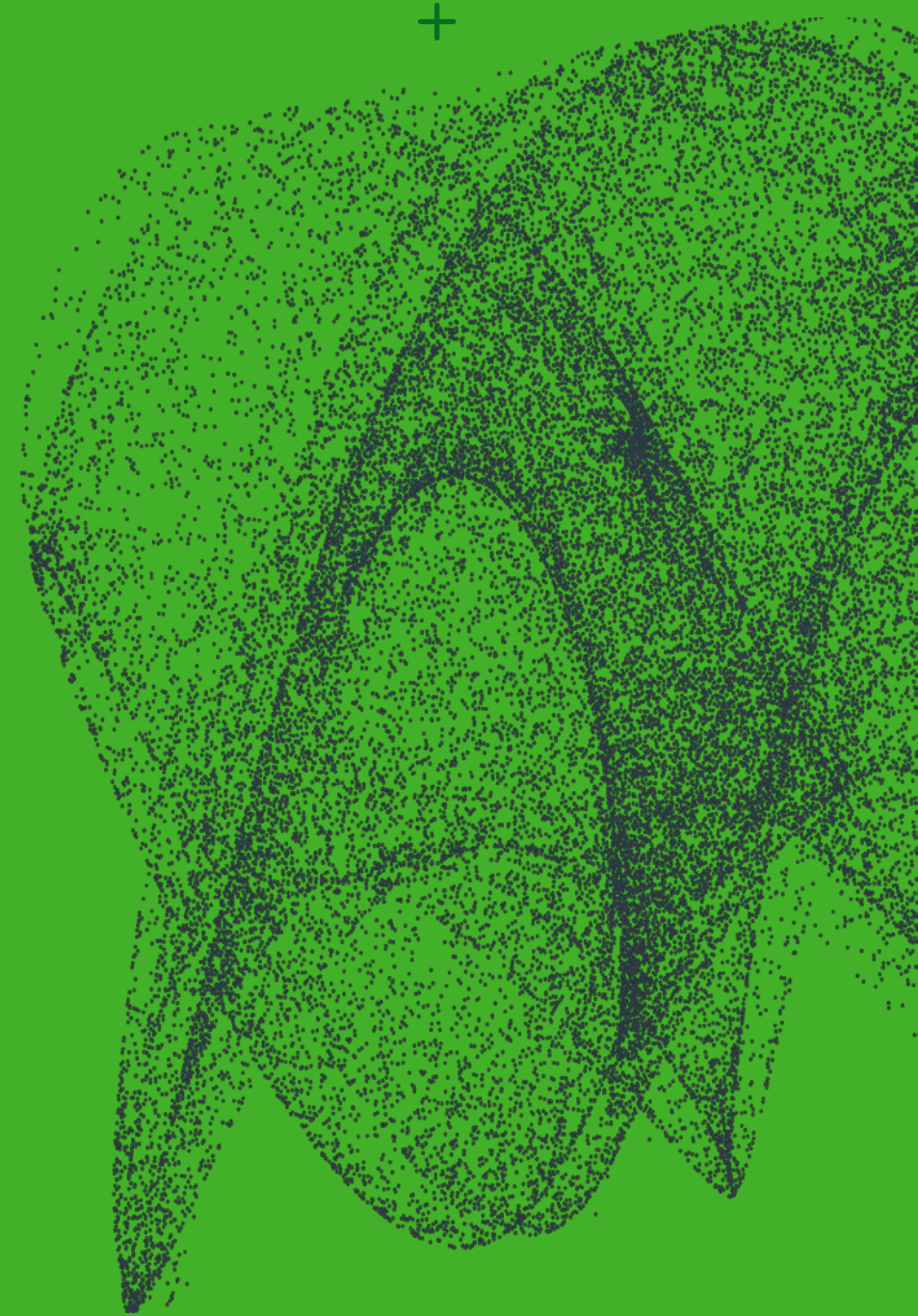


Drug Expenditure Dynamics 1995-2020

Understanding Medicine Spending in Context
Country Detail Appendix:

Italy

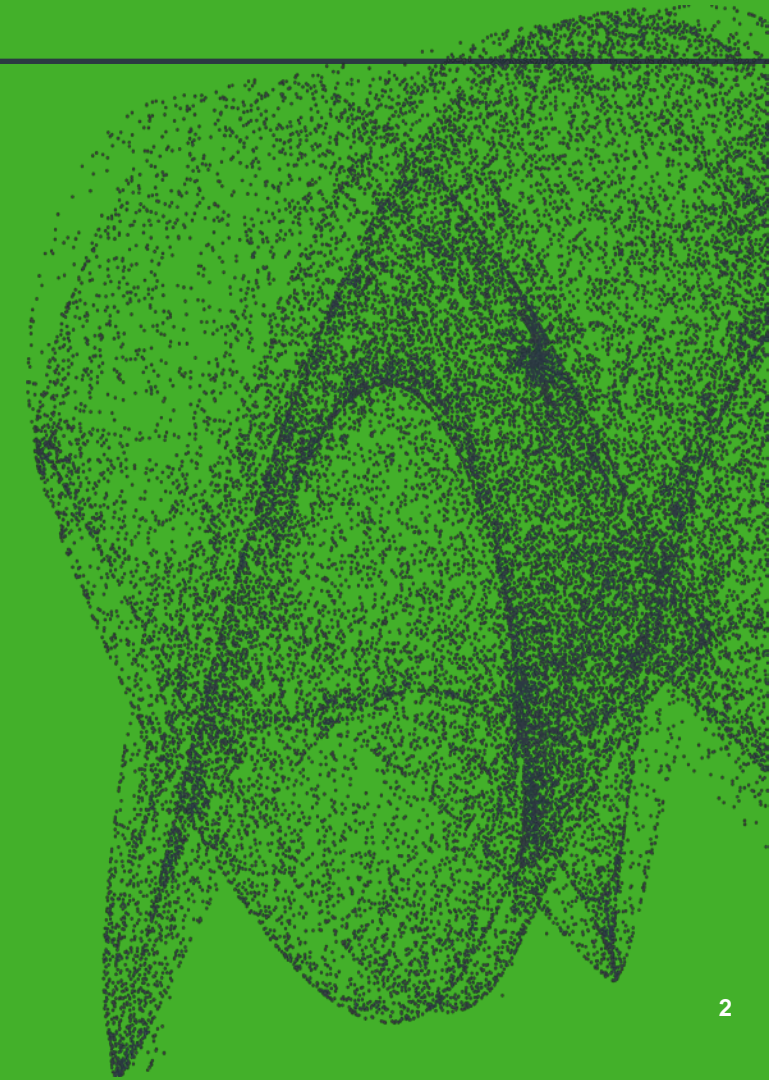


Introduction

- This document is intended as an accompanying appendix to the report Understanding the Dynamics of Drug Expenditure 1995-2020.
- 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 long-history 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.



Italy



Key findings

- Italian drug spending has been a relatively stable share of healthcare spending, with 16% in 1995 and 17% in 2018.
- Viral hepatitis spending peaked in 2016 at 11% of drug spending at list prices, but significant discounts were negotiated between industry and the government and total net drug spending only increased by 1% of net health spending.
- Drug spending includes retail pharmacy, drugs which represent 5% of total healthcare spending with an additional 12% of healthcare spending from non-retail, including high-cost medicines managed in a dedicated policy and considered non-retail despite some physical distribution via pharmacies.
- Spending has been distributed between brands and generics in relatively unchanged patterns for the past 10 years, despite significant increases in newer brand spending as generic volume itself continues to increase.
- The therapy area focus of spending has shifted from traditional classes, which dominated in the 1990s, to more specialty classes in 2020. Overall, the top four classes of 1995 (cardiovascular, immunology, pain, and anti-bacterials) represented about 47% of drug spending in 1995, but only 16% of spending in 2020, predominantly driven by genericization. The current leading classes (oncologics, immunology, antidiabetics, cardiovascular, and neurology) were 42% of spending in 2020, rising from 33% in 2000, illustrating a shift due to the influx of new treatment options in oncology and immunology and continued spending in diabetes, cardiovascular and neurology.
- Some classes (i.e., cholesterol, anti-ulcerants) have had important innovation early in the period followed by genericization resulting in dramatic declines in the cost of those medicines.
- Other classes (i.e., immunology, oncology) have had continuous introduction of new innovative drugs which are either added to regimens or supersede previous standards of care.

Italy drug spending share of healthcare is unchanged over 25 years, with more non-retail spending from managed innovation funding

Drug and Healthcare Spending 1995-2018

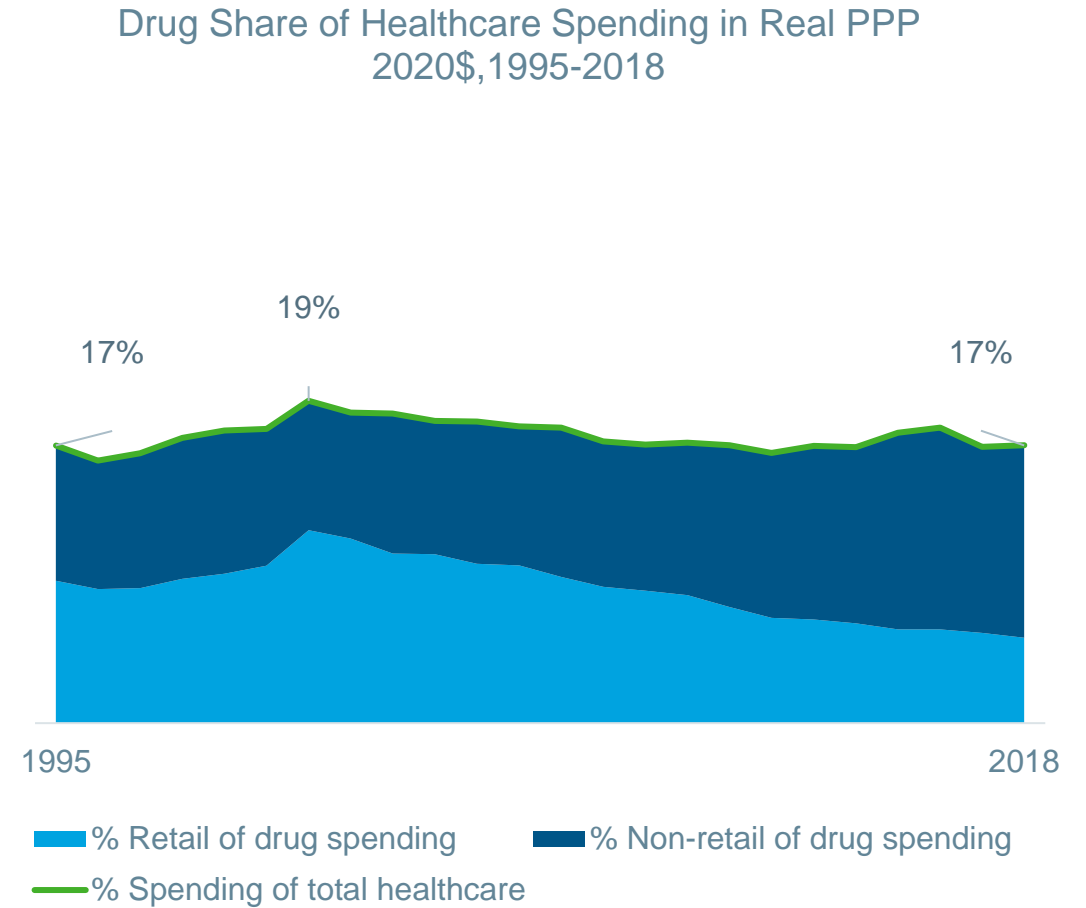
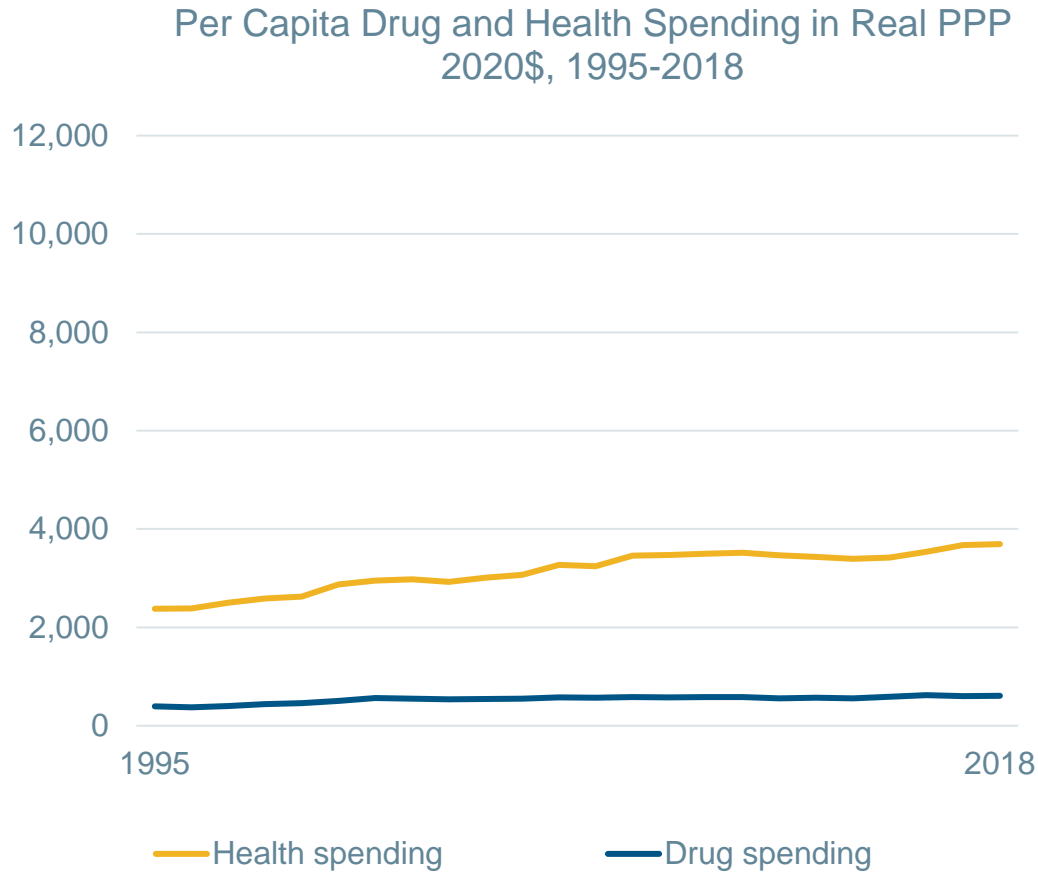
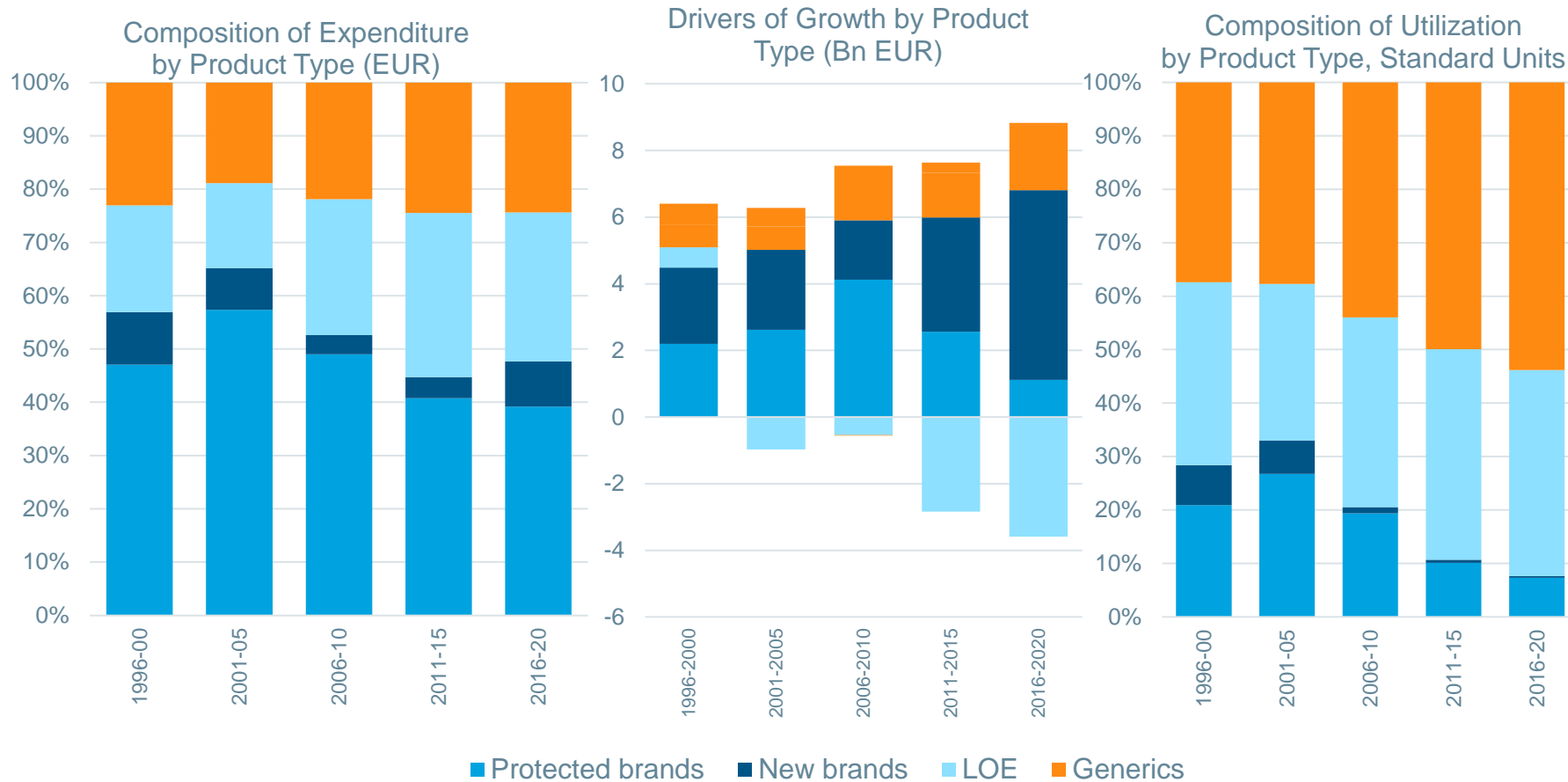


Chart Note: Methodology described in main report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*
Source: IQVIA Institute for Human Data Science, Sep 2021

Growth by new brands continues as the cycle of genericization results in lower costs in those medicines

Italy Drug Spending and Utilization 1995-2020

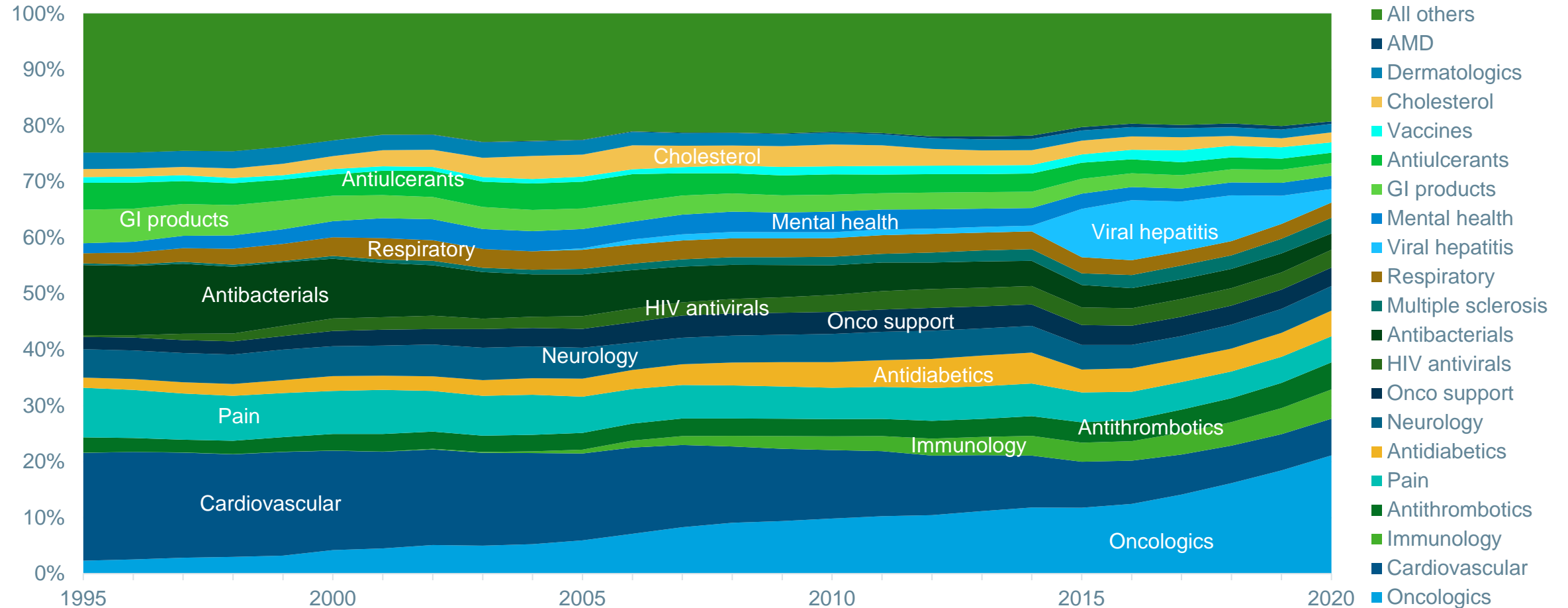


- Protected brands have a lower share of spending in the past decade consistent with shifts in national pricing policy
- Generic share of combined generic and LOE segments increasing is also consistent with shifts in policy
- Most growth is driven by new brands, including protected products, and offset by losses of exclusivity

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Significant spending on viral hepatitis has largely returned to pre-2015 levels, while oncology and immunology grow

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

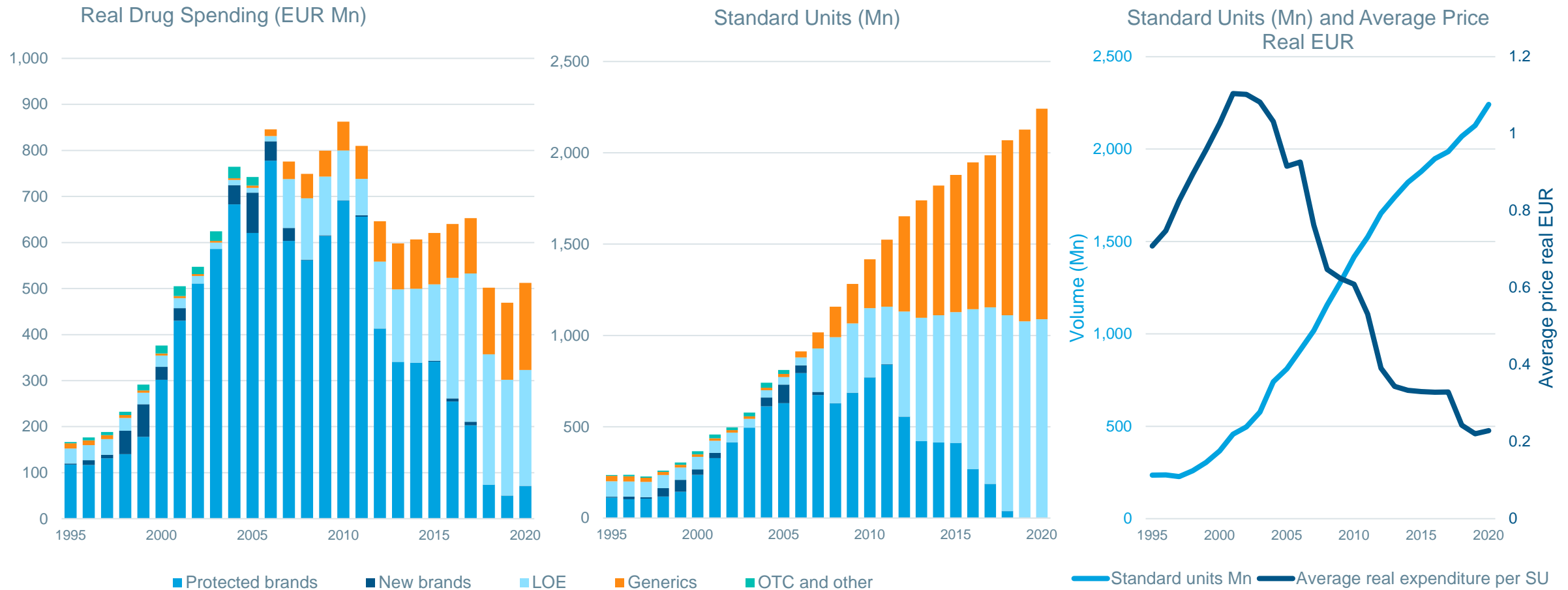


Note: Spending does not reflect discounts and rebates which are thought to be particularly impactful for viral hepatitis

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Cholesterol spending has dropped since the peak in 2010 but off-patent brands retain nearly half of the unprotected market

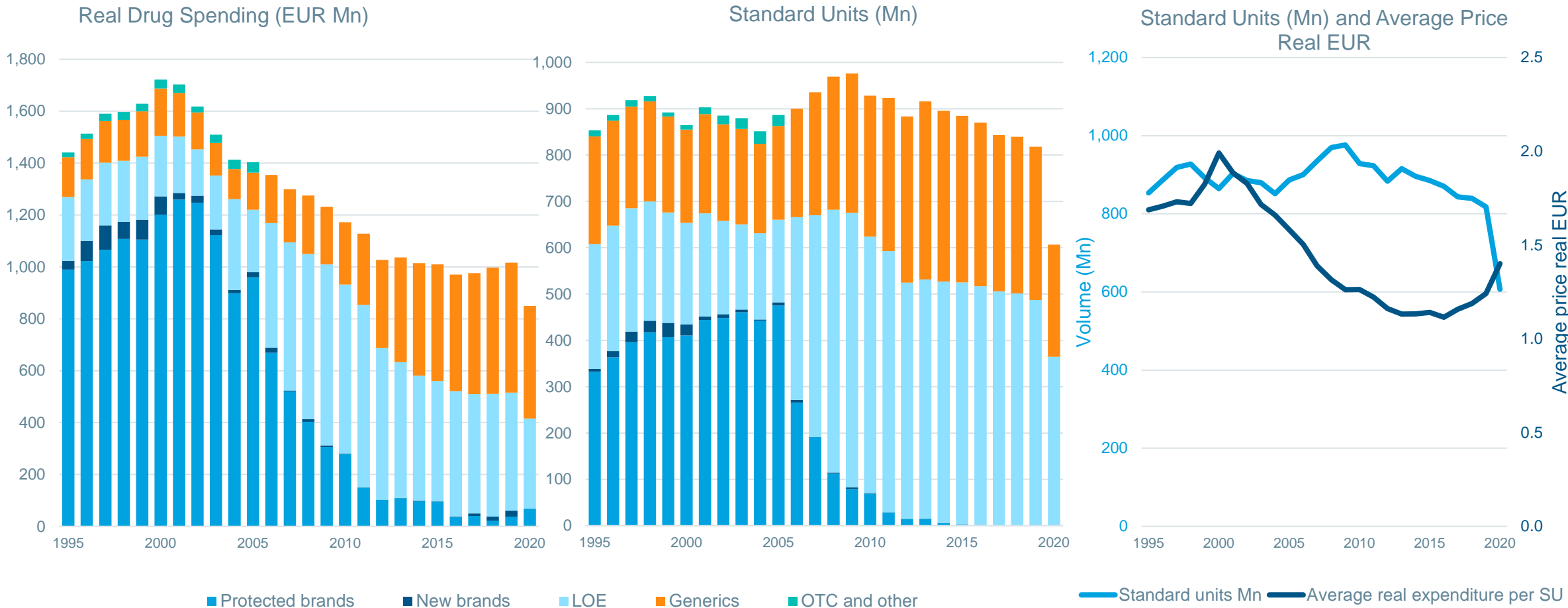
Italy Cholesterol Volumes, Average Prices and Spending by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Antibacterial volume has been declining, off-patent brands retain volume and revenue

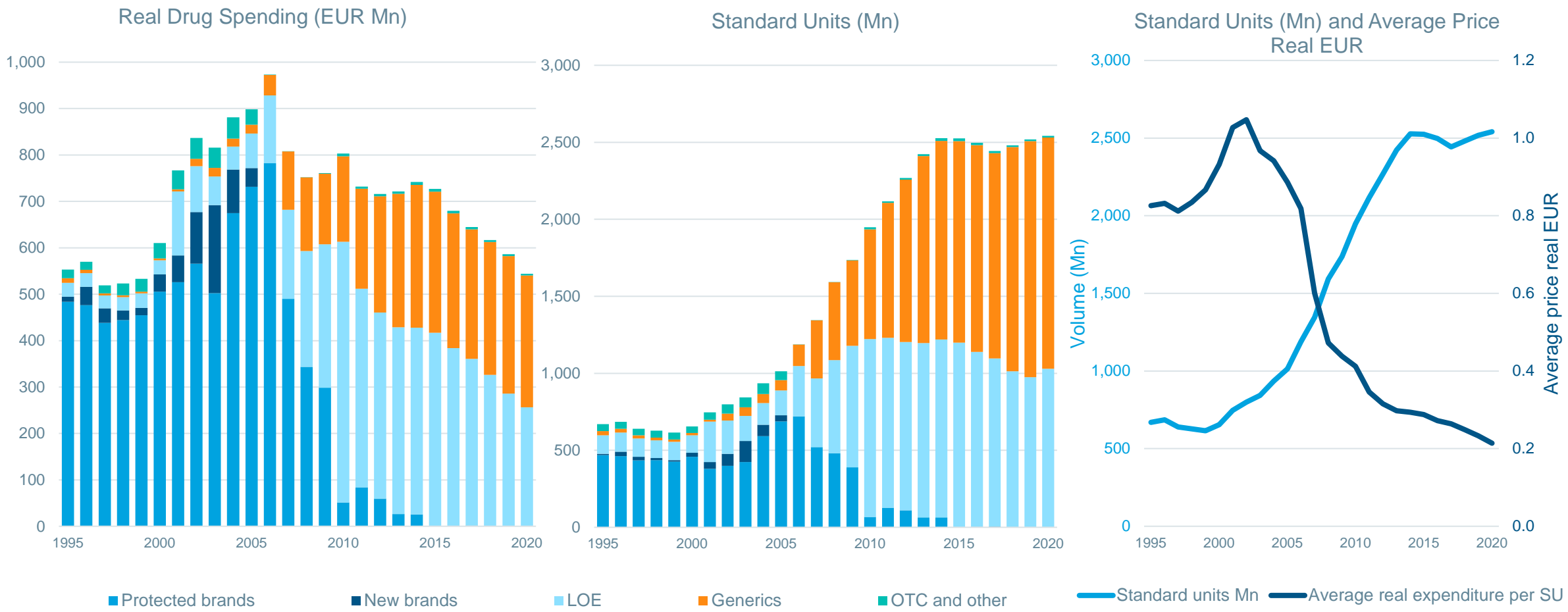
Italy Antibacterial Volumes, Average Prices and Spending by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Anti-ulcerant costs declined since early 2000s from expiries while off-patent brands retain volume and revenue at lower prices

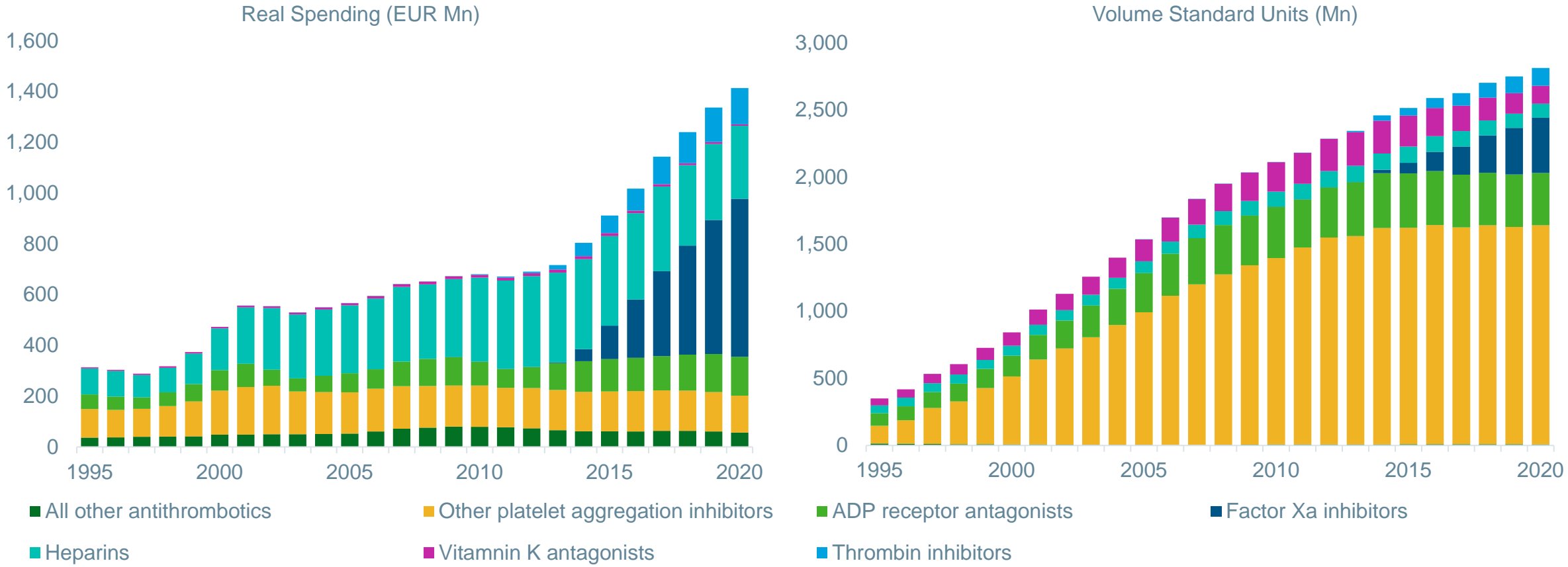
Italy Anti-Ulcerants Volumes, Average Prices and Spending by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

ADP receptors (clopidogrel) were not as widely adopted in Italy compared to other countries; growth was slower until Factor Xas

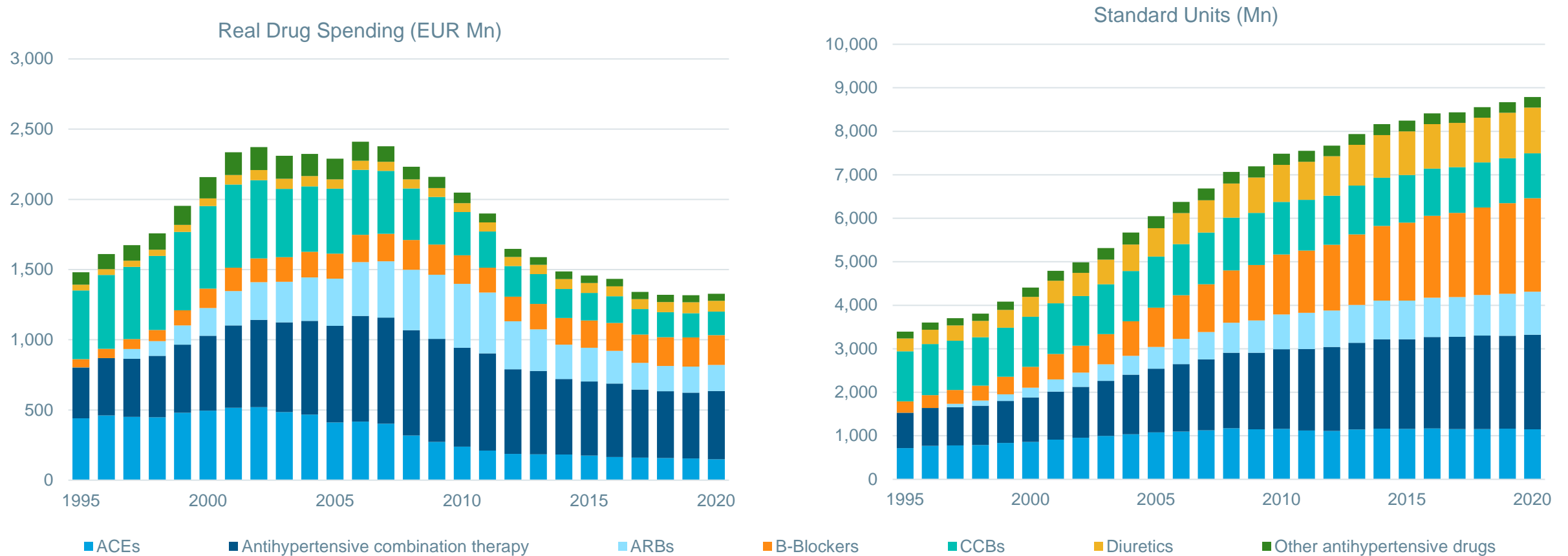
Italy Antithrombotics Spending and Volumes by Drug Type, 1995-2020



Source: IQVIA MIDAS, IQVIA Institute, December 2020

Hypertension spending declined by 45% since 1995 while B-Blockers and ARBs usage increased 12-fold

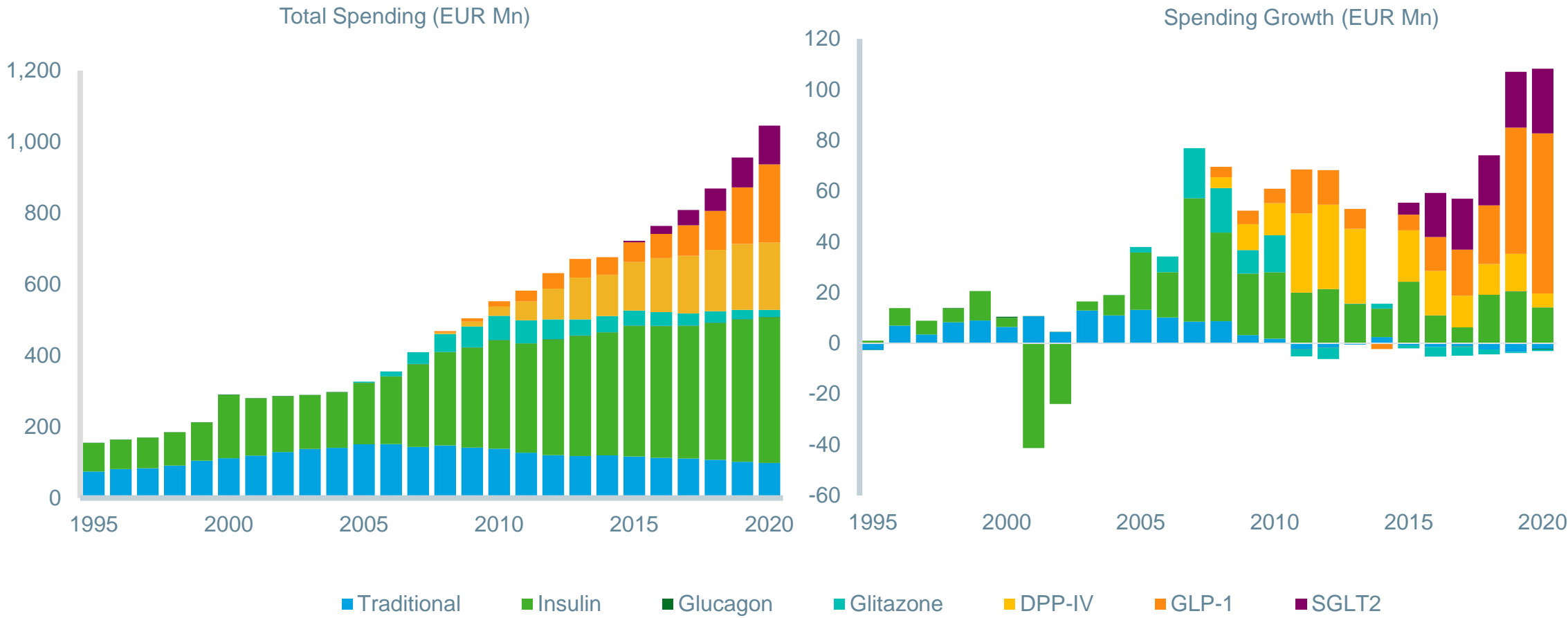
Italy Hypertension Spending and Volume by Mechanism, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Diabetes traditional therapy and insulin spending underpins diabetes while innovation drives all growth

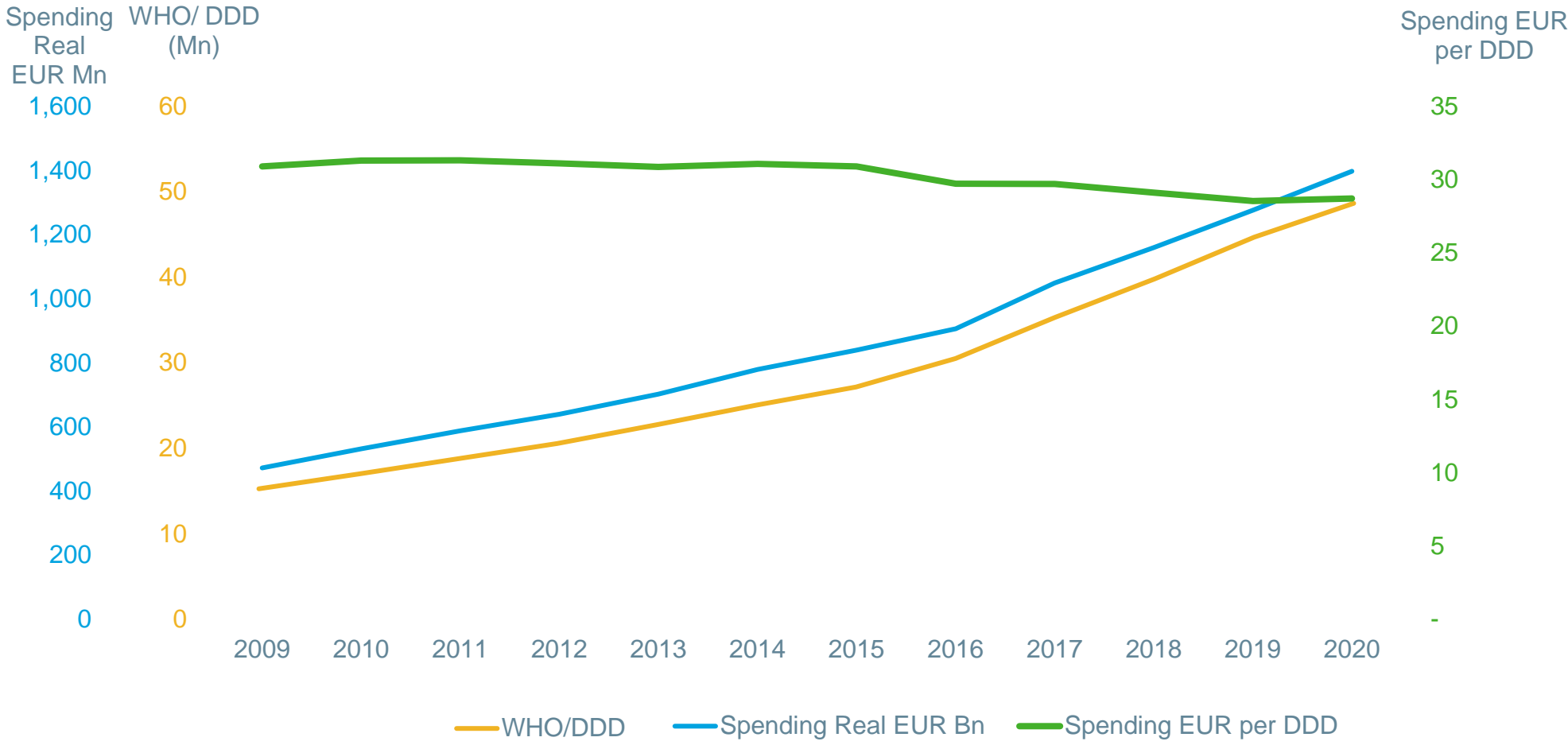
Italy Diabetes Real Spending and Growth EUR (Mn) by Drug Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Auto-immune cost per day of therapy stayed constant at 30€, while use more than tripled from roughly 15 Mn to 48 Mn days by 2020

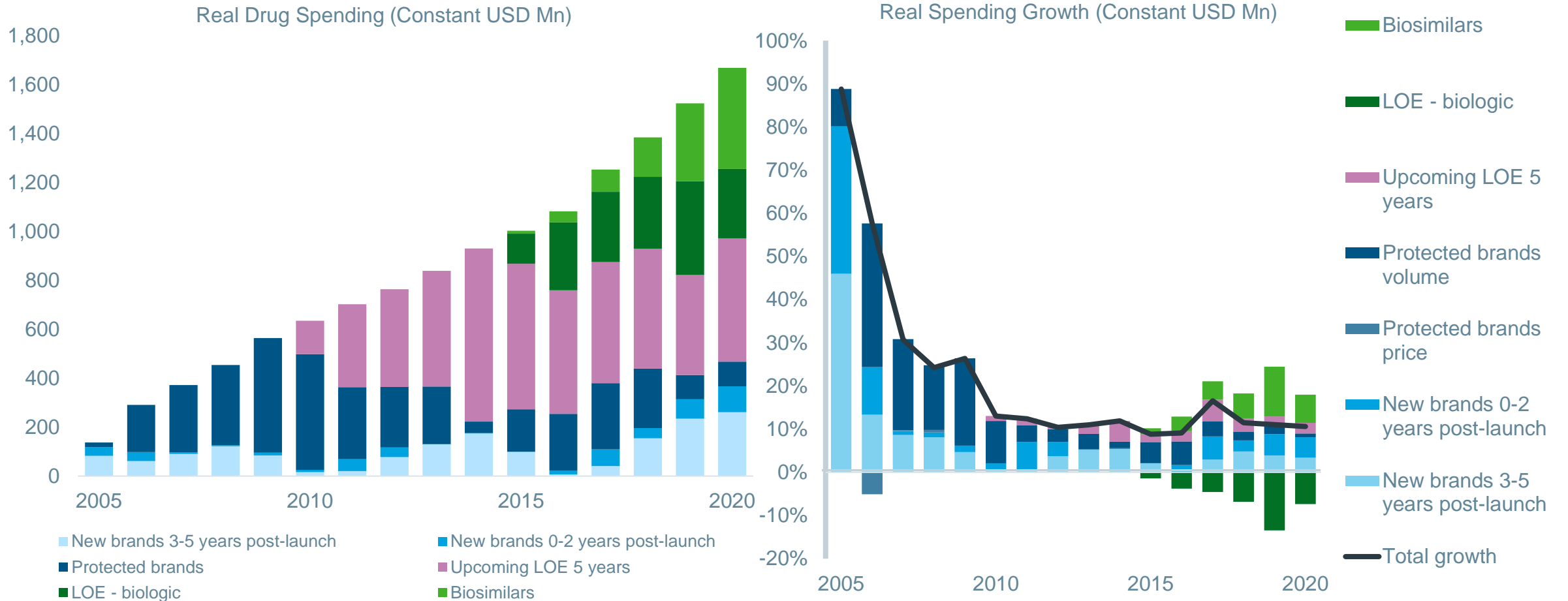
Italy Autoimmune Biologic Spending, DDD and Cost, 2009-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Auto-immune biologic growth slowing from biosimilar impact in the past 6 years and more expected through 2025

Italy Autoimmune Biologic Invoice Spending and Growth Drivers, 2005-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

HPV, meningitis, pneumonia, and shingles share of vaccine spending increased from 32% in 2007 to 60% in 2018

Italy Vaccine Spending and Volumes by Drug Type, 1995-2020

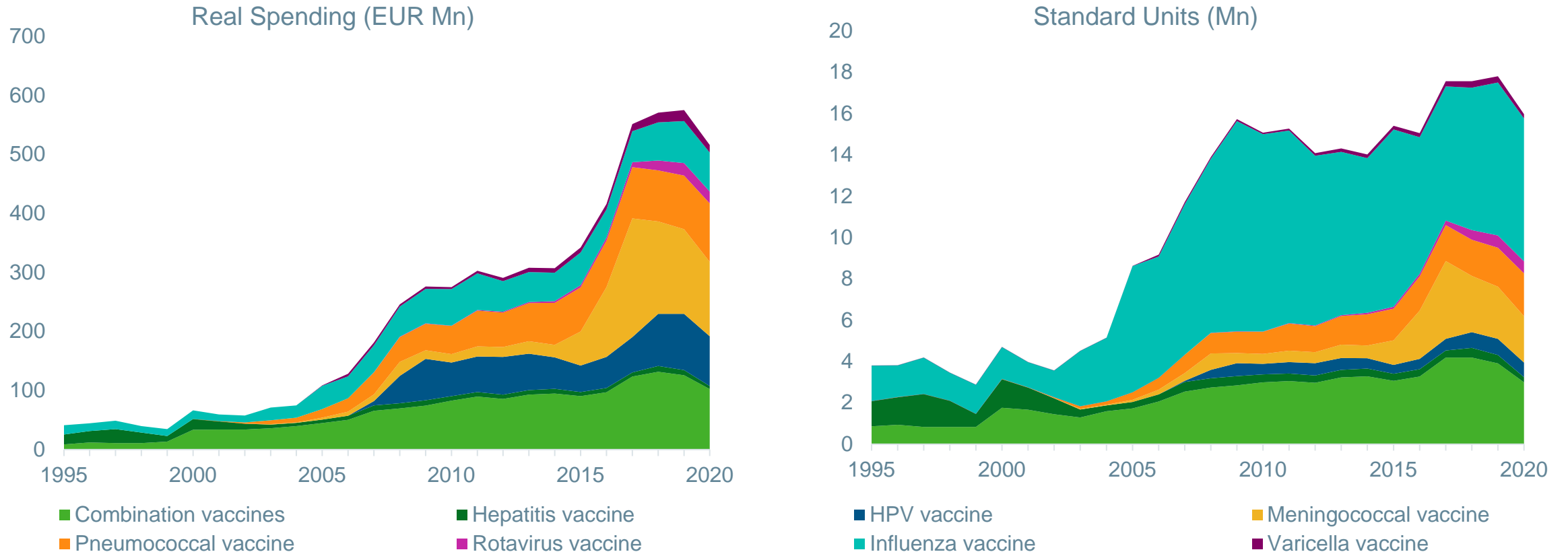
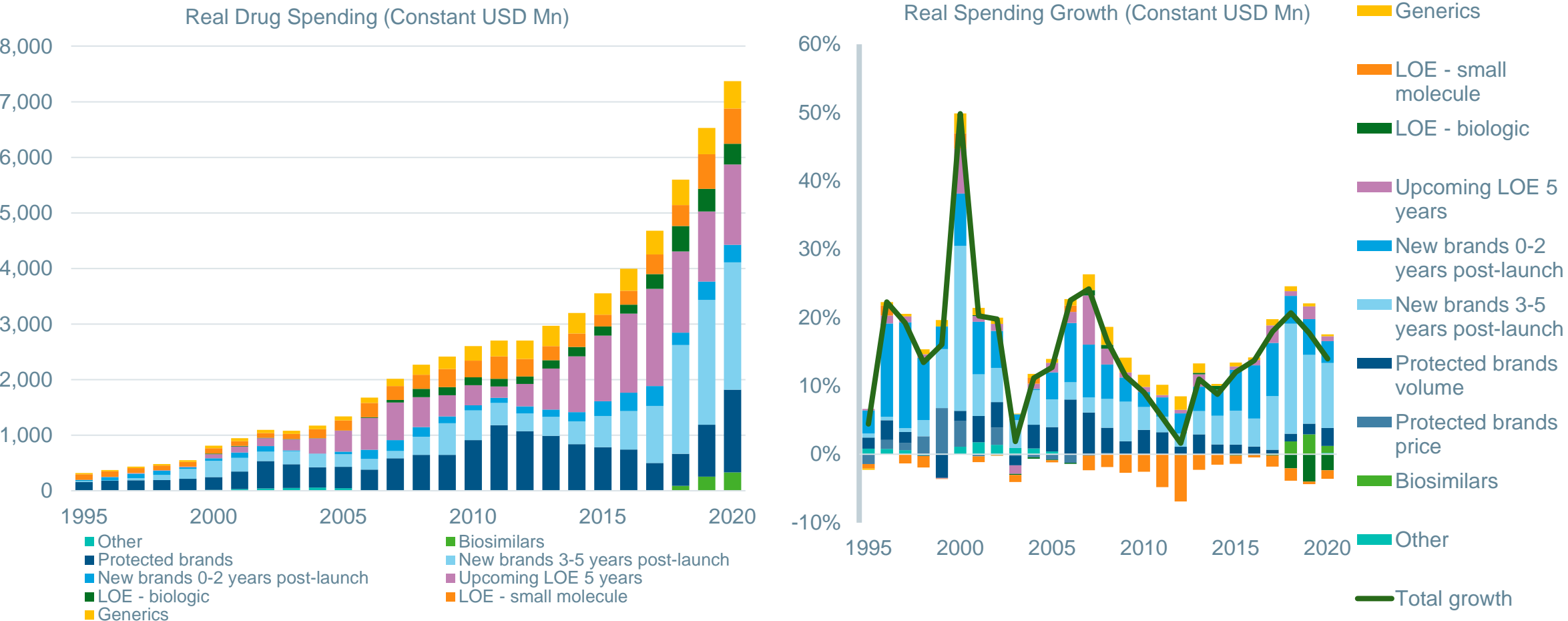


Chart notes: Combination vaccines represent combined vaccines (with measles, mumps, tetanus or other); HPV vaccine for human papillomavirus; Meningococcal vaccine for meningitis; Pneumococcal vaccine for pneumonia; Rotavirus vaccine for rotavirus; Influenza vaccine for the flu; Varicella vaccine for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

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Oncology growth is from new brands and offset by limited generic and biosimilar impact to date

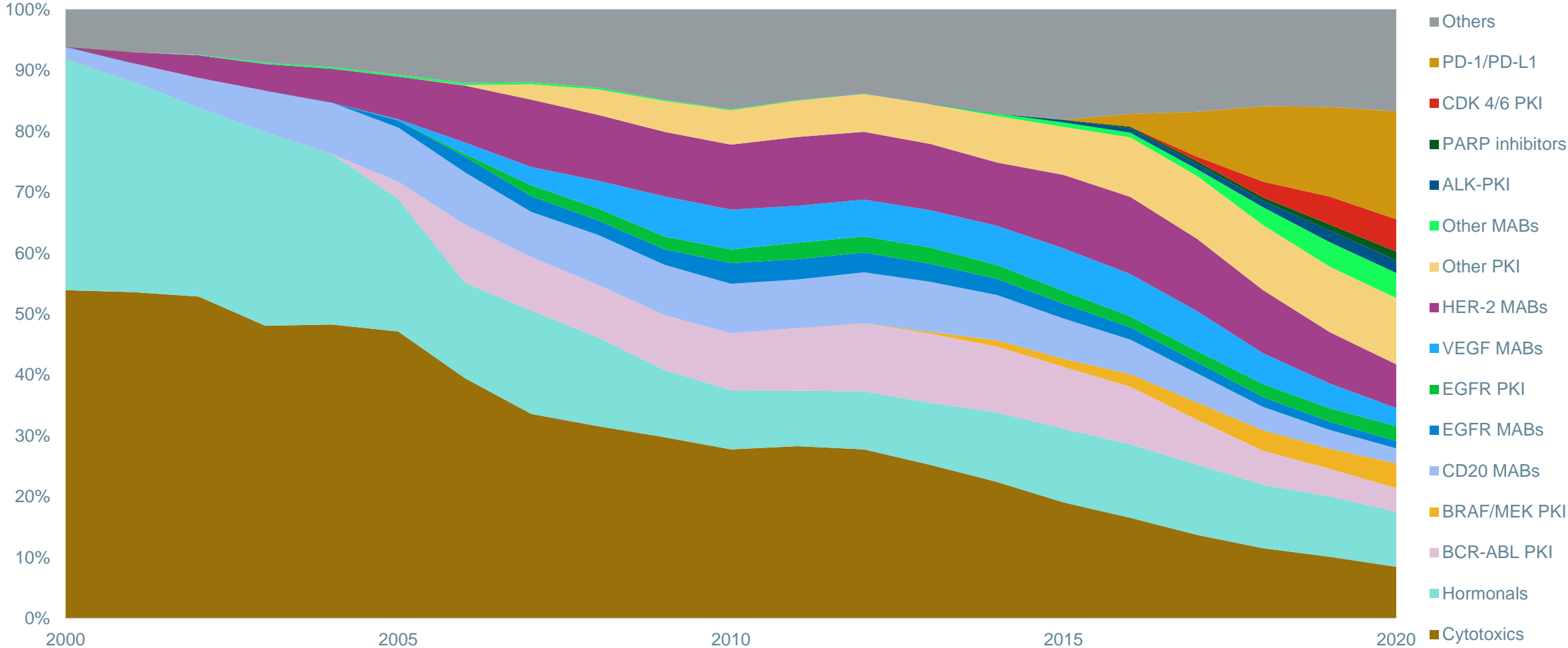
Italy Oncology Invoice Spending and Spending Growth Drivers, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Oncology spending growth over the last decade has been attributed to the introduction of innovative treatment alternatives

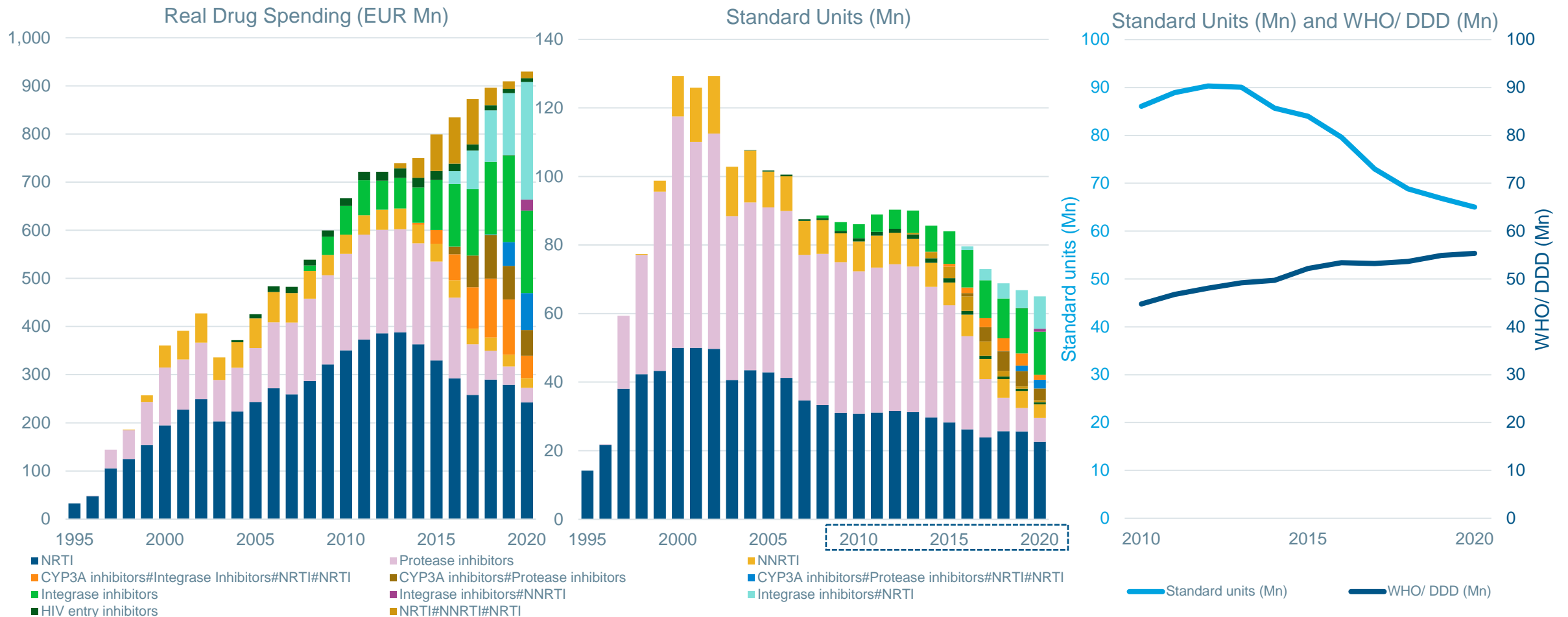
Italy Oncology Real Local Currency Spending by Mechanism, 2000-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Uptake of HIV fixed-dose combinations and newer mechanisms are shifting dosing patterns while days of therapy rise

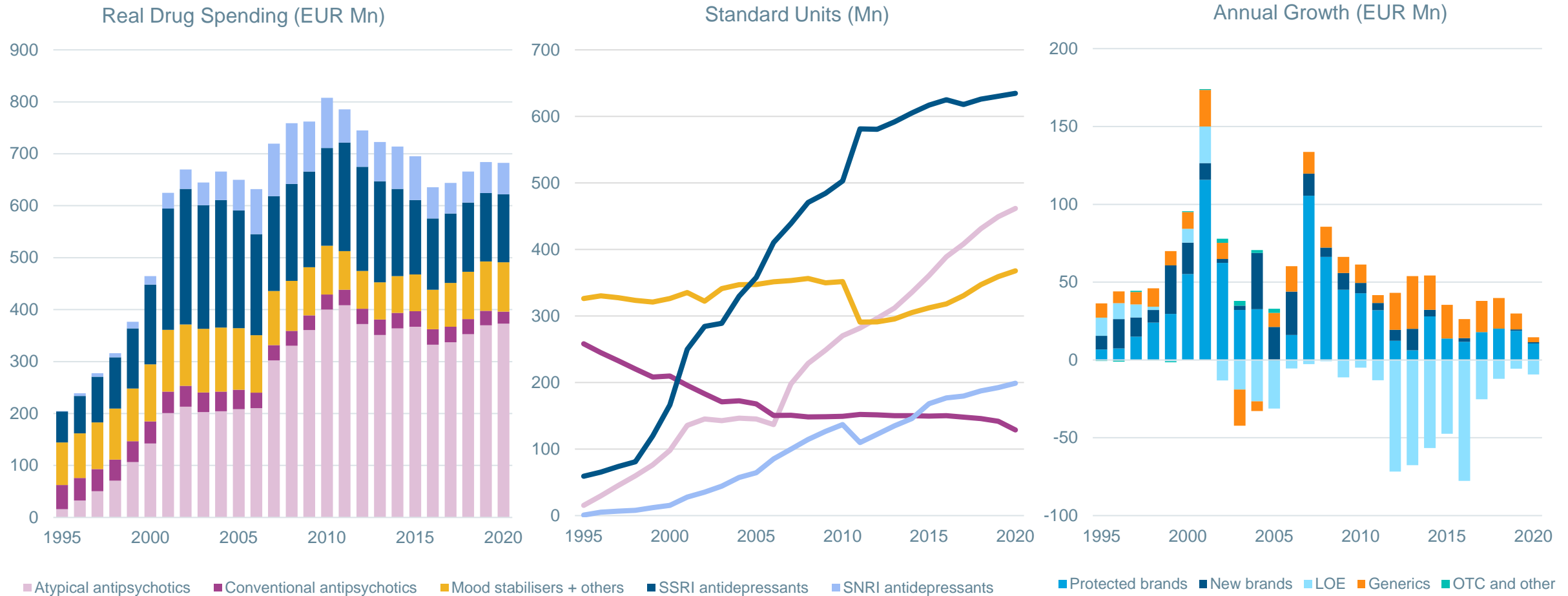
Italy HIV Spending and Volume by Mechanism, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Mental health spending has been growing slowly as most medicines are off-patent and growth is driven by volume

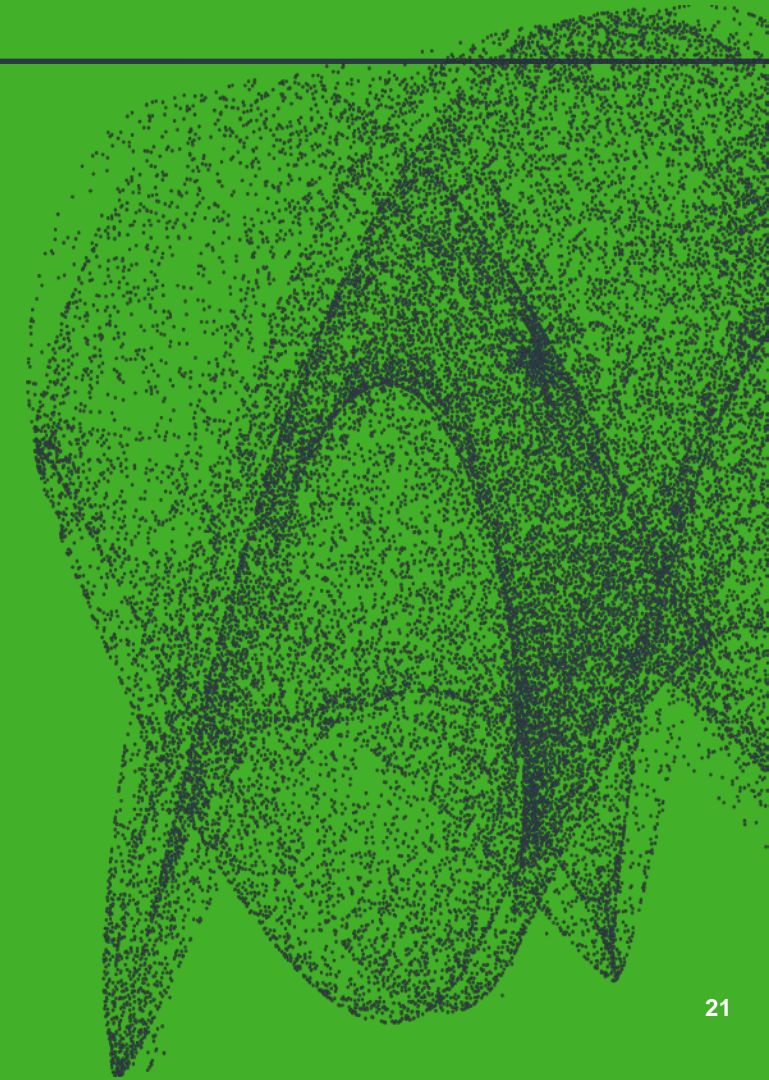
Italy Mental Health Spending, Volume by Mechanism and Growth by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020



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

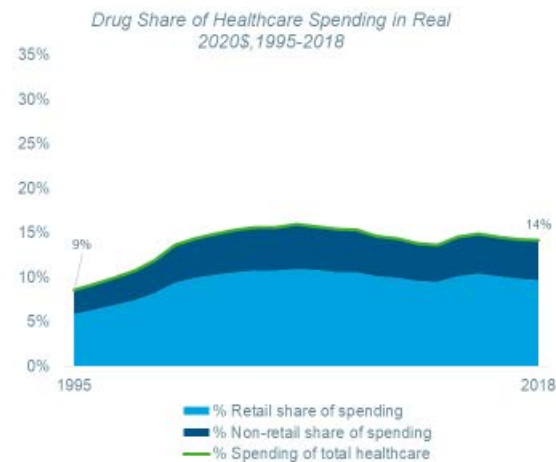
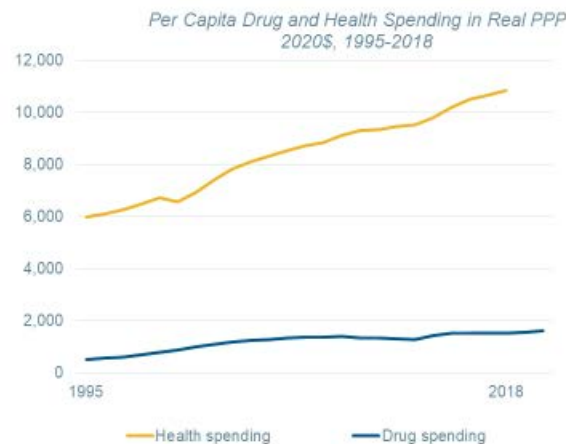


Chart Note: Methodology described in main report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*
Source: IQVIA Institute for Human Data Science, Sep 2021

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

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- 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

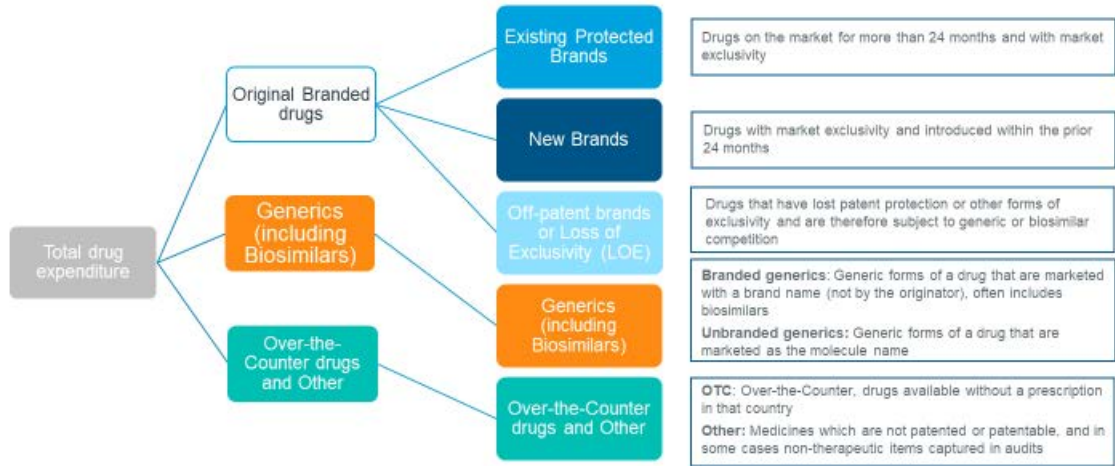


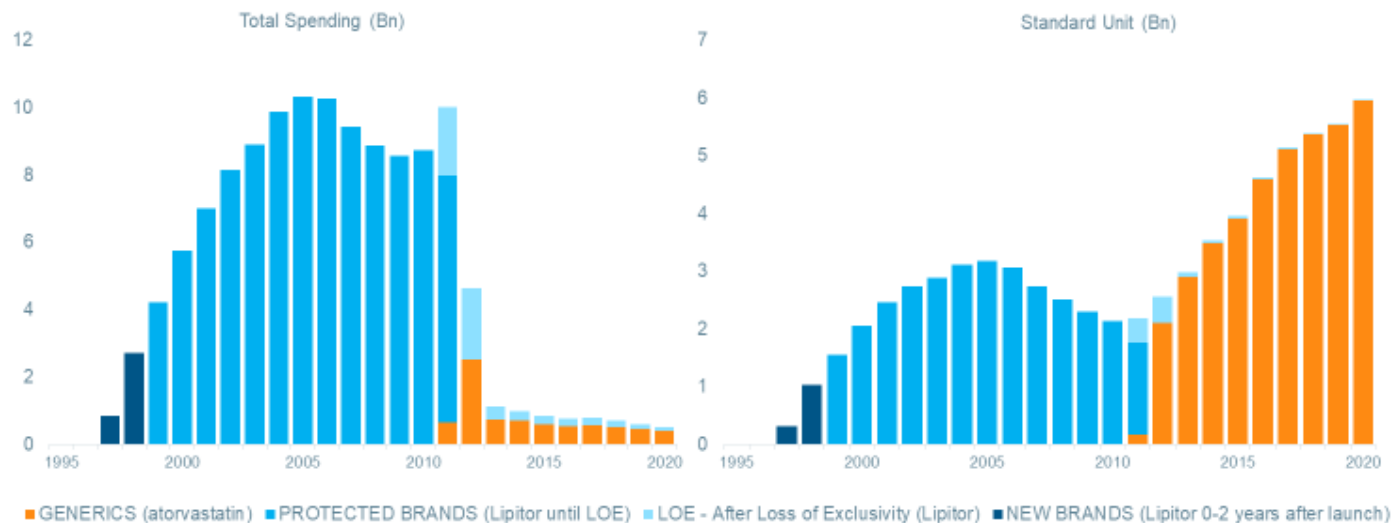
Chart notes: Protected brands include original protected brands, upcoming LOE and vaccines. New brands include original new brands; LOE include drugs that lost patent protection. Generics include non-original branded products as well as drugs that are marketed using the molecule name. OTC and other include 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

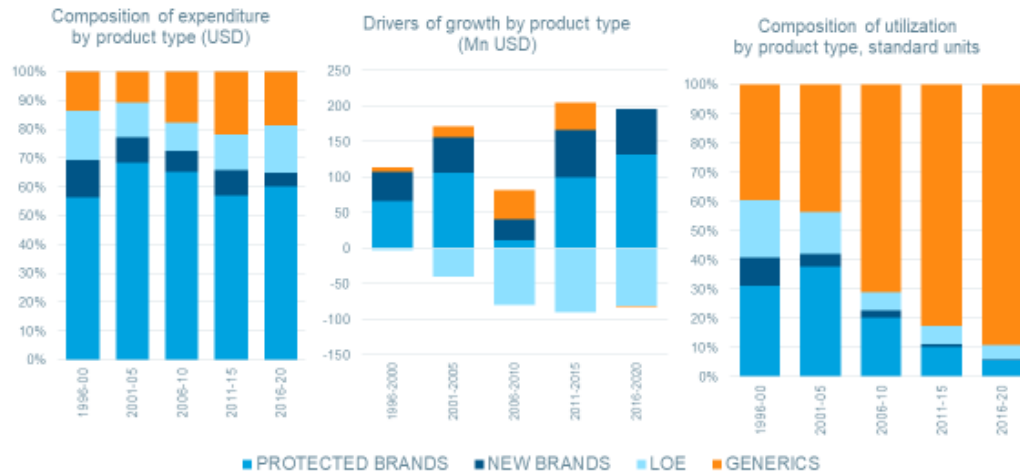


- In this example, the drug 'atorvastatin' begins life as a New Brand when Lipitor launched.
- The segmentation changes after 24 months to 'Protected Brand'. Analyses are based on quarterly time periods and a product may be considered new in 3 calendar years depending on the timing of launch in a country.
- 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



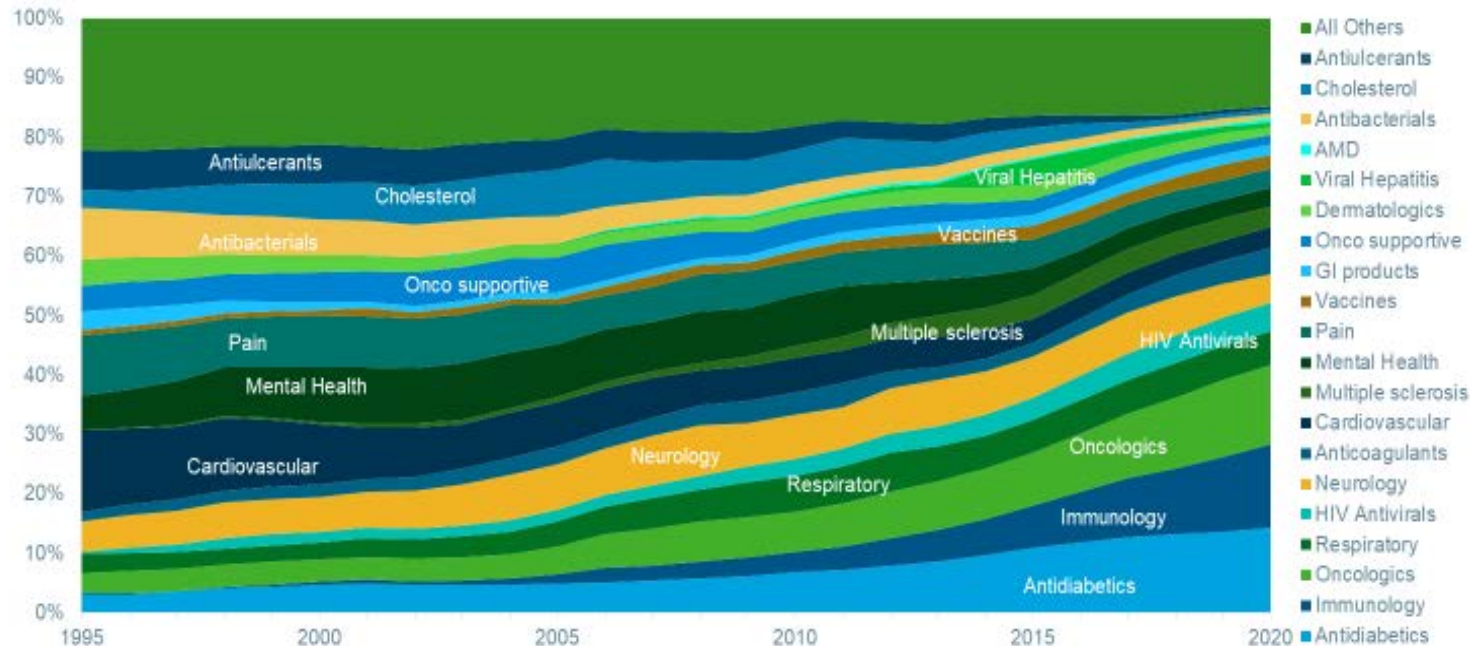
- Protected brands including new products average less than 70% of spending consistently
- Generic share of combined generic and LOE segments increasing steadily over time
- Generic share of volume increasing as generations of products shift to off-patent
- Most growth is driven by protected brands including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

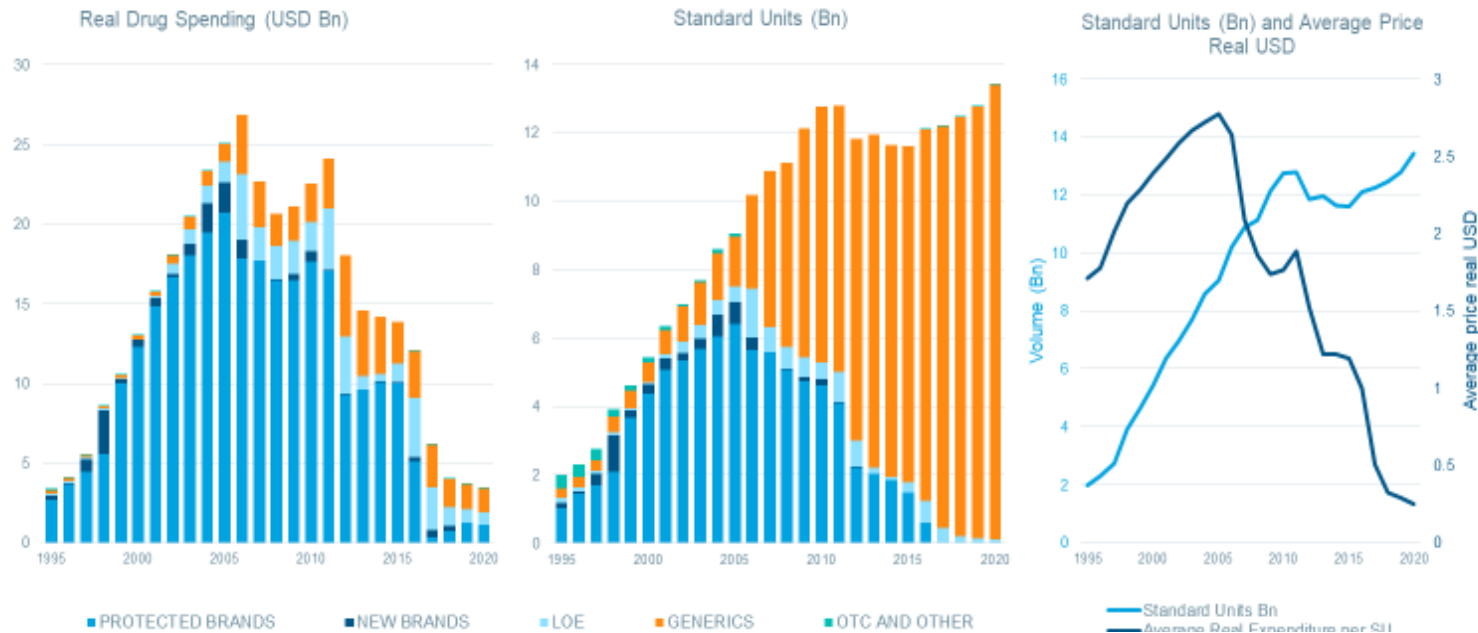


- Total IQVIA audited spending over 25 years has been collated and grouped by therapy areas.
- The therapy areas are defined by IQVIA with details of the definitions in the main report methodology section.
- The therapy areas called out by name are the classes that were ranked in the top 20 the most 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

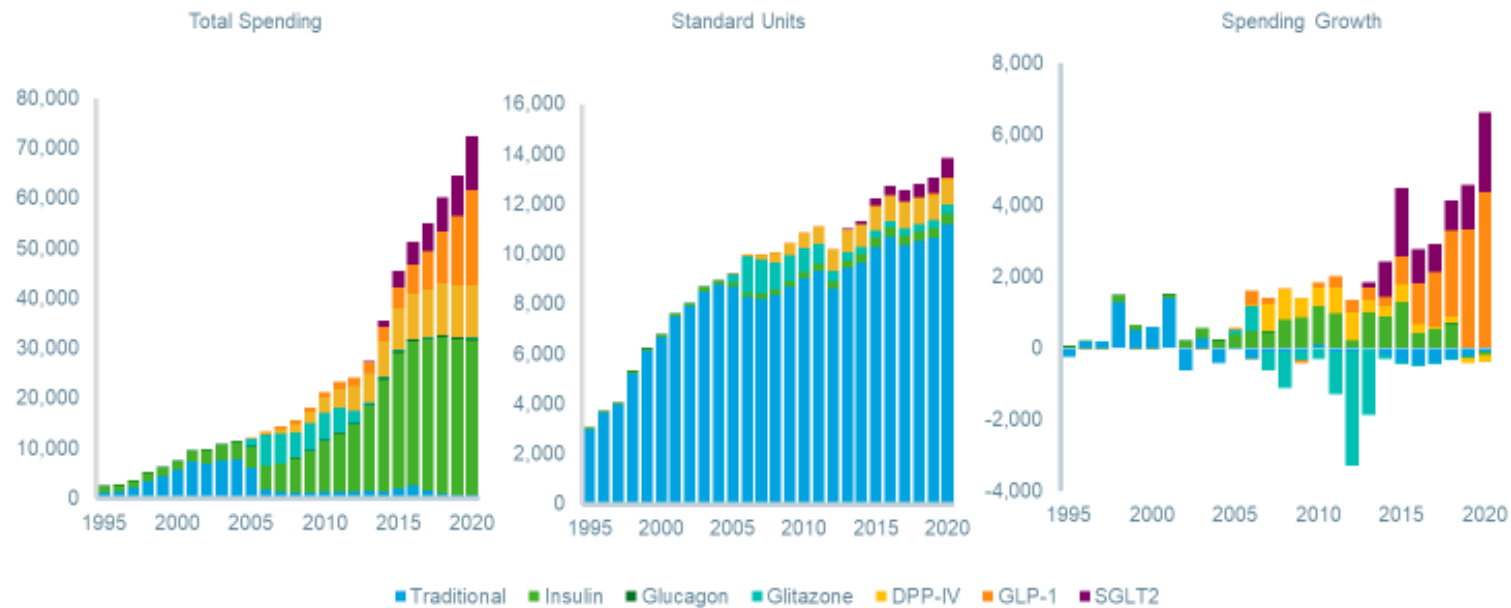


- Some analyses show three charts in this orientation, with spending, standard unit volume and finally a chart of volume and average cost per standard unit.
- Spending and cost are based on IQVIA audited data and do not reflect discounts and rebates.
- The segmentations shown in the charts are the same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



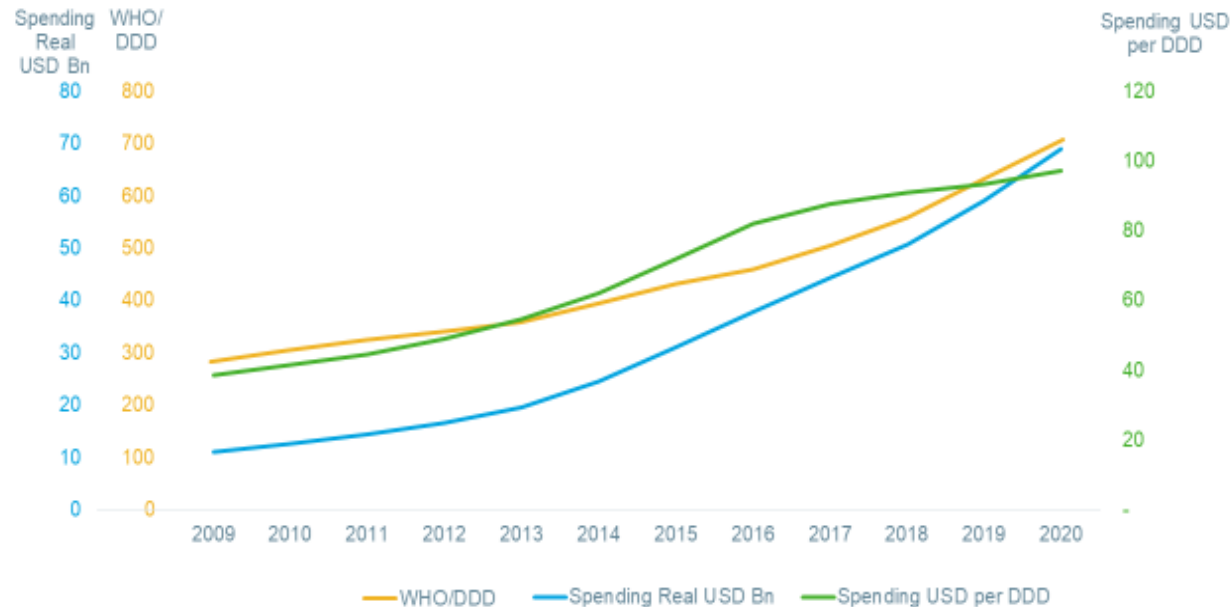
- Some therapy area charts include spending, standard units and spending growth.
- All are shown in the currency value noted.
- The colors of the chart indicate therapy sub segments, typically indicating shifts in the types of medicines used over time.

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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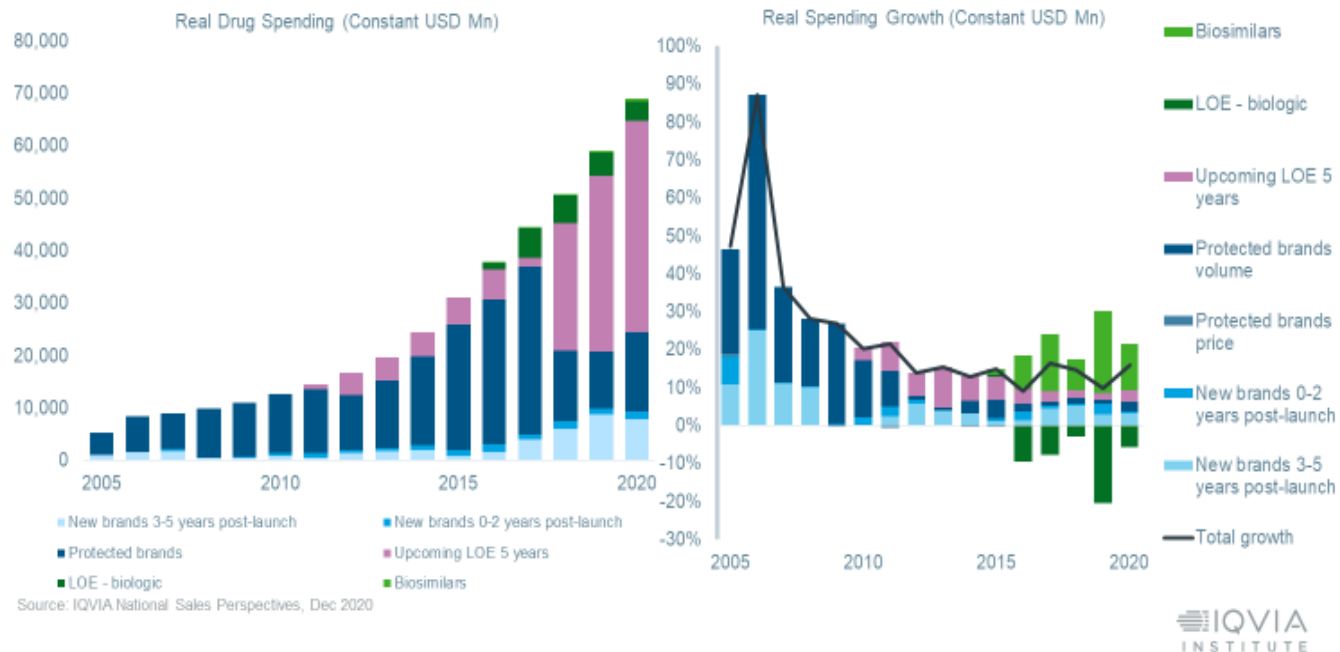
- This chart layout is used for the autoimmune biologic market.
- It has 3 axes which are color-matched to the lines
- Two axes are on the left (sales and volume in WHO Defined Daily Doses – WHODDD). The color of the lines matches the color used on the axis to show increments.
- WHODDD represent a standardized 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



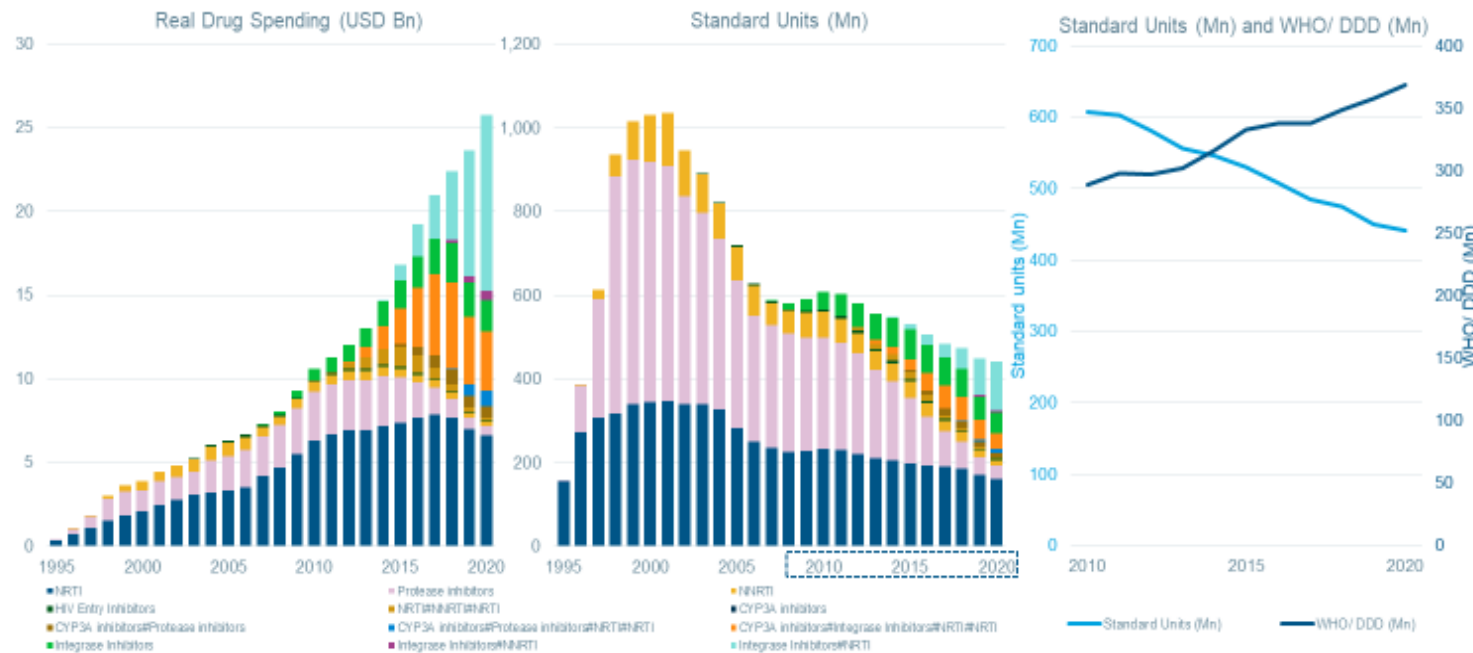
- Oncology and Autoimmune charts employ a more granular time-dependent segmentation of product type than other analyses in the report.
- Original biologics and small molecules when off-patent are identified separately as well as generics (small molecule) and biosimilars.
- The autoimmune charts are limited 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.iqviainstitute.org