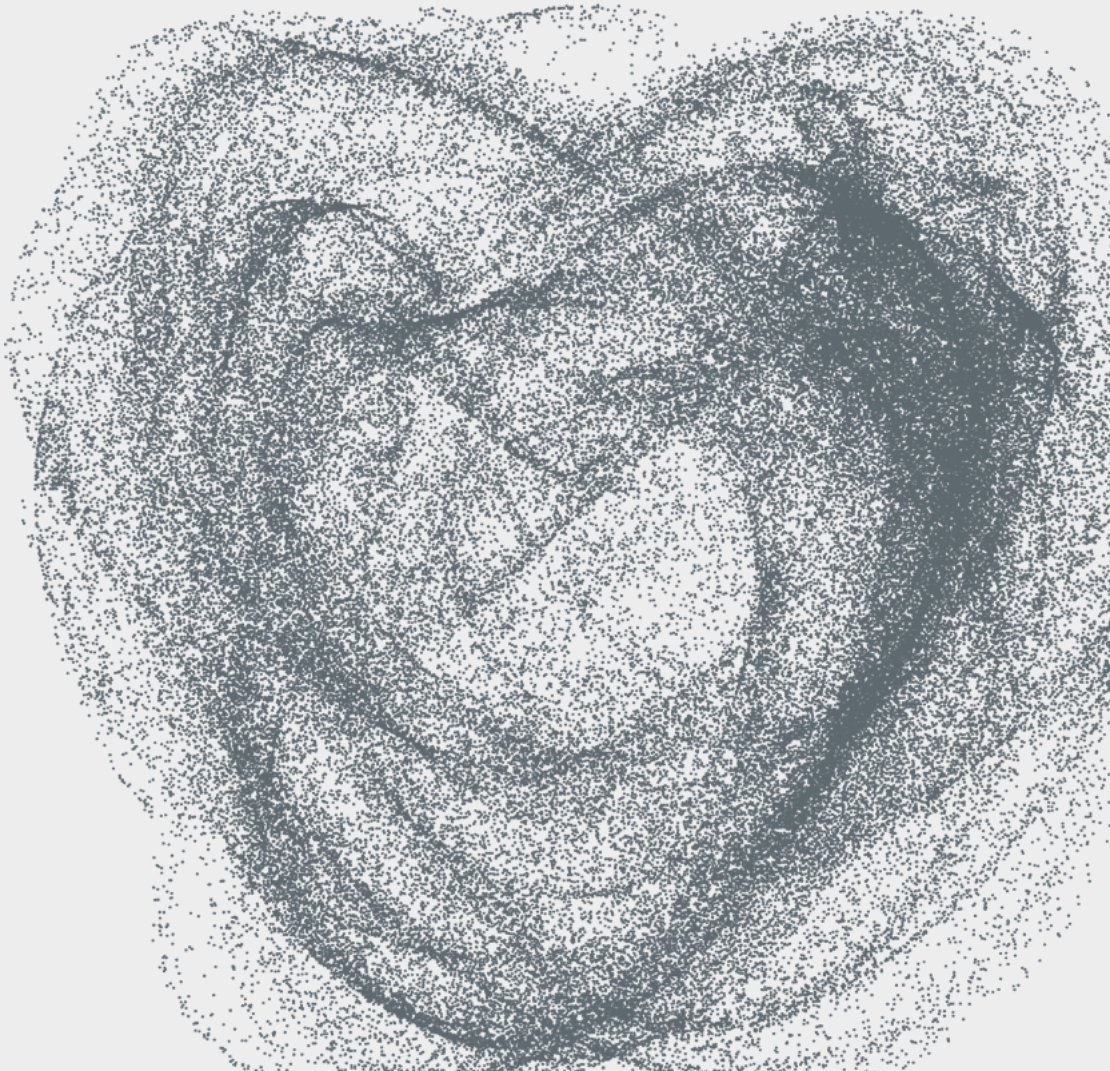
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

The Use of Medicines in the U.S.

SPENDING AND USAGE TRENDS AND OUTLOOK TO 2025



MAY
2021

Introduction

The impact of the COVID-19 pandemic on the people of the United States is hard to overstate. The direct and indirect impacts on people's health and their use of medicines is of critical importance now and as we manage the ongoing demands of this pandemic. As with many crises, other concerns are often pushed to the side, but the importance of healthcare for millions of Americans means these trends remain important. How quickly patients and providers return to 'normal' will impact health outcomes for decades to come.

This annual trends report is intended to provide a grounding in relevant information across a range of issues with both short- and long-term implications.

The impact of COVID-19 to-date on the regular running of the U.S. health system is one of the key elements that we can reference to judge the return to normalcy, and the Health Services Utilization Index we first introduced last summer is updated to show the recovery and what is still left to address.

Trends in the use of and spending on medicines illustrate the resilience of the system to the pandemic and in general are predominately driven by an aging population with chronic diseases or diseases of aging, including cancer. An overview of patient out-of-pocket costs provides insight into a key and significantly misunderstood area, and with these historic trends in mind, the outlook for the years ahead includes some key drivers and events to consider.

The 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 Onil Ghotkar, Luke Greenwalt, Elyse Muñoz, Urvashi Porwal, Priya Srivastava, Marcella Vokey, Terri Wallace and dozens of others at IQVIA are gratefully acknowledged.

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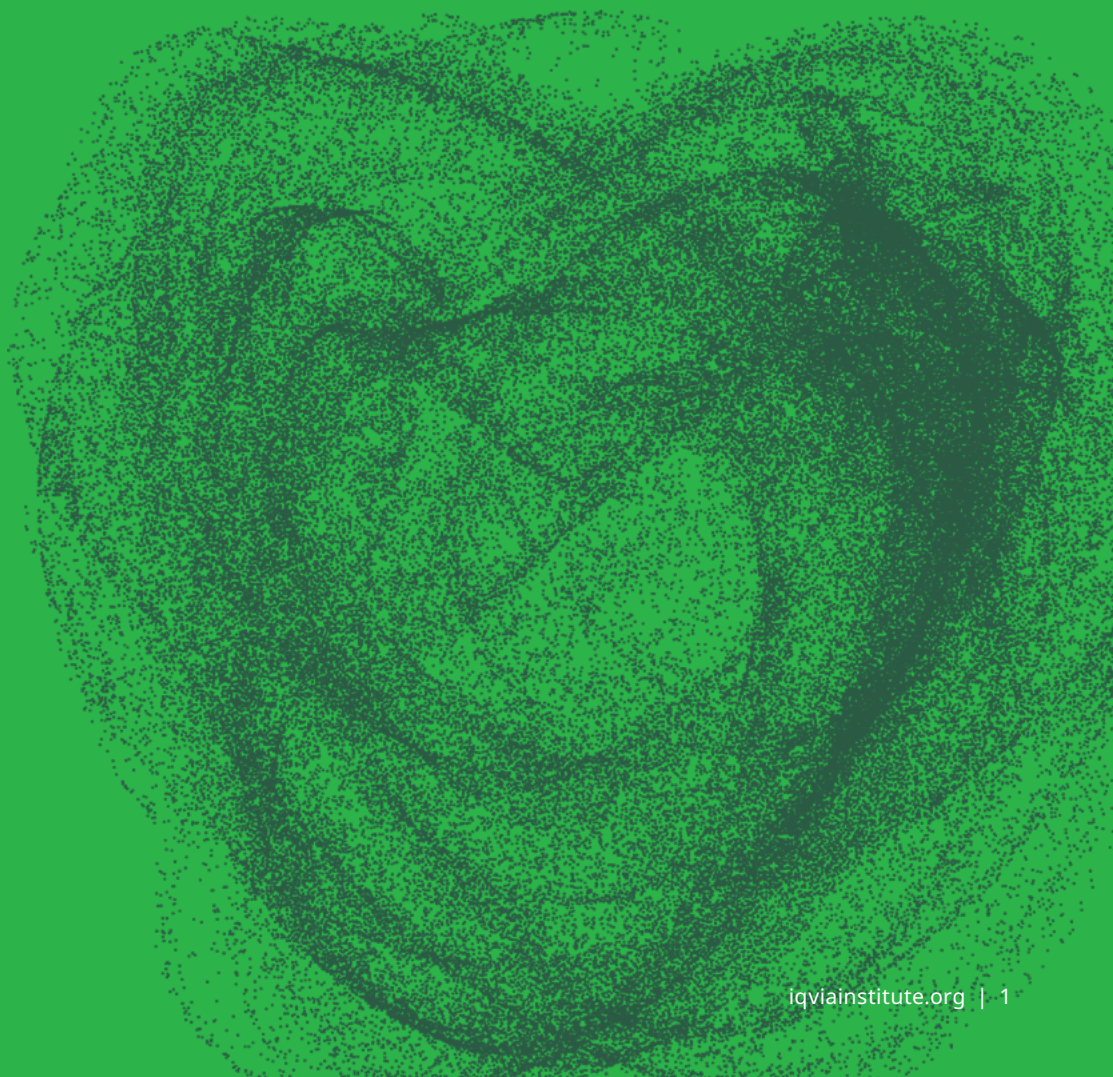
MURRAY AITKEN
Executive Director
IQVIA Institute for Human Data Science

Table of Contents



Overview

The U.S. health system demonstrated resilience and flexibility during 2020, recovering toward its pre-pandemic levels of activity and progressing into 2021, even as the backlog of missed or delayed activity remains substantial. Medicine supply was largely maintained and spending on medicines increased by less than 1% on a net price basis.

HEALTH SERVICES UTILIZATION INDEX DURING COVID-19

During the first quarter of 2021, the use of key health services — as measured by the IQVIA Health Services Utilization Index — was at 82% of pre-COVID-19 levels, up from a low of 42% at the peak of the first wave of the pandemic in April 2020. While the recovery has come closer to 100% levels in some of the component indices, it has yet to address the backlog of missed or delayed activity from earlier in the pandemic.

Elective procedures were only 15% of normal at the peak of the lockdowns in spring 2020 and have returned to 80%, but delayed procedures range from hip and knee replacements to procedures which are scheduled (rather than as emergencies) but are generally not seen as optional. Tests used to screen or monitor cancer dropped dramatically and then largely recovered, leaving a 11–23% deficit in key tests, including pap smears, and low-dose CT scans for lung cancer including colonoscopies, mammograms, pap smears, and low-dose CT scans for lung cancer.

Office visits, which are typically the entry point for patients, declined substantially, but a rapid shift to adopting telehealth across the system mitigated some of the decline. Telehealth now represents approximately 10% of visits, up from about 1% before the pandemic. These remote healthcare engagements are expected to remain an important part of healthcare delivery going forward.

Median Health Services Utilization Index indicates the U.S. is operating at 82% of pre-COVID-19 levels.

New prescriptions for acute and chronic therapies were disrupted in the pandemic while chronic continuing prescriptions were less affected. New prescriptions for chronic therapies are at 80% of normal, only recovering with the start of 2021.

MEDICINE USE

A total of 6.3 billion prescriptions were dispensed in 2020 with growth slowing to 1.7% after adjusting for the increased use of 90-day prescriptions for chronic therapies. Prescription growth has been mainly driven by the aging population and their greater use of medicines for chronic diseases and offset by disruptions for acute therapies during the pandemic. Millions of patients were still treated during 2020 for a wide range of diseases, many of them chronic, while some acute therapy areas had significant declines in usage in 2020, mostly associated with disruptions from COVID-19. Social changes also contributed to shifts in the use of behavioral and mental health therapies, notably increases in anxiety and depression, and shifts in the use of ADHD medicines (most often used in children).

MEDICINE SPENDING AND GROWTH DRIVERS

U.S. medicine spending increased 0.8% on a net price basis to $359 billion, which reflects an increasing gap between list or invoice prices and manufacturer net revenues. Real net per capita spending — adjusting for net prices, population and economic growth — declined in 2020 to $1,085 and has increased only $56 since 2010. Specialty medicines now account for 53% of spending, up from 27% in 2010 and driven by growth in autoimmune and oncology therapies.

List prices increased 4.4% while net manufacturer prices for protected brands declined 2.9% in 2020.

Manufacturer net revenues increased by $48 billion over the past five years, primarily driven by new products and brand volume. Protected brand list prices increased 4.4% in 2020, while net prices decreased by 2.9% - the fourth year at or below the level of consumer price inflation. Protected brand volume growth continues mostly in therapy areas with recent waves of innovation.. Generics

are now 90% of dispensed prescriptions, up from 72% ten years ago, and are dispensed 97% of the time when a generic is available. Biosimilar utilization is not as high as small molecules but newer biosimilars have seen volume share approach 60% within two years and have begun to contribute to savings at significant levels.

Immunology, diabetes, and oncology are the largest drivers of non-discounted spending growth. The introduction of biosimilars has contributed to oncology growth falling below 10% for the first time in seven years and new brand growth also slowed, despite a larger number of new drug launches. Diabetes growth slowed to 2% in 2020 on a net basis as off-invoice discounts and rebates drove protected brand prices down by 12%.

PATIENT OUT-OF-POCKET COSTS AND AFFORDABILITY

Out-of-pocket costs in aggregate for all patients — including retail prescriptions and non-retail medicines — increased $1 billion in 2020 to $77 billion. Patients without insurance coverage paid $14 billion for prescriptions, 97% of which were for generic medicines. Total out-of-pockets costs for these cash-pay patients has decreased by 16% over the past five years as many have become insured, offsetting exposure to higher list prices.

Across all types of insurance, the average amount paid out-of-pocket per retail prescription has dropped from $10.33 in 2015 to $9.81 in 2020, primarily reflecting lower generic costs.

While per-prescription costs are often a focus, insurance benefits are based on a plan year and overall, only 8% of patients reach annual out-of-pocket costs above $500. Medicare cost-exposure is higher, with 17% of patients reaching $500 of drug out-of-pocket costs in the year in part because cost-sharing is linked to list-prices which are higher than standardized copays, and because Medicare beneficiaries cannot use coupons to offset their costs. More than 92% of branded and generic prescriptions have a final out-of-pocket cost below $20, while 0.9% — about 57 million prescriptions — have a cost above $125 for a one-month supply. Patients were prescribed 55 million new therapy prescriptions by their doctors, which they abandoned at the pharmacy in 2020, about 9% of the total prescribed on average, with increasing frequency as costs rise. Those patients with commercial insurance are increasingly using savings programs offered by manufacturers to offset costs, especially in therapy areas such as immunology, mental health and diabetes.

More than 92% of branded and generic prescriptions have a final out-of-pocket cost below $20, while 0.9% — about 57 million prescriptions — have a cost above $125

OUTLOOK TO 2025

Total net spending on medicine is expected to reach $380–400 billion in 2025, up from $359 billion in 2020, reflecting a compound annual growth rate of 0–3%. This forecast is nearly unchanged from the pre-pandemic level, despite the disruptions from COVID-19 and short-term impact.

New brand launches are expected to continue at record levels, and the 50–55 new active substances forecast to be launched per year will contribute about $133 billion in spending growth through 2025, slightly higher than the past five years. Net prices for protected brands are expected to decline between 0 and 3% per year through 2025, reflecting more intense competition between manufacturers and aggressive negotiations by payers. Losses of exclusivity are forecast to result in $128 billion of lower brand spending through 2025, including $39 billion from branded biologics as the biosimilar market matures. Total saving to payers due to biosimilar introductions are forecast to be $133 billion ($85–183 billion range) in aggregate over the next five years.

Immunology, oncology and neurology will be the main sources of growth through 2025. Oncology spending will exceed $110 billion by 2025, up from $72 billion in 2020 and continuing at a slower growth rate due to the impact of biosimilars and new drug launches increasingly focused on rare cancers. Diabetes spending is expected to decline 2-5% on a net basis through 2025 due to heightened competition. Immunology will exceed $130 billion in the U.S. by 2025, with growth slowing after 2023 due to the launch of key biosimilars for adalimumab and ustekinumab in 2023 and 2024, respectively.

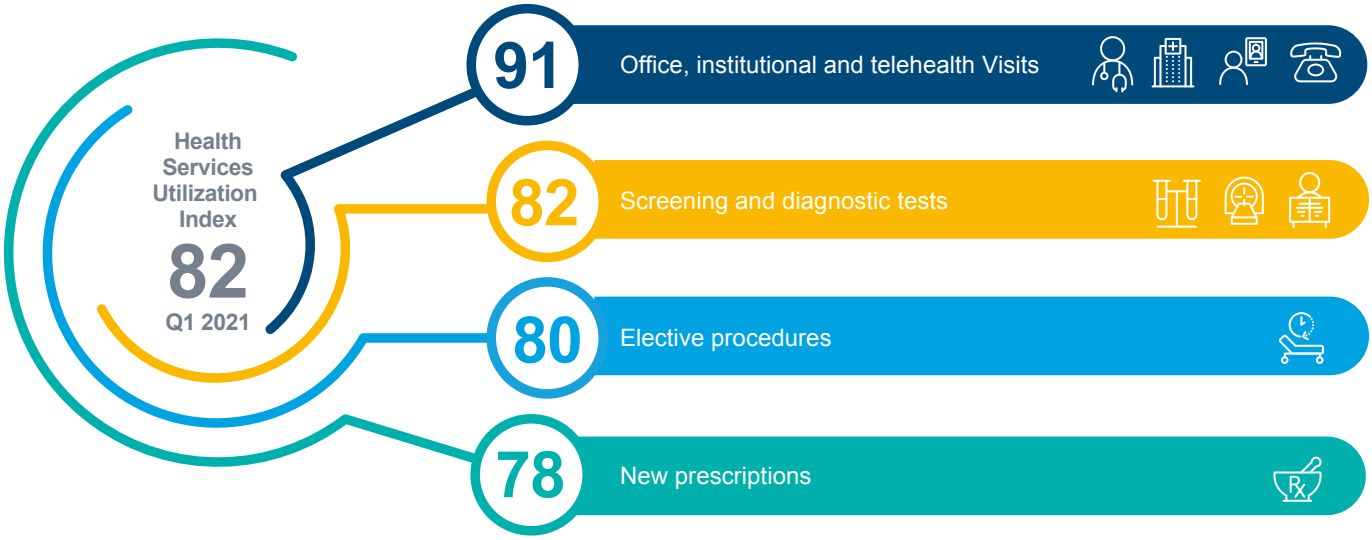
Health Services Utilization Index during COVID-19

- Median Health Services Utilization Index indicates the U.S. is operating at 82% of pre-COVID-19 levels.
- Health Services Utilization Index has recovered to 82% of pre-COVID-19 levels but has yet to address backlog from earlier.
- Elective procedures declined by 85% during system-wide shutdowns, returning to 80% of pre-pandemic levels by Q1 2021.
- Diagnostics used to screen and monitor cancer dropped dramatically and recovered, though an 11% –23% deficit remains.
- Patients and providers have shifted to telehealth but remain below baseline levels of healthcare engagement.
- New prescriptions for acute and chronic therapies were disrupted in the pandemic while chronic continuing prescriptions were less affected.
- The composite Health Services Utilization Index ranges from a high of 117 in UT to 78 in WV and a median value of 89.
- Prescription utilization by method of payment has shown little movement over the past year despite rising unemployment.

The U.S. is operating at 82% of pre-COVID-19 levels but has yet to address the backlog of missed or delayed activity from earlier in the pandemic.

Median Health Services Utilization Index indicates the U.S. is operating at 82% of pre-COVID-19 levels

Exhibit 1: Overview of Health Services Utilization Index



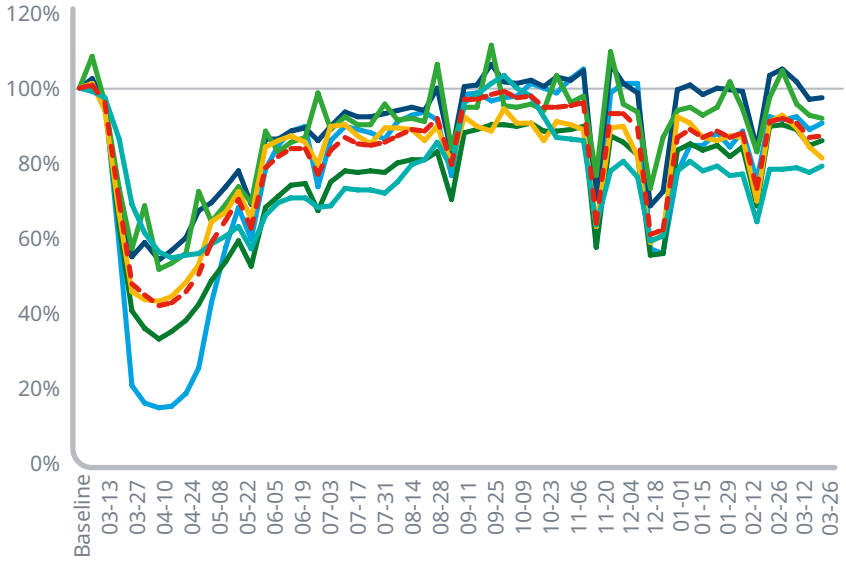
Source: IQVIA Institute; IQVIA Medical Claims Data; LAAD Prescription data, week ending 4/30/2021

- The return to a pre-pandemic level of utilization in the health system is critical to ensuring all Americans –including all 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 five 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 (office, institutional – hospital or clinic – or via telehealth), diagnostic lab results, and new brand or generic prescriptions filled.
- The first quarter of 2021, a period where millions of Americans have begun to be vaccinated for COVID-19, shows the overall utilization index recovered to 82, 18% below the pre-pandemic baseline but nearly double the index of 42 at the low-point in April 2020.

Exhibit 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.

Health Services Utilization Index has recovered to 82% of pre-COVID-19 levels but has yet to address backlog from earlier

Exhibit 2: Health Services Utilization Index and Component Metrics Percentage of 2020 Baseline



	% below baseline Peak (Apr 10, 2020)	FY2020	Q1 2021
Elective procedures	15	77	80
Office, institutional & telehealth visits	54	87	91
Institutional	52	86	90
Office	33	72	76
Screening and diagnostics	43	79	82
New prescriptions	56	76	78
Health Services Utilization Index	42	80	82

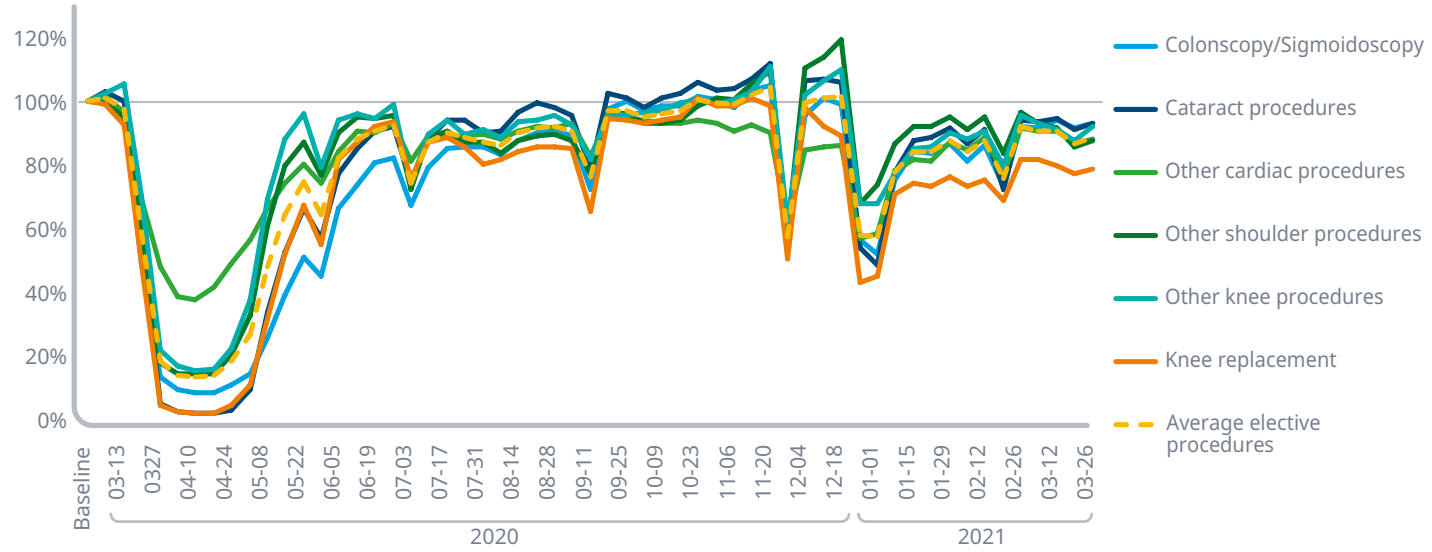
Source: IQVIA Medical Claims Data, LAAD Prescription data, week ending 4/30/2021

- Doctor visits - including office, institutional and telehealth – have rebounded strongly to an index of 91 relative to pre-pandemic baseline, the highest of the overall index components but still below prior levels and not yet making up the backlog in healthcare engagement that was created.
- Diagnostics and screening tests are often a part of a treatment sequence, starting with a visit and ultimately resulting in a procedure or drug therapy for many, and the gap in these tests from pre-pandemic levels allows risks for missing a cancer diagnosis or other such screening result.
- Elective procedures were largely stopped in the peak of the shutdowns from COVID-19, dropping to 15% of normal, but have since recovered to 80% nationally, though some states have begun to have above baseline levels.
- New prescription medicines have continued at well below the pre-pandemic baseline as a combination of factors are inhibiting prescribing, including lower visits and screening and diagnostics.
- It is notable that continuing prescriptions for chronic therapies have been trending above baseline as more patients have been filling longer three-month prescriptions or using mail-order in efforts to save money and/or avoid in-person pharmacy visits.
- The overall Health Services Utilization Index has recovered from 42 at the height of the shutdowns early in the pandemic to 80 for the full year 2020, and 82 in the first quarter of 2021.

Exhibit 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.

Elective procedures declined by 85% during system-wide shutdowns, returning to 80% of pre-pandemic levels by Q1 2021

Exhibit 3: Selected Elective Procedures Compared to Baseline



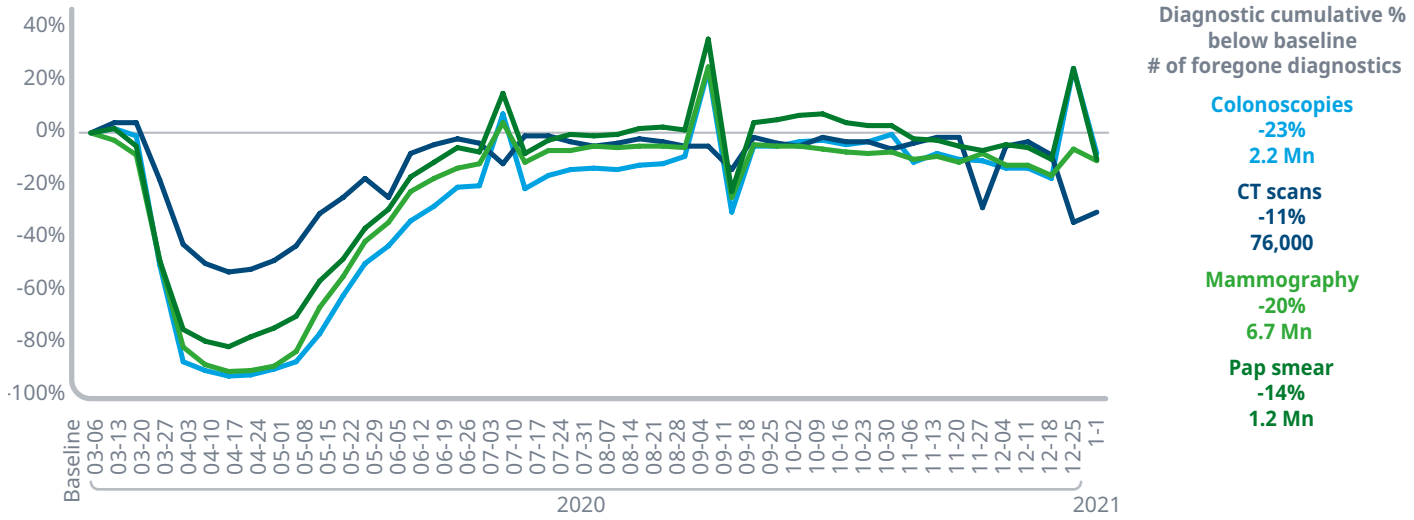
Source: IQVIA Medical Claims Data, week ending 4/30/2021

- Several elective procedures illustrate the decline in overall procedures during the height of the COVID-19 pandemic and the recovery since, with some above baseline for parts of the fourth quarter of 2020.
- For the most part, procedures for non-life-threatening conditions were rescheduled or canceled to a greater degree at the lowest point in April. Cardiac procedures dropped the least out of the procedures examined, to 38% of baseline, but have recovered to 89% as of the latest week.
- Aside from cardiac procedures, the other procedures dropped by 80-90% during the month of April but rebounded sharply in May and maintained a steady 80-90% of baseline through the summer, rebounding in the winter before dipping again in early 2021.
- Colonoscopies had one of the longer periods of disruption, recovering to 82% by the week before the Fourth of July holiday and steadily recovering since.
- As most restrictions in operating the health system safely have been well established for months, the absence of these procedures is most likely the result of the absence of initial diagnoses.
- The disruption to initial healthcare engagements such as doctor visits may be the cause of these lower elective procedure numbers, as patients who would otherwise have been seeking them may have delayed engaging with their doctor to start the sequence of events that would lead to a surgery.

Exhibit 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.

Diagnostics used to screen and monitor cancer dropped dramatically and recovered, though an 11–23% deficit remains

Exhibit 4: Selected Diagnostic Testing Procedures Compared to Baseline



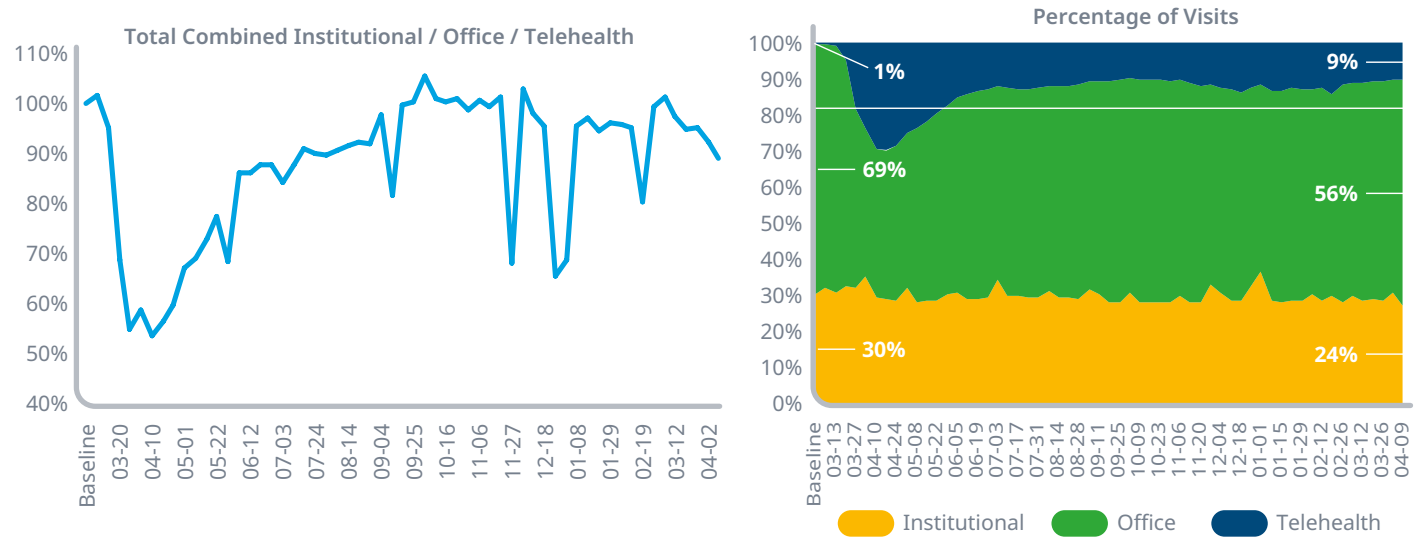
Source: IQVIA Real World Claims, Dec 2020; IQVIA Institute, Feb 2021

- Cancer screening diagnostics for several large prevalence tumors had significant disruptions during the height of the pandemic, which were sustained through midsummer.
- While the level has been largely near the pre-pandemic level since July, there has been little progress in addressing the backlog of missed screenings, affecting millions of tests.
- Low-dose CT scans for lung cancer screenings were the least disrupted, potentially as a result of an elevated focus of patients and providers on lung and breathing issues during the pandemic.
- Procedures for women such as pap smears for cervical cancer and mammograms for breast cancer finished 2020 down, 14% and 20% respectively, with 7.9 million expected diagnostic procedures not taking place.
- For a patient with an aggressive cancer, early diagnosis is often the key indicator of a better prognosis, even if only a small subset of those tested result in diagnosis of cancer.
- The benefits are clear for completing these regular screening tests and the size of this 'backlog', and the downward trend in 2021 are both concerning trends to oncologists.

Exhibit 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.

Patients and providers have shifted to telehealth but remain below baseline levels of healthcare engagement

Exhibit 5: Office, Institutional and Telehealth Visits Compared to Baseline



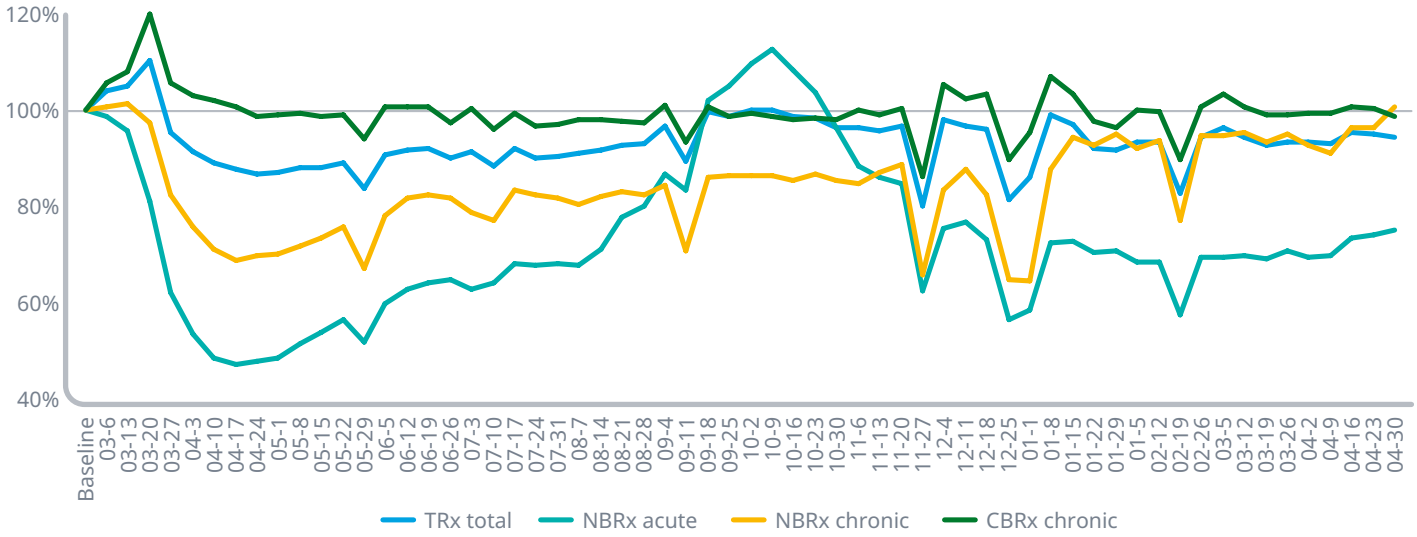
Source: IQVIA Medical Claims Data Analysis, Apr 2020

- With doctor's offices closed and hospitals not accepting anything but emergency visits, patient office visits to doctors dropped to 33% of normal in April 2020 compared to 52% of normal for institutional visits.
- As a result of the rapid adoption of telehealth, the combined group of visits were 54% of the pre-pandemic baseline, and telehealth adoption increased afterward.
- Telehealth represented roughly 1% of visits prior to the pandemic, rising to nearly 30% in April 2020 and then continuing at a consistent 9–11% since summer 2020.
- The shift of some kinds of health services to remote interactions has enabled a continued management of patients despite social distancing restrictions and hygiene requirements in hospitals and medical practices.
- Even as restrictions have been lifted, patients and providers have continued to use remote options, suggesting that the pandemic has resulted in some fundamental shifts in the ways patients and providers interact.
- Prior to the pandemic, telehealth was generally not covered for most interactions under Medicare or commercial insurance, and the extent to which insurers continue to reimburse providers for these remote interactions is the most significant driver of whether they will continue at current levels.

Exhibit 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 for acute and chronic therapies were disrupted in the pandemic while chronic continuing were less affected

Exhibit 6: Dispensed New and Continuing Prescriptions by Therapy Type as a Percent of 2020 Baseline



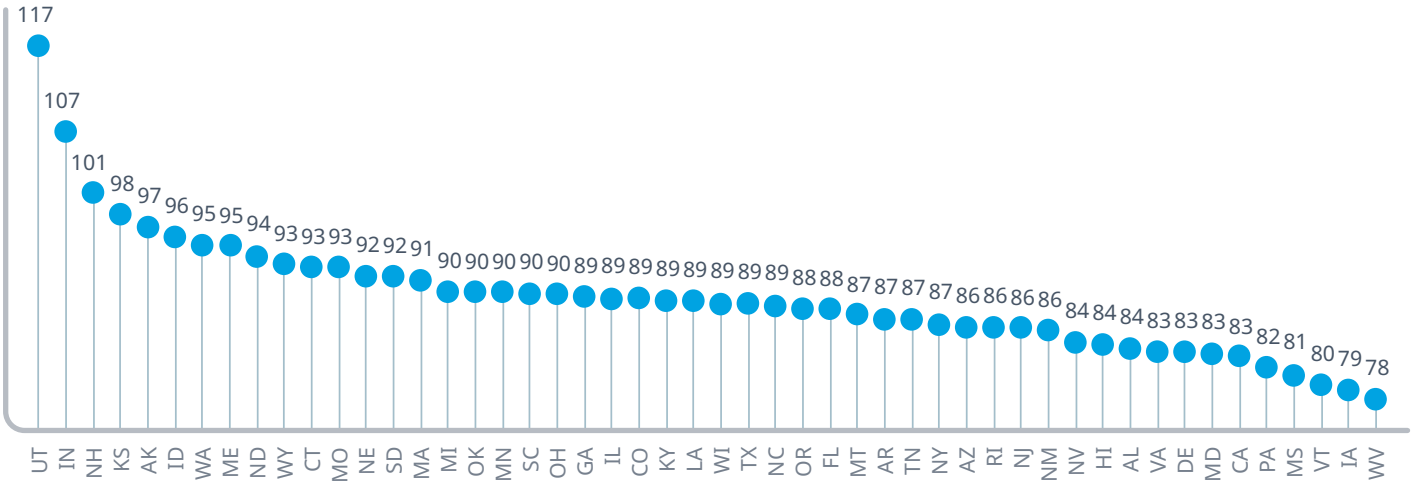
Source: IQVIA National Sales Perspective; IQVIA National Prescription Audit, Apr 2021

- Total prescriptions as of the end of March 2021 were at 94% of the baseline pre-pandemic level, as mostly acute therapies were far below normal while continuing chronic prescriptions have been trending at or just below baseline since the beginning of the pandemic.
- 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 both chronic and acute prescriptions.
- Acute care prescriptions were significantly disrupted, not because it was difficult to get them, but rather that patients didn't require them.
- Many antibiotics and pain management prescriptions are given as a result of an elective or emergency procedure, and as these were also disrupted, the normally resulting prescriptions were not filled.
- Later in the year, as the normal seasonal flu season was set to begin, most infections did not present, but following recommendations, an above average number of people got vaccinated for seasonal flu. As the flu season progressed without the typical rate of diagnoses, the impact is visible in overall acute NBRx.
- As the summer progressed though, new starts for chronic therapies have continued at 80% of normal, only recovering with the start of 2021.

Exhibit Notes: Difference between actual values per week and baseline average for the eight weeks from January 4 to February 28 are plotted. Prescriptions where patient has not a prescription of the same medicine in the past year, includes both new therapy starts and switched or added-on prescriptions.

The composite Health Services Utilization Index ranges from a high of 117 in UT to 78 in WV and a median value of 89

Exhibit 7: Health Services Utilization Index Q4 2020



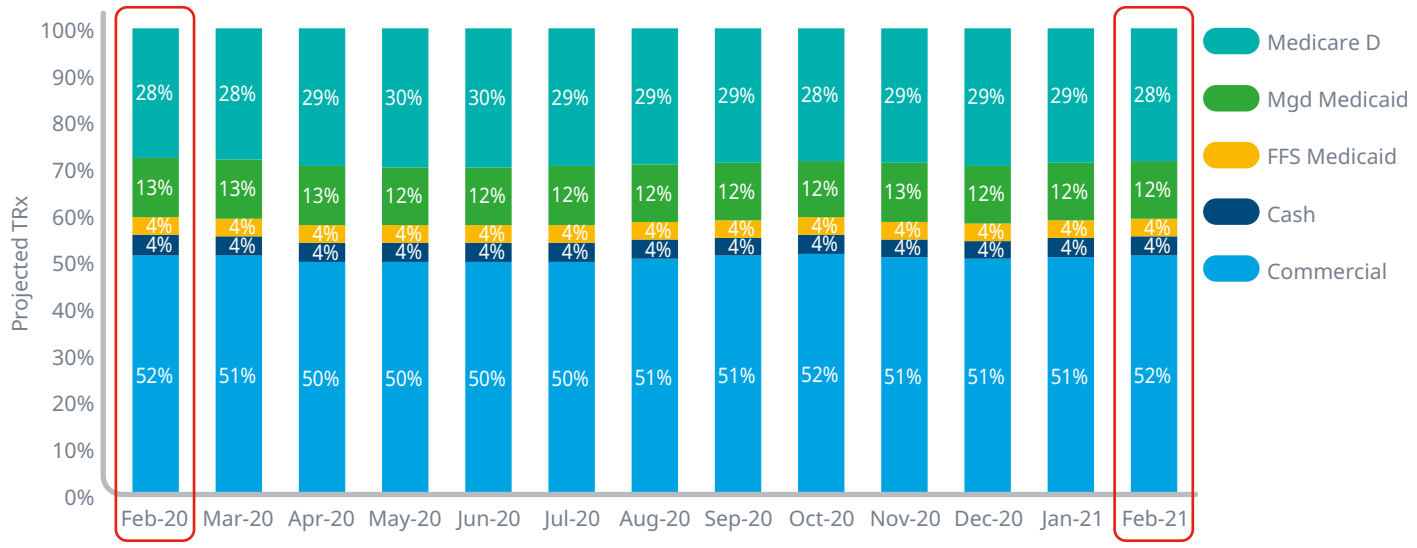
Source: IQVIA Real World Claims, 1/1/2021, Claims limited to processed within 14 days of service date for stability

- The Health Services Utilization Index ranged from 78 to 117 in the fourth quarter of 2020, with a median of 89.
- States have significantly different drivers of their overall indices, with elective procedures and lab tests above baseline for several states, while others lag far behind.
- Only three states have a Health Services Utilization Index (HSUI) above baseline: Utah, Indiana and New Hampshire, with 117, 107 and 101, respectively.
- Utah has lab tests at 145% of baseline and elective procedures at 128%, and combined doctor visits at 109%, all contributing the highest HSUI in the country – 117.
- By contrast, West Virginia, Iowa and Vermont all have HSUI below 80, with no component of the index above 100 for any of them.
- Diagnostic tests have a median index across states of 86, with 14 states below 80, the lowest in Vermont at 59.
- Combined doctor visits, including office, institutional and telehealth, have a median index in Q4 of 96, with a low in Vermont of 81 and a high of 116 in Indiana.
- Twelve states have visits above baseline levels, something key to addressing the burden of disease that may have built up during the pandemic.

Exhibit Notes: Index based on the average of the fourth quarter of 2020 at state level.

Prescription utilization by method of payment has shown little movement over the past year despite rising unemployment

Exhibit 8: Monthly Dispensed Prescriptions by Method of Payment



Source: IQVIA PayerTrak; US Market Access Analytic Solutions analysis, Feb 2021

- Despite significant and rapid shifts in employment nationally, prescription utilization does not yet show a significant shift to Medicaid, representing 8% of dispensed prescriptions through the year through February 2021.
- Some states operating under ACA Medicaid expansion have less stringent waiting periods to become eligible for Medicaid, but even with these shifts in enrollment, the overall utilization remains unchanged as a share of overall volume.
- These trends suggest that while unemployment and economic disruption were significant in the pandemic, the combined effects of stimulus payments and employers retaining staff or extending insurance during layoffs/furloughs had the result of diminishing the numbers of people who would be newly Medicaid eligible.

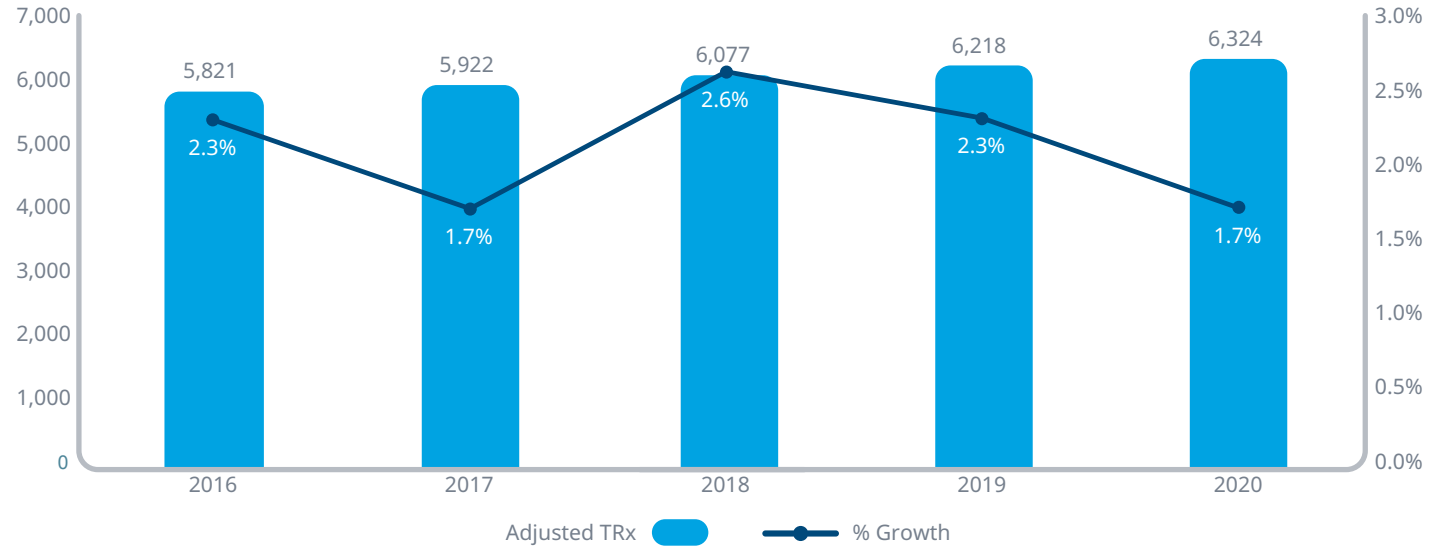
Medicine use

- Dispensed prescriptions reached 6.3 billion in 2020 while growth slowed to 1.7%.
- Prescriptions grew on an adjusted basis as more were filled as a three-month supply in retail channels.
- Chronic prescriptions account for nearly 80% of dispensed prescriptions and are increasingly dispensed in three-month supplies.
- Prescription growth has been driven mainly by the aging population as seniors use more medicines per capita.
- Millions of patients are treated annually for a wide range of diseases, many of them chronic and driven by the elderly.
- Some therapy areas had significant declines in usage in 2020.
- New prescriptions for acute and chronic therapies were disrupted in the pandemic while chronic continuing were less affected.
- New prescriptions were impacted during the early phase of the pandemic primarily from acute therapies.
- COVID-19 related social changes drove modifications in the use of behavioral and mental health therapies.
- During the COVID-19 pandemic, patients changed their use of over-the-counter medicines.
- Cash paid prescriptions declined 10% in 2020 but the trend preceded COVID-19.
- Medicaid rose as third-party growth slowed.
- Medicaid enrollees use 7.5 prescriptions per enrollee per year, and use generics more than commercial or Medicare Part D.
- States exceed national average per enrollee use of medicines for 23 of 37 expansion states and only 3 of 14 non-expansion states.

Chronic prescriptions account for nearly 80% of dispensed prescriptions and are increasingly dispensed in three-month supplies, contributing to improved medication adherence.

Dispensed prescriptions reached 6.3 billion in 2020 while growth slowed to 1.7%

Exhibit 9: Adjusted Dispensed Prescriptions



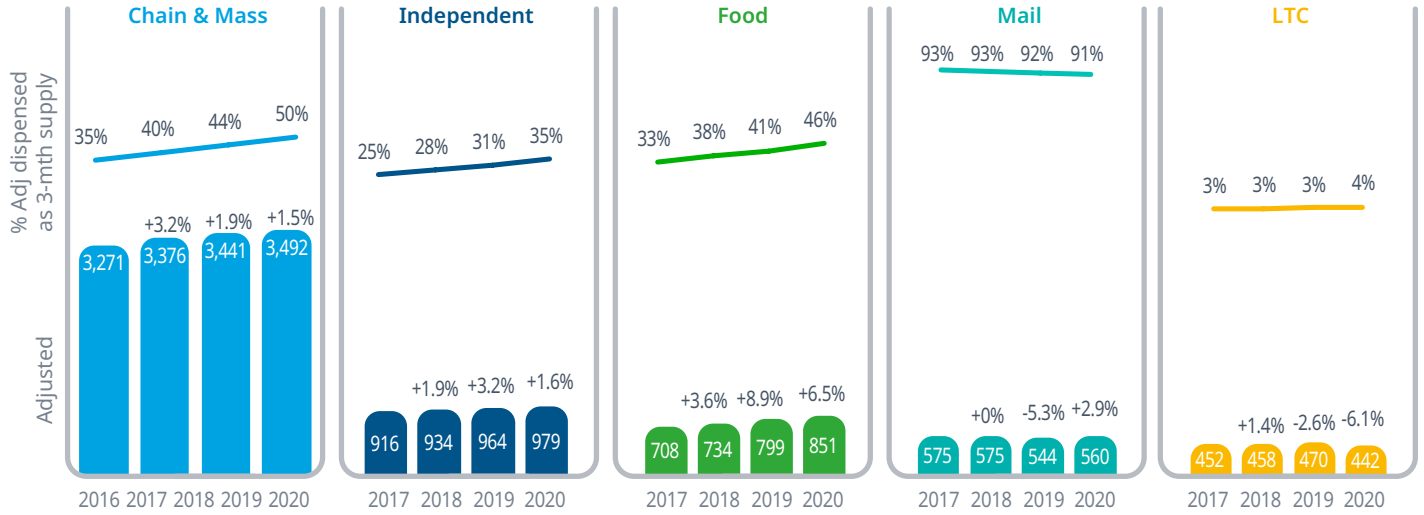
Source: IQVIA National Prescription Audit; IQVIA institute, Dec 2020

- Total prescriptions – adjusted for prescription length — reached nearly 6.3 billion in 2020, up from an estimated 5.8 billion in 2016.
- The increasing use of 90-day prescriptions is particularly notable as the rate of growth without adjustment for prescription length was -2.9% in 2020 but 1.7% after adjustment.
- Several incentives are in place for pharmacies, providers and Accountable Care Organizations (ACOs) based on achieving levels of medicine possession by patients, called percentage of days covered (PDC), and that are strongly linked to the rising use of 90-day prescriptions observed here.
- In 2020, the PDC for diabetes, cholesterol and hypertension all increased 3-4%, nearly the same percentage increase in 90-day prescriptions observed in those classes and in prescriptions overall.
- In total, dispensed prescriptions increased at an average 2.1% over the past four years.

Exhibit Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated. Prescriptions referred to as '90-day' are calculated based on transactions with 84 days supply are more to include medicines with up to one-week of fewer treatment days. Prescriptions for 84 days supply or more or factored by three, and those under 84 days unchanged. Due to changes in data collection after 2016, adjusted prescription total has been back-projected based on published growth rates from prior Institute reports to estimate the number of adjusted prescriptions in 2016.

Prescriptions grew on an adjusted basis as more were filled as a 3-month supply in retail channels

Exhibit 10: Adjusted Dispensed Prescriptions by Channel and Percentage of Adjusted Prescriptions Dispensed as 3-Month Supply



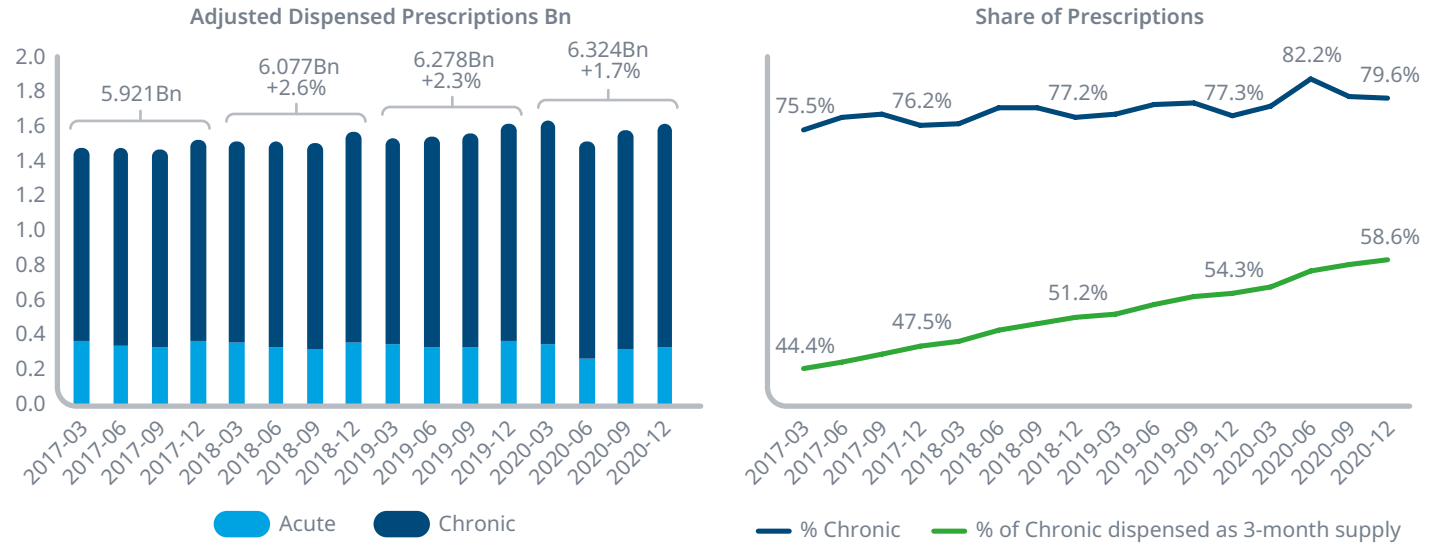
Source: IQVIA National Prescription Audit; IQVIA Institute, Dec 2020

- Over the past four years, prescriptions at retail pharmacies have risen faster than mail order.
- Retail pharmacies – including chain pharmacies, mass merchandisers, independent pharmacies and food stores - have increased at an average rate of 2.8% since 2017 compared to a decline of 0.9% in mail orders.
- Long-term care had been increasing, lifted by an aging population, but declined 6.1% in 2020, likely related to disruptions from COVID-19.
- The increases in prescriptions are also linked to the rising percentage dispensed as a three-month supply, limiting the number of opportunities for a patient to skip or miss a refill.
- Consistent and convenient access to chronic medicines is noted as one of the key drivers of medication adherence, which is linked to improved outcomes.
- It is also possible that some patients have unused or unneeded prescription medicines as a result of these dispensing patterns, which will require ongoing study and observation to manage the risks of these medicines being diverted to others and potentially causing harm.

Exhibit Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated. Prescriptions referred to as 90-day are calculated based on transactions with 84 days supply or more to include medicines with up to one fewer week of treatment days in the planned three-month duration. Prescriptions for 84 days supply or more are factored by three, and those under 84 days unchanged. Long-term care pharmacies (LTC).

Chronic prescriptions account for nearly 80% of dispensed prescriptions and are increasingly dispensed in 3-month supplies

Exhibit 11: Adjusted Dispensed Prescriptions by Acute/Chronic and % 3-Month Chronic Dispensing



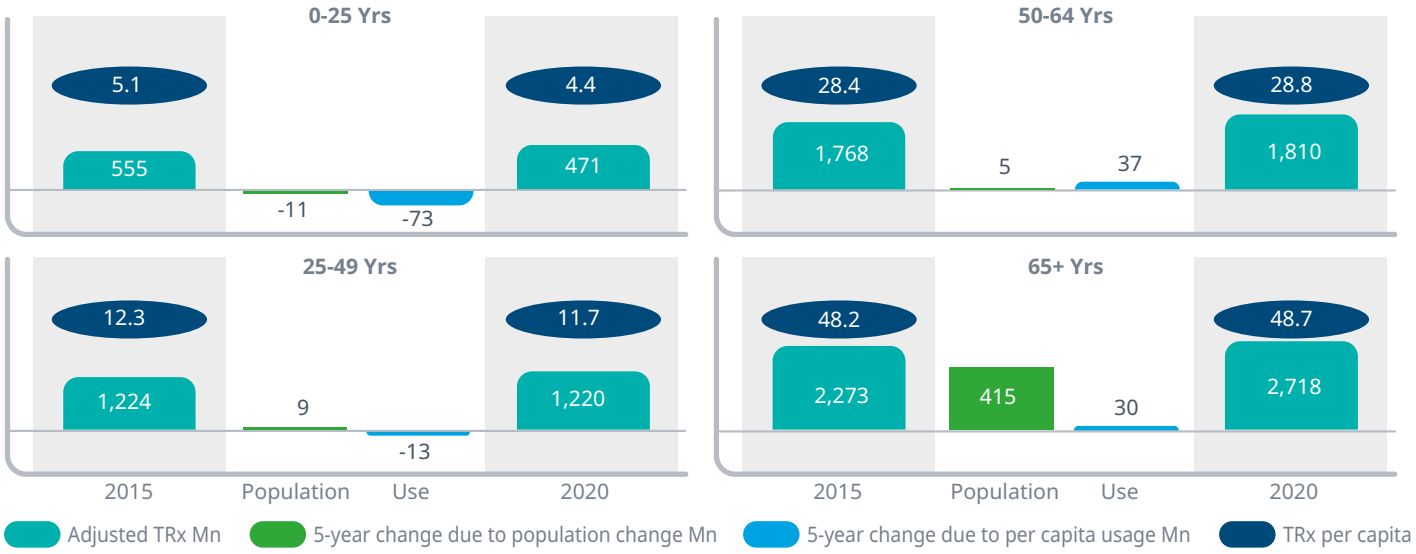
Source: IQVIA National Prescription Audit; IQVIA institute, Dec 2020

- Chronic prescriptions account for 79.6% of adjusted prescriptions as of Q4 2020, up from 75.5% at the beginning of 2017.
- Q2 2020 had a dip in acute prescriptions as some typical acute medicine uses were less likely to be required as people stayed home and were exposed less to common infections and had fewer elective procedures with associated discharge medications.
- The percentage of chronic prescriptions dispensed as a three-month supply has risen from 44.4% to 58.6% over that timeframe, adding 4.3 percentage points in just the last year.
- The dynamics of prescribing indicate that newer prescriptions — new and switch prescriptions are 5–20% of prescriptions in a therapy area — are less commonly dispensed this way, and that chronic continuing prescriptions are a slightly smaller share of overall prescriptions (65-72%) compared to total chronic of 79.6%.
- For those chronic prescriptions where it is potentially possible to dispense as three-month supplies, they are being dispensed that way over 80% of the time, consistent with the percentage of days covered (PDC) results which providers are achieving in Medicare STAR ratings.

Exhibit Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated. Prescriptions referred to as 90-day are calculated based on transactions with 84 days supply or more to include medicines with up to one fewer week of treatment days in the planned three-month duration. Prescriptions for 84 days supply or more are factored by three, and those under 84 days unchanged. 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 patent or prescription attributes and do not reflect the potential for some medicines to be used on a long-term basis against recommendations.

Prescription growth has been driven mainly by the aging population as seniors use more medicines per capita

Exhibit 12: Adjusted Prescriptions by Age and Drivers



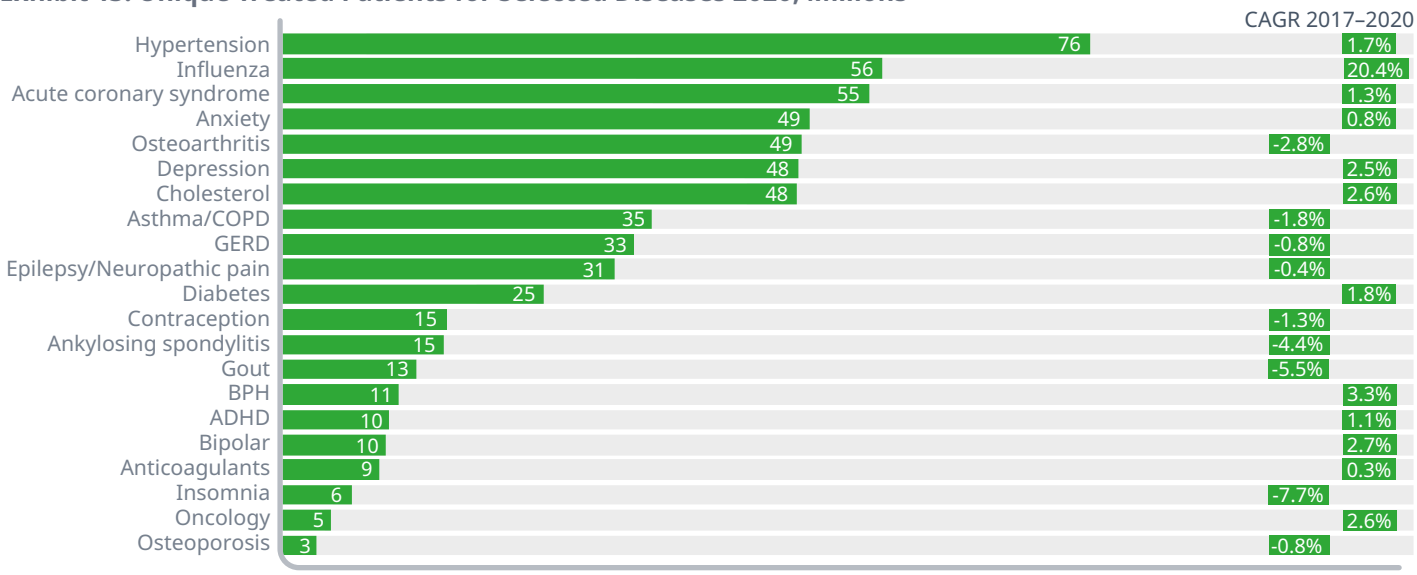
Source: IQVIA National Prescription Audit; US Census Bureau , Dec 2020

- Patients over 65 increased their per capita prescriptions per year only slightly — from 48.2 per year to 48.7 over the past five years.
- Seniors aged 50–64 also had a similar low change in per capita usage — from 28.4 to 28.8 per year.
- Younger adults from 26-49 decreased usage from 12.3 to 11.7, and younger people from birth to 25 years old also declined from 5.1 to 4.4 per person per year.
- Population changes associated with the aging population in the 'baby boom' generation drove almost all prescription growth over the past five years.
- The changes in coverage associated with the Affordable Care Act have had less effect on the younger age groups in this period than they did immediately after the initial implementation, as noted in an earlier report.

Exhibit Notes: Chart values not displayed to scale. Population-driven growth calculated as base period (2015) if it had grown at the rate of population growth for the specific age band. Use-driven growth are the associated changes in per capita usage that resulted over five years and are calculated as the remainder of change in per capita usage over five years. For earlier version of this analysis, see *IQVIA Institute Medicine Use and Spending In the U.S.: A review of 2016 and Outlook to 2021* https://www.iqvia.com/insights/the-iqvia-institute/reports/medicines-use-and-spending-in-the-us-a-review-of-2016.

Millions of patients are treated annually for a wide range of diseases, many of them chronic and driven by the elderly

Exhibit 13: Unique Treated Patients for Selected Diseases 2020, Millions



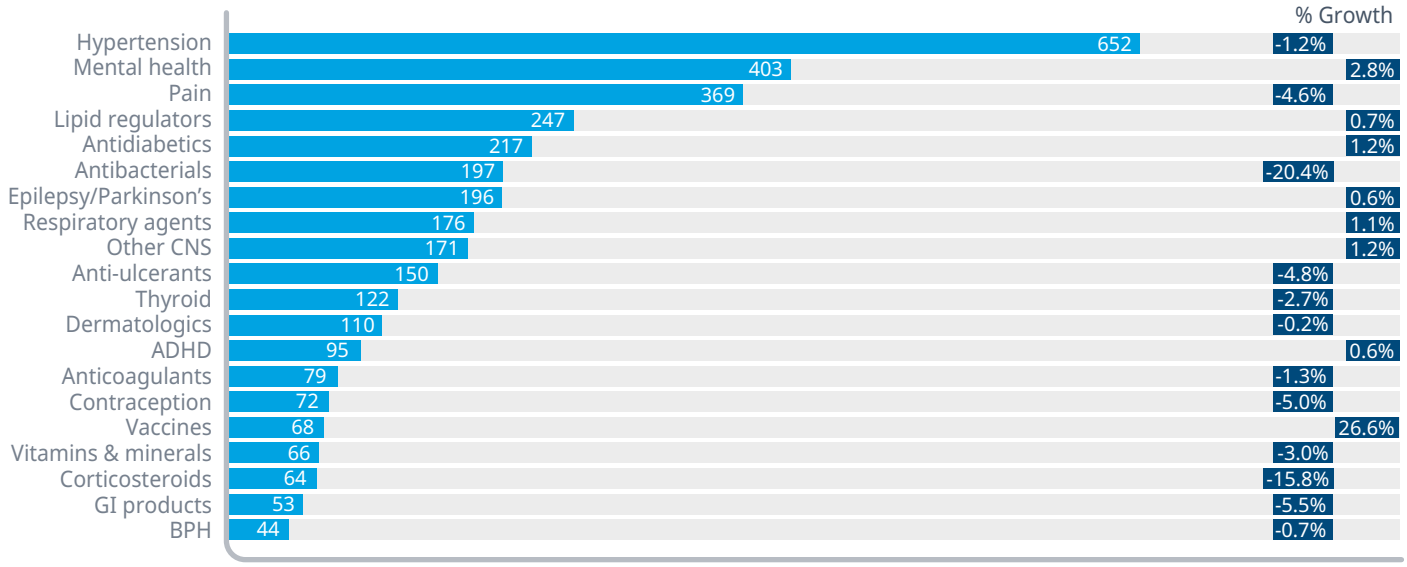
Source: IQVIA Medical Claims Data, Dec 2020

- Millions of Americans have a diagnosis and treatment for disease during the year, led by hypertension, with 76 million patients having filled at least one prescription in 2020, up 1.7% from 2017.
- Influenza — season flu — had more diagnoses resulting in a treatment in 2020, but this was predominately due to higher rates of vaccination as the seasonal flu was dramatically lower in the 2020/2021 flu season than in prior years.
- Insomnia had a decline of 7.7% in patients over the past four years, moving from 8.2 million to 6.4 million in 2020, with one-quarter of the decline happening in 2020 despite reports that many people are having trouble sleeping during the pandemic — suggesting the decline in 2020 would have been greater without the pandemic.
- There has been an average of 2.6% more oncology patients per year over the past 3 years, but that includes growth of 3.6% in 2018, 3.5% in 2019 and only 0.8% in 2020 as cancer screenings and treatment delays disrupted or slowed diagnoses, potentially putting thousands at risk for worse prognosis than if their cancers were detected earlier.

Exhibit Notes: Disease definitions are not mutually-exclusive and do not correspond perfectly to therapy areas reported elsewhere in this report. Annual unique patients does not reflect the number of patients on-therapy at any one time as some patients start and stop therapy during the year. Medical claims are unprojected and reflect the data captured in IQVIA's audits.

Some therapy areas had significant declines in usage in 2020

Exhibit 14: Unadjusted Dispensed Prescriptions 2020 and % Growth from 2019



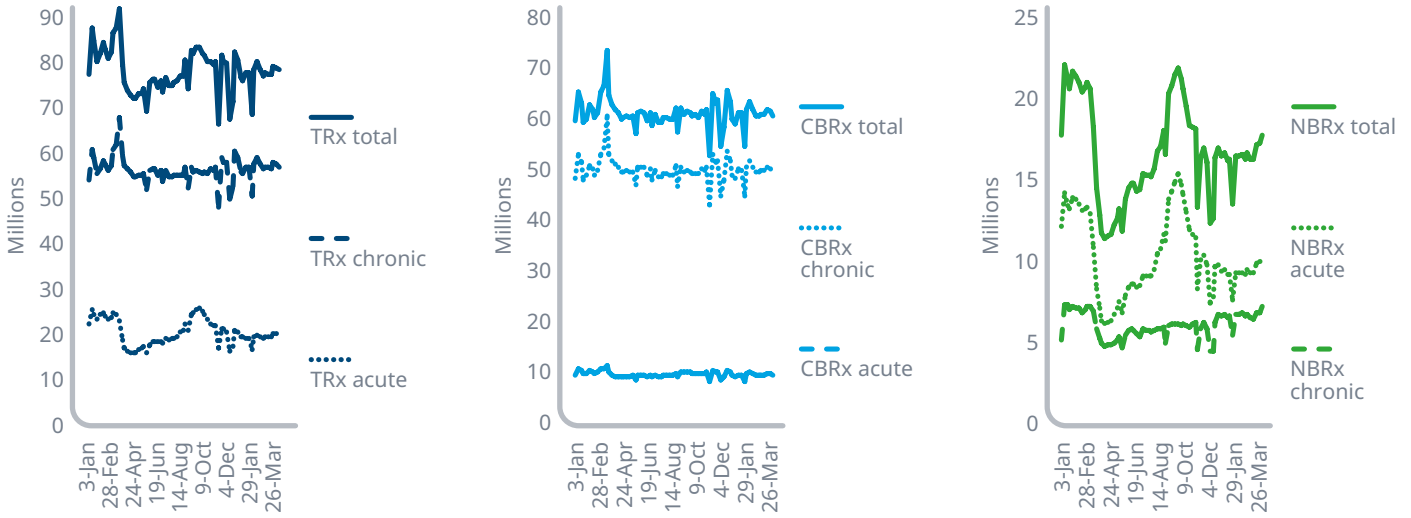
Source: IQVIA National Prescription Audit, Dec 2020

- Patients filled 652 million prescriptions (of any length) for hypertension medicines in 2020, down 1.2% without adjusting for prescription size, but increasing when adjusted for the increase in three-month supplies.
- Mental health prescriptions increased 2.8% in 2020 on an unadjusted basis, suggesting increases from both chronic users with improved adherence and new patients prompted by issues during the pandemic.
- The broad pain management therapy area declined 4.6%, largely because there were fewer elective procedures requiring pain medicines at discharge, even as pain medicine usage has been slowly declining, particularly with prescription opioids.
- Antibacterials were down 20.4% from the combined effects of fewer elective procedures and fewer bacterial infection as people socially-distanced.
- Vaccines were up 26% primarily from higher seasonal flu vaccines in 2020.
- Corticosteroids down 15.8% as a common treatment for injuries, infections and other acute events which didn't happen as often in 2020.

Exhibit Notes: Therapy definitions are mutually exclusive. Prescriptions are unadjusted for length or volume of medicine prescribed.

New prescriptions for acute and chronic therapies were disrupted in the pandemic while chronic continuing were less affected

Exhibit 15: Dispensed Total, Continuing and New Prescriptions by Therapy Type



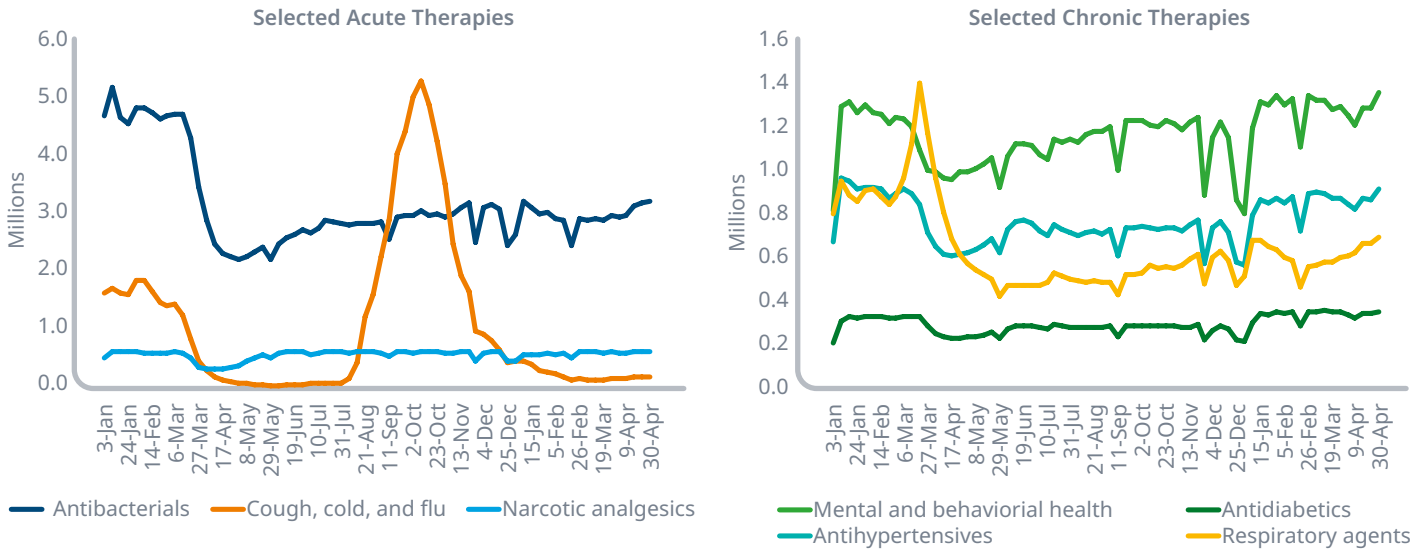
Source: IQVIA National Prescription Audit, Apr 2021

- The impact on prescriptions from the COVID-19 pandemic is particularly notable for acute prescriptions, which had a sharp decline in spring 2020 as the initial lockdown phase of the pandemic took hold.
- Acute prescriptions recovered during the remainder of the year as reopening spread and aided by an above average seasonal flu vaccination cycle, which had been recommended by experts to mitigate risks of being co-infected with COVID-19 and influenza; many people heeded the advice.
- Later in the year, acute prescriptions dropped again, largely as a result of the absence of the seasonal flu in the population from the combined effects of higher vaccination rates and social-distancing and mask-wearing.
- Chronic continuing prescriptions were relatively stable through 2020, with week-to-week variations following normal patterns and marked by disruptions surrounding weeks containing public holidays.
- There has been a steady increase in new to brand (NBRx) chronic prescriptions, but the level has remained below the first eight weeks of 2020 before the pandemic, suggesting that these 'missing' new patients may still be present with their illnesses but are undiagnosed, and is an area of ongoing concern for long-term chronic health outcomes.

Exhibit Notes: 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 patent or prescription attributes and do not reflect the potential for some medicines to be used on a long-term basis against recommendations.

New prescriptions were impacted during the early phase of the pandemic primarily from acute therapies, chronic showing rise later

Exhibit 16: New to Brand Prescriptions (NBRx) Selected Acute and Chronic Therapies



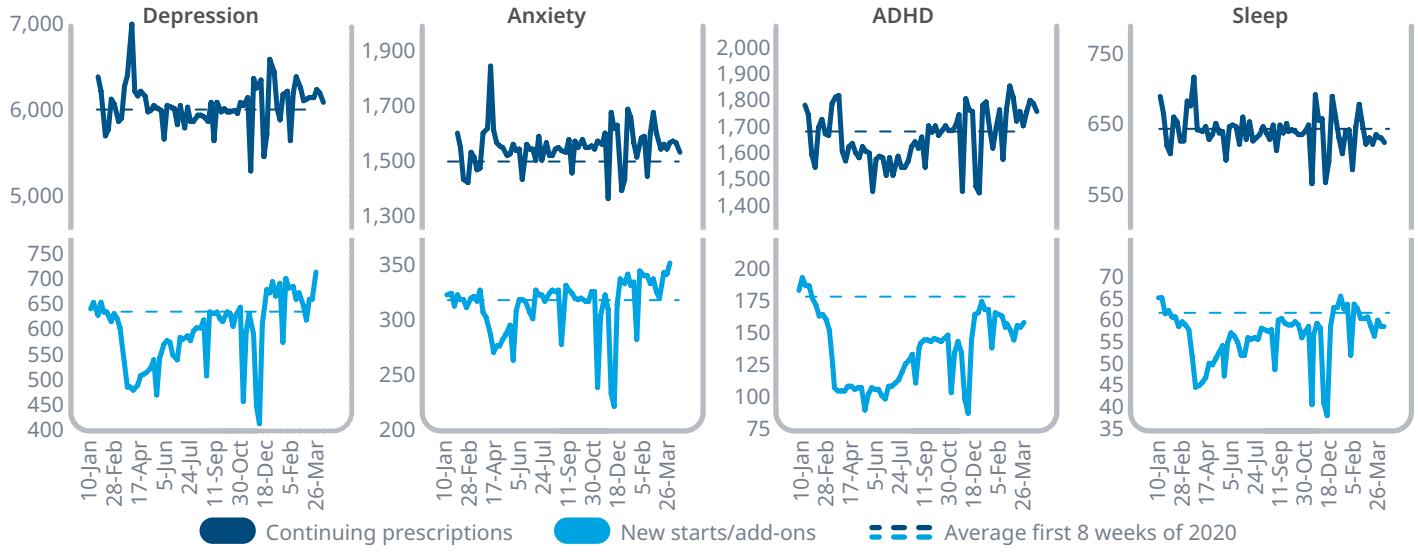
Source: IQVIA National Prescription Audit, Apr 2021

- Disruptions to patterns of life during the pandemic resulted in clear changes in prescribing for acute therapies.
- Antibacterial therapies are used for community-acquired infections and as prophylaxis after a medical procedure where there is a risk of infection, and both types of usage were affected as fewer procedures took place and fewer person-to-person interactions limited community spread of infections.
- Narcotic analgesics declined less in terms of new prescriptions as some patients required pain management for delayed procedures.
- New starts for respiratory therapies, often for chronic asthma, had a sharp increase early in the pandemic as some hospitals increased use of rescue inhalers for COVID-19 patients and existing asthma patients stocked up fearing supply shortages.
- Hypertension and diabetes new starts have rebounded more slowly after the initial shutdown period, suggesting there may have been a time-displacement of some patients who would have been diagnosed earlier, but the increases in 2021 suggest that there could be a larger burden of disease emerging due to the lifestyle changes millions went through adapting to the pandemic.
- Early diagnosis is critical to better outcomes for most chronic diseases, and the degree to which annual health checks are restarted at previous levels will determine whether these patients are identified early enough to have a meaningful impact on their disease progression.

Exhibit Notes: 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.

COVID-19 related social changes drove changes in use of behavioral and mental health therapies

Exhibit 17: Selected Mental and Behavioral Health Therapies New and Continuing Prescriptions, Thousands



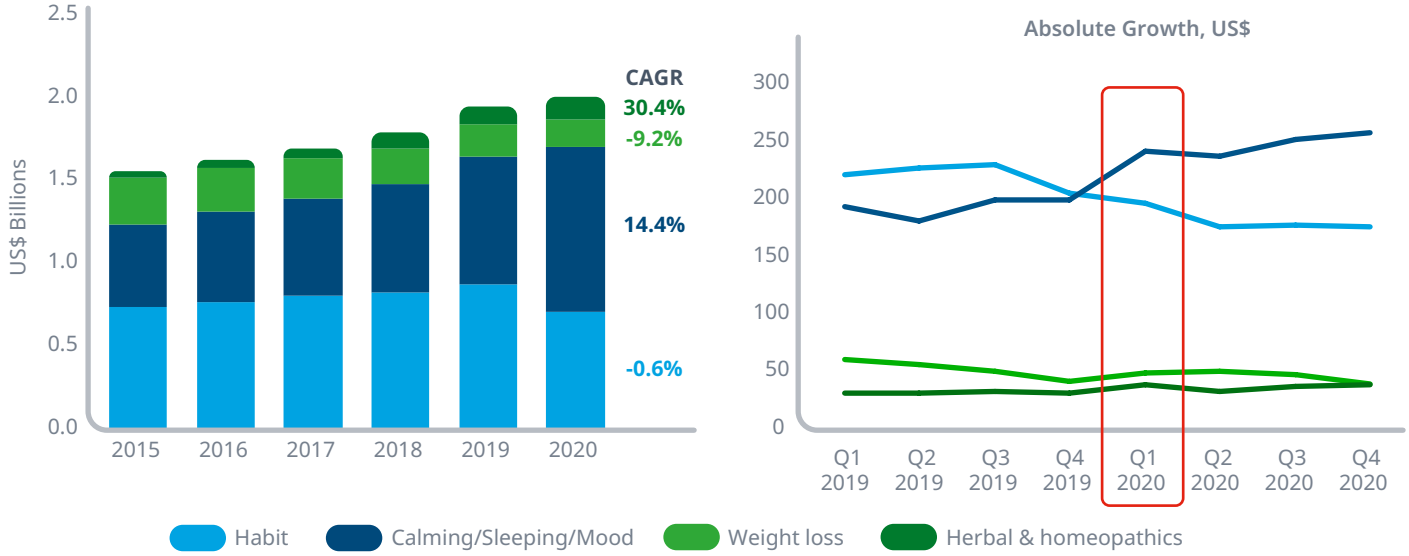
Source: IQVIA National Sales Perspective; IQVIA National Prescription Audit, Apr 2021

- Reports of increasing mental health burden during the COVID-19 pandemic appear warranted and may represent a complex challenge for providers to identify patients in the future.
- Anxiety and depression both exhibited a sharp disruption in new therapy starts early in the pandemic but have recovered to above the baseline average (first eight weeks of 2020) in the late summer, and now continue above those average levels.
- These increases could be the result of simply shifting new patients later in time or because of personal or social reasons that patients have not presented themselves for treatment as soon after reopening as they have with other conditions.
- This could also reflect a limited capacity of providers to cope with an influx of new patients and protocols that would delay drug therapy until it has been deemed appropriate.
- Attention Deficit Hyperactivity Disorder (ADHD) typically experiences a trough in usage during the summer as some parents choose to take a prescription holiday, but the pattern in 2020 was a greater degree of decline and for longer than is typical, likely related to school closures, and levels of new starts have not returned to previous levels.
- Sleep (insomnia) prescriptions have been declining for several years and the decline in new starts may represent a continuation of that trend partly offset by new patients with sleep issues during the pandemic.

Exhibit Notes: Prescriptions are unadjusted. New to Brand or new starts/add ons (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.

During the COVID-19 pandemic patients changed their use of over-the-counter medicines

Exhibit 18: Selected Over-the-Counter Medicines Spending 2015–2020



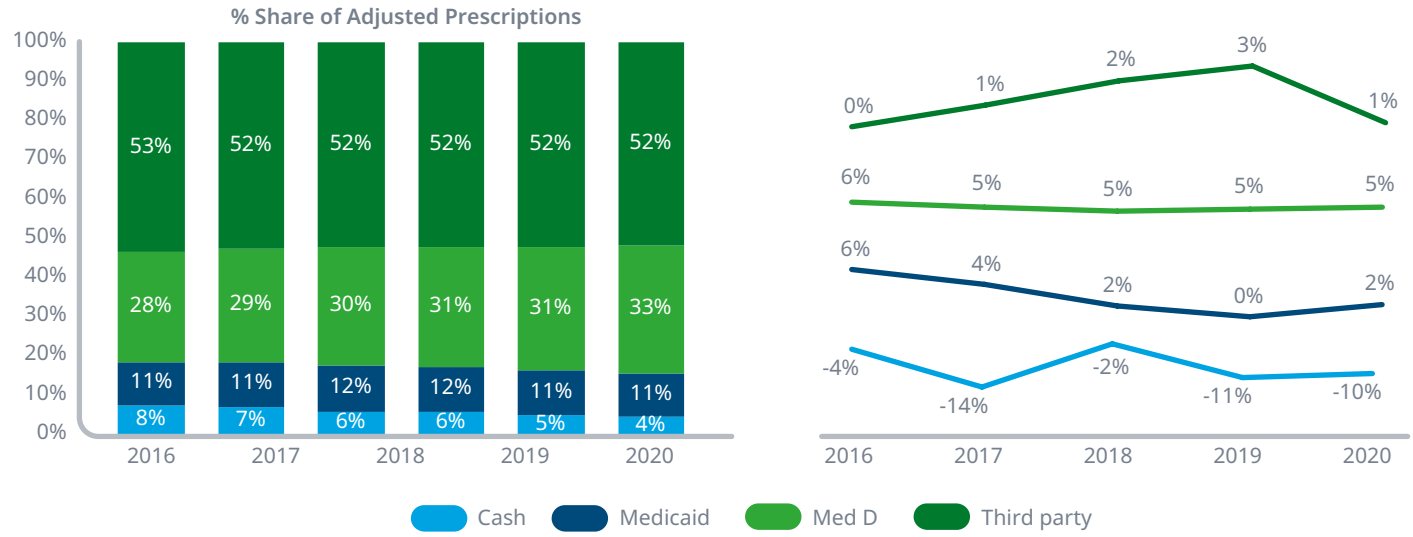
Source: IQVIA Consumer Health data licensed from Nielsen, Dec 2020

- COVID-19 has created a surge in internal well-being, exercise regimens and healthy-eating sectors.
- Calming/sleeping/mood medicines were up significantly in Q1 2020 and since, as many have reported increased stress levels, and over-the-counter medications offer potential relief without the burden of a doctor visit.
- Smoking cessation — the largest component of the habit categor -— was declining prior to the pandemic as more patients were switching from branded anti-smoking products to store-brands or 'private-label' with a lower cost, and this accelerated during the pandemic.
- OTC diet and weight loss therapies have also been declining before the pandemic but may be a signal of a growing burden if they increase following further re-opening as COVID-19 vaccinations progress.

Exhibit Notes: Data are reported spending in dollars, and most over-the-counter (OTC) medicines are relatively low cost, with few changes in cost over time.

Cash paid prescriptions declined 10% in 2020 but the trend preceded COVID-19; Medicaid rose as third-party growth slowed

Exhibit 19: Adjusted Dispensed Prescriptions and % Growth by Method of Payment



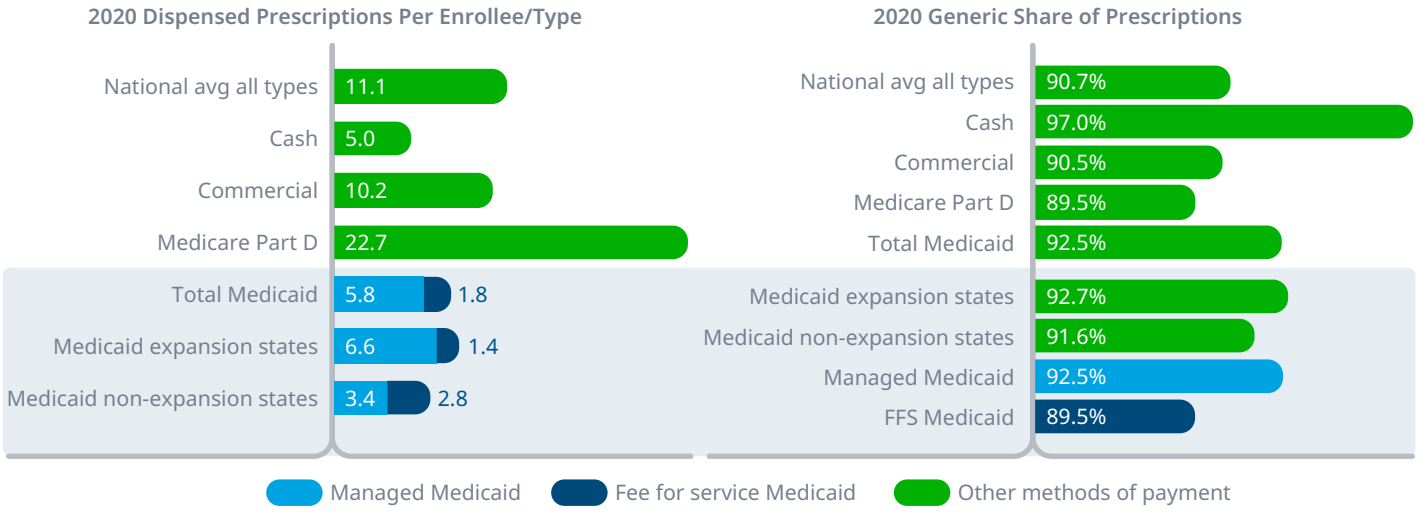
Source: IQVIA National Prescription Audit; IQVIA institute, Dec 2020

- Over the past five years as levels of insurance coverage have increased, cash-paid prescriptions have been in decline, accounting for just 5% of adjusted prescriptions in 2019 compared to 8% in 2015.
- Cash prescriptions declined 10% in 2020, not because more people got insurance but rather because of disruptions from COVID-19.
- Third-party insurance — including employer-sponsored, private group market and health insurance exchanges — grew only 1% in 2020 after increasing faster over the prior three years, as people with insurance used fewer prescriptions and people lost their insurance with layoffs or furloughs.
- Medicaid prescriptions had been slowing prior to the pandemic, with prior growth driven primarily by some states adopting Affordable Care Act Medicaid expansion in the last three years, and the 2020 rebound in growth driven to a degree by increased enrollment.
- Medicare Part D has been relatively unchanged in the prescription growth rate at 5%, only slightly above the population growth rate for those 65+ years old.

Exhibit Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated. Prescriptions referred to as '90-day' are calculated based on transactions with 84 days supply or more to include medicines with up to one-week fewer treatment days. Prescriptions for 84 days supply or more or factored by three, and those under 84 days unchanged. Due to changes in data collection data after 2016, adjusted prescription total has been back-projected based on published growth rates from prior Institute reports to estimate the number of adjusted prescriptions in 2016. Medicare Part D includes dual eligible for Medicare and Medicaid.

Medicaid enrollees use fewer prescriptions per enrollee per year, but use generics more than commercial or Medicare Part D

Exhibit 20: Dispensed Prescriptions per Enrollee and Generic Share of Prescriptions by Insurance Type, 2020



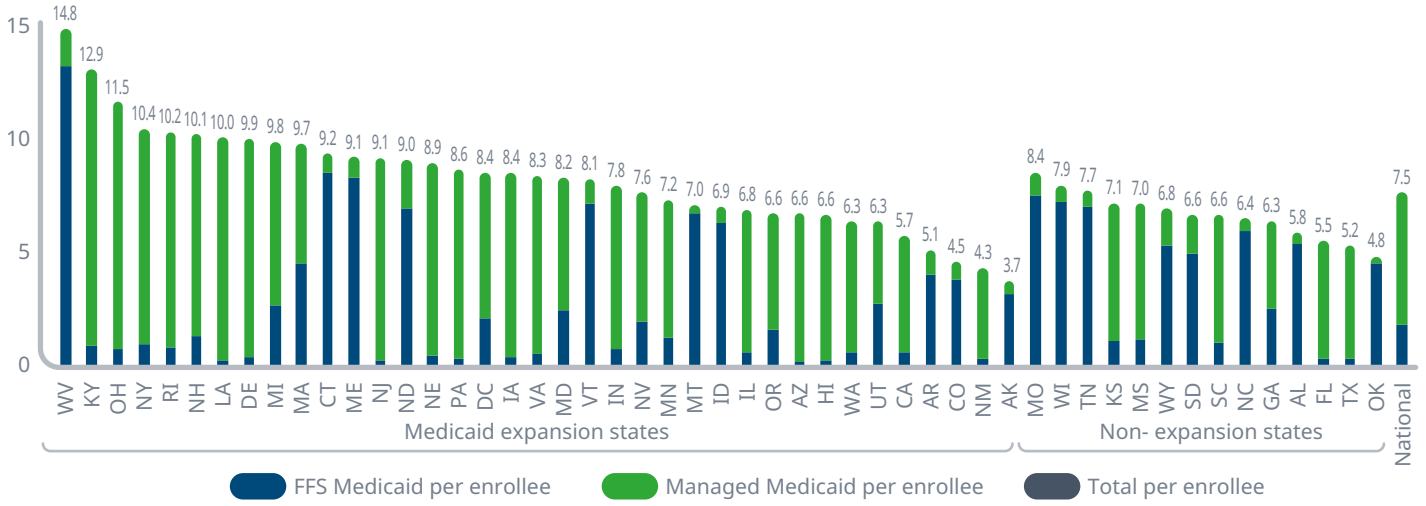
Source: IQVIA National Prescription Audit, Dec 2020;
https://www.kff.org/medicaid/issue-brief/status-of-state-medicaid-expansion-decisions-interactive-map/ accessed 5/18/2021.

- As expanded Medicaid enrollment has been following the economic disruption from the pandemic, the patterns in usage of medicine by insurance types are helpful to understand the burden Medicaid programs will face.
- Commercially-insured patients use almost twice as many prescriptions per person than the average Medicaid enrollee, potentially increasing the burden of increased enrollment.
- Notably, states that have not expanded Medicaid eligibility under the ACA have the lowest per capita medicine usage.
- Generic utilization is one of the more effective mechanisms to control drug costs and yet generic utilization varies considerably across insurance types, with commercial 1% higher than Medicare and states that have expanded Medicaid 1.1% higher than those that have not, and usage under Managed Medicaid 3% higher than under fee for service.
- Differences in generic usage may be related to the types of enrollees, diseases and treatments that are being covered, but also reflect plan designs and incentives.

Exhibit Notes: Prescriptions are unadjusted. Medicare Part D utilization significantly understates per capita usage due to the high degree of three-month supply prescriptions known to be present in the over-65 years old population (see exhibit 12).

States exceed national average per enrollee use of medicines for 23 of 37 expansion states and only 3 of 14 non-expansion states

Exhibit 21: Dispensed Prescriptions per Enrollee, 2020



Source: IQVIA National Prescription Audit, Dec 2020;
https://www.kff.org/medicaid/issue-brief/status-of-state-medicaid-expansion-decisions-interactive-map/ accessed 5/18/2021

- States operate the Medicaid program independently, receiving subsidies from the federal program but having the option to run it with state management, or outsource to a managed care organization.
- All states have some part of their program run by the state on a fee for service basis, usually for complex diseases or specific diseases, while most have a very large share run by managed care organizations on their behalf.
- For the most part, higher Managed Medicaid volume correlates with higher overall prescription volume per enrollee, as better disease management often leads to lower overall healthcare costs.
- While only 3 of the 14 non-expansion states exceed the national average per capita prescription volume, all three have majority fee for service usage.

Exhibit Notes: Prescriptions are unadjusted for prescription length.

Medicine spending and growth drivers

- U.S. medicine spending reflects an increasing gap between invoice level spending and manufacturer net revenues.
- Diverse measures of medicine spending illustrate differing trends depending on the party doing the spending.
- There are large differences between list prices and the amounts spent by payers and patients or received by manufacturers.
- Real net per capita manufacturer revenues declined as specialty discounts, rebates and coupons increased significantly in 2020.
- Specialty medicines now account for 53% of spending, up from 27% in 2010 and driven by growth in autoimmune and oncology.
- Manufacturer net revenues increased by $48 billion over the past five years, primarily driven by new products and brand volume.
- New brand spending in the U.S. has averaged higher than in the last five years but represents a smaller share of spending

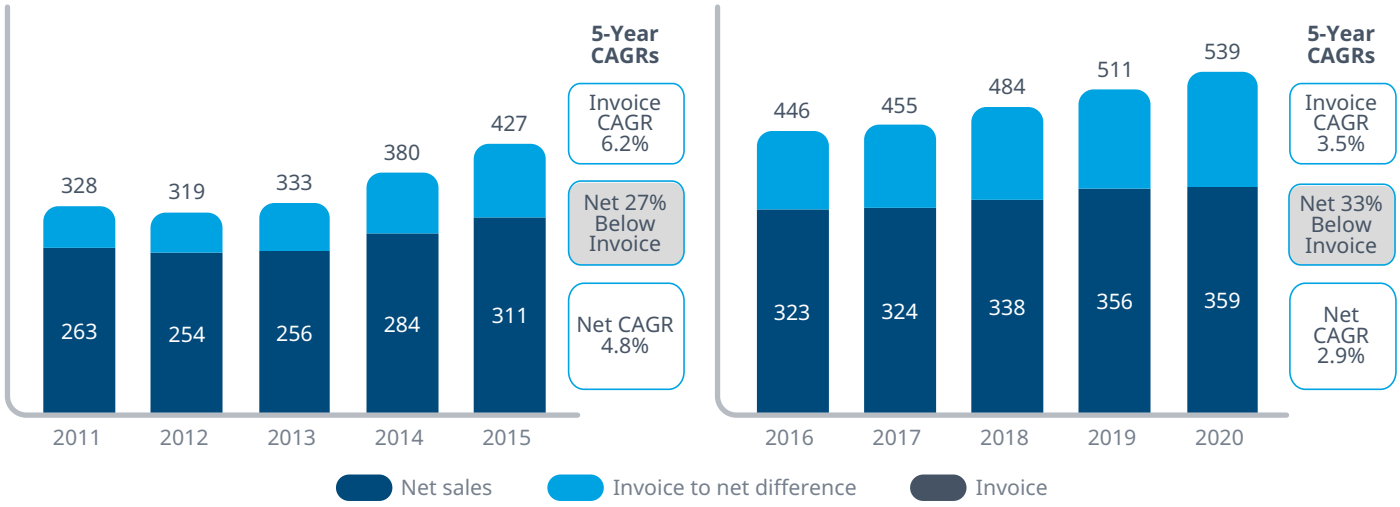
- Protected brand list prices increased 4.4% in 2020, while net prices decreased -2.9% - the fourth year at or below the CPI.
- The impact of losses of exclusivity of biologics has increased dramatically in the past three years.
- Generics are 90% of dispensed prescriptions, up from 72% 10 years ago, and dispensed 97% of the time when possible.
- Biosimilars mature as volume tracks toward 60% for newer molecules and originators begin to decline in accessible markets.
- Specialty classes – Immunology and oncologics drive non-discounted spending growth.
- Biosimilars bring oncology growth below 10% for the first time in seven years as new brand growth also slowed.
- Diabetes growth slowed to 2% in 2020 on a net basis as off-invoice discounts and rebates drive protected brand costs down by 12%.
- Autoimmune grew $10.8 billion to $77.1 billion in 2020, driven by products launched in the past five years and those with upcoming biosimilars.

A NOTE ON NOMENCLATURE

In this report, "spending on medicines" and "invoice-price spending" refer to the amounts paid to distributors by their pharmacy or hospital customers. It does not relate directly to either the out-of-pocket costs paid by a patient, except where noted, nor does it refer to the amount health plans or Medicare pay for medicines, and does not include mark-ups and additional costs associated with dispensing or other services associated with medicines reaching patients. "Net-Price Spending" or "Net Manufacturer Revenue" are proprietary derived estimates of the amount received by pharmaceutical manufacturers after rebates, off-invoice discounts and other price concessions have been made by manufacturers to government for statutory discounts and rebates, distributors, health plans and intermediaries. See the Methodology section for more details.

The U.S. spending reflects an increasing gap between invoice level spending and manufacturer net revenues

Exhibit 22: U.S. Medicine Spending and Growth at Invoice-level and Estimated Net 2011–2020



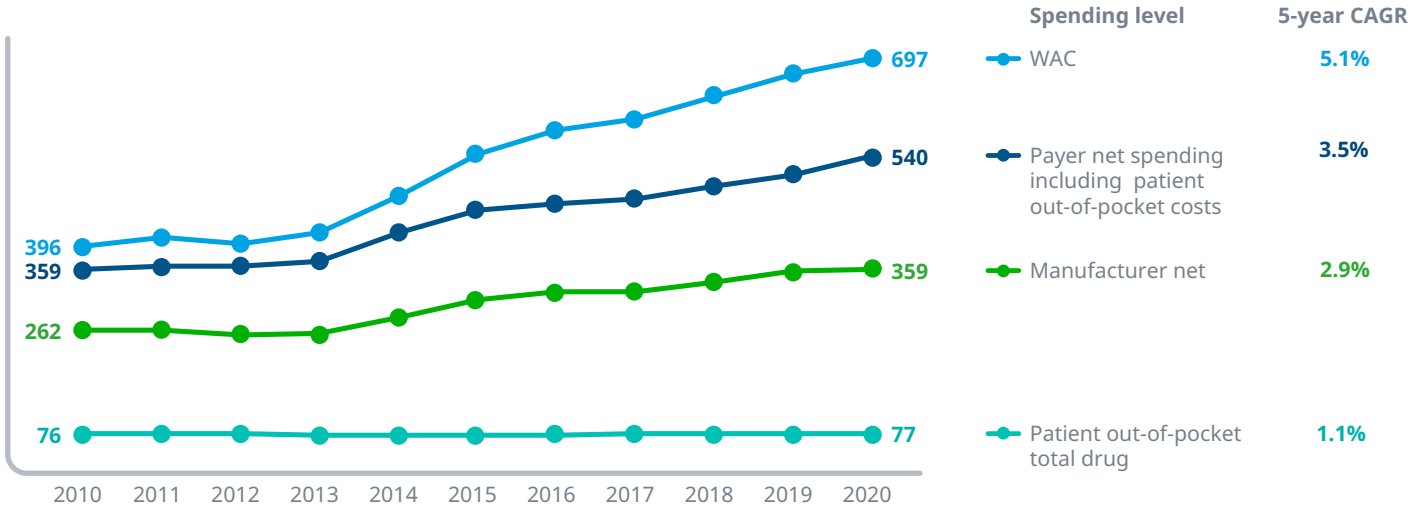
Source: IQVIA Institute, May 2021

- In 2020, spending grew 0.8% net of off-invoice discounts and rebates, while growth at the invoice-level was 5.5%.
- Discounts, rebates and other price concessions on brands reduced absolute invoice spending by an estimated 33% to $359 billion.
- Off-invoice discounts and rebates paid by manufacturers to other stakeholders include statutory discounts and rebates to government programs like the pharmaceutical fee paid by branded companies, Medicaid and 340B, negotiated rebates with pharmacy benefit managers, supply chain discounts and fees, and coupons provided to patients, among others.
- Spending grew in 2020 due in part to the launch of new branded products as well as an increase in the volume of current branded products, and offset disruptions that mostly affected generic volume from the COVID-19 pandemic.
- On an invoice basis, spending has risen 64% since 2011, from $328 to $539 billion in 2020, but only 37% on a net basis, from $263 to $359 billion in 2020.
- The past decade has included both the most impactful concentration of patent expiries in 2011 and 2012 as well as the largest impact from new brand launches from late 2013 through 2015, while periods since have shown more modest growth dynamics, punctuated by the COVID-19 pandemic in 2020.

Exhibit Notes: Measures total value of spending on medicines, including generics, branded products, biologics, small-molecules, retail and non-retail channels. Invoice spending is based on IQVIA reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied. Includes all medicines in both pharmacy and institutional settings. Pricing is at the manufacturer level.

Diverse measures of medicine spending illustrate differing trendsdepending on the party doing the spending

Exhibit 23: Medicine Spending at Selected Reporting Levels, US$Bn



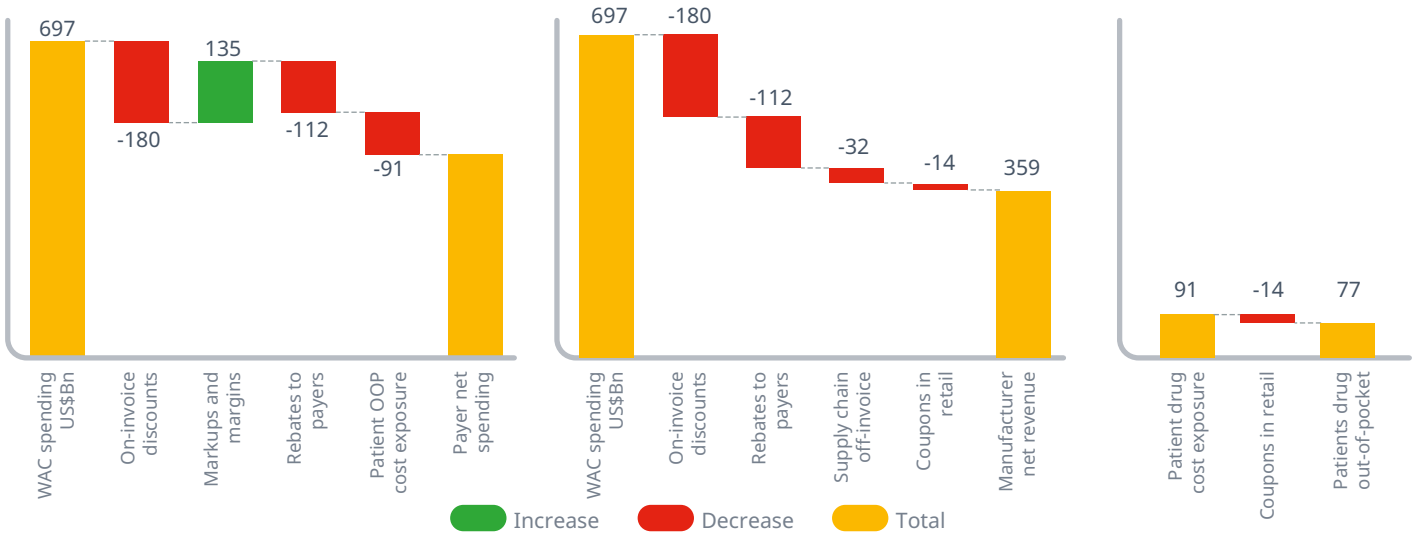
Source: IQVIA Institute, May 2021; CMS National Health Expenditures (NHE), Dec 2020

- Over the past five years, spending at list prices [Wholesaler Acquisition Cost (WAC)] has increased from $543 billion to $697 billion — an average of 5.1% per year.
- Manufacturer net revenues from these sales, including all products, are estimated to have grown an average of 2.9% over five years and 0.8% from 2019 to 2020.
- 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 remained relatively unchanged, rising from $76 billion 2010 to $77 billion in 2020.
- Manufacturer net revenue is lower than other measures of spending based on a combination of statutory discounts to Medicaid, discounts for 340b eligible institutions, the branded pharmaceutical fee in the ACA, donut-hole subsidies in Medicare Part D, supply chain discounts (often for generic drugs), as well as the value of coupons given to patients.
- Payers (including government and private insurance and patient out-of-pocket costs) have seen their spending rise an average 3.5% over the past five years to $540 billion, mostly driven by higher insurer cost exposure.

Exhibit Notes: 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 amount 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 that reduce payer responsibility. Payer net spending is derived from an analysis of CMS National Health Expenditure (NHE) data, IQVIA audited sales, and IQVIA estimates of manufacturer invoice-level and net revenue. Patient out-of-pocket costs are derived from CMS NHE. Due to lag-times in reporting, CMS-derived measures are projections for 2019 while IQVIA-derived metrics are actual.

There are large differences between list prices and the amounts spent by payers and patients or received by manufacturers

Exhibit 24: Differences Between Various Spending Levels for U.S. Prescription Medicines in 2020, US$Bn



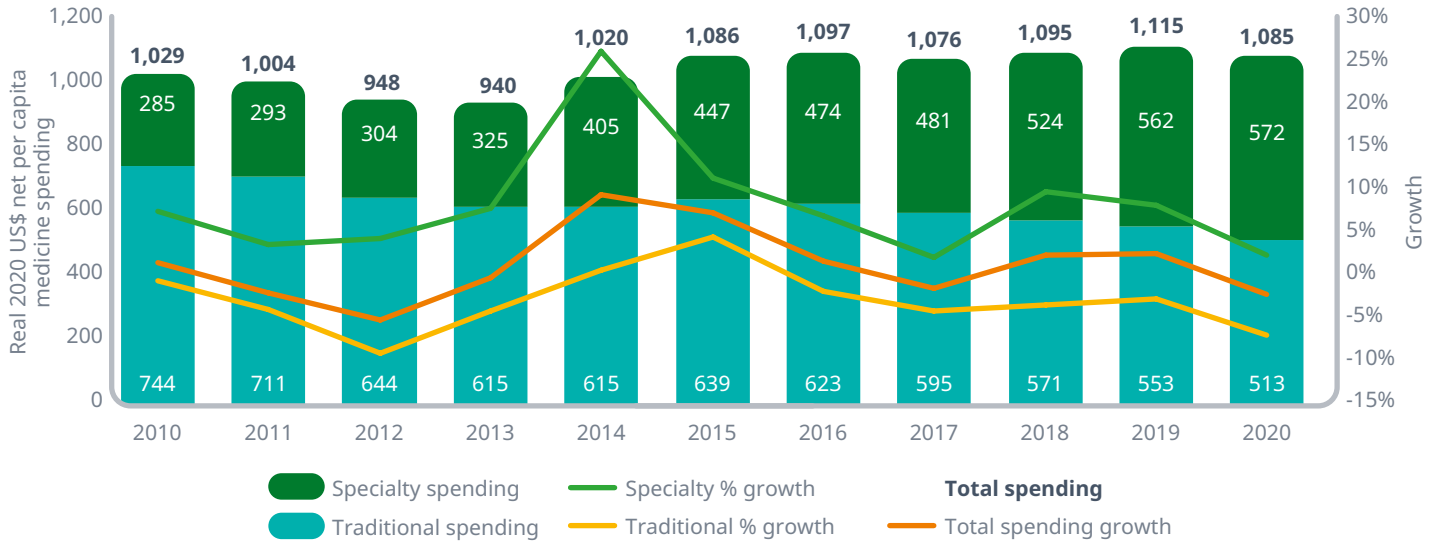
Source: IQVIA Institute, May 2021; CMS National Health Expenditures (NHE), Dec 2020

- Wholesaler acquisition costs (WAC) represent list prices that influence the costs paid by others in the supply chain and some patients. WAC does not reflect elements like discounts and rebates, which cause significant differences in the prices experienced by various stakeholders and individuals.
- Payers (including patients), in aggregate, paid $540 billion in 2020 for medicines, including those paid through a patient's medical benefit for doctor-administered drugs or drugs used during a hospitalization, which are often excluded from official statistics.
- Manufacturers offer supply chain discounts, rebates to insurers, and coupons to patients, resulting in net revenues of $359 billion - $338 billion lower than at WAC prices.
- Patient costs are much lower overall due to insurance coverage but still represent a substantial amount: $77 billion in 2019. This value accounts for $14 billion in savings for patients as a result of manufacturer coupons (including the use of manufacturer-provided pre-paid debit cards).

Exhibit Notes: 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. Patient out-of-pocket costs are derived from CMS NHE. Due to lag-times in reporting, CMS-derived measures are projections for 2020 while IQVIA-derived metrics are actual.

Real net per capita manufacturer revenues declined as specialty discounts, rebates and coupons increased significantly in 2020

Exhibit 25: Real Net per Capita Medicine Spending and Growth by Product Type US$



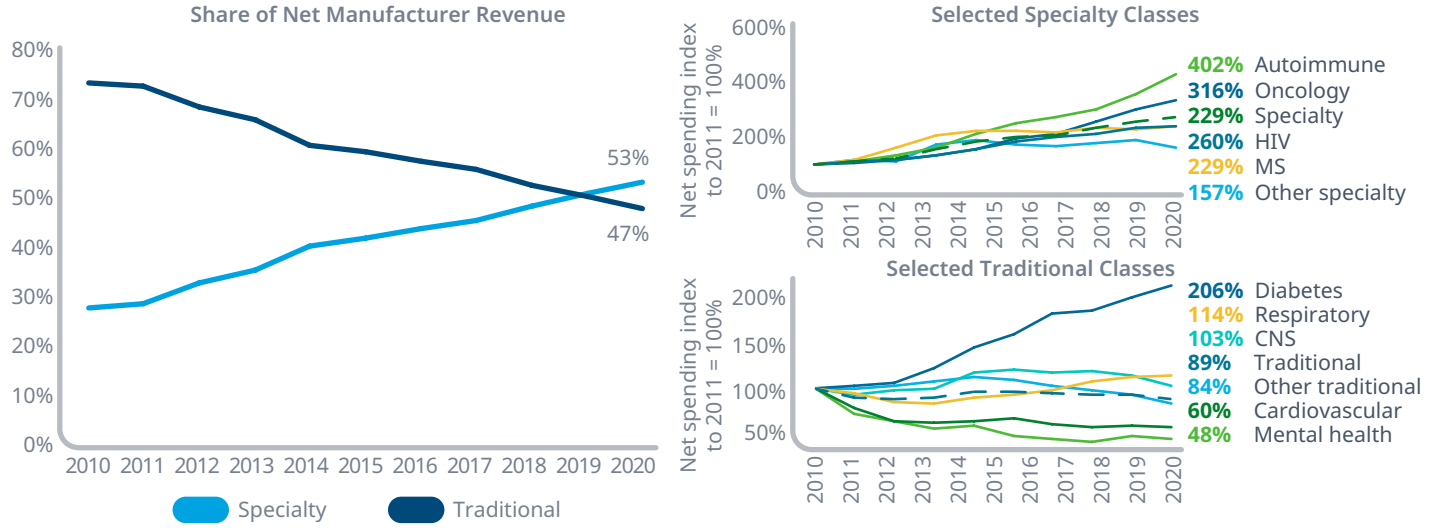
Source: IQVIA National Sales Perspectives, IQVIA Institute, May 2021; U.S. Census Bureau; U.S. Bureau of Economic Analysis (BEA), Dec 2020

- Medicine spending per capita, adjusted for population growth and shown in current (2020) dollars, grew only $56 since 2010.
- Real net per capita spending declined by 2.7% in 2020 as a result of the economic impact of COVID-19, while net growth of 0.8% was only slightly above reported population growth.
- Over 10 years, real net per capita spending grew an average 0.5% per year but was trending at 0.9% through 2019.
- Specialty share of net spending across institutional and retail settings rose from 27% in 2010 to 53% in 2020, driven by innovation, and the declining share for traditional medicines as growth has slowed due to 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 five years has been specialty drugs, and specialty spending per person has doubled from $285 in 2010 to $572 in 2020, while traditional net medicine spending has declined by $231 per person over the same period.
- Across all settings, specialty medicines treat relatively few patients and have costs far higher per patient than traditional medicines.

Exhibit Notes: Real medicine spending reflected in 2020 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 53% of spending, up from 27% in 2010, driven by growth in autoimmune and oncology

Exhibit 26: Share of Net Manufacturer Revenue



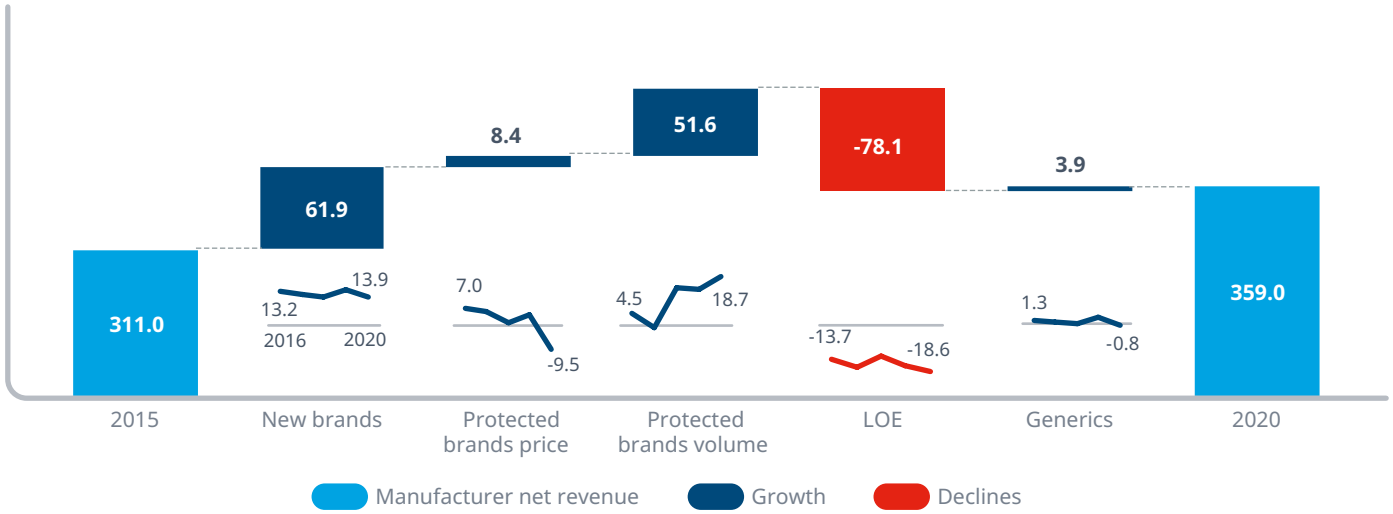
Source: IQVIA Institute, May 2021

- 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 53% of net manufacturer revenue.
- The rise in specialty spending has been predominately driven by oncology and autoimmune diseases, where spending has increased 316% and 402% respectively since 2011 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 48% and 60% respectively of their 2011 level of net spending as of 2020.
- Diabetes has increased to 206% of the 2011 level as a result of significant innovation, with three new classes of treatments (DPP-IV, GLP-1, and SGLT-2) treatments 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.

Exhibit 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.

Manufacturer net revenues increased by $48 billion over the past five years, primarily driven by new products and brand volume

Exhibit 27: Net Manufacturer Revenues and Growth 2015–2020, All Channels, US$Bn



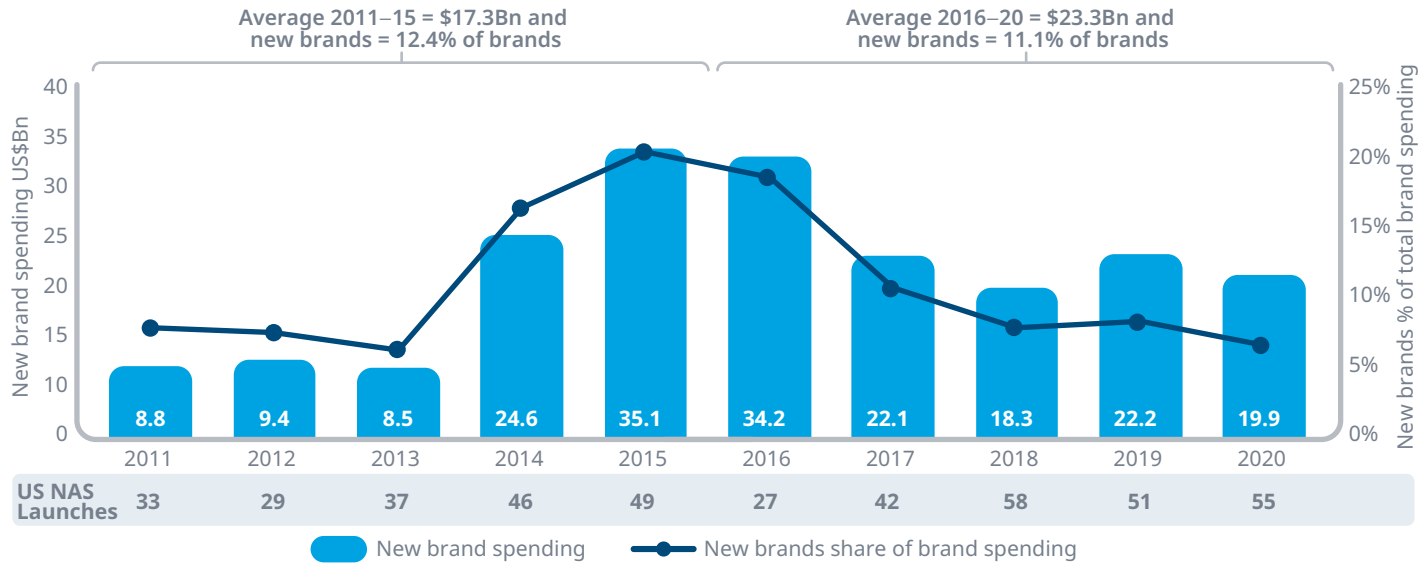
Source: IQVIA Institute, May 2021

- New products, including 233 new active substances that launched from 2016 through 2020, contributed $62 billion to net manufacturer revenue growth over the past five years.
- Price increases for protected brands, which have slowed substantially in recent years, contributed $8.4 billion to growth over five years, averaging a 0.8% increase per year, including the net decline in 2020.
- Volume growth experienced by protected brands — most often driven by brands in the three to five-year period since their launch when adoption by HCPs grows — contributed $52 billion 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 also lower brand sales for the originator. These contributed a decline of $78 billion to manufacturer net revenues.
- The impact of LOE had a significant inflection from biosimilars in 2020, with brand losses of $7.4 billion on an invoice basis (see exhibit 31).
- During the past five years, generic prices have been deflating, driven by an increase in the number of generic approvals, shrinking a previous backlog in applications at FDA and bringing new competition to existing generic molecule markets as well as the impact from new patent expiries during the period.

Exhibit Notes: IQVIA estimates of net manufacturer revenue and growth 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.

New brand spending in the U.S. has averaged higher than in the last five years but represents a smaller share of spending

Exhibit 28: U.S. New Brand Invoice Spending



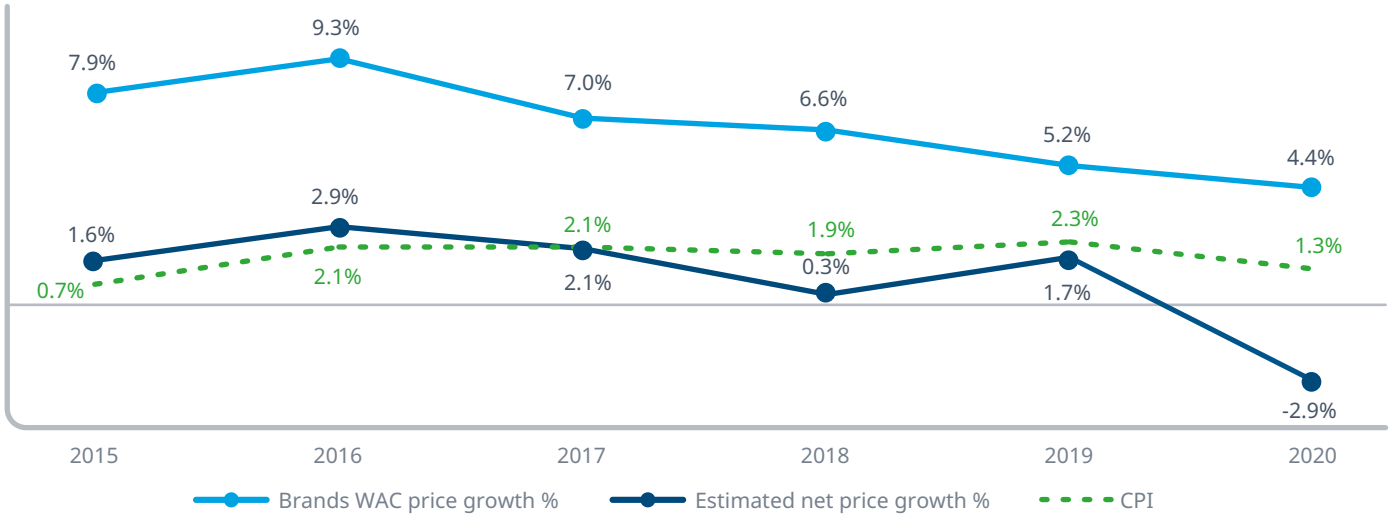
Source: IQVIA Institute, Feb 2021

- New medicines launched in the past two years drove spending of $19.9 billion on an invoice basis in 2020, down from $22.2 billion in 2019 as new launches had lower average sales in 2020.
- There were 55 novel active substances (NAS) launched in 2020, including three emergency use authorizations (EUA) for COVID-19 whose sales are not reflected in the totals.
- The number of NAS launches per year was 50 or more for the third year in a row even as spending for new products has trended down overall as a share of brand spending.
- Increasingly, new medicines are specialty, niche and orphan disease drugs, driving most of the increase in new medicines and in the spending which has been elevated since 2014 with the launch of drugs for hepatitis C and a range of other specialty conditions.
- New launches were impacted in 2020 by disruptions from COVID-19, with newer products performing worse than comparators, both from a skew to more orphan products in the launch group, as well as lack of promotion due to shutdowns.
- Large contributors to new brand spending in 2020 were remdesivir (Veklury) for COVID-19, quadrivalent flu vaccines (Fluzone HD Quadrivalent and Fluad Quadrivalent), and a reformulation of daratumumab (Darzalex Faspro), which brings a shorter treatment duration with a subcutaneous injection compared to prior infusion for multiple myeloma.

Exhibit Notes: New brands are defined as brands launched in the last 24 months and defined separately for each year. NAS = new active substance.

Protected brand list prices increased 4.4% in 2020, while netprices decreased -2.9% - the fourth year at or below the CPI

Exhibit 29: Wholesaler Acquisition Cost (WAC) Growth and Net Price Growth for Protected Brands



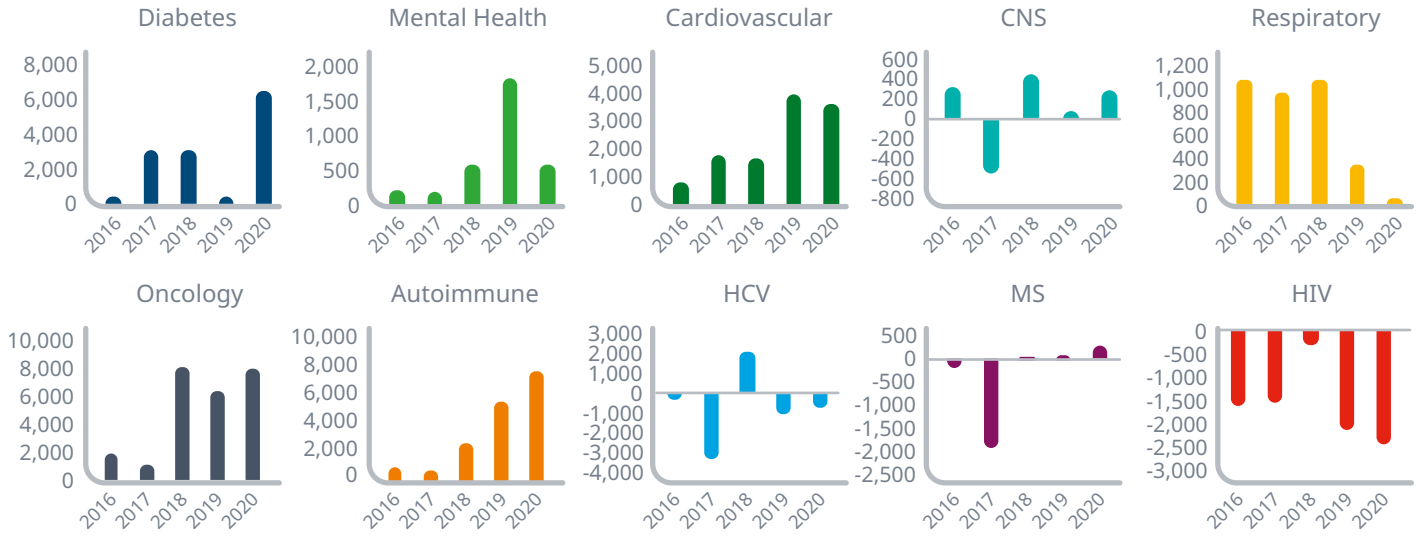
Source: IQVIA Institute: IQVIA National Sales Perspectives, Dec 2020; Bureau of Labor Statistics, CPI Data, Dec 2015–Dec 2020

- The list prices of protected branded products — those products more than two years after launch having not yet lost patent protection — increased 4.4% in 2020.
- Net manufacturer prices — the cost of medicines after all discounts and rebates have been paid — declined 2.9% in 2020, continuing a downward trend for the past five years that was interrupted in 2019.
- 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. 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.

Exhibit 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). CPI = consumer price index.

Protected brand volume growth continues mostly in therapy areas with recent waves of innovation

Exhibit 30: Protected Brand Volume Growth at Net Prices US$Bn



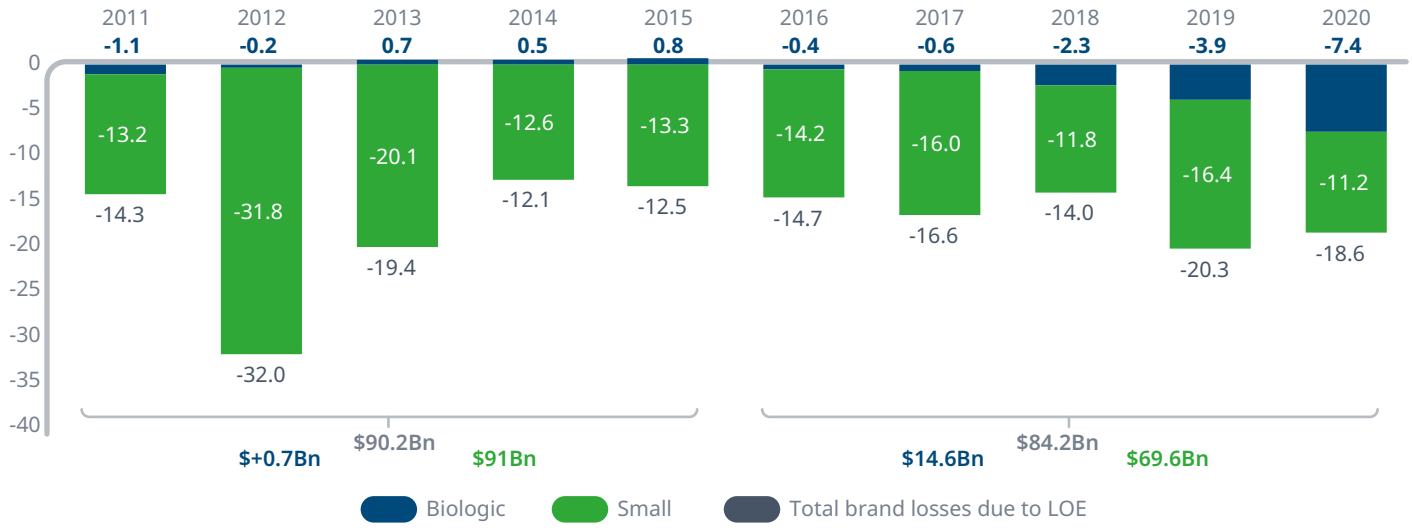
Source: IQVIA Institute; IQVIA National Sales Perspectives, Dec 2020

- Volume growth — sales measured at prior year estimated net prices for products older than two years after launch but not yet off-patent — has grown to widely differing degrees across therapy areas.
- Diabetes, despite net price declines due to rising discounts and rebates, had volume growth of nearly $6.5 billion 2020 as the wider use of newer protected brands has continued.
- Oncology volume growth has been more than $6 billion per year for the last three years, largely as products launched from 2013–2015 began to be included.
- Autoimmune similarly includes a group of products first launched from 2013 to 2016 and which are growing through volume even as competition is driving up off-invoice discounts, rebates and the use of patient savings programs (coupons).
- Hepatitis C volume has been declining as fewer patients are being treated after the initial waves when the drugs were first introduced.

Exhibit Notes: Volume growth measured as sales at constant prices, adjusted to net prices. Volume growth measured at invoice level may have different trends as some products experience net price changes without changing list prices.

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

Exhibit 31: Impact of Brand Losses of Exclusivity 2011–2020, US$Bn



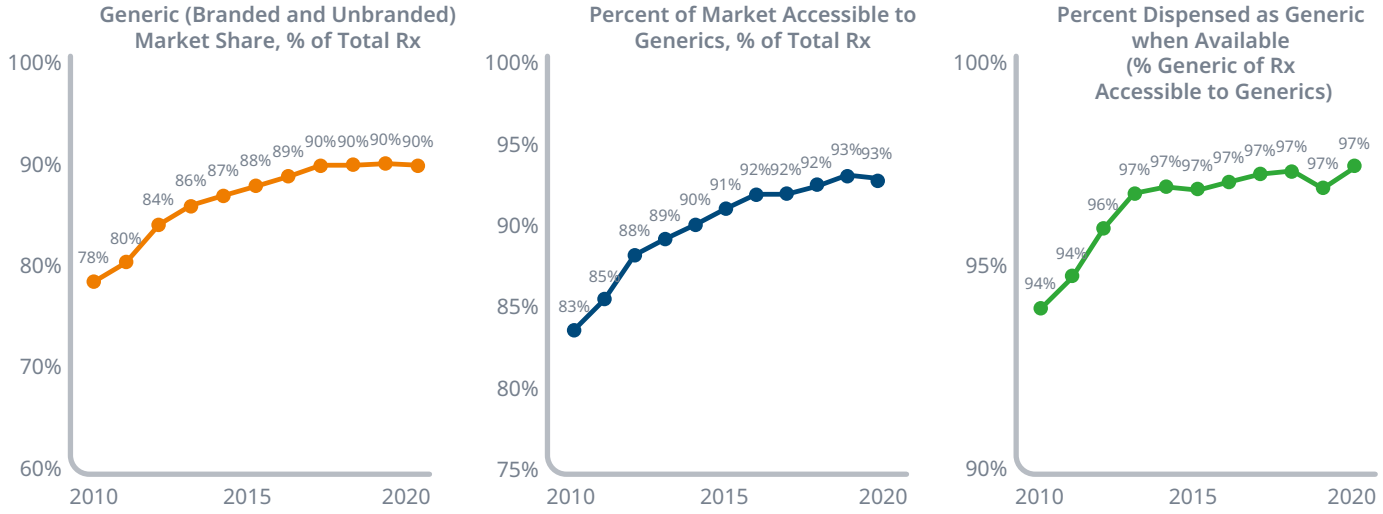
Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

- The introduction of multiple biosimilars for three molecules in the oncology market — bevacizumab, rituximab, and trastuzumab — have contributed to a significant increase in brand losses due to losses of exclusivity (LOE) in 2020.
- Biologic brand losses were $7.4 billion 2020, an increase from the 3.9 billion in 2019 and totaling $14.6 billion in the past five years.
- Small molecule brand losses continued at historic rates and contributed $69.6 billion over the past five years, down from $91 billion in the prior five years.
- In total, the $84.2 billion of brand losses from LOE in the past five years was down from the $90.2 billion in the prior five years which included the ‘patent cliff’.
- Notably, biosimilars earlier in the period actually didn’t reduce brand sales in the early periods and resulted in an increase of $700 million in invoice level spending for brands facing competition, though these increases were likely offset by off-invoice discounts and rebates.

Exhibit 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 invoice level.

Generics are 90% of dispensed prescriptions, up from 72% 10 years ago, and dispensed 97% of the time when possible

Exhibit 32: Generic Shares of Dispensed Prescriptions, Accessible Market and Generic Share when Available



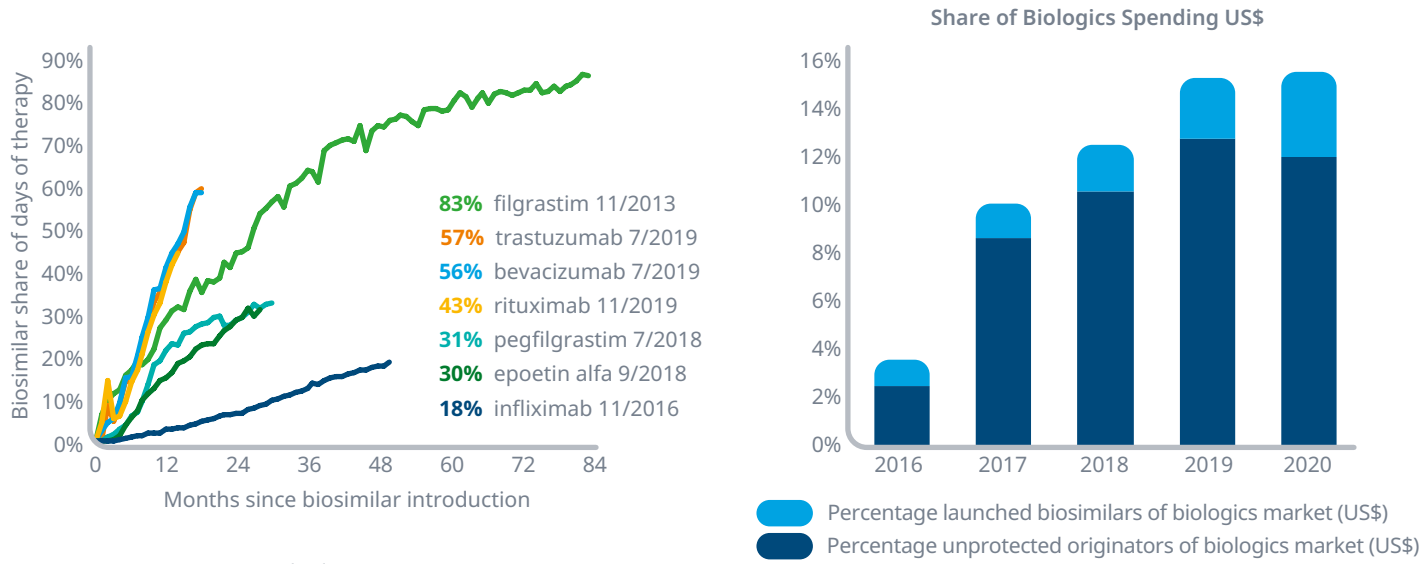
Source: IQVIA National Prescription Audit, Dec 2020

- The overall level of generic dispensing of prescription medicines has risen from 78% in 2010 to 90% in 2020.
- The market accessible to generics, measured as that part of the market where generics have launched, has risen from 83% of prescriptions to 93% over 10 years.
- The overall rate of generic dispensing, when it is possible to do so, rose from 94% to 97% by 2013, and has remained steady for the past seven years.
- The high level of generic dispensing is consistent with significant financial incentives for patients and providers to make use of the lowest cost alternatives where possible.
- In many therapy areas, however, the rate of generic dispensing is at or near 100%.

Exhibit Notes: If a generic or branded generic is available in the market for a medicine (e.g., a molecule, molecule combination, of a specific formulation) it is considered to be available, whether or not the FDA Orange Book indicates that they are substitutable.

Biosimilars mature as volume tracks toward 60% for newer molecules and originators begin to decline in accessible market

Exhibit 33: Biosimilar Share of Days of Therapy and Share of Biologic Spending



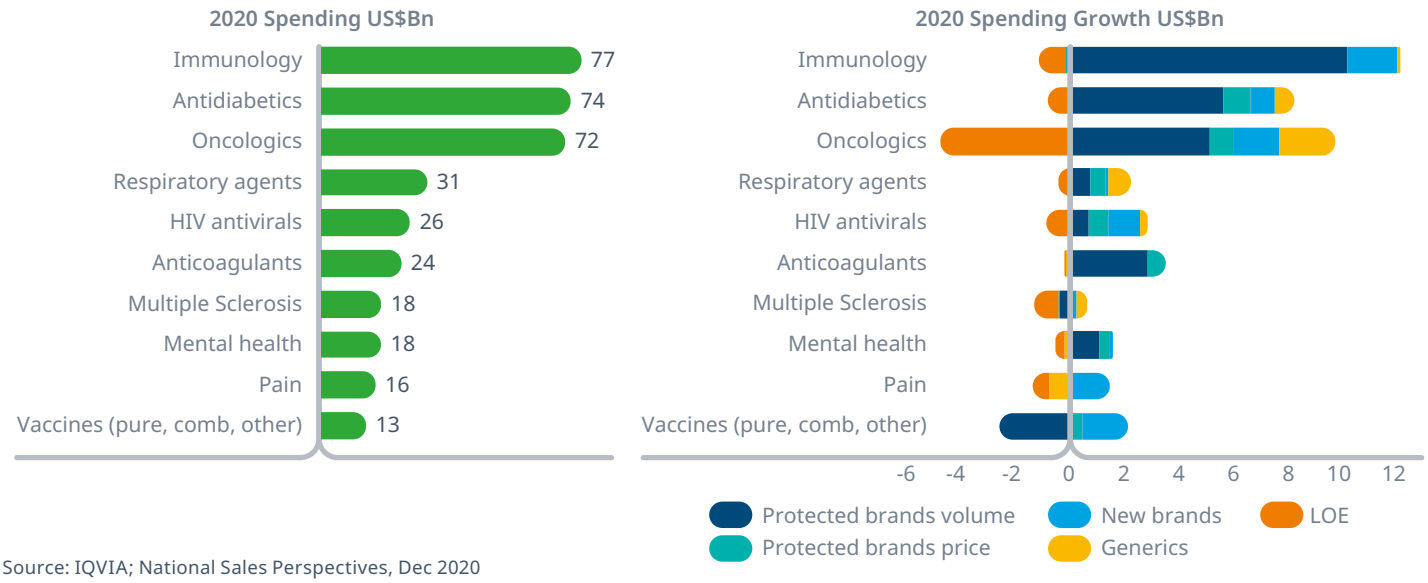
Source: IQVIA Institute; National Sales Perspectives, Dec 2020

- The last three biologics to lose exclusivity have had much faster and higher biosimilar uptake, trending to nearly 60% volume share by the end of their second year on the market.
- Older biosimilars had lower trajectories or took longer to achieve such levels.
- As new molecules have become available as biosimilars, the share of the market that is accessible to biosimilars has risen to almost 14% of spending, and as biosimilars have taken share, and had lower prices, they have taken a larger share of the competitive market.
- The rapid uptake of these newer biosimilars may be helped by the way the medicines are used, largely in treatment episodes with an independently measurable clinical outcome such as tumor shrinkage, indicating if another cycle of therapy should be used.
- This usage pattern is a marked contrast to chronic therapies, where switching from the reference brand to the biosimilar would need to be considered, and to date there have been no approvals deemed interchangeable by the FDA.

Exhibit Notes: Days of therapy are based on the World Health Organization Defined Daily Dose concept (WHO-DDD) where each molecule has a set volume of medicine that is assumed to represent a day of therapy. Spending is at invoice level.

Specialty classes — immunology and oncologics — drive non-discounted spending growth

Exhibit 34: Leading Therapy Classes Non-Discounted Spending Growth by Segment ($BN), 2020

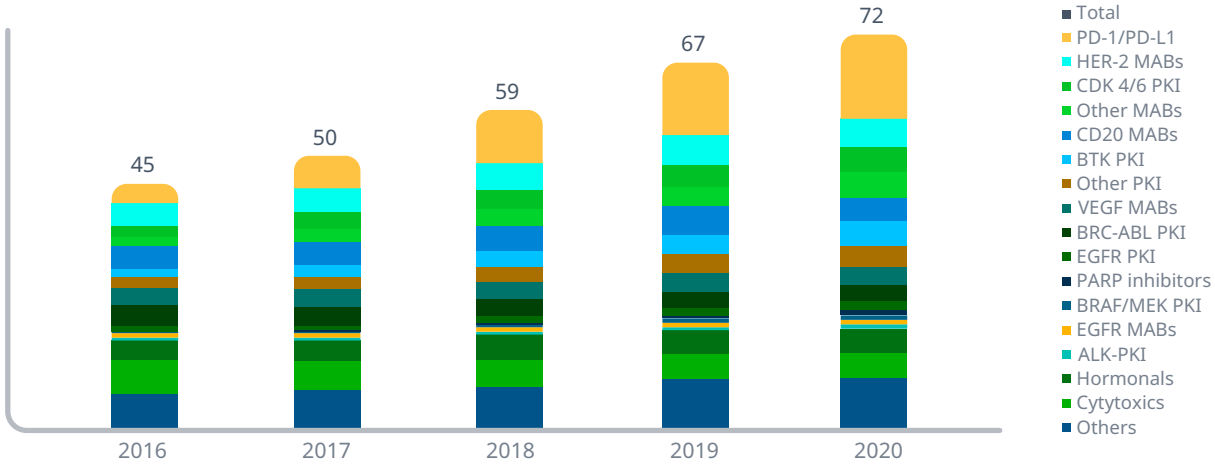


Source: IQVIA; National Sales Perspectives, Dec 2020

- Spending in leading therapy areas has been led by immunology, diabetes and oncology, with these three classes accounting for 60% of spending growth on an invoice basis.
- Oncology drivers of growth include declines from losses of exclusivity, including biosimilars, as well as the continued uptake from new drugs launched in the past five years, though that slowed in 2020.
- The fourth largest therapy area by growth is anticoagulants, as novel anticoagulants continue to grow steadily.
- Vaccines had a significant decline in 2020 as existing vaccinations were disrupted as medical practices were closed for COVID-19, while the new quadrivalent flu formulations drove uptake during the extra high level of seasonal flu vaccination in late 2020.

U.S. Oncology spending has been growing from the uptake of PD-1/PD-L1s and a myriad of other new mechanisms

Exhibit 35: U.S. Oncology Invoice Spending by Mechanism



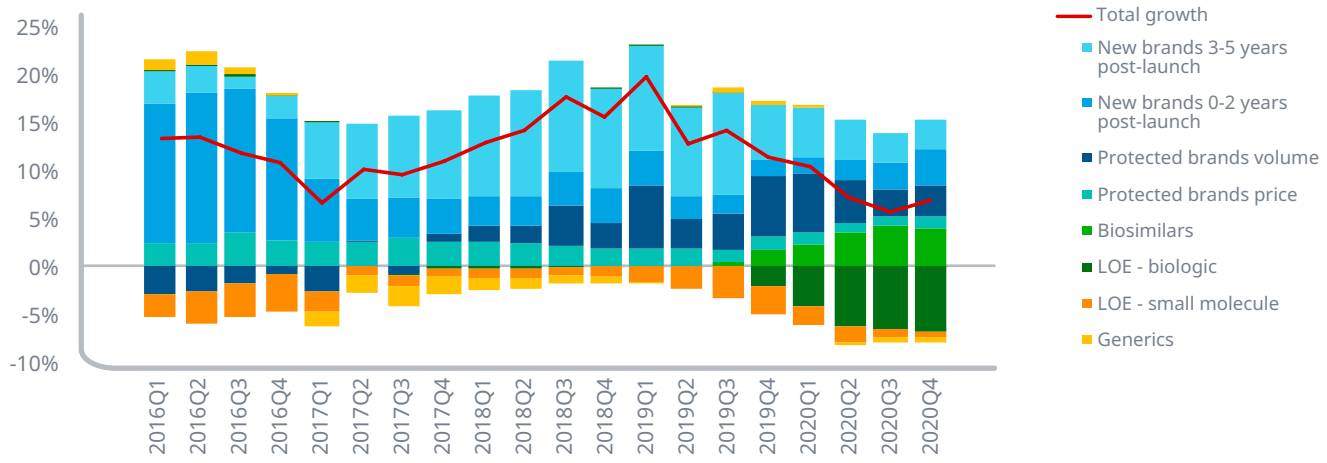
Source: IQVIA National Sales Perspectives, Dec 2020

- Oncology spending increased $5 billion in the past year and $27 billion over the past four years to $72 billion in 2020.
- Oncology growth has been driven by new products, particularly PD-1/PD-L1 as well as a proliferation of mechanisms for small molecule and antibody targeted agents.
- Each of these various mechanisms is typically identified as the result of a biomarker test where the particular tumor exhibits mutations where the drugs have been shown to be effective.
- This fragmentation of therapy options has brought new options with better outcomes to many cancer patients.
- Mechanisms related to new biosimilars were HER-2 MABs, VEGF MABs and CD20 MABs, where spending declined as a result.
- HER-2 MABs declined from $5.3 billion in 2019 to $5 billion in 2020, while CD20 MABs declined from $5 billion to $4.4 billion, and VEGF MABs from $3.6 billion to $3.3 billion, with most of the negative contribution to growth from the impact of biosimilars.

Exhibit Notes: Mechanisms represent a summary of all drugs of the same types.

Biosimilars bring oncology growth below 10% for the first time in seven years as new brand growth also slowed

Exhibit 36: U.S. Oncology Invoice Spending Growth Drivers



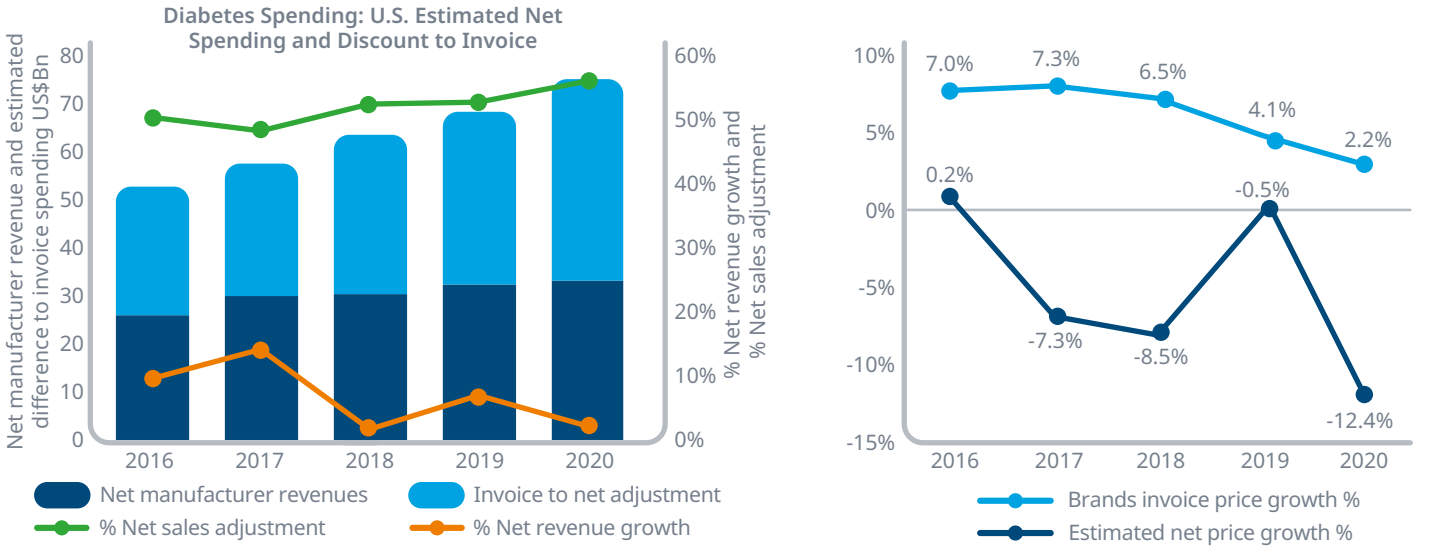
Source: IQVIA National Sales Perspectives, Dec 2020

- Despite the continued flow of new products – including another 17 new active substance (NAS) launches in oncology in 2020 — there has been a relative slowing of growth from new products. This reflects the niche and often rare cancer focus of newer drugs, with 16 of the 17 NAS orphan designated in 2020.
- Older launches have been continuing to drive growth, as illustrated in the new brands three to five years after launch segment, which has been driving more than half of positive growth for most of the last five years, slowing in 2020.
- Protected brand volume growth includes those drugs more than five years after launch, and their increased growth starting in 2018 represents launches from 2012 and 2013, which are continuing to grow strongly.
- Price growth has remained historically low, contributing only 1% to growth in 2020.
- Biosimilars dramatically reduced spending for bevacizumab, trastuzumab and rituximab and while that was offset by biosimilar spending, the impact on growth was considerable.

Exhibit Notes: New brands are assigned to the <2 years or 3-5-year segments based on their launch date relative to each quarter in the analysis. Products are included in different segments over time, and upon being more than 5 years after launch are in the protected brand segment until patent expiry. Protected brands are segmented by growth due to price changes on an invoice basis and growth due to volume. Generics and biosimilars are shown separately.

Diabetes growth slowed to 2% in 2020 on a net basis as off-invoice discounts and rebates drive protected brand costs down 12%

Exhibit 37: Diabetes Invoice and Net Spending and Growth



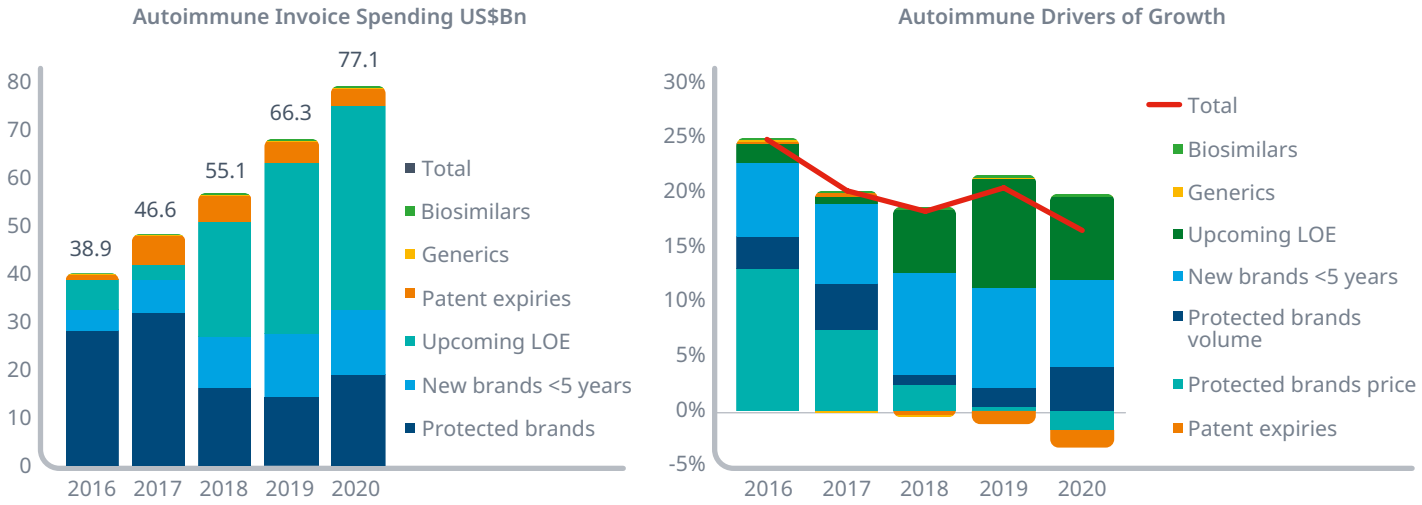
Source: IQVIA Institute, May 2021; IQVIA National Sales Perspectives, Dec 2020

- Diabetes was the second largest therapy area in the U.S. in 2020 at invoice prices, but nearly 60% off-invoice discounts and rebates resulted in net manufacturer revenue that is $40 billion lower.
- Protected brands in diabetes had invoice price increases of only 2.2% in 2020, but net prices declined 12.4%.
- Several factors are contributing to net price declines in diabetes, including the expansion of the 340B program and market competition.
- The 340B program allowing outpatient drug purchases to be made at the lowest net prices in the market for covered entities which serve the poor, and which has grown significantly in recent years.
- Market competition is a significant factor with multiple brands in newer mechanisms (DPP-IV, GLP-1, SGLT-2) offering negotiated discounts as well as patient savings programs (coupons), all of which lower net revenues even as the experience of diabetes costs for some are linked to list prices.
- Net revenue increased at 2% in 2020 and rose $7 billion since 2016 to $33 billion.

Exhibit Notes: Measures total value of spending on medicines, including generics, branded products, biologics, small-molecules, retail and non-retail channels. Invoice spending is based on IQVIA reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied. Includes all medicines in both pharmacy and institutional settings.

Autoimmune grew $10.8Bn to $77.1 Bn in 2020 driven by products launched in past five years and those with upcoming biosimilars

Exhibit 38: Autoimmune Invoice Spending and Growth Drivers



Source: IQVIA National Sales Perspectives, Dec 2020

- Autoimmune was the leading therapy area by invoice spending in 2020, but with more than half of current spending due to face loss of exclusivity by 2025, including adalimumab (Humira) in 2023 and ustekinuamb (Stelara) in 2024.
- Products facing upcoming losses of exclusivity through 2025 were contributing 7.6% to the total 16.4% growth in 2020, suggesting that spending will decline sharply when biosimilars appear in 2023.
- New brands in the past five years now represent $13 billion in spending of the total market $77 billion, though it is estimated that off-invoice discounts and rebates for brands mean net revenues are on average 35-40% lower.as many newer products have significant negotiated discounts and patient savings (coupon) programs.
- Invoice prices for protected brands declined in 2020 after having slowed to near zero in 2019.
- Biosimilars, in this market relating to infliximab (Remicade), have relatively little contribution to spending ($523 million in 2020) but contribute to the declining growth from off-patent brands (LOE), which lowered 2020 growth by 1.5%.

Exhibit Notes: Spending at invoice levels. Autoimmune includes drugs which are indicated for a variety of autoimmune disorders including rheumatoid arthritis, psoriasis, ulcerative colitis, Crohn's disease, atopic dermatitis and others), and includes small molecules and biologics. Estimates of net revenues are based on comparisons of IQVIA audited spending at invoice levels to company-reported net revenues in public filings (see Methodology).

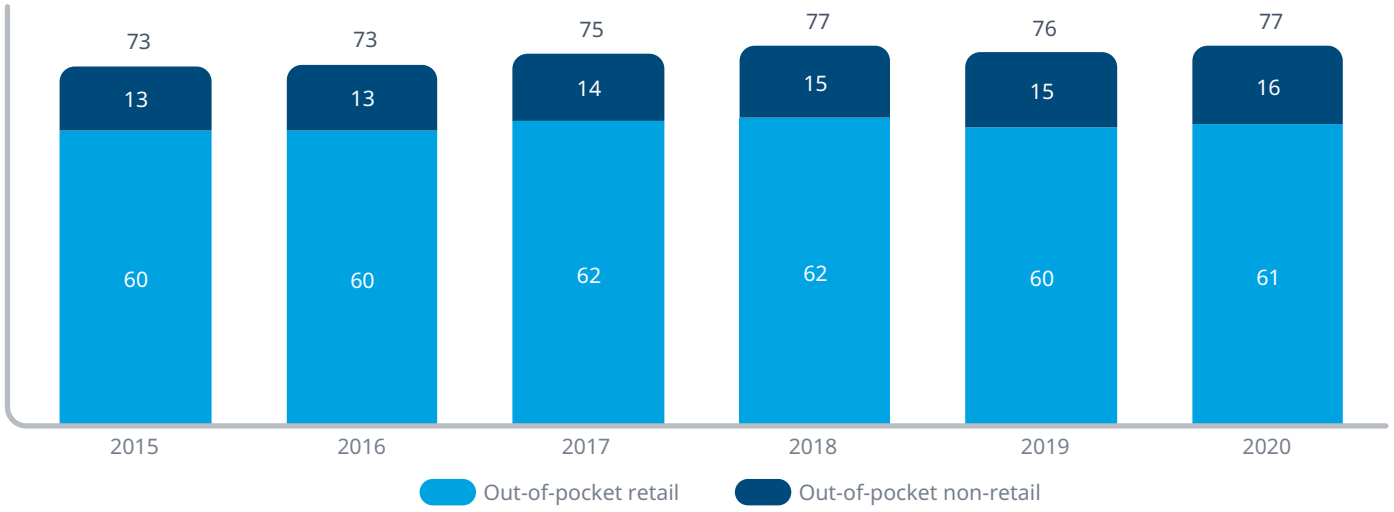
Patient out-of-pocket costs and affordability

- Out-of-pocket costs in aggregate increased $1 billion in 2020.
- Medicare aggregate out-of-pocket costs have risen over the past five years, with population increases offset by declining cost sharing.
- The average amount paid out-of-pocket per retail prescription has dropped from $10.33 in 2015 to $9.81 in 2020.
- Generics and branded generics account for 19% of invoice-level spending but represent 65% of patient out-of-pocket costs.
- Overall, 8% of patients reach annual out-of-pocket costs above $500 compared to 17% in Medicare, in large part due to benefit design.
- Over 92% of branded and generic prescriptions have a final out-of-pocket cost below $20, and only 0.9% have a cost above $125.
- Patients starting new therapy abandoned 55 million prescriptions at pharmacies in 2020 with increasing frequency as costs rise.
- Increasingly patients are using savings programs offered by manufacturers to offset costs.

While average prescription costs are declining, large numbers of patients — in private plans, Medicare and the uninsured — are faced with higher costs.

Out-of-pocket costs in aggregate increased $1 billion in 2020

Exhibit 39: Aggregate Patient Out-of-Pocket Cost for Medicines Dispensed in Retail and Non-Retail Settings, US$Bn



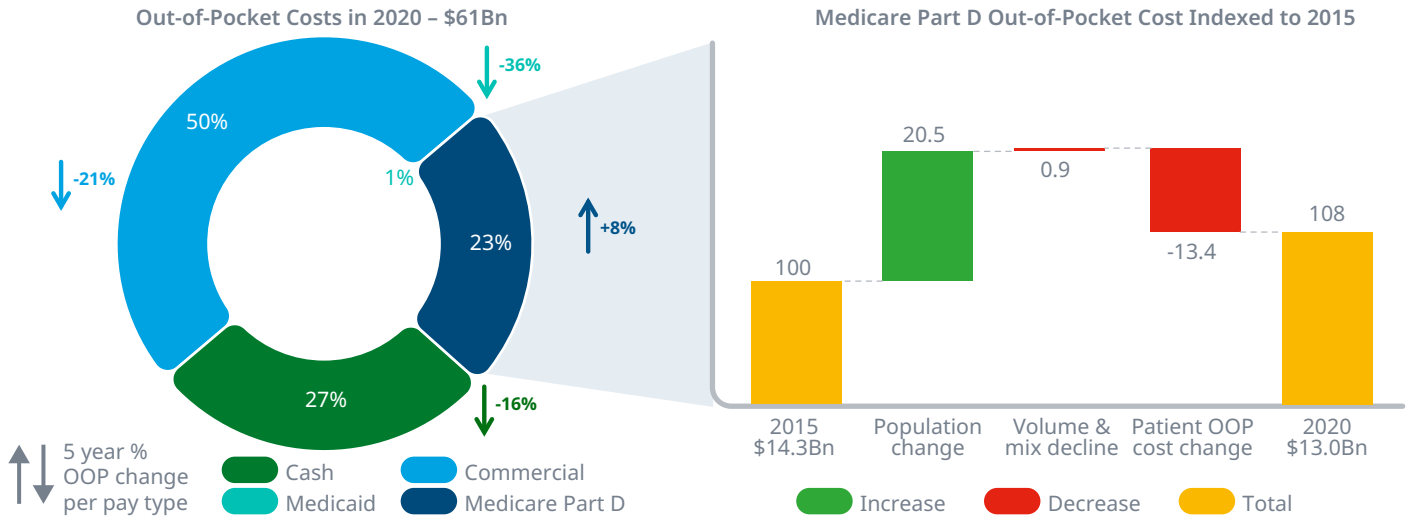
Source: IQVIA Xponent; IQVIA LAAD Sample Claims Data, Jan 2015–Dec 2020; IQVIA Institute, May 2021; CMS National Health Expenditures (NHE), Dec 2020

- Retail pharmacy out-of-pocket costs have risen from $60 billion in 2015 to $61 billion in 2020, though some patients have seen their costs decline during this period.
- Patients with Medicare Part D or high-deductible private health plans have seen individual prescription costs rise in line with the rising list prices of drugs but be offset by the Medicare "donut hole" subsidy program or the use of coupons, respectively.
- As out-of-pocket costs have risen, coupons for commercially-insured patients have reached $14 billion in 2020, including the use of pre-paid debit cards issued to eligible patients by manufacturers.
- This use of coupons and debit cards is occurring alongside benefit-design changes, including the preponderance of deductibles in most private insurance plans and a rising number of them termed high-deductible plans, which expose patients to the list price of a drug until a deductible is met.
- Among commercially-insured patients on branded medications, 14% of them used coupons to reduce their out-of-pocket costs in 2020.
- Patient out-of-pocket costs for non-retail medicines reached $16 billion in 2020, up from $13 billion in 2015, which represent a smaller share of total costs for patients with deductibles or out-of-pocket maximums, but can be significant for those few in private insurance without a maximum or for Medicare patients who do not have supplemental insurance and who pay 20% of medical costs without a cap.

Exhibit Notes: OOP costs are estimated based on prescription volumes and observed OOP costs. OOP costs are projected from a sample in the IQVIA LAAD sample claims data to a national estimate using national adjusted prescriptions, which were back-projected to estimate the trend prior to a trend break after 2016 due to restatement of NPA volumes (see Methodology). Values have been restated from past reports.

Medicare patient out-of-pocket costs have decreased over the past five years, as population increases offset by declining cost sharing

Exhibit 40: Aggregate Patient Out-of-Pocket Cost for Prescriptions and Value Offset by Coupons



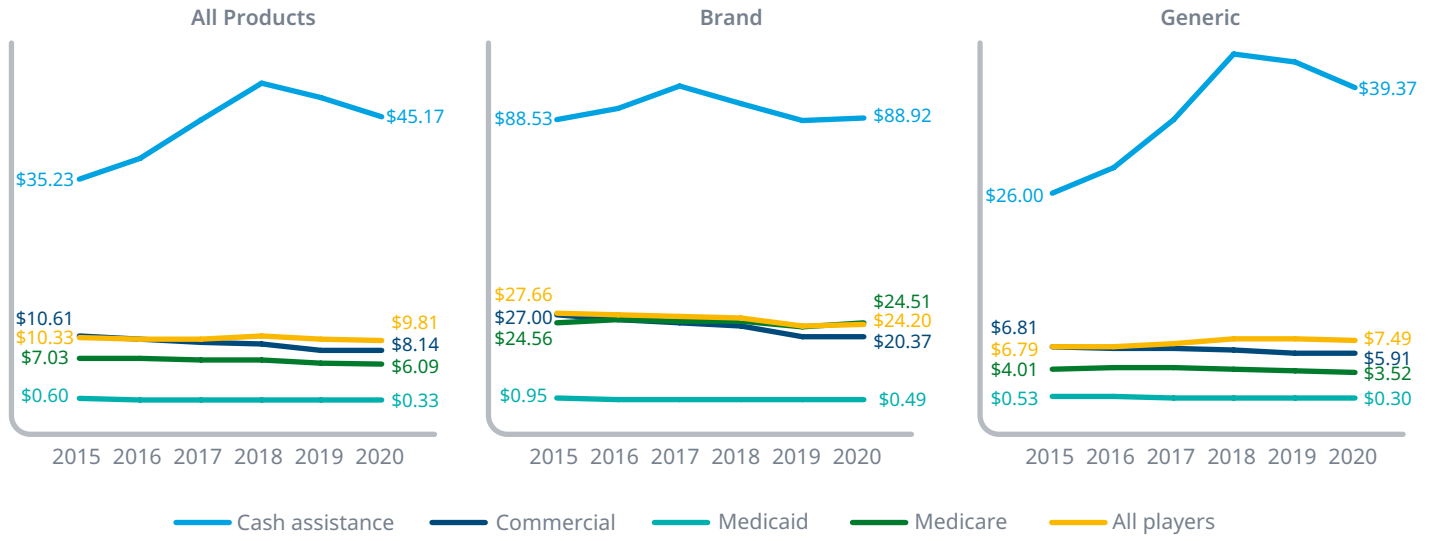
Source: IQVIA Xponent; IQVIA LAAD Sample Claims Data, Jan 2015–Dec 2020; US Census Bureau; IQVIA Institute, May 2021; CMS National Health Expenditures (NHE), Dec 2020

- Medicare out-of-pocket costs rose, in aggregate, by 8% from $11.1 billion to 11.9 billion in 2020, as total spending by beneficiaries would have risen 21% due to population growth, but declined a combined 14% due to the mix of products used and the closure of the donut hole.
- Commercially insured patients or "third party" insured overall out-of-pocket costs declined 21% over five years as patients shifted coverage to Medicare and Medicaid, while cash patients saw their aggregate out-of-pocket costs decline by 16% as the number of uninsured dropped even as rising costs linked to list prices raised their cost exposure per prescription.
- Patients paying cash account for 27% of overall patient out-of-pocket costs and paid $14 billion in 2020, for only 4% of prescriptions, for which they received 97% generic medicines (see exhibit 20).
- Medicaid patients account for 11% of prescriptions and 1% of patient out-of-pocket costs as most of their costs are waved as the basis for the program.

Exhibit Notes: OOP = 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. Note, 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, or where a mode pay type was impossible to determine. Volume and mix growth is the remainder of all growth minus population and price growth.

The average amount paid out-of-pocket per retail prescription has dropped from $10.33 in 2015 to $9.81 in 2020

Exhibit 41: Average Final Out-of-Pocket Cost per Retail Prescription by Type and Method of Payment, 2015–2020



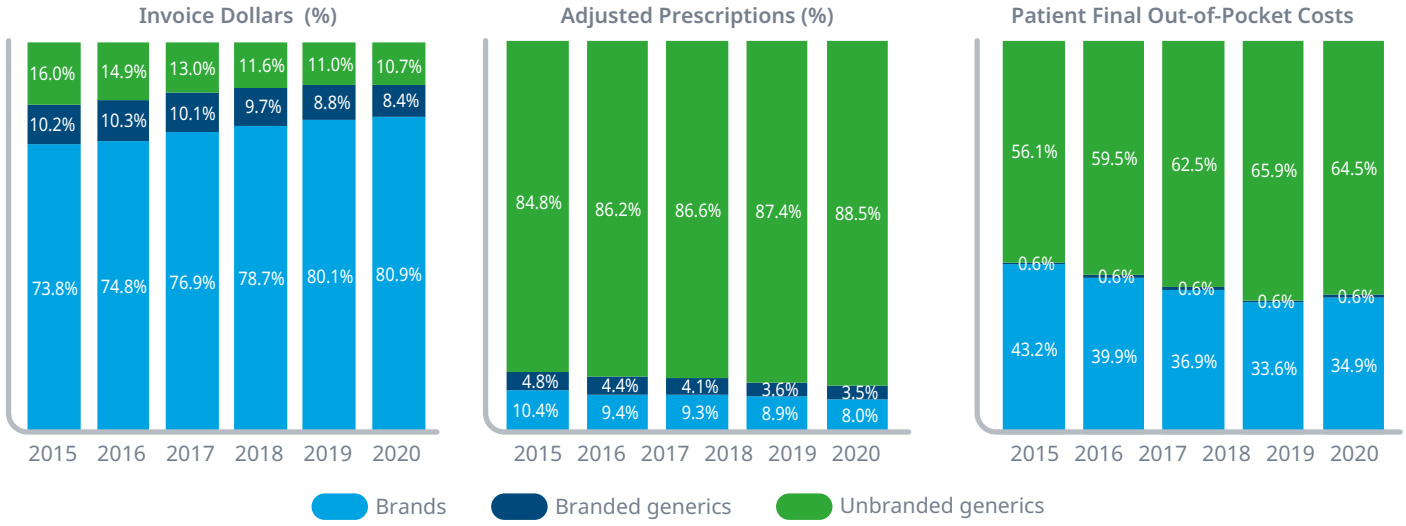
Source: IQVIA LAAD Sample Claims Data, Jan 2015–Dec 2020

- Overall, average out-of-pocket costs are not rising rapidly, with an average cost declining from $10.33 in 2015 to $9.81 in 2020 across all products and all payers.
- Uninsured patients paying with cash have seen costs rise for all types of products from $35.23 to $45.17, largely driven by generic prices which rose until 2018 and then have been declining.
- Medicare average prescription costs dropped from $7.03 to $6.09 as brand costs declined $0.05 and generic costs declined $0.49 but generics were used more often; all of these cost changes embed the benefit design changes associated with closing the 'donut hole'.
- Commercially-insured patient prescription costs have declined from $10.61 to $8.14 as brand costs dropped from $27.00 to $20.37 over five years, predominately from the use of coupons to offset higher list prices.
- For generics, commercial and Medicare patients have seen their costs decline while cash-paying patients saw costs rise from $26.00 in 2015 to $43.60 in 2018 and then drop to $39.37 in 2020.

Exhibit 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 19% of invoice-level spending but represent 65% of patient out-of-pocket costs

Exhibit 42: Share of Spending, Prescriptions and Patient Out-of-Pocket Costs by Product Type, 2016–2020



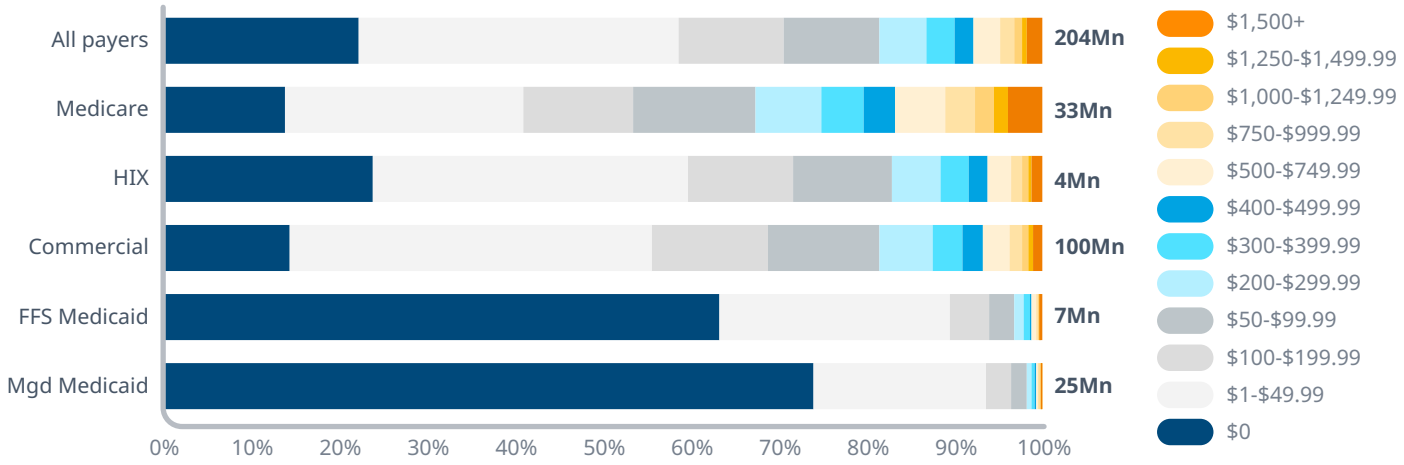
Source: IQVIA National Sales Perspectives; IQVIA National Prescription Audit, Dec 2020; IQVIA LAAD Sample Claims Data, Dec 2020

- 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 19.1% invoice-level spending, they account for 65.1% of patients' out-of-pocket costs.
- Over the past five years generic share of invoice-level spending has dropped from 26.2% to 19.1% while the share of prescriptions has risen from 89.6% to 92.0%, 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.

Exhibit Notes: Prescription counts are adjusted for length of prescriptions and re-aggregated. Prescriptions referred to as '90-day' are calculated based on transactions with 84 days supply or more to include medicines with up to one week fewer treatment days. Prescriptions for 84 days supply or more or factored by three, and those under 84 days unchanged. Due to changes in data collection data after 2016, adjusted prescription total has been back-projected based on published growth rates from prior Institute reports to estimate the number of adjusted prescriptions in 2016.

Overall, 8% of patients reach annual out-of-pocket costs above $500 compared to 17% in Medicare largely due to benefit design

Exhibit 43: Patients by Annual Prescription Out-of-Pocket Cost in 2020



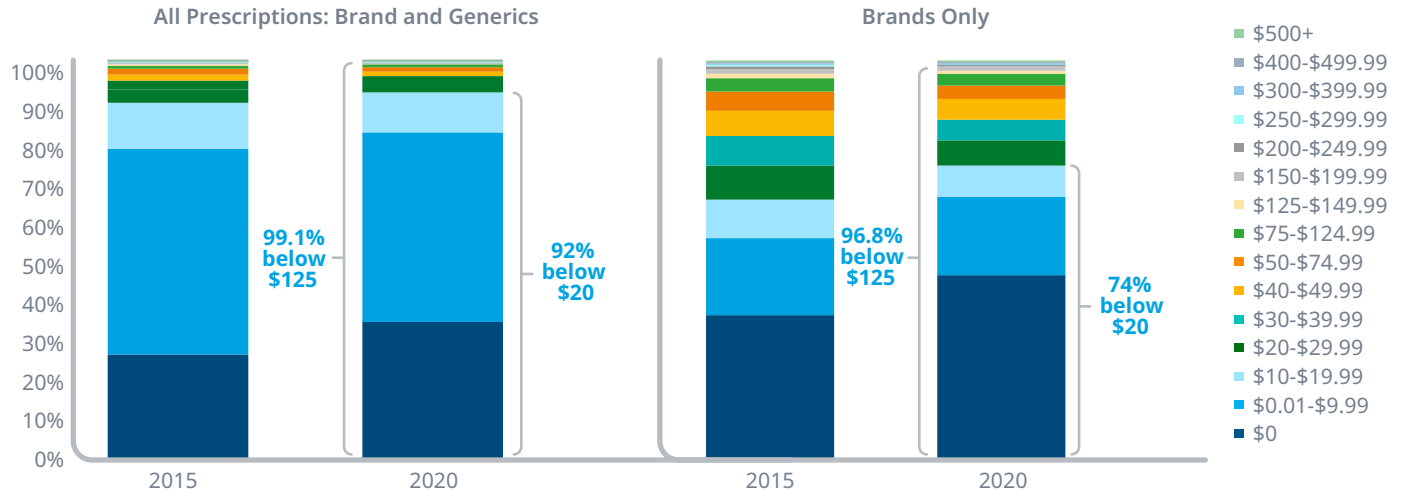
Source: IQVIA LAAD Sample Claims Data, Dec 2020

- Across all pay types, 8% of patients pay more than $500 and 1.8% pay more than $1,500 out-of-pocket for prescriptions.
- In Medicaid, only 1.9% of patients pay more than $500 out-of-pocket for prescriptions, and only 0.3% pay more than $1500, and these most likely relate to patients on a different kind of insurance for part of the year.
- In Medicare, 17% 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.
- As a result, seniors have higher cost exposures than the commercially-insured population.
- In commercial coverage, 6.7% of patients pay more than $500 compared to 6.3% in ACA health insurance exchanges (HIX) and 1.1% pay more than $1,500 in both kinds of commercial plans.
- For the millions of seniors who become Medicare eligible each year, the cost exposure difference as their insurance changes can be a significant shock, which could lead to changes in adherence to planned medication.

Exhibit Notes: Patients who filled at least one prescription in our sample were included. Patients were grouped into cohorts by mode pay type and costs aggregated in the year.

Over 92% of branded and generic prescriptions have a final out-of-pocket cost below $20, and only 0.9% have a cost above $125

Exhibit 44: Distribution of Prescriptions by Out-of-Pocket Cost in 2020, All Channels



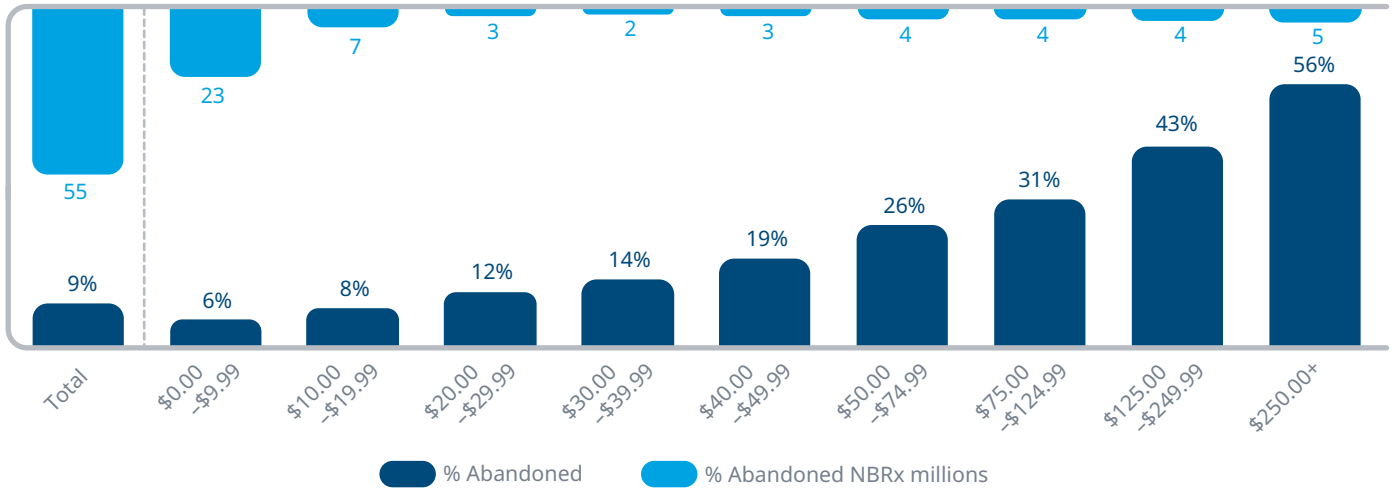
Source: IQVIA LAAD Sample Claims Data, Jan 2015–Dec 2019

- Over 92% of all prescriptions have final out-of-pocket costs below $20, which is up 2.4 percentage points from 2015.
- Branded prescriptions with final out-of-pocket costs below $20 account for 74% of brands filled in 2020, up from 65% in 2015.
- Out-of-pocket costs above $125 for a normalized monthly prescription account for 0.9%, down from 1.1% in 2015.
- Only 3.2% of branded prescriptions have out-of-pocket costs above $125, down from 4.2% in 2015.
- Many patients have paid lower costs year-over-year due to a variety of shifts in benefit designs, coupon programs, patient assistance programs, rising Medicaid enrollment, and mandated supports, such as the Medicare Part D donut-hole subsidy.
- While relatively few patients fill prescriptions at higher cost levels, abandonment is higher, and those prescriptions may be underrepresented as those prescriptions might have been abandoned due to cost (see exhibit 45).
- A rising number of prescriptions are now dispensed with a $0 payment by the patient and now amount to 46% of all branded prescriptions in 2020, up from 36% in 2015.
- 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.

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

Patients starting new therapy abandoned 55 million prescriptions at pharmacies in 2020 with increasing frequency as costs rise

Exhibit 45: 14-day Abandonment Share of New-to-Product Prescriptions by Final Out-of-Pocket Cost in 2020, All Payers, All Products



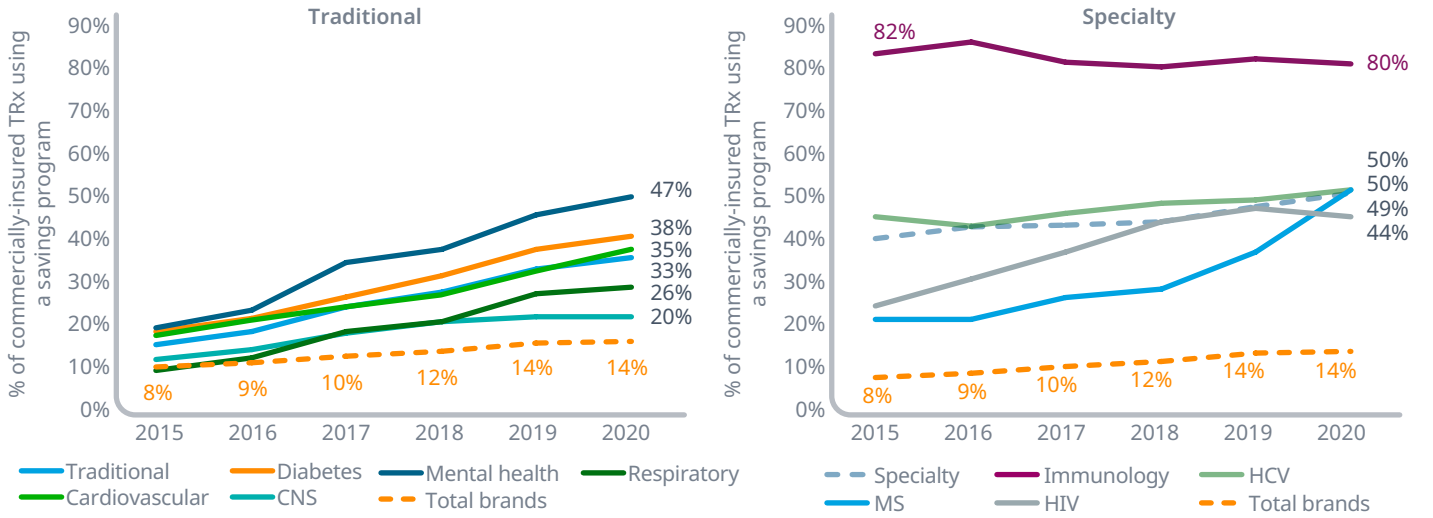
Source: IQVIA LAAD Sample Claims Data, Dec 2020

- The number of prescriptions written and transmitted to pharmacies by doctors, either by traditional paper, by phone or electronically, exceeds the number that patients actually had filled, for a variety of reasons.
- Some patients choose not to fill a prescription if they don't agree with the doctor's advice or find it inconvenient to do so, but the more common reason is the cost of the prescription.
- Of prescriptions with a final cost above $500, 56% are not picked up by patients, as compared with 6% of patients who do not fill when the cost is less than $10.
- The overall abandonment rate for all prescriptions across all pay types is 9% but rises consistently as cost exposure increases.
- Of the 55 million new-to-product prescriptions abandoned in 2020, 23 million were abandoned when costs were under $10, while the remaining 32 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 12% or less. This can be compared to a non-preferred brand copay of $75 with an abandonment of 26% 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.

Exhibit 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.

Increasingly patients are using savings programs offered by manufacturers to offset costs

Exhibit 46: Percent Utilization of Savings Programs for Commercial Branded Prescriptions, Selected Traditional and Specialty Therapy Areas



Source: IQVIA LAAD Sample Claims Data, Dec 2020

- As out-of-pocket costs have risen, coupons for commercially-insured patients have been increasingly used, reaching $14 billion in 2020, including an estimate of pre-paid debit cards – and helping lower commercially-insured patients out-of-pocket costs over the period.
- Of commercially-insured patients on branded medications, 14% of them used coupons to reduce their out-of-pocket costs in 2020.
- Coupon usage in some therapy areas is far higher, however, and reached 47% in mental health and 80% in immunology.
- Savings programs include coupons, e-coupons, pre-paid debit cards, and average 50% of brand prescriptions in some of the highest overall spending specialty therapy areas, compared to 33% of leading traditional medicine therapy areas.
- The use of coupons is also a relatively good indicator of the competitive intensity in the therapy area where multiple competitors are negotiating with payers for market access and using coupons to help patients with costs in the event they lose those contracts.

Exhibit Notes: Prescriptions for patients with commercial insurance are assessed for whether there was a supplementary payer identified by IQVIA as a coupon or savings program.

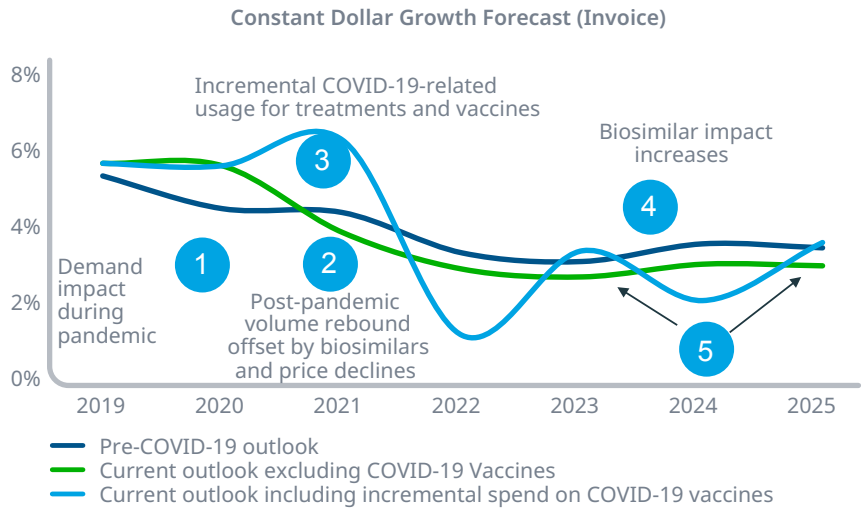
Outlook to 2025

- U.S. market growth will return to pre-pandemic projections by 2025 despite year-to-year fluctuations.
- Policy changes impacting the use of medicines are likely to be phased in over the next five years.
- The U.S. spending forecast reflects an increasing gap between invoice level spending and manufacturer net revenues.
- New brand spending in the U.S. is projected to be higher than the last five years but a smaller share of spending.
- Net price growth for protected brands is forecast to be 0 to -3% through 2025.
- Losses of exclusivity expected to result in $128 billion of lower brand spending through 2025 with $39 billion from branded biologics.
- Biosimilars mature, and the impact of medicines facing new biosimilar competition in 2023 and 2024 will have a large impact.
- Immunology, oncology, and neurology drive growth.
- U.S. oncology spending to exceed $110 billion by 2025, with growth slowing to 10% from biosimilar savings.
- Diabetes spending to decline 2-5% through 2025 as off-invoice discounts and rebates continue to offset list prices.
- Treatments for autoimmune disorders to exceed $130 billion in the U.S. by 2025, slowing after 2023 due to key biosimilars.

Total net spending on medicine is expected to reach $380–400 billion in 2025, reflecting a compound annual growth rate of 0–3%.

U.S. market growth will return to pre-pandemic projections by 2025 despite year-to-year fluctuations

Exhibit 47: Comparison of Current Outlook to Pre-COVID-19 Outlook



Key Changes in the Outlook

1. 2020: +1.0 (~$5 billion)
2. 2021: -0.4% below pre-COVID-19 growth; -1.5% below 2020 growth as volume returns but biosimilars offsets growth
3. Current outlook for 2021 including vaccines +2% over outlook that excludes vaccines due to ~$9–12 billion of vaccine spending, later reduced as volume shifts to biennial boosters and prices drops over time
4. Biosimilar market impact expected to be substantial in 2023–25, offset by flow of innovative products
5. Vaccine spending declines as biennial boosters and costs decline in the endemic phase, followed by overall growth returning to expected levels

Source: IQVIA Market Prognosis, Sep 2020; IQVIA Institute, Mar 2021

- While the short-term impact from COVID-19 in 2020 and 2021 has been significant, the long-term impact on growth trends is more muted.
- Including estimates of higher spending growth from COVID-19 vaccines and lower spending from existing treatments due to disruptions from the pandemic, the five-year CAGR to 2025 is unchanged compared to the pre-COVID-19 outlook and the forecasts differ by only 0.2% within the range of uncertainty of 2-5%.
- These dynamics reflect the relative resilience of spending levels in the U.S. market compared to other countries and the already rapid progress in the unprecedented mass vaccination program.
- The spending associated with COVID-19 vaccines is expected to add approximately 2% of spending growth in 2021, dipping in 2022 as fewer need new shots, and rebounding in 2023 and 2025 with expected need for booster shots.
- Because the effectiveness of current vaccines against new variants, as well as the duration of immunity, remains uncertain, it is expected that many people will need to receive new booster vaccinations in future years.
- If vaccinations fail to reach herd immunity levels, it is likely that continued waves of infections and economic and health impacts will be felt for years to come, though based on current trends, this may be rarer and isolated to certain geographic areas within the U.S.

Exhibit Notes: Pre-COVID-19 outlook based on IQVIA Market Prognosis, Sept. 2019 edition. Current outlook based on IQVIA Market Prognosis Sept. 2020 edition. Incremental COVID-19 vaccine scenario based on current outlook combined with incremental spending for vaccines.

Policy changes impacting the use of medicines are likely to be phased in over the next five years

Exhibit 48: Selected Policy Areas with Likely Legislation or Executive Order Implementation through 2025

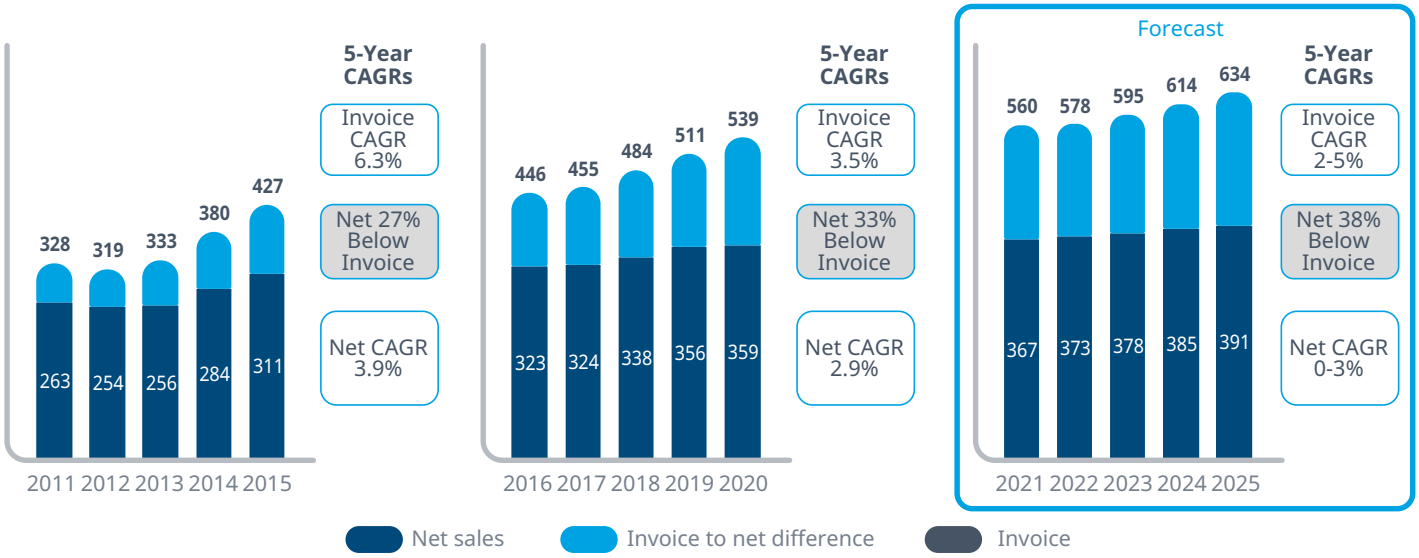
Medicaid	Medicare	Commercial
• Medicaid 5% increase in matching funds from stimulus • Medicaid drug rebate cap removal in 2024 resulting in some rebates >100%	• Medicare buy-in options at lower ages • Price negotiation in Medicare • Cost sharing changes for patients in Medicare including caps in out-of-pocket • Changes in rebate structure for manufacturers, payers and CMS	• Exchange subsidies temporary boost through 2022 • Expanded ACA Open Enrollment periods • Reform to accumulator adjuster / maximizer plan designs • Net-price cost sharing for deductible / co-insurance

Source: IQVIA Institute, May 2021

- Policies affecting medicine costs could include the legislation H.R.3, which as passed the House but not the Senate (where this looks uncertain), as well as policies included in the stimulus in March 2021.
- One provision was to remove the cap on Medicaid rebates at 100%, which if removed could affect some established branded products if price increases were faster than inflation for a sustained period, and which would result in additional rebates flowing to Medicaid, which states benefit from.
- The stimulus bill also included a 5% increase in matching funds to states for Medicaid, which will help during the pandemic as states have significant tax revenue shortfalls but will also potentially encourage the 14 remaining states to consider Medicaid expansion.
- Medicare policies include expanding eligibility to younger enrollees in the so-called Medicare at 60 or allowing younger people to buy into the program by choice, are part of a mosaic of issues including caps on out-of-pocket costs as well as reforms to pricing and rebate structures that would help pay for these changes.
- As with the last administration, it is notable that policies affecting Medicare are potentially addressable with executive orders, and this could occur particularly if legislation stalls in Congress.
- States have also entered these debates, with nearly a dozen enacting restrictions on accumulator adjuster/ maximizer plans to ensure patients receive their share of negotiated rebates.

The U.S. spending forecast reflects an increasing gap between invoice level spending and manufacturer net revenues

Exhibit 49: U.S. Medicine Spending and Growth at Invoice-Level and Estimated Net 2011–2025



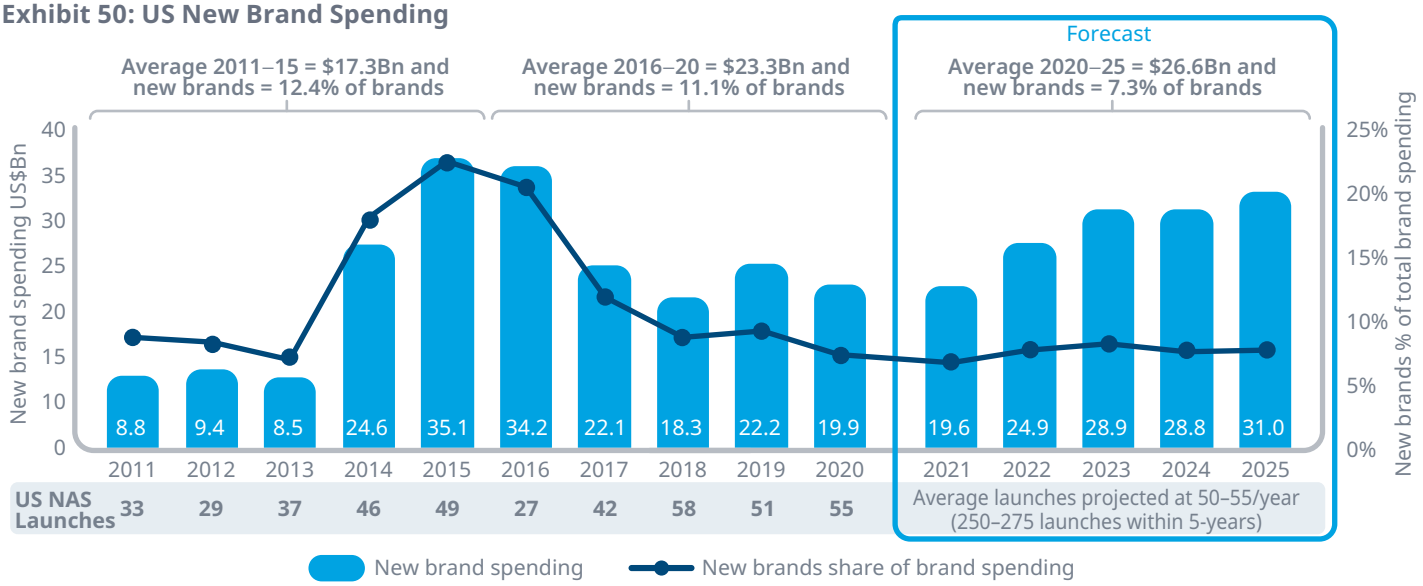
Source: IQVIA Institute, Feb 2021

- Total net spending on medicines is expected to reach $380-400 billion in 2025, up from $359 billion in 2020, and includes spending across all channels and product types.
- Over the next five years, medicine spending will grow between 2–5% on an invoice basis and 0–3% after off-invoice discounts and rebates.
- Growth will be driven by adoption of newly launched innovative products, which are expected to occur at higher levels than in past years 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 effect of price growth on overall spending over the next five years is expected be 0 to -3% as list price increases continue at historically low levels and net prices will decline in markets with significant competitive intensity.

Exhibit Notes: Invoice spending is based on IQVIA reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied. Includes all medicines in both pharmacy and institutional settings.

New brand spending in the U.S. is projected to be higher than the last five years but a smaller share of spending

Exhibit 50: US New Brand Spending



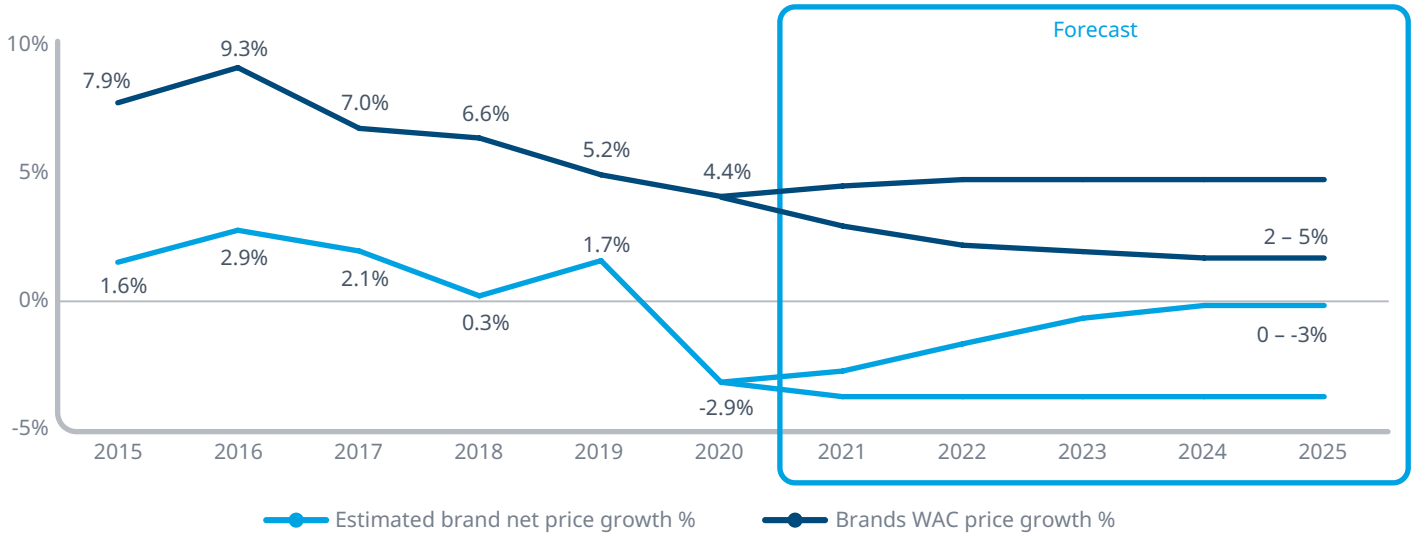
Source: IQVIA Institute, Feb 2021

- The growing output of R&D is expected to continue to result in an average 50–55 NASs per year and an aggregate of $133 billion of new drug spending over five years.
- NAS launches in 2020 reached 55, even as the aggregate amount of new brand spending dipped partly because more medicines are for smaller populations and generate less spending per drug.
- Over the next five years, 250–275 NAS launches are expected but are anticipated to represent 7.3% 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.

Exhibit Notes: NAS = new active substance. New brands are protected branded products on the market less than 24 months during the year reported.

Net price growth for protected brands is forecast to be 0 to -3% through 2025

Exhibit 51: Protected Brand Invoice and Net Price Growth



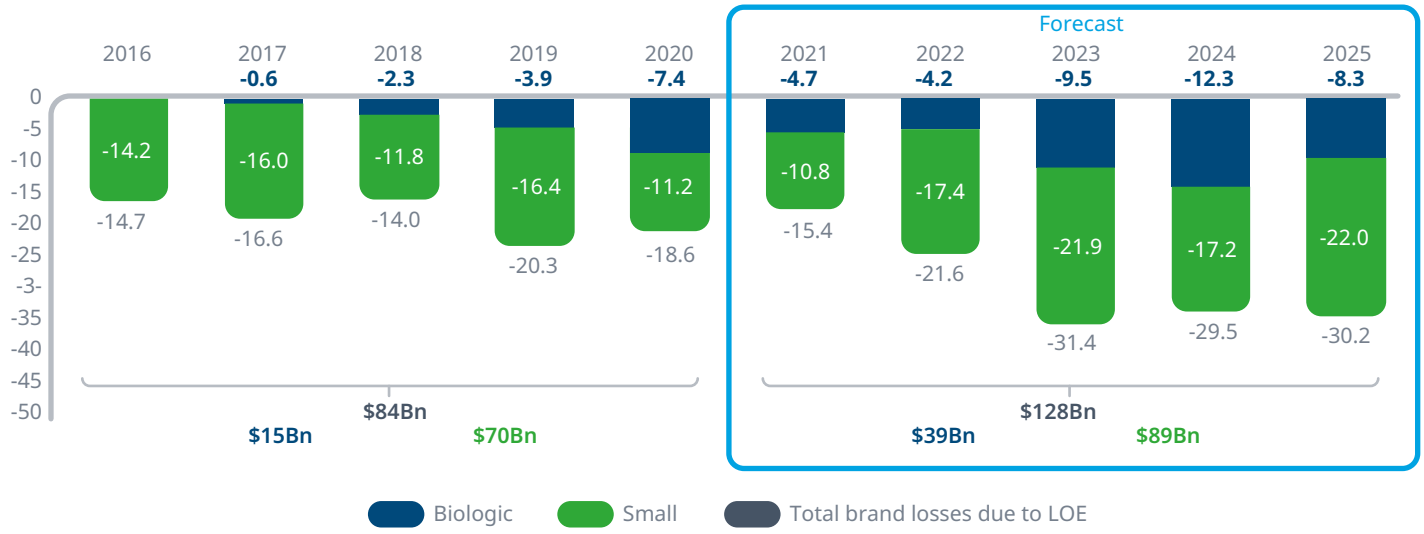
Source: IQVIA Institute, May 2021

- As public pressure on drug pricing has escalated, list price increases have slowed to 4.4% in 2020 and are expected to average 2–5% per year through 2025.
- Net price growth is likely to continue to see declines in the 0 to -3% range as the structural drivers of low net price growth are expected to remain in effect and be amplified by increased competitive intensity in many therapy areas, especially those with new launches and/or upcoming biosimilar events such as diabetes and immunology.
- Some products and therapy areas may be able to increase net prices to a greater or lesser extent, linked to the level of differentiation and/or competition in their markets.
- The lower level of net price growth and the continued gap between invoice and net price growth reflect the higher levels of off-invoice discounts, rebates and price concessions, which began to increase in 2012 and have continued.
- While there is a clear expectation that drug pricing policies will be reformed, there are likely impacts of those policies on either invoice prices, consumer out-of-pocket costs or net prices, and the exact nature of those changes remain significantly uncertain.

Exhibit 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).

Losses of exclusivity to result in $128 billion of lower brand spending through 2025 with $39 billion from branded biologics

Exhibit 52: Impact of Brand Losses of Exclusivity 2016–2025, US$Bn



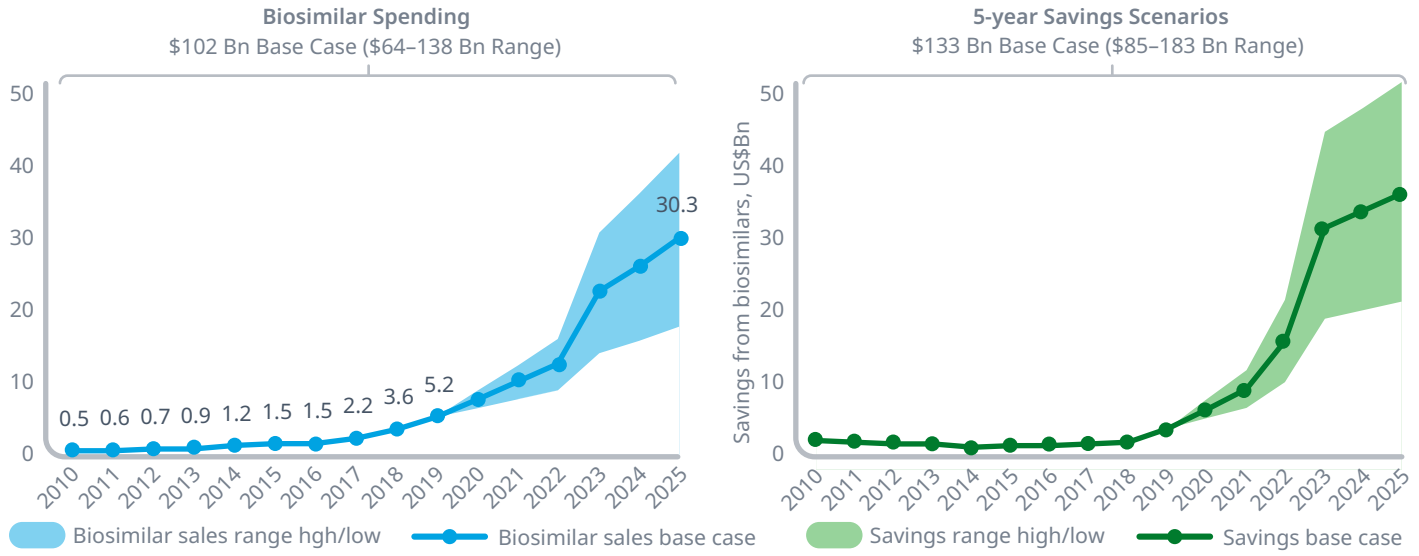
Source: IQVIA National Sales Perspectives; IQVIA Market Prognosis; IQVIA Institute, Feb 2021

- The impact of patent expiries is expected to increase over the next five years as both small molecules and biologics will increase by almost $30 billion in brand losses compared to the last five years.
- The largest biologic impact is expected in 2023 when adalimumab (Humira) is expected to face competition. While biosimilars for this drug are already approved, litigation and settlements between originators and biosimilar companies have agreed 0n market entry in early 2023.
- While 2020 has seen some of the largest overall impact on branded spending from biosimilars, mainly from those that entered in 2019 — bevacizumab, rituximab and trastuzumab — and to a lesser extent, new biosimilars in 2018 — pegfilgrastim, insulin lispro and epoetin alfa.
- Small molecule expiry impact in 2023 is the largest in the outlook with medicines expiring in 2022, such as Januvia and Spiriva, fully impacting the market in 2023.

Exhibit 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.

Biosimilars mature and the impact of medicines facing new biosimilar competition in 2023 and 2024 will have a large impact

Exhibit 53: Biosimilar Spending and Savings Scenarios



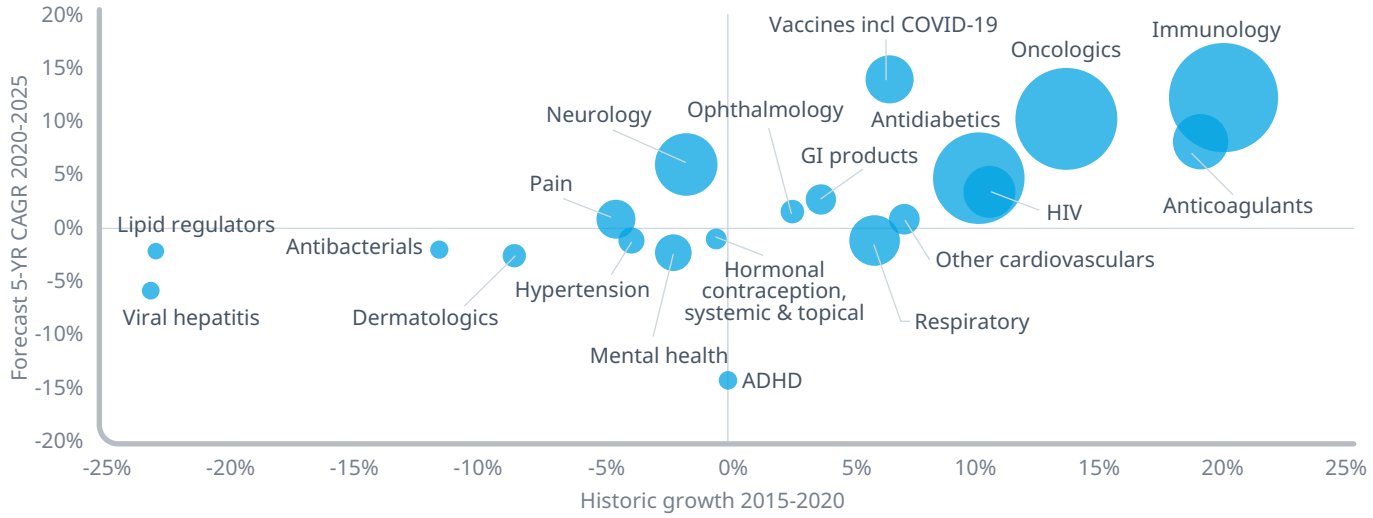
Source: IQVIA Institute, Dec 2020

- The first biosimilars approved in the U.S. captured an average 15–30% share of their respective molecules and averaged 15% from Q2 2013 to Q3 2016.
- Since then, newer biosimilars have generated much higher volume shares and projected biosimilar spending is expected to reach $30 billion in 2025 and a total of $102 billion over the next five years.
- Savings from biosimilars — the difference between projected spending with and without biosimilars — is expected to be $35-40 billion in 2025 and a cumulative five years total of $133 billion, but with significant uncertainties around these projections.
- Future biosimilars may continue to achieve very high-volume shares as recent entrants have, but that will depend on the number of competitors in each molecule, their decisions as well as the competitive actions of originators and the cost negotiating tactics of insurers and drug purchasers.
- In some cases, negotiations may even spill over into other still-patent-protected brands in the same therapy areas, resulting in higher discounts, rebates, and use of coupons.
- With the scale of savings potentially in the balance, there will be significant attention focused on the evolution of these markets, and if savings are below expectations, policymakers will likely review policies which incentivize biosimilar development and uptake as well as those around originator periods of exclusivity.

Exhibit Notes: Biosimilar spending projections based on pricing and volume assumptions, extended to 2025 (See *IQVIA Institute Report Biosimilars in the United States 2020-2024*, Oct 2020).

Immunology, oncology, neurology drive growth through 2025 along with COVID-19 vaccines

Exhibit 54: US Historic and Forecast Growth for Top 20 Therapy Areas



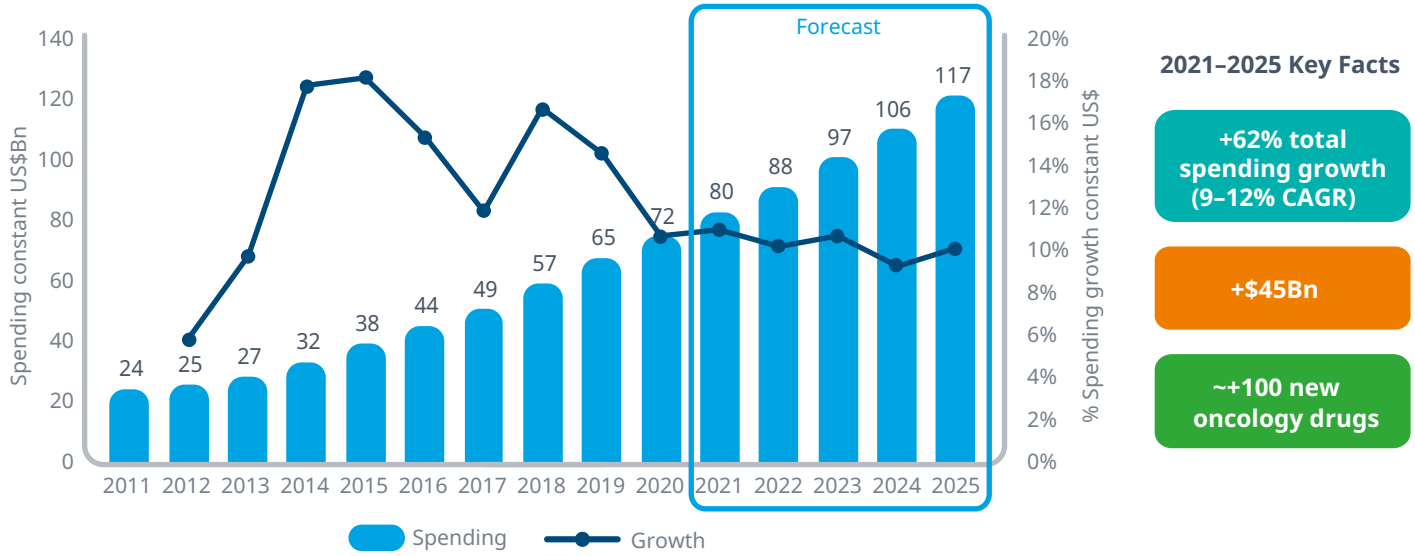
Source: IQVIA Institute, Feb 2021

- Immunology, oncology and neurology represent the largest aggregate contributors to growth in the next five years, predominately from a continued flow of new medicines and offset by losses of exclusivity.
- Overall growth in neurology is not significantly lower than diabetes but has much lower discounts and rebates and embeds significant upside uncertainty related to Alzheimer's and Parkinson's therapies as well as rare neuromuscular disorders.
- Therapy areas with lower growth in the next five years than in the last five, including ADHD, dermatology, mental health and respiratory, are consistently those focused in more traditional therapy areas where fewer new launches have happened and where savings from losses of exclusivity are contributing to lower growth.

Exhibit Notes: Bubble size represents forecast in 2025; COVID vaccine estimates based on estimates of periodic booster shots; neurology includes nervous system disorders such as epilepsy, Parkinson's, Alzheimer's, other neurological disorders but excluding mental health or pain. Neurology estimate based on risk-adjusted potential for Alzheimer's approval and uptake.

U.S. oncology spending to exceed $110 billion by 2025,with growth slowing to 10% from biosimilar savings

Exhibit 55: Oncology Non-Discounted Spending and Growth



2021–2025 Key Facts

+62% total spending growth (9–12% CAGR)

+$45Bn

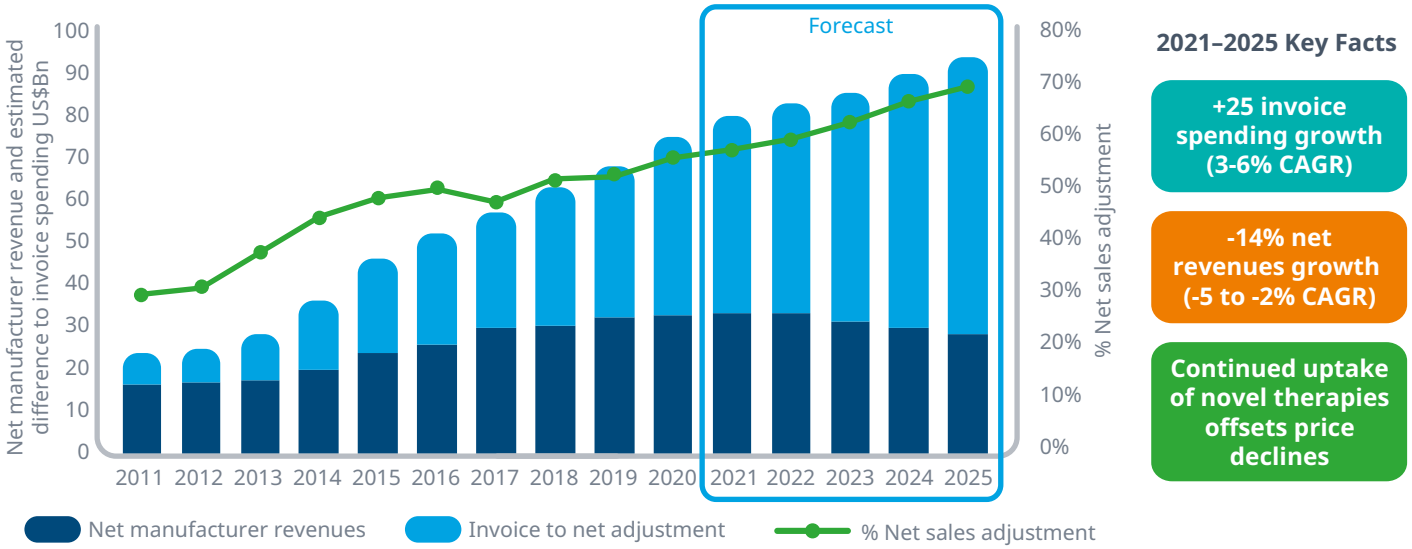
~+100 new oncology drugs

Source: IQVIA Institute, Feb 2021

- U.S. oncology spending is expected to slow to 9-12% through 2025 as biosimilars offset a continued flow of newer treatments.
- Over the next five years spending is expected to increase 62%, an average of 9-12% per year, and add $45 billion in spending.
- More than 100 new oncology drugs are anticipated based on current pipeline, although they are expected to be increasingly narrowly focused as precision medicine and biomarker-driven therapies become more common.
- While some therapies are being developed with wide tumor applicability and are being approved based on biomarkers or mutations and termed ‘tissue-agnostic’ approvals, there are also a continued flow of treatments for very specific tumor or biomarker situations which do not translate to wider use.
- In addition to the flow of more biomarker-driven therapeutic choices, developed markets will benefit from wider use of next-generation sequencing technologies (NGS), which can test for multiple potential mutations at once and guide therapy selection more precisely.
- While still in earlier stages of adoption, the use of liquid biopsies where NGS is used on blood samples has the potential to identify tumors much earlier and drive much more effective outcomes for patients.
- Savings from biosimilars are expected to contribute to slower spending growth despite the wide range of expected innovations.

Diabetes spending to decline 2-5% through 2025 as off-invoice discounts and rebates continue to offset list prices

Exhibit 56: Diabetes Spending and Growth at Net and Non-Discounted Levels



2021–2025 Key Facts

+25 invoice spending growth (3-6% CAGR)

-14% net revenues growth (-5 to -2% CAGR)

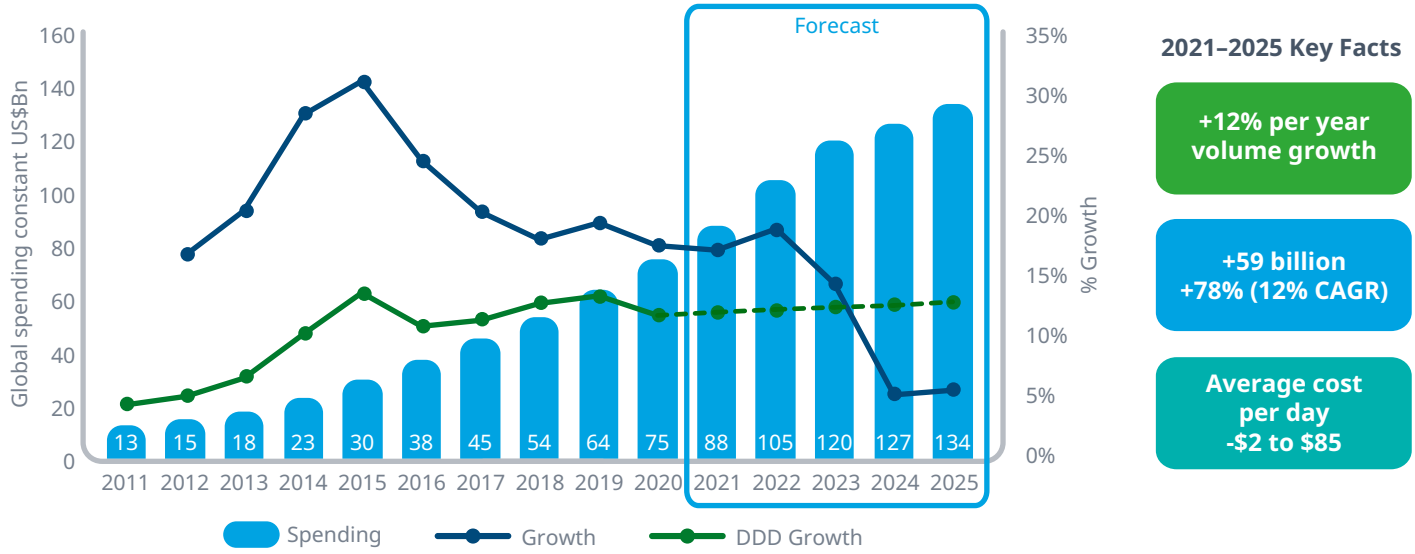
Continued uptake of novel therapies offsets price declines

Source: IQVIA Institute, Feb 2021

- 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.
- The key element in assessing trends in diabetes is the current 56% lower-than-net revenue in the U.S. compared to invoice and projected to increase to 70% lower by 2025, far higher than other therapy areas.
- Over the next five years net revenues for manufacturers will decline by 14%;at -2% to -5% CAGR as net price declines continue.
- Demographic shifts which will likely increase the number of diabetes patients will contribute to greater volume but be offset by net price reductions.

Treatments for autoimmune disorders to exceed $130 billion in the U.S. by 2025, slowing after 2023 due to key biosimilars

Exhibit 57: U.S. Autoimmune Non-discounted Spending Growth



2021–2025 Key Facts

+12% per year volume growth

+59 billion +78% (12% CAGR)

Average cost per day -$2 to $85

Source: IQVIA Institute, Feb 2021

- Over the past 10 years, immunology treatments have consistently been driven by increasing volume, averaging 12% volume growth in days of therapy and averaging 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 increase 78% or $59 billion.
- The average cost per day has been rising throughout the past 10 years as prices were rising but are expected to drop once new biosimilars enter the market in 2023.
- The introduction of biosimilar adalimumab (Humira) in 2023 and ustekinumab (Stelara) in 2024 will contribute significantly to lower costs for immunology treatments, with the full impact visible in 2024 when spending growth slows to 5%.
- Spending is expected to grow at a 12% CAGR through 2025, to exceed $134 billion.

Notes on sources

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

NATIONAL SALES PERSPECTIVES (NSP)™ 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.

REAL WORLD EVIDENCE is a suite of services that provides clinical evidence regarding the usage and potential benefits or risks of medical products or procedures derived from analysis of IQVIA Real World Data (RWD). IQVIA's RWD are a variety of information assets that represent the healthcare experiences of the patient. IQVIA's RWD provides near census-level coverage of dispensed prescription information at a prescriber and insurance plan level and tracks deidentified anonymous patient records over time to analyze distinct use patterns. Additionally, IQVIA's RWD captures information about the patient's medical, hospital, EMR, consumer, and laboratory experiences, among other details.

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

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

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

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.

Diagnosis, telehealth and procedural claims have been derived based on IQVIA's medical claims database through the week ending 5/29/2020. Normal claims processing lags are adjusted for by IQVIA using a methodology called "date control" in order to estimate claim levels where the full number of claims has not yet been received. The methodology considers historic patterns of lag periods between service dates and receipt of claims to project missing claims.

Disruptions from COVID-19 may result in claim lags that differ from historic patterns. IQVIA's medical claims database is dynamic and IQVIA will always employ the latest available information to consider in its estimates — therefore estimates of growth may change from publication to publication.

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

Methodologies

DISPENSED PRESCRIPTIONS ADJUSTED FOR 90-DAY PRESCRIPTIONS (method used in appendix tables)

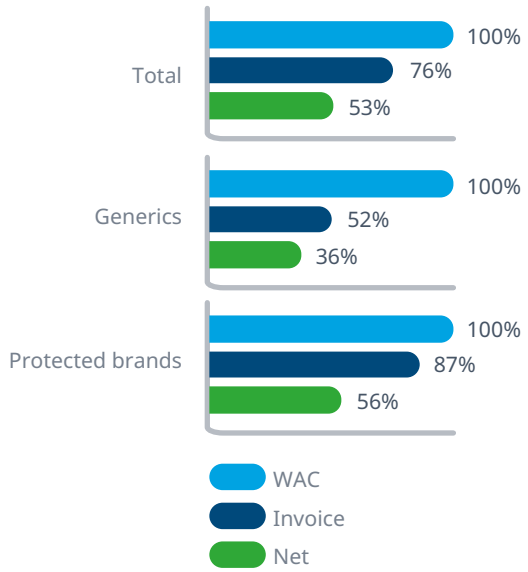
Prescriptions with >84 days supply to the patient are assumed to represent a three-month prescription, and all other prescriptions are assumed to represent a one-month prescription. Three-month prescriptions are factored by three to normalize prescriptions to one-month durations.

ESTIMATES OF NET MANUFACTURER REVENUE AND PRICES

IQVIA audits reflect invoice-based pricing derived from proprietary information gathered from wholesalers and company direct sales. While IQVIA invoice prices reflect supply-chain price concessions, they do not reflect the off-invoice discounts and rebates separately paid to insurers, or other price concessions paid to patients or other health system participants. Estimated net prices and revenue are projected from a sample of large and mid-sized companies analyzed from 2011–2020. Branded products are included in the sample if their net sales amount is disclosed in financial filings with the Securities and Exchange Commission (SEC) and if the volume of sales captured in IQVIA audits is consistent with information provided directly by manufacturers in support of IQVIA proprietary datasets. Net prices are calculated by dividing publicly reported net sales values by volumes for the same products reported to IQVIA. Estimated brand net price growth for the total market is projected from the analysis sample to the total market. Net prices represent an estimate of the average manufacturer realized price, reflecting any reductions in net revenues due to off-invoice discounts, rebates, copay assistance or other price concessions, and do not necessarily reflect the net costs paid by insurers, the federal government, or patients, which all vary significantly and independently. For generic companies, a sample of five large generic companies' generic portfolios were analyzed in aggregate consistent with their SEC filings, as specific generic product analyses are not possible. See Medicine Use and Spending in the United States, April 2019 for more details.

The IQVIA "net sales adjustment" analysis is based on ex-manufacturer invoice sale prices, which are lower than wholesaler acquisition cost (WAC). In the market overall, invoice prices are 24% below WAC, with net prices are 47% below that list price.

Exhibit 58: WAC, Invoice and Net Prices, 2020



Source: IQVIA Institute, Mar 2020

About the authors

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

About the Institute

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

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

Research Agenda

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

- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

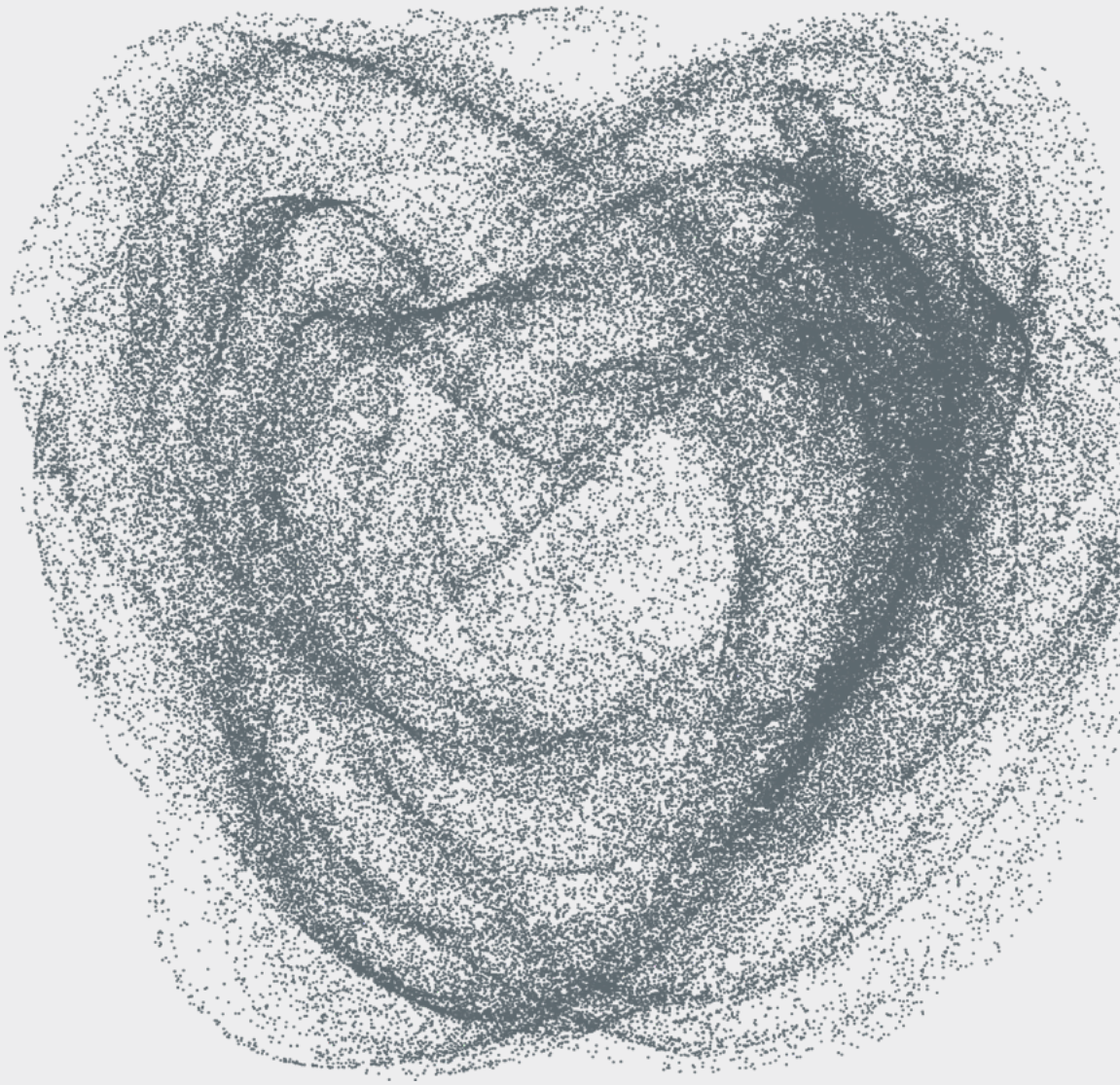
Guiding Principles

The Institute operates from a set of guiding principles:

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

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

The data is based on medical claims and dispensed new prescriptions related to the utilization of health services in the U.S. after the start of the COVID-19 pandemic as explored in the first chapter of this report.



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