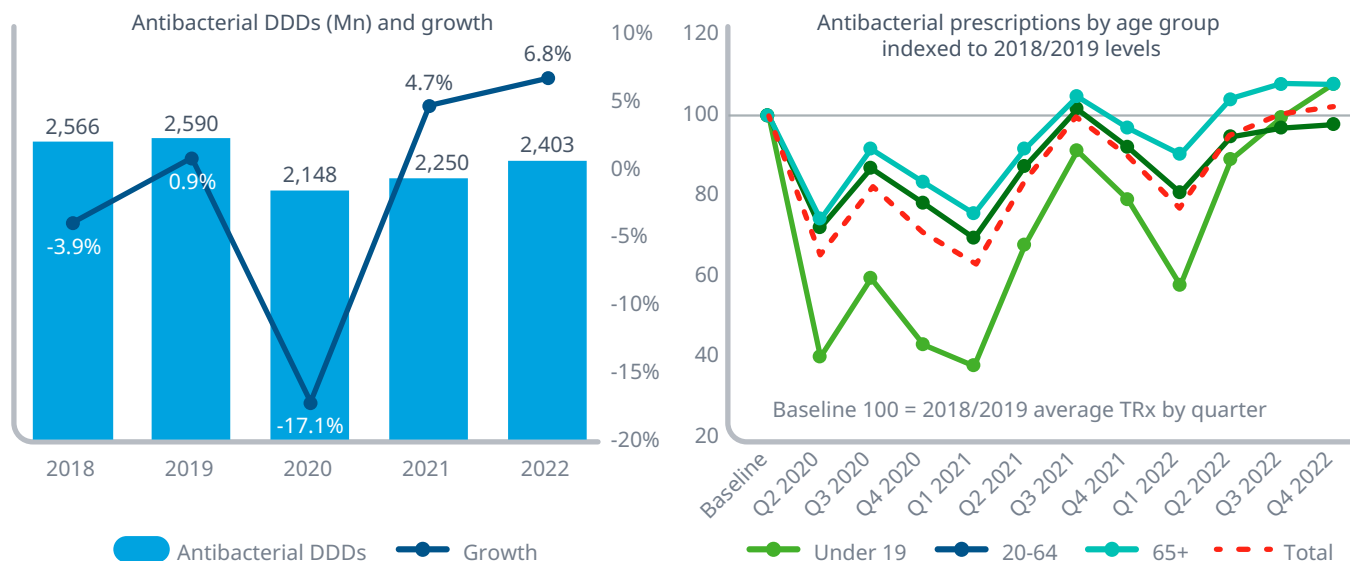
- Prescriptions across most therapy areas grew in 2022 after disruptions in growth earlier in the pandemic and following notable shifts in use (Exhibit 12).
- A severe respiratory illness season (Exhibit 5) contributed to significant growth across a range of acute therapies, including 22.3% growth in infectious disease and 12.2% growth in antibacterials.
- Mental health prescriptions reached 567 million in 2022, up from 544 million in 2021 and 515 million in 2020 as more Americans seek care for mental health disorders in the U.S.
- Corticosteroids grew 10.3% in 2022 after growing 10.5% in 2021, with use in managing COVID-19 remaining high and use for allergies and asthma recovering following significant declines during the pandemic, likely due to fewer asthma attacks.<sup>14</sup>
- Contraception and vitamins/minerals were the only therapy areas that saw declines in 2022. Contraception use has declined 6.6% since 2019, while vitamin/mineral use has returned to pre-pandemic levels following increases in treatments for vitamin D and potassium deficiency.

Notes: Therapy definitions are mutually exclusive. Excludes COVID-19 vaccines and therapeutics.



# Use of antibacterials grew 6.8% in 2022 to 2.4Bn days of therapy but remains below pre-pandemic levels

Exhibit 14: Antibacterial Defined Daily Doses (DDD) (Mn) and antibacterial prescriptions by age group



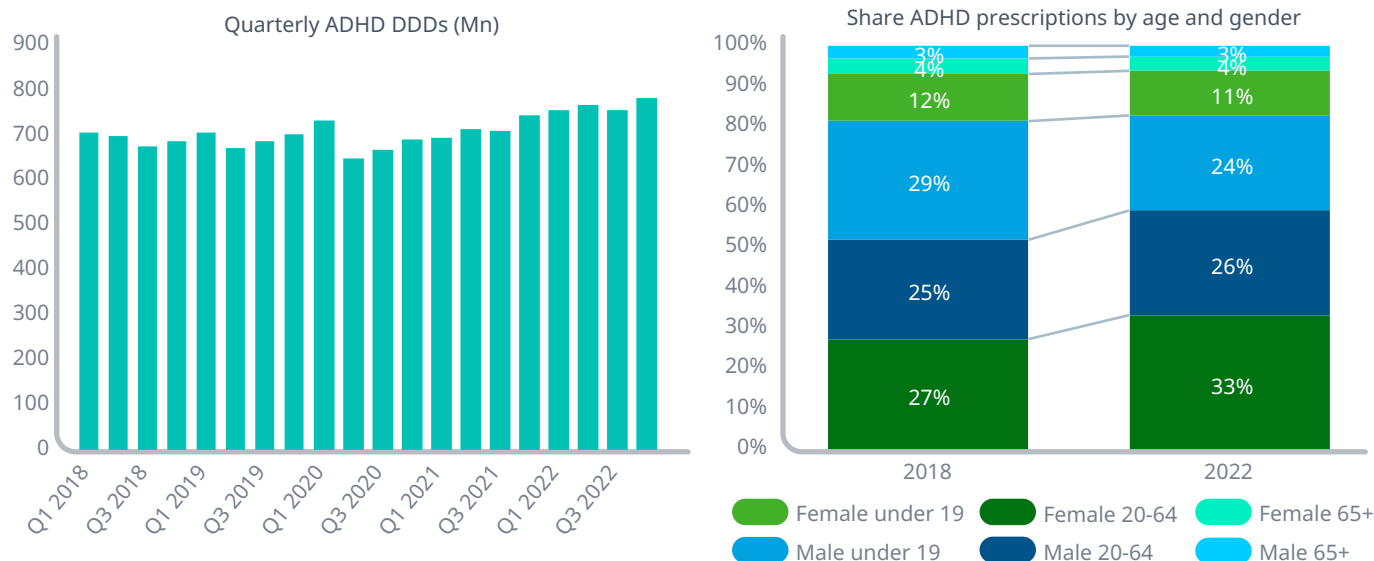
Source: IQVIA National Sales Perspective, IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Feb 2023.

- Antibacterial use grew to 2.4 billion days of therapy in 2022, up 6.8% from 2021 but 7.2% below pre-pandemic levels, likely due to social distancing and public health measures to reduce the spread of COVID-19 decreasing transmission of bacterial infections.
- Despite lower volumes of antibacterials utilized in the U.S., there is growing concern about antimicrobial resistance as deaths rose 15% in 2020 and nearly 80% of patients hospitalized with COVID-19 received an antibiotic — most upon admission — despite being ineffective.<sup>15</sup>
- Children under 19 saw the largest declines in antibacterial usage early in the pandemic, down 50% on average from pre-pandemic levels through Q2 2021. As schools re-opened and children returned to regular activities, antibacterial use climbed to 8% above baseline by the end of 2022.
- Return to baseline levels of antibacterial usage across age groups is likely driven by the return of seasonal levels of strep and ear infections, with the CDC noting particularly concerning levels of severe invasive group A strep infections in children.<sup>16</sup> These atypical patterns of demand throughout the pandemic have led to a widely reported shortage of pediatric amoxicillin commonly prescribed for these infections.<sup>17</sup>

Notes: Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology). Prescriptions by age based on prescriptions unadjusted for length of prescription. Index baseline based on the 2018 and 2019 average prescriptions in each month to adjust for seasonality of usage. Monthly indices are aggregated into quarterly averages.

## Use of ADHD medicines grew 11% over the last 5 years with women 20–64 now accounting for one-third of prescriptions

Exhibit 15: ADHD Defined Daily Doses (DDD) and share of prescriptions by age and gender, 2018–2022



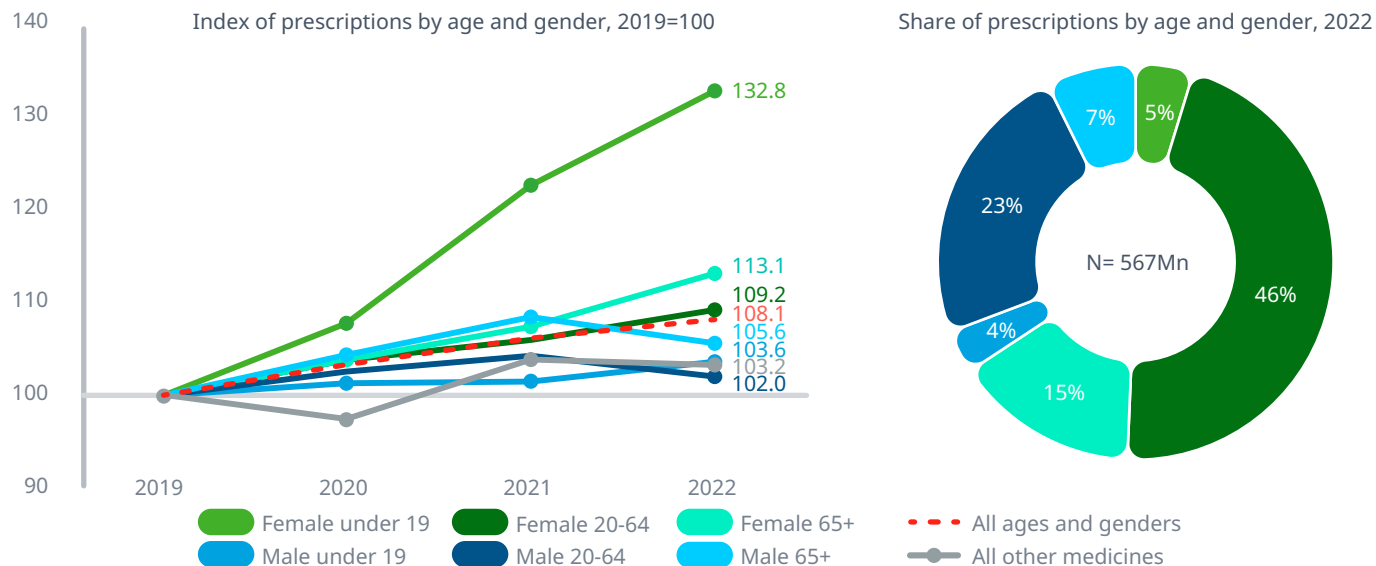
Source: IQVIA National Sales Perspective, IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023.

- Use of medicines for attention-deficit/hyperactivity disorder (ADHD) exceeded 3 billion days of therapy in 2022, up from 2.8 billion in 2018 and 2.5 billion a decade ago.
- Growth in ADHD medicines remained stable from 2018–2020, declining on average less than 1% annually over the three years; however, after a substantial decline in Q2 2020, use has risen significantly through 2021 and 2022, up 11% from 2018.
- Shortages for amphetamine mixed salts (e.g., Adderall) across a range of manufacturers throughout 2022 have been exacerbated by the rising demand for these medicines, however other medicines for treating ADHD, including extended-release versions of amphetamine, remained available.<sup>18</sup>
- In 2018, boys under 19 accounted for 29% of ADHD prescriptions and represented the largest share of prescriptions, however prescriptions in this age group were the most impacted by the pandemic, falling 7% below 2018 levels in 2020 and remaining 4% below in 2022.
- Adults aged 20–64 have seen the highest growth over the last five years, with prescriptions in women up 46% and in men up 26% from 2018, and women aged 20–64 now accounting for one-third of prescriptions.
- These shifts in usage likely reflect the impacts of remote work on adults and an increasing awareness of diagnosis criteria among clinicians.<sup>19</sup>

Notes: Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology). Includes prescription psychostimulants and non-stimulant ADHD medicines; does not include OTC psychostimulants such as caffeine. Prescriptions by age and gender based on prescriptions unadjusted for length of prescription.

# Mental health prescriptions have increased 8% since 2019 with girls under 19 seeing a 33% increase in use

Exhibit 16: Mental health prescriptions indexed to 2019 values and 2022 share by age and gender



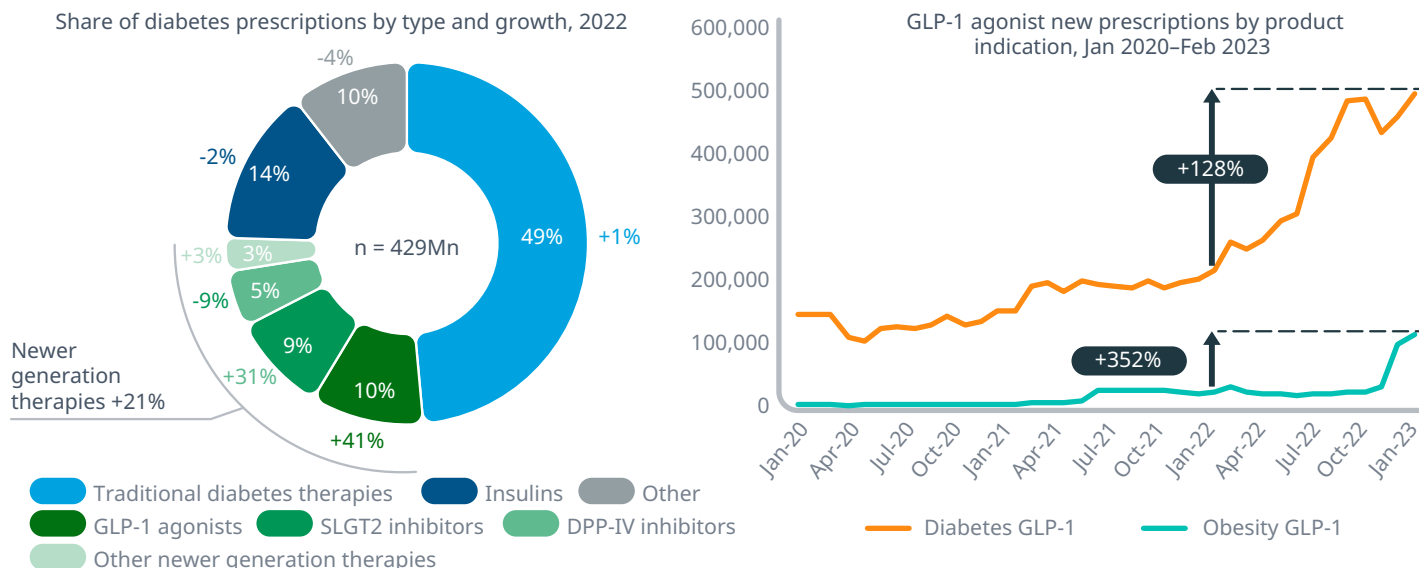
Source: IQVIA National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023.

- Mental health prescriptions — unadjusted for length of prescription — across all ages and genders are up 8.1% in 2022 from 2019 levels, compared to just 3.2% for all other medicines, as the pandemic exacerbated an ever-growing mental health crisis in the U.S.
- Ketamine, traditionally used for anesthesia and illicit recreational purposes, was approved for use in depression in 2019. Although use is limited to treatment-resistant depression and major depressive disorder, it has gained traction, with more than 100,000 prescriptions in 2022, more than tripling over the last three years.
- While all age groups and genders saw increasing usage of mental health prescriptions, there are apparent differences in usage between males and females, with females accounting for two-thirds of prescriptions in 2022 and women aged 20–64 accounting for 46%.
- Girls under the age of 19 have experienced the highest growth in mental health prescriptions, up 33% from 2019. This coincides with a concerning trend noted by the CDC among high school students where female students are more likely to experience poor mental health and suicidal thoughts and behaviors, and the percentage has increased more rapidly through 2021 than in male students.<sup>20</sup>
- Although not evident from medicine usage, LGBTQ+ students had the highest levels of depression and suicidal thoughts among demographic groups, with 22% of LGBTQ+ in 2021 reporting attempting suicide in the past year compared to 10% for all students – a concerning metric for a demographic group where more data and support is needed.<sup>20</sup>

Notes: Prescriptions by age and gender based on prescriptions unadjusted for length of prescription.

# Newer diabetes therapies have seen significant growth with GLP-1 agonist use rising across both diabetes and obesity late in 2022

Exhibit 17: Adjusted diabetes prescriptions by type and GLP-1 agonist new prescriptions by indication



Source: IQVIA National Prescription Audit, Feb 2023; IQVIA Institute, Mar 2023.

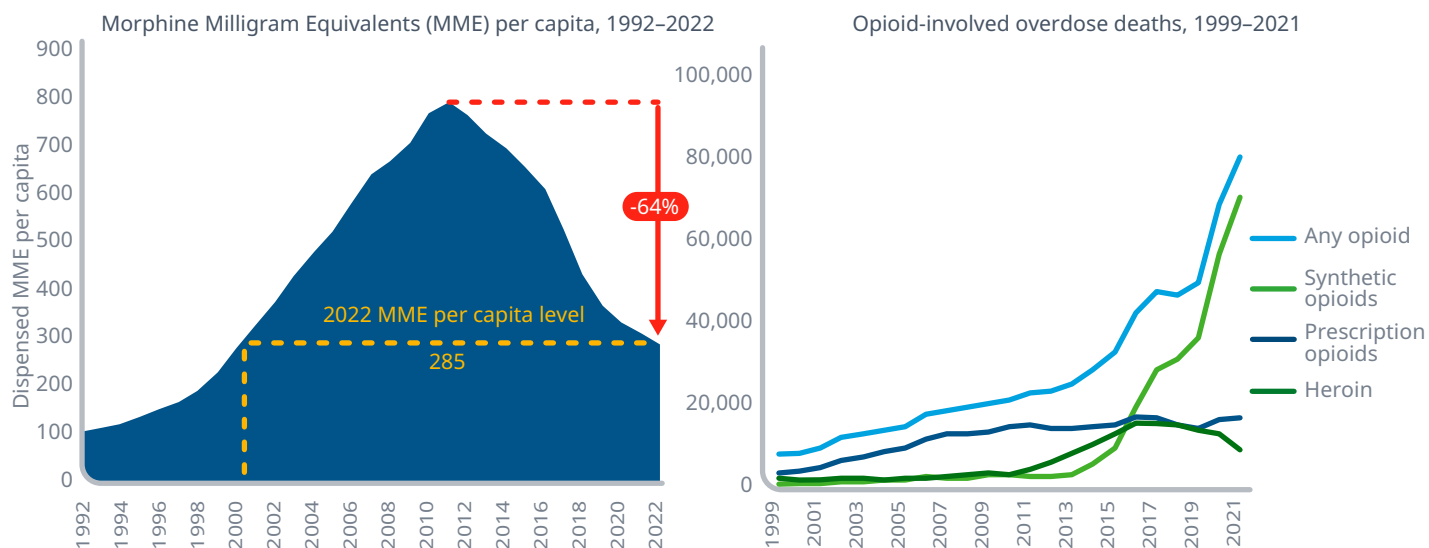
- In 2022, 429 million prescriptions were dispensed to treat diabetes, growing 4.4% in 2022 and 7.9% over the last two years.
- Nearly half of diabetes prescriptions in 2022 were for traditional therapies, including metformin and sulphonylureas, with metformin accounting for 74% of traditional diabetes therapies.
- Insulins, which have received significant attention related to out-of-pocket costs (Exhibit 41), account for 14% of diabetes prescriptions and have been declining in use, down 2% in 2022.
- Newer generation diabetes therapies, including DPP-IV inhibitors, SGLT2 inhibitors, and GLP-1 agonists, have had high growth in recent years, with all combined growing 21% in 2022.
- GLP-1 agonists were the fastest growing class of diabetes medicines in 2022 at 41%. Some of these medicines are approved for treating both diabetes and obesity, but under different products, at different dosages, and with different prescribing information.
- GLP-1 agonists across both diabetes and obesity saw rapid increases in new prescriptions at the end of 2022 and in early 2023, with diabetes new prescriptions up 128% in February 2023 compared to the prior year and obesity up 352%.
- The increasing popularity of GLP-1 agonists led to shortages in 2022 for semaglutide, which is approved for use as Ozempic and Wegovy in diabetes and obesity, respectively, potentially leaving existing patients to find alternative options.<sup>21</sup>

Notes: Other diabetes prescriptions include diabetes tests and glucagon for treating severe hypoglycemia. GLP-1 agonist products are grouped based on indication listed on latest FDA label and do not reflect off-label use.



## Per capita prescription opioid use continues to decline to levels seen in 2000, however overdose deaths continue to rise

Exhibit 18: Prescription opioid use overall and opioid-involved overdose deaths



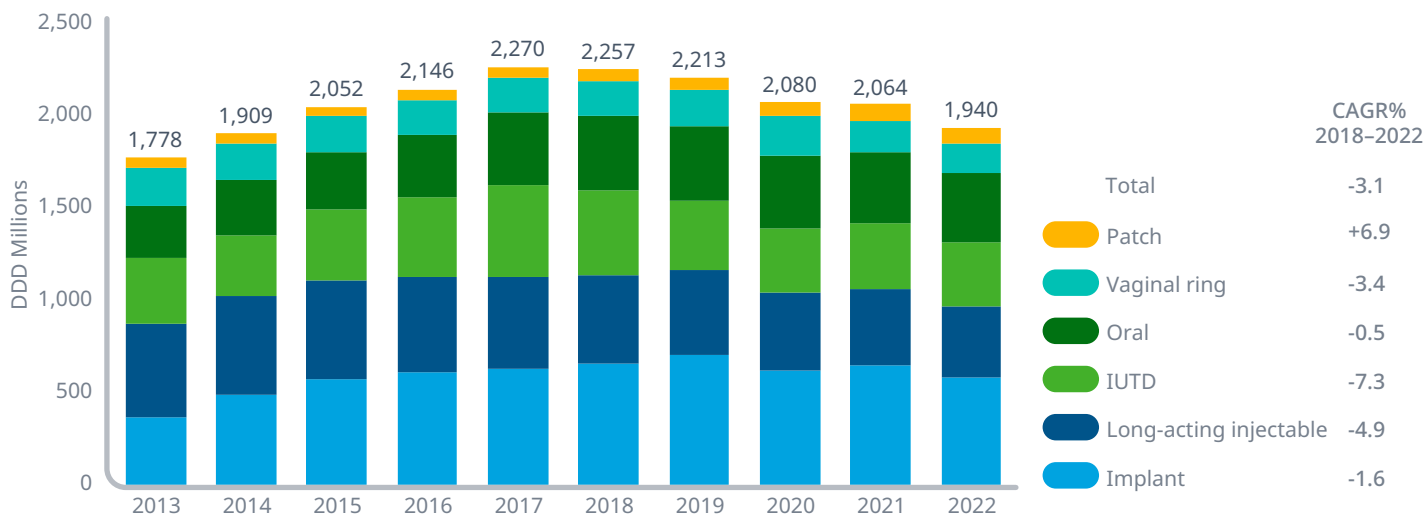
Source: IQVIA Xponent, IQVIA National Prescription Audit, Sep 2022; IQVIA Institute, Mar 2023; National Institute on Drug Abuse, Feb 2023.

- Prescription opioid volume declined for the 11th consecutive year after peaking in 2011.
- In 2022, use of opioids declined by 7.4% to 95 billion MMEs, with per capita levels down 64% from the peak in 2011 and dropping back to levels of use seen in the year 2000.
- The greatest reductions in prescription opioid volume — measured in morphine milligram equivalents — have been in higher-risk segments receiving greater than 90 MMEs per day.
- These decreases in volume have been driven by changes in clinical usage, regulatory and reimbursement policies, and progressively more restrictive legislation enacted since 2012, including class-wide guidance from FDA in 2016.
- Despite significant progress in reducing opioid prescriptions to combat the opioid overdose epidemic, overdose deaths have been rising, primarily due to illicit synthetic opioids.<sup>22</sup>
- Overdose deaths involving prescription opioids averaged nearly 16,000 annually from 2017-2021 and were declining prior to the pandemic, but experienced setbacks in 2020 and 2021. Provisional numbers indicate prescription opioid overdose deaths may have trended downward again in 2022.<sup>23</sup>

Notes: Historical NPA archive data for periods 1992-2005 combined with Xponent analysis for periods 2006-2022. Analysis is based on opioid medicines for pain management and excludes those medicines used for medication-assisted opioid use dependency treatment (MAT) or overdose recovery. Opioid medicines are categorized and adjusted based on their relative intensity to morphine, called a morphine milligram equivalent (MME), consistent with methods defined by the Centers for Disease Control and Prevention (CDC). Prescription data is through the retail channel only. Drug overdose deaths may involve multiple drugs and therefore may be included in more than one category.

## Contraception use peaked in 2017 and has been declining over the last 5 years driven by lower use of long-acting birth control

Exhibit 19: Contraception Defined Daily Doses (DDDs) (Mn) by type, 2013–2022



Source: IQVIA National Sales Perspective, Dec 2022; IQVIA Institute, Mar 2023.

- Contraception use fell to 1.9 billion days of therapy in 2022, down, on average, 3.1% annually over the last five years.
- These declines in recent years were driven by lower use of long-acting birth control such as intrauterine devices (IUDs), implants, and long-acting injectables, which can provide contraception from a few months to years.
- Oral contraception accounts for 20% of contraceptive days of therapy, and levels have remained stable over the last five years.
- Contraception is required to be covered by most health insurance plans, with no out-of-pocket costs; however, a survey of women conducted in 2022 showed that more than 40% were unaware of this requirement.<sup>24</sup>
- It is possible that declines in prescription contraception use in 2022 could be associated with potentially rising levels of permanent contraception (i.e., male and female sterilization) following the Supreme Court ruling in *Dobbs v. Jackson* in June 2022.<sup>25,26</sup>

Notes: Defined daily doses (DDD) are based on WHO definitions where each medicine is assigned a volume of medicine per day (see methodology). Contraception types are based on product descriptions and EphMRA New Form Codes (NFC) assigned to each product.

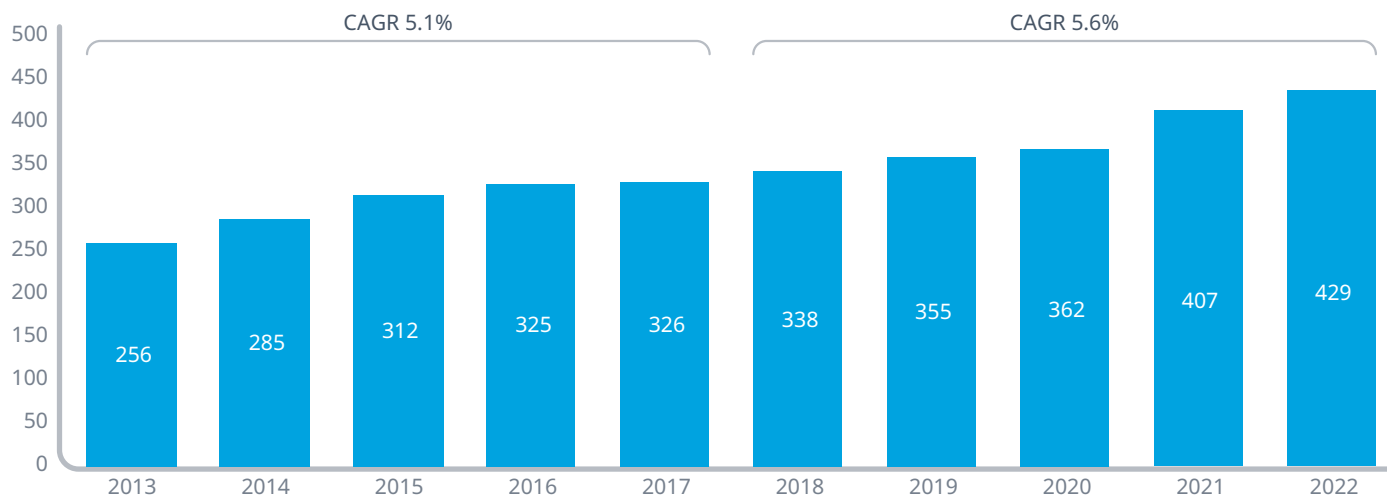
# Medicine spending and growth drivers

- The U.S. market at net prices grew by 5.3% in 2022, including the contribution of COVID-19 vaccines and therapeutics, while spending without COVID-19 vaccines and therapeutics grew by only 5.1%.
- Spending at list prices grew at 7.4% over the past five years, but payers' spending grew at 4.5% and patients' costs grew at 1.4%.
- Spending at list prices has increased faster than all-payer net spending but far slower than 340B institutions.
- Net spending growth in non-retail channels over the past five years has been more than double the rate of growth in retail channels, and non-retail now makes up almost 38% of the market.
- When adjusted for population growth and inflation, real per capita spending at estimated net manufacturer revenues grew 2.5% in 2022 and 31% over the past decade
- Specialty medicines now account for 51% of spending, up from 32% in 2012 and driven by growth in immunology and oncology.
- Costs of new medicines launched in the prior two years have been rising, particularly those in oncology and rare diseases, with the median annual cost of treatment exceeding \$250,000.
- Patients with a rare disease have seen new orphan drug approvals total 372 over the past five years, and spending on these drugs at invoice prices reached \$67Bn in 2022, up 57% in 5 years.
- Total drug spending at estimated net manufacturer prices increased by \$103Bn over the past five years, primarily driven by new products and brand volume.
- Average protected brand list price increases have fallen to a low of 3.7% in 2022, while net prices were unchanged on average, marking the fifth consecutive year with net price increases of less than 1%.
- The difference between list and net prices varies considerably across therapy areas, with diabetes nearing 80%, immunology nearing 50%, and oncology below 10%.
- Volume growth for protected brands has been driven by immunology, oncology, COVID-19 and diabetes, from expansion of indications, longer duration of use, and increased prevalence and diagnosis.
- Losses of exclusivity for biologics and introduction of biosimilars have increased dramatically in the past three years, with brand sales of those products dropping by \$33Bn over the past five years compared to \$4Bn over the prior five years and reflecting a growing role for biosimilars.



## The U.S. market at net prices grew by 5% in 2022, including the contribution of COVID-19 vaccines and therapeutics

Exhibit 20: U.S. medicine spending at estimated net manufacturer prices, 2013–2022, US\$Bn



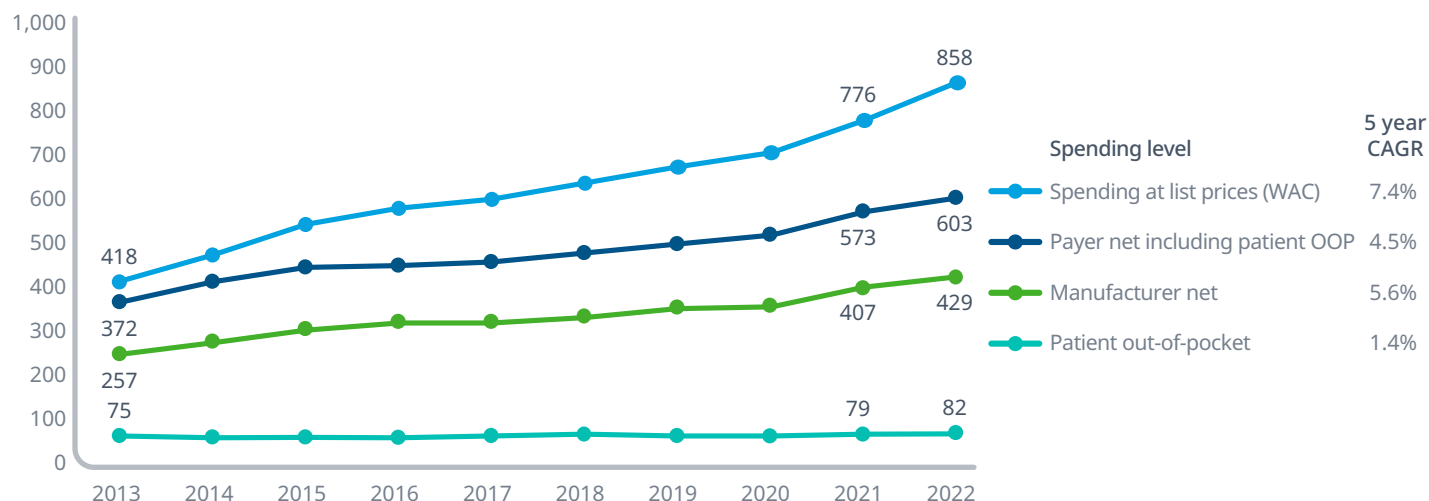
Source: IQVIA Institute, Mar 2023.

- U.S. medicine spending at estimated net manufacturer prices reached \$429Bn, up 5.3% in 2022, including the contribution of COVID-19 vaccines and therapeutics.
- Vaccines and therapeutics for COVID-19 contributed \$28.9Bn in 2022, up from \$26.6Bn in 2021 and \$3.2Bn in 2020.
- Spending growth for all other medicines was 5.1% in 2022, down slightly from 6.0% in 2021 and 1.1% in 2020.
- Net spending in the past five years increased \$103Bn with a 5.6% CAGR, up from 5.1% in the prior five years.
- Over the past decade, spending has increased by \$174Bn or 69% in aggregate over the \$254Bn net spending in 2012.

Notes: Measures total value of spending on medicines, including generics, branded products, biologics, small-molecules, retail and non-retail channels. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied. Estimates of COVID-19 vaccine and therapeutic spending are based on company financials. Company financials report net revenues recognized by the companies in the U.S. but not necessarily consumed by U.S. patients and it is understood a substantial value of the vaccines were donated to other countries.

## Spending at list prices grew at 7.4% over the past 5 years, but payers' spending grew at 4.5% and patients' costs grew at 1.4%

Exhibit 21: Medicine spending at selected reporting levels, US\$Bn



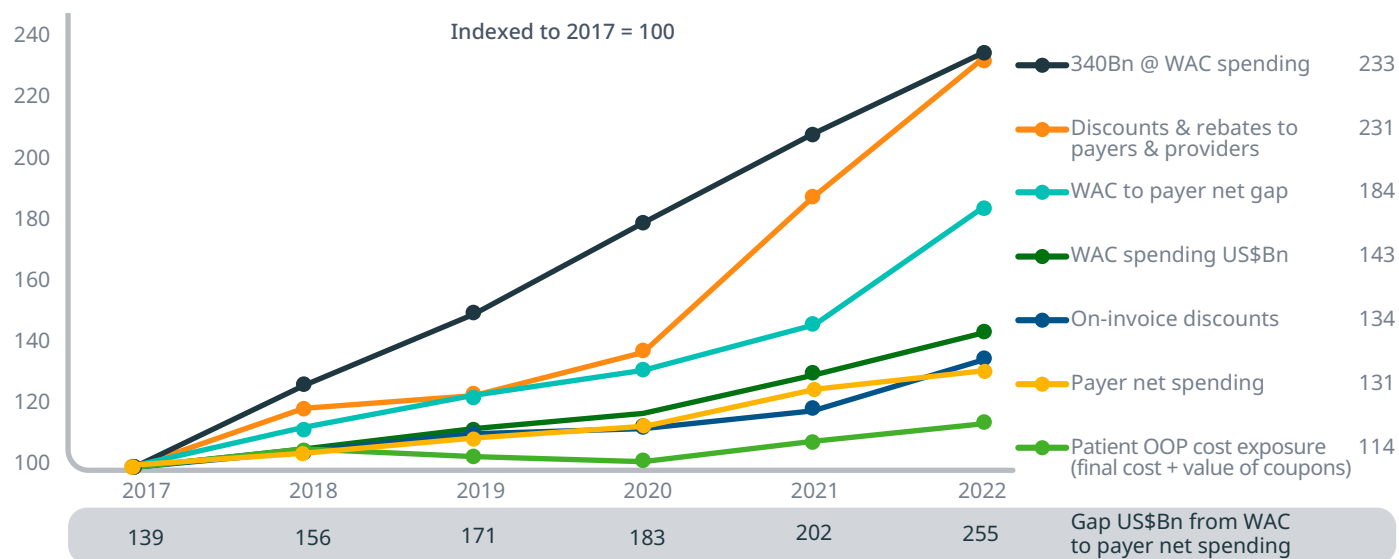
Source: IQVIA Institute, Mar 2023; CMS National Health Expenditures (NHE), Mar 2022.

- Over the past five years, spending at list prices [Wholesaler Acquisition Cost (WAC)] has increased from \$600Bn to \$858Bn — an average of 7.4% per year.
- Payer net spending has increased from \$461Bn to \$603Bn over five years at a compound annual growth rate of 4.5%.
- Spending at manufacturer net prices, including all products, are estimated to have grown an average of 5.6% over five years.
- Patient out-of-pocket costs for drugs dispensed in a retail setting and those costs for drugs dispensed in hospitals or at doctor's offices have both risen and fallen over the past decade, totaling \$75Bn in 2013 and rising to \$82Bn in 2022 with CAGR of 1.4% in the past five years.
- Patient out-of-pocket costs have continued to grow more slowly than manufacturer net or payer net as insurance has continued to absorb more costs.

Notes: Includes COVID-19 vaccines and therapeutics. IQVIA audits include measures of sales at Wholesaler Acquisition Cost (WAC) or list prices. Additionally, the IQVIA Institute has analyzed company reported net revenues for a sample of companies and products and projected a total market estimate (see Methodology section). Payer net spending reflects the total amounts spent by payers for medicines in both retail and non-retail settings, including all insurance types, and cash paying patients, offset by the estimates of rebates or payments which reduce payer responsibility. Payer net spending is derived from an analysis of CMS NHE data, IQVIA audited sales, and IQVIA estimates of manufacturer invoice-level and net revenue. Payer net spending has been estimated to include non-retail drug spending which is otherwise not reported by CMS. Patient out-of-pocket costs are derived from IQVIA audited measures of pharmacy out-of-pocket costs and informed by IQVIA audited non-retail sales and CMS NHE out-of-pocket costs share of non-retail healthcare costs. Due to lag times in reporting, CMS-derived measures are projections for 2022 while IQVIA-derived metrics are actual.

## Spending at list prices has increased faster than all-payer net spending but far slower than 340B institutions

Exhibit 22: Selected elements of differences between list price spending (WAC) and payer net spending



Source: IQVIA Institute, Apr 2023; CMS National Health Expenditures (NHE), Mar 2022; The 340B Drug Discount Program Exceeds \$100B in 2022 – IQVIA Market Access Center of Excellence, Apr 2023.<sup>27</sup>

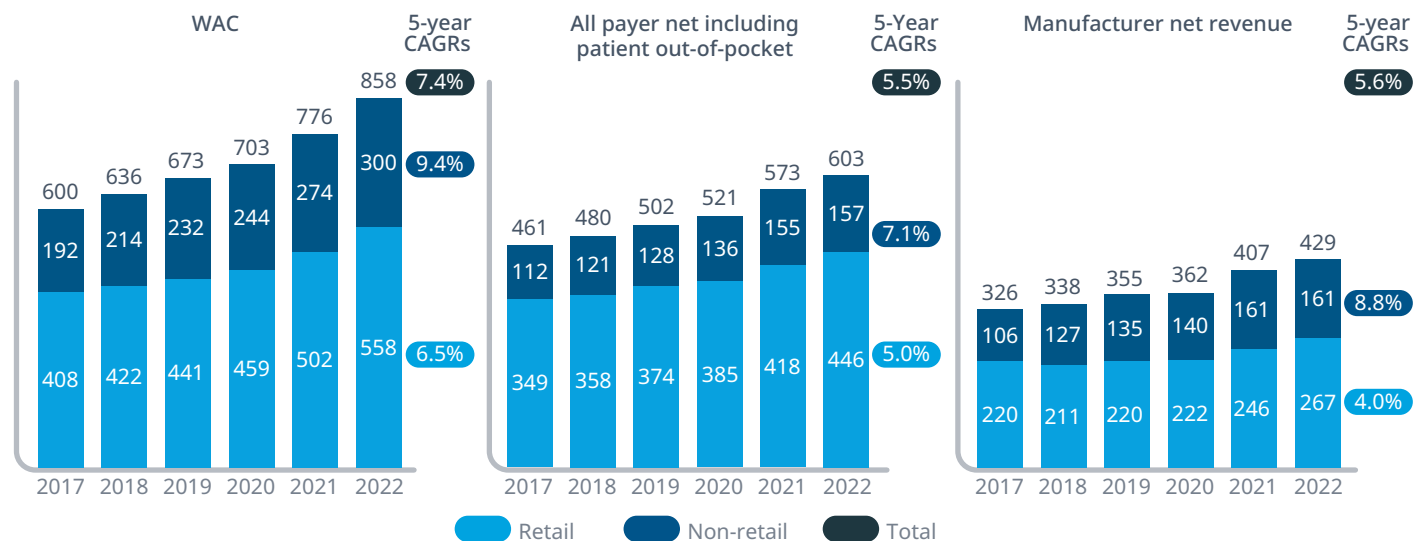
- Differences between list price (WAC) spending and payer net spending reached \$255Bn in 2022, up from \$139Bn in 2017 as negotiated discounts and rebates to payers and providers increase in competitive markets and 340B organizations account for a larger share of medicine use.
- Wholesaler acquisition costs (WAC) represent list prices that influence the costs paid by others in the supply chain and some patients. Spending at list prices has increased dramatically, 43% higher than the level in 2017.
- List price spending does not reflect discounts and rebates, which cause significant differences in the prices experienced by various stakeholders and individuals.
- Payer net spending for medicines increased 25% over five years to reach \$603Bn in 2022, including those paid through a patient’s medical benefit for doctor-administered drugs or drugs used during a hospitalization.
- Patient out-of-pocket costs have generally not changed as much in aggregate for reasons explored in more detail in the next chapter.

Notes: Includes COVID-19 vaccines and therapeutics. IQVIA Audits include measures of sales at Wholesaler Acquisition Cost (WAC) or list prices. Additionally, the IQVIA Institute has analyzed company reported net revenues for a sample of companies and products and projected a total market estimate (see Methodology section). Payer net spending reflects the total amounts spent by payers for medicines in both retail and non-retail settings, including all insurance types, and cash paying patients, offset by the estimates of rebates or payments which reduce payer responsibility. Payer net spending is derived from an analysis of CMS NHE data, IQVIA audited sales, and IQVIA estimates of manufacturer invoice-level and net revenue. Payer net spending has been estimated to include non-retail drug spending which is otherwise not reported by CMS. Patient out-of-pocket costs are derived from IQVIA audited measures of pharmacy out-of-pocket costs and informed by IQVIA audited non-retail sales and CMS NHE out-of-pocket costs share of non-retail healthcare costs. Due to lag times in reporting, CMS-derived measures are projections for 2022 while IQVIA-derived metrics are actual.



# Net spending growth in non-retail channels over the past 5 years has been more than double the rate of growth in retail channels

Exhibit 23: U.S. medicine spending levels and segmentation by channel, 2017–2022



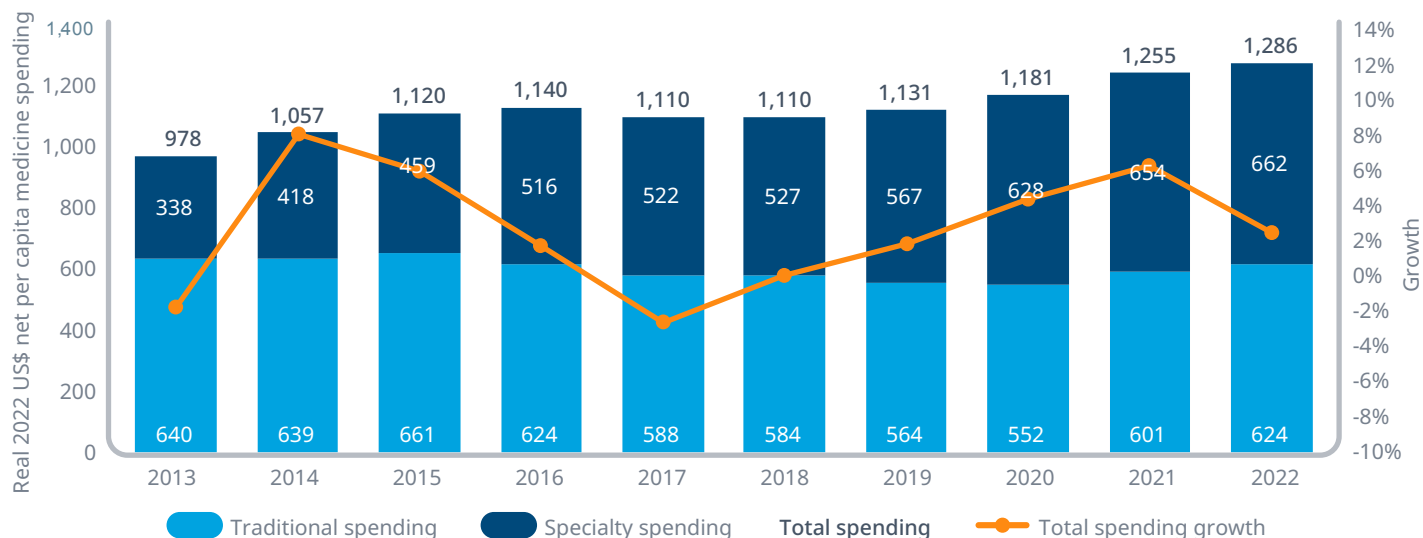
Source: IQVIA Institute, Mar 2023; CMS National Health Expenditures (NHE), Mar 2022.

- Measures of drug spending often mirror reimbursement structures, which are split by pharmacy and medical benefits and roughly correspond to distribution channels for retail and non-retail.
- Non-retail spending includes hospitals, clinics, and long-term care pharmacies as well as a variety of other non-traditional outlets, and now represents almost 38% of manufacturer net revenue compared to 26% of payer net spending.
- Whether spending is measured at list prices, payer net, or manufacturer net, non-retail drug spending is growing faster than retail spending, consistent with shifts in the types of medicines which drive spending, including oncology.
- Over the past five years, non-retail spending at list prices grew at 9.4% compared to 7.1% at payer net level and 8.8% for manufacturers as discounts and rebates grew faster than list prices in this channel.
- For retail pharmacies including mail order, list price spending grew at 6.5% while payer net spending increased at 5.0% and spending at manufacturer net prices grew at 4.0%, including the significant increases due to COVID-19 vaccines and therapeutics in the past two years.

Notes: Includes COVID-19 vaccines and therapeutics. IQVIA audits include measures of sales at Wholesaler Acquisition Cost (WAC) or list prices. Additionally, the IQVIA Institute has analyzed company reported net revenues for a sample of companies and products and projected a total market estimate (see Methodology section). Payer net spending reflects the total amounts spent by payers for medicines in both retail and non-retail settings, including all insurance types, and cash paying patients, offset by the estimates of rebates or payments which reduce payer responsibility. Payer net spending is derived from an analysis of CMS NHE data, IQVIA audited sales, and IQVIA estimates of manufacturer invoice-level and net revenue. Payer net spending has been estimated to include non-retail drug spending which is otherwise not reported by CMS. Patient out-of-pocket costs are derived from IQVIA audited measures of pharmacy out-of-pocket costs and informed by IQVIA audited non-retail sales and CMS NHE out-of-pocket costs share of non-retail healthcare costs. Due to lag times in reporting, CMS-derived measures are projections for 2022 while IQVIA-derived metrics are actual.

## Real per capita spending at estimated net manufacturer revenues grew 2.5%, up 31% since 2013

Exhibit 24: Real per capita spending and growth by product type at estimated net manufacturer prices in 2022 US\$



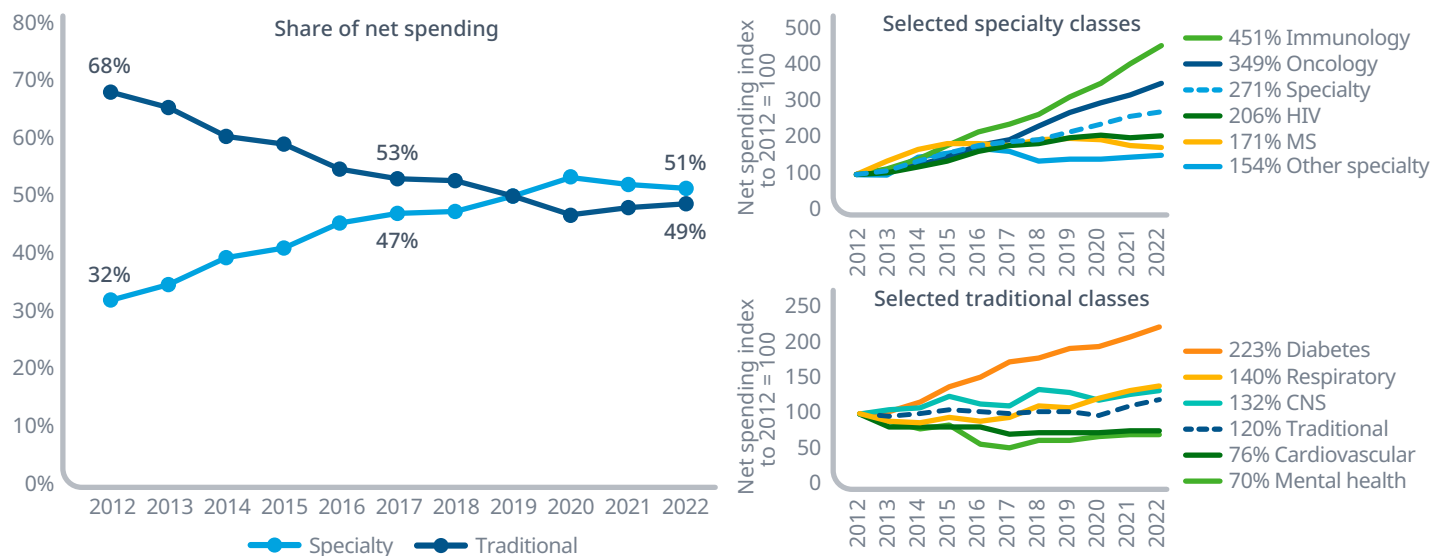
Source: IQVIA National Sales Perspectives, IQVIA Institute, Mar 2023; U.S. Census Bureau; U.S. Bureau of Economic Analysis (BEA) [https://apps.bea.gov/iTable/index\\_nipa.cfm](https://apps.bea.gov/iTable/index_nipa.cfm) accessed Mar 30, 2022.

- Medicine spending per capita, adjusted for population growth and shown in current (2022) dollars, grew \$290 since 2012 (not shown), a 2.6% compound annual growth rate.
- Real net per capita spending grew by 2.5% in 2022 as nominal spending grew 5.3% overall and 5.1% excluding the contribution from COVID-19 vaccines and therapeutics.
- Specialty share of net spending across institutional and retail settings rose from 35% in 2013 to 51% in 2022, driven by innovation and the declining share for traditional medicines, as growth has slowed due to higher off-invoice discounts and rebates and patent expiries.
- Growth in real net per capita spending for specialty medicines peaked in 2014, when it grew by 21.0% with the introduction of several breakthrough therapies for the hepatitis C virus, cancer and autoimmune diseases.
- The largest proportion of new medicines launched in the past decade has been specialty drugs, and specialty spending per person has nearly doubled from \$338 in 2013 to \$662 in 2022, while traditional net medicine spending has declined by \$16 per person over the same period.
- Across all settings, specialty medicines treat relatively few patients, accounting for 3% of volume measured in defined daily doses (WHO DDD) and have costs far higher per patient than traditional medicines (Exhibit 26).

Notes: Includes COVID-19 vaccines and therapeutics. Real medicine spending reflected in 2022 US\$. Specialty and traditional medicines are defined by IQVIA. Specialty medicines – those that treat chronic, complex or rare diseases, and possess additional distribution, care delivery and/or cost characteristics which require special management by stakeholders. Includes all medicines in both pharmacy and institutional settings, and all brands and generics. Totals may not sum due to rounding.

# Specialty medicines now account for 51% of spending, stable in the past 3 years as COVID treatments have lifted traditional

Exhibit 25: Share of spending at estimated net manufacturer prices



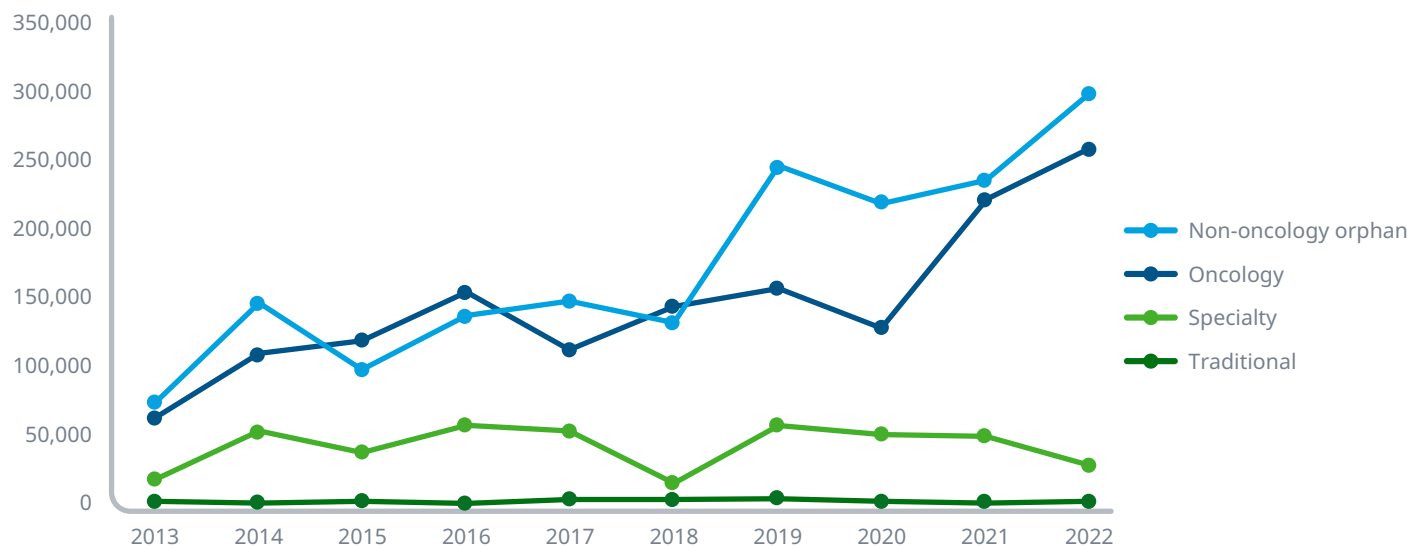
Source: IQVIA Institute, Mar 2023.

- Specialty medicines — those that treat chronic, complex or rare diseases and possess additional distribution, care delivery and/or cost characteristics which require special management by stakeholders — now represent 51% of net manufacturer revenue.
- The contribution of COVID-19 vaccines and oral therapeutics have lifted traditional share of spending in 2021 and 2022, pausing the rise of specialty share but likely only temporarily.
- The rise in specialty spending has been predominately driven by immunology and oncology, where spending has increased 451% and 349% respectively since 2012 on a net basis.
- Traditional therapies have generally faced declining spending as many had faced patent expiries and had not had newer generation therapies introduced into the classes over time.
- This pattern has driven mental health and cardiovascular classes to 70% and 76%, respectively, of their 2012 level of net spending as of 2022.
- Diabetes has increased to 223% of the 2012 level as a result of significant innovation, with three new classes of treatments (DPP-IV, GLP-1, and SGLT-2) introduced and gaining wide usage during the period, as well as novel insulin products, and offset by some of the highest off-invoice discounts and rebates in the market.

Notes: Specialty and traditional medicines are defined by IQVIA. Specialty medicines — those that treat chronic, complex or rare diseases, and possess additional distribution, care delivery and/or cost characteristics which require special management by stakeholders. Includes all medicines in both pharmacy and institutional settings, and all brands and generics. Totals may not sum due to rounding.

## Median annual costs of new medicines have been rising particularly those in oncology and rare diseases

Exhibit 26: Median annual cost of treatment at launch for brands US\$, 2013–2022



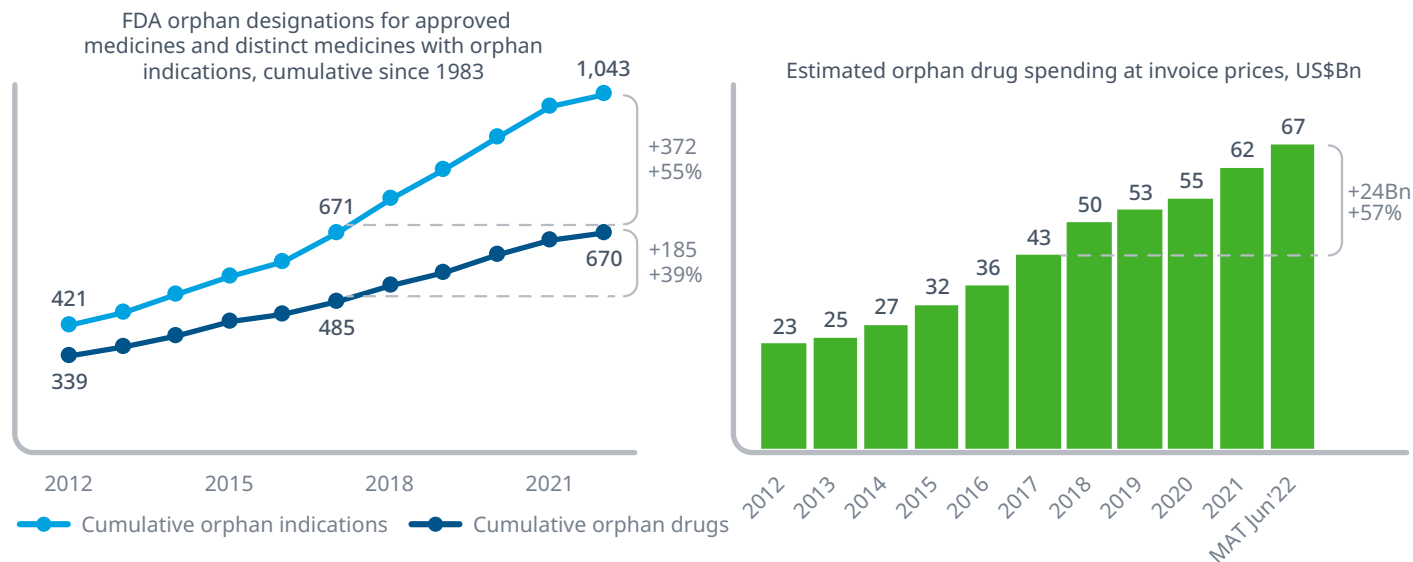
Source: IQVIA National Sales Perspectives, Dec 2022; IQVIA Institute, Mar 2023

- One aspect common across specialty, oncology and orphan medicines is their cost, which has notably been higher than traditional medicines, which is also rising each year.
- There is wide variability in the expected annual costs of treatment with medicines within each of the four types analyzed, though these median annual costs do provide a useful frame of reference.
- The four mutually exclusive types of drugs shown reflect patterns in the pricing of the new drugs, however it is notable that together, oncology, non-oncology orphan, and all other specialty drugs typically represent less than 3% of medicine volume used in the U.S., so while these costs are high, use is typically very rare.
- New non-oncology orphan drugs had a median cost of \$300,000 in 2022, the highest ever, and up from \$237,000 in 2021.
- New oncology drugs had a median annual cost of \$260,000 in 2022, up from 223,000 in 2021, reflecting the unmet needs for some tumors as well as significant advances in survival and specificity of biomarker determined treatments, which are most commonly linked to the higher cost new treatments.
- This is the ninth consecutive year with oncology median annual costs above \$100,000, once thought to be a ceiling for cancer drug costs.

Notes: Annual costs based on invoice prices. Products are included in medians based on segment assignments. Oncology includes both orphan and non-orphan products. All other products which have orphan indications are grouped together and some products have both orphan and non-orphan indications in this group. Specialty and traditional products exclude orphan or oncology products but are otherwise defined according to IQVIA definitions. Costs do not reflect the real-world experience for patients.

# Patients with a rare disease have seen 372 new orphan drug approvals and spending increase 57% over the past 5 years

Exhibit 27: Number of orphan drug approvals and invoice spending, US\$Bn



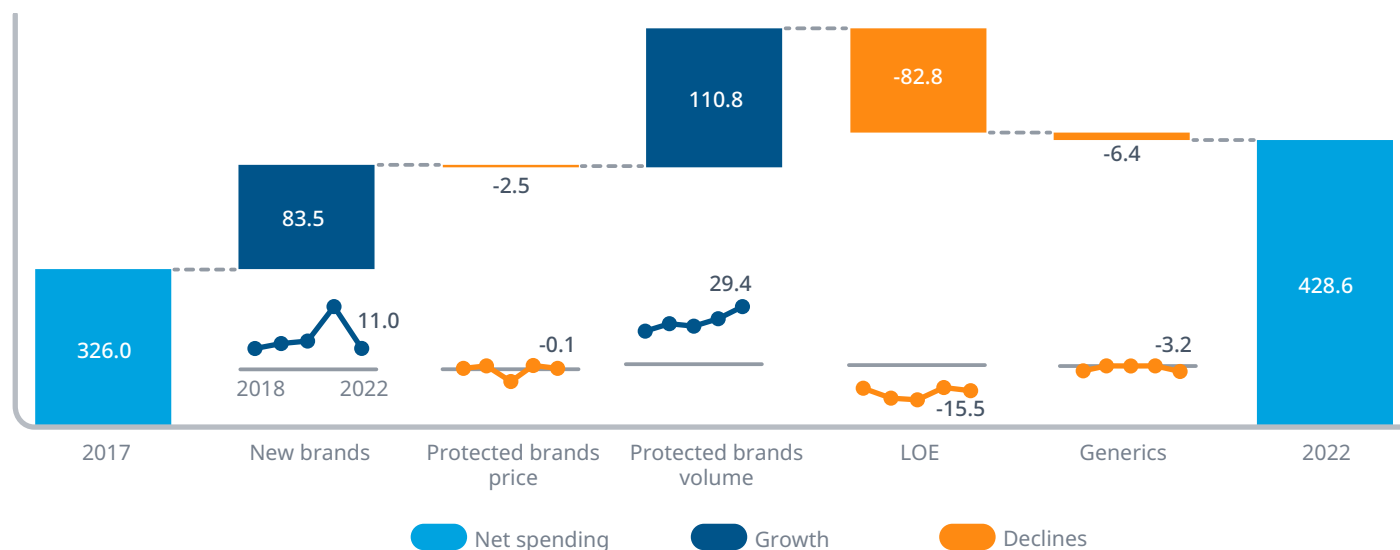
Source: IQVIA National Sales Perspectives, Jun 2022, IQVIA Institute, Mar 2023.

- In the 40 years since the passage of the Orphan Drug Act (ODA), treatments for hundreds of rare diseases have been developed and launched.
- The total number of approved orphan indications since the passage of the ODA in 1983 reached 1,043 in 2022, up from 671 five years ago, a 55% increase.
- Drugs often have multiple orphan indications or a mix of orphan and non-orphan indications, especially in oncology and immunology, making the term “orphan drugs” an ambiguous one.
- The number of distinct drugs with any orphan indication reached 670 in 2022, adding 185 in the past five years.
- Those 670 medicines account for 29% of medicine spending in the U.S. in 2022 at invoice prices, but after adjusting for those drugs with a mix of orphan and non-orphan uses, the orphan indications account for 11% of total spending.
- Orphan spending has increased \$24Bn in the past five years, lifting orphan share of total spending two percentage points in that period.

Notes: The Orphan Drug Act (1983) grants the orphan designation to treatments for smaller populations, since clarified to be less than 200,000 pe year, as well as to therapies where it may be unlikely the innovator would make a financial return. Indications included in this analysis are those that are designated orphan for medicines at their market approval or for already approved medicines and do not include pre-approval orphan designations from FDA. Distinct drugs receiving multiple orphan indications have been assessed and compiled by the IQVIA Institute from the FDA Orphan Drug Database. Estimates of orphan indication spending are based on assessments of the approved uses of a drug, and the best available estimates of usage from IQVIA data, or published epidemiological estimates.

# Spending increased by \$102.6Bn over the past 5 years driven by new products and brand volume, offset by expiries

Exhibit 28: Spending and growth at estimated net manufacturer prices 2017–2022, all channels, US\$Bn



Source: IQVIA Institute, Mar 2023

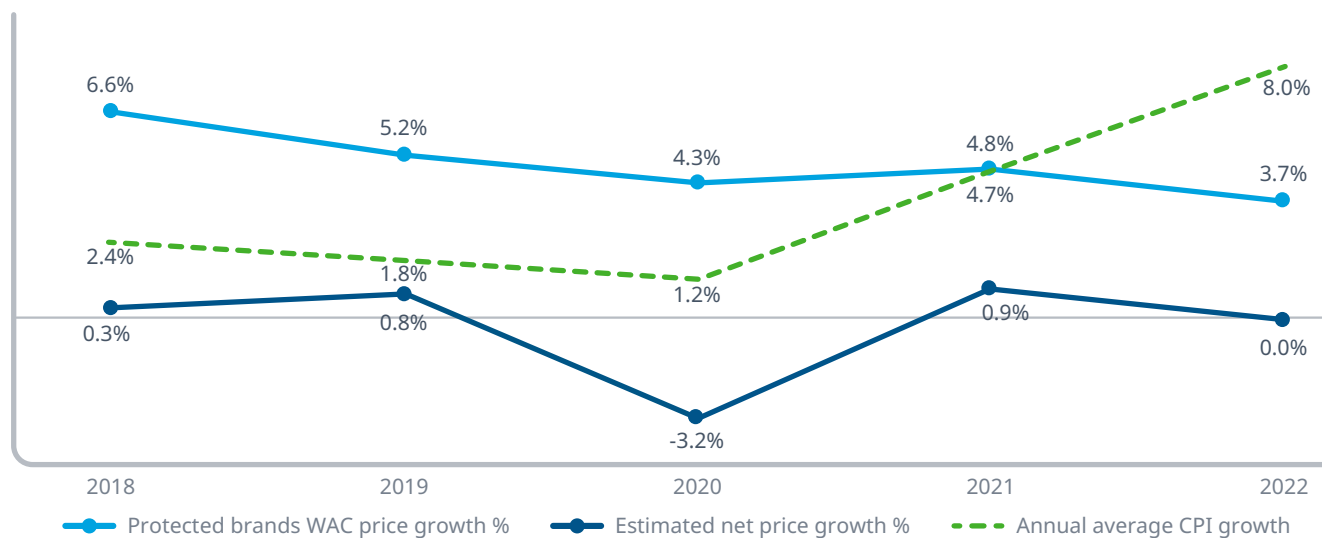
- New products, including 268 new active substances that launched from 2018 through 2022, contributed \$83.5Bn to spending at manufacturer net prices over the past five years.
- Price increases for protected brands, which have slowed substantially in recent years, declined by \$2.5Bn over five years.
- Volume growth experienced by protected brands — most often driven by brands in the three- to five-year period since their launch when adoption by healthcare providers grows — contributed \$110.8Bn to growth over the five-year period.
- Losses of Exclusivity (LOE), or patent expiries, typically result in a dramatic shift of volume to generics and lower brand sales for the originator. These contributed a decline of \$82.8Bn to manufacturer net revenues.
- During the past five years, generic prices have been deflating, driven by an increase in the number of generic approvals and despite the significant brand losses of exclusivity. Generic spending did not grow over the period.

Notes: Includes COVID-19 vaccines and therapeutics. IQVIA estimates of spending at net manufacturer prices are based on comparisons of IQVIA audited data and company reported net revenues (see Methodology section). Products are assigned to segments in each month based on time relative to launch or patent expiry and product type. Growth is calculated annually on a like-for-like product segment basis and then aggregated to five-year totals.



## Protected brand list prices increased 3.7% in 2022, while net prices were unchanged at the market level

Exhibit 29: Wholesaler Acquisition Cost (WAC) growth and net price growth for protected brands



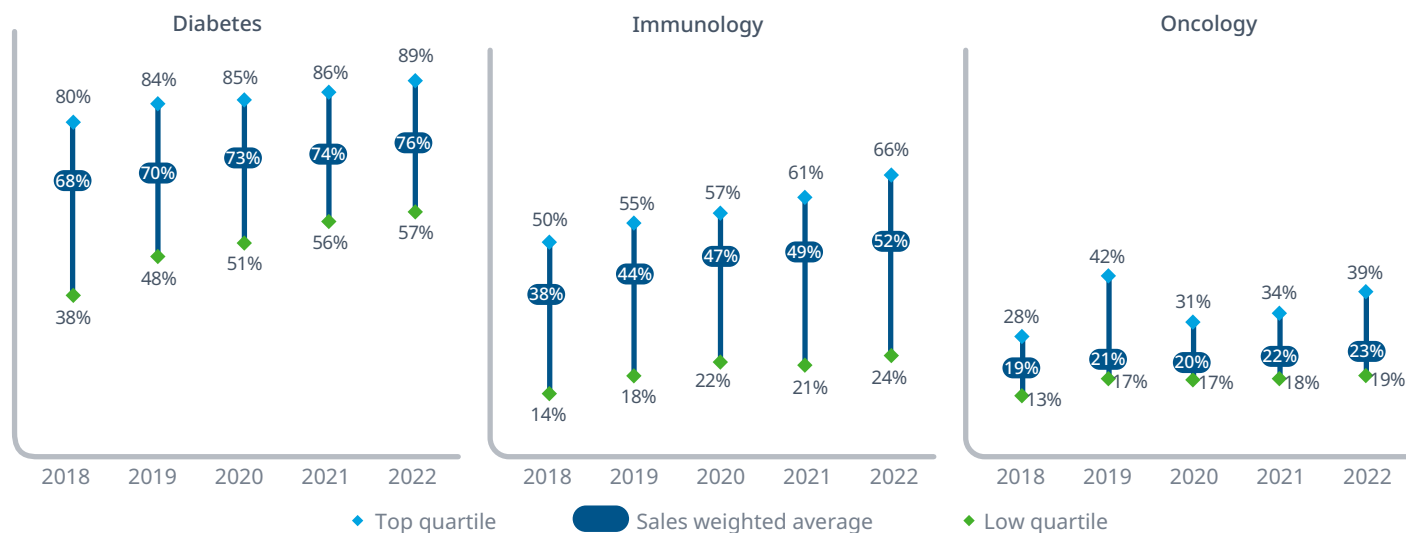
Source: IQVIA Institute, National Sales Perspectives, Dec 2022; Bureau of Labor Statistics, Annual Average Monthly CPI Growth, Dec 2022.

- The list prices of protected branded products — those products more than two years after launch having not yet lost patent protection — increased 3.7% in 2022.
- Net manufacturer prices — the cost of medicines after all discounts and rebates have been paid — were unchanged in 2022 and continued below inflation for the fifth year.
- Overall U.S. annual average inflation increased sharply in 2021 and remains high, but net price growth for drugs is notably not following the same patterns in the wider economy.
- Prices paid by different stakeholders in the U.S. health system are based to varying degrees on list prices and the discounts and rebates they negotiate or receive and do not apply uniformly to all parties.
- Most discounts are offered to wholesalers and pharmacies and do not necessarily result in lower out-of-pocket costs for patients.
- Some of the rebates and other price concessions manufacturers pay (resulting in lower net prices) are statutory payments to government programs such as Medicaid or to 340B eligible entities. Price concessions also include coupons offered to patients using private insurance, whereas those with government insurance cannot use coupons.
- These complexities mean that the price for each medicine can be unique, reflecting the drug, the insurance type, the other medicines a patient takes during the year, the time of year, the pharmacy, the coupons offered by manufacturers, and whether a patient chooses to use them.

Notes: Segments of growth are mutually exclusive in each monthly time period, calculating growth over the prior year for that cohort of products independent of the products' previous status or segment. Protected brands are brands more than 24 months after first launch and not yet off-patent. Net price growth estimates based on public information compared to IQVIA data (see Methodology section). CPI = consumer price index is averaged annually.

## List prices are higher than net prices but vary considerably by therapy area

Exhibit 30: Selected therapy area protected brand net sales % below list price sales (WAC)



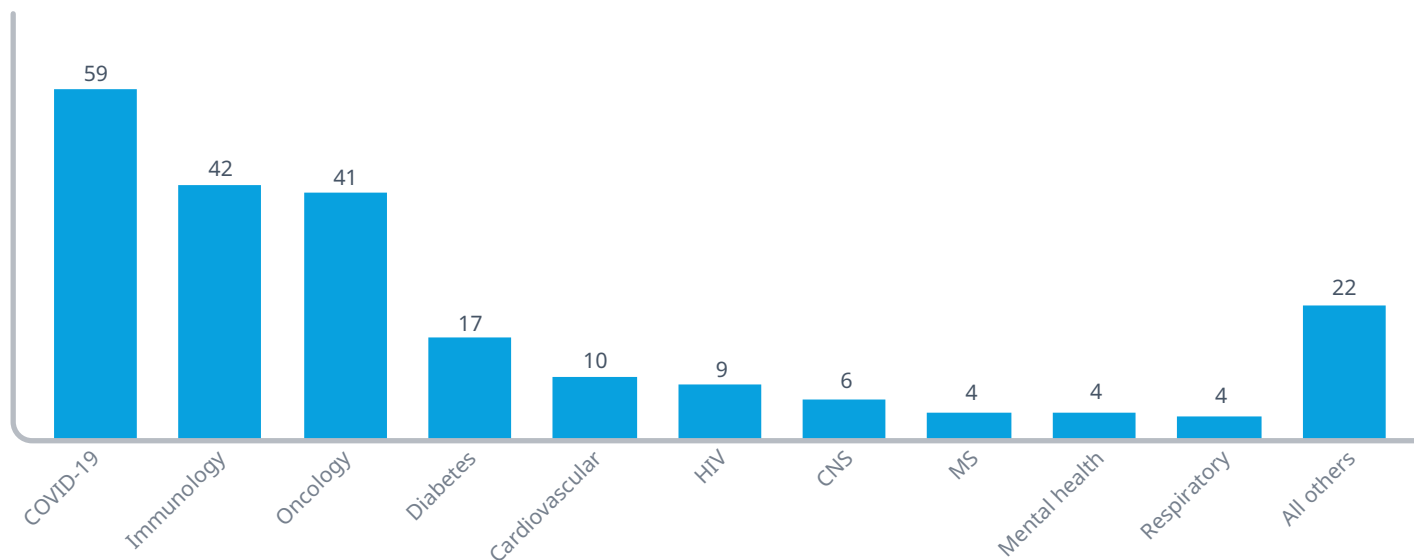
Source: Company annual financial reports, IQVIA National Sales Perspectives, IQVIA Institute, Mar 2023.

- The difference between list prices measured at wholesaler acquisition cost (WAC) and net prices is sometimes significant but varies across and within therapy areas.
- Diabetes, immunology and oncology represent three different therapy area dynamics, with off-invoice discounts and rebates representing a significantly different importance and role in the commercialization and distribution of products.
- In diabetes, for a sample of protected branded products, the weighted average net price is 76% below the WAC price but the highest quartile of products average 89% and the lowest quartile average 57%.
- In immunology, a collection of diseases including rheumatoid arthritis, psoriasis, ulcerative colitis and Crohn’s disease, the average WAC to net difference has risen from 38% five years ago to 52% in 2022 and is expected to continue to rise as competitive intensity in the class is amplified by large numbers of competitors and the introduction of biosimilars for key products.
- Oncology most often represents products that don’t compete directly with each other or that are paid via the medical benefit where there is less rebate negotiation generally and specifically doesn’t take place in Medicare part B.

Notes: IQVIA audits include measures of sales at Wholesaler Acquisition Cost (WAC) or list prices. IQVIA Institute has analyzed company reported net revenues for a sample of companies and products and projected a total market estimate (see Methodology section). Selected therapy areas shown based on sample analyzed protected brand products including weighted average difference between WAC and net, and the average of the top and lowest quartiles of sample products.

## New and existing medicines drove \$218Bn in spending growth over the past 5 years excluding impact of expiries and prices

Exhibit 31: Medicine net spending growth 2018-2022 for new brands and protected brands volume, US\$Bn



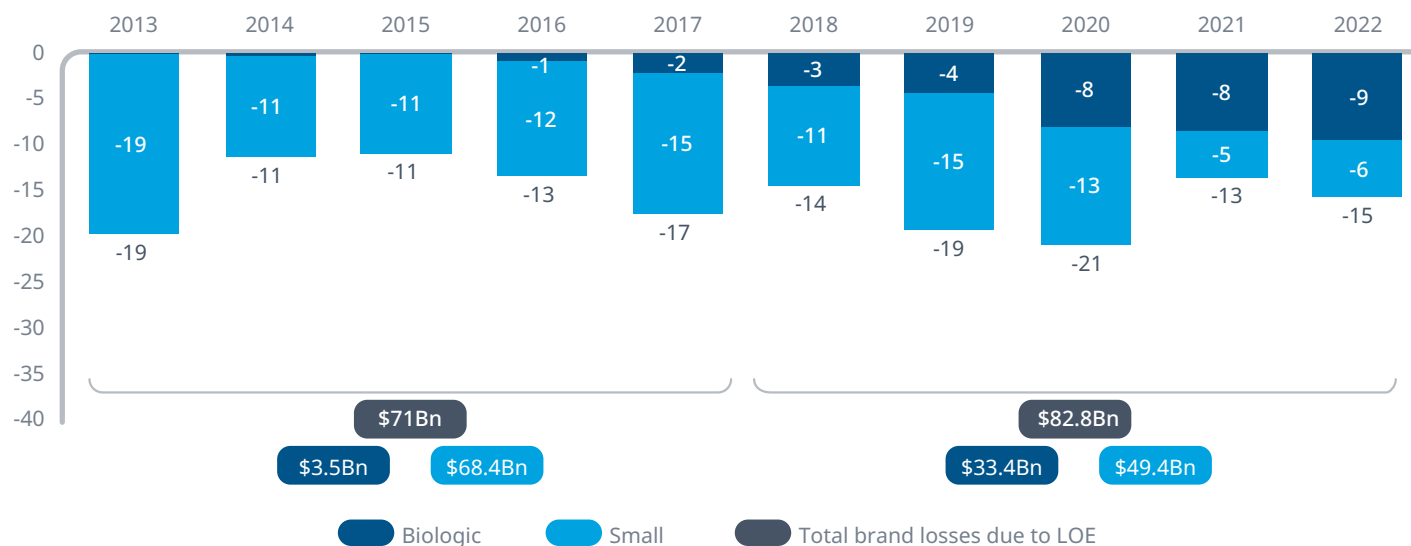
Source: IQVIA National Sales Perspectives, IQVIA Institute, Mar 2023.

- Positive growth drivers for protected brands — including volume growth which added \$110.8Bn and new products which added \$83.5Bn — in total contributed \$194.3Bn in growth over five years led by immunology, oncology and diabetes, as well as the \$59Bn from COVID-19 vaccines and therapeutics.
- Volume growth — growth without the impact of net price changes and covering products older than two years after launch but not yet off-patent — has grown to widely differing degrees across therapy areas.
- Immunology products including those for a wide range of autoimmune conditions had net growth from both new products and volume of \$42Bn over five years.
- Oncology added \$41Bn, driven by the largest number of new products of any therapy area in the period but lifted more by volume growth of previously launched products, especially immuno-oncology checkpoint inhibitors, which have rapidly moved to become a standard of care in many solid tumors.
- Diabetes added \$17Bn in net new spending or increased volume, reflecting the significant benefits of new mechanisms including GLP-1s, SGLT-2s and DPP-IV treatments as well as other novel insulins.

Notes: New original branded products and protected brands growth due to volume growth, excluding the impacts of price growth as well as the impact of losses of exclusivity. Spending growth is measured at manufacturer net price level. Includes COVID-19 vaccines and therapeutics. Overall growth over 5 years has been included.

# The impact of losses of exclusivity of biologics has increased dramatically in the past 3 years

Exhibit 32: Impact of brand losses of exclusivity 2013–2022, spending at estimated net manufacturer prices, US\$Bn



Source: IQVIA MIDAS, IQVIA Institute, Mar 2023.

- Most of the impact from losses of exclusivity (LOE) in 2020 through 2022 was from biosimilars introduced in the prior three years, including three molecules in the oncology market —bevacizumab, rituximab, and trastuzumab — which have contributed to a significant increase in brand losses due to LOE.
- Biologic brand losses were \$8Bn each in 2020 and 2021 and \$9Bn in 2022, lifting the total to \$33.4Bn in the past five years.
- Small molecule brand losses were much less than historic averages in the past two years as few products with higher spending lost exclusivity, and deflationary effects of earlier expiries were not as strong.
- Small molecule LOE effects are also more muted when measured at estimated net spending levels than when measured at list prices, as the originator products generally have higher discounts and rebates than biologics.
- Small molecules contributed \$49.4Bn in brand losses to LOE over the past five years, down from \$68.4Bn in the prior five years.
- Notably, biosimilars earlier in the period didn't reduce brand sales as much as there were relatively fewer products and net savings were offset by increased volume to a greater degree, resulting in only \$3.5Bn in brand losses from 2013 to 2017.

Notes: Chart reflects the lower spending for branded products which have lost exclusivity but does not reflect the increased spending for generics or biosimilars. Analysis at manufacturer net price level.

## Patient out-of-pocket costs

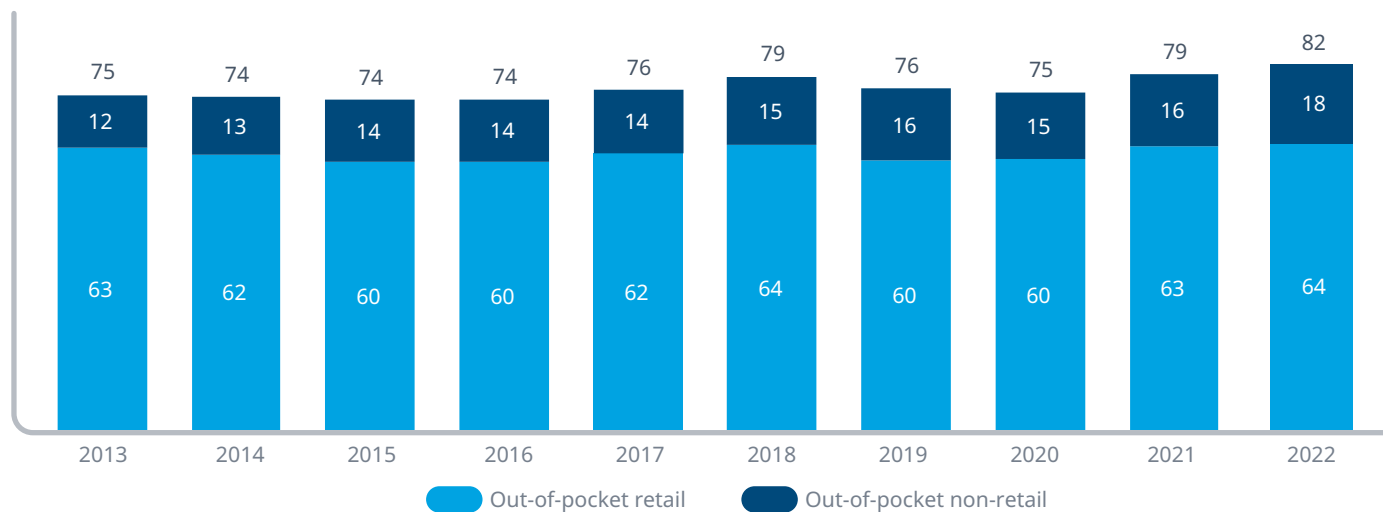
- Out-of-pocket costs in aggregate increased \$3Bn in 2022 to \$82Bn but represent a smaller share of all-payer net spending than a year ago.
  - Manufacturer copay assistance bought down patient costs by nearly \$19Bn in 2022 and nearly \$80Bn over the last five years.
  - Medicare aggregate out-of-pocket costs have risen over the past five years, with population and volume increases accounting for most of the increase offset by price reductions.
  - The average amount paid out-of-pocket per retail prescription has dropped from \$10.15 in 2017 to \$9.38 in 2022.
  - Generics and branded generics account for 15% of invoice-level spending but represent 66% of patient out-of-pocket costs.
- Overall, 7% of patients reach annual out-of-pocket costs above \$500 compared to 15% in Medicare, in large part due to benefit design.
  - More than 92% of branded and generic prescriptions have a final out-of-pocket cost below \$20, and only 1% (66 million) have a cost above \$125.
  - Patients starting new therapy abandoned 94 million prescriptions at pharmacies in 2022 with increasing frequency as costs rise.
  - Insulin costs continue to decline but patient payments above \$35 are more common for these drugs than in the overall market.
  - Insulin out-of-pocket costs have declined by \$394Mn since 2019 and would further decline by \$561Mn if costs were capped at \$35 as a result of policy changes and manufacturer price reductions.

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*Patients had to pay more than \$80Bn in total out-of-pocket costs for the first time in 2022, even as the average patient cost per retail prescription remained under \$10.*

## Out-of-pocket costs in aggregate increased \$3Bn in 2022, mostly driven by non-retail drugs

Exhibit 33: Aggregate patient out-of-pocket cost for medicines dispensed in retail and non-retail settings, US\$Bn



Source: IQVIA LAAD Sample Claims Data, Dec 2022; IQVIA Institute, Mar 2023; CMS National Health Expenditures, Mar 2022.

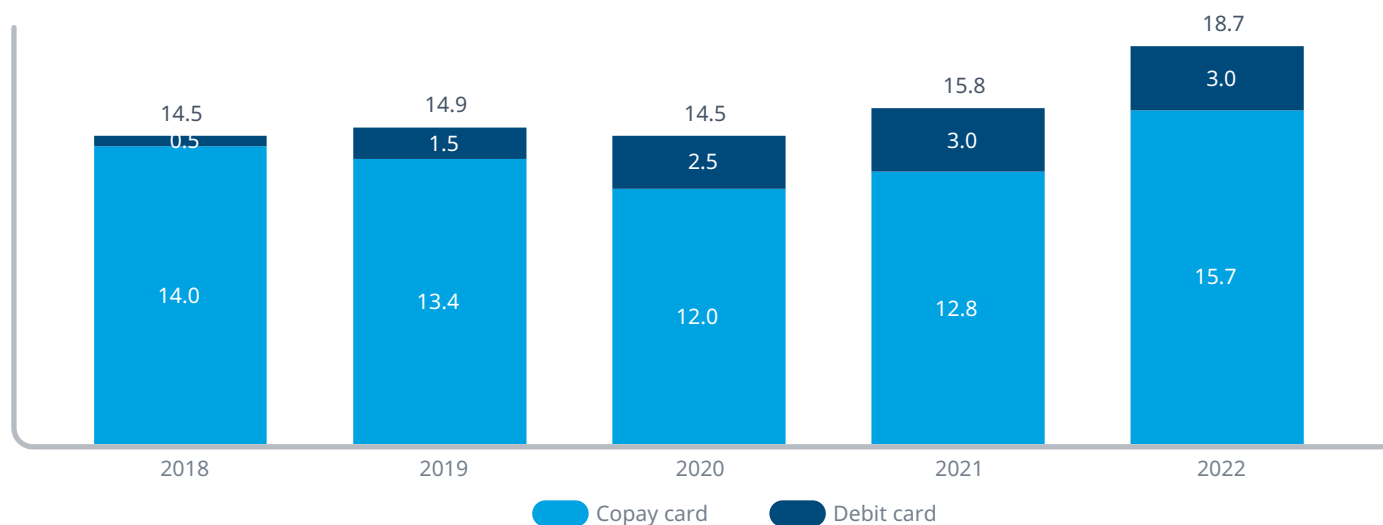
- Patient out-of-pocket costs increased \$2.1Bn in 2022, exceeding peak levels last seen in 2018.
- This growth was driven by non-retail out-of-pocket costs, which grew \$1.2Bn, or 7.5%, in 2022, returning to pre-pandemic growth rates following a significant decline in 2020.
- Retail out-of-pocket costs grew \$949Mn, or 1.5%, in 2022 and have remained relatively stable over the last five years, growing an average 0.7% annually.
- Total patient out-of-pocket costs were highest in 2022, with out-of-pocket costs increasing \$4.9Bn, or 6.3%, over the last decade, driven by increasing non-retail out-of-pocket costs while retail out-of-pocket costs have decreased 1.5%.
- As the vast majority of prescriptions are dispensed as generic drugs and individual prescription costs fall, overall out-of-pocket costs have risen, driven by population changes, the mix of medicines used, and offset by the use of coupons.

Notes: Retail OOP based on LAAD sample prescription data, grossed up to NPA adjusted prescriptions normalizing for 90-day prescription dispensing. Non-retail estimates based on CMS NHE for personal healthcare excluding retail prescription drugs. IQVIA estimates of non-retail drug (modified by estimates of rebates and offset by applying the estimated net cost of insurance and typical channel markups) with CMS PHC OOP % applied to those amounts.



## Manufacturer copay assistance bought down patient costs by nearly \$19Bn in 2022 and nearly \$80Bn over the last 5 years

Exhibit 34: Estimated total copay and debit card costs, 2018–2022, US\$Bn



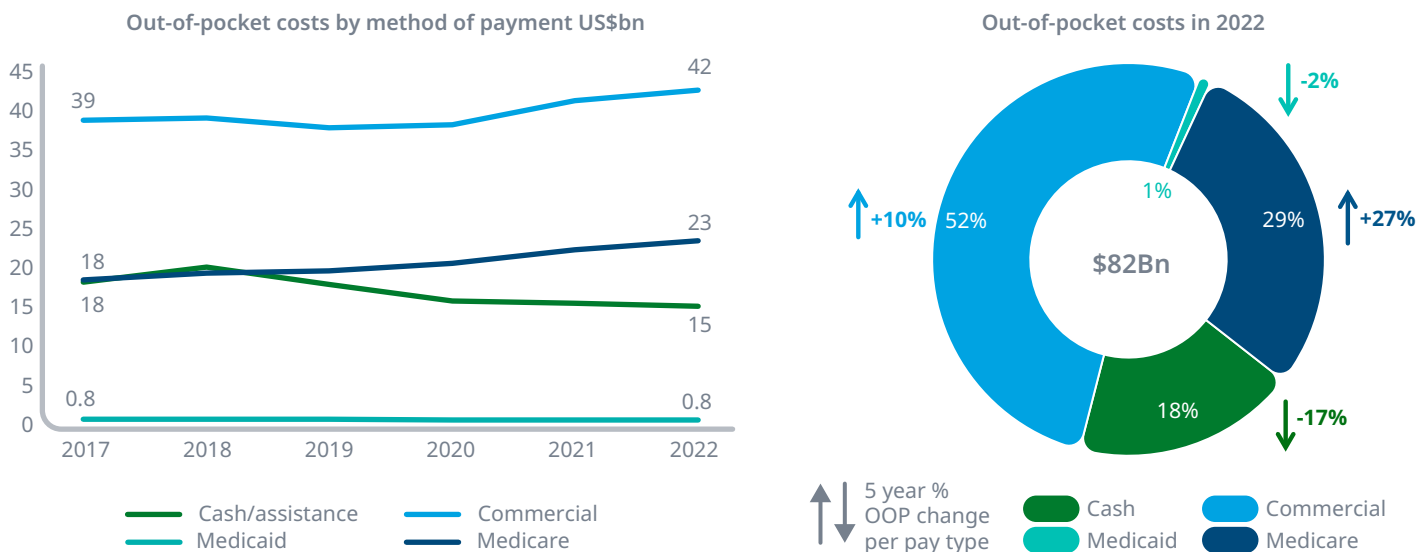
Source: IQVIA LAAD 3.0 Claims Data; Xponent PlanTrak Projected Data, PAAS Data; IQVIA US Market Access Strategy Consulting Analysis, Dec 2022.

- Manufacturer copay assistance has been a large and growing aspect of the market for the past five years.
- Patients’ exposure to costs is often based on the list prices of the medicines they are prescribed if they have a high-deductible health plan, or if their plan does not cover the medicine.
- The use of coupons or pre-paid debit cards enables patients who might otherwise have abandoned to fill their prescriptions.
- Coupons and debit cards offset patient cost exposure by \$18.7Bn in 2022, 23% of what retail prescription costs would have been without them.
- Trends in copay assistance are coinciding with rising list prices and the increasing prevalence of insurance designs, which discourage coupon use.
- These so-called ‘accumulator’ benefit designs only allow patients to accumulate progress to their deductible or out-of-pocket maximum if they paid the amounts themselves without such copay assistance.
- Pre-paid debit cards are a relatively recent development but have increased dramatically.

Notes: Estimate does not capture point-of-sale programs denial conversion, bridge programs, and other non-traditional support. All brands; Commercial/Assistance.

# Commercial and Medicare out-of-pocket costs for drugs have risen in the past 5 years while cash has declined

Exhibit 35: Out-of-pocket costs by method of payment, US\$Bn



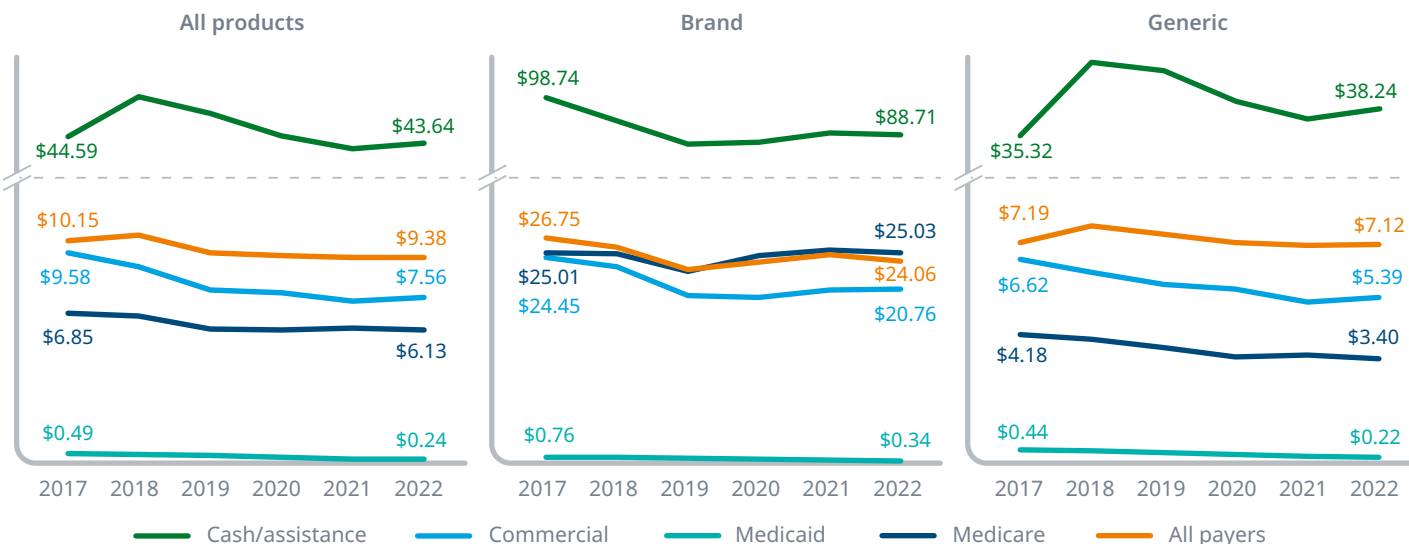
Source: IQVIA LAAD Sample Claims Data, Dec 2022; IQVIA Institute, Mar 2023; CMS National Health Expenditures, Mar 2022.

- Out-of-pocket costs rose in aggregate for commercial and Medicare beneficiaries while those who paid cash declined due to reduced volumes, potentially linked to abandonment of prescriptions due to costs.
- Commercial insurance out-of-pocket costs, which account for 52% of overall patient out-of-pocket costs, rose 10% in aggregate over five years, all within the last two years from increased volume despite declining enrollment and shifts in the mix of prescriptions to those carrying higher costs.
- Medicare out-of-pocket costs rose, in aggregate, by 27%, from \$18Bn in 2017 to \$23Bn in 2022, driven by increased volume and enrollment as well as shifts in the mix of prescriptions.
- Uninsured patients account for 18% of overall patient out-of-pocket costs and paid \$15Bn in 2022 for only 4% of prescriptions. Cash out-of-pocket costs have declined, in aggregate, 17% over five years, primarily from declines in volume and the number of people uninsured.
- Medicaid patients account for 12% of prescriptions and 1% of patient out-of-pocket costs, as most of their costs are waived as the basis for the program.

Notes: Out-of-pocket (OOP) costs estimated based on prescription volumes and observed OOP costs. OOP costs were projected from a sample in the IQVIA LAAD sample claims data to a national estimate using national adjusted prescriptions. Method of payment is determined based on the most common or mode pay type in recorded claims. Cash method of payment includes those where patients used no insurance, including those who received some assistance from charities, foundations or other programs.

## The average amount paid out-of-pocket per retail prescription has dropped from \$10.15 in 2017 to \$9.38 in 2022

Exhibit 36: Average final out-of-pocket cost per retail prescription by product type and method of payment, 2017–2022



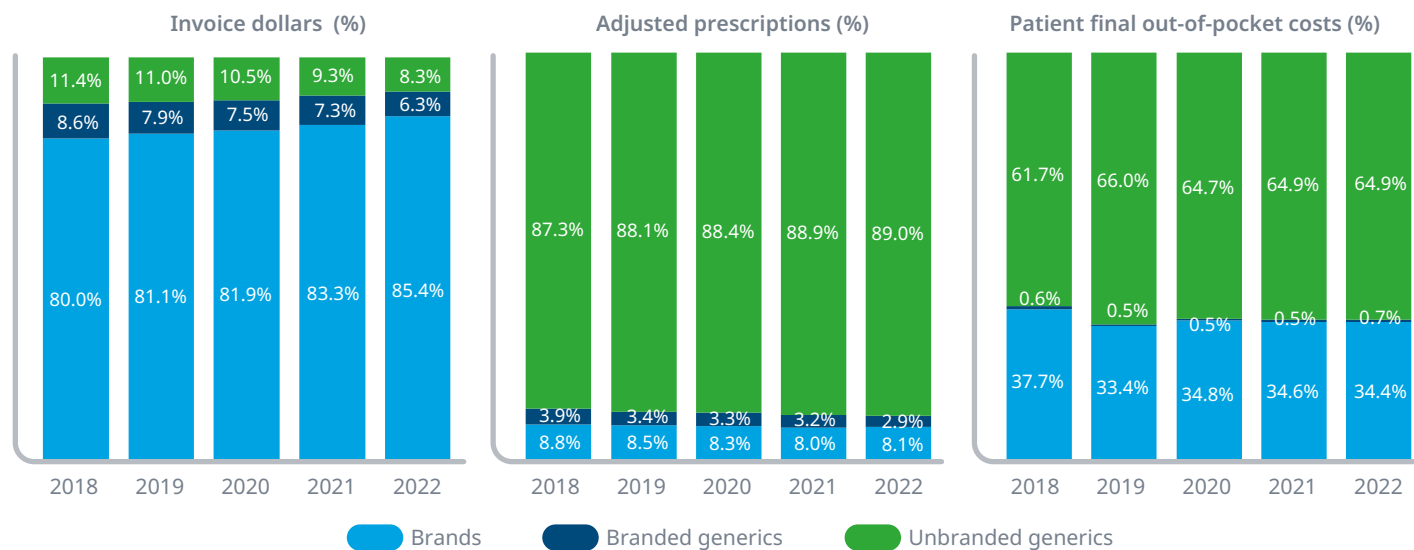
Source: IQVIA LAAD Sample Claims Data, Dec 2022.

- Overall, average out-of-pocket costs are not rising rapidly, with average prescription cost declining from \$10.15 in 2017 to \$9.38 in 2022 across all products and all payers.
- Uninsured patients paying with cash have seen costs decline slightly for all types of products, from \$44.59 to \$43.64, with generic prices higher than in 2017 but below the peak in 2018, while brand prices have dropped \$10.03 per prescription.
- Medicare average prescription costs dropped from \$6.85 to \$6.13 as brand costs remained flat, rising just \$0.02, and generic costs declined \$0.78 but were used more often; these cost changes embed the benefit design changes associated with closing the ‘donut hole.’
- Commercially-insured patient prescription costs have declined from \$9.58 to \$7.56 as brand costs dropped from \$24.45 to \$20.76 over five years, predominately from the use of coupons to offset higher list prices.
- For generics, costs across all payers have remained relatively flat, with commercial and Medicare patients seeing their costs decline while cash-paying patients saw costs rise from \$35.32 in 2017 to \$43.27 in 2018 and then drop to \$38.24 in 2022.

Notes: Includes paid claims only for patients filling at least one prescription. Prescriptions and costs normalized to 30 days.

## Generics and branded generics account for 15% of invoice-level spending but represent 66% of patient out-of-pocket costs

Exhibit 37: Share of spending, prescriptions and patient out-of-pocket costs by product type, 2018–2022



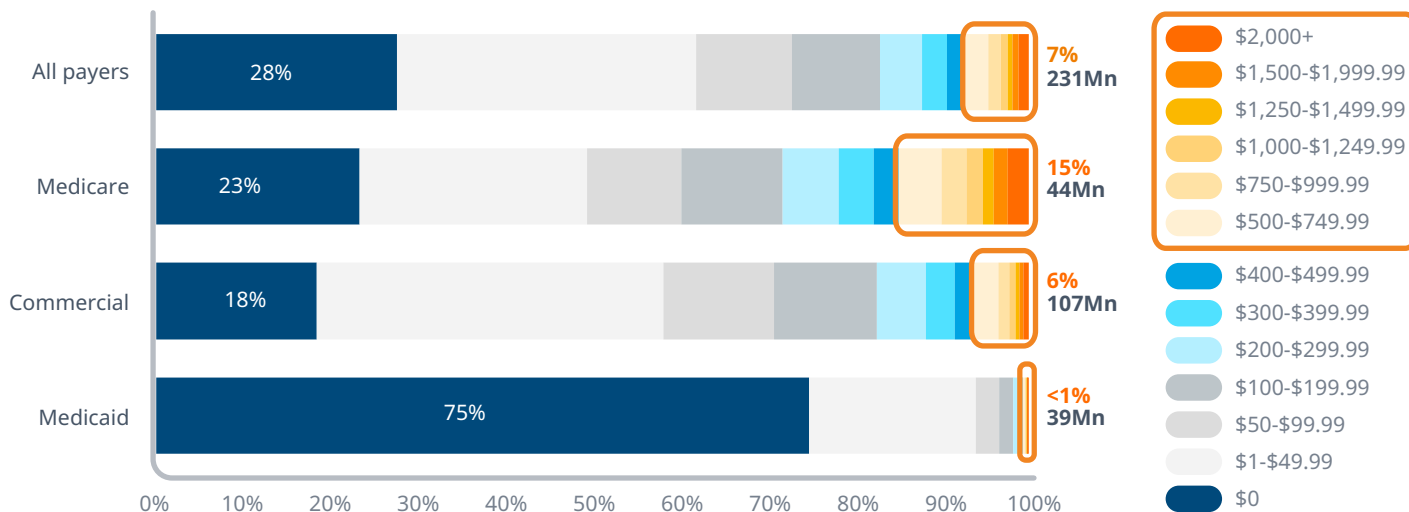
Source: IQVIA National Sales Perspectives; IQVIA National Prescription Audit; IQVIA LAAD Sample Claims Data, Dec 2022.

- Patent expiries over decades for products used by millions of patients have contributed to overall generic share of adjusted prescriptions reaching 92% — including branded generics.
- While these products are relatively inexpensive, accounting for 14.6% of invoice-level spending, they account for 65.6% of patients’ out-of-pocket costs.
- Over the past five years, generic share of invoice-level spending has dropped from 20.0% to 14.6% while the share of prescriptions has risen from 91.2% to 91.9%, and yet patient out-of-pocket costs have risen.
- Generics have seen a rising share of out-of-pocket costs as some are paid by cash-paying patients at list prices.
- While brand invoice spending has risen to 85.4%, a declining share of prescriptions are for brands with just 8.1% in 2022 and share of out-of-pocket costs for brands has declined 3.3% since 2018, driven by use of coupons to offset higher prices.

Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated (see methodology). Excludes COVID-19 vaccines and therapeutics.

## Overall, 7% of patients reach annual out-of-pocket costs above \$500 compared to 15% in Medicare largely due to benefit design

Exhibit 38: Patients by annual prescription out-of-pocket cost in 2022



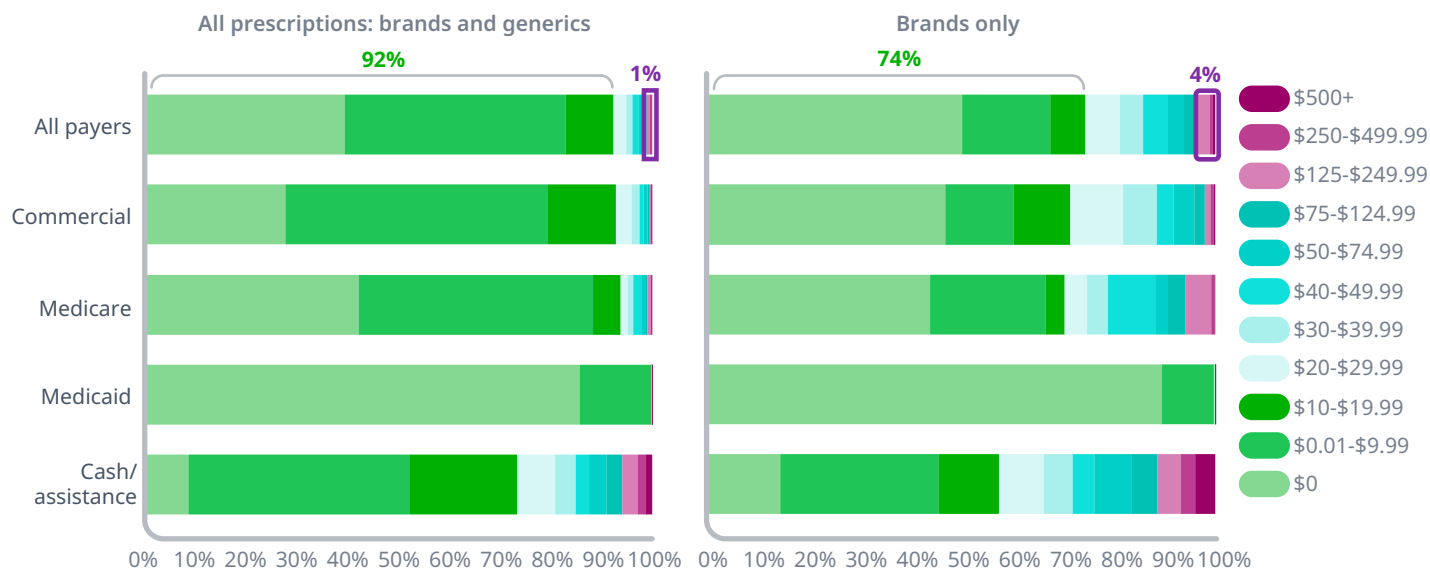
Source: IQVIA LAAD Sample Claims Data, Dec 2022.

- Across all patients, 7% reach annual out-of-pocket costs above \$500 and 1.9% pay more than \$1,500 out-of-pocket for prescriptions.
- In Medicaid, 75% of patients have no annual out-of-pocket costs for prescriptions, with less than 1% of patients paying more than \$500 out-of-pocket for prescriptions.
- In Medicare, 15% of patients pay more than \$500 out-of-pocket — the amount where cost-sharing starts for patients with standard coverage under Medicare Part D and patients become responsible for 25% of costs. Four percent also pay more than \$1,500.
- Following the passage of the Inflation Reduction Act, Medicare Part D out-of-pocket costs will be capped at \$2,000 annually starting in 2025.<sup>28</sup> In 2022, 1 million Medicare enrollees reached prescription out-of-pocket costs over \$2,000 and the new cap would save these patients \$1.8Bn in aggregate or \$1,700 per patient on average.
- In commercial coverage, 6% of patients pay more than \$500 and 1.1% pay more than \$1,500. For the millions of seniors who become Medicare eligible each year, the cost exposure difference as their insurance changes can be a significant shock as seniors have higher cost exposure than the commercially-insured.

Notes: Patients who filled at least one prescription in our sample were included. Patients were grouped into cohorts by method of payment and costs aggregated in the year.

# Over 92% of prescriptions have a final out-of-pocket cost below \$20, 1% (66 million) prescriptions have costs above \$125

Exhibit 39: Distribution of prescriptions by out-of-pocket cost in 2022, all channels



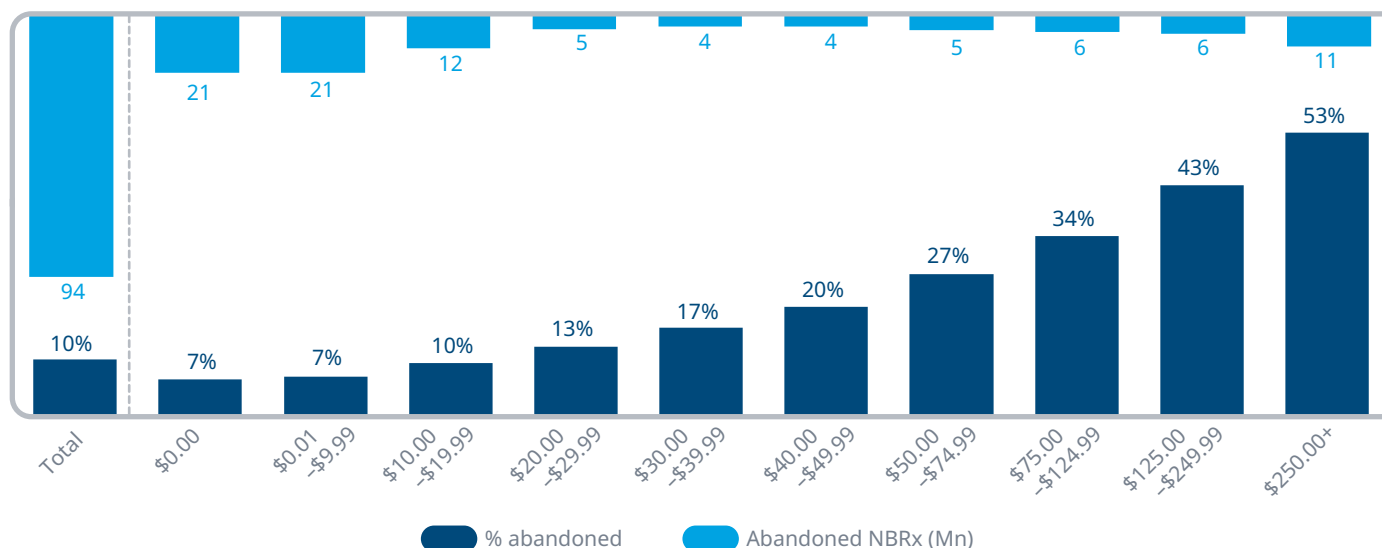
Source: IQVIA LAAD Sample Claims Data, Dec 2022.

- About 66 million prescriptions — 1% of the total — were filled in 2022 with a final out-of-pocket cost above \$125, and with more than 9.8 million prescriptions with an out-of-pocket cost over \$500.
- While 92% of all prescriptions across all payers have an out-of-pocket cost under \$20, this drops to 73% of prescriptions for the uninsured costing less than \$20, while 6% of prescriptions cost above \$125 for the uninsured.
- Four percent of brands have a final out-of-pocket cost over \$125, with Medicare beneficiaries exposed to higher prescription costs and with 6% of prescriptions for brands having an out-of-pocket cost over \$125.
- Cash paying patients have significantly higher costs for brand prescriptions, with 11% having out-of-pocket costs greater than \$125, likely leading to higher abandonment of brands among these patients.
- While relatively few patients fill prescriptions at higher cost levels, abandonment rates are higher, and those prescriptions may be underrepresented as those prescriptions might have been abandoned due to cost (Exhibit 40).
- A rising number of prescriptions are now dispensed with a \$0 payment by the patient and amount to 50% of all branded prescriptions and 39% of all product prescriptions in 2022.
- These zero cost prescriptions are driven by a combination of factors, including patients reaching out-of-pocket maximums, receiving coupons (some of which lower costs to zero), or being driven by benefit designs, which provide free products in certain classes, or from Medicaid.

Notes: Includes paid claims only for patients filling at least one prescription. Prescriptions and costs normalized to 30-days.

## Patients starting new therapy abandoned 94Mn prescriptions at pharmacies in 2022 with increasing frequency as costs rise

Exhibit 40: 14-day abandonment share of new-to-product prescriptions by final out-of-pocket cost in 2022, all payers, all products



Source: IQVIA National Prescription Audit: New to Brand, LAAD Sample Claims Data, Dec 2022; IQVIA Institute, Mar 2023.

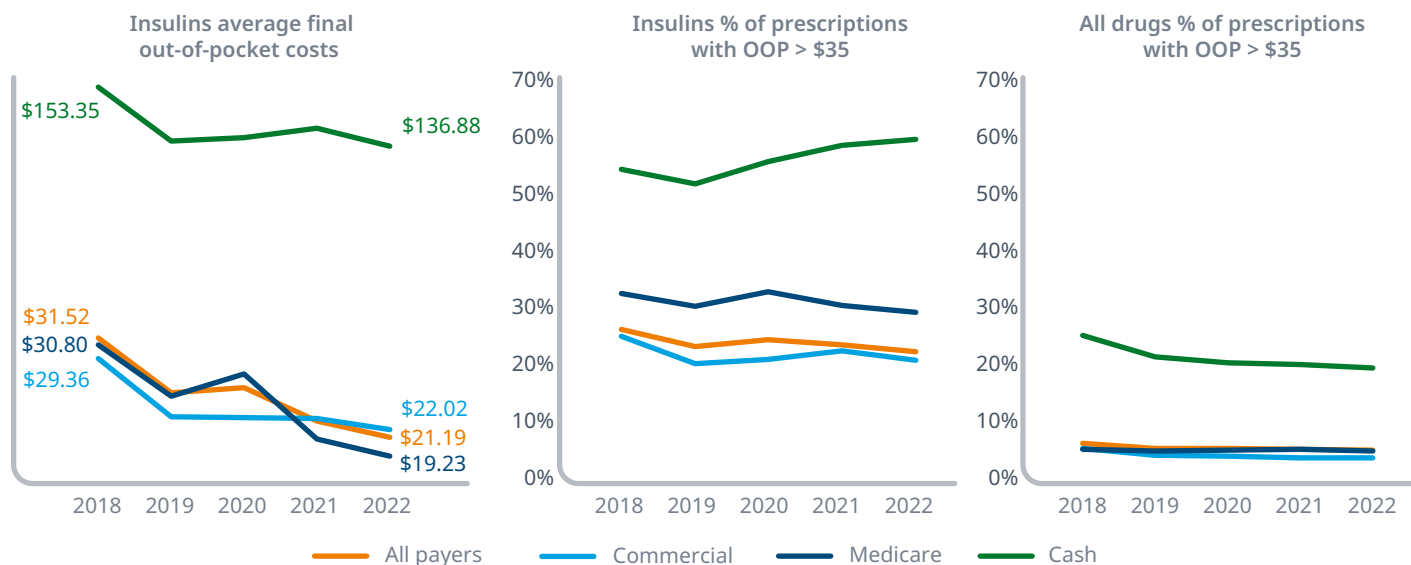
- The number of prescriptions written and transmitted to pharmacies by doctors, either by traditional paper, by phone or electronically, for a variety of reasons exceeds the number that patients filled by 10%, the most common reason being the cost of the prescription, with the effect rising as costs rise.
- Of prescriptions with a final cost above \$250, 53% are not picked up by patients, as compared with 7% of patients who do not fill when the cost is less than \$10.
- Of the 94 million new-to-product prescriptions abandoned in 2022, 42 million were abandoned when costs were under \$10, including zero cost prescriptions, while the remaining 52 million were abandoned at greater rates as costs rise.
- Many traditional insurance plans with a fixed copay design include brand copays of less than \$30 for preferred products, with abandonment of 13% or less. This can be compared to a non-preferred brand copay of \$75 with an abandonment of 34% or higher.
- Benefit designs that inherently expose patients to costs use this patient behavior relating to costs to encourage the use of lower-cost medicines, but can equally result in patients not taking necessary medicines.
- Some therapy areas where branded products are often more costly at list prices, including oncology and immunology, have notable rates of abandonment exceeding 30% for the pharmacy-dispensed medicines in those therapy areas.

Notes: New to product prescriptions are those where patients have not had a prescription for the specific brand or generic drug within the prior year. Pharmacies in the sample provide information on prescriptions which were prepared for dispensing and whether they were dispensed, with abandonment defined as the prescription in question not being dispensed to the patient within 14 days of the initial fill. Analyses on a sample of claims projected to national totals.



## Insulin costs have declined but patient payments above \$35 are more common for these drugs than in the overall market

Exhibit 41: Insulin average out-of-pocket costs and share of prescriptions with costs >\$35



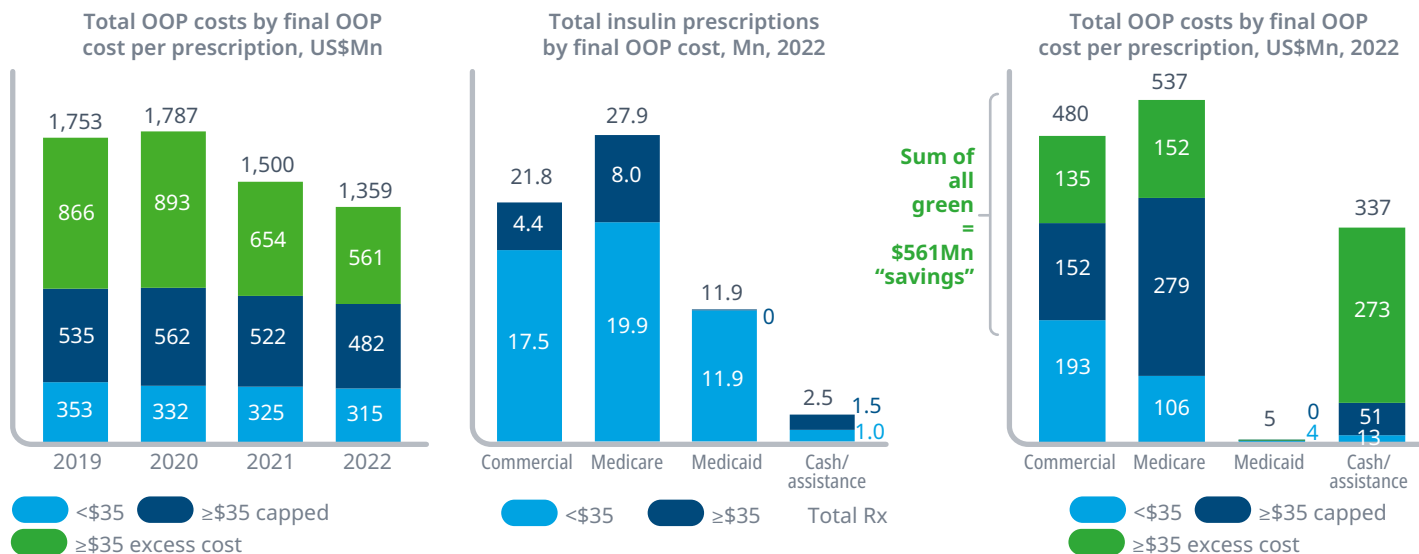
Source: IQVIA LAAD Sample Claims Data, Dec 2022.

- The costs of insulins when paid without insurance are over \$136 per month, and while insulin prescriptions paid with cash represent 4% of insulin volumes, cash insulin volumes are likely understated because of high list prices and the likely abandonment of these high-cost prescriptions.
- Across all medicines, patients abandon 43% of new prescriptions that cost from \$125 to \$249.99 and 53% of those costing more than \$250, which would reflect the costs uninsured patients could pay depending on their pharmacy.
- Insurance influences what patients pay for insulin, with 59% of cash-paid prescriptions costing those patients more than \$35 compared to 17% of cash-paid prescriptions across all medicines.
- Even among those with insurance, commercially insured patients pay over \$35 for insulin 20% of the time, consistent with how many patients have high deductible health plans. Medicare patients pay over \$35 about 29% of the time, down from 32% in 2018.
- Across all patients, benefit design changes combined with the availability of biosimilars are contributing to falling insulin costs.

Notes: Includes paid claims only for patients filling at least one prescription. Prescriptions and costs normalized to 30 days. Does not reflect initial cost exposure.

# Insulin out-of-pocket costs have declined by \$394Mn since 2019 and would further decline by \$561Mn if costs were capped at \$35

Exhibit 42: Number of insulin prescriptions with final out-of-pocket cost above and below \$35 and potential savings if costs were capped at \$35, US\$Mn



Source: IQVIA LAAD Sample Claims Data, National Prescription Audit, Dec 2022; IQVIA Institute, Mar 2023.

- Total out-of-pocket costs paid by patients with insulin prescriptions amounted to \$1.4Bn in 2022, and 77% of those costs are linked to the 21% of prescriptions that cost patients more than \$35.
- The Inflation Reduction Act caps insulin out-of-pocket costs for Medicare beneficiaries at \$35 per month beginning in 2023. Although this does not apply to commercially insured or uninsured patients, three of the major insulin manufacturers have announced significant price reductions taking effect by 2024.
- If costs were capped at \$35 for all patients, they would save \$561Mn: \$135Mn in commercial plans, \$152Mn in Medicare, and \$273Mn for cash-paying patients (typically the uninsured).
- In 2022, there were 13.8 million insulin prescriptions costing more than \$35, down 10% (1.5 million) from 2019, with some of this driven by a decline in overall insulin prescriptions.
- Patients spent \$480Mn in commercial plans, \$537Mn in Medicare, and \$337Mn when paying cash, and per prescription savings would average \$31 in commercial, \$19 in Medicare, and \$188 for cash.
- While the potential savings from capping insulin costs is less than 1% of total patient out-of-pocket costs in 2022, the reductions in prescription costs ensure these essential medicines are more accessible to patients who need them.

Notes: Values may not sum due to rounding. Prescriptions in retail pharmacies were adjusted to consistent 30-day prescription lengths for cost and volume comparison purposes. Final out-of-pocket cost reflects the final patient responsibility after insurance and the use of coupons or other assistance for cash or commercial patients. Savings calculated as out-of-pocket cost minus \$35 per month for prescriptions costing above \$35. Savings could be offset in future if lower-cost prescriptions have higher costs.

## Outlook to 2027

- U.S. market growth will return to pre-pandemic projections by 2024 but embeds new pressures on net growth in later years.
- U.S. spending on medicines is forecast to be largely unchanged over the next five years, with growth expected between -2 to 1%.
- Effects of policy changes in the Inflation Reduction Act and American Rescue Plan Act will impact stakeholders differently and are subject to final regulations and implementation of these far-reaching pieces of legislation.
- New brand spending in the U.S. is projected to be lower than the last five years.
- Net prices for protected brands are forecast to decline -2 to -5%, while list prices will grow 0 to 3%, including impacts of price cuts.
- The impact of exclusivity losses will drop to \$63Bn over the next five years, including the impact of biosimilar introduction, and mostly reflects the timing of specific molecule patent expiries.
- Aggregate savings over the next five years as a result of biosimilars entering the market are projected to exceed \$180Bn, though uncertainties remain.
- Oncology, neurology and obesity drive growth through 2027 while diabetes, immunology and COVID-19 will slow.
- U.S. oncology spending to reach \$125Bn by 2027, with growth slowing to 9% from biosimilar savings.
- List price cuts dramatically change diabetes pricing while net spending will decline 36-39% by 2027 from expiries and competition.
- Costs for autoimmune disorders will drop by 41% from biosimilars and competition while volume grows 45% through 2027.
- Next-generation biotherapeutics are expected to reach \$12Bn by 2027, up from \$4Bn in 2022, with a wide range of potential scenarios.
- Obesity spending has accelerated in the past 2 years from novel GLP-1 inhibitors with upside if more widely reimbursed.

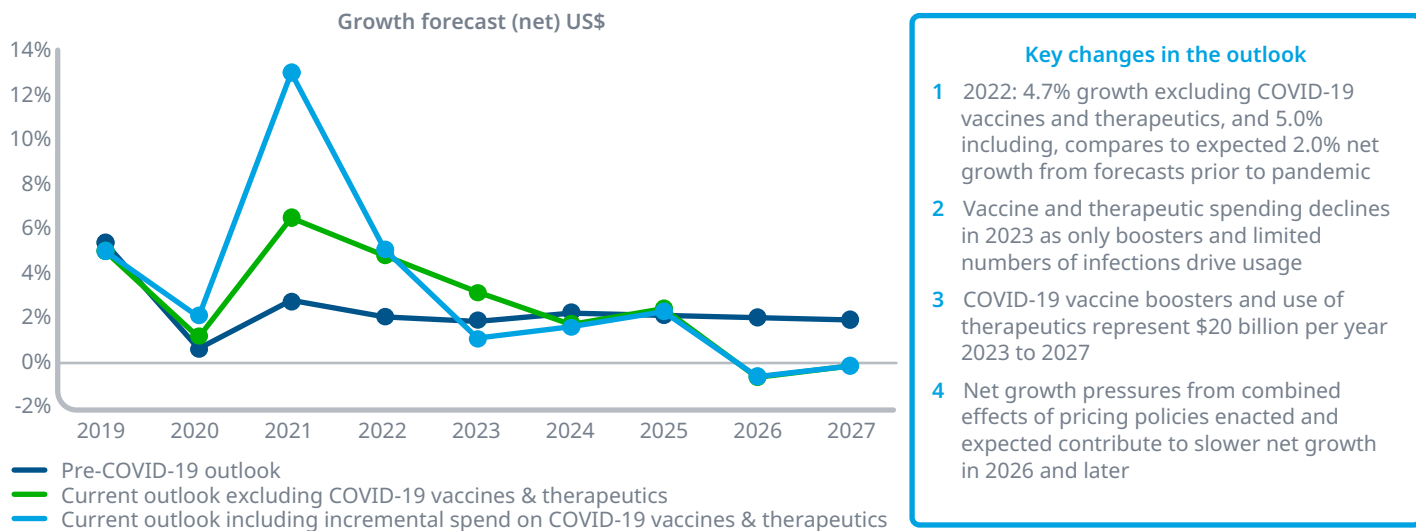


*Medicine spending is projected to be unchanged over five years for the first time reflecting structural market dynamics and competition as well as the effects of new policies and legislation.*



# U.S. market growth will return to pre-pandemic projections by 2024 but embeds new pressures on net growth in later years

Exhibit 43: Comparison of current outlook to pre-COVID-19 outlook



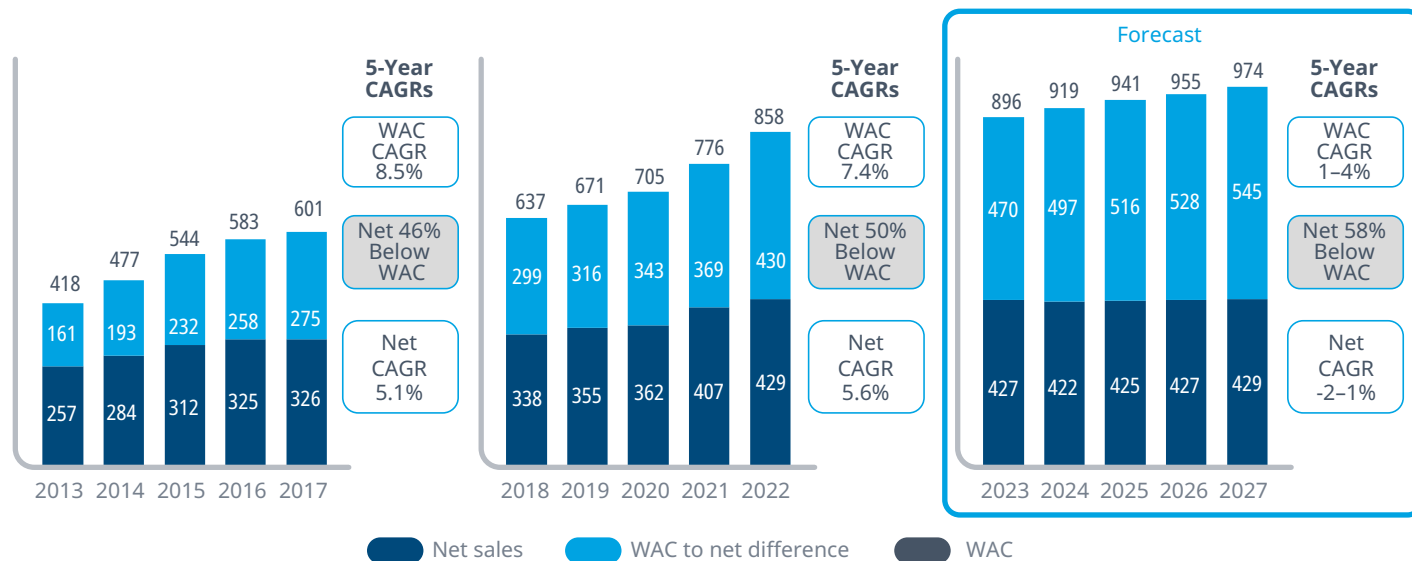
Source: IQVIA Market Prognosis, Mar 2023; IQVIA Institute, Mar 2023.

- While the impact from COVID-19 has been significant, the long-term impact on growth trends is expected to be more muted and the market will return to pre-pandemic trends by 2024.
- The significant slowdown in market growth in 2026 and 2027 was not modeled in earlier editions of the forecasts and reflects the impact of new pricing policies enacted in 2022.
- Policymakers have been focusing on drug pricing for most of the last decade with both federal and state level legislation being passed, the most impactful of which is thought to be the Inflation Reduction Act (2022).
- The new legislation includes wide-ranging provisions affecting Medicare insurance design, cost-sharing and adding drug price inflation penalties to Medicare plans.
- Many of these provisions are phased in and the key elements are expected to have the most impact in 2026 and beyond.

Notes: Pre-COVID-19 outlook based on IQVIA Market Prognosis, Sept. 2019 edition. Current outlook based on IQVIA Market Prognosis Sept. 2022 edition but updated reflecting year-end 2022 actual data. Incremental COVID-19 vaccine & therapeutics scenario based on current outlook combined with incremental spending for vaccines & therapeutics. The growth shown here are estimated at manufacturer net prices.

## U.S. spending on medicines is forecast to be largely unchanged over the next 5 years with growth expected between -2 to 1%

Exhibit 44: U.S. medicine spending and growth at WAC and estimated net 2013–2027



Source: IQVIA Institute, Mar 2023.

- Total net spending on medicines in 2027 is expected to be unchanged compared to 2022 as volume growth drivers will be fully offset by drivers of lower prices, including patent expiries and the effects of legislation.
- Over the next five years, medicine spending will grow between 1–4% on a list price basis and -2 to 1% after discounts and rebates.
- Growth will be driven by adoption of newly launched innovative products, with an average of 50–55 new medicines launching per year over the next five years, including those in oncology or with specialty or orphan status.
- Spending growth will be offset by losses of exclusivity and continued emergence and uptake of biosimilars, the impacts of legislation and stakeholder responses, and a shift in COVID-19 spending to reflect a shift to endemic status.
- List price growth will continue at historically low levels with protected brands expected to increase 0 to 3%, while net prices are expected to decline -2 to -5%, especially later in the forecast.

Notes: Spending is based on IQVIA reported values from wholesaler transactions measured at list (WAC) prices and exclude discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after both invoice and off-invoice discounts, rebates and price concessions are applied. Includes all medicines in both pharmacy and institutional settings. Includes COVID-19 vaccines and therapeutics from company reported values.

## There are a range of expected effects from the Inflation Reduction Act, American Rescue Plan Act impacting stakeholders differently

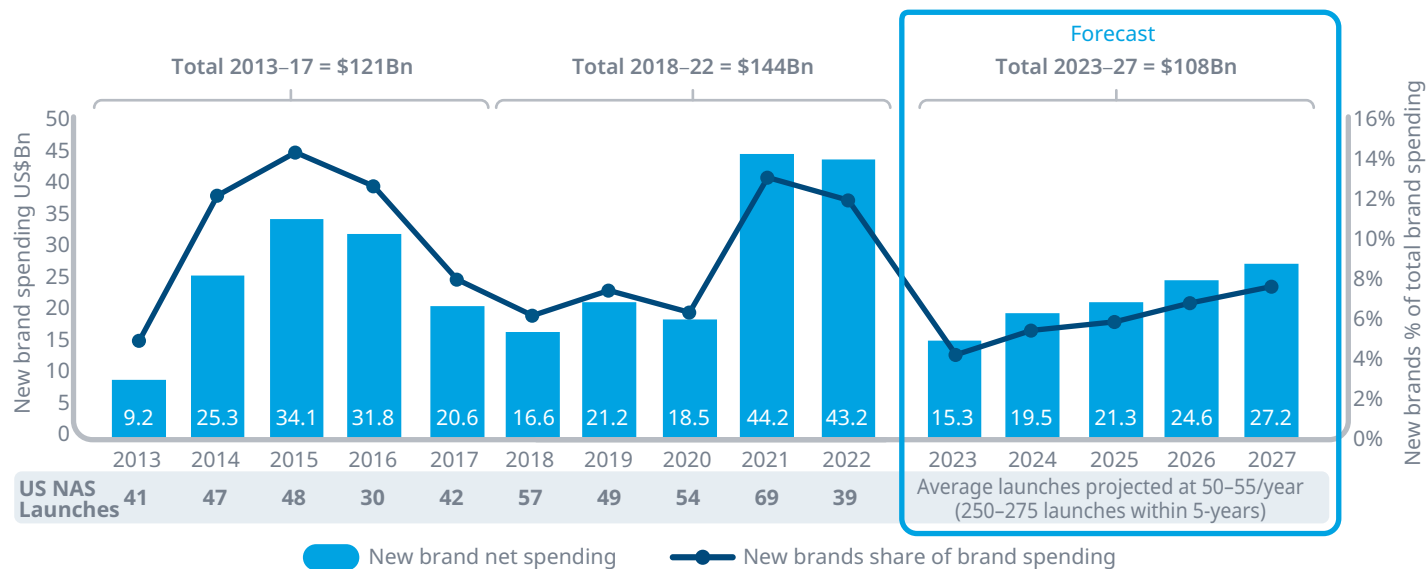
Exhibit 45: Notable expected effects of U.S. policy reforms

	FIRST ORDER EFFECTS	SECOND ORDER EFFECTS
Medicine usage	Cost-sharing reductions, out-of-pocket limits result in increased fill rates on previously abandoned prescriptions	Incremental volume may result in more restricted access to some medicines
Medicine spending	Likely neutral effects on overall net spending as increased volumes offset impact from lower prices most of which come into effect later in the decade	Changes in the amount of absolute difference from gross to net spending impact payers' and will likely contribute to greater access restrictions and/or rising premiums
Patient spending	Medicare Part D patients' annual costs reduced from \$2,000 cap, in addition to spreading costs across the year to avoid billing shocks, while those taking insulin will be capped at \$35/month	Insulin companies, expecting to be exposed to rebates >100% in Medicaid from 2024 have cut list prices, affecting all patients, not just Medicare Part D. Additional therapy areas/products may follow
Patient insurance premiums	Medicare Part D insurance premiums are capped at 6% increases per year	If approved plans have premiums rising more than 6%, CMS makes up the difference to the plans
Government payer spending	Medicare catastrophic phase shifting responsibility from government to insurers and the drug industry	Offsetting premium increases above the patient cap will likely reduce these savings
Private payer spending	Plan spending will rise as they absorb responsibility for catastrophic phase of part D, and cover patients who would have previously not filled prescriptions	Formulary controls become more stringent as out-of-pocket caps make some patients less influenced by the cost of their drugs
Brand manufacturers net revenue	Drug price negotiation likely to result in maximum fair prices below current net prices.	Companies with greater exposure to inflation penalties cut list prices, dramatically reducing off-invoice discounts and rebates to be paid to payers while having less impact on net prices and potentially reducing the impact of MFP on final negotiated prices
Brand manufacturers operating costs	Limited direct effects on operating model	Companies reduce operating expenditures as a result of expected lower revenue, could impact R&D, drive greater operating efficiencies elsewhere or result in reduced operating profit
Generic/biosimilar manufacturers revenue	Reduced differences between brand list prices and generic/biosimilar prices and patient cost caps reduce patient incentives to choose generics or biosimilars	Utilization increases benefit generics more than brands in volume terms
Wholesalers / pharmacies	Neutral effects from legislative provisions	Greater focus on fee-based payments than % of list price and potential for payers to prefer more restrictive supply chain and care delivery networks as a mechanism to control costs, ultimately benefitting wholesalers and providers

Source: IQVIA Institute, Apr 2023.

# New brand spending in the U.S. is projected to be lower than in the last 5 years

Exhibit 46: U.S. new brand spending at estimated manufacturer net prices



Source: IQVIA Institute, Mar 2023.

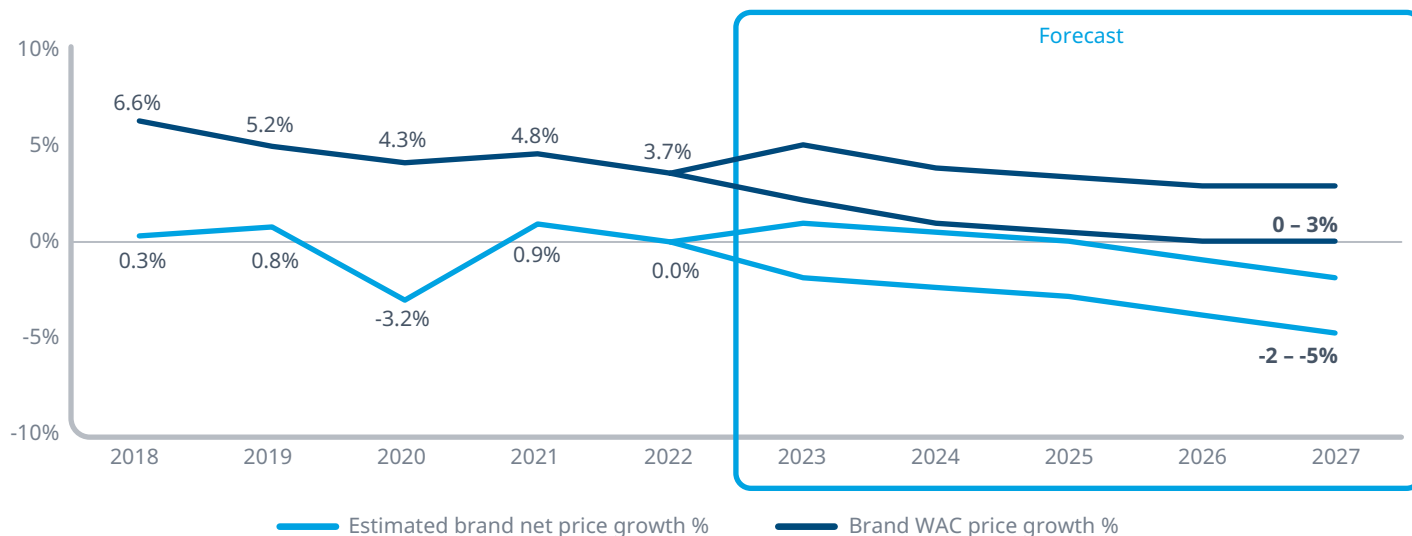
- The growing output of drug R&D is expected to continue to result in an average 50-55 NASs per year and an aggregate of \$108Bn of new drug spending over five years, lower in aggregate than the past two five-year periods.
- The number of NAS launches in 2022 slowed to 39 after a record year in 2021, and notably differing from reports of drug approvals due to the inclusion of Emergency Use Authorizations, cell and gene therapies, and launches from prior years' approvals.
- The aggregate amount of new brand spending rose sharply from \$27Bn in 2021 and \$29Bn in 2022 from COVID-19 vaccines and therapeutics.
- New brand spending, excluding COVID-19, would have been below \$20Bn for three successive years, a trend projected to continue in 2023.
- Over the next five years, 250-275 NAS launches are expected but are anticipated to represent an average 6-7% of brand spending compared to 11% in the past five years.
- New brands in the next five years are expected to include large numbers of oncology, immunology and neurology drugs as well as a significant proportion of rare disease treatments.

Notes: NAS = novel active substance. New brands are protected branded products on the market less than 24 months during the year reported. New brand spending is at estimated net manufacturer price levels.



## Net prices for protected brands are forecast to decline -2 to -5%, while list prices will grow 0 to 3%, including impact of price cuts

Exhibit 47: Wholesaler Acquisition Cost (WAC) growth and net price growth for protected brands



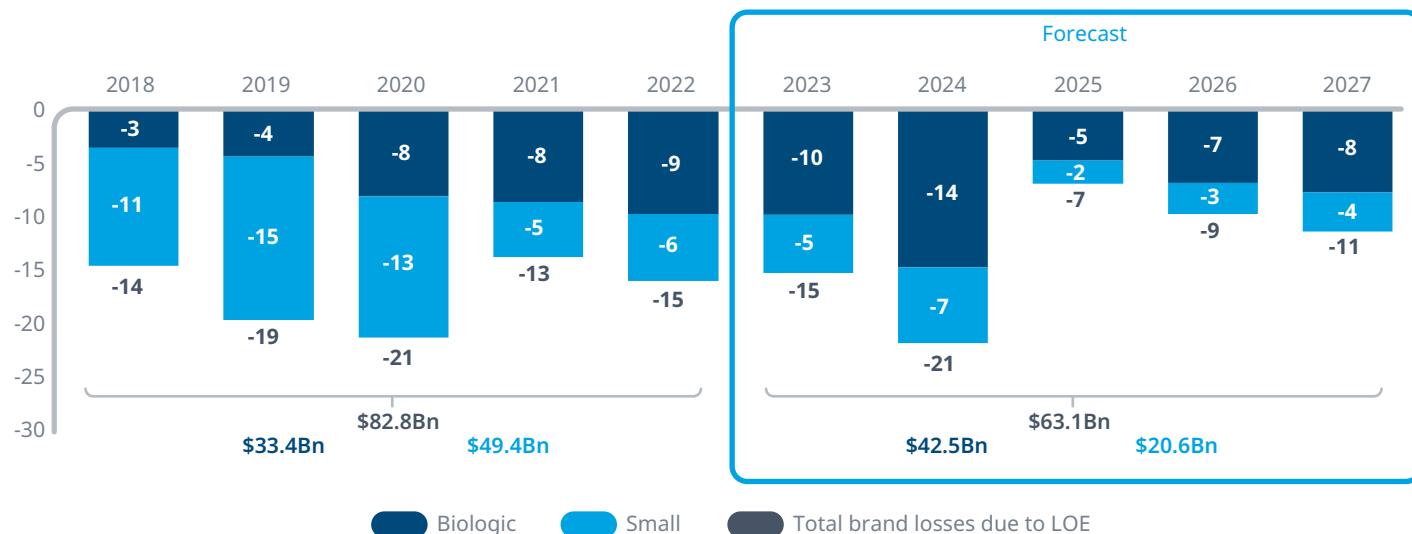
Source: IQVIA Institute, Mar 2023.

- As public pressure on drug pricing has escalated, list price increases have slowed to 3.7% in 2022 and are expected to average 0–3% per year through 2027, including the expected effects of the Inflation Reduction Act.
- Net price growth is likely to continue to see declines in the -2 to -5% range as the structural drivers of low net price growth are expected to remain in effect and be amplified by new legislation and increased competitive intensity in therapy areas with new launches and/or upcoming biosimilar events, such as diabetes and immunology.
- The price cuts for insulin products announced by manufacturers in early 2023 are expected to lower list prices from 2024 forward and be followed by additional products in other therapy areas, contributing to slowing list price growth through 2027.
- The key driver of these price cuts is the combination of provisions of the Inflation Reduction Act as well as provisions of the American Rescue Plan Act (2021), which would have dramatically increased Medicaid rebates for the affected insulin products in the absence of these price cuts.
- The combined effects of the legislative changes, anticipated stakeholder actions, and ongoing market dynamics are expected to reduce net prices progressively over the five-year period.

Notes: Wholesaler Acquisition Cost (WAC) price. Protected brands are brands more than 24 months after first launch and not yet off-patent. Net price growth estimates based on public information compared to IQVIA data (see Methodology section).

## The impact of exclusivity losses will drop to \$63Bn over 5 years, including significant biosimilars impact through the period

Exhibit 48: U.S. impact of brand losses of exclusivity 2018–2027, US\$Bn



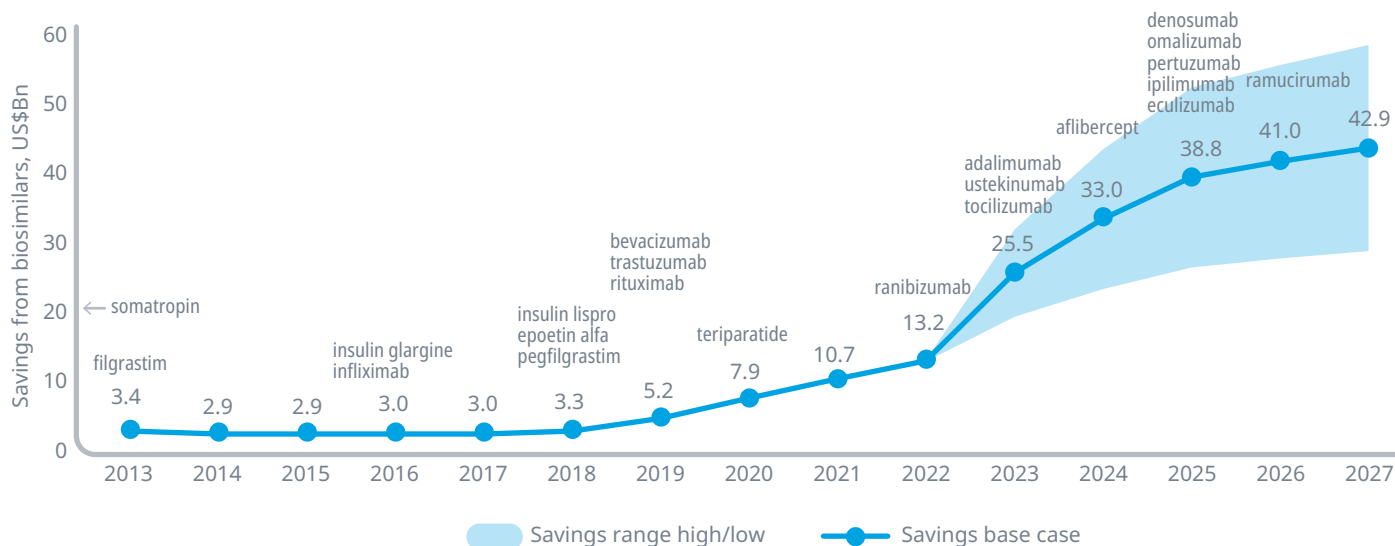
Source: IQVIA Market Prognosis, Sep 2022; IQVIA Institute, Mar 2023.

- The impact of patent expiries is expected to decrease over the next five years measured at net prices.
- Small molecule impact is expected to be only \$20.6Bn, down from \$49.4Bn in the past five years as small molecule impacts are fewer and key events are later in the forecast period.
- Biologics impact will increase to over \$42.5Bn of brand losses on a net basis from the continued impact of earlier biosimilar events as well as from large LOE impacts in 2023–2024 when products such as ranibizumab (Lucentis) which began in 2022, adalimumab (Humira) already underway in January 2023, and ustekinumab (Stelara) expected later in the year.
- The largest biologic impact is expected to be adalimumab (Humira), although uncertainty still surrounds provider willingness to prescribe non-interchangeable versions as well as formulation differences between the newer versions of the originator and some of the biosimilars. Multiple additional biosimilars expected to launch in July 2023 will set the stage for the most anticipated and competitive biosimilar market to date in the U.S.

Notes: Lower brand spending based on invoice prices. Forecast impacts are modeled by projecting individual products sales growth to the point of patent expiry and then modeling expected impact based on historical analogues and actual data for in-progress events. Chart totals may not sum due to rounding. Estimates are based on manufacturer net price levels and estimated future evolution of associated discounts and rebates.

# Savings over the next 5 years as a result of biosimilars are projected to exceed \$180Bn, though uncertainties remain

Exhibit 49: Biologic estimated savings from biosimilars at invoice prices



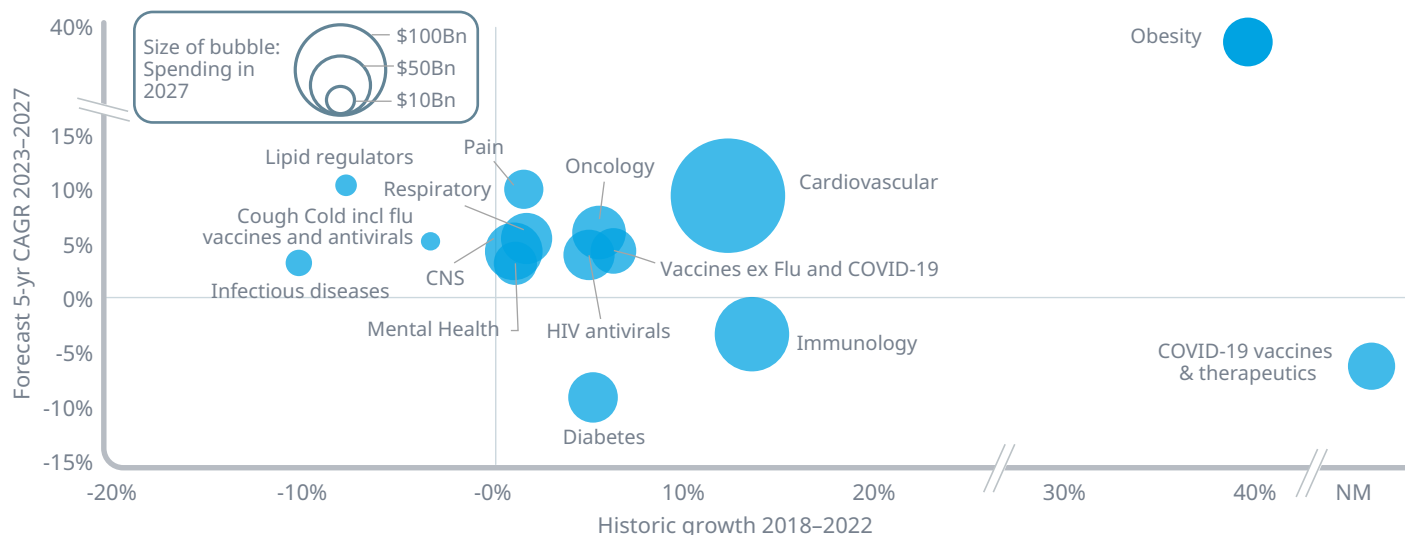
Source: Biosimilars in the United States 2023–2027 – Competition, Savings, and Sustainability. January 2023. Report by the IQVIA Institute for Human Data Science.

- In the last 10 years, \$36Bn of biosimilar spending was associated with savings of \$56Bn compared to what spending would have been without biosimilars.
- The next five years are expected to result in an increase in savings to \$181Bn, more than four times savings seen over the past five years (\$40Bn), as newly approved biosimilars launch and existing biosimilars see continued uptake and price reductions.
- The most impactful biosimilars in the next five years — those referencing adalimumab — have already begun to appear earlier this year as a result of negotiated patent litigation settlements.
- Other significant biosimilar launches for high value ustekinumab in 2023 and aflibercept in 2024 are also expected to contribute significantly to future savings.
- In addition to new biologic molecules facing biosimilars from 2023–2027, recent biosimilars launched in 2018 and 2019 (mainly in oncology) are continuing to generate substantial savings as uptake increases and prices decline.
- Data to date suggest that a wide range of market outcomes are still possible, ranging from lower biosimilar volume uptake with lower discounts relative to the original brand, or alternatively higher volume shares, and bigger discounts.

Notes: Historical savings were calculated by comparing actual molecule spending to projected spending if total molecule volume had been at originator pre-expiry prices. Projected future savings based on estimated continuing impact of biosimilar events in progress, as well as future expected expiries. The range of savings values shown in the biosimilar savings scenarios include assumptions for high, low, and average (base case) biosimilar volume uptake and price discounts relative to originators. Timing of expected biosimilar entry based on patent information and litigation/settlements as of Oct 2022.

# Oncology, neurology and obesity drive growth through 2027 while diabetes, immunology and COVID-19 contribute to slowing

Exhibit 50: Historic and forecast net spending growth for leading therapy areas



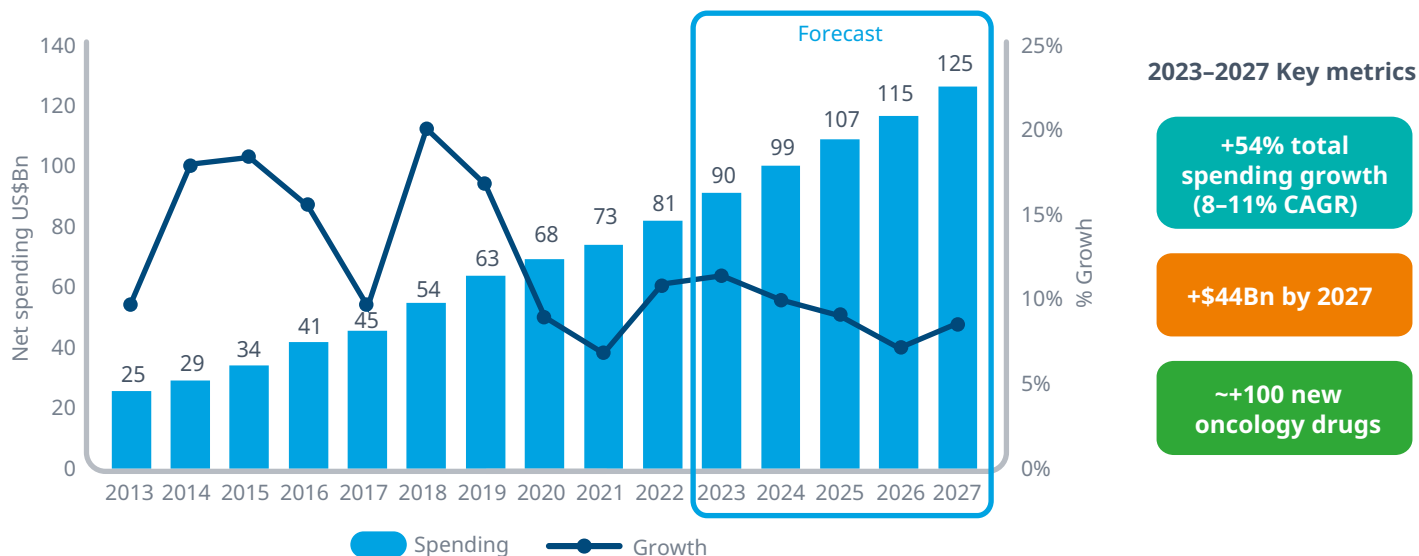
Source: IQVIA Institute, Mar 2023.

- Oncology, obesity and a selection of neurology classes represent the largest aggregate contributors to net growth in the next five years, predominately from a continued flow of new medicines and offset by losses of exclusivity.
- Net spending on COVID-19 vaccines and therapeutics rose to the current \$29Bn in spending and are expected to reduce to \$21Bn by 2027. Volumes reduce offsetting rises in costs.
- Immunology is expected to grow at -3% CAGR from the combined effects of patent expiries and the maturation and slowing growth of launches in the past five years.
- Diabetes growth is expected to slow significantly over the period as the effects of biosimilars, continued high gross-to-net effects, and small molecule expiries all contribute to declining growth.
- Overall growth in neurology is expected to shift to positive in the next five years as continued innovation in wider population areas as well as significant potential upside related to Alzheimer’s and Parkinson’s therapies, in addition to rare neuromuscular disorders that are not included in the base case forecast.
- Pain – defined broadly to include chronic pain relief, anesthesia and other pain treatments such as migraines – is expected to be the fastest growing area over the next five years of the selected high spending classes, lifted in the near term by continued growth in migraine.

Notes: NM = not meaningful, where COVID-19 5-year compound annual growth would reflect a not meaningful growth comparator to the other classes. Selected therapy areas shown. IQVIA Forecast Link modeling of company reported and analyst consensus forecasts has been utilized for therapies with the exception of oncology, immunology, diabetes, and COVID-19 which have been modeled separately by the IQVIA Institute.

# U.S. oncology spending to reach \$125Bn by 2027, with growth slowing to 8–11% from biosimilar savings

Exhibit 51: Oncology spending at estimated manufacturer net prices, US\$Bn



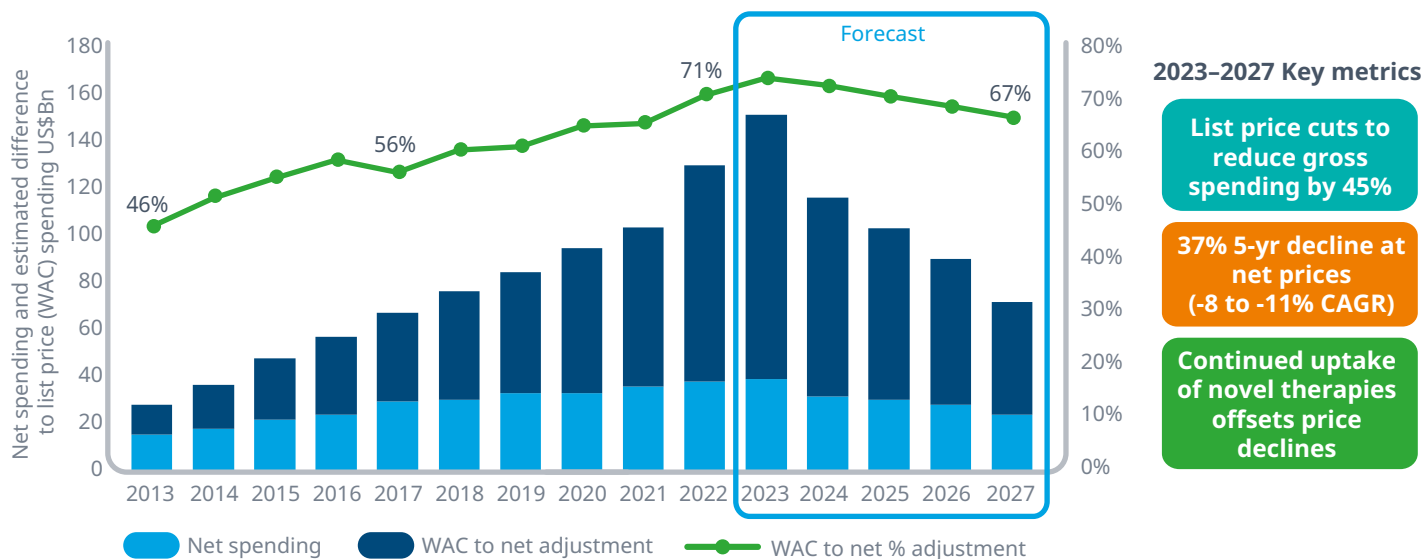
Source: IQVIA Institute, Mar 2023.

- U.S. oncology spending is expected reach \$125Bn on a net basis and to slow to 8–11% through 2027 as patent expiries for both small molecules and biosimilars offset a continued flow of newer treatments.
- Over the next five years, spending is expected to increase 54% on a net basis and add \$44Bn in spending.
- More than 100 new oncology drugs are anticipated based on the current pipeline, although they are expected to be increasingly narrowly focused as precision medicine and biomarker-driven therapies become even more common.
- New modalities are expected to drive oncology spending with cell and gene therapies, bispecific antibodies, and antibody-drug conjugates making up an increasing part of novel medicines in both solid and hematological malignancies.
- In addition to the flow of more biomarker-driven therapeutic choices, the use of next-generation sequencing technologies (NGS) is expanding which can test for multiple potential mutations at once and guide therapy selection more precisely, including the timing of shifting lines of therapy for more optimal results.
- In addition to robust innovation, the continued wider use of novel immunotherapies, shifting to earlier lines of therapy and used for longer treatment durations, are bringing significant survival benefits to many patients.

Notes: Oncology includes therapeutics and not supportive care.

# List price cuts dramatically change diabetes pricing while net spending will decline 36–39% by 2027 from expiries and competition

Exhibit 52: Diabetes spending at net and list price (WAC) levels



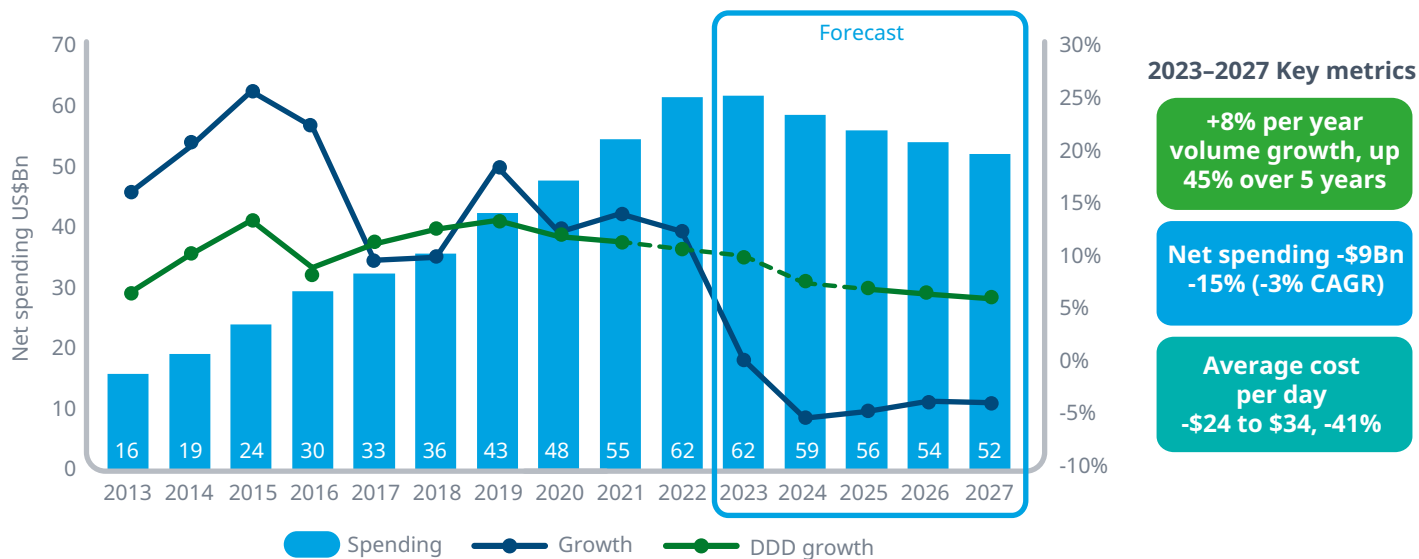
Source: IQVIA Institute, Mar 2023.

- Diabetes spending in the U.S. reflects both the consistent use of older therapies as patients’ Type 2 disease progresses and the adoption of novel therapies later in the treatment pathway, as well as the therapy area with the largest difference between spending at list and net prices.
- Diabetes therapies have among the highest levels of discounts and rebates with list prices 76% higher overall than net manufacturer prices for all products, with wide variations by product (Exhibit 30).
- Over the next five years, net revenues for manufacturers will decline by 36-39%, at -8% to -11% CAGR, as net price declines continue for protected brands as well as biosimilars and generics.
- In addition to the net price reductions, the changes in list prices of insulin products already announced may be followed by similar actions for other diabetes therapies.
- The continued uptake of novel therapies in the GLP-1 and SGLT-2 mechanisms continue to contribute to spending growth.
- Demographic shifts, which will likely increase the number of diabetes patients, will contribute to greater volume but will be offset by net price reductions.

Notes: Diabetes does not include obesity drugs using the GLP-1 target which have begun to be marketed as these are categorized elsewhere.

# Costs for autoimmune disorders will drop by 41% from biosimilars and competition while volume grows 45% through 2027

Exhibit 53: Immunology spending at estimated manufacturer net prices, US\$Bn



Source: IQVIA Institute, Mar 2023.

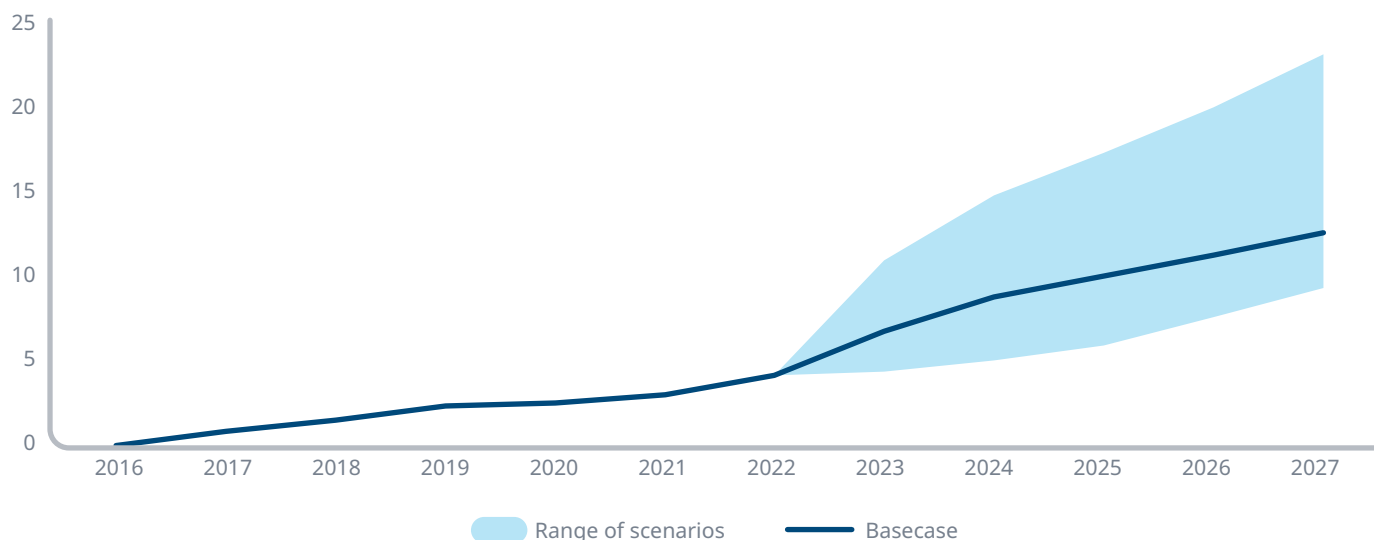
- Over the past 10 years, immunology treatments have consistently been driven by increasing volume, averaging 12% volume growth in days of therapy and a higher rate of growth in spending as newer products with higher prices have contributed to growth.
- In the next five years, spending is expected to drop 15% or \$9Bn and slowing to an average -3% CAGR.
- The average cost per day has been rising for most of the past 10 years as prices were rising faster than volume growth, but costs are expected to drop considerably as key biosimilar events begin in 2023.
- The introduction of biosimilar adalimumab (Humira) and ustekinumab (Stelara) in 2023 will contribute significantly to lower costs for immunology treatments, with the full impact visible in 2024 when spending growth declines -5%.
- The entrance of biosimilars for leading products is expected to have both direct and indirect effects on competition and contribute to slowing net growth as companies increase discounts and rebates as part of negotiations for formulary position.
- Overall, costs at net manufacturer prices are expected to decline \$24 to \$34 per day, although these costs are not the same as patient cost exposure, which can be significantly different based on insurance type and benefit design.

Notes: Immunology includes small molecule and biologic immunology treatments for a range of diseases including but not limited to rheumatoid arthritis, psoriasis, atopic dermatitis, lupus, ulcerative colitis, severe asthma. Defined daily doses are based on the most common indication and stable maintenance dosing in the label, using body weight assumptions rather than real-world data. These dose assumptions are consistent with the World Health Organization defined daily dose metric (see Methodology section).



## Next-generation biotherapeutics to reach \$12Bn by 2027, up from \$4Bn in 2022 with a wide range of potential scenarios

Exhibit 54: U.S. next-generation biotherapeutics spending at estimated net manufacturer prices, US\$Bn



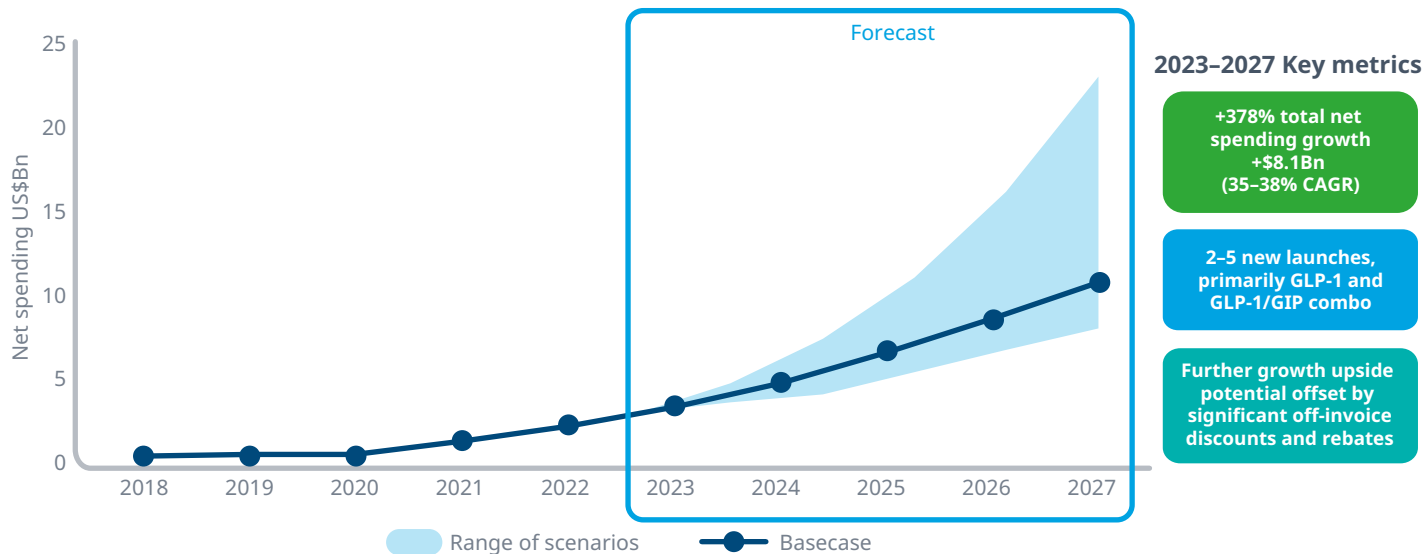
Source: Company financials for medicines launched in the U.S., Dec 2022, IQVIA Institute, Mar 2023.

- There are currently 33 cell, gene or RNA-based therapies launched globally to-date but only 18 of them are currently marketed in the U.S. An additional 55–65 new therapies could be launched globally by 2027, with a dozen new per year on average, up from the average of three per year in the past five years; about 60% of those are expected to be available in the U.S.
- While there is considerable R&D activity related to these mechanisms of action, there remains significant uncertainty about the emergence of safety risks and the pace of clinical trials and regulatory reviews, and as has happened for some existing treatments, some may be removed from the market after launch for commercial reasons.
- Total U.S. spending to date has reached \$4Bn, which is 60% of the global spending on these drugs. Total spending is expected to rise to \$12Bn by 2027, but with the potential for both higher or lower scenarios ranging from \$9Bn to \$23Bn.
- Even considering the large numbers of these products, they will not be more than 20% of all new drugs expected to be launched in the next five years and less than 10% of the spending on new drugs in the same period.
- The lower end of expectations would be driven by lower uptake due to more limited reimbursement, resulting in more risk-sharing agreements and lower net prices or outcomes-based contracts.
- Demonstration of significant clinical benefits could coincide with evolving provider comfort with complex logistics for cell and gene therapies, and significant demonstrated efficacy perhaps using real-world data.

Notes: Spending estimates based on company financials and IQVIA audited data to address potential underreporting of therapies with unique distribution methods. Excludes mRNA vaccines.

# Spending on obesity drugs has accelerated in the past 2 years from novel GLP-1 agonists with upside if more widely reimbursed

Exhibit 55: Obesity spending at estimated manufacturer net prices, US\$Bn



Source: IQVIA Institute, Mar 2023.

- U.S. obesity spending at net manufacturer prices reached nearly \$2.1Bn in 2022, up from just \$0.5Bn in 2018 and largely driven by the uptake of novel treatments.
- The newest obesity treatments are glucagon-like peptide 1 agonists or GLP-1 agonists, the mechanism initially developed in diabetes, which often generates weight loss for patients, and which has been developed by several companies as novel weight loss treatments with efficacy and safety rivaling traditional bariatric surgery.
- The potential for obesity treatments to be extended in guidelines to patients with lower body mass indices (BMI) could dramatically increase eligible populations.
- The epidemiology of adults, particularly in the U.S. and other higher income markets categorized as obese, with associated comorbidities and health risks, is prompting significant reassessment of benefits of wider treatment of obesity.
- If guidelines are not expanded and payers are reluctant to extend coverage, spending could grow to \$7Bn by 2027, primarily paid out-of-pocket by patients with likely copay support from manufacturers.
- The base case is more optimistic with an expected \$10Bn net spending in 2027, and \$22Bn in a higher scenario where access is less restricted.
- While the direct cost expansion in these scenarios could be significant, it is likely that these costs would offset other disease costs and prevent worse cardiometabolic outcomes, which is likely the basis upon which many of these decisions will be decided by clinicians and payers.

Notes: Obesity includes medicines specifically indicated for the treatment of obesity excluding dietetics or medical foods.

# Notes on sources

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## **THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW**

**IQVIA's Longitudinal Prescription Data:** IQVIA receives nearly 4 billion prescription claims per year with history from January 2006 with coverage over 90% for the retail channel, 60–85% for mail service, and 75– 80% for long-term care. Longitudinal data derives from electronic data received from pharmacies, payers, software providers and transactional clearinghouses. This information represents activities that take place during the prescription transaction and contains information regarding the product, provider, payer, and geography. Rx data is longitudinally linked back to an anonymous patient token and is linkable to events within the data set itself and across other patient data assets.

**IQVIA's Medical Claims Data:** Dx data are pre-adjudicated claims collected from office-based physicians and specialists. These data are sourced from CMS-1500 form-based claim transactions, the standard reimbursement form for all non-cash claims. Medical claims data includes patient-level diagnosis and procedures for visits to U.S. office-based individual professionals, ambulatory and general healthcare sites. The medical claims data includes more than 205 million patients, over 1.7 billion claims and 3 billion service records obtained annually.

**IQVIA's National Prescription Audit (NPA):** NPA is the industry standard source of national prescription activity for all pharmaceutical products. It measures demand for prescription drugs, including dispensed pharmaceuticals to consumers across three unique channels: retail, mail service, and long-term care pharmacies. From sample pharmacies, IQVIA collects new and refilled prescription data daily. NPA represents and captures over 92% of all outpatient prescription activity in the United States and covers all products, classes, and manufacturers.

## **IQVIA's National Prescription Audit: New To Brand (NPA NTB)**

NPA New to Brand provides enhanced visibility into the volume of a patient's true, first-time use of a brand versus continued therapies. IQVIA's longitudinal data allows users to analyze new therapy starts, switched to/add-on products, as well as continued therapies. In addition to reporting the new or refill information from a prescription, the therapy history for the patient is taken into account in order to categorize that prescription. New to Brand RX (NBR) = New Therapy Start Rx + Switch/Add-On Rx

**NATIONAL SALES PERSPECTIVES (NSP)<sup>™</sup>** measures revenue within the U.S. pharmaceutical market by pharmacies, clinics, hospitals and other healthcare providers. NSP reports 100% coverage of the retail and non-retail channels for national pharmaceutical sales at actual transaction prices. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

**IQVIA<sup>™</sup> 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.

# Methodologies



## DISPENSED PRESCRIPTIONS ADJUSTED FOR 90-DAY PRESCRIPTIONS

Prescriptions with >84 days supply to the patient are assumed to represent a three-month prescription, and all other prescriptions are assumed to represent a one-month prescription. Three-month prescriptions are factored by three to normalize prescriptions to one-month durations.

**WHO Defined Daily Doses (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 most often 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/](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

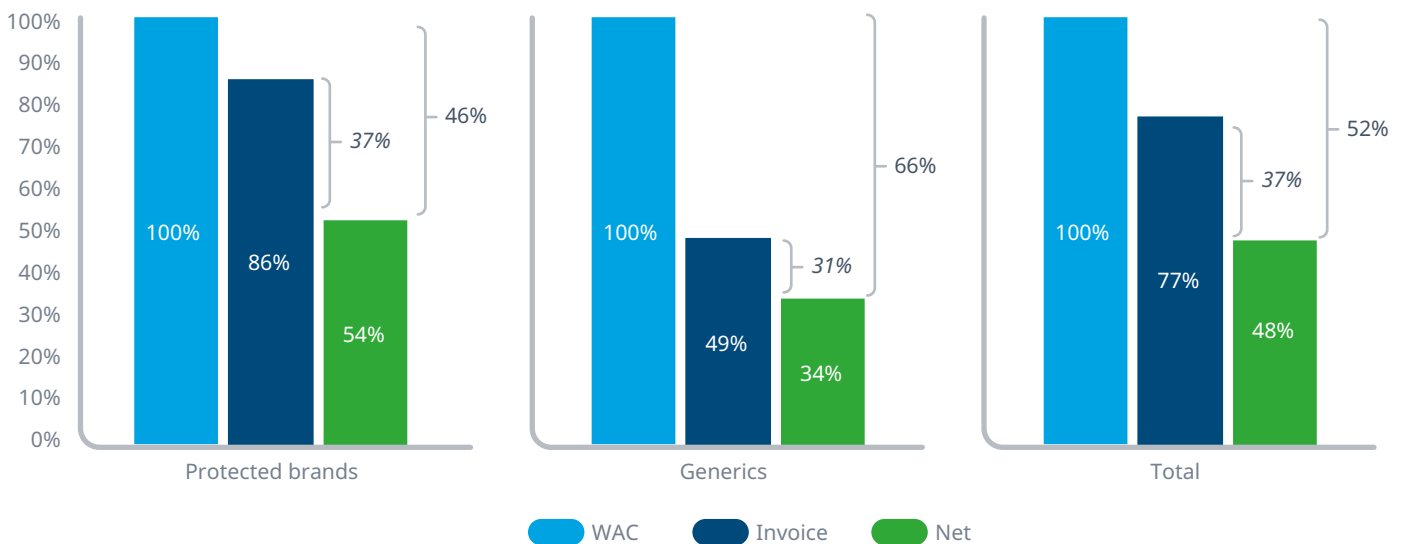
of pills per day in the case of chronic medicines such as hypertension. WHO provides guiding principles for calculating DDDs for fixed-dose combination products.

The IQVIA institute has developed additional factors using the same or highly similar concepts to represent more than 75% of audited standard unit volume. DDDs have been estimated for other products based on the standard unit to DDD ratios per product type and therapy area, where specific DDD values had already been determined.

## ESTIMATES OF SPENDING AT NET MANUFACTURER PRICES

IQVIA audits reflect invoice-based pricing or list prices 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. Estimated net prices and revenue are projected from.

**Exhibit 56: WAC, invoice and net prices, 2022**



Source: IQVIA Institute, Mar 2023.

The Use of Medicines in the U.S.: Usage and Spending Trends and Outlook to 2027. Report by the IQVIA Institute for Human Data Science.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.



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Jamie Pritchett is Thought Leadership Manager for the IQVIA Institute, managing aspects of IQVIA Institute projects and conducting research and analysis within global healthcare. Prior to joining IQVIA in 2021, he held positions with the North Carolina Department of Health and Human Services and the Duke Human Vaccine Institute, where he developed skills in understanding and addressing the array of physical, environmental, and social contributors to individual health. Jamie uses his experience in public health, health communication, and drug development and research to understand current trends in healthcare and the life sciences industry. He holds a Bachelor of Science in Animal Science and Zoology and a Master of Toxicology from North Carolina State University.



# About the Institute

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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 five areas considered vital to contributing to the advancement of human health globally:

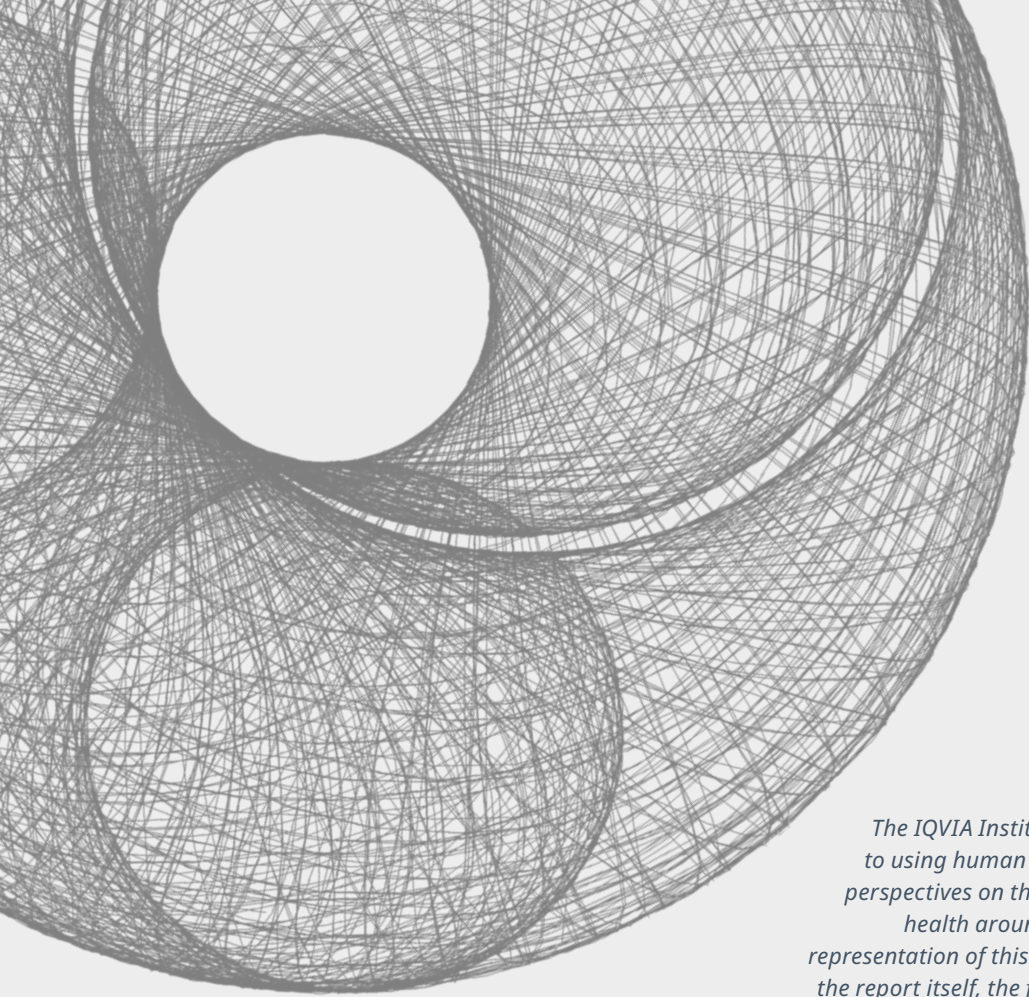
- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing 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.*

*This algorithmic art on this report cover is based on U.S. medicine usage data in notable therapy areas over the last five years.*



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