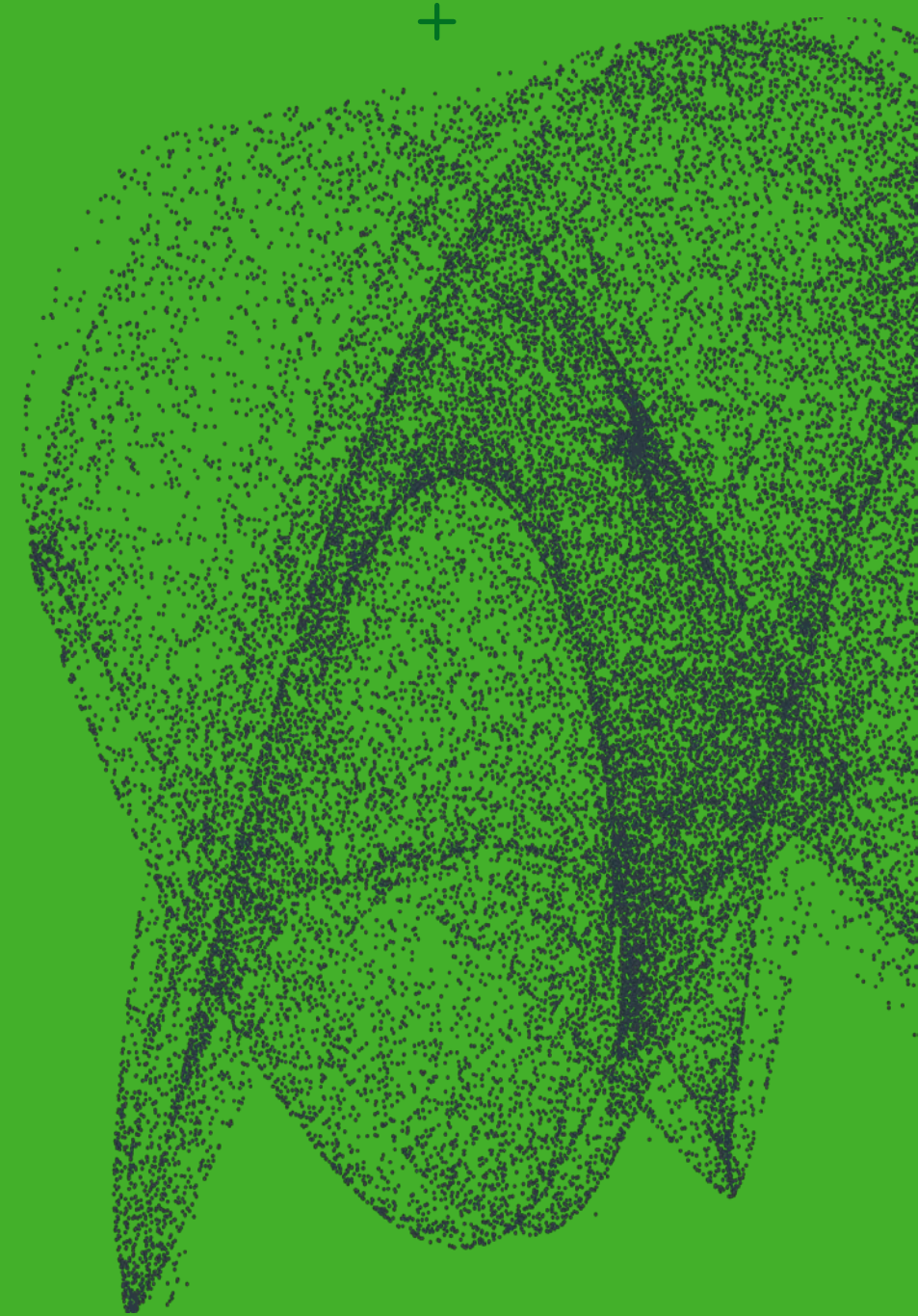




# Drug Expenditure Dynamics 1995-2020

Understanding Medicine Spending in Context  
Country Detail Appendix:

**U.S.**

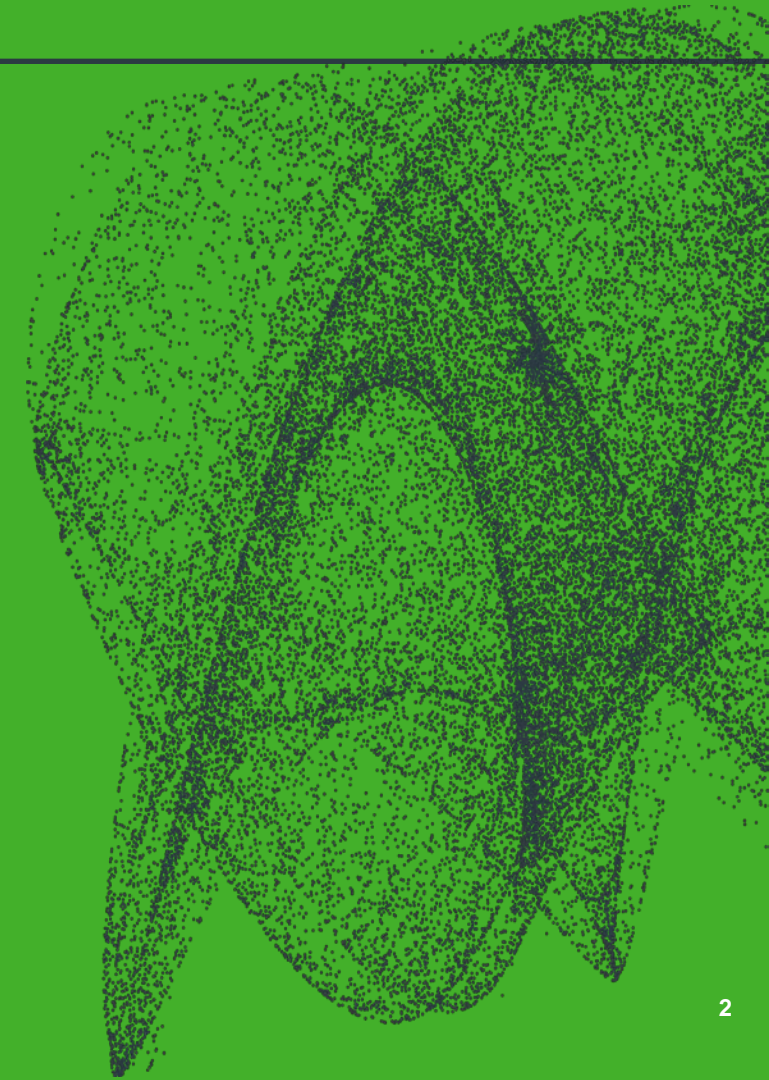


# Introduction

- This document is accompanying appendix to the report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*
- The report includes analyses of 11 major countries and provides cross-country and aggregate analyses of these markets.
- This document includes specific country analyses mirroring the main report and intended to illustrate the same dynamics in each country that are shown across countries.
- In some cases, there are important differences from cross-country trends and those are illustrated and highlighted.
- The key findings in relation to each country are summarized and each page represents a specific analysis of interest.
- This document is not an exhaustive analysis or summary of the country, and the primary purpose is to provide the extended historic periods analyses which are unique to this report.
- The exhibits in this report are sometimes complex or include multiple graphics per page. This document ends with several annotated examples of the layout of important exhibits to enable the reader to better understand how to read and understand them.



**U.S.**



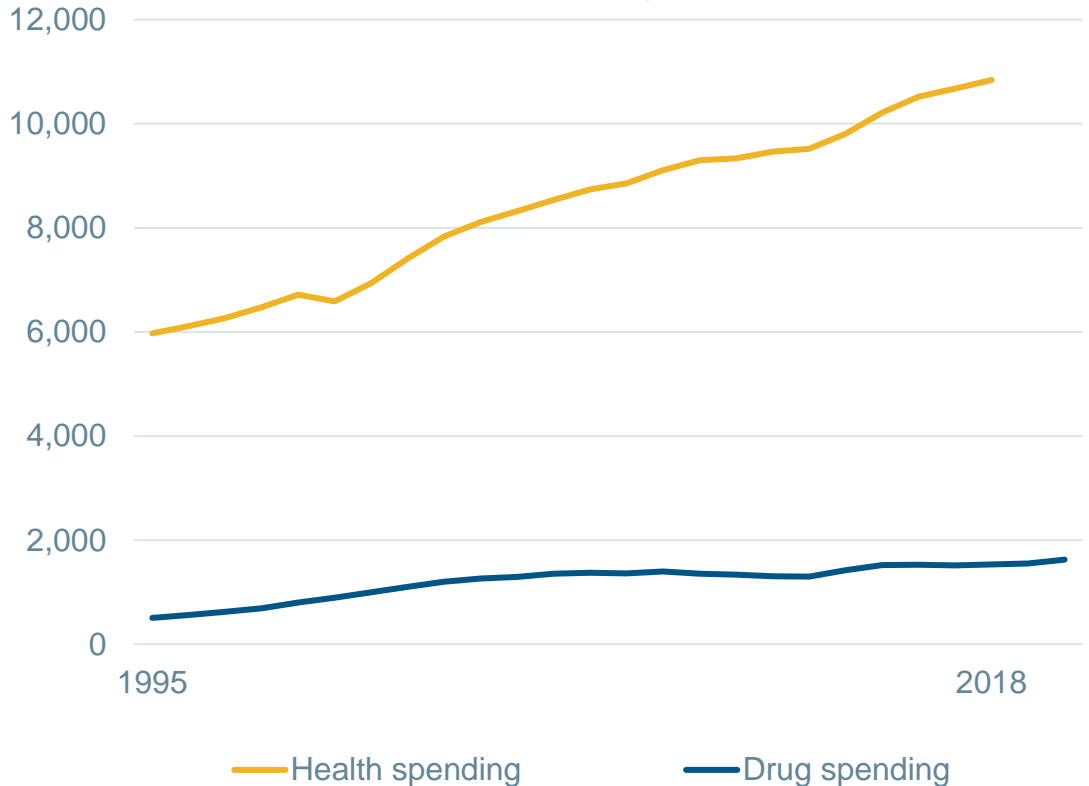
# U.S. drug spending is 14% of healthcare spending with growth below medical inflation or declined for most of the last decade

- U.S. drug spending represents 14% of overall healthcare spending, including 4% of spending in non-retail settings
- Net drug spending (by all payers) in the U.S. has risen by 20% over the past 10 years for an average of 2% per year, while manufacturer net revenue has grown by 5% for an average of under 1% per year.
- Medicine net spending (by all payers) includes markups by intermediaries, less the discounts and fees companies pay, whereas manufacturer net revenue reflects all the discounts, rebates, fees, and other payments companies have made, and are applied to the gross revenue they generate prior to intermediary markups.
- Drug spending in this analysis includes retail pharmacy drugs, which represent 10% of total healthcare spending, as well as hospital, clinic or doctor administered drugs, which add another 4% of healthcare spending and are not generally included in published official analyses; together total drug spending has been growing below medical inflation for most of the last decade and has sometimes declined.
- The cycle of genericization results in lower costs for those medicines, while newer medicines grow without as significant impact on total spend; as a result, branded medicines' share of spending has remained largely unchanged over two decades.
- Leading therapy areas in the 90s accounted for nearly half of spending, a pattern similar to the current group of leading classes, but the classes have changed from the older, traditional, large-population treatments to the current group of specialty therapy areas.
- Some therapy areas have seen significant innovation-led growth for a time, but then have seen spending decline following genericization (e.g., cholesterol and anti-ulcerants).
- Classes such as oncology and immunology have seen continued innovation drive constant evolution of treatments, while spending has continued to rise, driven by new therapies and wider usage.
- Each therapy area demonstrates differing dynamics based on innovation, volume usage of different medicines, and losses of exclusivity and generic (or biosimilar) uptake.

# U.S. drug spending represents 14% of overall healthcare spending, including 4% of spending in non-retail settings

## Drug and Healthcare Spending 1995-2018

Per Capita Drug and Health Spending in Real PPP 2020\$, 1995-2018



Drug Share of Healthcare Spending in Real 2020\$, 1995-2018

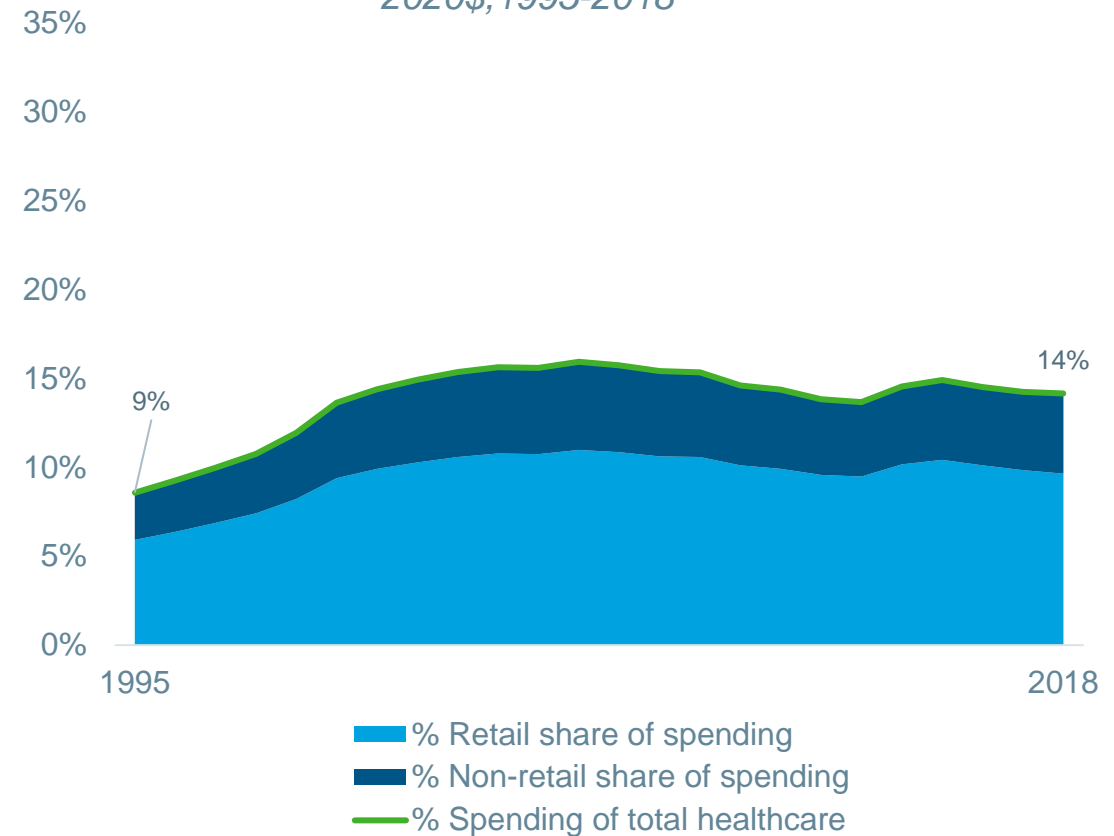


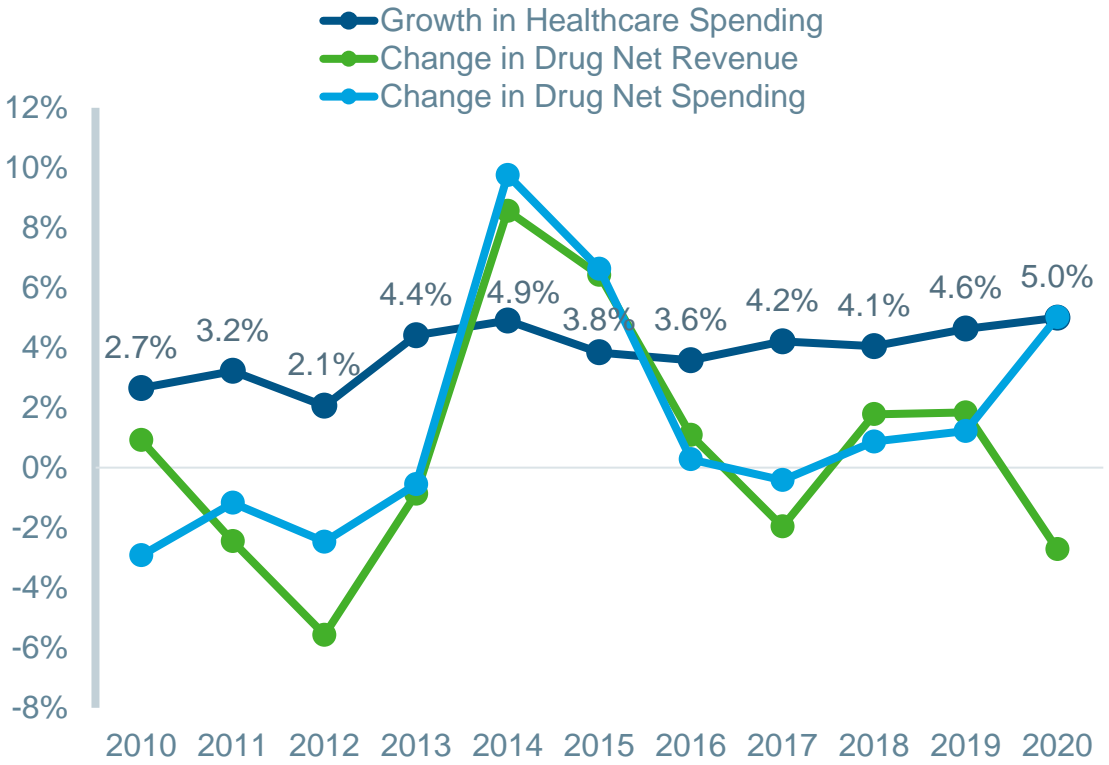
Chart Note: Methodology described in main report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*  
 Source: IQVIA Institute for Human Data Science, Sep 2021



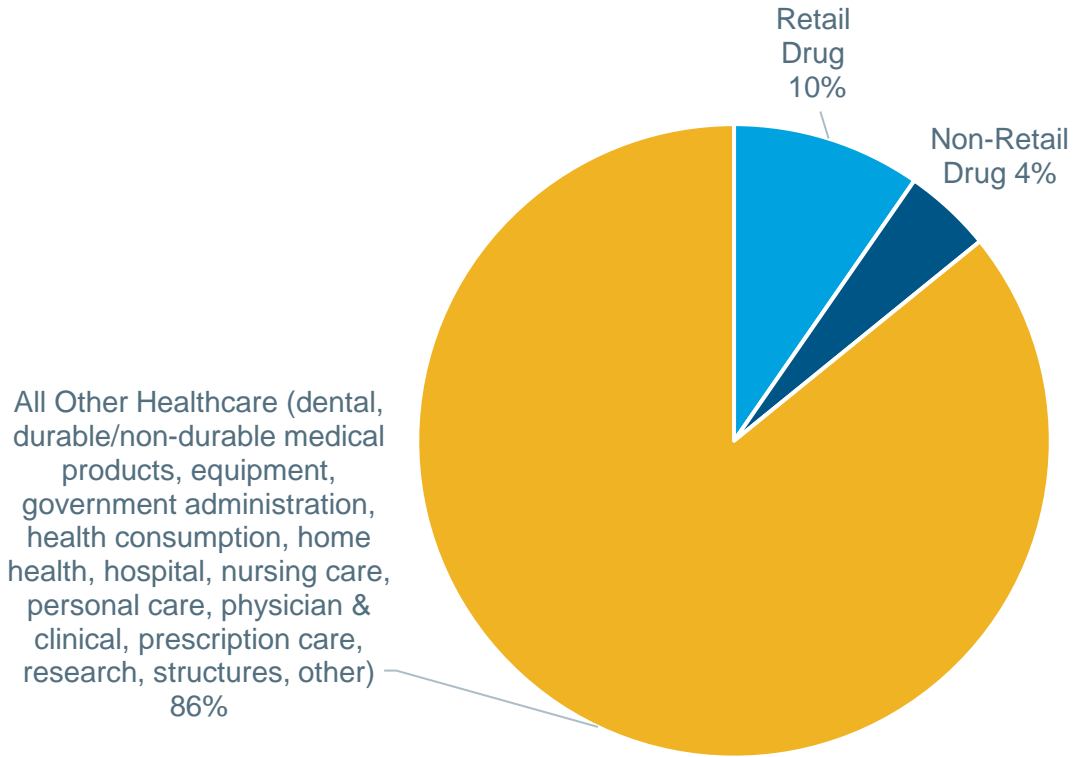
# Drug costs are 14% of total spending, a minor part of U.S. healthcare expenses and growing more slowly than medical inflation for the last decade

## Drug and Healthcare Spending Growth and Share 2010-2020

Annual Change in Spending since 2010



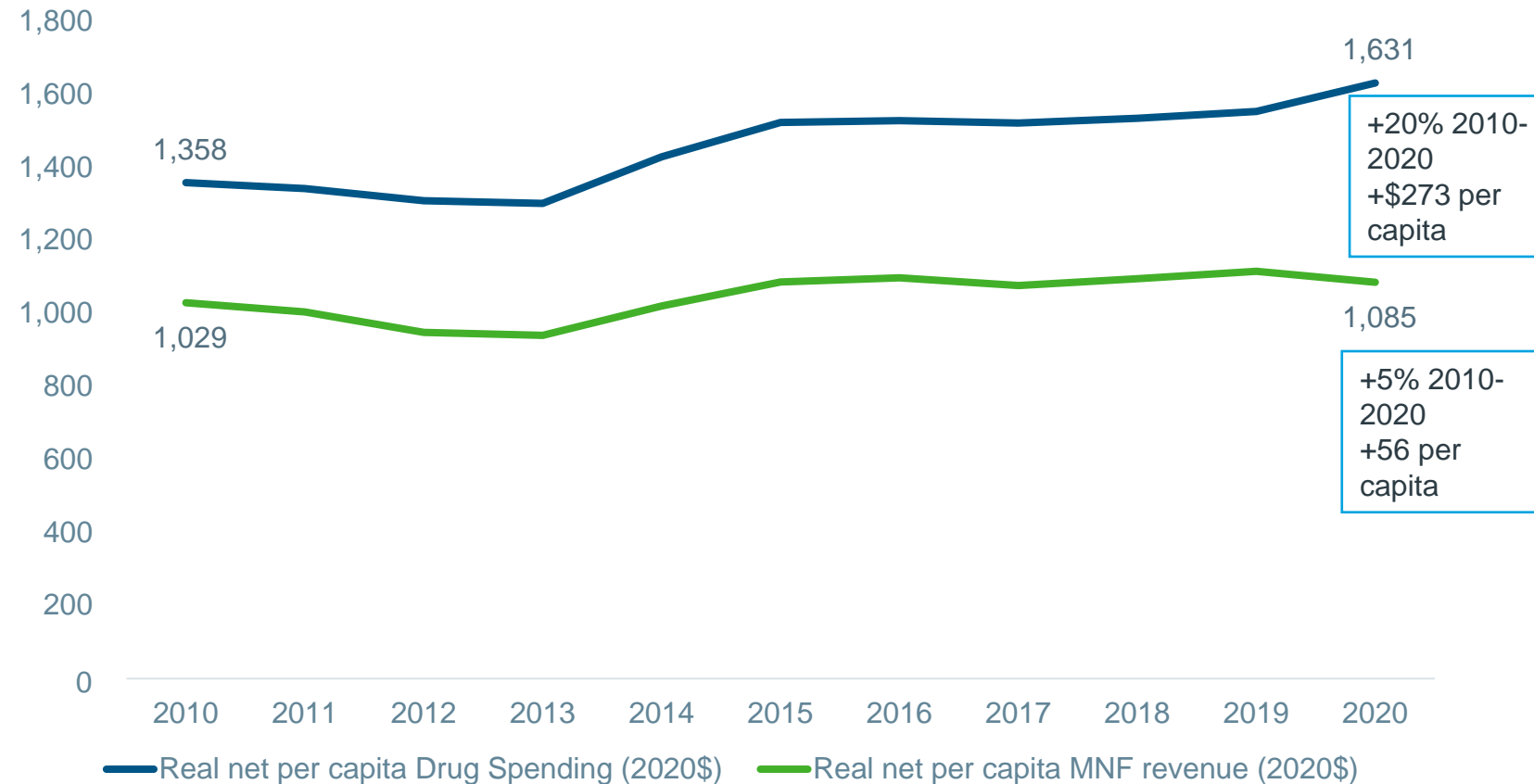
Segments of National Health Expenditure



Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021; IQVIA Institute Sep 2021; CMS National Health Expenditure (NHE) projections Dec 2020, accessed July 2021

# Net spending (by all payers) in the U.S. has risen by 20% over the past 10 years, while manufacturer net revenue has grown by 5%

*U.S. Real Net Per Capita Drug Spending and Manufacturer Net Revenue 2020\$*



- Drug spending by all payers (including patients) is a different measure than the revenue that pharmaceutical companies earn.
- Medicine net spending (by all payers) includes markups by intermediaries, less the discounts and fees companies pay.
- Manufacturer net revenue reflects all the discounts, rebates, fees and other payments companies have made, and are applied to the gross revenue they generate prior to intermediary markups.

Chart notes: Drug spending represents the amount spent by all payers after the discounts and rebates they receive. Net revenue represents the estimated amount of revenue received by manufacturers after the discounts and rebates they provide to payers and patients. The difference between the two analyses are markups and margins applicable to transactions for wholesalers, pharmacies and other intermediaries.

Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021; IQVIA Institute, Sep 2021

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

Real Net per Capita Medicine Revenue and Growth by Product Type US\$

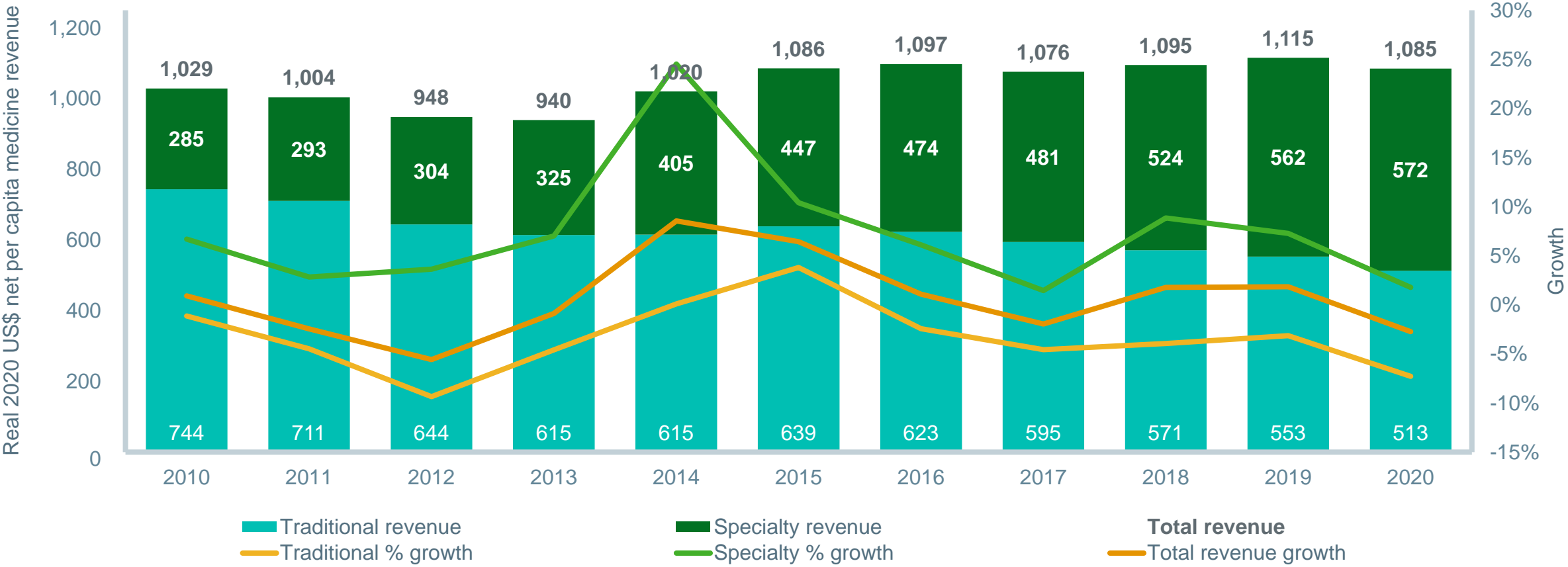


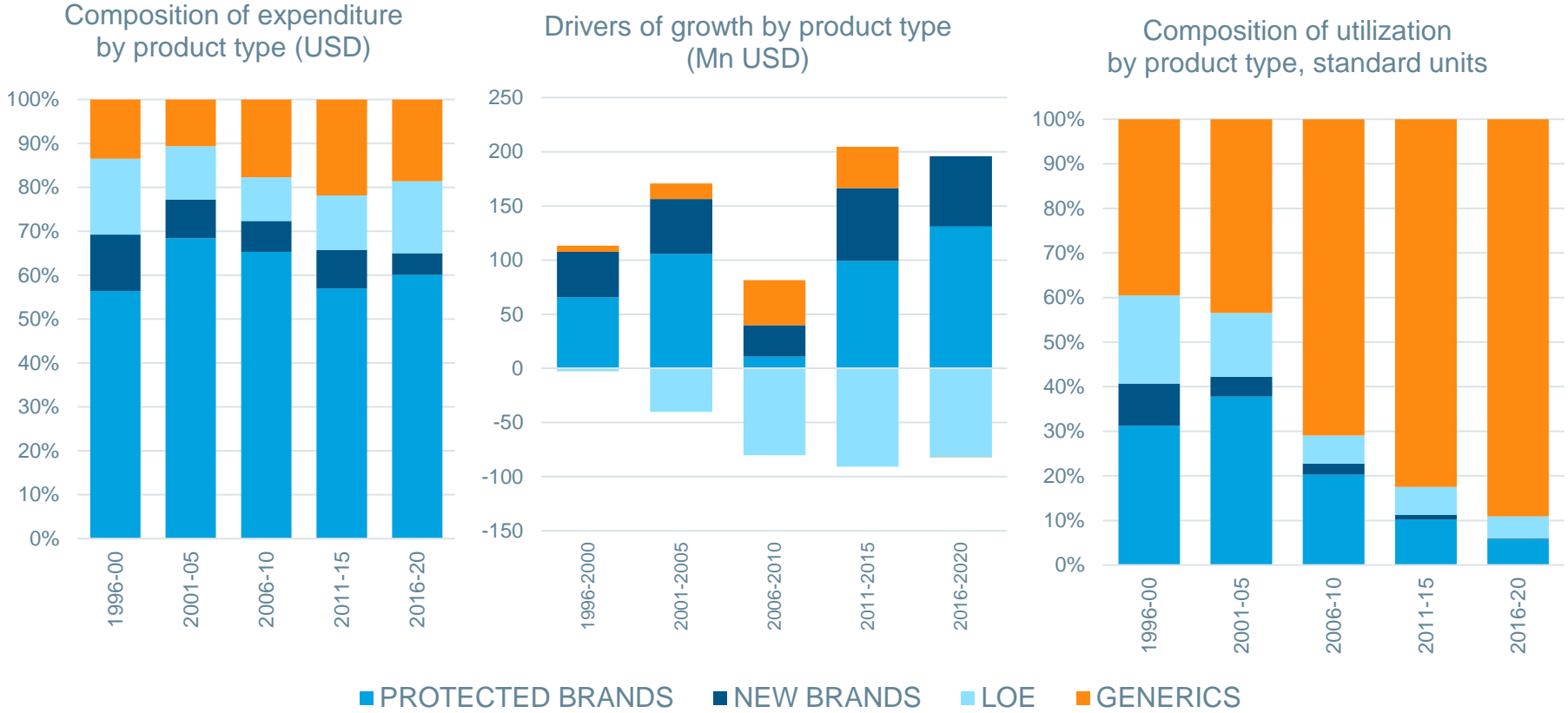
Chart notes: Analysis represents net manufacturer revenues. When originally published in May 2021 the chart was labeled as “net spending” but is now labeled “net revenue,” which is a terminology change with no other changes to the analysis.

Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021



# The cycle of genericization results in lower costs for those medicines, while newer medicines have grown without significant impact on total spend

## U.S. Drug Spending and Utilization 1995-2020

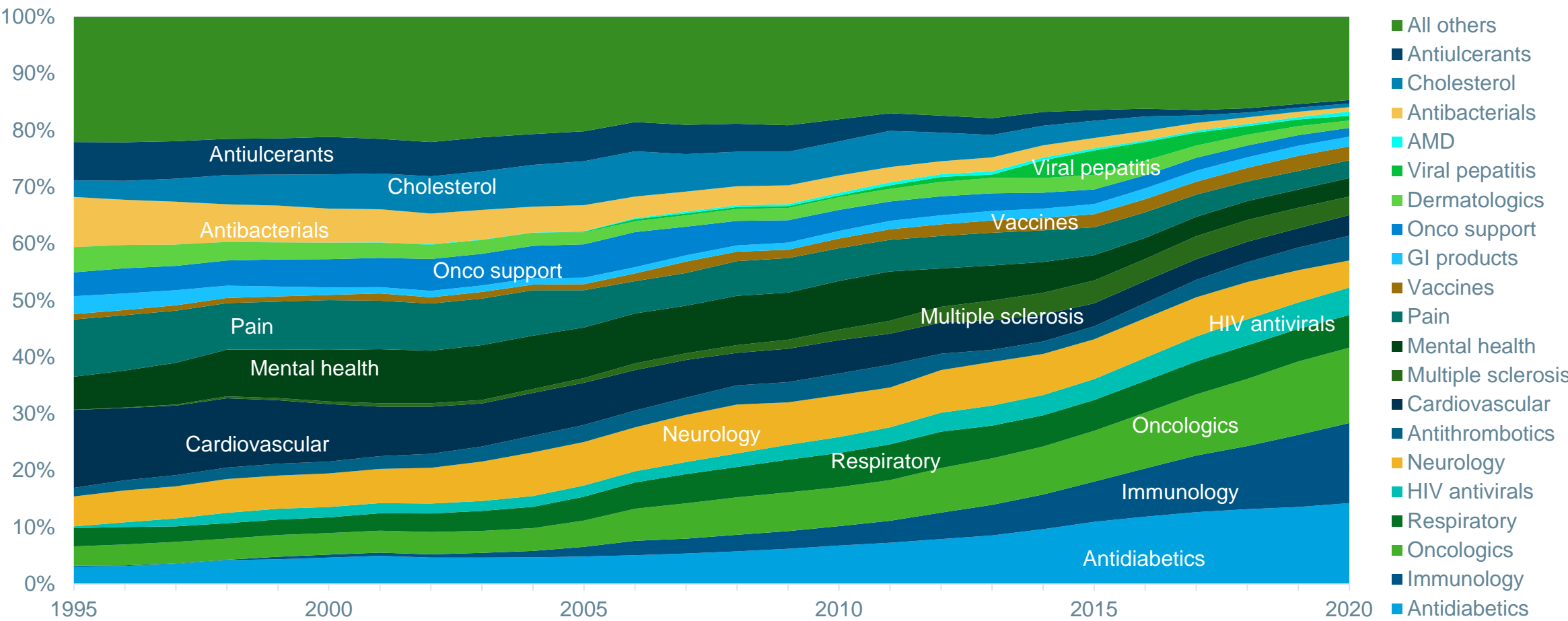


- Protected brands, including new products, average less than 70% of spending consistently
- Generic share of combined generic and LOE segments are increasing steadily over time
- Generic share of volume are increasing as generations of products shift to off-patent
- Most growth is driven by protected brands, including new products, and offset by losses of exclusivity

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Leading classes in the 1990s are now a much smaller share of spending while current leading classes were much smaller before

*U.S. Composition of Drug Real Local Currency Spending by Drug Class, 1995-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Classes dominated by new and protected brands characterize the focus of innovation in a period and shift over time

U.S. Composition of Protected Brands Real Local Currency Spending by Drug Class, 1995-2020

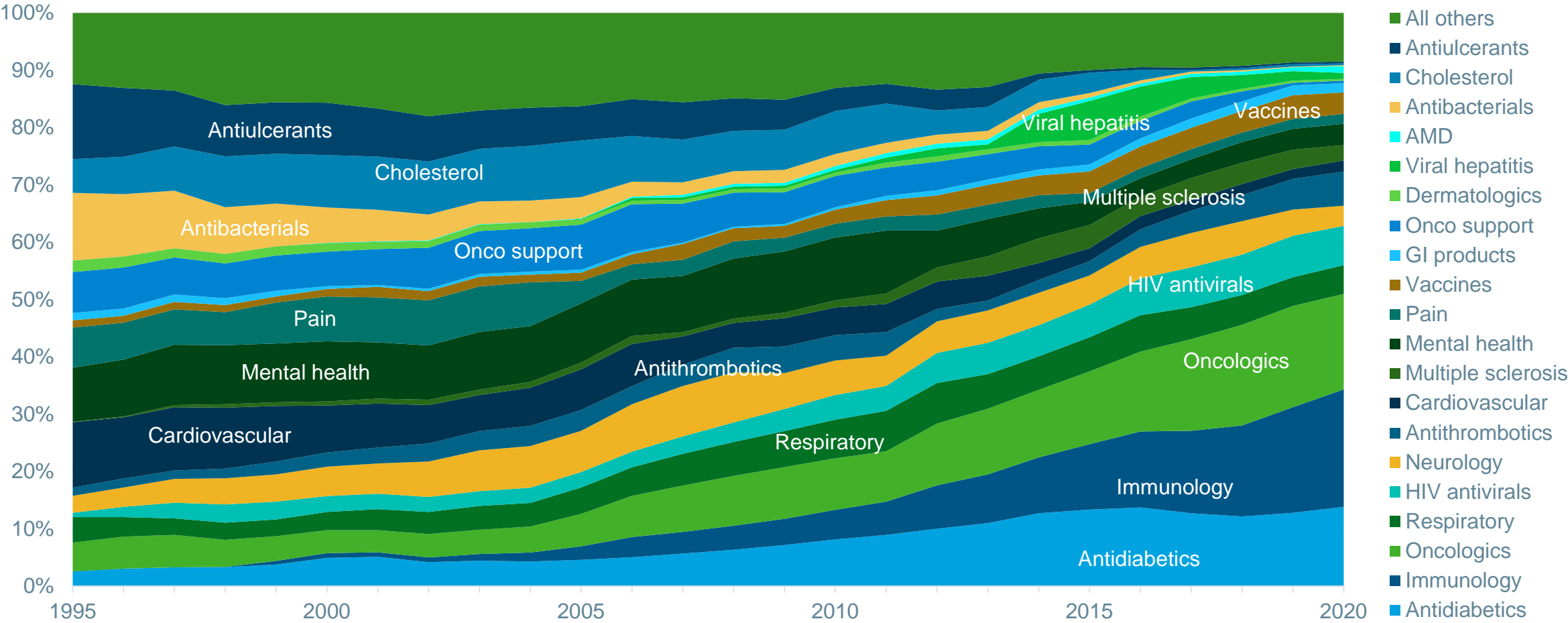
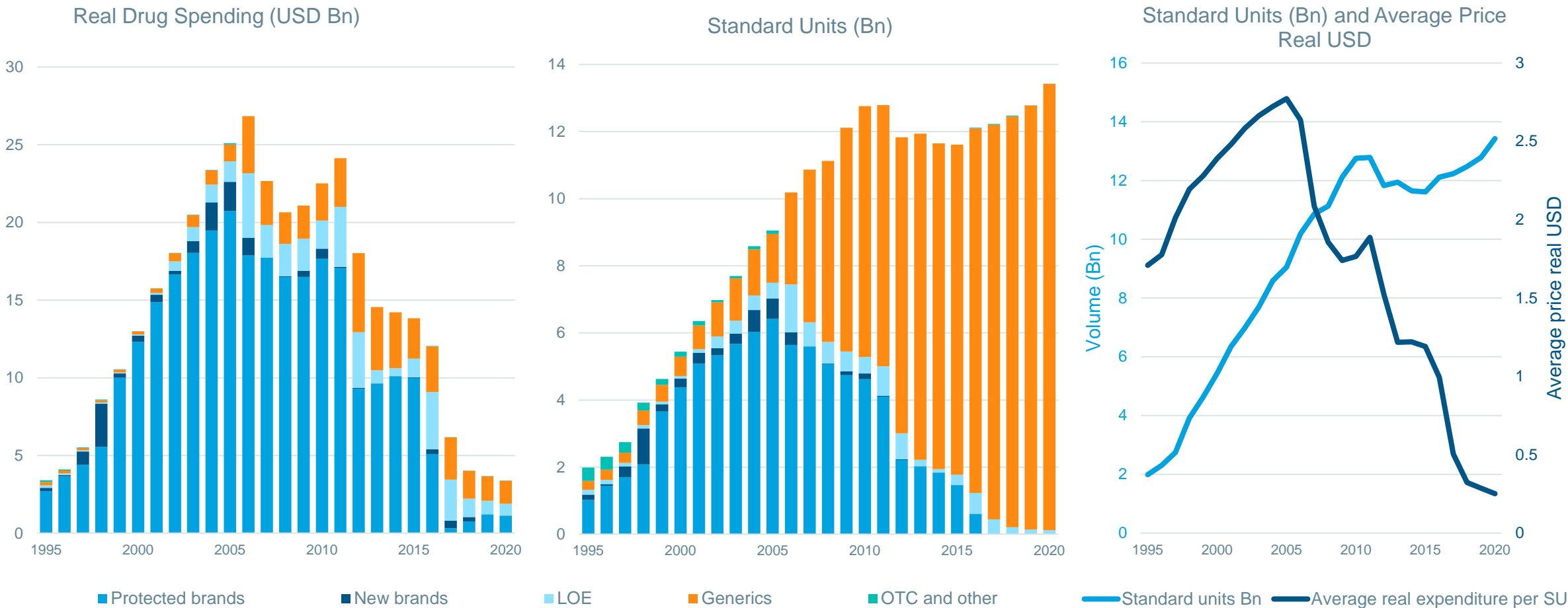


Chart notes: Protected brands includes new original brands, protected original brands, upcoming LOE and vaccines.  
 Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# The cholesterol market rose dramatically until patent expiries drove lower spending; volume continues to grow while costs fall

*U.S. Cholesterol Volumes, Average Prices and Spending by Product Type, 1995-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Anti-bacterial drug spending declined by 72% from peak in 2003 due to patent expiries, while volumes declined (avoiding misuse)

*U.S. Antibacterial Volumes, Average Prices and Spending by Product Type, 1995-2020*

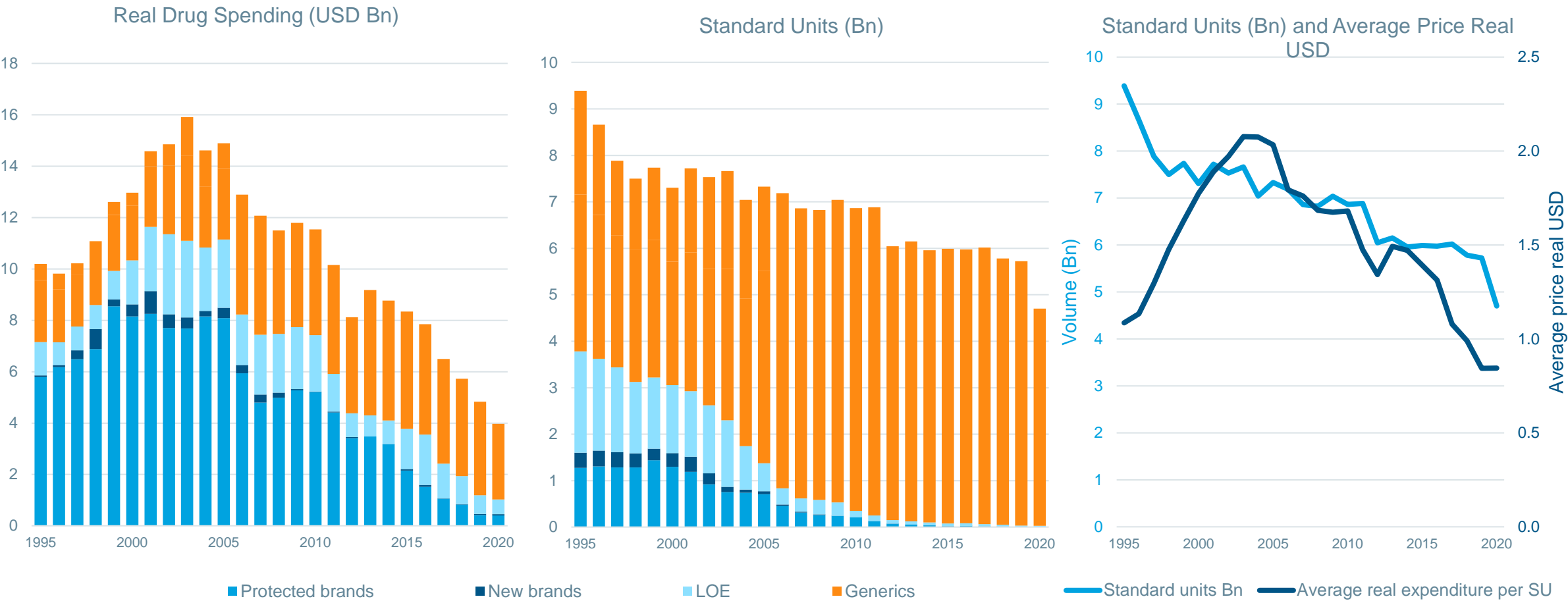
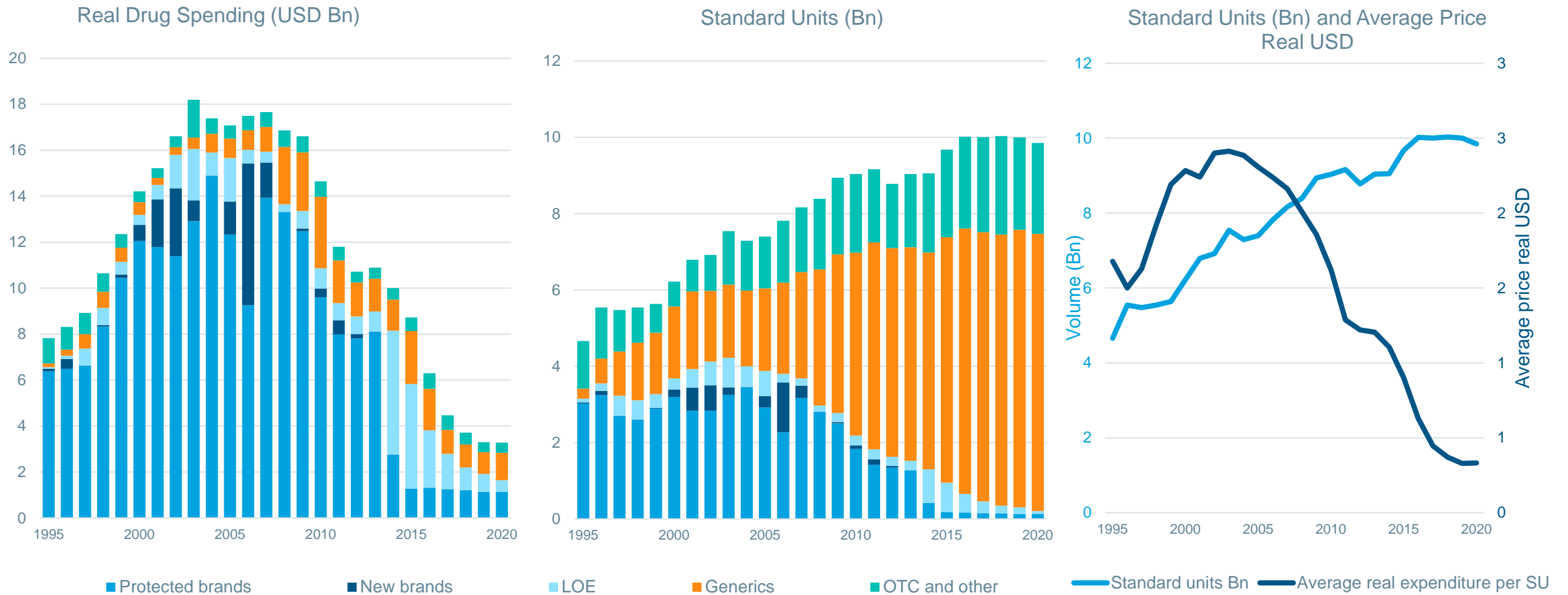


Chart notes: Products which are no longer marketed but had spending or volume in 2005 or earlier are included in the 'other' segment as specific segmentation was not possible.  
 Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Anti-ulcerant spending peaked in 2003 and remained stable until 2010, where it declined by more than 82% due to loss of exclusivity

*U.S. Anti-Ulcerants Volumes, Average Prices and Spending by Product Type, 1995-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020



# Use of hypertension therapies has continued to increase, while spending has reduced by 50% in the past 10 years

*U.S. Hypertension Spending and Volume by Mechanism, 1995-2020*

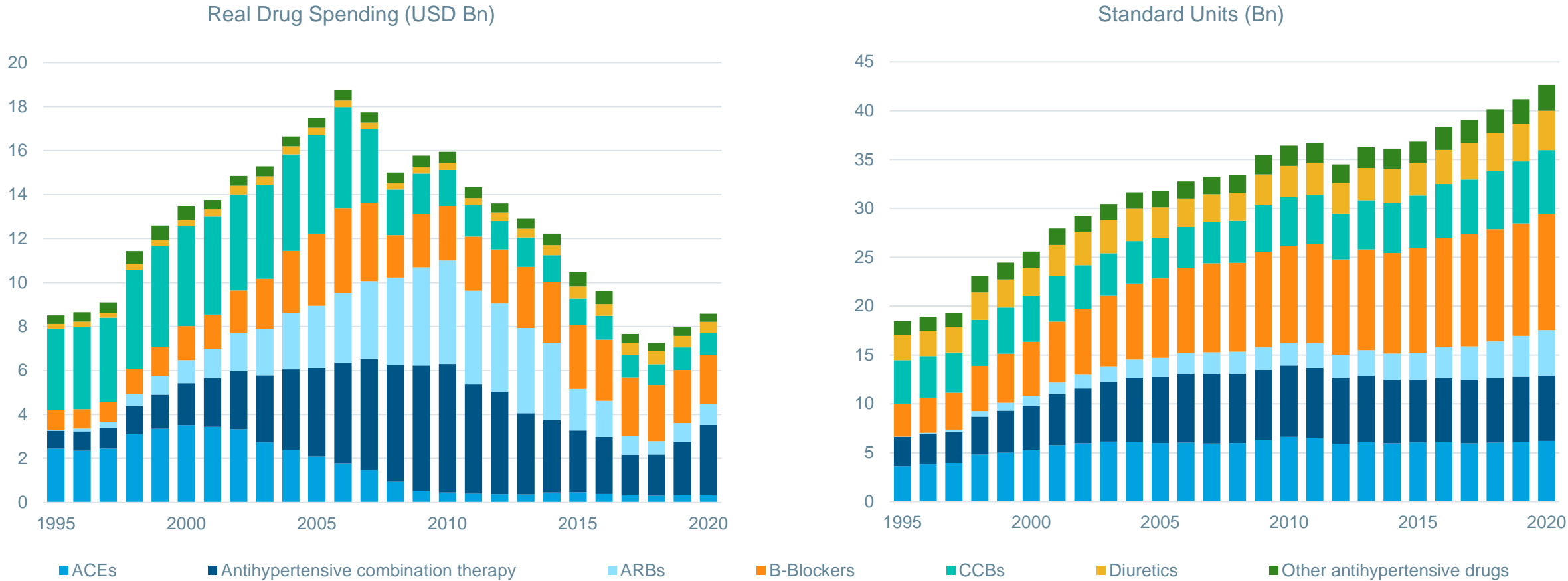
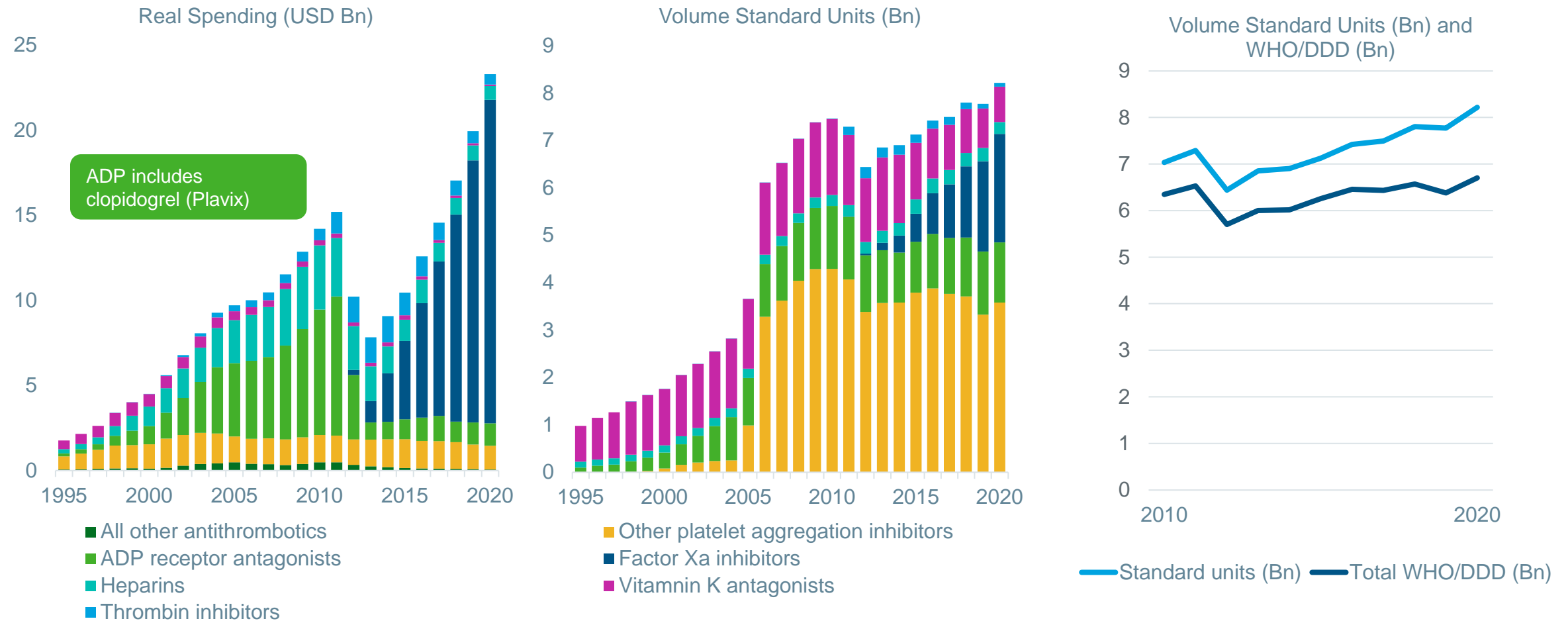


Chart notes: ARBs: Angiotensin II receptor antagonists, CCBs: Calcium channel blockers; ACEs: Angiotensin-converting enzyme.  
 Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Antithrombotics have continued to grow by volume even as some mechanisms have seen significant expiries

*U.S. Antithrombotics Spending, Volumes and DDD by Drug Type, 1995-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Diabetes spending growth has been driven by the adoption of novel classes, including SGLT2, GLP-1, and DPP-IV

*U.S. Diabetes Real Spending, Volume and Growth USD (Mn) by Drug Type, 1995-2020*

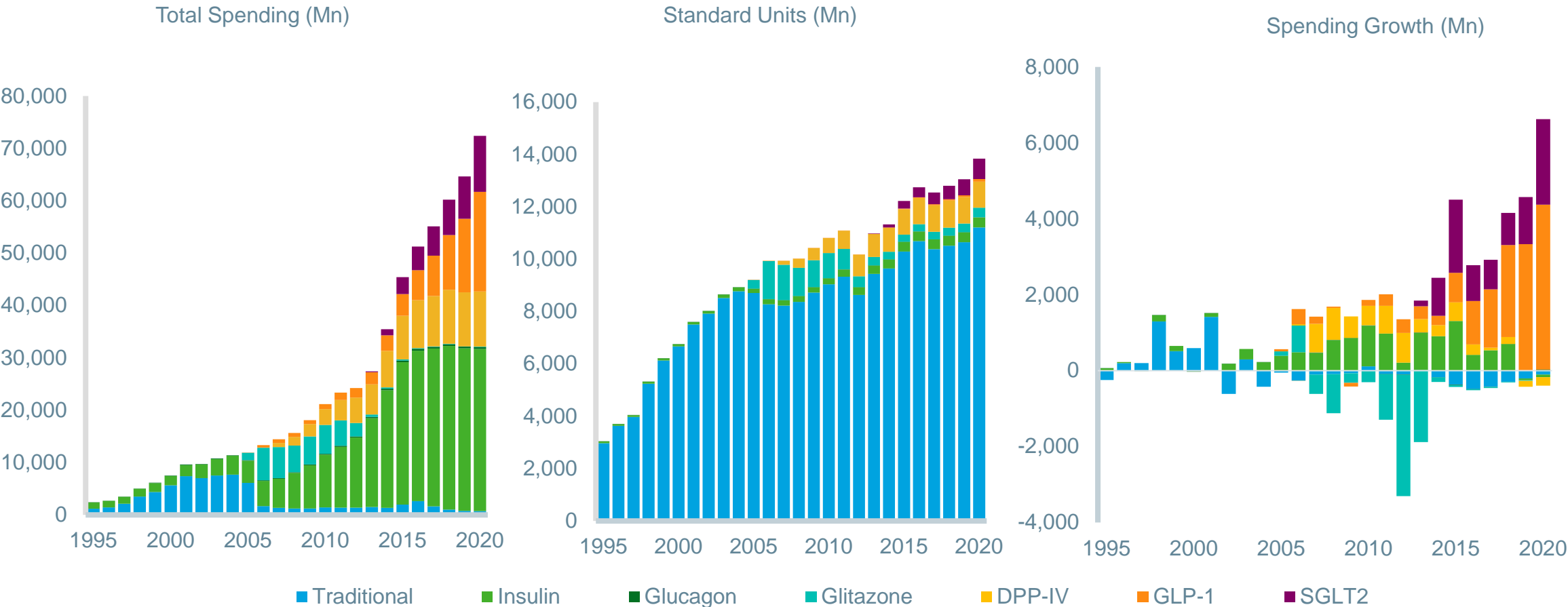


Chart notes: Analysis is without adjusting for off-invoice discounts and rebates which are understood to be reduce diabetes spending by nearly 2/3rds.  
 Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Diabetes growth slows to 2% on a net basis as off-invoice discounts and rebates drive protected brand costs are down 12%

## Diabetes Invoice and Net Spending and Growth

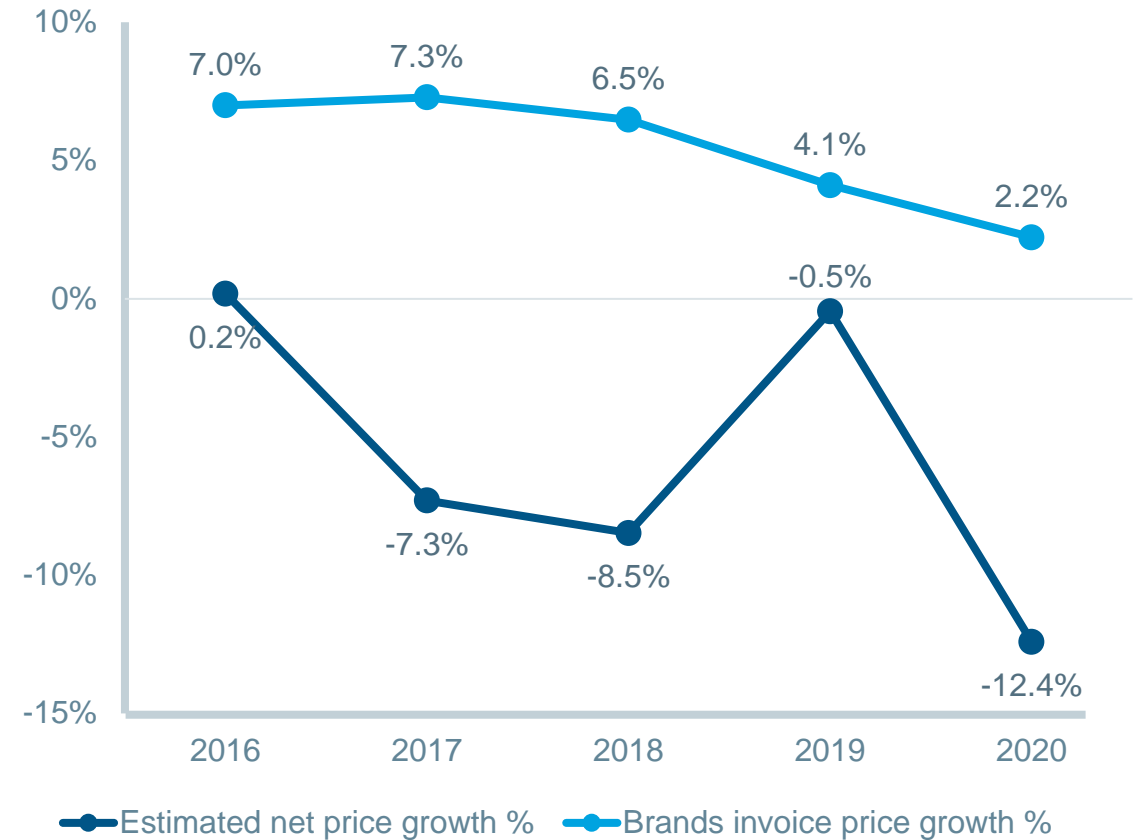
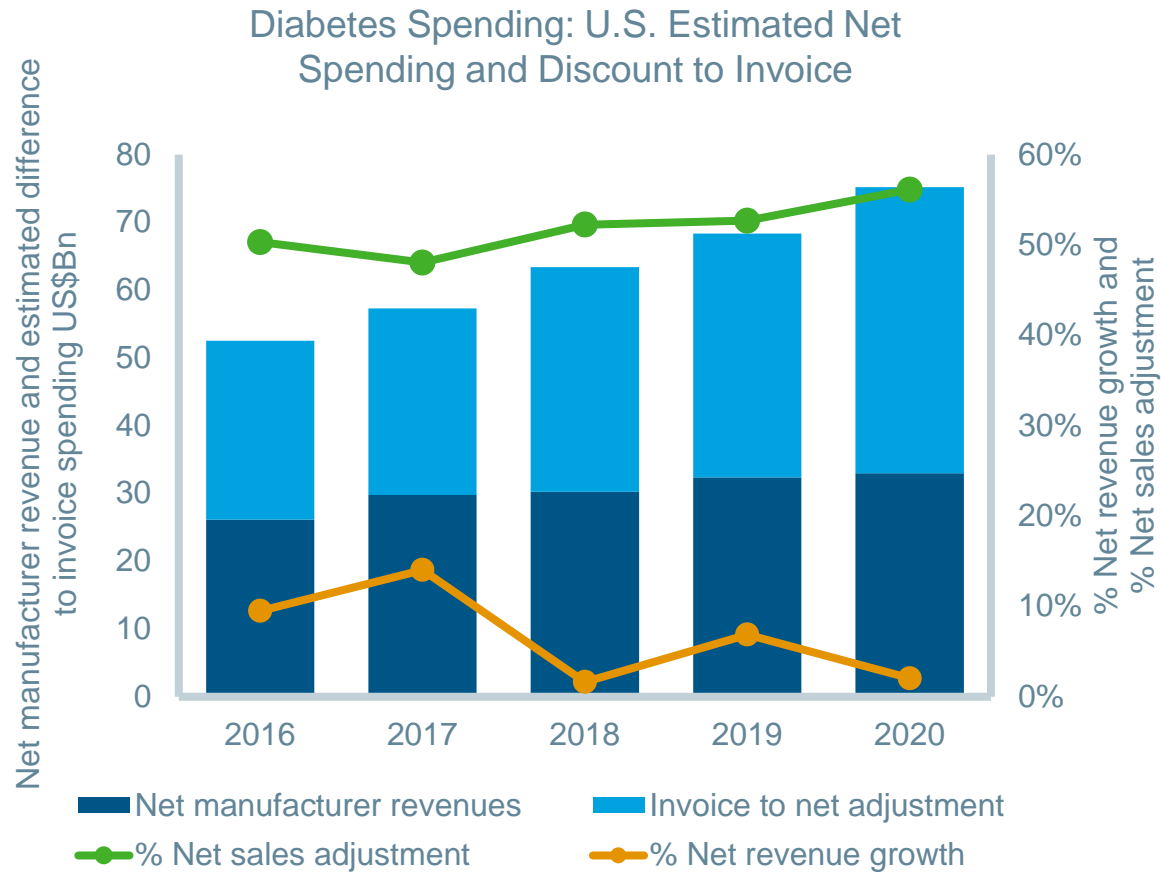
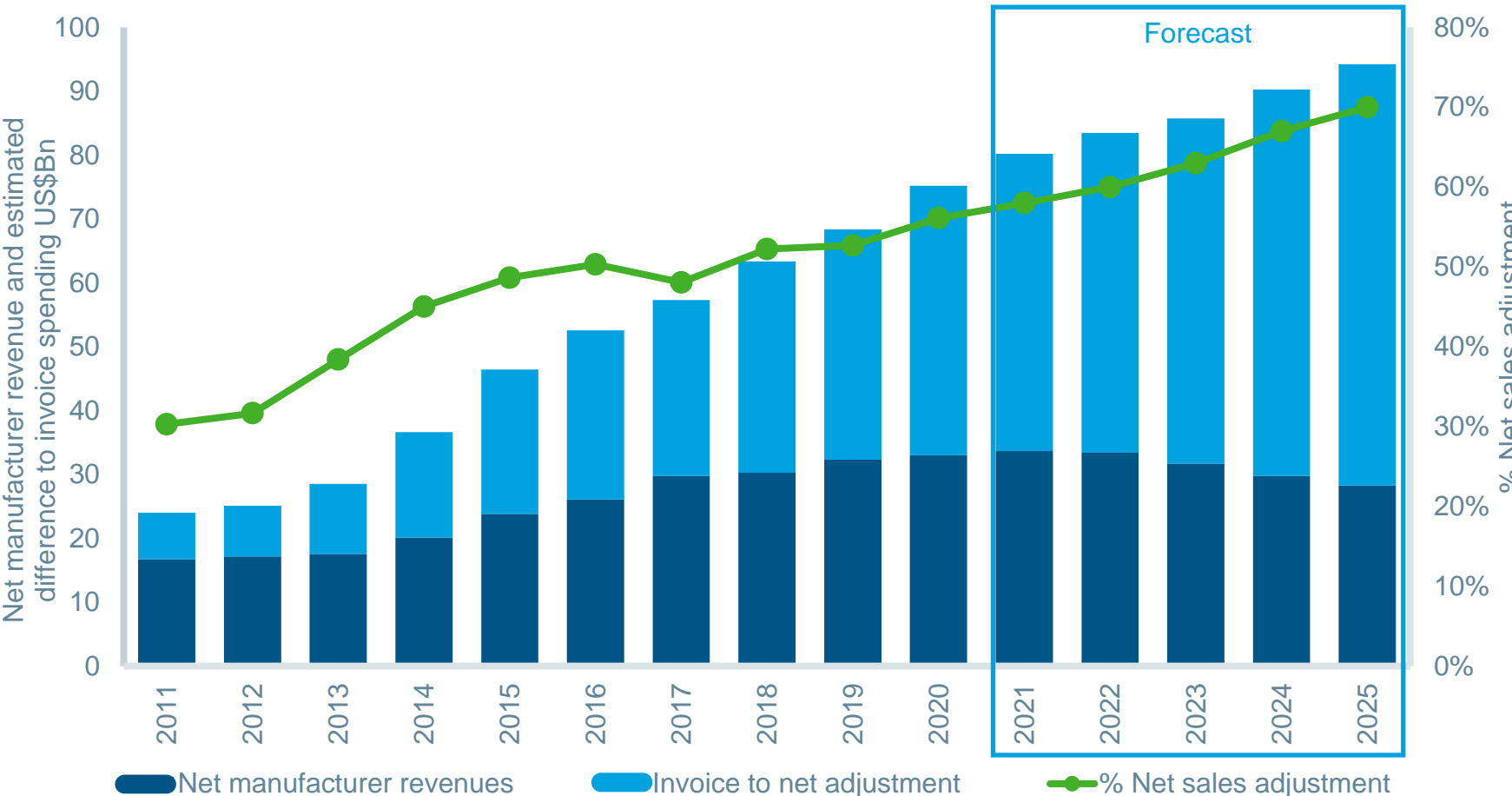


Chart notes: This exhibit is reproduced from another report to illustrate the pattern of off-invoice discounts and rebates.  
 Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021

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

Diabetes Spending and Growth at Net and Non-Discounted Levels



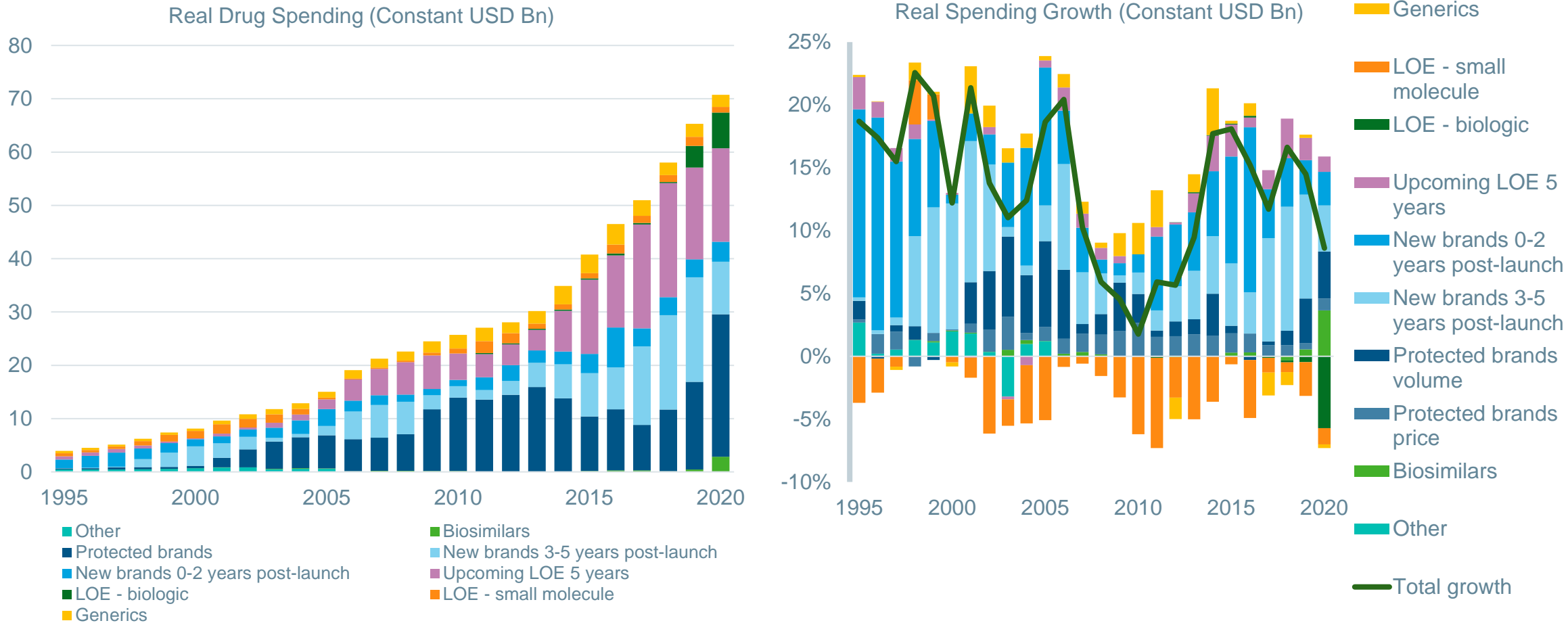
### 2021–2025 Key Forecast Drivers

- +25 invoice spending growth (3-6% CAGR)
- 14% net revenues growth (-5 to -2% CAGR)
- Continued uptake of novel therapies offsets price declines

Note: This exhibit is reproduced from another report to illustrate the pattern of off-invoice discounts and rebates.  
 Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021

# Oncology growth has been driven by new products while slowing recent growth is driven by the impact of biosimilars

U.S. Oncology Invoice Spending and Spending Growth Drivers, 1995-2020



Source: IQVIA MIDAS, IQVIA Institute, Dec 2020



# Oncology has seen successive waves of innovation driving growth while older mechanisms are superseded or genericize

*U.S. Oncology Real Local Currency Spending by Mechanism, 2000-2020*

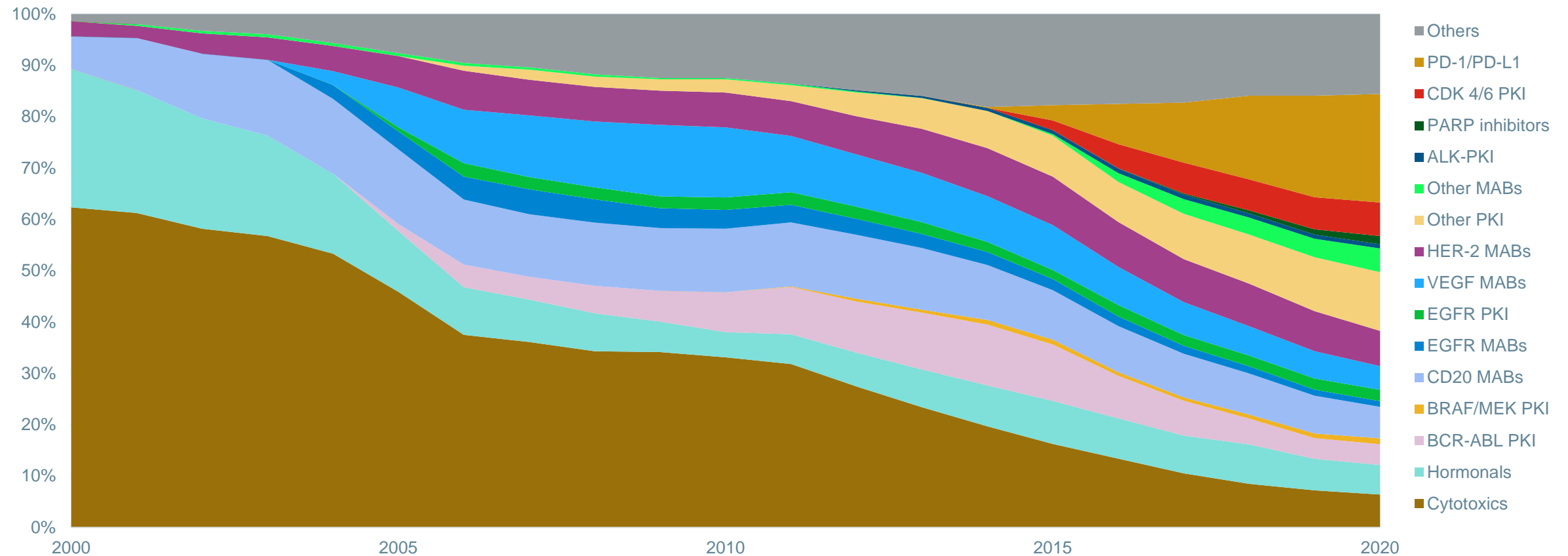
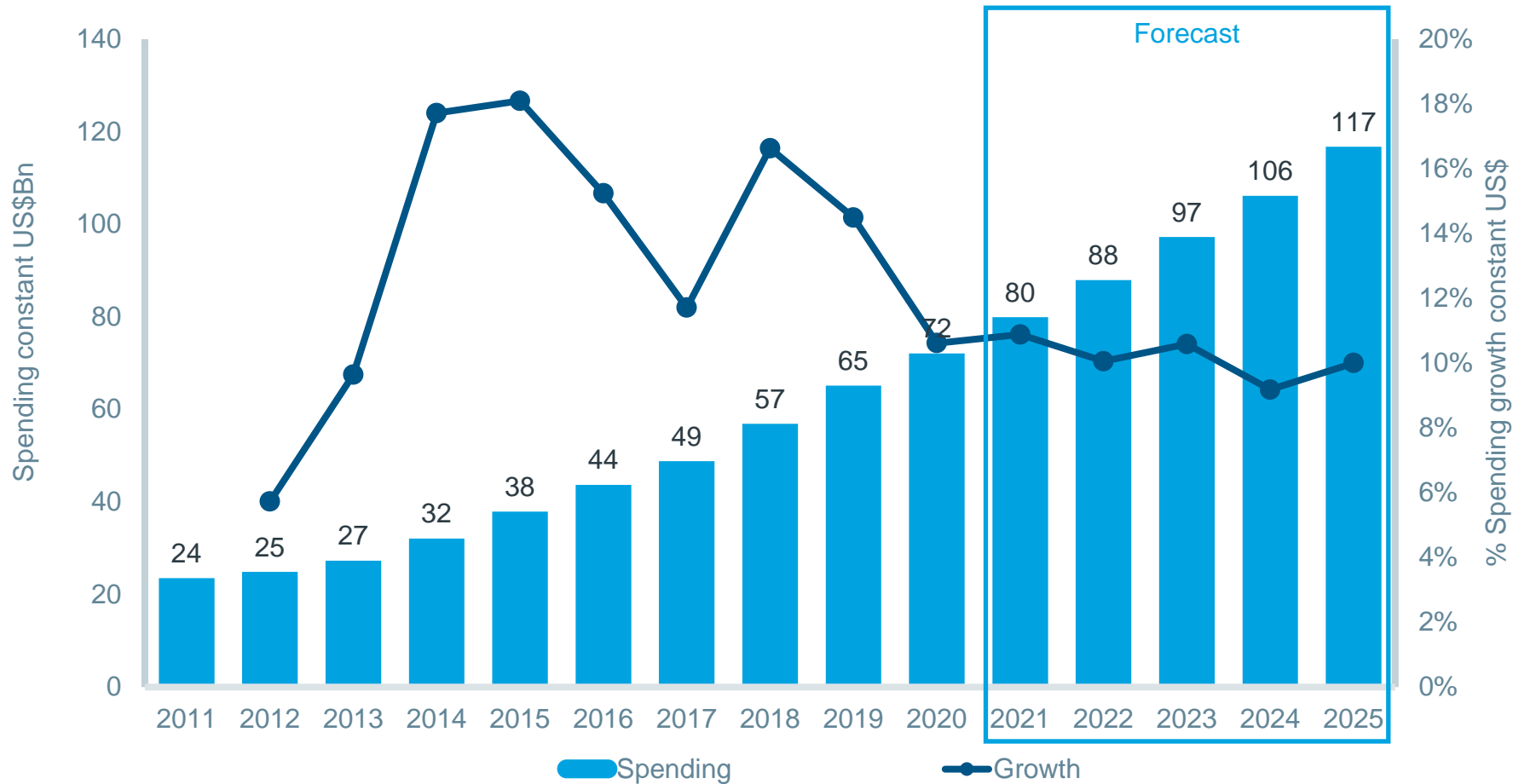


Chart notes: Cytotoxics include antimetabolites, taxane, alkylating agents, camptothecin, platinum, lidomide, podophyllotoxin, vinca alkaloid and other antineoplastics, aromatase inhibitors; Hormonals include cytostatic anti-androgens, gonadotropins, gonadotropin releasing hormones, progestogens, estrogens, anti-estrogens; others include all other neoplastics.

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

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

*Oncology Non-Discounted Spending and Growth*



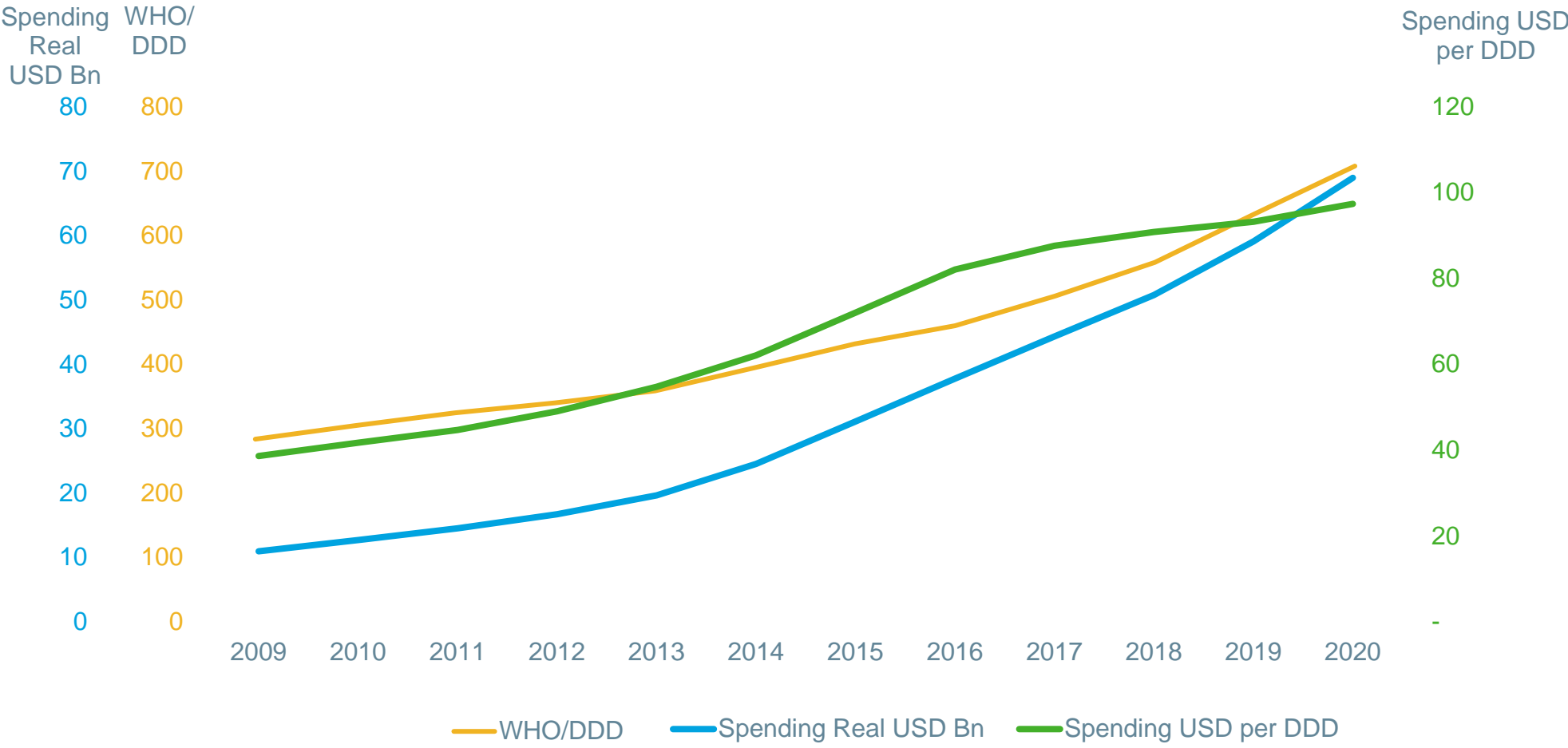
## 2021–2025 Key Forecast Drivers

- +62% total spending growth (9–12% CAGR)
- +\$45Bn
- ~+100 new oncology drugs

Chart notes: This exhibit is reproduced from another report to illustrate the expected forecast outlook for the therapy area.  
 Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021

# Immunology grew from usage and rising costs per day until 2016; biosimilars and brand competition have slowed cost growth since

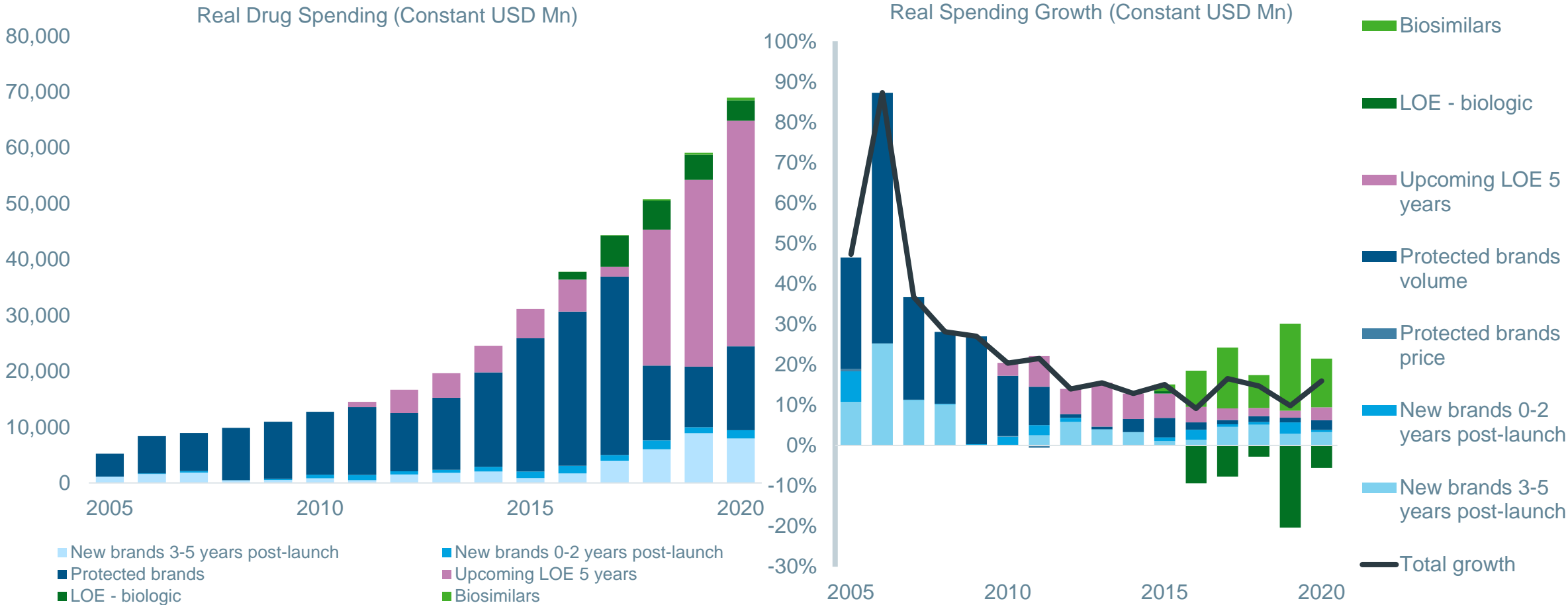
*U.S. Autoimmune Biologic Spending, DDD and Cost 2009-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# More than half of auto-immune biologic spending will lose exclusivity by 2025, including adalimumab and ustekinumab

*U.S. Auto-immune Biologic Invoice Spending and Growth Drivers, 2005-2020*



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

# Treatments for auto-immune disorders to exceed \$130 billion in the U.S. by 2025, slowing after 2023 due to key biosimilars

Autoimmune Non-Discounted Spending Growth

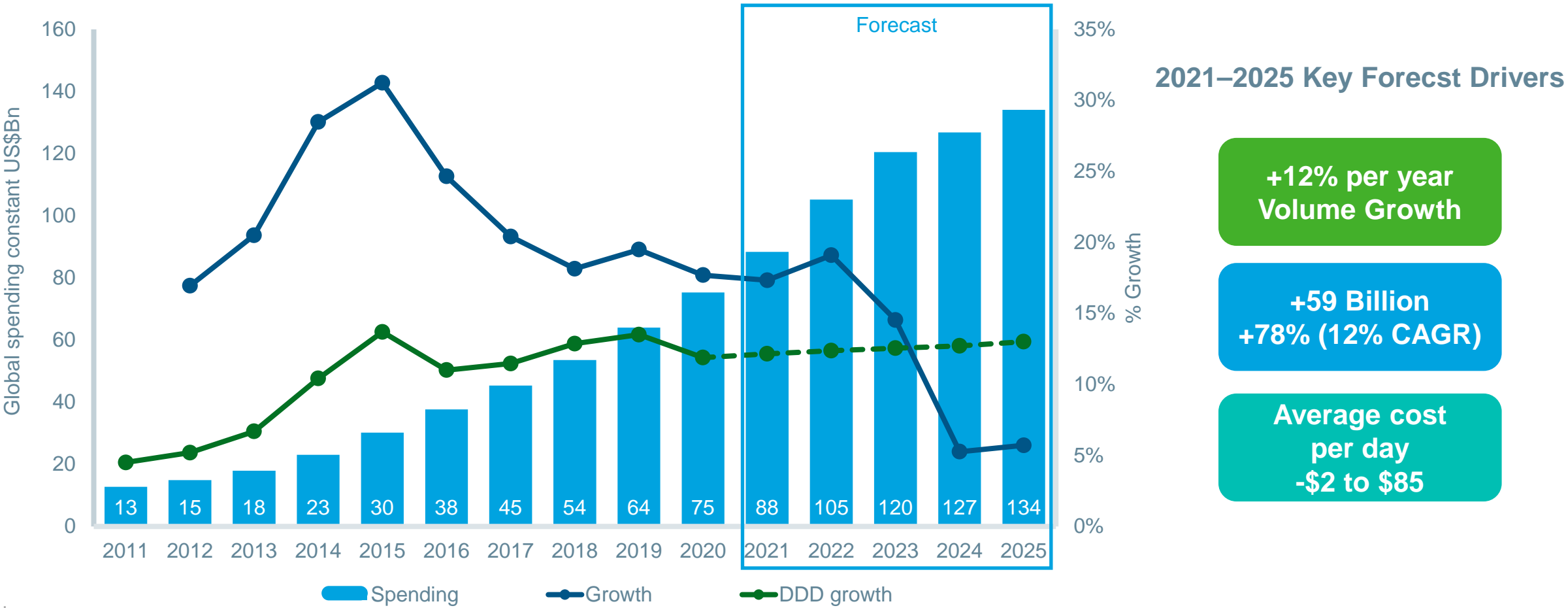


Chart notes: This exhibit is reproduced from another report to illustrate the expected trend for forecast spending and for volume growth measured in WHO-DDD. Source: IQVIA Institute, *The Use of Medicines in the U.S.: Spending and Usage Trends and Outlook to 2025*, May 2021

# Innovative vaccines in last 15 years for HPV, meningitis, pneumonia and shingles drove spending while flu drives volume

*U.S. Vaccine Spending and Volumes by Drug Type, 1995-2020*

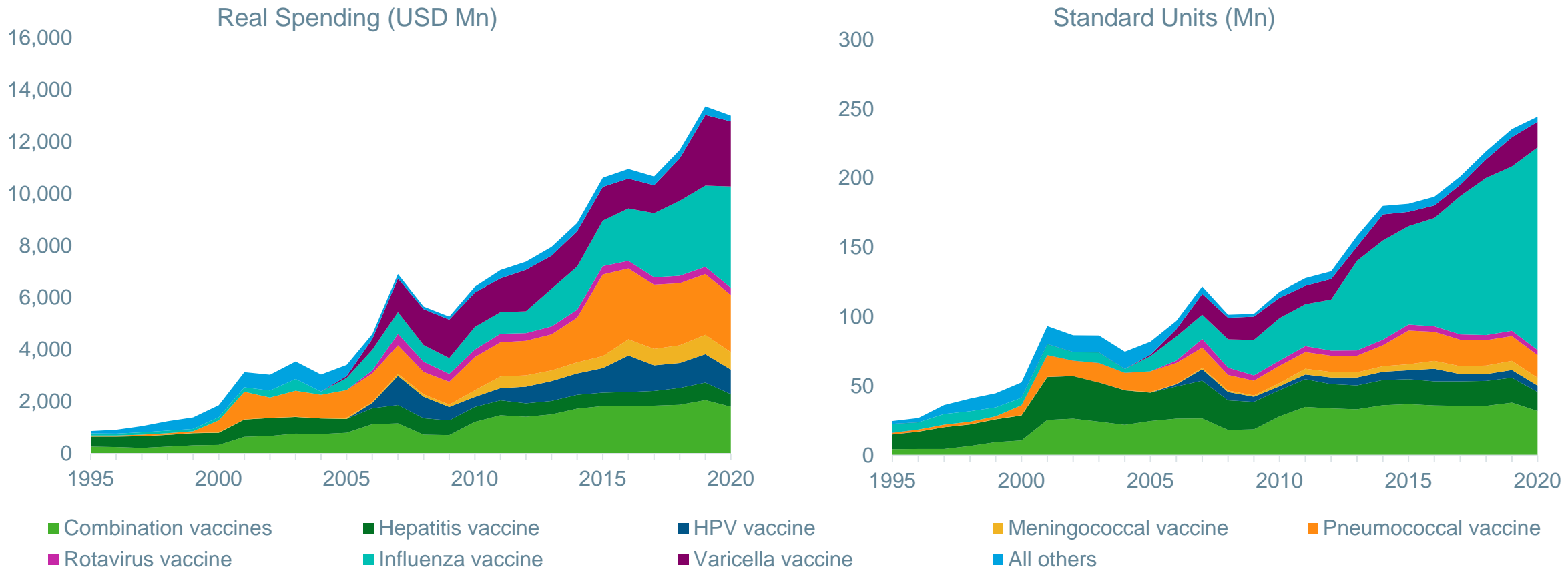


Chart notes: Combination vaccines represent combined vaccines (with measles, mumps, tetanus or other); HPV vaccine for human papillomavirus; Meningococcal vaccine for meningitis; Pneumococcal vaccine for pneumonia; Rotavirus vaccine for rotavirus; Influenza vaccine for the flu; Varicella vaccine for shingles; and All others for cholera, tetanus, typhoid and other viral/bacterial vaccines.  
 Source: IQVIA MIDAS; IQVIA Institute, Dec 2020



# New HIV combination treatments led to lower pill volume, even as days of therapy continued to increase, especially integrase inhibitors

*U.S. HIV Spending and Volume by Mechanism 1995-2020 and DDD, 2010-2020*

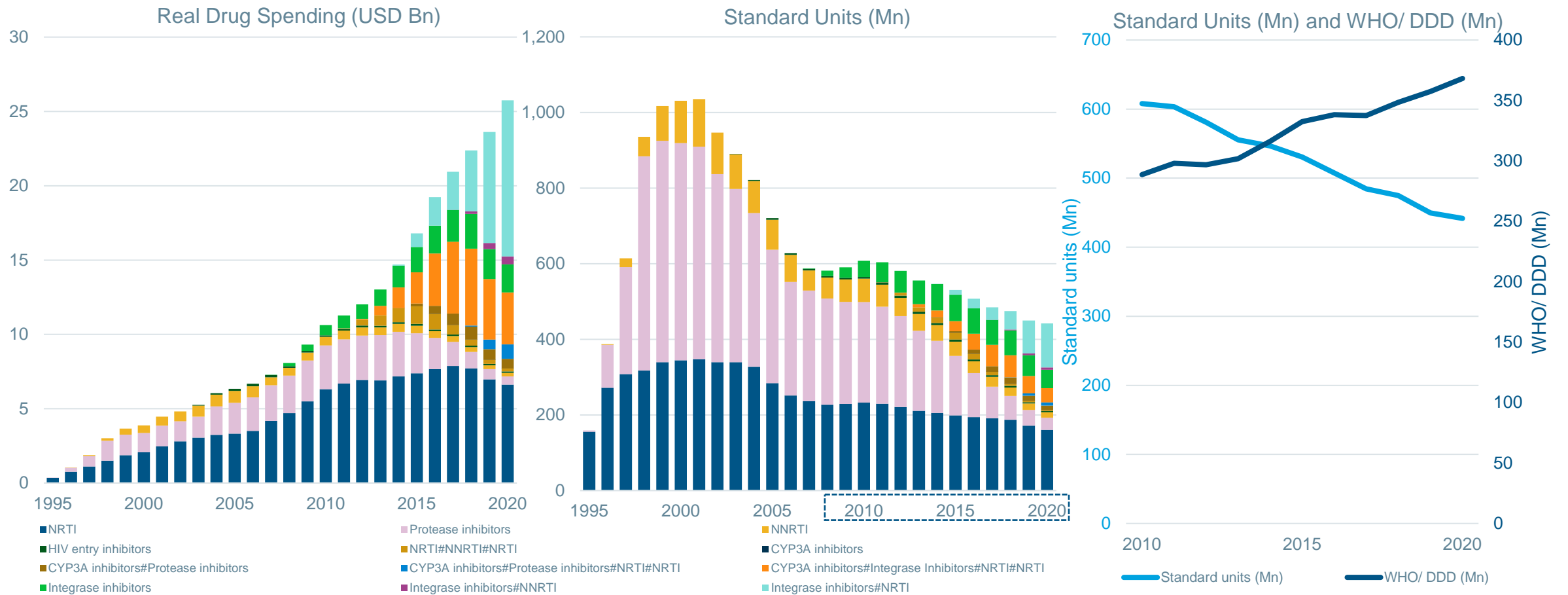


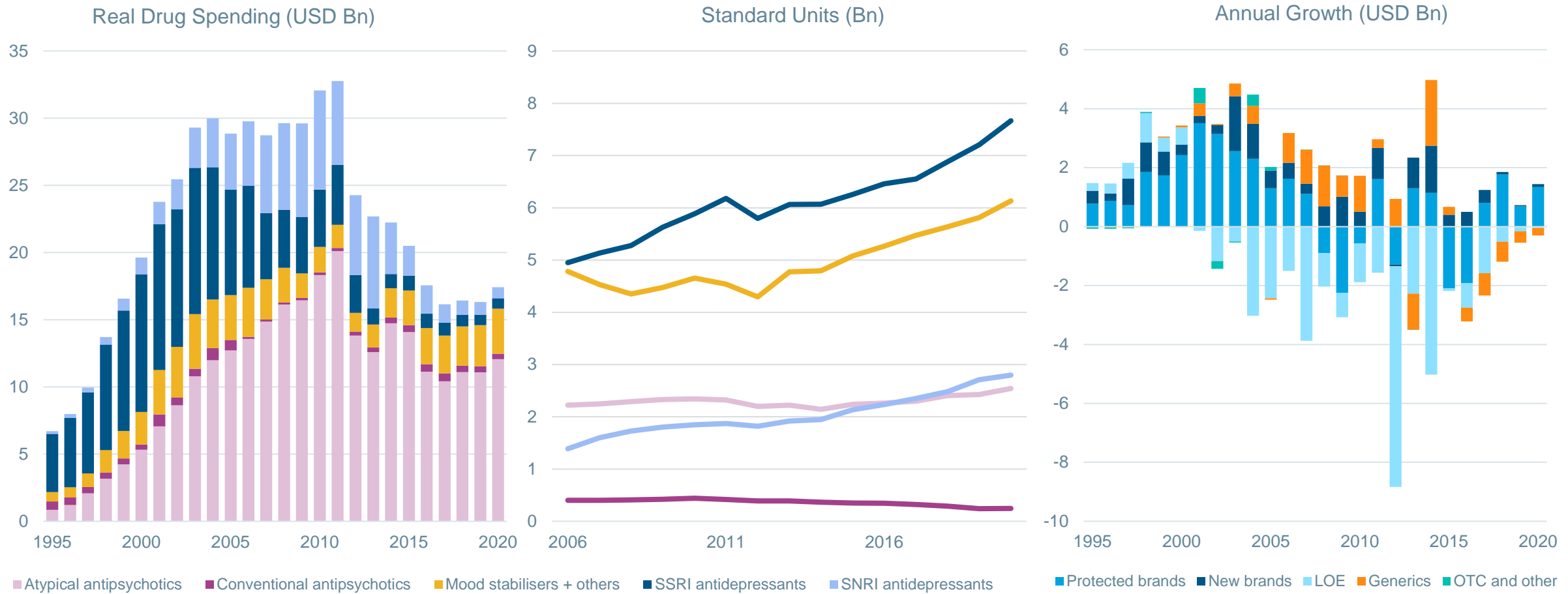
Chart notes: NRTI - Nucleos(t)ide reverse transcriptase inhibitor; NNRTI - Non- nucleoside reverse transcriptase inhibitor; CYP3A inhibitors - cytochrome P450 3A CYP3A inhibitors; # is used to define the combinations of mechanisms used in respective categories.

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context U.S Detail Appendix

# Mental health spending is half the 2012 peak as most mechanisms have genericized; volume growth continues

*U.S. Mental Health Spending, Volume by Mechanism and Annual Growth by Product Type, 1995-2020*

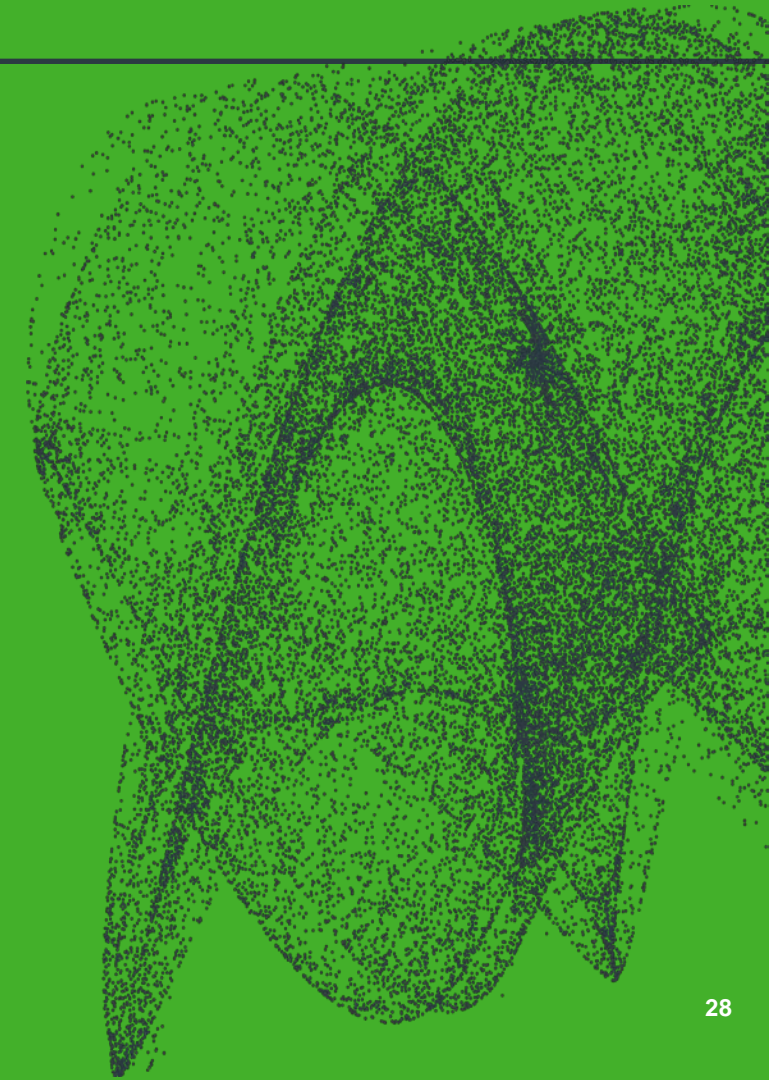


Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context U.S Detail Appendix



# Illustration and explanation of data and chart layouts



# Drug and Healthcare Spending Analyses

Key elements to note for interpreting charts

Drug and Healthcare Spending 1995-2018

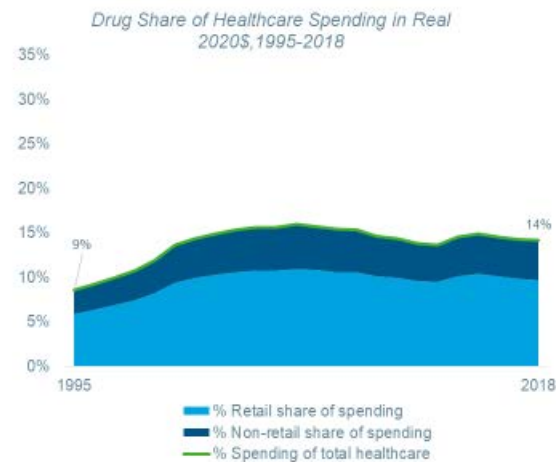
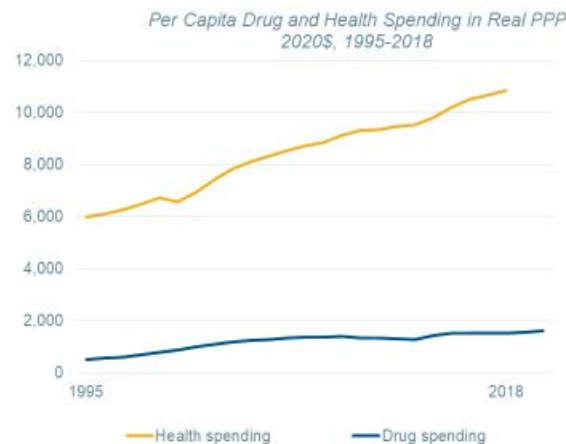


Chart Note: Methodology described in main report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*  
Source: IQVIA Institute for Human Data Science, Sep 2021

Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context U.S Detail Appendix

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4

- Drug and healthcare spend have been adjusted for economic growth ('real' GDP growth has been removed), population growth, and for cost of living differences (Purchasing Power Parity – PPP).
- Drug spending as a percentage of healthcare spending uses estimates of total drug spending in all channels (retail and hospital) and after discounts and rebates.
- The hospital drug spend adds 1-11 percentage points, depending on the country, to the retail drug share of healthcare that is most often reported by governments (OECD).
- The right-most chart illustrates how much of overall drug spending is attributable to non-retail spending, which is significant and varies over time.

# Drug spending is segmented by type of product, changing over time for some products to enable more complex analyses

*Illustrating the Drug Type Segmentation Used in the Report*

## Drug Expenditure Segmented by Type of Drug

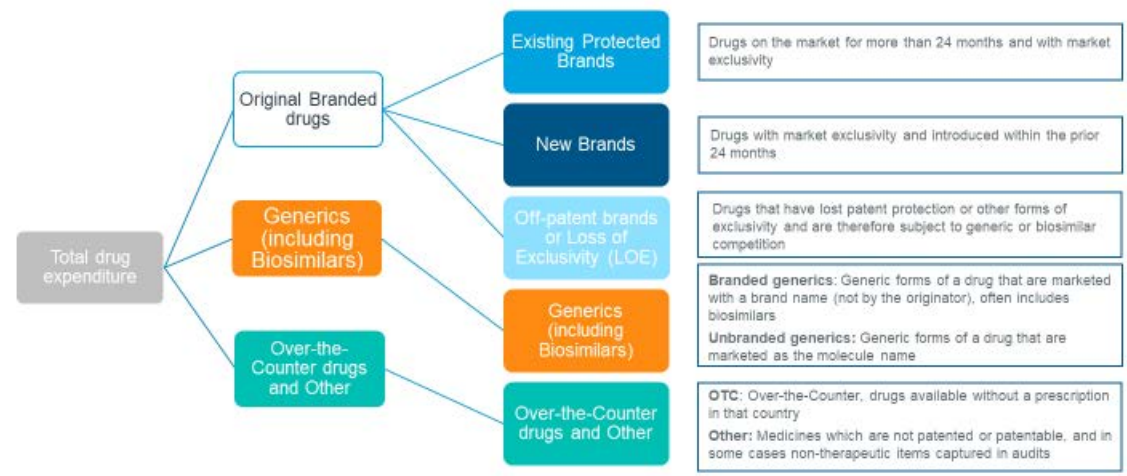


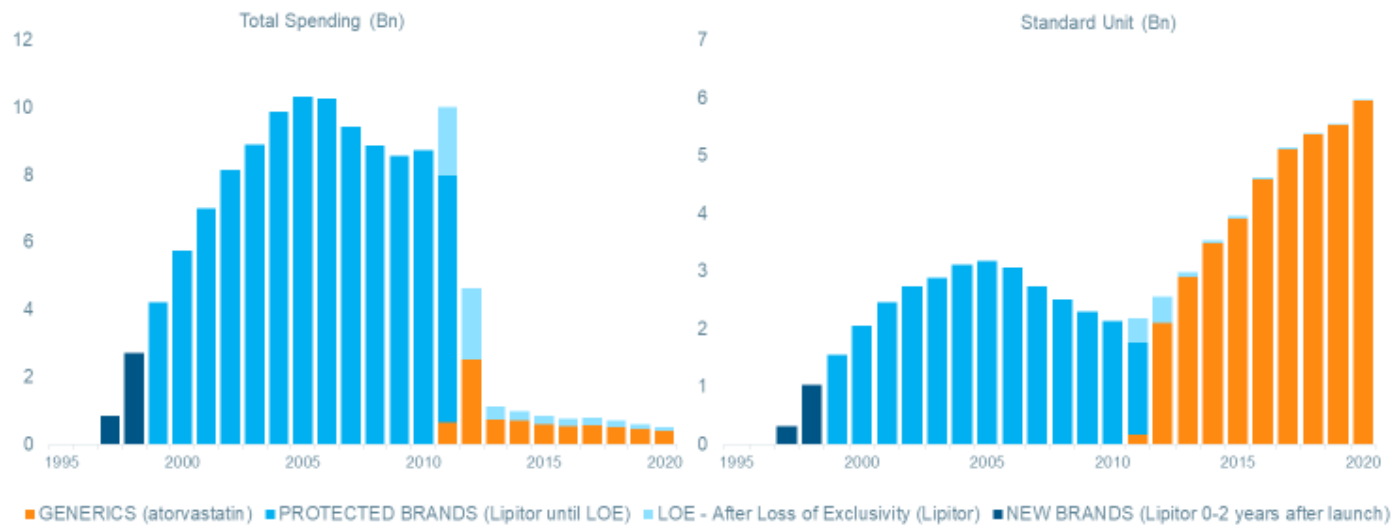
Chart notes: Protected brands include original protected brands, upcoming LOE and vaccines. New brands include original new brands; LOE include drugs that lost patent protection. Generics include non-original branded products as well as drugs that are marketed using the molecule name. OTC and other include non-prescription bound products and not patentable products. Due to the methods of combining multiple archived databases, products which are no longer marketed but had spending or volume in 2005 or earlier are included in the 'other' segment as specific segmentation was not possible.

- Analyses in this report that use product segmentations as shown here are based on IQVIA audited data. They do not reflect payer net spending due to the confidential nature of some of the discounts and rebates. Unless a page indicates a non-IQVIA source, the analysis would not be adjusted for off-invoice discounts and rebates.
- Products have been segmented both by the way they are marketed (brands, generics, biosimilars, Over-the-counter) as well as by the status of their patent or other types of protection.
- Existing Protected brands are those which are no longer 'new' and are not yet off-patent.
- New brands are defined as those products within their first 2 years in the market; however, some analytics in this report specifically identify older new brands from 3-5 years after launch.
- Loss of exclusivity is the status for branded products that are off-patent or no longer protected (but still had sales in the market) and these terms are used interchangeably in the report.
- Generics and biosimilars are treated in the same segment unless noted specifically on the chart.
- Over-the-counter status is a country-specific regulatory status and some drugs have both prescription-bound and OTC packs in the market.
- Other is a status where products either do not have typical brand or generic or protection statuses or where the product is no longer marketed and it was not possible to apply segmentation.

# Illustration: product segmentation drug lifecycle dynamics

*Example of Drug Type Segmentation using a single medicine*

*Exhibit x: Illustration of U.S. branded and generic segmentation, Lipitor and Atorvastatin generics*



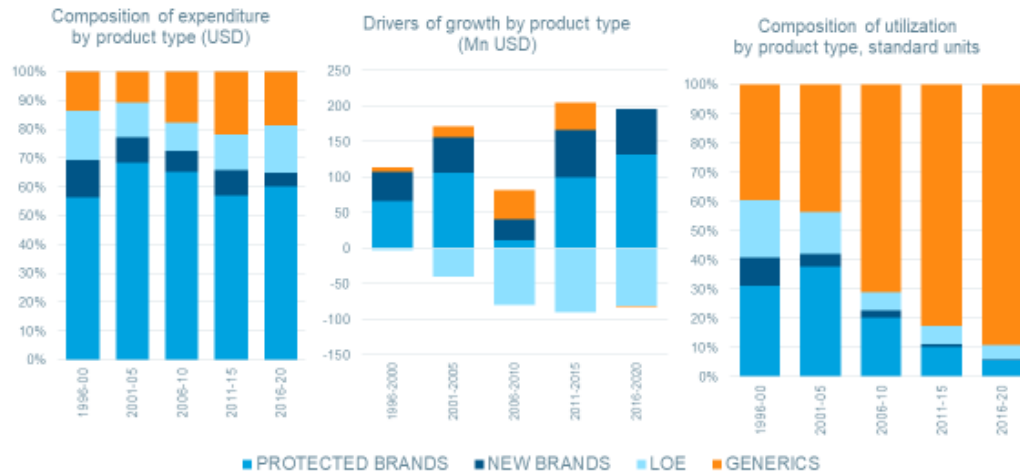
- In this example, the drug 'atorvastatin' begins life as a New Brand when Lipitor launched.
- The segmentation changes after 24 months to 'Protected Brand'. Analyses are based on quarterly time periods and a product may be considered new in 3 calendar years depending on the timing of launch in a country.
- At the point of patent expiry, the brand Lipitor becomes LOE, and new competing Generics enter the market.
- The left chart shows 'spending,' which is reflected in the currency noted on each chart. In the report the currencies are most often normalized to real 2020\$ with constant US\$ exchange rates, but in the country appendix local currencies are used.
- The right chart shows values in standard units. Standard units vary by form and are generally not recommended to report in this aggregated way. However most drugs in the therapy areas were similar enough to enable this analysis.



# Illustration of data and charts in this report

## Country level overview of product types

### Drug Spending and Utilization 1995-2020



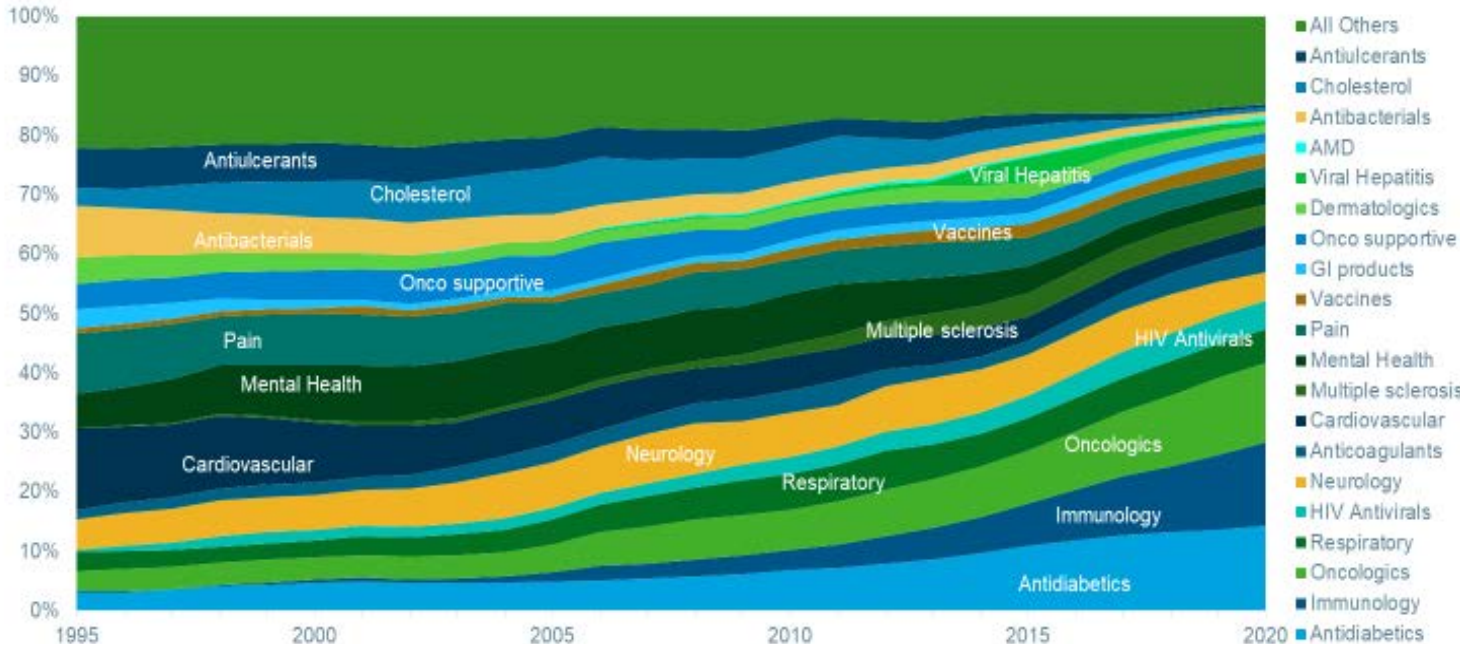
- Protected brands including new products average less than 70% of spending consistently
- Generic share of combined generic and LOE segments increasing steadily over time
- Generic share of volume increasing as generations of products shift to off-patent
- Most growth is driven by protected brands including new products, and offset by losses of exclusivity

- This analysis includes three views of drug spending, growth and volume in standard units, each present in the cross-country comparison section of the report and repeated in the beginning of each country section of the appendix.
- Spending is IQVIA audited sales and does not reflect off-invoice discounts and rebates.
- The drivers of growth chart is represented in absolute values of the currency noted.
- Products each have a segment status in each time period, and growth is a representation of the current group of products and their growth compared to prior periods. The product status in the prior period is not considered.
- Growth on an annual basis has been added together into 5-year groupings.
- Standard units are highly dissimilar by formulation and not recommended.

# Illustration of data and charts in this report

Total drug spending over time on 100% scale by top 20 Therapy areas

US Composition of Drug Real Local Currency Spending by Drug Class, 1995-2020

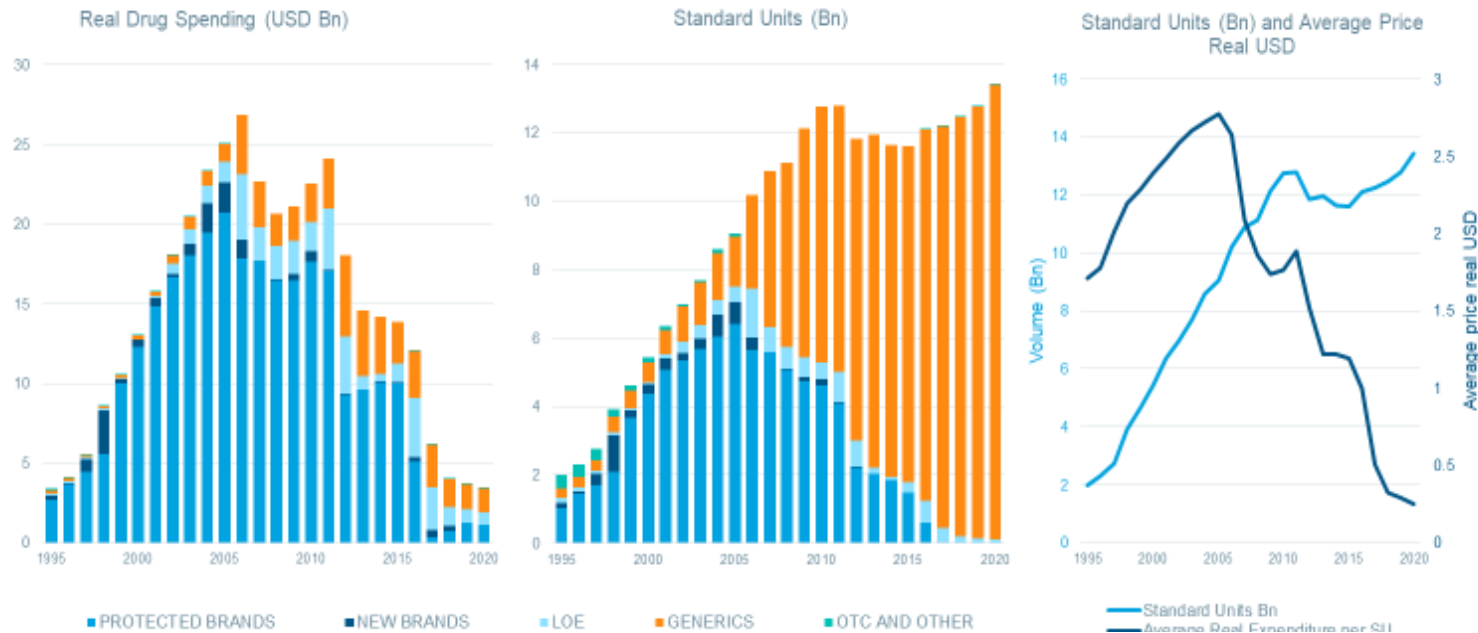


- Total IQVIA audited spending over 25 years has been collated and grouped by therapy areas.
- The therapy areas are defined by IQVIA with details of the definitions in the main report methodology section.
- The therapy areas called out by name are the classes that were ranked in the top 20 the most often across the eleven countries studied across the 25 years. This can mean that some classes which have declined in sales outside the top 20 in the most recent period are still shown.

# Therapy area charts with sales, volume and cost by type of drug

Example of single therapy area with multiple metrics analyzed

US Cholesterol Volumes, Average Prices and Spending by Product Type, 1995-2020

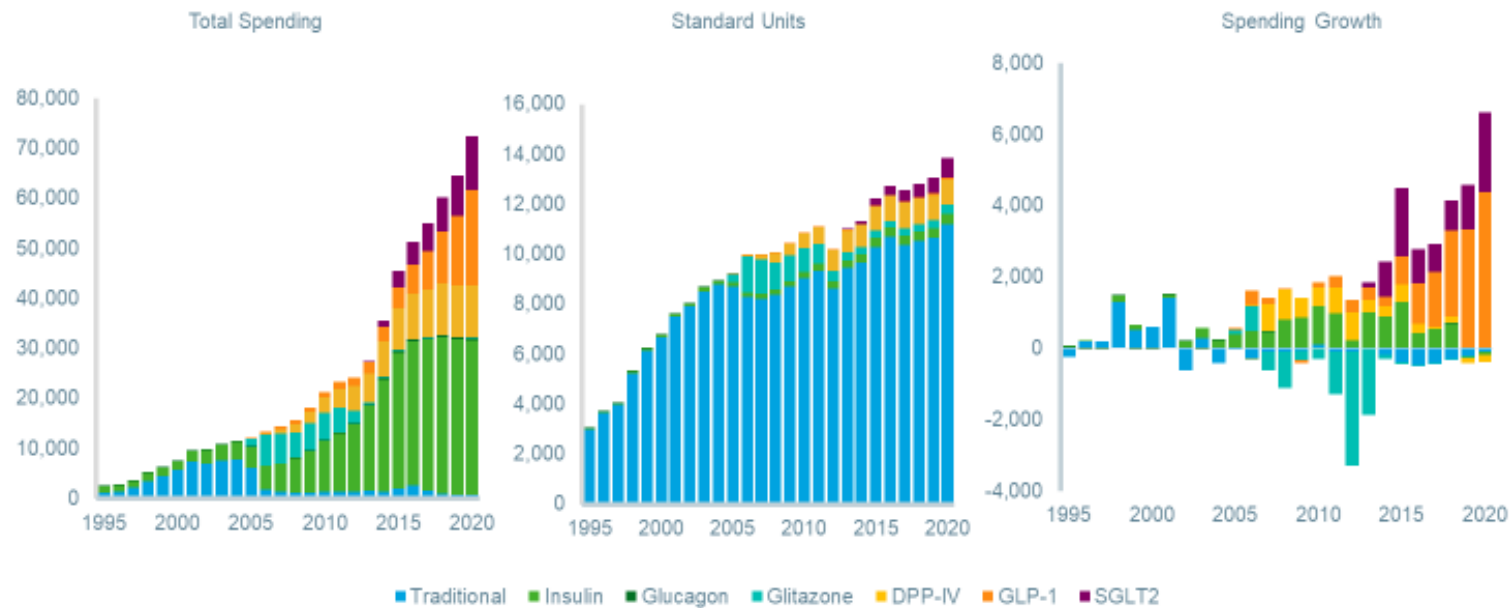


- Some analyses show three charts in this orientation, with spending, standard unit volume and finally a chart of volume and average cost per standard unit.
- Spending and cost are based on IQVIA audited data and do not reflect discounts and rebates.
- The segmentations shown in the charts are the same as described earlier.
- The average cost calculation is at the therapy area level.

# Therapy areas showing subclasses by mechanism of action

*Illustration of a therapy area using multiple analysis metrics*

U.S. Diabetes Real Spending, Volume and Growth USD (Mn) by Drug Type, 1995-2020



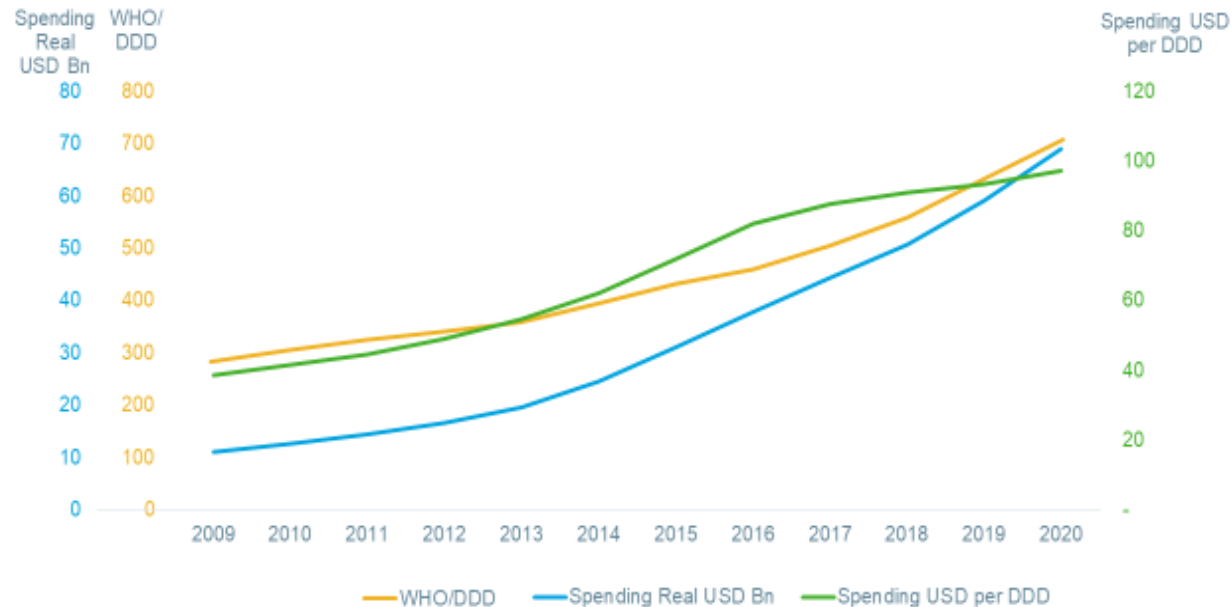
- Some therapy area charts include spending, standard units and spending growth.
- All are shown in the currency value noted.
- The colors of the chart indicate therapy sub segments, typically indicating shifts in the types of medicines used over time.

# Autoimmune biologic charts

Illustration of three metrics on three axes on the same chart

## Cost per day in immunology had been rising rapidly but has slowed since the first introduction of biosimilars in 2016

US Auto-immune Biologic Spending, DDD and Cost 2009-2020



Sources: IQVIA MIDAS, IQVIA Institute, December 2020

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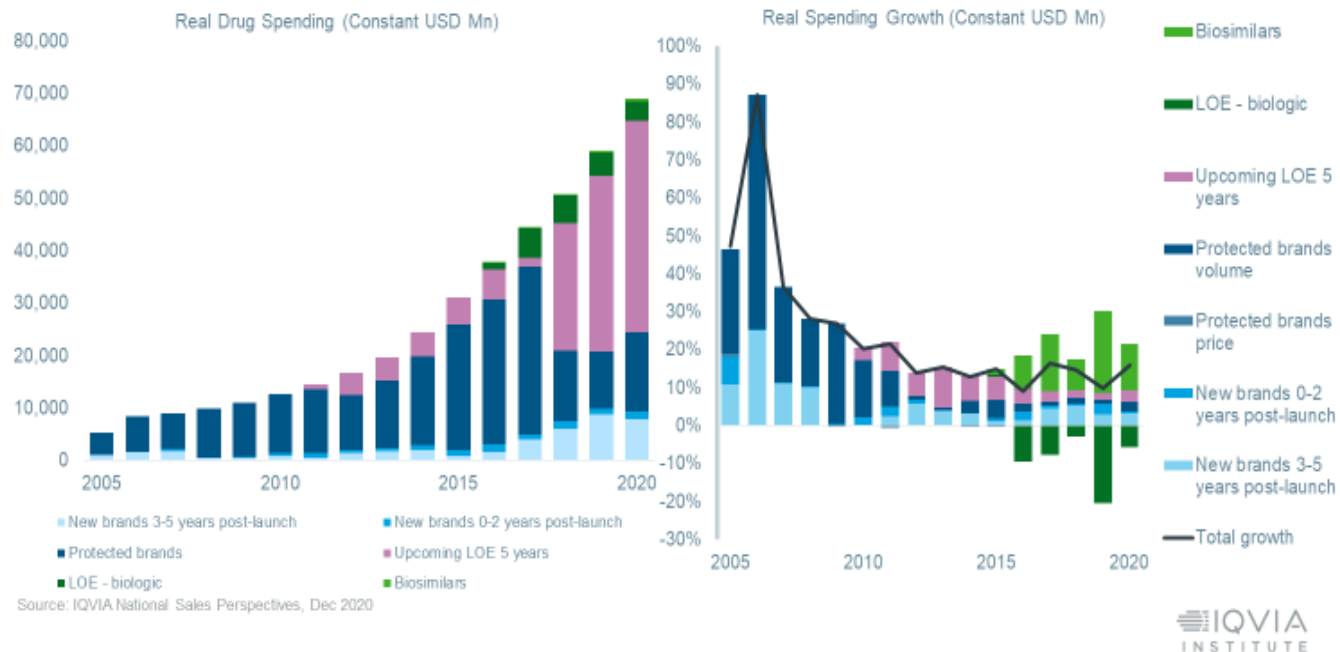
- This chart layout is used for the autoimmune biologic market.
- It has 3 axes which are color-matched to the lines
- Two axes are on the left (sales and volume in WHO Defined Daily Doses – WHODDD). The color of the lines matches the color used on the axis to show increments.
- WHODDD represent a standardized dose used for all patients and normalized for packaging and formulation differences which are common with some products in this therapy area.
- WHODDD is particularly helpful for comparisons when original and biosimilar products are packaged differently from each other.

# Charts using a more granular product type view

*Illustration of product type segmentation with forward-looking segment*

## More than half of autoimmune biologic spending is due to lose exclusivity in next 5 years

*U.S. Auto-immune Biologic Invoice Spending and Growth Drivers, 2005-2020*



- Oncology and Autoimmune charts employ a more granular time-dependent segmentation of product type than other analyses in the report.
- Original biologics and small molecules when off-patent are identified separately as well as generics (small molecule) and biosimilars.
- The autoimmune charts are limited to biologic products and therefore exclude some small molecule products that could be relevant in some analyses such as JAK inhibitors.
- The upcoming LOE 5 years segment is composed of different products each year as their status changes, and refers to the expected entry of biosimilars in key products in future years.
- New products are shown with both 0-2 years and 3-5 year segments.
- Brands that are not 'new' and not LOE are shown as 'protected' and growth charts are split by price and volume.

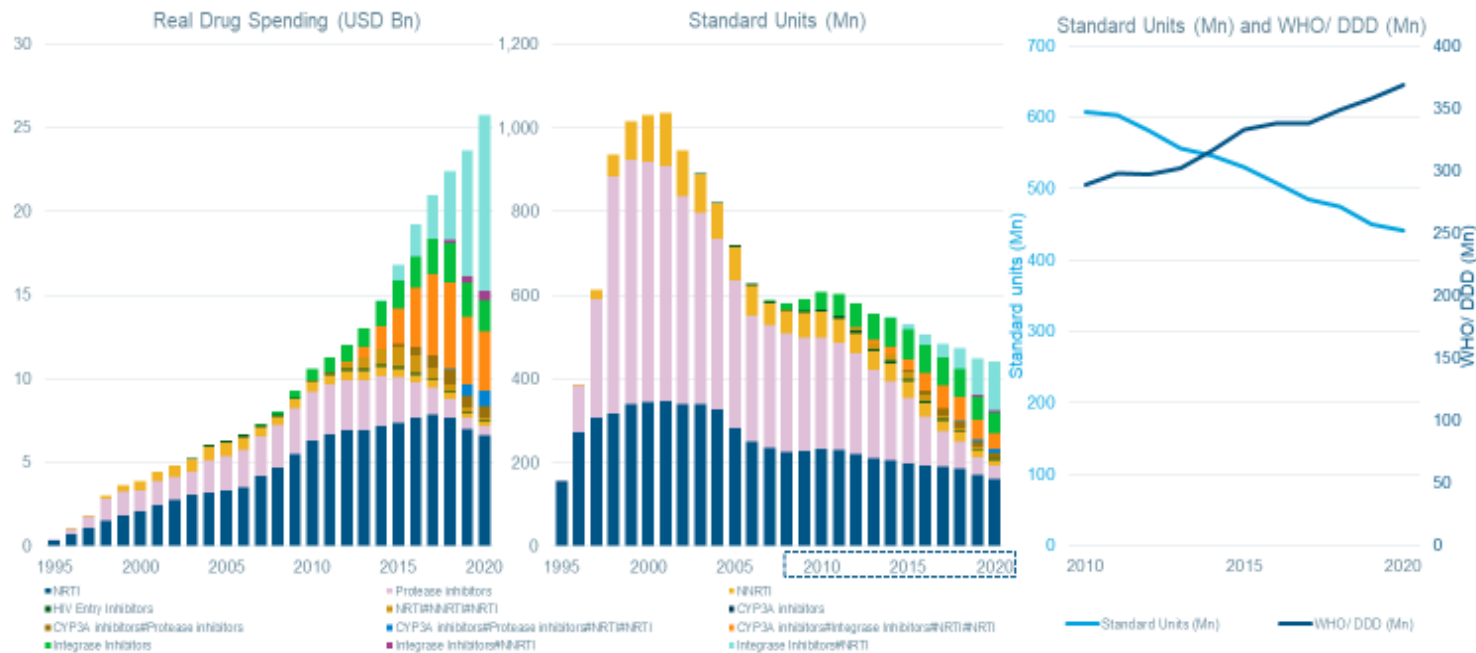


# HIV market charts

*Illustration of products with varying mechanisms of action*

## New combination treatments with low dosing regimens led to reduction in volume, offset by an increase of days of therapy

*US HIV Spending and Volume by Mechanism 1995-2020 and DDD, 2010-2020*



Sources: IQVIA MIDAS, IQVIA Institute, December 2020  
 Chart notes: NRTI - Nucleos(t)ide reverse transcriptase inhibitor; NNRTI - Non-nucleoside reverse transcriptase inhibitor; CYP3A inhibitors - cytochrome P450 3A CYP3A inhibitors; # is used to define the combinations of mechanisms used in respective categories



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- Products in this market have been grouped by mechanism of action.
- Fixed-dose combination products are grouped by the type of mechanism of each ingredient, with each mechanism separated by a '#' symbol.
- Volume is measured in standard units in the middle chart.
- In the right chart, volume is in both standard units and WHO DDD, and the shift in the trajectory of these two measures suggests a changing number of doses per day as combination products become more common.



Access the full report at [www.iqvainstitute.org](http://www.iqvainstitute.org)