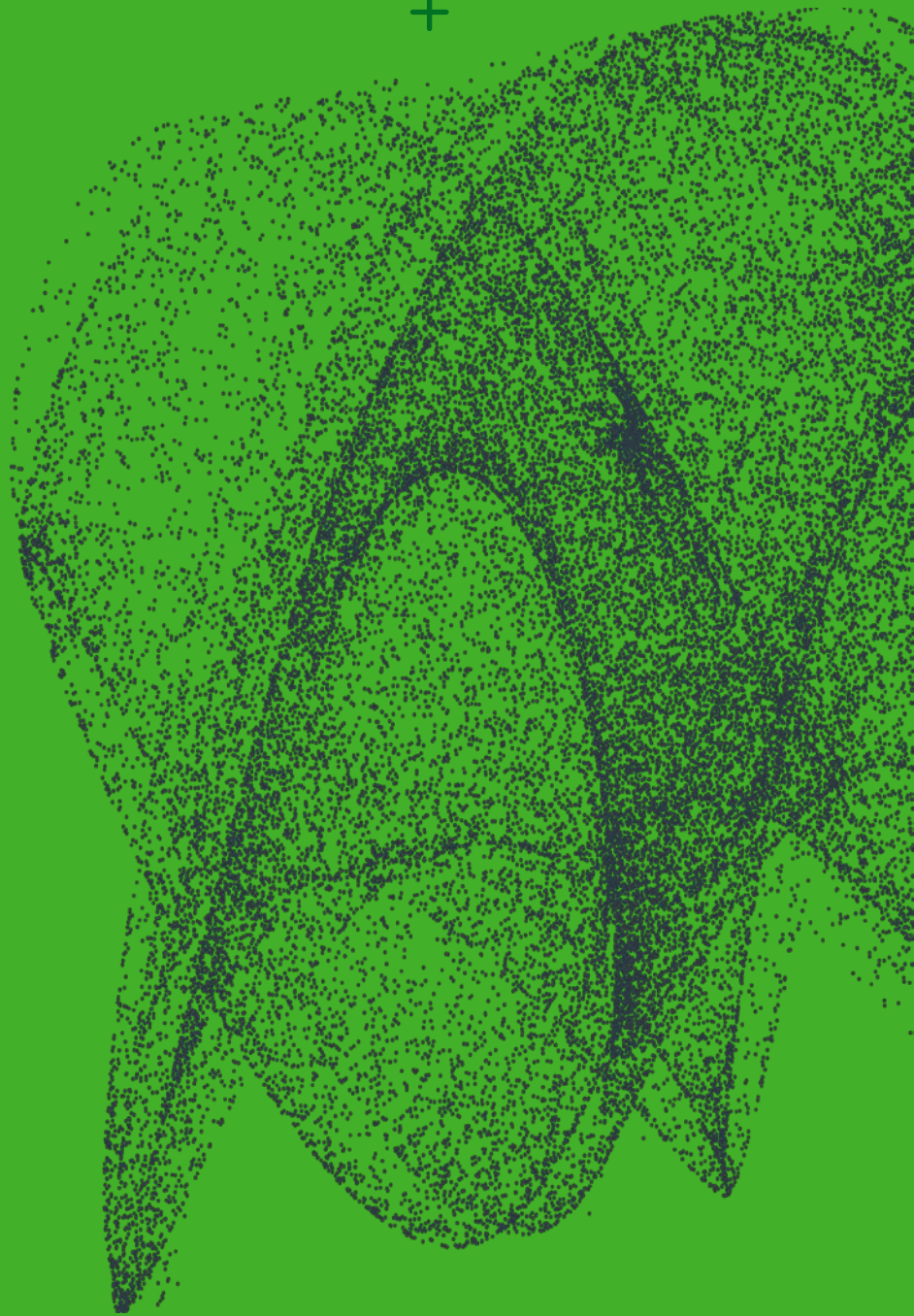
IQVIA INSTITUTE FOR HUMAN DATA SCIENCE

Drug Expenditure Dynamics 1995-2020

Understanding Medicine Spending in Context

Country Detail Appendix:

Japan



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.

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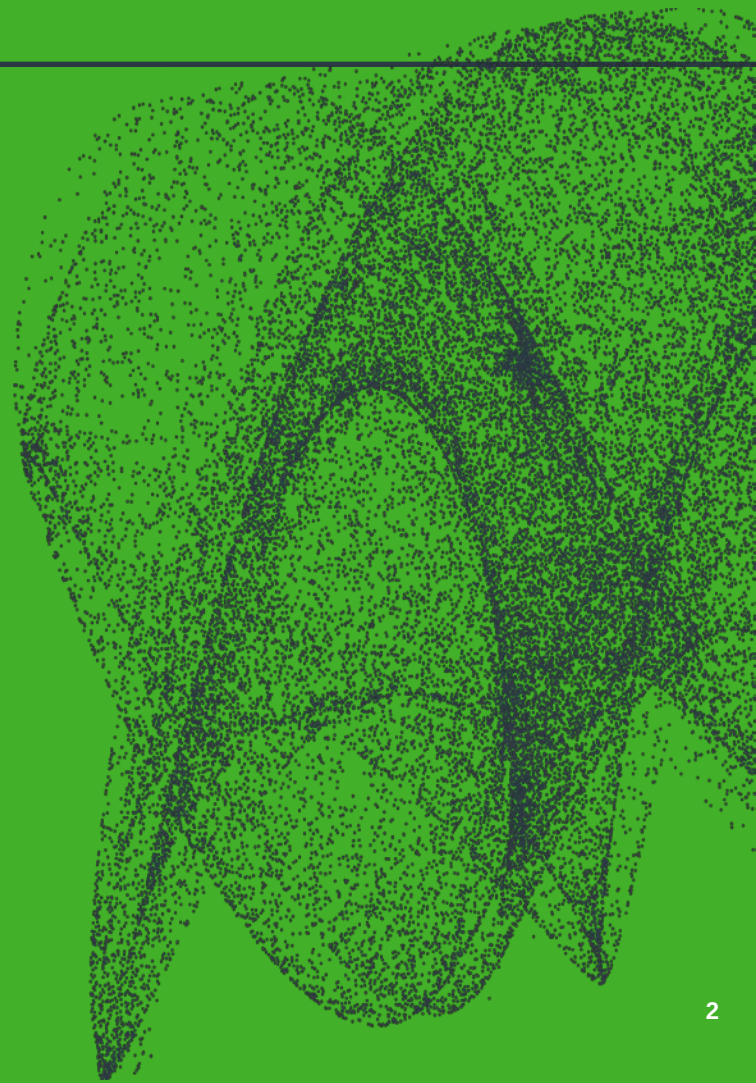
Japan



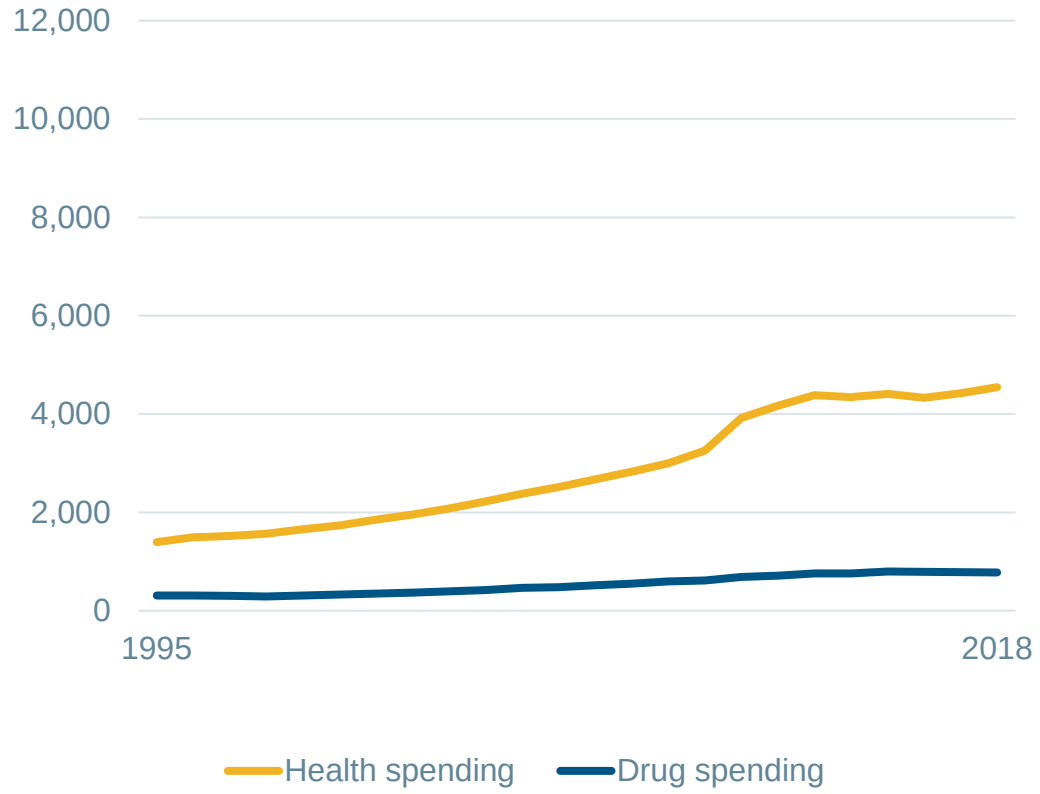
Key findings

- Japan drug spending as a share of overall healthcare spending declined from 22% in 1995 to 17% in 2018, partly due to healthcare spending rising faster over the same period.
- Healthcare spending in Japan rose from $1,395 in 1995 to $4,547 in 2018 as a result of aging, a shrinking population, and a shift in focus to greater access to novel medicines supporting healthcare policy.
- The therapy area focus of spending has shifted from traditional classes which dominated in 1995 to more specialty classes in 2020. Overall, the top five classes in 1995 (cardiovascular, cholesterol, anti-ulcerants and anti-bacterial) represented about 53% of drug spending, declining to under 6% in 2020, predominantly driven by genericization. The current leading classes (oncologics, immunology, anti-diabetics, cardiovascular, and neurology) were 43% of spending in 2020, rising from 27% in 2000, illustrating a shift due to the influx of new treatment options.
- In more recent periods, Japan has observed an increasing share of protected brand spending in the number of therapy classes (e.g., oncology, immunology, antithrombotics) as a result of shifts in the biennial price cut system to encourage innovation by subjecting long-listed brands and generics to greater price cuts than innovative products.
- In therapy classes such as cholesterol, anti-bacterial and anti-ulcerants, the continued utilization and spending for brands that were no longer protected illustrates how differently the Japanese market operated from other countries, though the differences are shrinking in more recent years with an active shift toward generics.
- Some therapy areas such as oncology, HIV and mental health have seen significant growth driven by new therapies and wider utilization.
- Policies have begun to encourage earlier launches relative to international markets, while the historic lag between global launch and availability in Japan is reducing, notably for the utilization of the newest mechanisms in cancer at similar timing and share of spending to other markets.

Japan drug spending as a share of overall healthcare spending has declined from 22% in 1995 to 17% in 2018

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

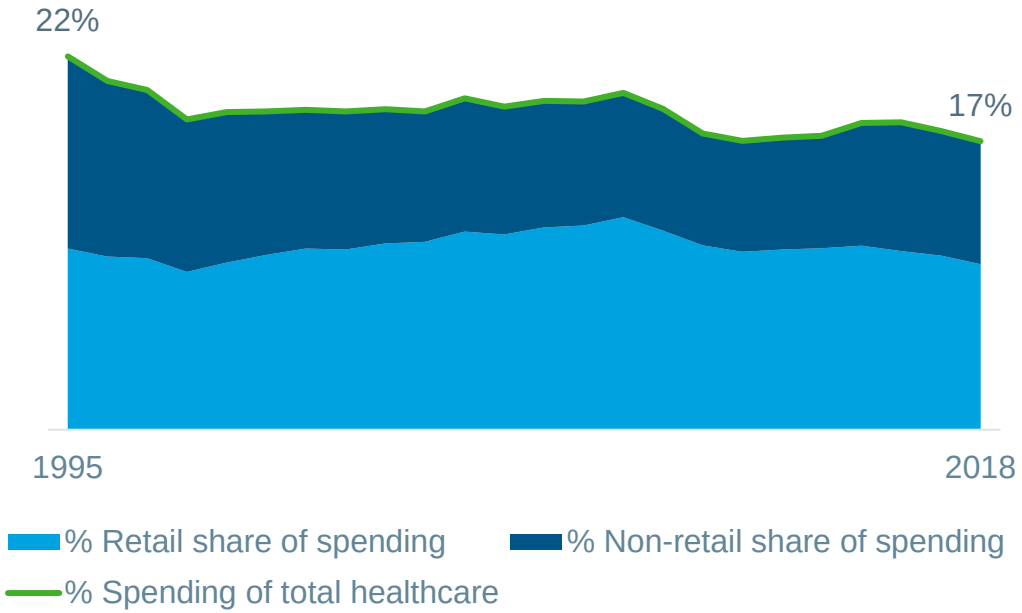
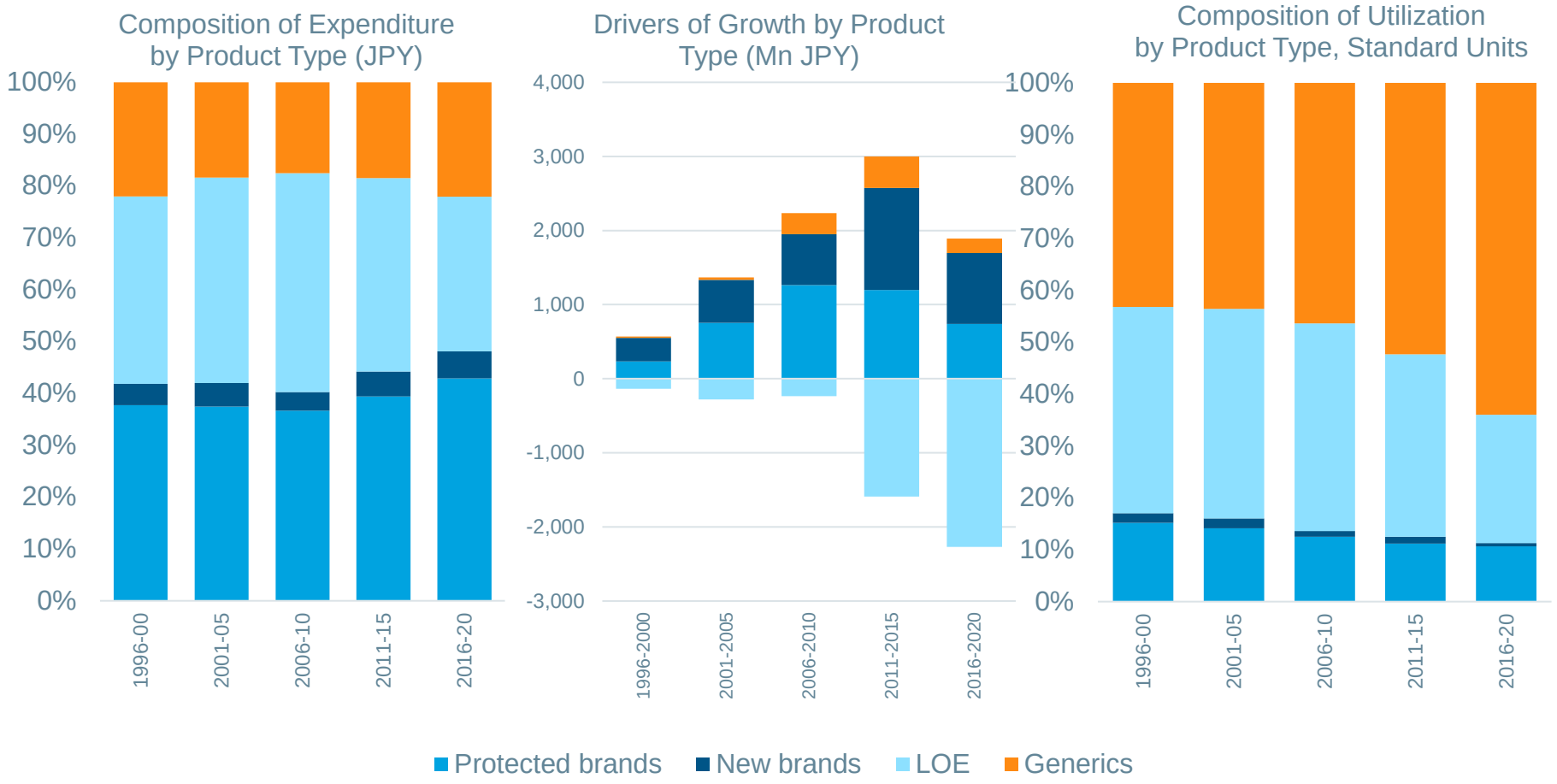


Chart Note: Methodology described in main report *Drug Expenditure Dynamics 1995-2020: Understanding Medicine Spending in Context*
Source: IQVIA Institute for Human Data Science, Sep 2021

Generic contribution to overall spending and utilization has increased during last few years as a result of policy change

Japan Drug Spending and Utilization 1995-2020

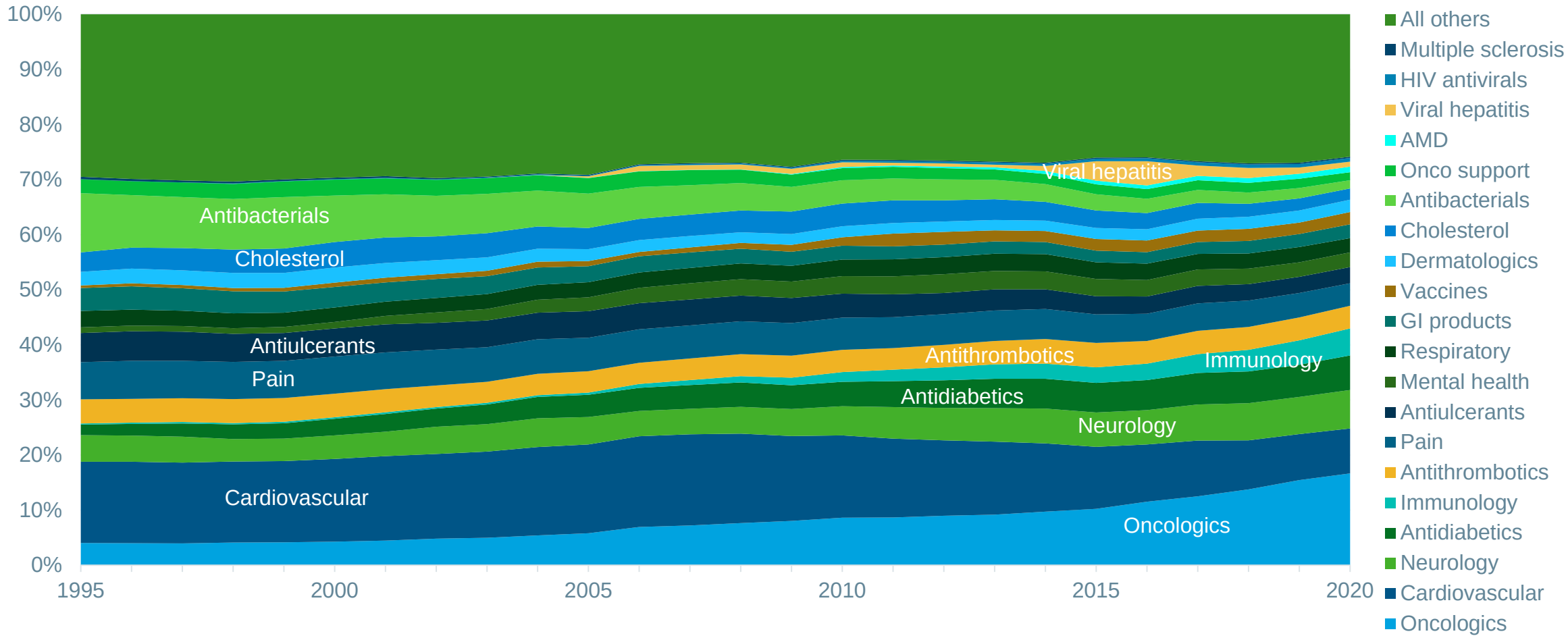


- Protected brands, including new products, have an increasing share of spending in the past decade consistent with shifts in national pricing policy
- Uptake of generic drugs increased to ~60% in the most recent period, up from 40% during 1996-2000
- Most growth is driven by protected brands, including new products, and offset by losses of exclusivity

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Anti-bacterials and cardiovascular, which accounted for 25% of overall spending in 1995, have dropped to below 10% in 2020

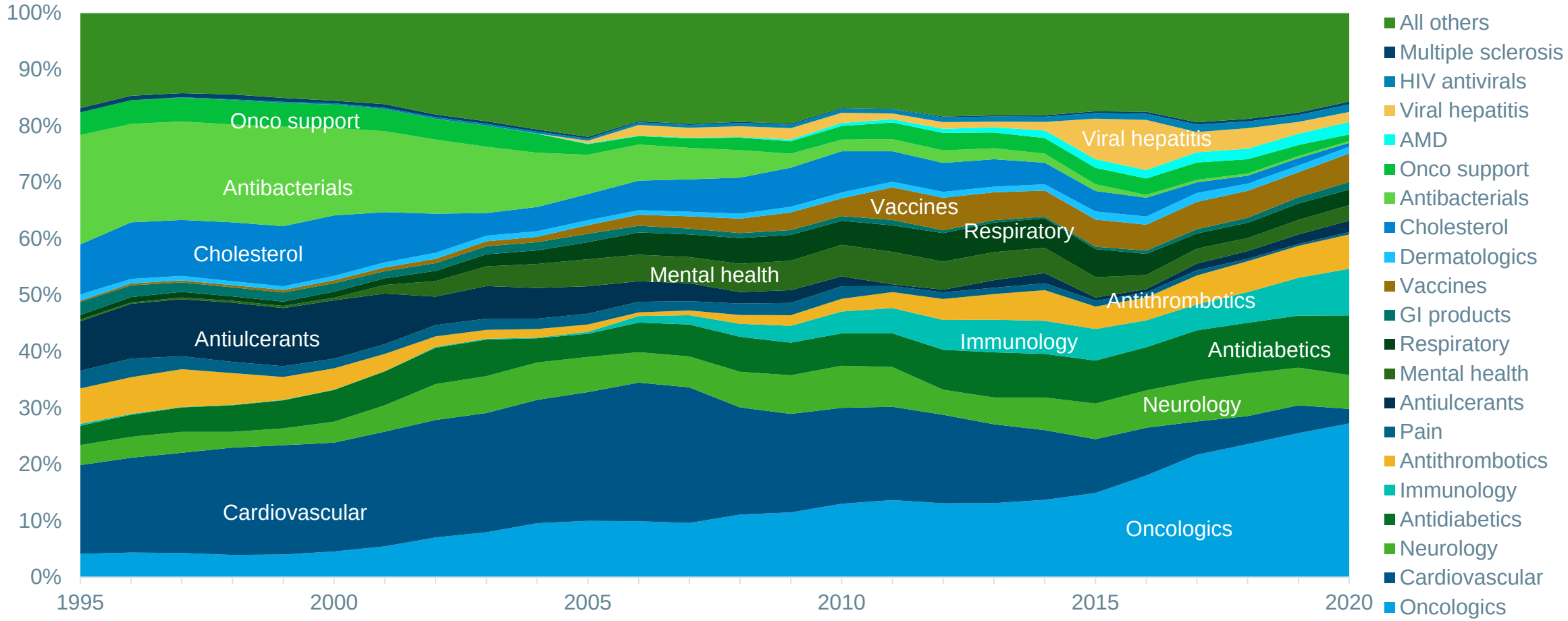
Japan Composition of Drug Real Local Currency Spending by Drug Class, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Oncologics, cardiovascular, neurology, diabetics, and immunology contribute to more than half of total spending in recent years

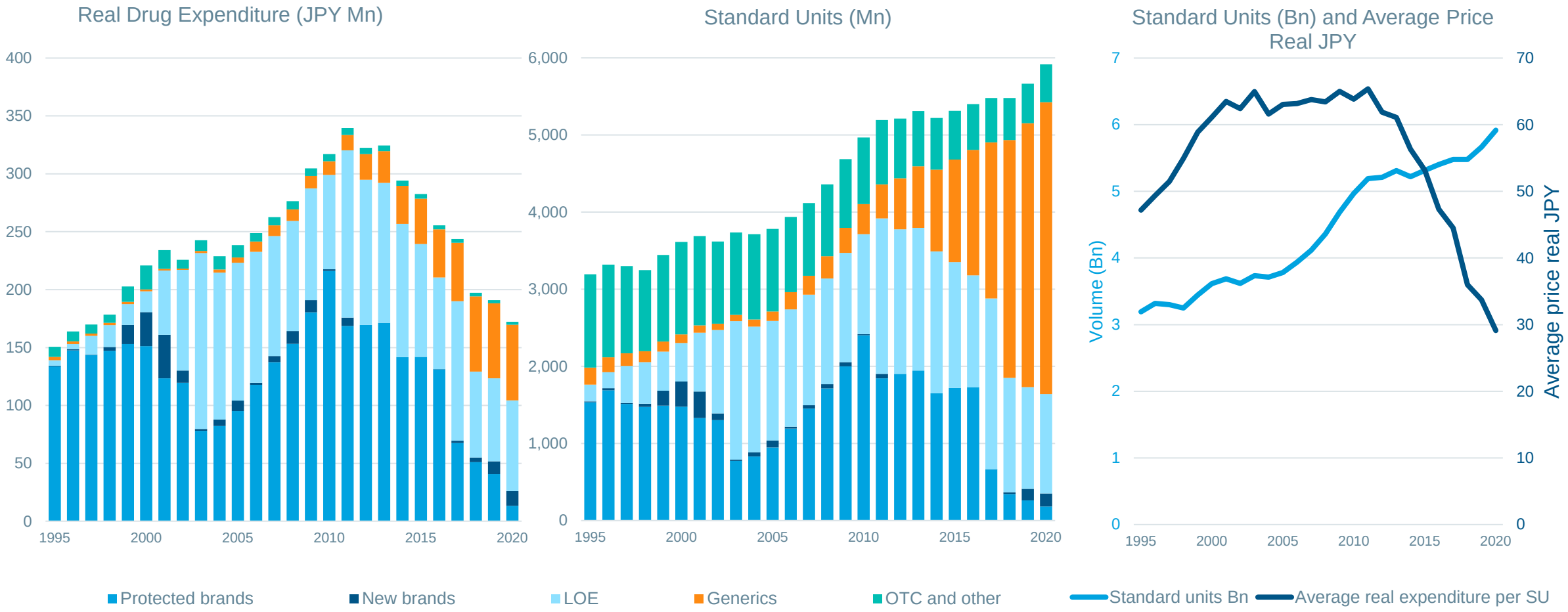
Japan Composition of Protected Brands Real Local Currency Spending by Drug Class, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Generic cholesterol drug use has increased in Japan in the last 10 years due to drop in costs and their increased availability

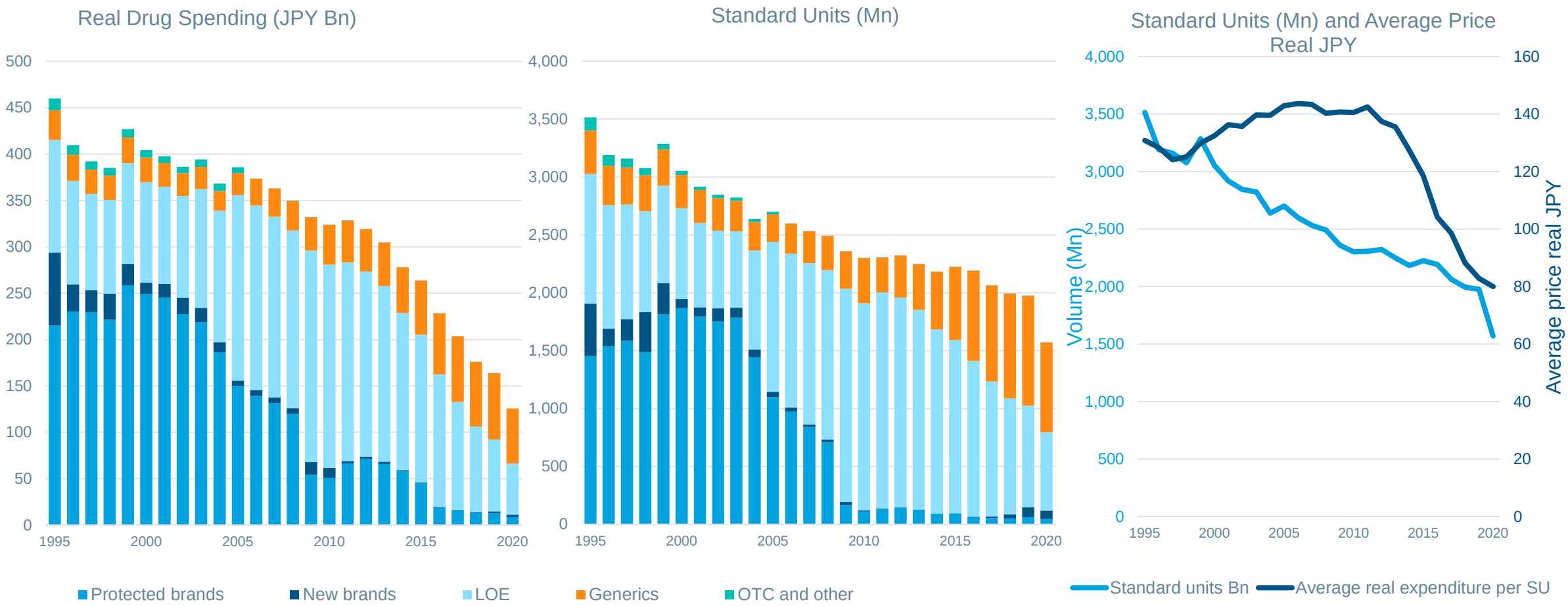
Japan Cholesterol Volumes, Average Prices and Spending by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

High usage of off-patent or long-listed branded anti-bacterials began to shift to generics in the last 10 years

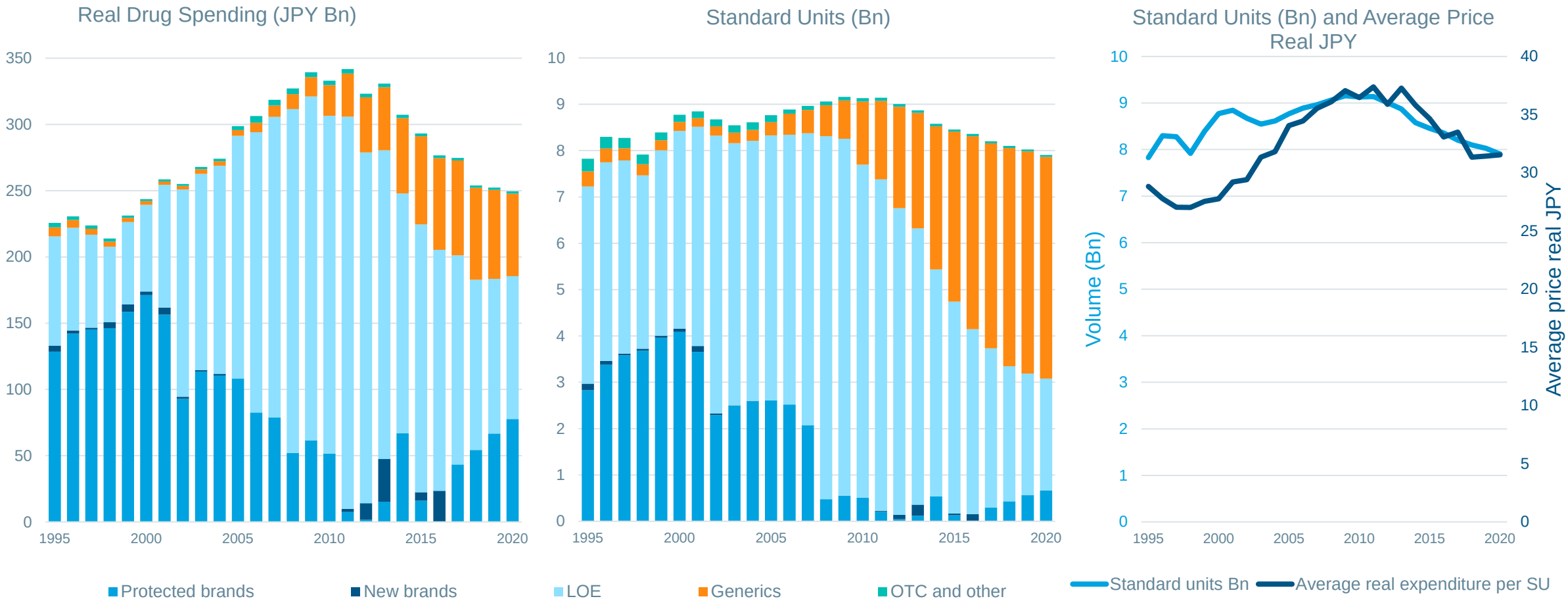
Japan Anti-bacterial Volumes, Average Prices and Spending by Product Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Anti-ulcerant drug use shifted to generics from long-listed brands while costs declined slightly, illustrating the intended policy shift

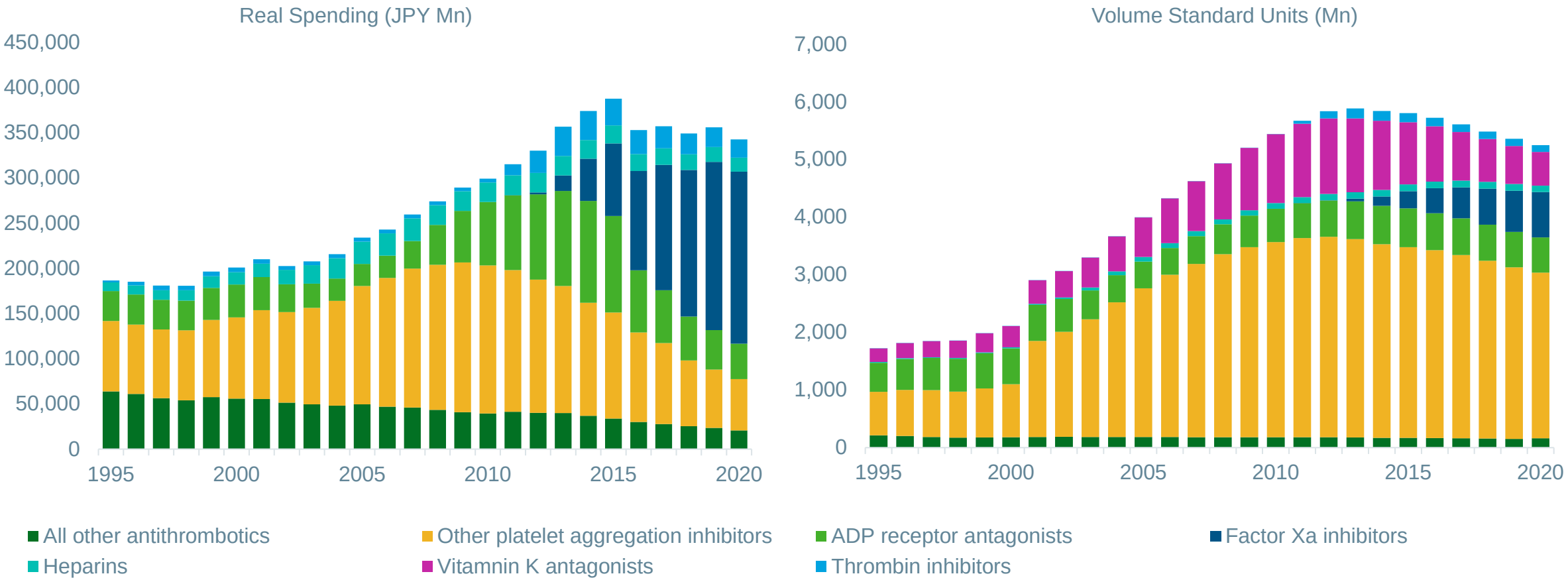
Japan Anti-Ulcerants Volumes, Average Prices and Spending by Product Type 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Antithrombotic spending rose from Factor Xa inhibitors while ADP receptor antagonists and others declined

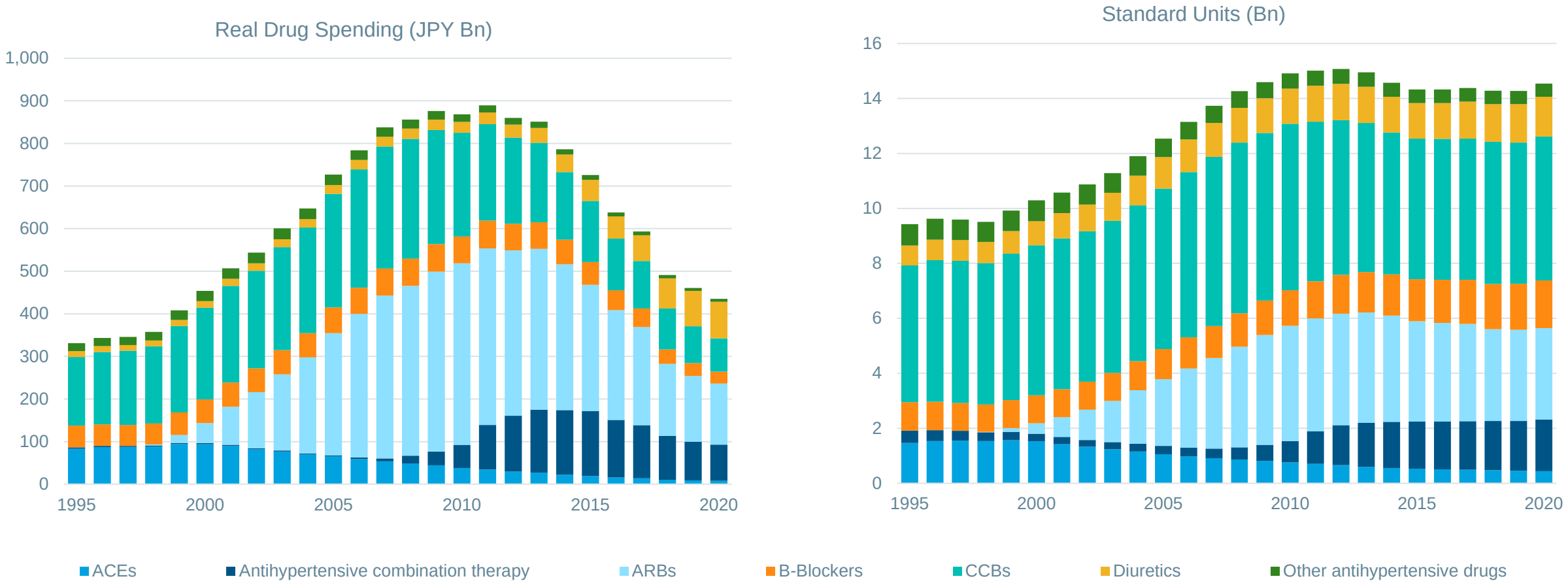
Japan Antithrombotics Spending and Volumes by Drug Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Hypertension usage has continued steadily for the past 15 years while spending has begun to decrease due to patent expiries

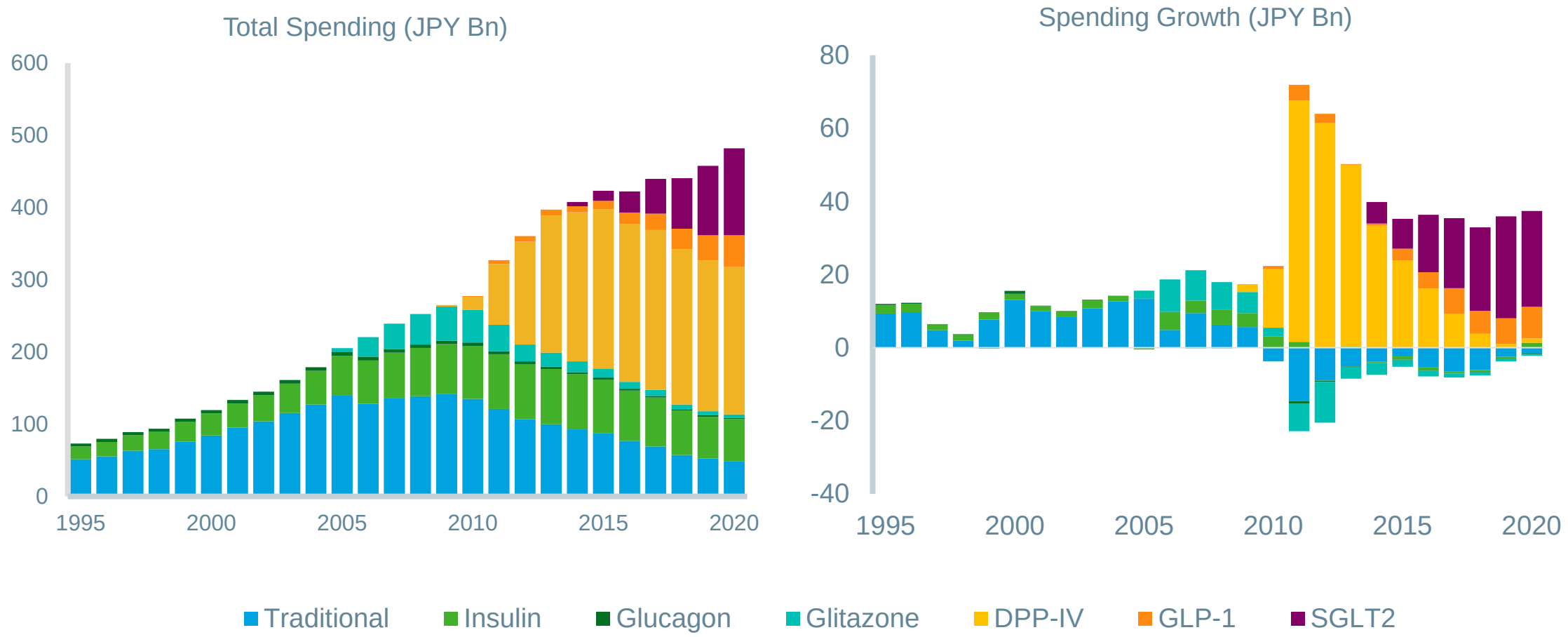
Japan Hypertension Spending and Volume by Mechanism, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Diabetes spending in Japan is driven by innovation, while older therapies have reduced spending from biennial price cuts

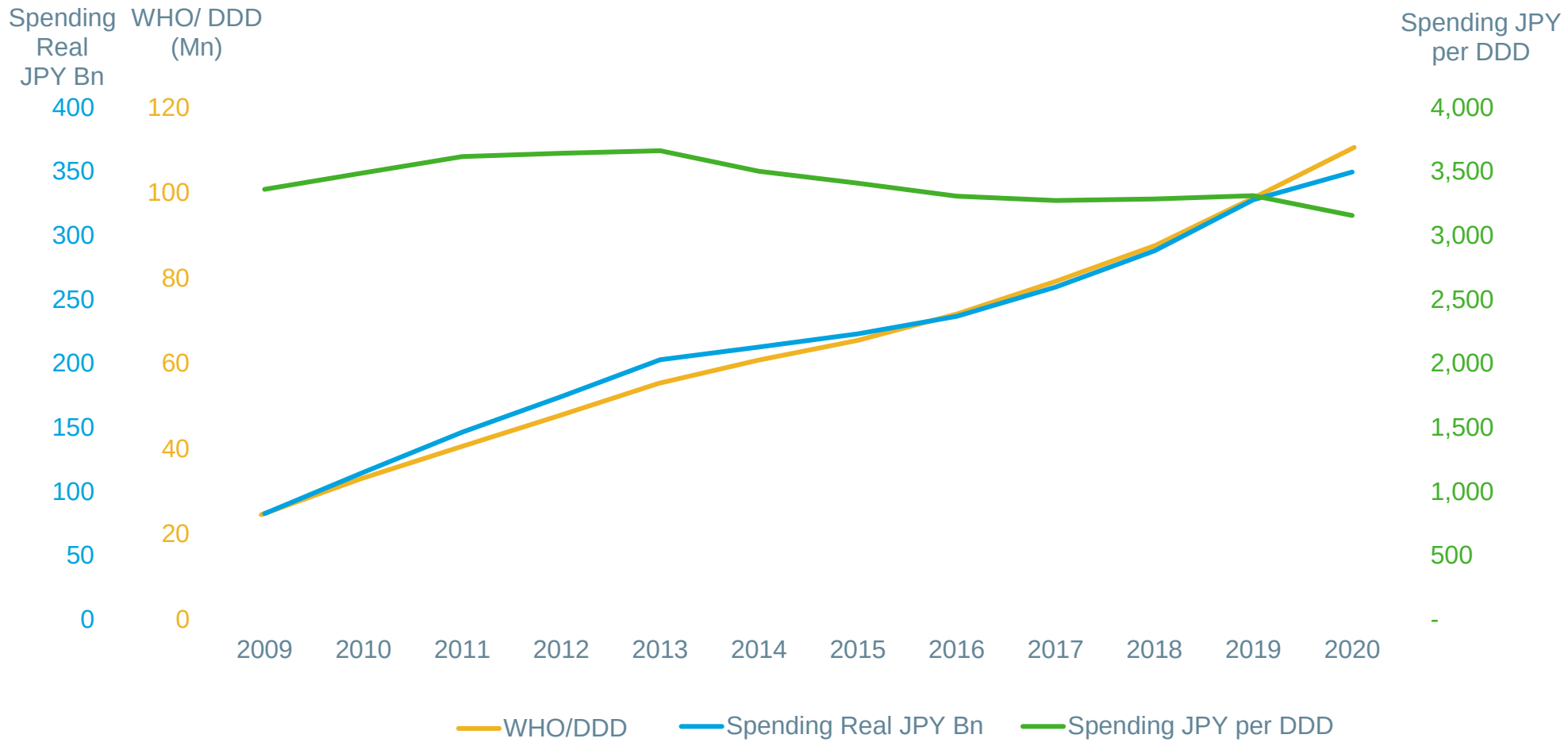
Japan Diabetes Real Spending and Growth JPY (Bn) by Drug Type, 1995-2020



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Spending in immunology has been driven by increasing volume, which is up >200% since 2010, while cost per day declined 10%

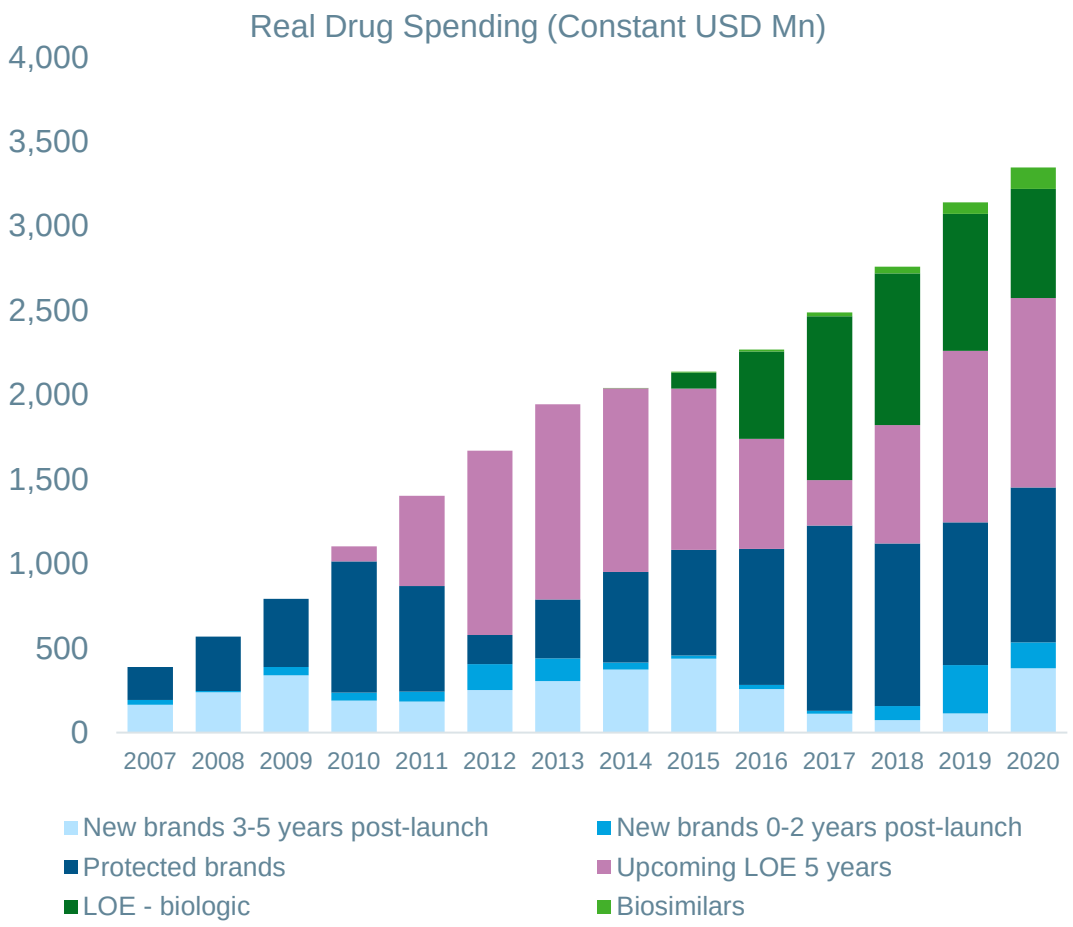
Japan Autoimmune Biologic Spending, DDD and Cost, 2009-2020

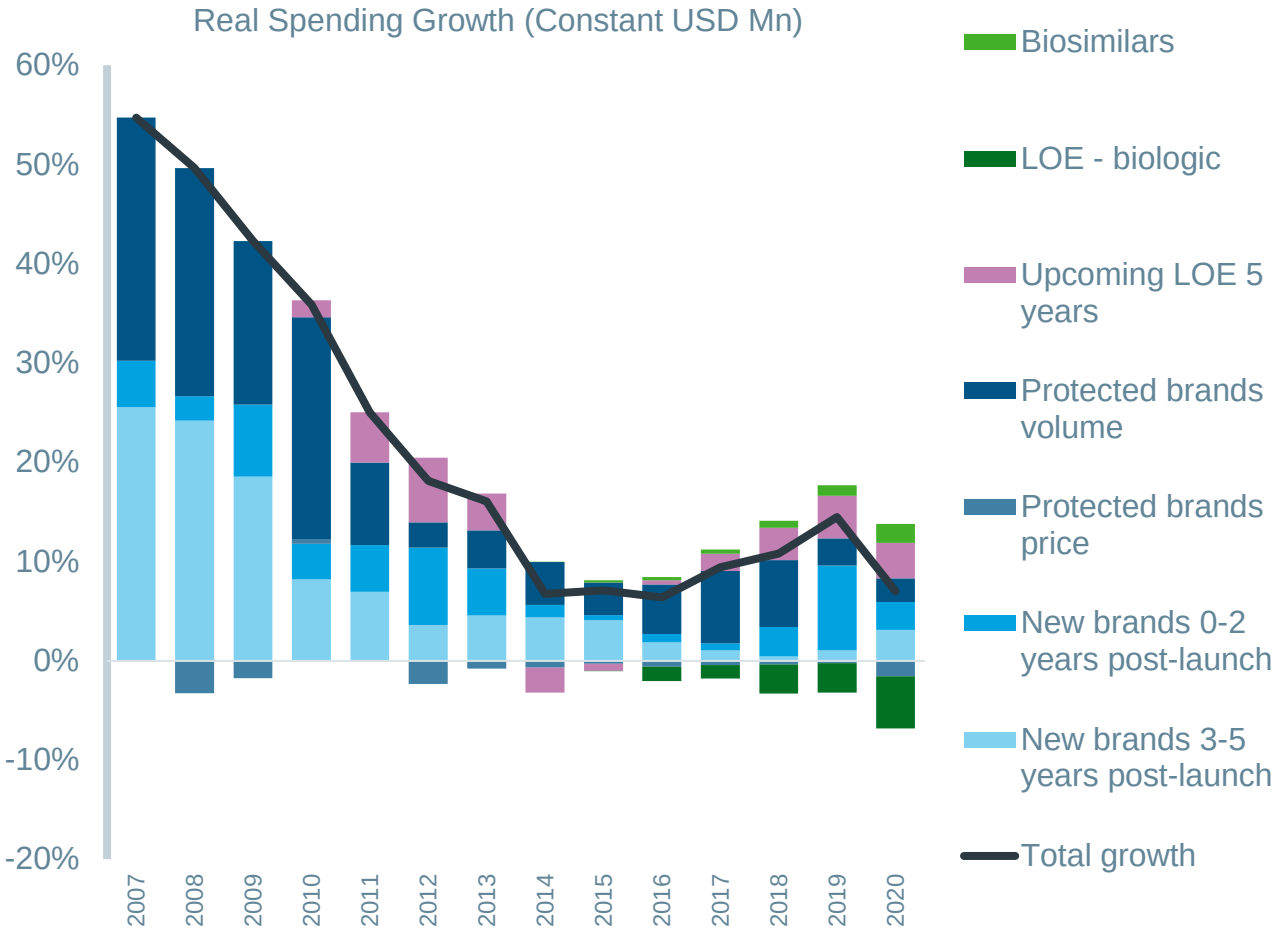


Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Auto-immune biologic spending growth has slowed as biosimilars have impacted the market since 2015

Japan Autoimmune Biologic Invoice Spending and Growth Drivers, 2007-2020





Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Vaccination spending increased in the past decade from new adult vaccines; HPV peak in 2011 followed by withdrawn recommendation in 2013

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

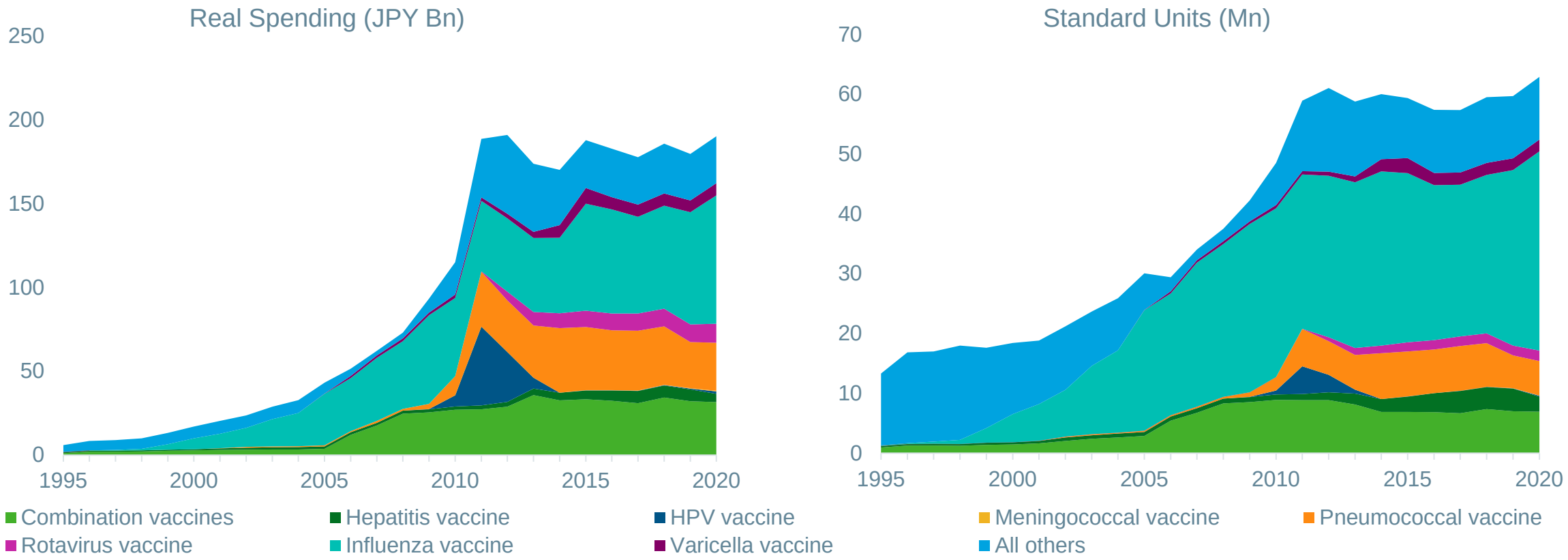
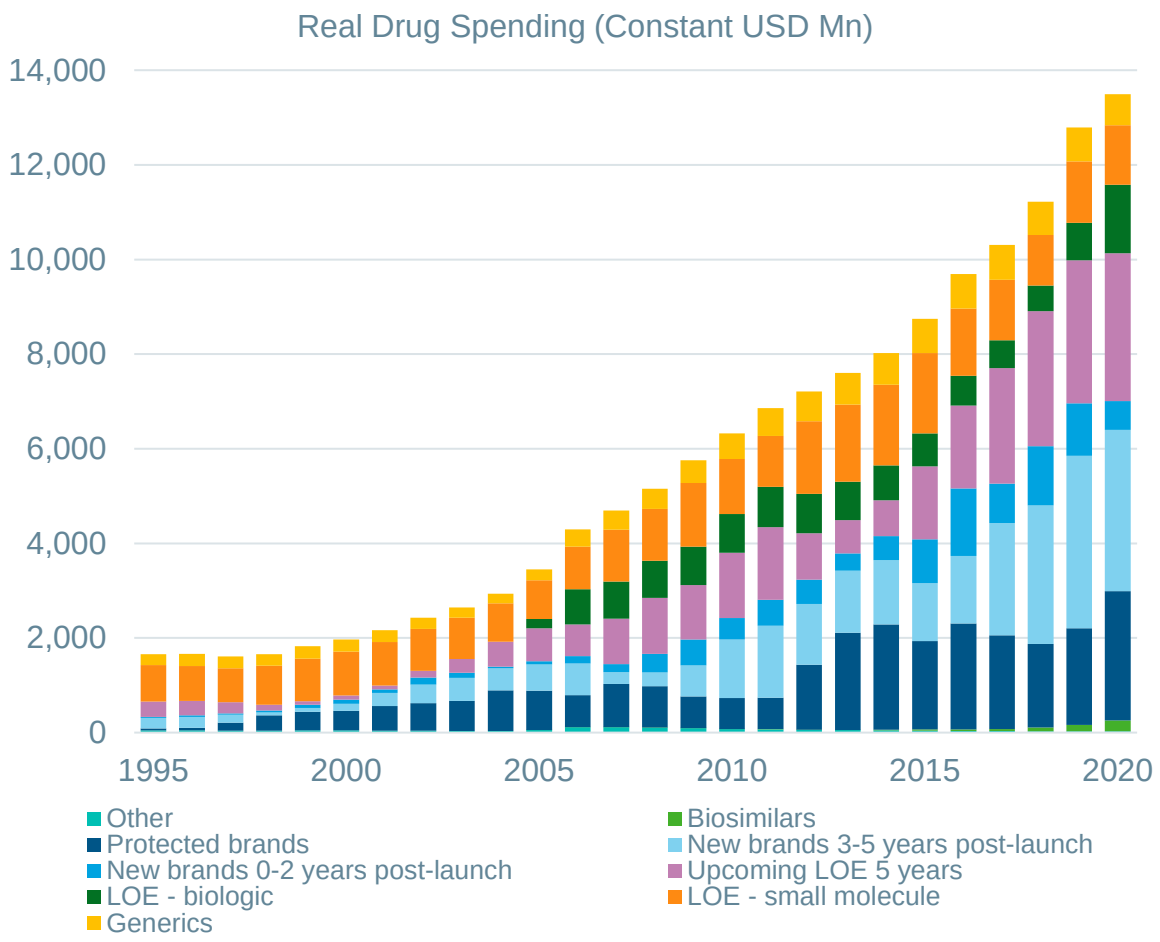


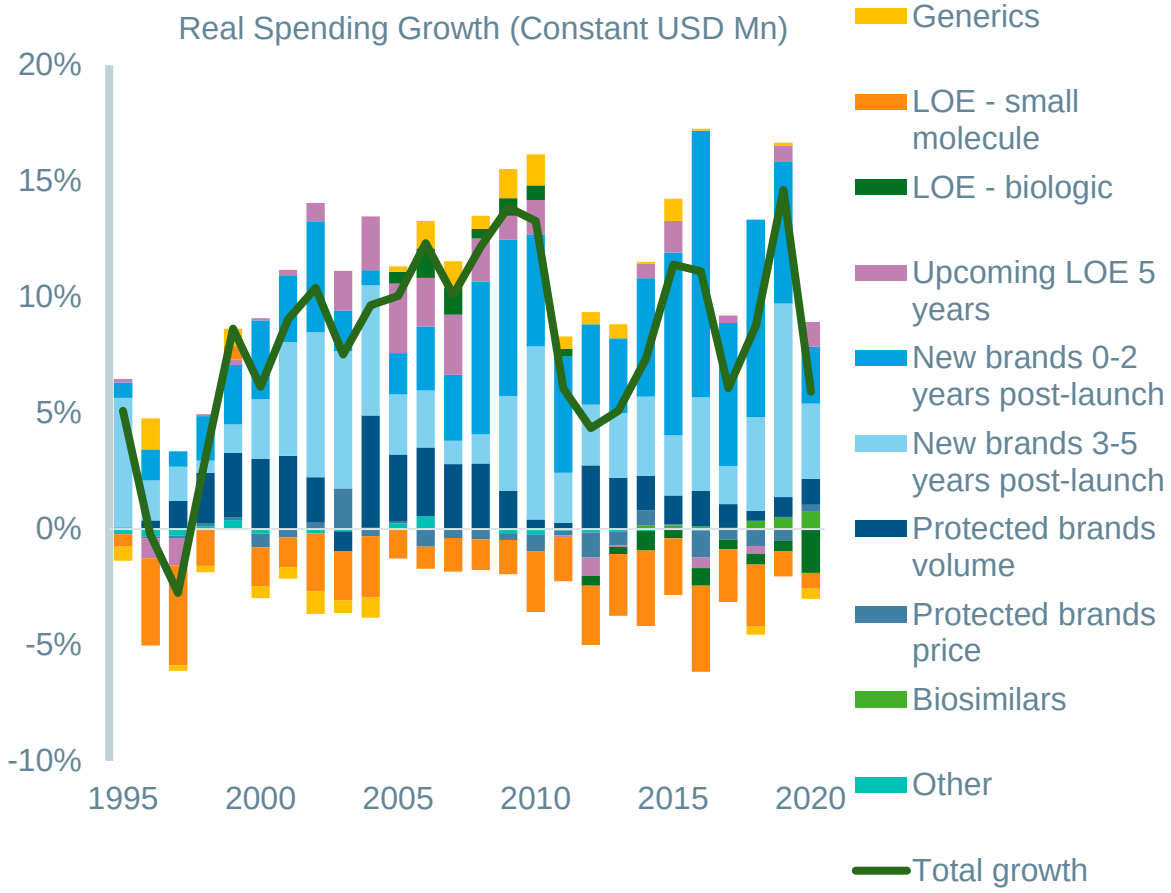
Chart notes: Combination vaccines represent combined vaccines (with measles, mumps, tetanus or other); HPV vaccine for human papillomavirus; Meningococcal vaccine for meningitis; Pneumococcal vaccine for pneumonia; Rotavirus vaccine for rotavirus; Influenza vaccine for the flu; Varicella vaccine for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

Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Oncology spending increasingly driven by new drugs and global launch lags are becoming shorter

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

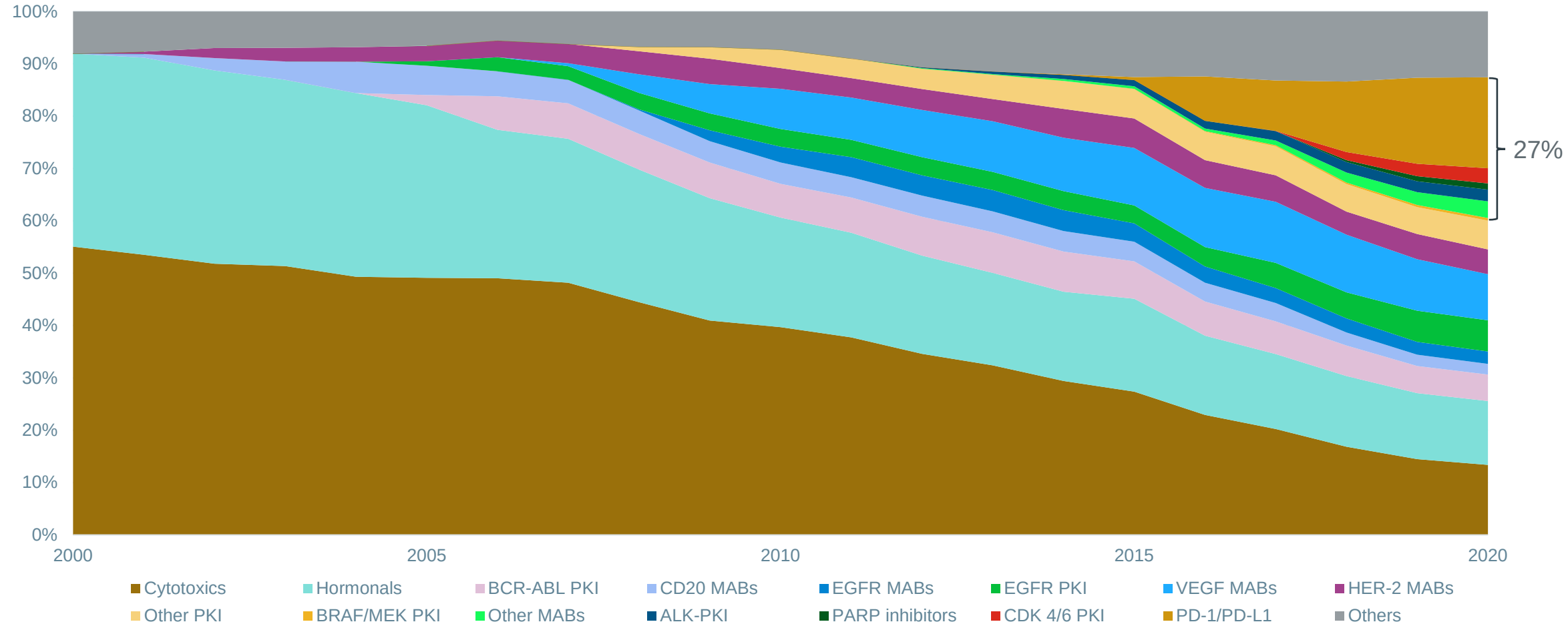




Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Adoption in the oncology market of new mechanisms in last 10 years contributed to 27% of total oncology spending in 2020

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



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

Newer HIV treatments, especially integrase inhibitors and combinations, drive growth; volume shows shift to 1/day dosing

Japan HIV Spending and Volume by Mechanism, 1995-2020

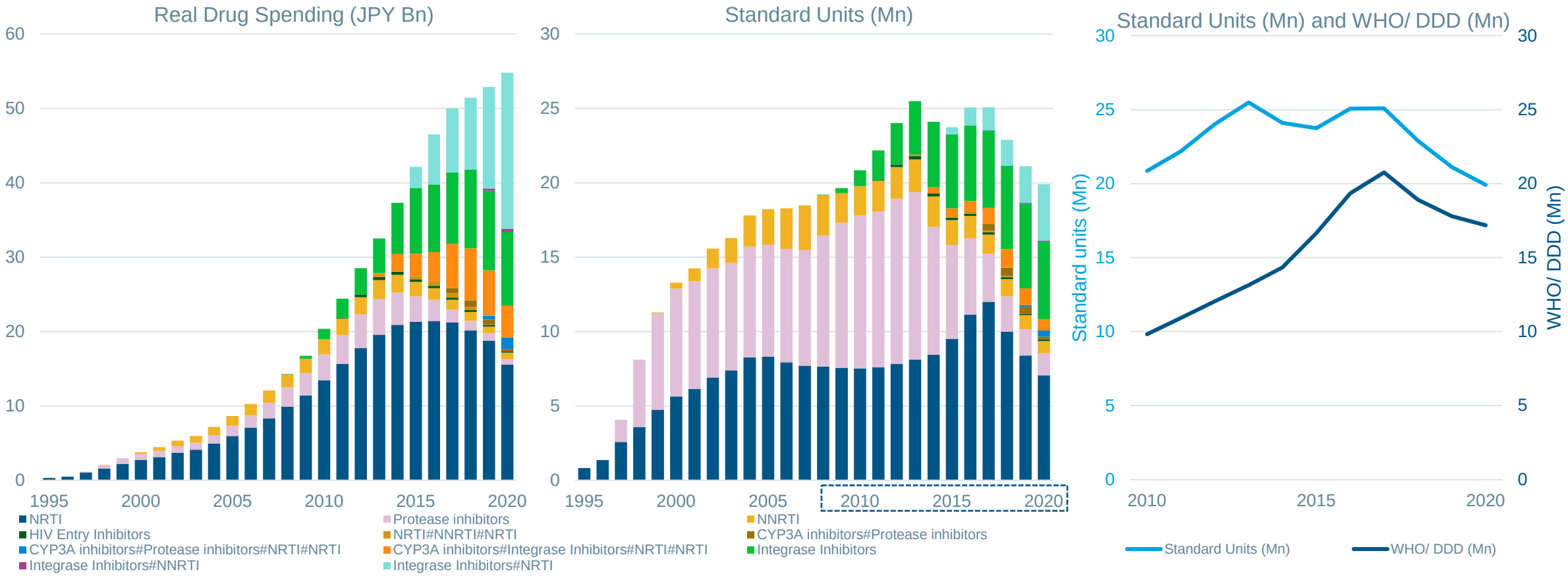
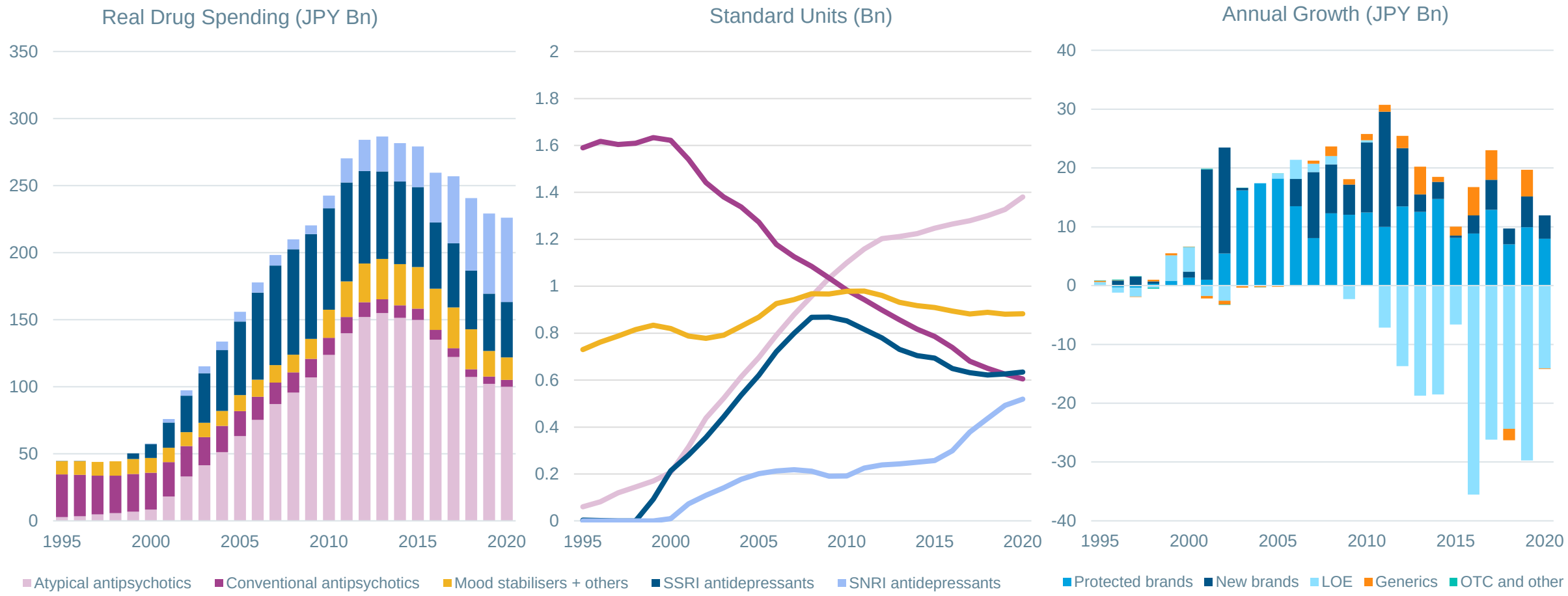


Chart notes: NRTI - Nucleos(t)ide reverse transcriptase inhibitor; NNRTI - Non- nucleoside reverse transcriptase inhibitor; CYP3A inhibitors - cytochrome P450 3A CYP3A inhibitors; # is used to define the combinations of mechanisms used in respective categories. Standard units and WHO/DDD trend in parallel in last four years illustrate that doses per day usage patterns are not changing as much as in earlier years.

Source: IQVIA MIDAS, IQVIA Institute, December 2020

Mental health total spending increased from ¥44 Bn to ¥226 Bn over the 25-year period, with influx of new treatment options

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



Source: IQVIA MIDAS; IQVIA Institute, Dec 2020

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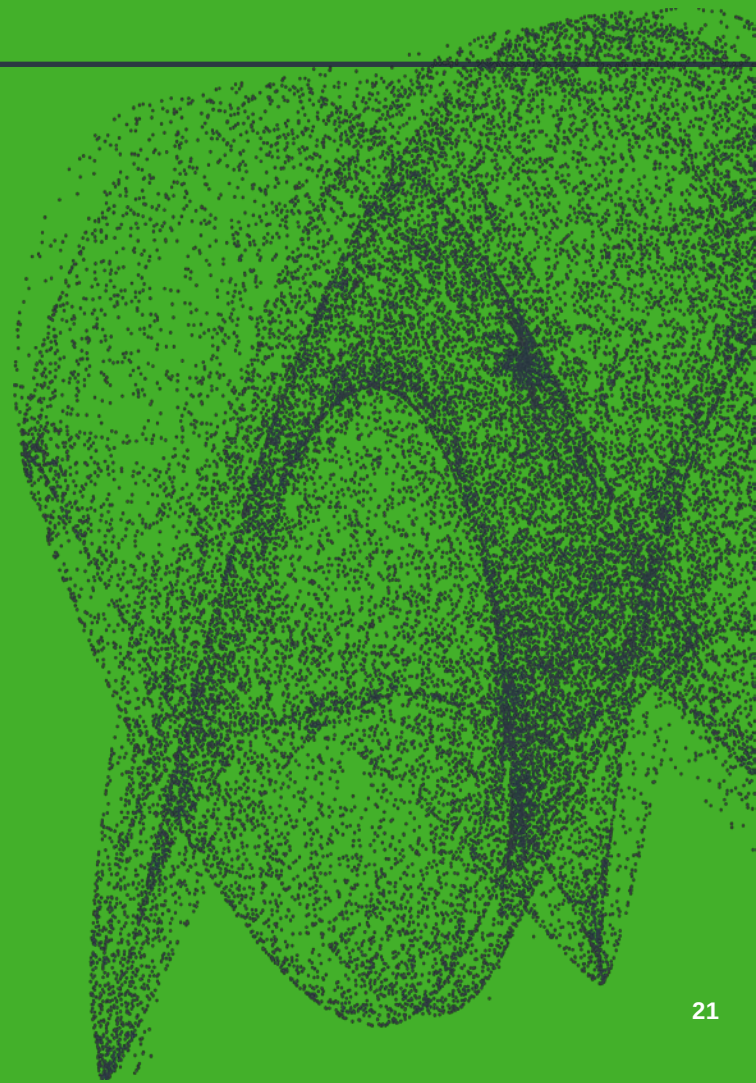
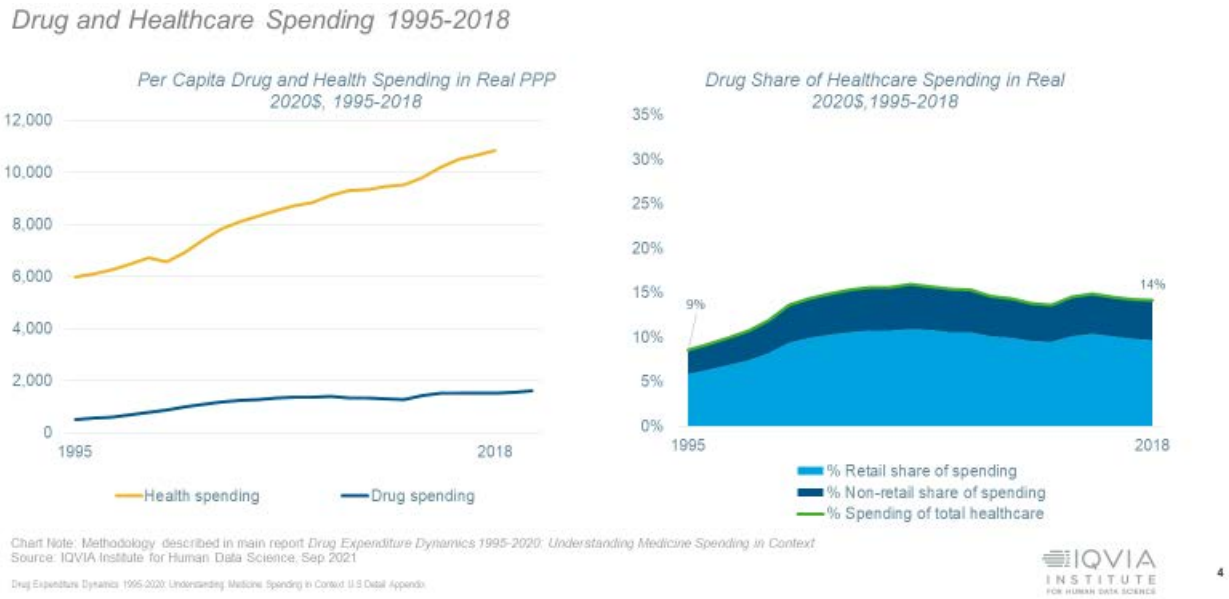
Illustration and explanation of data and chart layouts



Drug and Healthcare Spending Analyses

Key elements to note for interpreting charts



- **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

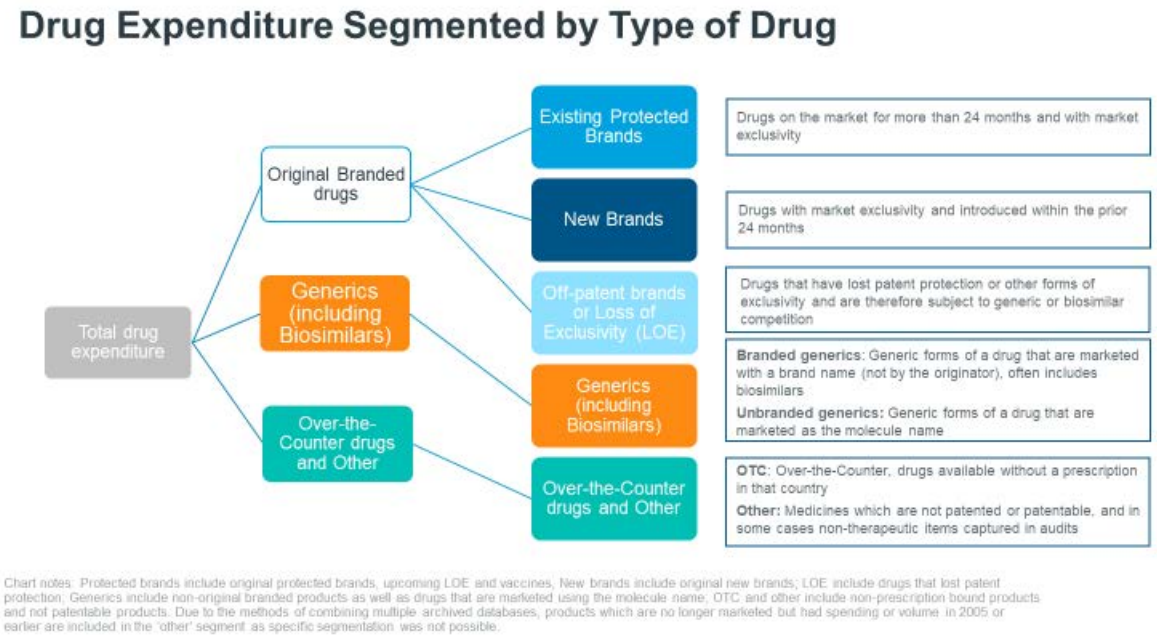


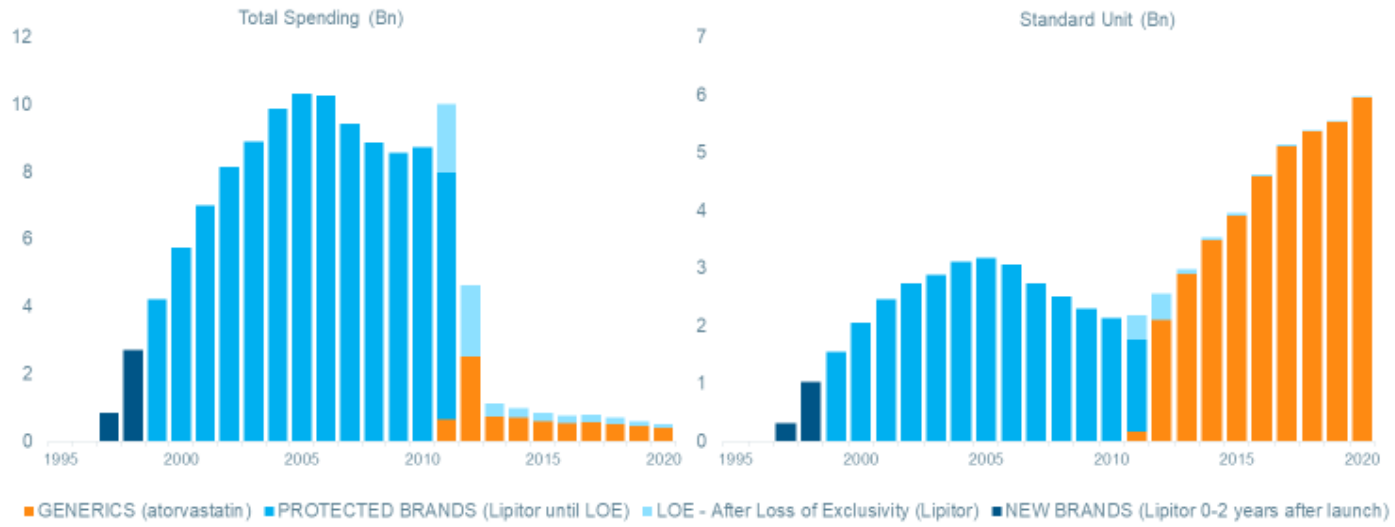
Chart notes: Protected brands include original protected brands, upcoming LOE and vaccines, New brands include original new brands; LOE include drugs that lost patent protection; Generics include non-original branded products as well as drugs that are marketed using the molecule name; OTC and other include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

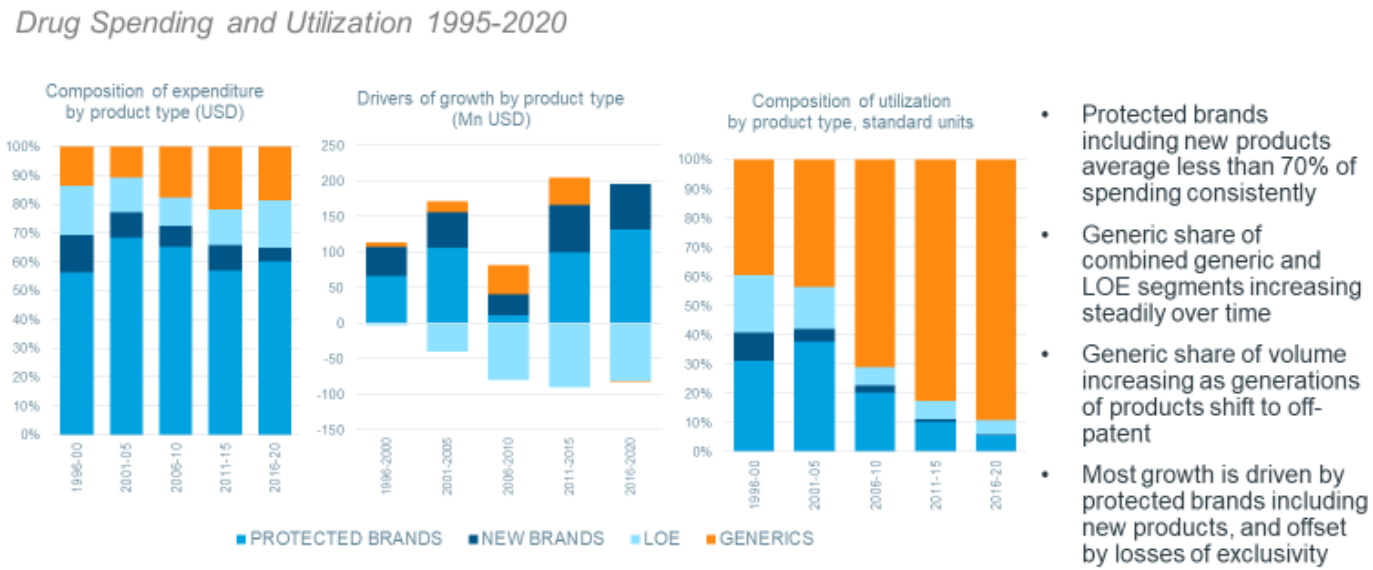
Exhibit x: Illustration of U.S. branded and generic segmentation, Lipitor and Atorvastatin generics



- **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

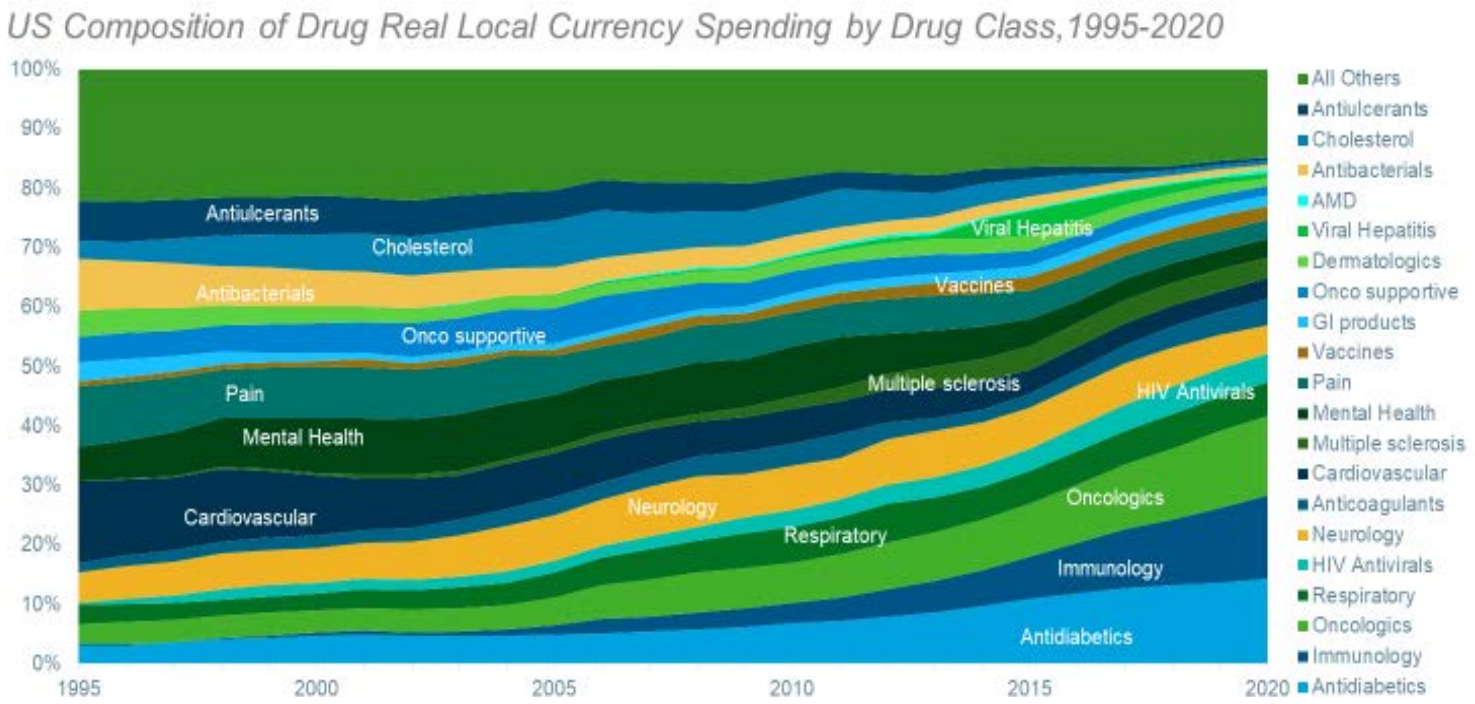


- Protected brands including new products average less than 70% of spending consistently
- Generic share of combined generic and LOE segments increasing steadily over time
- Generic share of volume increasing as generations of products shift to off-patent
- Most growth is driven by protected brands including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

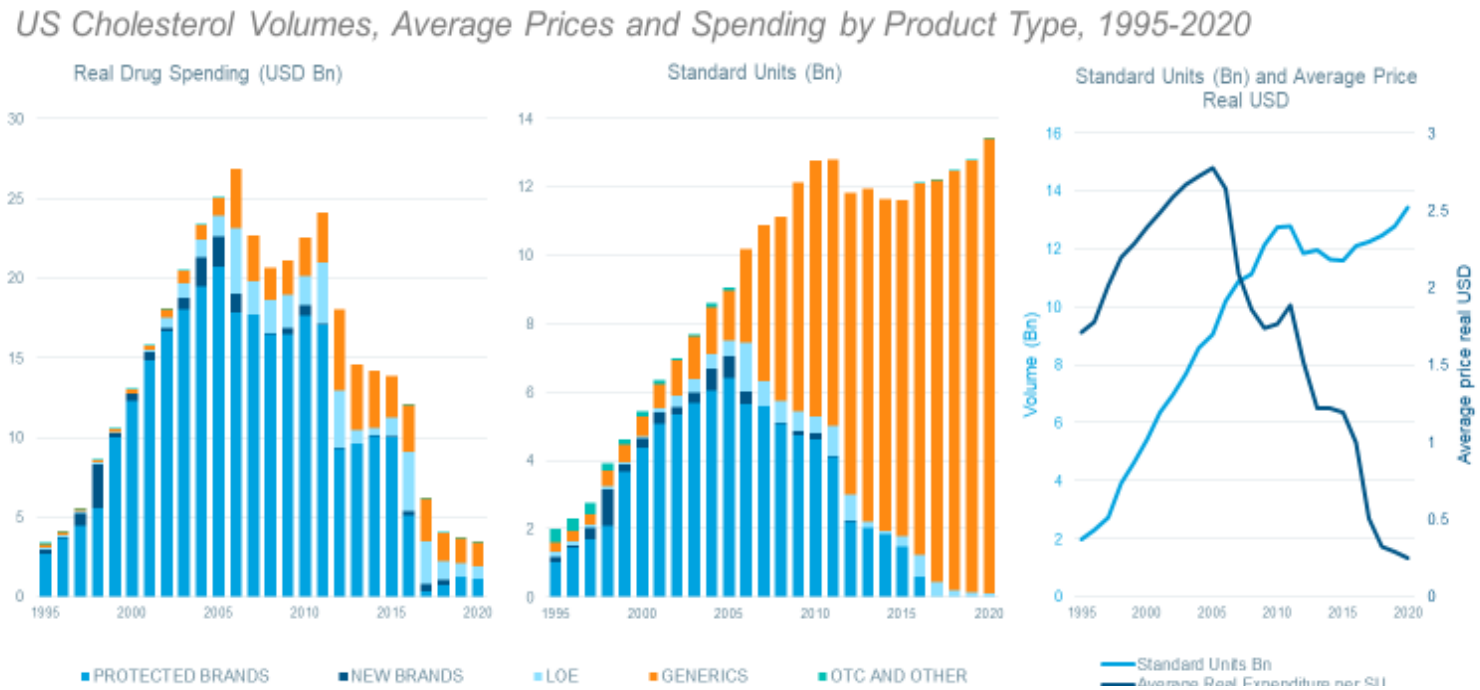
Total drug spending over time on 100% scale by top 20 Therapy areas



- **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

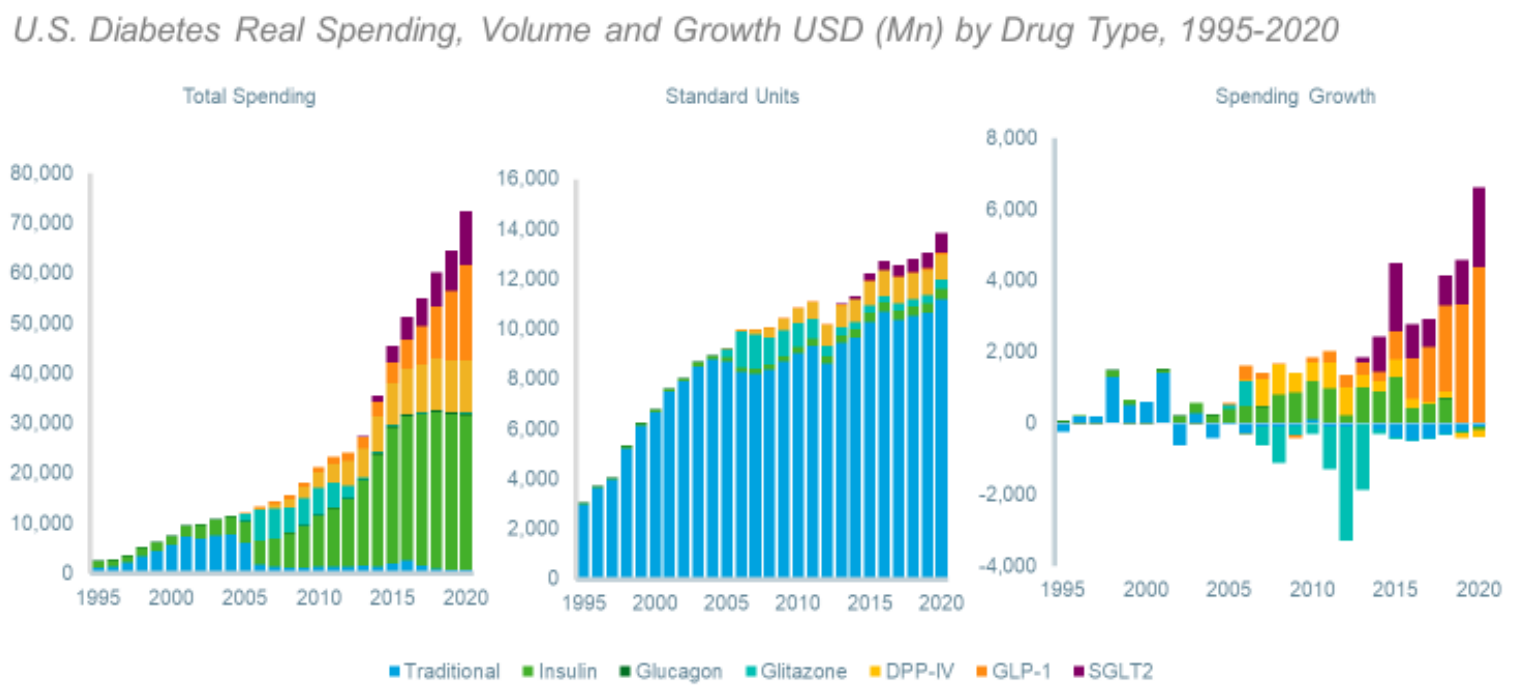
Example of single therapy area with multiple metrics analyzed



- **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

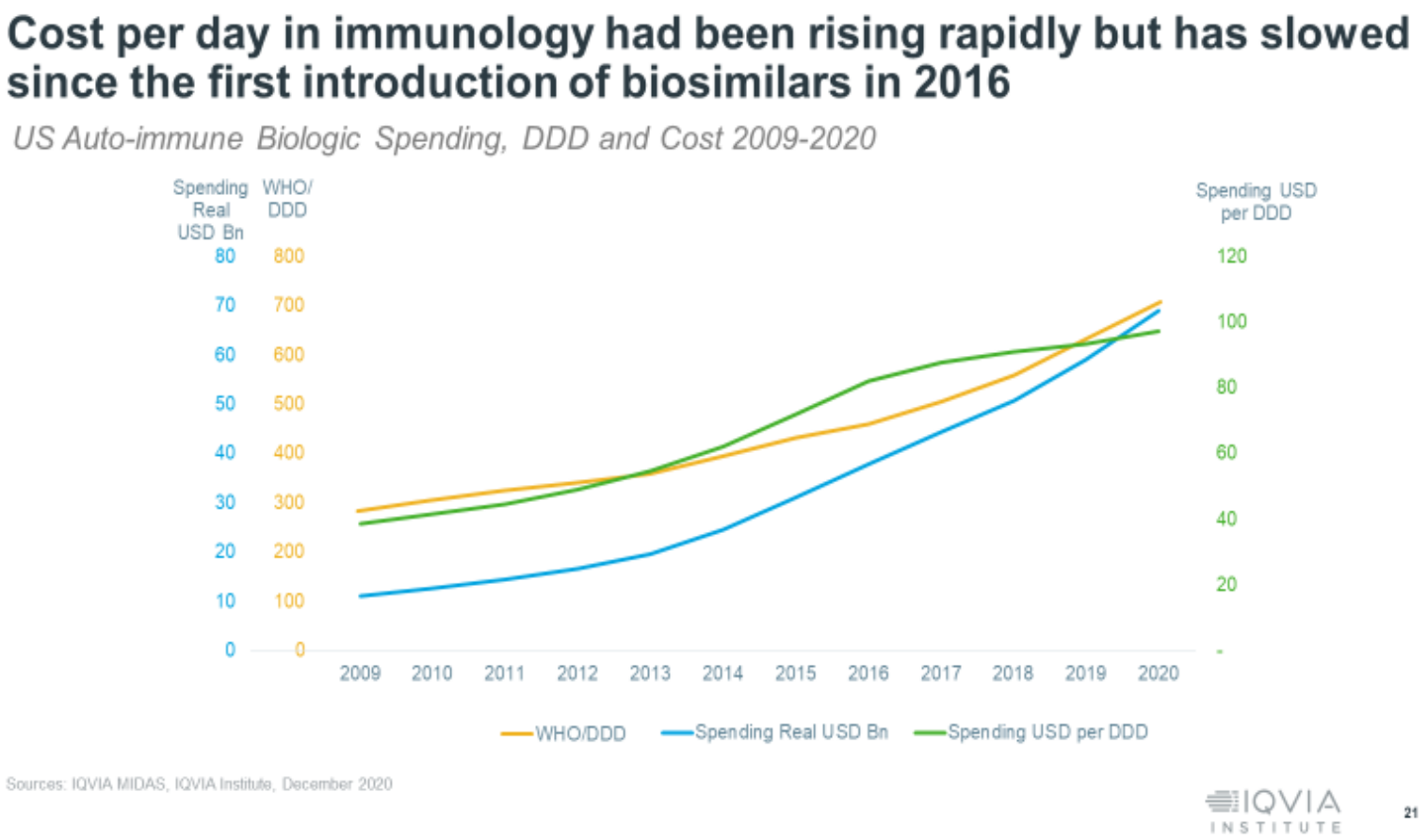
Illustration of a therapy area using multiple analysis metrics



- 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

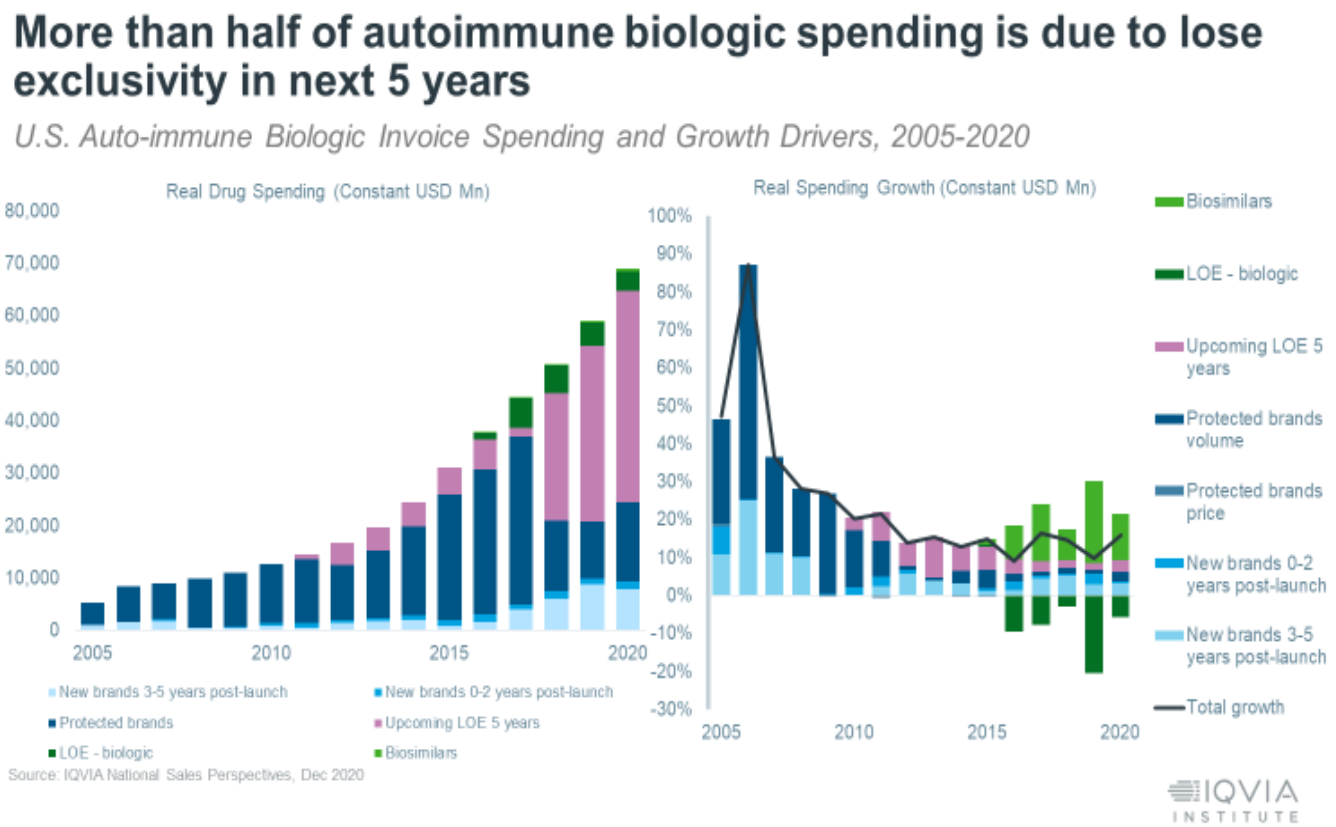
Illustration of three metrics on three axes on the same chart



- 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

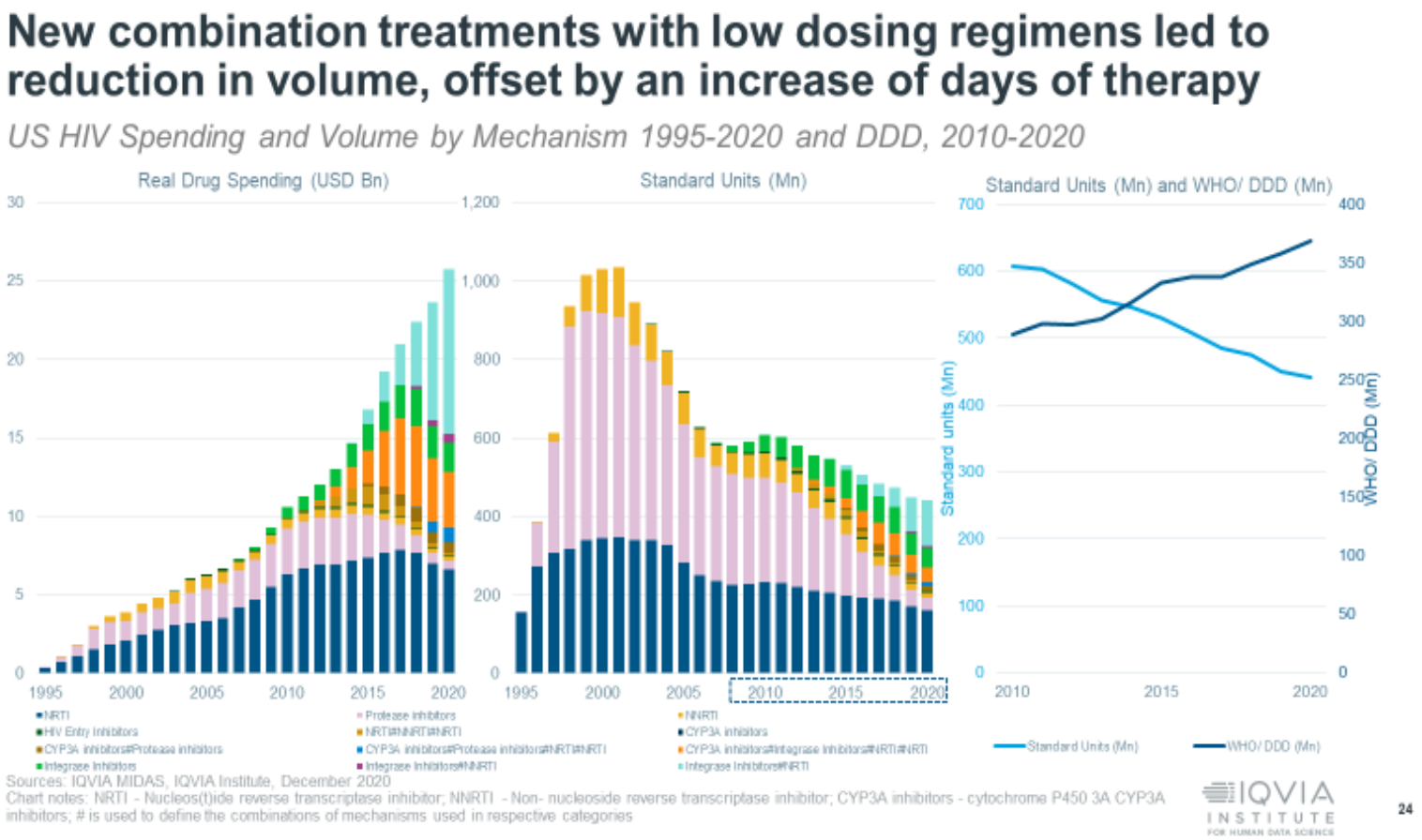
Illustration of product type segmentation with forward-looking segment



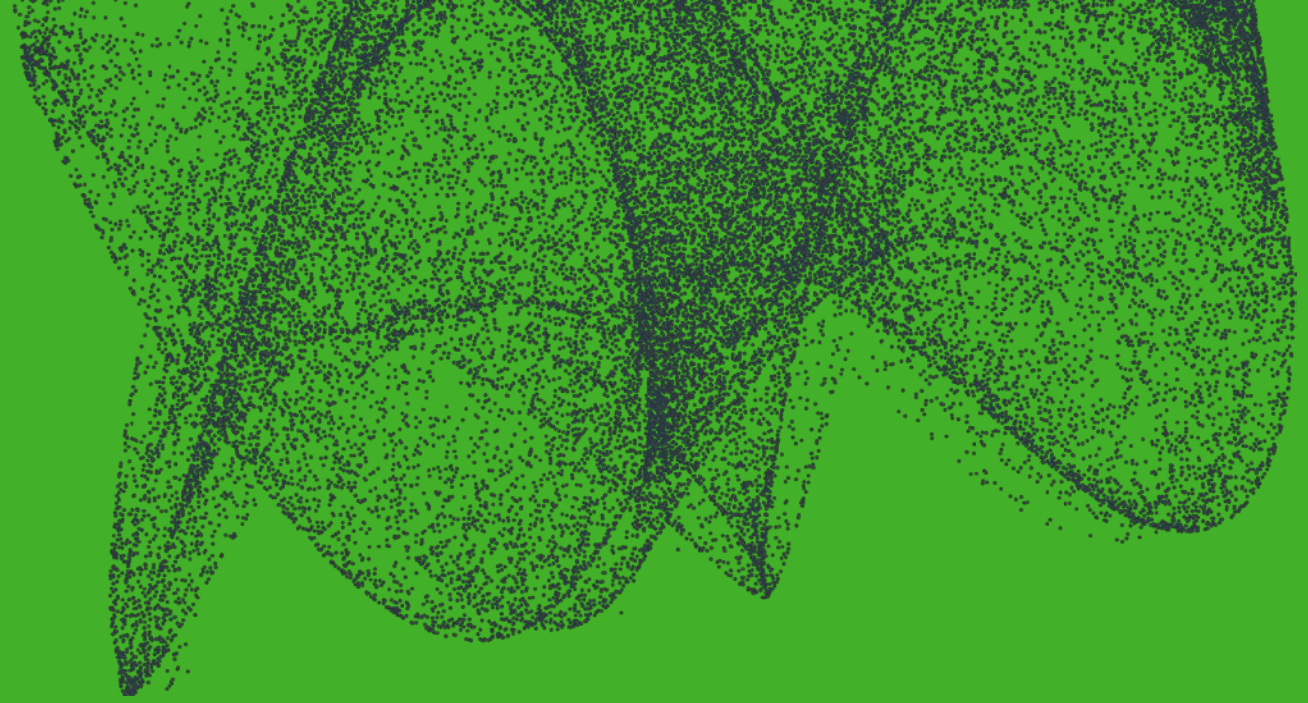
- **Oncology and Autoimmune charts employ a more granular time-dependent segmentation of product type than other analyses in the report.**
- **Original biologics and small molecules when off-patent are identified separately as well as generics (small molecule) and biosimilars.**
- **The autoimmune charts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



- **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.**



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