

April 2015

Medicines Use and Spending Shifts

A Review of the Use of Medicines
in the U.S. in 2014



Introduction

Growth in spending on medicines was higher in 2014 than any year since 2001, and exceeded forecast overall healthcare spending growth for the first time since 2011. As 2014 was also a landmark year in the implementation of the Affordable Care Act, understanding the specific drivers of medicine spending growth is important for decision-makers across the healthcare system.

In this report we bring together several perspectives on 2014: total system spending on medicines at an aggregate and segmented level; the evolution of healthcare demand, delivery and payment systems; patient out-of-pocket costs for medical and pharmacy benefits including retail prescription co-pays; and transformations in disease treatment resulting from newly approved medicines.

It is clear that the U.S. healthcare system is in a state of flux. The past year brought fundamental changes and heightened uncertainty to patients, payers, providers, government and lawmakers. The goal of this report is to bring context and perspective to the complex interplay of factors that determine the level of spending on medicines and their role in our healthcare system.

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Executive summary

Medicine spending increased at the highest rate since 2001, driven by innovative new medicines, lower patent expiry impact and higher list prices. Demand for healthcare services declined in 2014 despite this being the first year of insurance coverage for millions of people under the Affordable Care Act (ACA). Some newly insured individuals, particularly in Medicaid, drove a substantial increase in dispensed prescriptions. Hospital networks are increasingly integrated and coordination of care is seen as a key approach to improving outcomes and lowering costs in the ACA, but nationally health systems remain highly fragmented. Commercially insured patients face increasingly high deductibles, and reduced their prescription usage substantially in 2014.

Healthcare costs and spending on medicines

Spending reached \$373.9 billion in 2014, up 13.1%, the highest level since 2001 when growth was 17.0%. Innovative new drugs for the treatment of hepatitis C, cancer and multiple sclerosis and higher spending on diabetes drugs contributed the most to spending growth. The impact of patent expiries has consistently slowed spending growth in the past five years but the level in 2014 was the lowest in that period at only \$11.9 billion, compared to the peak amount in 2012 of \$29.3 billion. A period of fewer patent expiries since the middle of 2013 drove most of the reduced impact, but off-patent brands that did not face generic competition reduced the impact in 2014 by an estimated \$4-5 billion. Prices for branded products rose in 2014 at an average rate of 13.5% on an invoice basis, but were reduced to 7-8% taking into account off-invoice discounts and rebates which offset most of the increases. Much of the innovation-led spending growth was from specialty medicines which grew by 26.5% and reached one-third of medicine spending, up from 23% five years ago. New medicines contributed \$20.3 billion to growth in 2014, including \$11.3 billion from four new hepatitis C treatments as nearly ten times as many patients were treated in 2014 than in 2013.

Changes in the demand and payment for medicine

In the first full year of enrollment for expanded Medicaid and exchanges under the ACA, patients with Medicaid in states that expanded eligibility filled prescriptions 25.4% more than the prior year, and 2.8% more in non-expansion states. Newly covered patients in Health Insurance Exchanges (HIX) had slightly lower levels of increase, and the group of other commercially insured patients had reduced usage, either because they had become Medicaid or HIX insured or because of the impact of rising co-pays and deductibles. Doctor office visits and hospitalizations declined in 2014, but some types of hospital admissions increased.

When examined by insurance type, usage of hospital services shifted from emergency services to outpatient in general. Medicaid patients had an increase overall in ER visits, but considering the size of the new enrollee population, the increase was relatively modest. Hospital networks have increasingly pursued an integrated care delivery model and the corporate entities and their hospitals, group practices and other aligned service providers now account for over a quarter of all prescriptions dispensed in the U.S. As care becomes more coordinated through ownership or new incentives like the Accountable Care Organization (ACO) shared savings program and patient-centered medical homes (PCMH), it remains to be seen whether patient care will become more consistent and high quality. Early evidence suggests that networks are pursuing quite different protocols and while they may be highly rigorous in managing protocols within networks, care remains highly variable because of network to network differences which exceed the variability in care by doctors not aligned to any network. Changing insurance designs and persistent fragmentation of care patterns can put patients at risk because shifting treatment courses and cost-sharing models can reduce medication adherence and impact health outcomes.

Transformations in disease treatment

The number of new medicines reaching patients has increased in the last few years and in 2014 42 New Active Substances were launched, up from 36 in 2013, and the most since 2001. Clusters of new medicines in hepatitis C, multiple sclerosis and oncology each brought major efficacy, tolerability or convenience benefits. The drug R&D pipeline has shifted to specialty medicines over the past decade and 42% of the late stage pipeline is now specialty, up from 33% ten years ago. Ten Breakthrough Therapies launched in 2014 after the 2012 FDASIA Act granted new approval authorities to the FDA. The FDA has a range of new incentive programs including efforts to encourage drug development for antibacterial resistance. In addition the number of orphan drugs launched peaked again with 18 in 2014 and 61 in the last five years. Cancer remains the most common orphan category, and increasingly very rare “ultra-orphan” drugs, for populations fewer than 10,000, are being developed. Perhaps the most anticipated innovations were “generic” versions of biologic drugs, called biosimilars because exact copies are not possible, which began to be filed for review by the FDA in 2014 and approvals began in 2015.

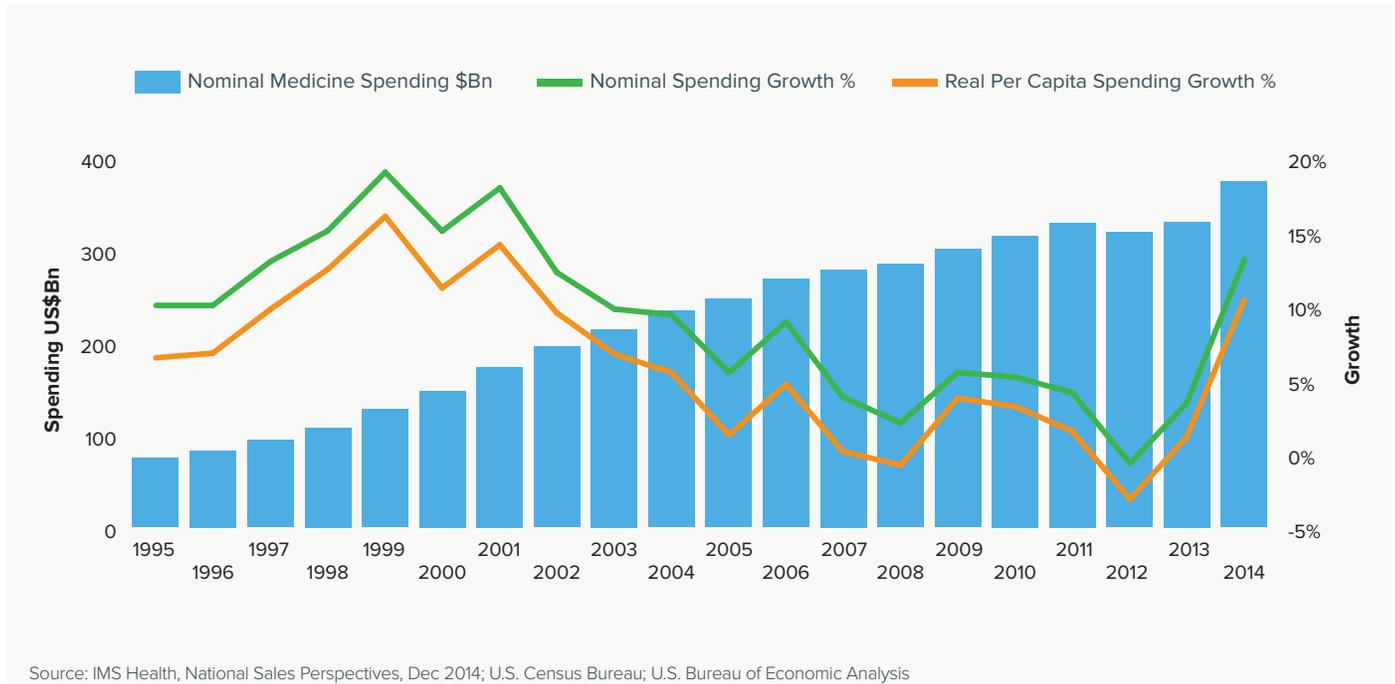
Healthcare costs and spending on medicines

Spending on medicines rose 13.1% on a nominal basis – and 10.3% on a real per capita basis – driven by innovation, higher levels of price increases and lower patent expiry impact.

- Nominal spending on pharmaceuticals reached \$373.9 billion in 2014, an increase of 13.1%, the highest increase since 2001 when spending increased 17.0%.
- Losses of patent exclusivity led to \$11.9 billion lower spending on branded medicines, almost one-third the level in 2012 when expiry impact peaked.
- Price increases for protected brands increased spending by \$26.3 billion, contributing 8.2% to total market growth on an invoice price basis; estimated net price growth was substantially lower as rising off-invoice discounts and rebates offset incremental price growth and reduced net price contribution to growth to 3.1%.
- Specialty medicines now account for one-third of spending, driven by a wave of recent innovations.
- Spending on new brands increased dramatically in 2014 as new treatment options for hepatitis C, cancer, multiple sclerosis and diabetes had stronger uptake than new medicines in prior years.
- Over 161,000 patients started treatment for hepatitis C in 2014, more than four times the previous peak and nearly ten times more than in the previous year as spending on widely adopted new treatments totaled \$12.3Bn.
- Other new medicines including treatments for multiple sclerosis, cancer and diabetes drove \$8.9 billion of increased spending in 2014.
- Diabetes spending increased 30.5% to \$32.2 billion in 2014, driven by innovation and partially offset by off-invoice discounts and rebates, resulting in net spending growth of 22.4%.

Spending on medicines increased 13.1% in 2014, the highest level since 2001 when spending growth reached 17.0%

Medicine Spending & Growth 1995-2014



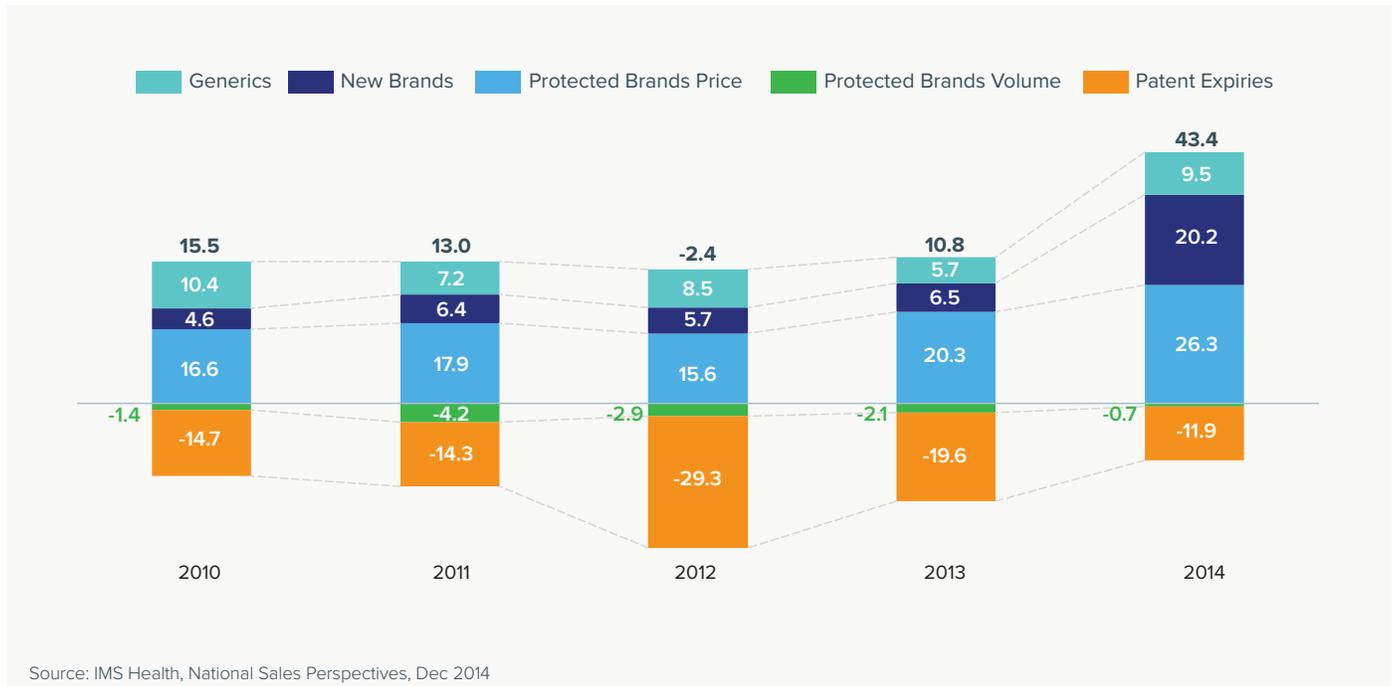
- Real per capita spending was \$995 in 2014 and has nearly tripled since 1995 when it was \$339, both measured in 2005 dollars.
- Higher spending growth between 1997 and 2003 reflected the period when the largest number of blockbuster drugs launched and were increasingly used by millions of Americans.
- Lower levels of growth in spending between 2002 and 2013 were due to lower volume growth, increased use of generics, loss of patent protection for major branded products and reduced spending on new drugs.
- The sharp increase in spending in 2014 was driven by new brands, lower impact from patent expiries and increases in the list prices of branded medicines.

Chart notes:

Measures total value of pharmaceutical spending, including generics, branded products, biologics, small-molecules, retail and non-retail channels. Value measured at Trade Price – the price paid to wholesalers or manufacturers by retail and non-retail pharmacies and excluding off-invoice discounts and rebates that lower net prices received by manufacturers. Real Per capita adjustments based on data from U.S. Census Bureau and U.S. Bureau of Economic Analysis.

Overall spending increased in 2014 due to record spending on new medicines, brand price increases, and lower expiry impact

Spending Growth Drivers US\$Bn



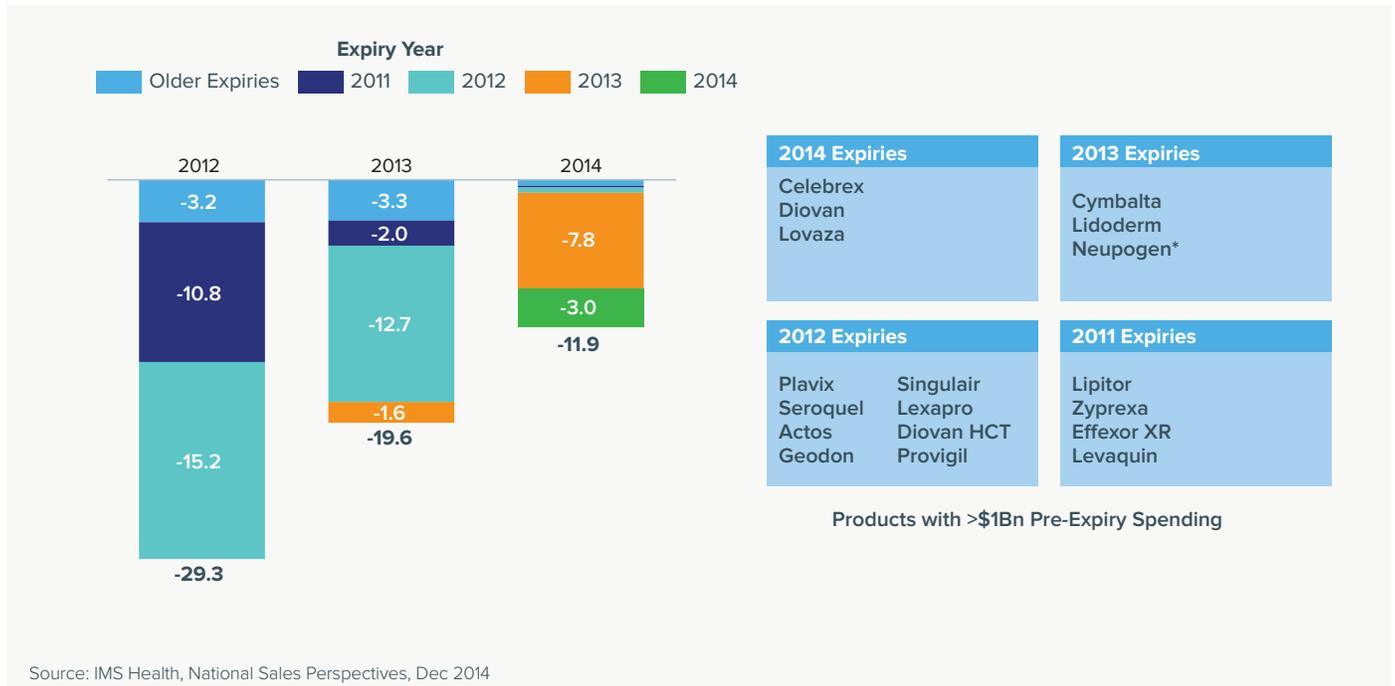
- Total spending on medicines increased \$43.4Bn to \$373.9Bn in 2014.
- Spending on new brands increased by \$20.2Bn in 2014, triple the previous level.
- Spending on protected brands increased \$25.6Bn in 2014 following an increase of \$18.3Bn in 2013.
- The decline in the volume of protected brand products reduced spending by \$700Mn in 2014.
- Increases in the invoice prices of protected brands raised spending by \$26.3Bn.
- Recent patent expiry events resulted in an \$11.9Bn reduction in spending, the lowest expiry impact in five years.
- Generic spending increased \$9.5Bn in 2014, driven by increased spending on generic mental health, pain and cancer medicines.

Chart notes:

Segments are mutually exclusive. Protected brand growth is split by volume and price growth. New Brands segment includes products launched in the last two years. Patent expiry category represents the impact of products that lost exclusivity.

The impact of patent expiries in 2014 was nearly \$8 billion less than 2013 and \$17 billion less than 2012

Negative Brand Growth from Loss of Exclusivity US\$Bn



- Patent expiry events resulted in a reduction in spending of \$11.9Bn in 2014, mostly from the impact of the loss of exclusivity for Cymbalta in 2013 and Celebrex in 2014.
- Despite the lower level of expiry impact, the share of prescriptions dispensed as generics increased by 2% to 88% in 2014.
- In the 21 months between Diovan’s September 2012 patent expiry and the June 2014 generic entry, sales of the brand named blood pressure medication totaled \$3.8Bn.
- In January 2015, safety concerns prompted the FDA to revoke Ranbaxy’s exclusive right to market a generic copy of AstraZeneca’s Nexium – off patent since May 2014 – and instead grant approval to Teva’s generic heartburn medication.
- Granix, a non-original version of the biologic Neupogen (filgrastim), was launched in November 2013 and captured approximately 11% of filgrastim volume in 2014.

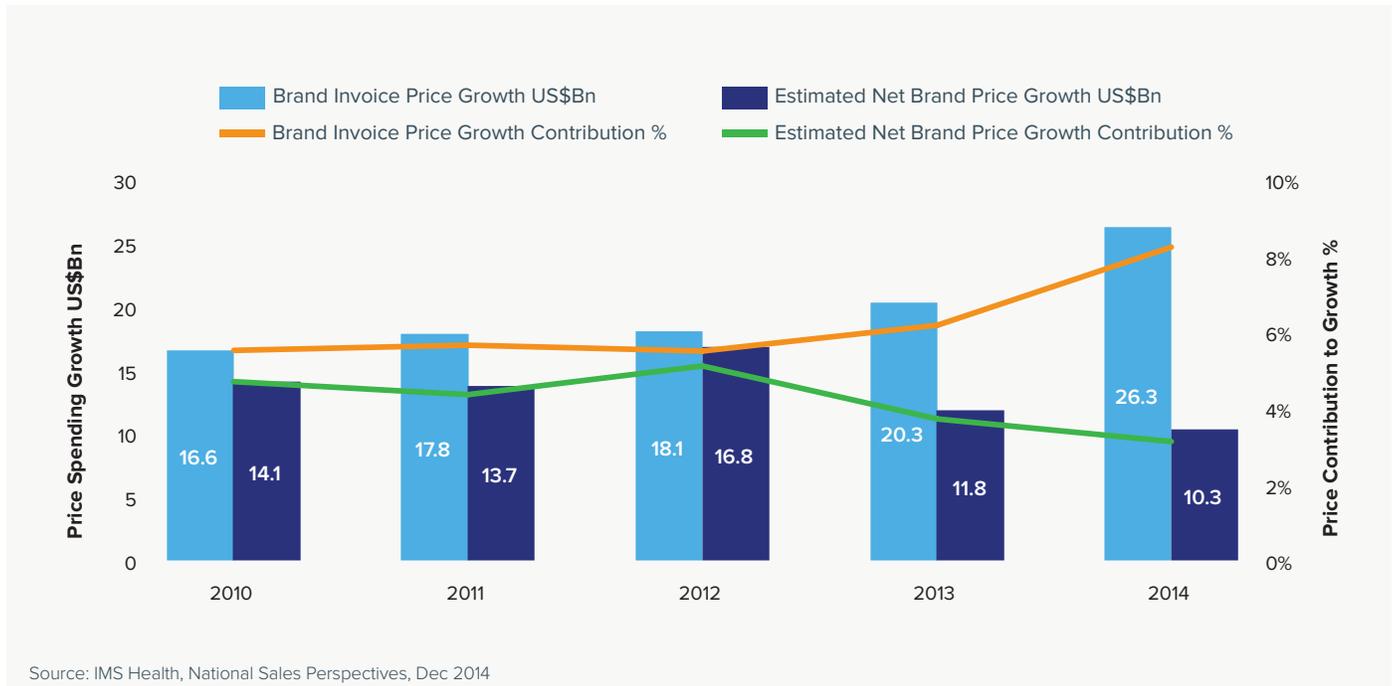
Chart notes:

Older expiries includes products that lost exclusivity in earlier period. LOE – Loss of Exclusivity – includes branded products that have lost patent exclusivity and faced generic competition to date. Loss of exclusivity year is determined primarily by patent expiry date, but adjusted to reflect when generic competition entered the market.

*Neupogen (filgrastim) faced non-original competition from Granix which was approved as an original Biologic (BLA) in November 2013; a biosimilar competitor was approved in 2015 through the FDA’s new approval process.

Invoice prices increased in 2014, but were offset by off-invoice discounts, rebates and other price concessions

Protected Brand Price Spending Growth



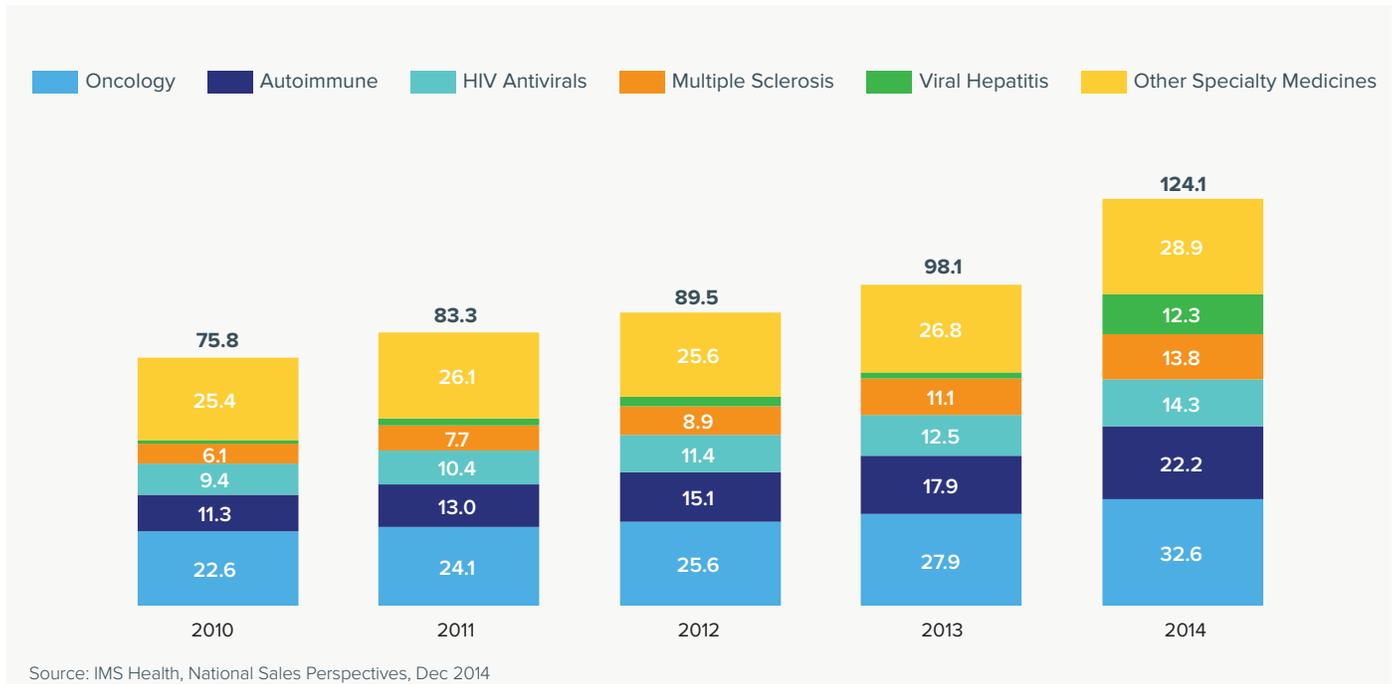
- Spending on protected brands increased by \$26.3Bn in 2014 due to invoice price changes, compared to \$20.3Bn in the prior year.
- Spending growth due to protected brand invoice pricing contributed 8.2% to overall growth in 2014, up from 6.2% in 2013.
- Protected brands invoice price increases averaged 13.5% in 2014, up from 12% in 2013.
- When adjusted for changes in the aggregate level of rebates and discounts, net price growth of an estimated \$10.3Bn contributed 3.1% to spending growth in 2014.
- The net prices for some brands in particularly competitive therapy areas have declined, while others have continued to increase at levels consistent with historic trends, with brand net prices estimated to have increased 5-7% on average in 2014.

Chart notes:

Total IMS Health reported price growth is dollar growth driven by invoice price changes and excludes the impact of rebates and contract pricing agreements. Brand invoice price growth contribution is the contribution to market growth and does not reflect a rate of price increases. Estimated net price growth is based on a comparison of company reported net sales and IMS Health reported sales at invoice prices from wholesaler transactions. Comparisons were made at company level for a sample representing 75% of total U.S. medicines spending, and at product level for branded products representing 64% of brand spending, and results of both methods were consistent within +/- 0.5%.

Specialty medicines now account for one-third of spending driven by a wave of recent innovations

Spending on Specialty Medicines US\$Bn



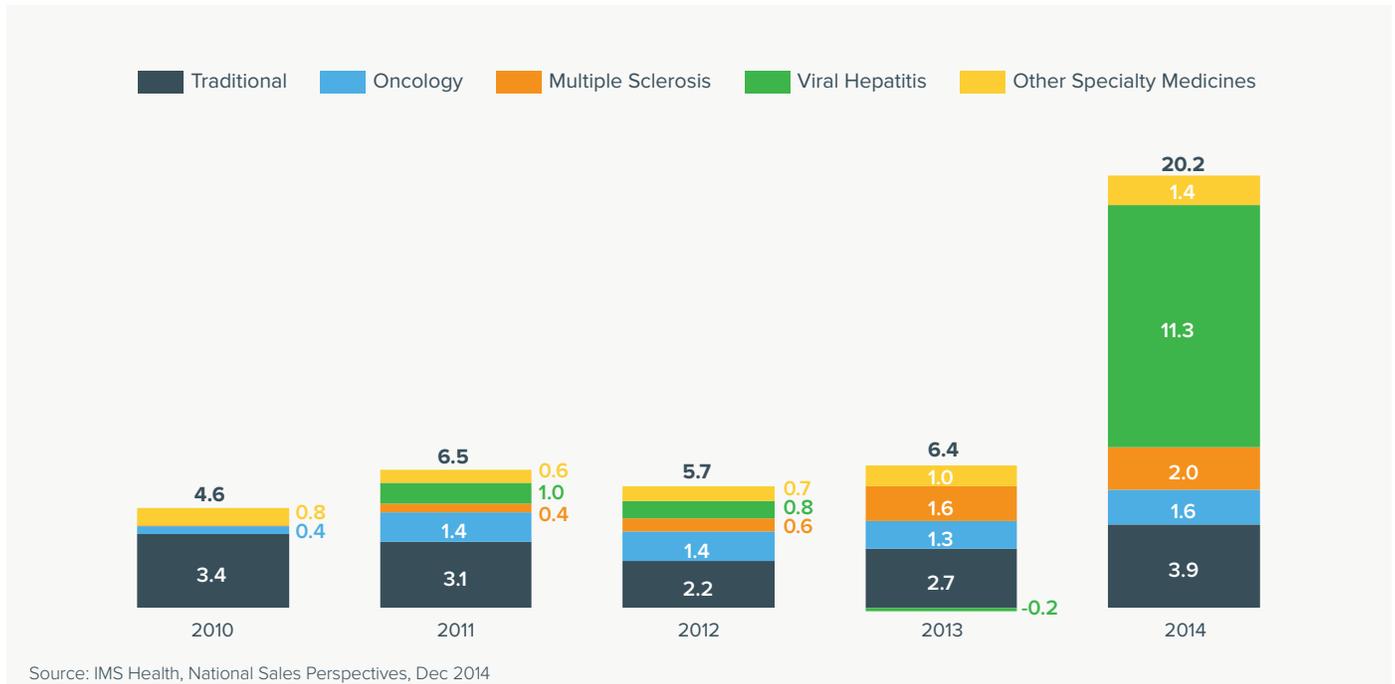
- Spending on specialty medicines has increased by \$54.0Bn in the last five years, contributing 73% of overall medicine spending growth in that period.
- Increased specialty spending was driven by innovations in treatment for autoimmune diseases, hepatitis C and oncology, accounting for \$34.7Bn of increased spending.
- Specialty medicine spending increased by 26.5% to \$124.1Bn in 2014; the increase was 16.3% excluding hepatitis C treatments.
- The biggest driver of specialty spending growth, \$12.3Bn in spending on treatments for hepatitis C, caught many payers by surprise, forcing budget holders to weigh the cost and the value of new cures.
- Spending on oncology and autoimmune treatments increased by 16.8% and 24.0% respectively.
- Multiple sclerosis spending increased 24.4%, driven by new treatment options offering new mechanisms of action and more convenient dosing.

Chart notes:

Specialty therapies are defined by IMS Health as products that are often injectable, high-cost, biologics or require cold-chain distribution. They are mostly used by specialists, and include treatment for cancer and other serious chronic conditions. Specialty therapies often involve complex patient follow-up and monitoring. Oncology includes therapeutic treatments and not supportive care.

Specialty drugs for hepatitis C, multiple sclerosis and cancer drove new brand spending growth

New Brand Spending Growth US\$Bn



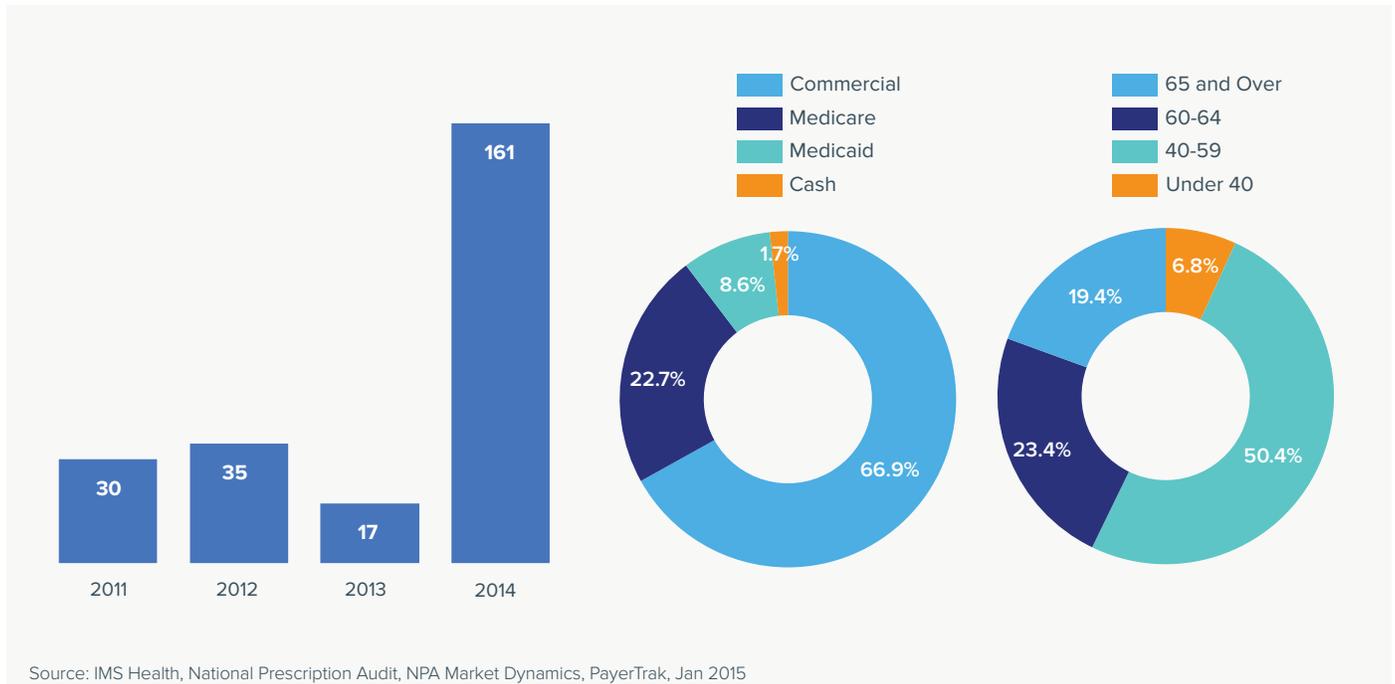
- The unprecedented \$20.2Bn increase in spending on new brands contributed 6.1% points to overall 13.1% growth in 2014.
- Four new treatments for hepatitis C, which offer drastically improved patient outcomes, increased spending by \$11.3Bn.
- Other new treatments increased new brand spending by \$8.9Bn, somewhat higher than past years.
- Two of the most successful brand launches of 2011, both treatments for hepatitis C, were withdrawn from the market in 2014, having been replaced by newer generation treatments.
- Specialty medicines accounted for \$19.2Bn or 78% of the \$24.5Bn total new brand spending, reflecting a continued shift of R&D towards specialty diseases, and their growing share of overall drug spending.
- New cancer and multiple sclerosis medicines contributed \$1.6Bn and \$2.0Bn respectively.
- Traditional medicines included entirely new mechanisms for treating diabetes and contributed \$3.5Bn to spending.

Chart notes:

New brands defined as brands launched in the last two years. Specialty therapies are defined by IMS Health as products that are often injectable, high-cost, biologic or requiring cold-chain distribution. They are mostly used by specialists, and include treatment for cancer and other serious chronic conditions, and often involve complex patient follow-up and monitoring. Oncology includes therapeutic treatments and not supportive care.

Over 161,000 patients started treatment for hepatitis C in 2014, far more than during the earlier cluster of innovation

New Hepatitis C Patients (Thousands) by Age and Insurance Type



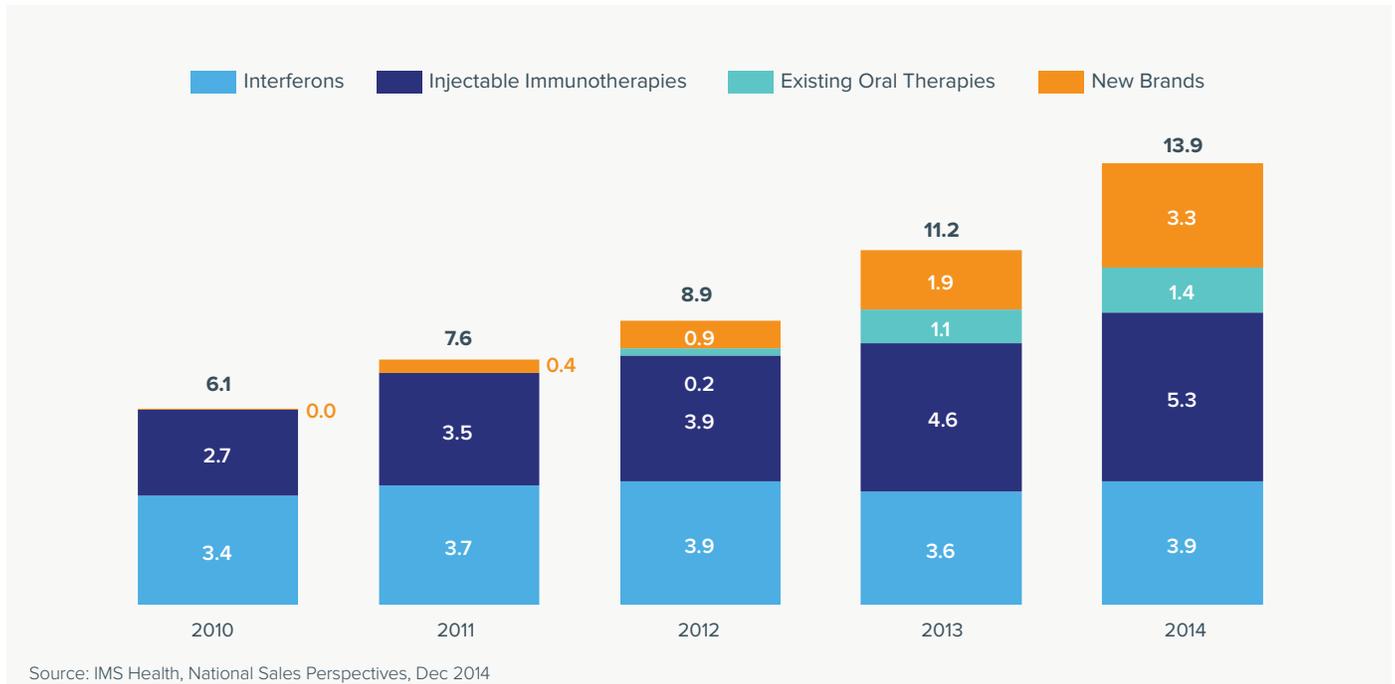
- Over three million people in the U.S. are infected with the hepatitis C virus but low treatment rates persisted due to the slow disease progression and intolerable side effects of older therapies.
- Six medicines launched since 2011 have provided tolerable and effective new options for people living with hepatitis C.
- The number of patients seeking treatment for hepatitis C jumped nearly tenfold in 2014, from 17 to 161 thousand, owing to new treatments with cure rates over 90% and dramatically fewer side effects.
- Much of the discussion of these medicines during 2014 focused on their prices, over \$80,000 for a twelve week course of treatment and even higher when add-on therapies are included.
- Most insurance plans limit patient costs with annual out-of-pocket maximums, but price was a dominant theme in patient, payer and doctor discussions of treatment during 2014.
- The majority of patients who received treatment in 2014 had commercial insurance.

Chart notes:

New patients are defined as new to brand prescriptions for Incivek, Victrelis, Sovaldi, Olysio, Harvoni and Viekira Pak. Patient estimates are adjusted based on company reports and IMS Health estimates of supplier data restrictions. Medicaid includes both fee for service and managed Medicaid. Commercial insurance includes exchange plans (HIX). Medicare Part D coverage is available for disabled patients who are under 65. Insurance type is estimated for mail order pharmacies based on distribution of commercial and Medicare Part D prescriptions in over 65 and under 65 populations in retail pharmacies.

Multiple sclerosis spending rose 24% to \$13.9 billion in 2014 driven by new oral and self-administered medications

Multiple Sclerosis Spending US\$Bn



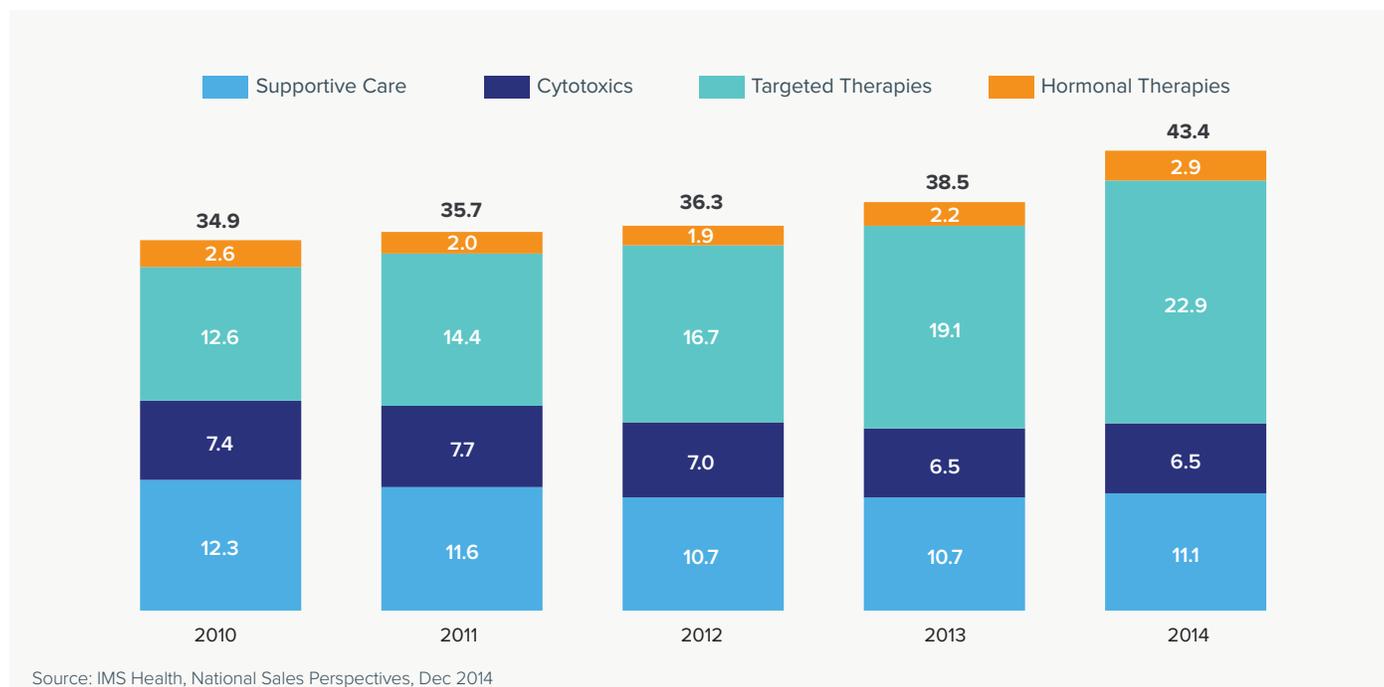
- Multiple sclerosis spending rose 24.4% to \$13.9Bn in 2014, driven by \$4.7Bn in new brands and oral therapies.
- Patients with MS still face considerable burdens from their disease but newer medicines have brought a range of new options over the past five years.
- Injectable interferons accounted for \$4.3Bn or 30.9% of total multiple sclerosis spending.
- Spending on injectable immunosuppressants, such as glatiramer acetate and natalizumab increased 14% to \$5.3Bn.
- The once-daily glatiramer acetate 20mg will likely face generic competition in late 2015, but as of the end of 2014, nearly two-thirds of new prescriptions for the medicine were started with a new long-acting injection formulation.
- Spending on oral treatments – including new brands – reached \$4.3Bn in 2014, the largest was dimethyl fumarate which surpassed \$3.5Bn in spending less than two years since its launch.

Chart notes:

Multiple sclerosis market defined as L3B2 interferons, dimethyl fumarate, fingolimod, glatiramer acetate, natalizumab and teriflunomide. New Brands segment includes products launched in the last two years.

Oncologics spending reached \$43.4 billion in 2014 lifted by new melanoma, lung, breast and prostate cancer therapies

Therapeutic Oncology and Supportive Care Spending US\$Bn



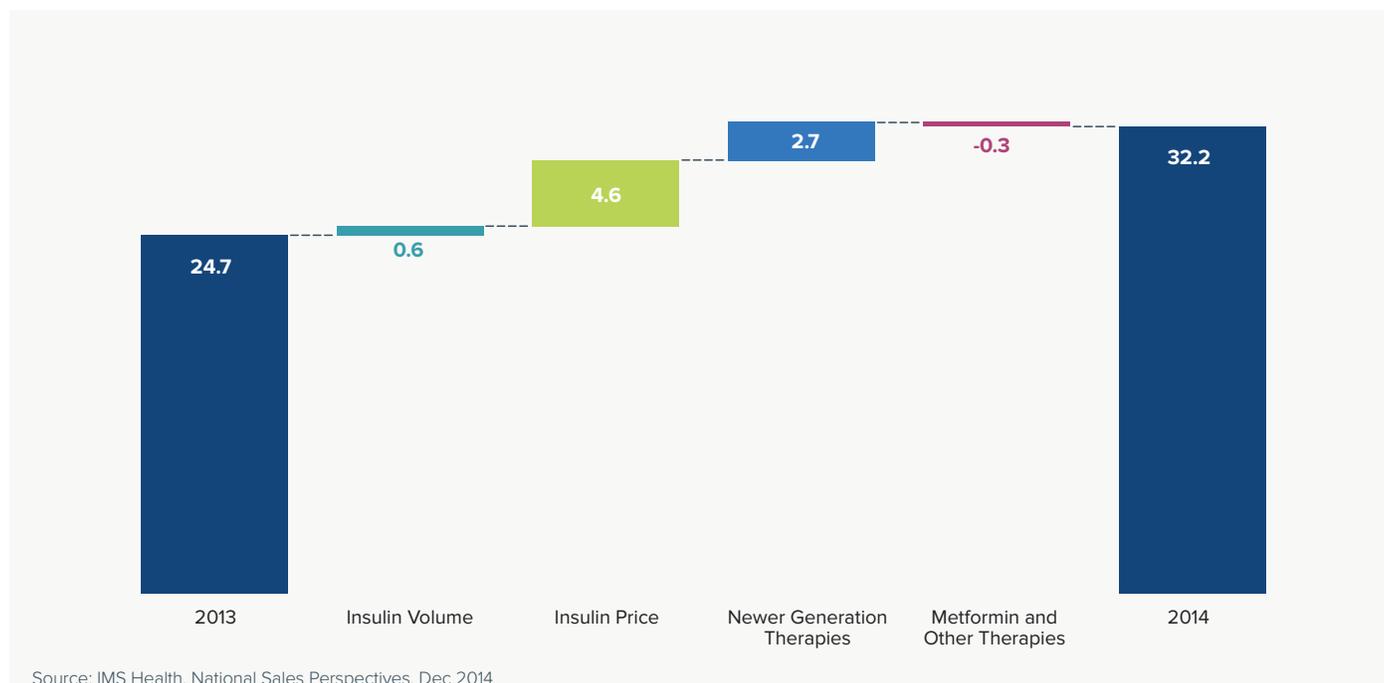
- Oncologics led all classes in spending in 2014 with \$32.3Bn in spending, or \$43.4Bn including supportive care treatments.
- Spending grew by nearly \$4.9Bn, mostly from new targeted therapies, which had the fourth straight year of \$1Bn or more growth from new brands, and many of those earlier medicines have continued to expand usage and contribute more to spending.
- Treatment options launched in the last two years account for 30% of spending increases.
- Supportive care treatments such as erythropoietins, anti-nauseants, and bisphosphonates contributed little to spending growth but often allow patients to continue on other treatments.
- Granix, a non-original version of the biologic Neupogen, used to reduce the risk of infection during chemotherapy, became available in November 2013 and now accounts for 11% of filgrastim volumes.

Chart notes:

Therapeutic oncology defined as EphMRA ATC classification L1 - cytotoxics, L2 hormonal treatments, V3C radiotherapeutics, as well as molecules classified elsewhere noted to be therapeutic oncolgoids (lenalidomide, denosumab (when used for bone metastases it is marketed as Xgeva), aldesleukin, pomalidomide). Supportive care includes erythropoietins, colony-stimulating factors, anti-nauseants for cancer, and chemotherapy protectants.

Diabetes spending increased 30.5% to \$32.2 billion in 2014, offset by off-invoice discounts and rebates to net spending growth of 22.4%, driven by innovation

Components of Diabetes Spending Growth US\$Bn



- Spending on treatments for diabetes reached \$32.2Bn in 2014, increasing 30.5% on an invoice-price basis over 2013, the second highest therapy area growth rate among leading classes (after hepatitis C).
- Total diabetes spending grew by an estimated 22.4% net of off-invoice discounts and rebates, driven equally by new products (\$2.7Bn) and net price growth (\$2.6Bn).
- Insulins accounted for 63.3% of diabetes spending and 61.3% of spending growth in 2014, driven by price increases, with an estimated 44% of the increase conceded in discounts or rebates.
- Cost savings for insulins – the largest part of diabetes spending – are on the horizon with the first filings with FDA for non-original biologic or biosimilar insulin therapies made in 2014, and the first biosimilars likely to launch in the U.S. in 2015-16.
- Newer therapies, such as DPP-IVs, GLP-1s and SGLT2s now account for 31.4% of diabetes spending.
- Spending on other diabetes therapies, including sulphonylureas, biguanides and glitazones decreased by 16.3%, declining \$337Mn to \$1.7Bn.

Chart notes:

Newer generation diabetes drugs include dipeptidyl peptidase-4 inhibitors (DPP-IVs), glucagon-like peptide-1 agonists (GLP-1s) and sodium-glucose cotransporter 2 inhibitors (SGLT2s).

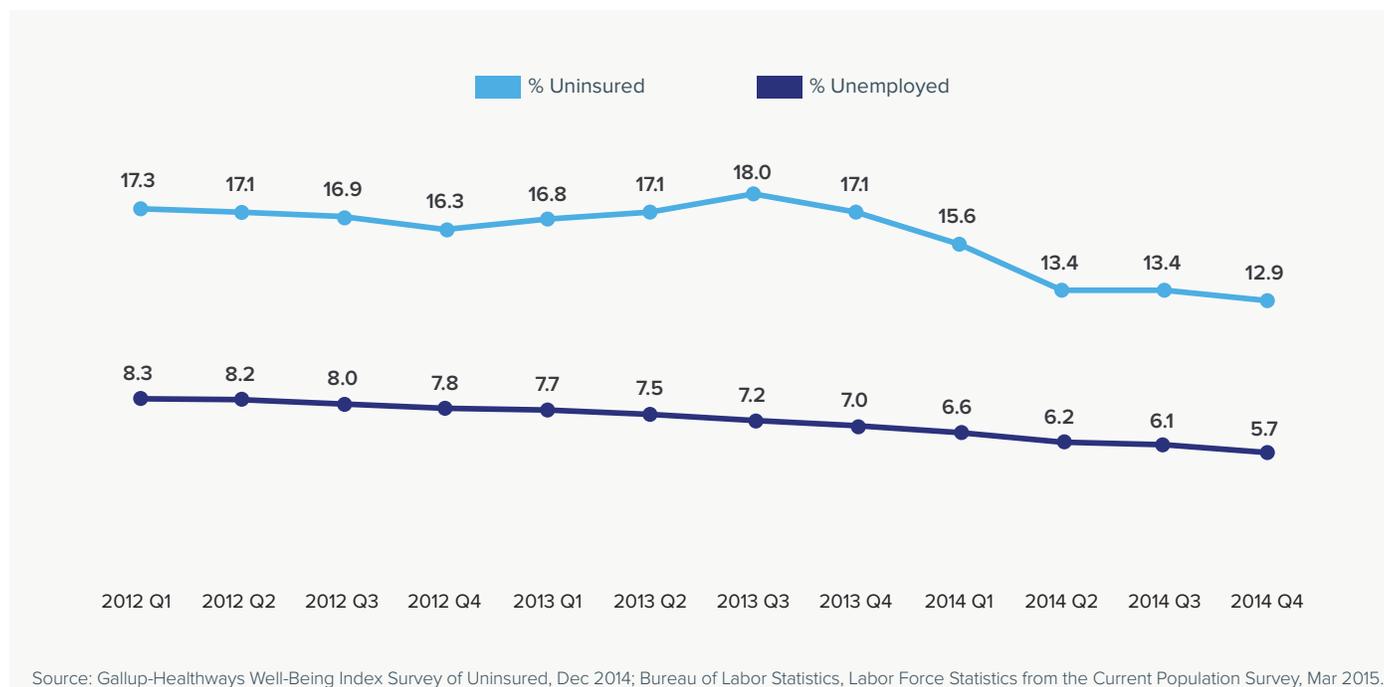
Changes in demand and payment for medicines

Demand for healthcare services was impacted by the Affordable Care Act (ACA) and also by changes in cost sharing between patients and payers.

- 15.7 million people gained health insurance coverage in 2014 due to the ACA's Medicaid expansion, Health Insurance Exchanges (HIX) and continued economic recovery.
- Macro-level demand for healthcare shifted in 2014 as patients made 3.0% fewer office visits, had 1.7% fewer hospital admissions, but filled 2.1% more prescriptions as newly insured patients drove increased prescription demand.
- The decline in overall hospital visits was driven mainly by a decline in outpatient visits for commercially insured and Medicaid patients, and offset by a 3.8% increase in ER visits by Medicaid beneficiaries, including those who were new to coverage.
- Integrated Delivery Networks (IDNs) are increasingly a part of the U.S. healthcare system, as integration is key to many ACA goals and programs, but some geographies remain highly fragmented.
- Integrated health systems promote highly uniform care within their networks, but in some therapy areas there are significant variations in the protocols of choice, leading to very different treatments depending on network and/or geography.
- Medicaid patients used dramatically more prescriptions, lifting overall prescription demand nationally, suggesting that new enrollees were sicker than previously enrolled patients.
- Nine percent of patients filling Medicaid prescriptions in 2014 and 24% of those with exchange plans may have been previously uninsured, representing a substantial shift in coverage.
- Many Americans with employer-sponsored insurance continued to see increases in premiums and out-of-pocket costs, but 93% of beneficiaries have annual maximums and out-of-pocket costs capped at less than \$6,350.
- There is some evidence that exposure to costs affects patient behavior and adherence as more patients move to health plans with deductibles.
- High out-of-pocket costs can be mitigated with various forms of co-pay assistance, including coupons and vouchers, and as many as half of all branded prescriptions in newer diabetes treatments are supported in this way, compared to 8% of brands in all therapy areas.

The uninsured rate in the U.S. declined in 2014 driven by the Affordable Care Act and an improving economy

Quarterly Unemployment and Uninsured Rates



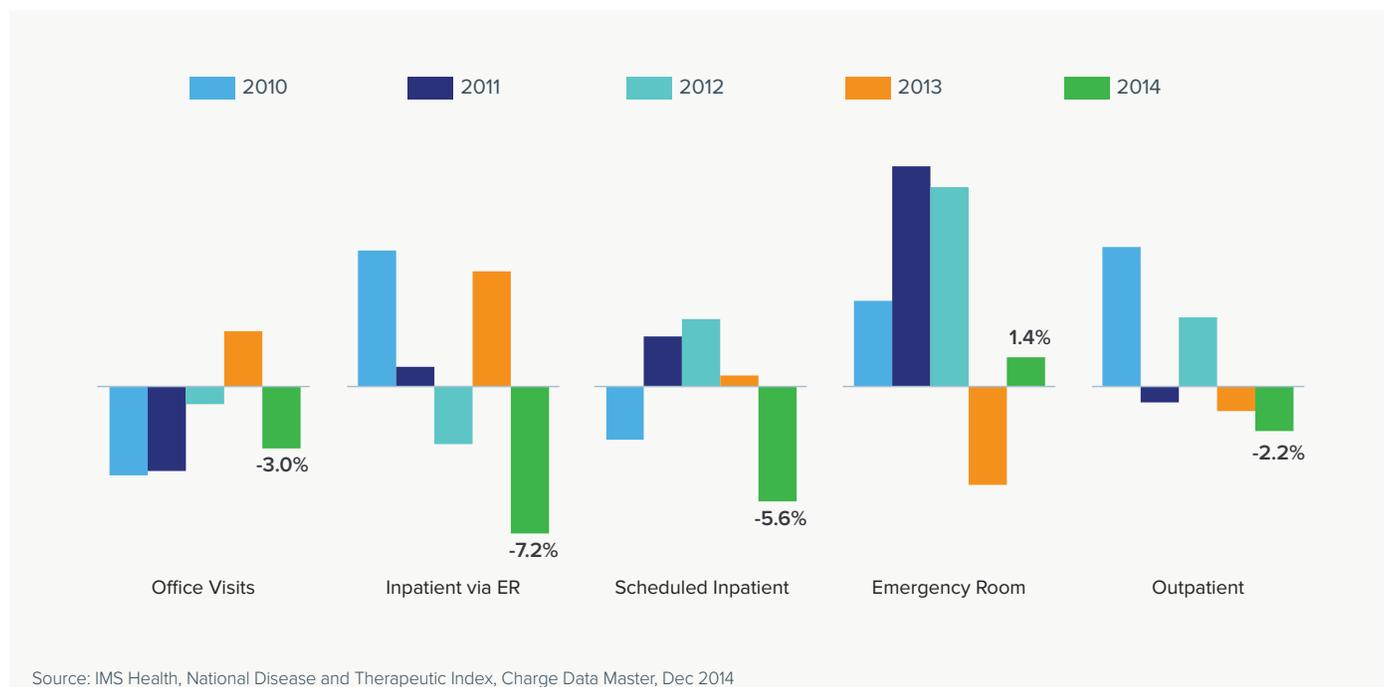
- Medicaid expansion and health exchanges began enrolling patients in October 2013 and benefits became available in January 2014.
- Enrollment continued until April 2014 and the fullest impact of new enrollees became apparent in the second quarter of 2014.
- From the end of September 2013 to the end of 2014, the uninsured rate was reduced by 5.1%, adding 15.7 million people to the insured population.
- The unemployment rate dropped 1.5% in that period and some of the 2.3 million newly employed were offered new coverage by their employers.
- Medicare enrollment also increased as more baby-boomers reached the age of eligibility, some of whom may have been uninsured previously.

Chart notes:

Uninsured rate is the percentage of U.S. adults without health insurance among adults aged 18 and older. Unemployment rate is based on the non-disabled >16 years labor force. Other public estimates of the newly insured population include 19-25 year-olds who gained coverage starting in 2010, and those who gained coverage starting in January 2015, which are excluded from this analysis as they do not impact the newly insured in 2014.

Patients made fewer visits to hospitals in 2014 with a large drop in outpatient visits and slight increase in ER visits

Percent Change in Office and Hospital Visits



- Twenty-six states and the District of Columbia expanded Medicaid to millions of adults with incomes up to 138% of the federal poverty level in 2014, and millions more gained insurance coverage through exchanges, but overall doctor visits and hospital admissions declined.
- Americans made 1.2Bn visits to the doctor in 2014, a decline of 3.0% over 2013.
- Hospital visits dipped 1.7% in 2014, driven mainly by a decline in outpatient visits.
- Inpatient stays declined 6.2%, driven by 7.2% fewer inpatient admissions via the emergency room.
- Scheduled inpatient visits dropped 5.6%.
- Emergency room visits increased 1.4%, driven by a 3.8% increase by Medicaid patients, though this was a lower rate than the increased enrollment.
- Outpatient visits declined 2.2% as commercially insured and Medicaid patients scheduled 5.6 and 5.3 million fewer outpatient procedures, respectively.

Chart notes:

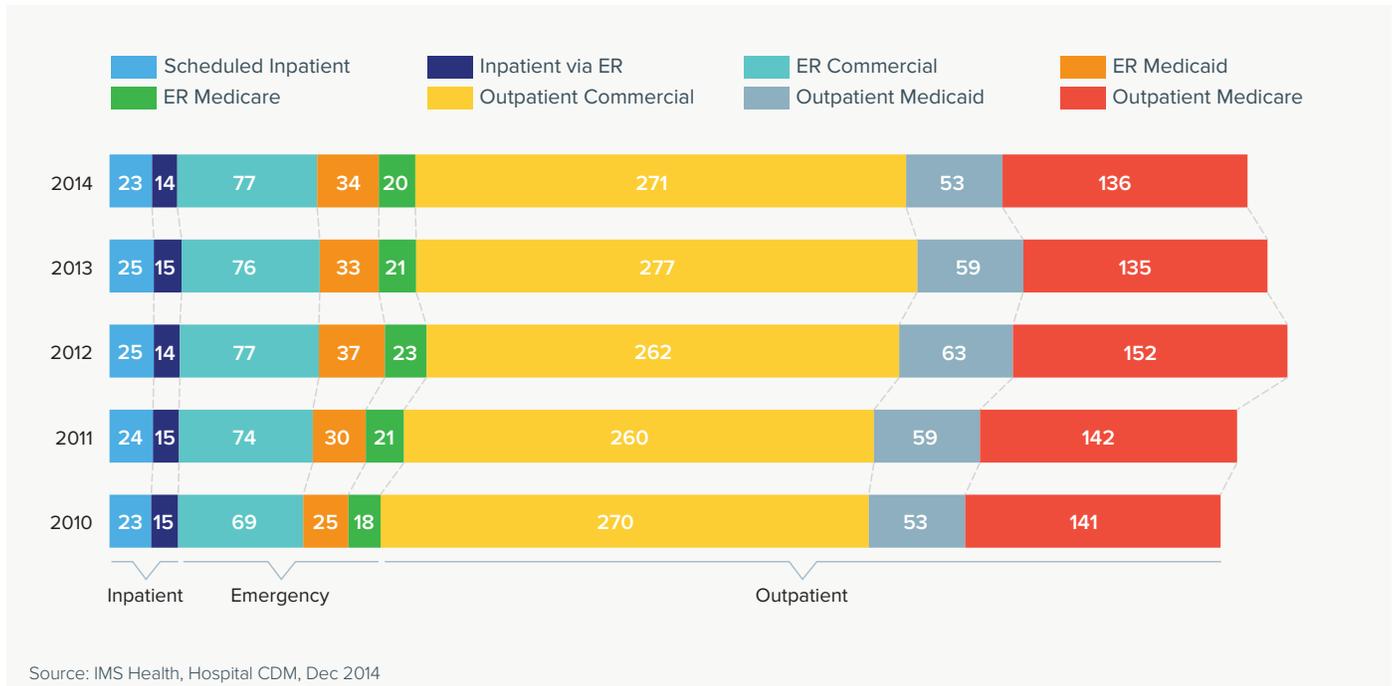
Patient visits projected from a survey of office-based physicians.

ER (emergency room) includes patients who visit the ER and are released without being admitted.

IMS Charge Data Master includes hospital-based admissions based on a sample of private hospitals. Outpatient admissions represent outpatient services provided by a wholly-owned hospital facility, and do not include standalone infusion centers or cancer centers.

Hospital utilization declined as the commercially insured and Medicaid patients scheduled fewer outpatient procedures

Trends in Hospital Admissions by Pay Type (Mn)



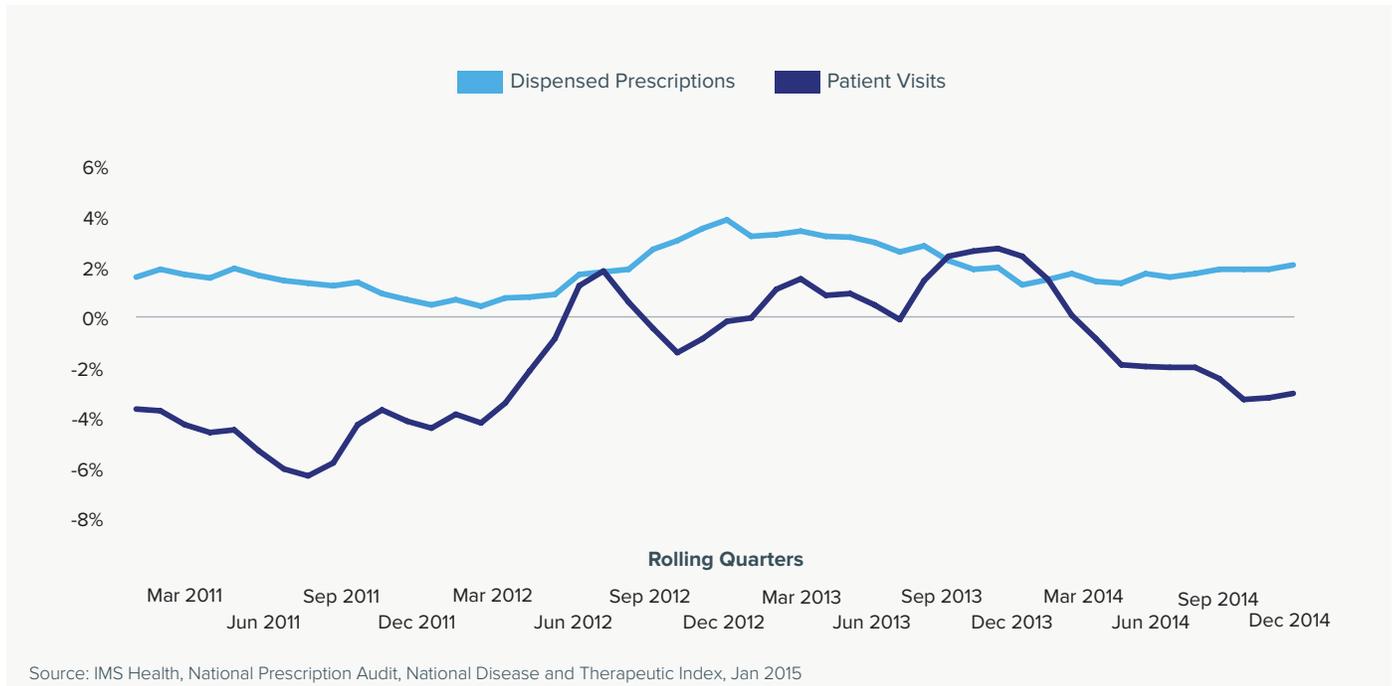
- Americans made 629 million hospital visits in 2014, a decline of 1.7%.
- The decline included 10.3 million fewer outpatient visits, 2.5 million fewer inpatient visits, and 1.8 million more emergency room visits in 2014.
- All aspects of hospital utilization declined except for outpatient Medicare visits, and emergency room visits by commercially and Medicaid insured patients, each increasing by 1 million and offset by declines in other types of usage for those patient groups.
- ACA provisions to encourage coordinated care, prevent hospital readmissions and avoidable complications may have influenced the reduction in usage in some cases.
- Rising use of ER services by Medicaid and commercially insured patients was relatively modest in 2014, but represents the kind of health system usage that reforms have been intended to discourage.

Chart notes:

Scheduled inpatients are those patients who are admitted as inpatients not via the ER. Inpatient via ER are patients who are admitted as inpatients after first visiting the emergency department during the episode of care. Emergency admissions where the episode of care does not result in an inpatient admission can also be called day-patients. Outpatient treatments in hospitals can include patients treated by physicians in clinics or practices owned or operated by hospitals, or day-surgeries. All such determinations are based on the type of reimbursement submitted by the hospital to the relevant insurers.

Office visits declined 3.0% and dispensed prescriptions increased 2.1% in 2014

Patient Office Visits and Prescription Growth (%)



- Prescription growth has remained relatively stable over the last several years but office visits have demonstrated greater volatility.
- Trends in office visits are, in part, linked to prescription trends and visits can be seen as an influence on future prescription trends.
- The relationship between office visits and prescription demand is substantially lagged and distorted, perhaps in recent periods by the large group of newly insured patients with substantial disease burdens entering the health system.

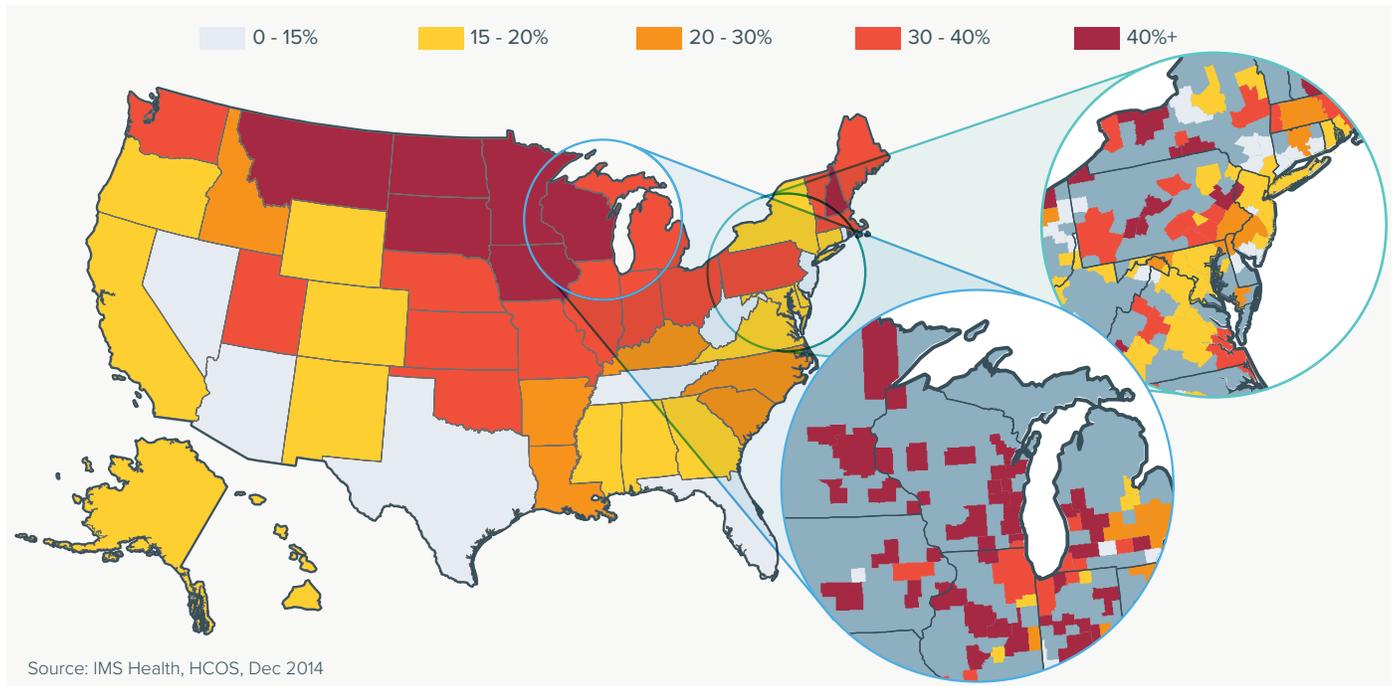
Chart notes:

Patient visits projected from a survey of office-based physicians. Some states allowed newly enrolled Medicaid patients to begin using coverage immediately instead of waiting until January 1st 2014.

Analysis reported on a rolling quarterly basis to remove monthly prescribing-day volatility.

Integrated health networks are associated with the majority of prescriptions in some geographies while others remain highly fragmented

Integrated Delivery Network Concentration by State and Metropolitan Area



- Integrated health systems have grown dramatically over the past decade and they now own or are affiliated with 80% of hospitals nationally, own or control 60% of group practices, have affiliations with 70% of doctors and directly employ half of all doctors.
- In 2010 there were approximately 750 IDNs nationally, up from 300+ in 2004, and continuing to grow to over 1,000 in 2014.
- Despite this growth, the U.S. health system remains highly fragmented with almost 75% of prescriptions written by providers not part of an integrated health system.
- The number of unaffiliated prescribers is higher in many urban areas where residents often have the highest burden of disease and the lowest access to coordinated care.
- The Northern Midwest has the most integrated healthcare in the country, while major urban centers like New York are highly fragmented.

Chart notes:

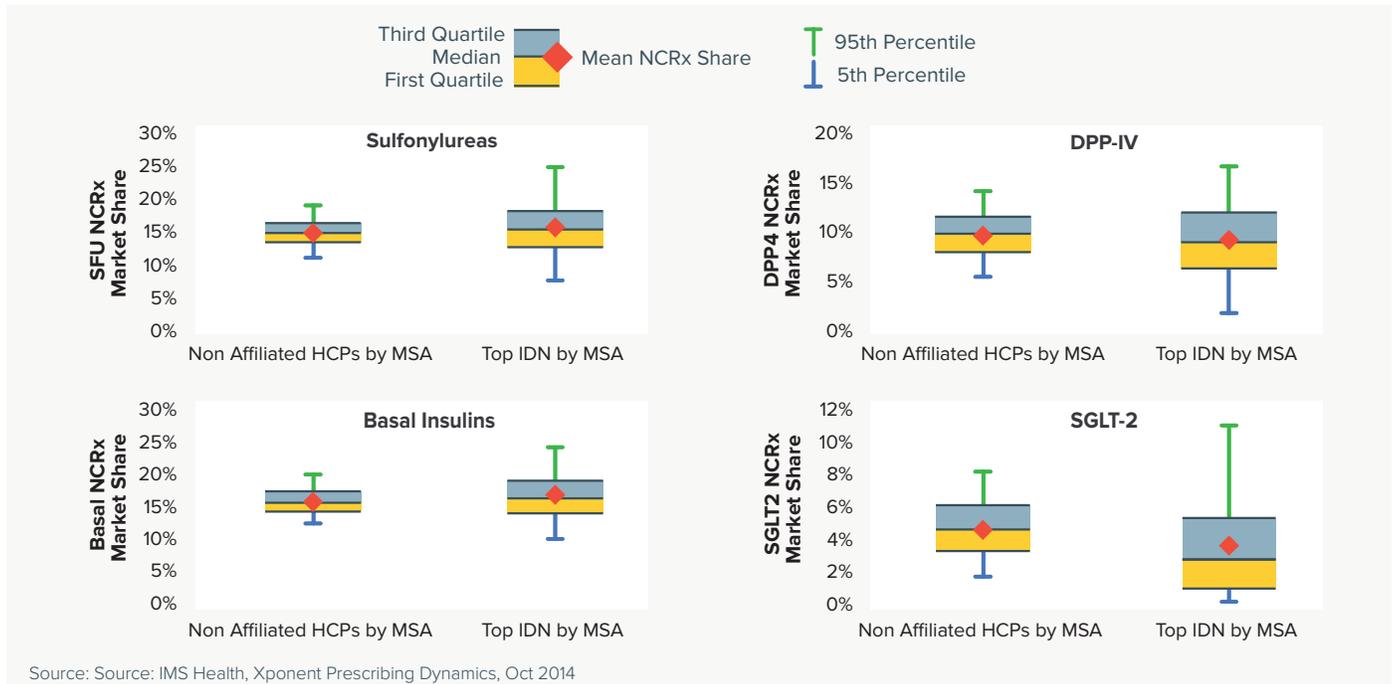
The map colors represent the percentage of dispensed prescriptions by doctors affiliated with Integrated Delivery Networks either at a state or metropolitan area in 2014. Gray areas indicate non-metropolitan areas, which are included in state averages.

Maps represent the concentration of diabetes treatments only.

An integrated healthcare delivery network (IDN) is a healthcare organization that has direct responsibility for centralizing the purchasing or contracting of its affiliated hospitals and ancillary-care facilities; it also offers a continuum of care through services at acute and non-acute sites.

Uniform treatment protocols are followed within networks but vary widely across networks

IDN vs. Non-IDN Class Utilization



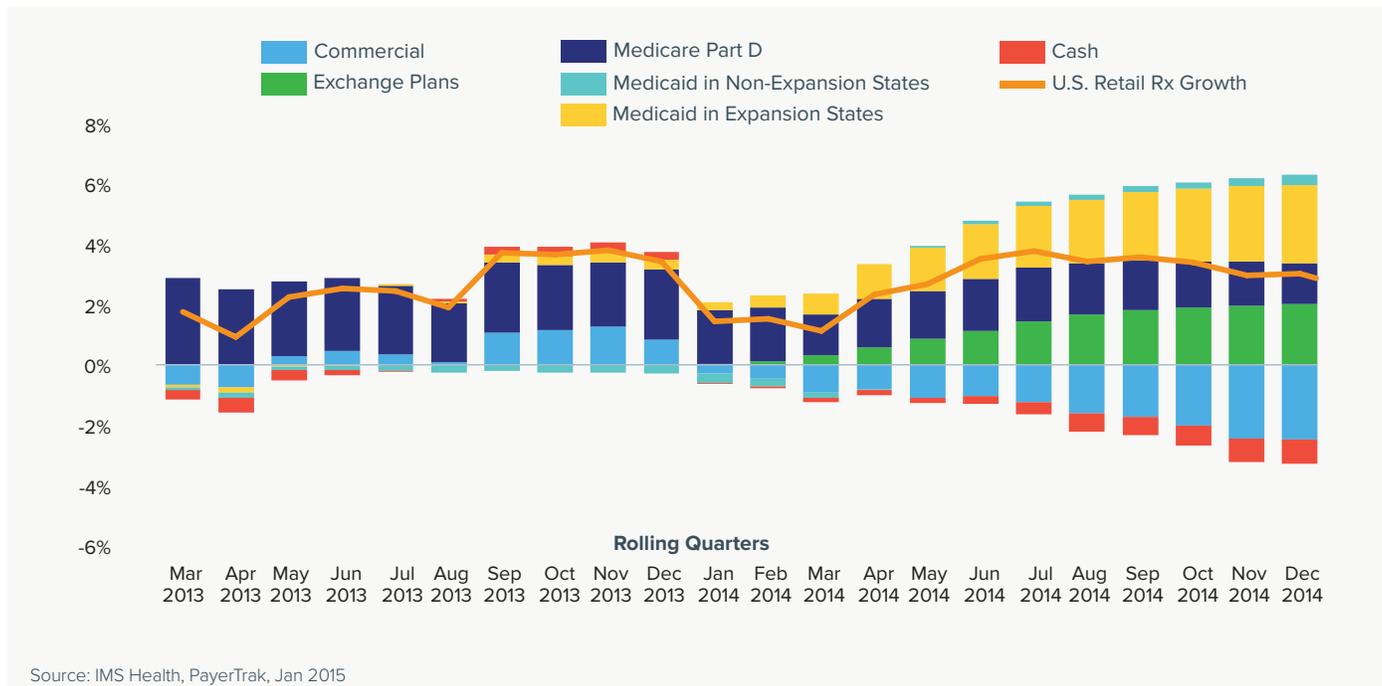
- Integrated Health Delivery Networks (IDNs) standardize protocols, resulting in lower variability in treatment within that network for similar patients and improving outcomes.
- This analysis specifically compares IDNs to each other within specific metropolitan areas and identifies variations at a macro-level view of IDNs approach to diabetes treatment.
- There is substantially more variability in prescribing patterns in diabetes between IDNs than there is in unaffiliated physicians in the same geographies, and those differences have important implications for the treatments a patient is likely to receive.
- In general, IDNs skew to using older diabetes medicines more often than non-affiliated providers, but there are substantial variations across IDNs with some choosing to focus on immediate management of proxy measures like blood sugar control while some prefer newer treatments.

Chart notes:

The chart shows the mean, first quartile, median, third quartile, and the high and low lines represent the 5th and 95th percentile of prescribing activity in non-affiliated prescribers and IDNs by MSA nationally. Metrics compare MSAs to each other, comparing either non-affiliated prescribers or top IDNs from MSAs. Top IDN in an MSA includes IDNs which form part of the top 80% of the IDNs in the MSA, thus excluding the bottom 20% of IDNs in each MSA. New to Class Rx (NCRx) share represents the sub-class share of prescriptions for patients new to any therapy in the broader diabetes class.

Medicaid was the leading driver of retail prescription growth in the first year of expanded coverage under the Affordable Care Act

Contribution to Retail Prescription Growth (%)



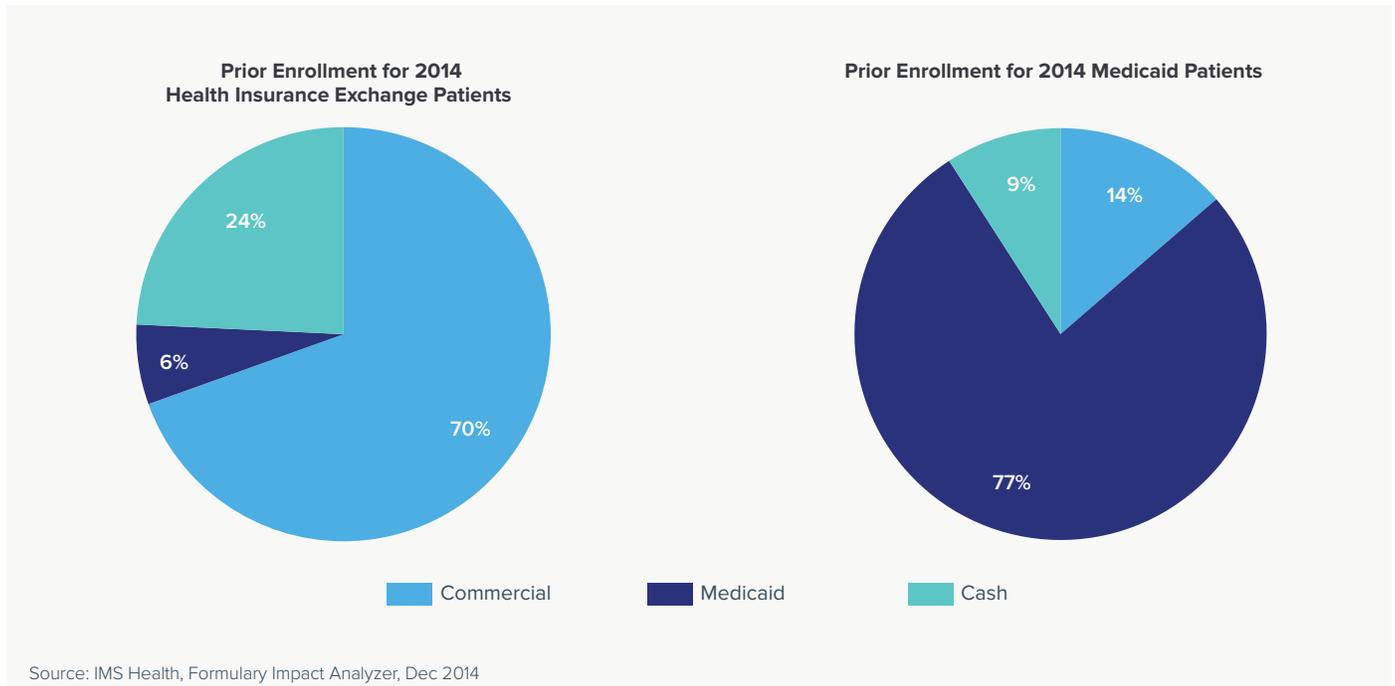
- Retail prescriptions rose 2.4% in 2014, the first year of major coverage expansion.
- Overall Medicaid prescriptions increased 16.8% in 2014, accounting for 70% of the growth in retail prescription demand.
- Medicaid prescriptions increased 25.4% in states that expanded Medicaid coverage, and 2.8% in states that did not expand Medicaid coverage.
- Cash prescriptions, typically filled by uninsured patients, declined 5.5%.
- An estimated 12.6 million prescriptions were filled through exchange plans in 2014.
- The commercially insured, including patients who purchased coverage on the exchanges, filled 8.4 million fewer scripts in retail pharmacies in 2014 than in 2013.
- Prescription demand dipped in the first quarter of 2014 as plan cancellations and website glitches plagued the autumn enrollment period.
- Seniors with coverage through Medicare Part D filled almost 1 billion prescriptions in retail pharmacies in 2014.

Chart notes:

Retail prescriptions only. Medicaid includes fee for service and Managed Medicaid. Growth represents three-month rolling average. The Medicaid expansion category includes 27 states and the District of Columbia. Estimates of retail prescriptions filled by patients with exchange plans is based on IMS Health’s analysis of commercial plan names.

Nearly a quarter of exchange plan patients and 9% of Medicaid patients may have been previously uninsured

Prior Enrollment of Patients Filling Prescriptions in 2014



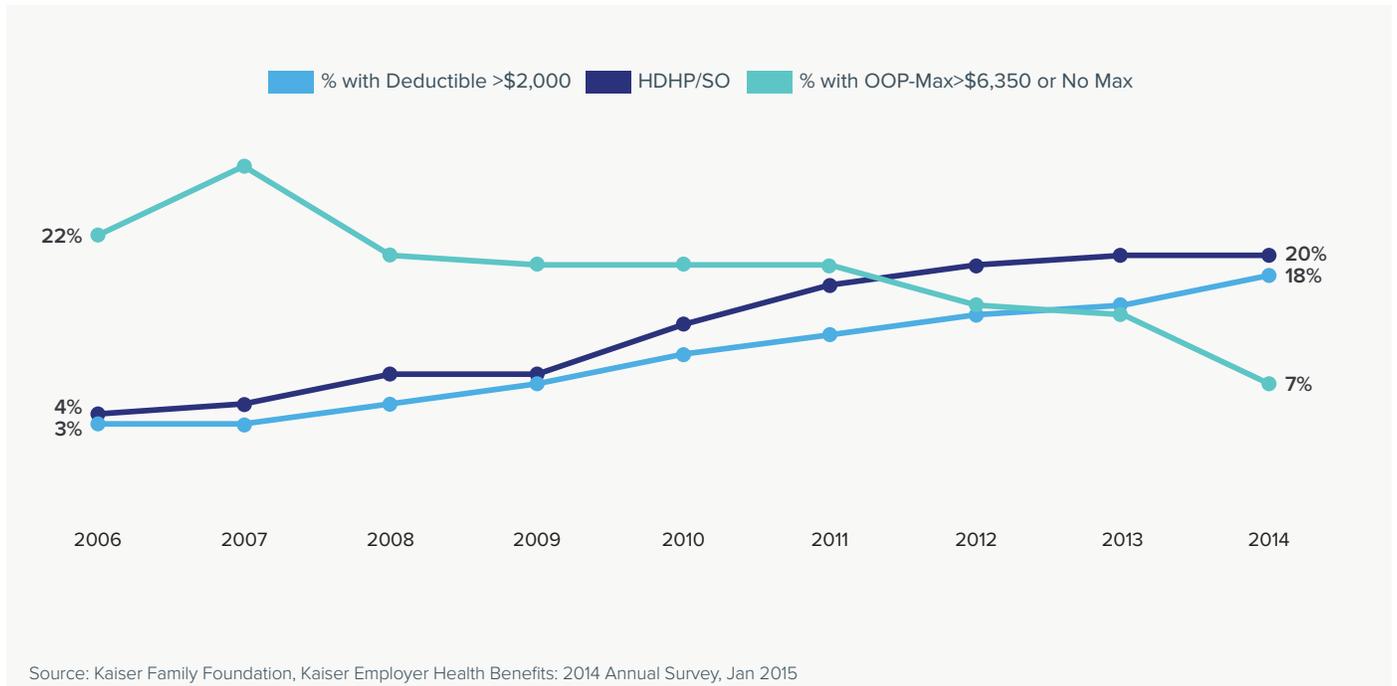
- Almost a quarter of patients with coverage through the newly formed Health Insurance Exchanges who filled prescriptions in 2014 may have been uninsured in 2013.
- Fourteen percent of Medicaid patients were previously covered by commercial plans, another 9% paid for prescriptions in cash.
- Although Medicaid expansion increased enrollment by 10–15% in 2014, nearly a quarter of Medicaid prescriptions were filled by newly enrolled patients, suggesting that many of them were carrying significantly higher disease burdens than existing patients.

Chart notes:

Patients were selected by having a mode payer in 2014 that is either a Health Exchange or Medicaid plan. The 2013 mode payer for these patients is supplied as their prior enrollment. Patients that had no claims, and no reliable indication of the type of insurance coverage they had in 2013 were excluded from the analysis (38% of 2014 HIX prescriptions, 34% of 2014 Medicaid prescriptions).

Insurance coverage has been shifting to higher deductibles and to capping out-of-pocket costs over the past decade

Percentage of Employer-Based Insurance 2006–2014

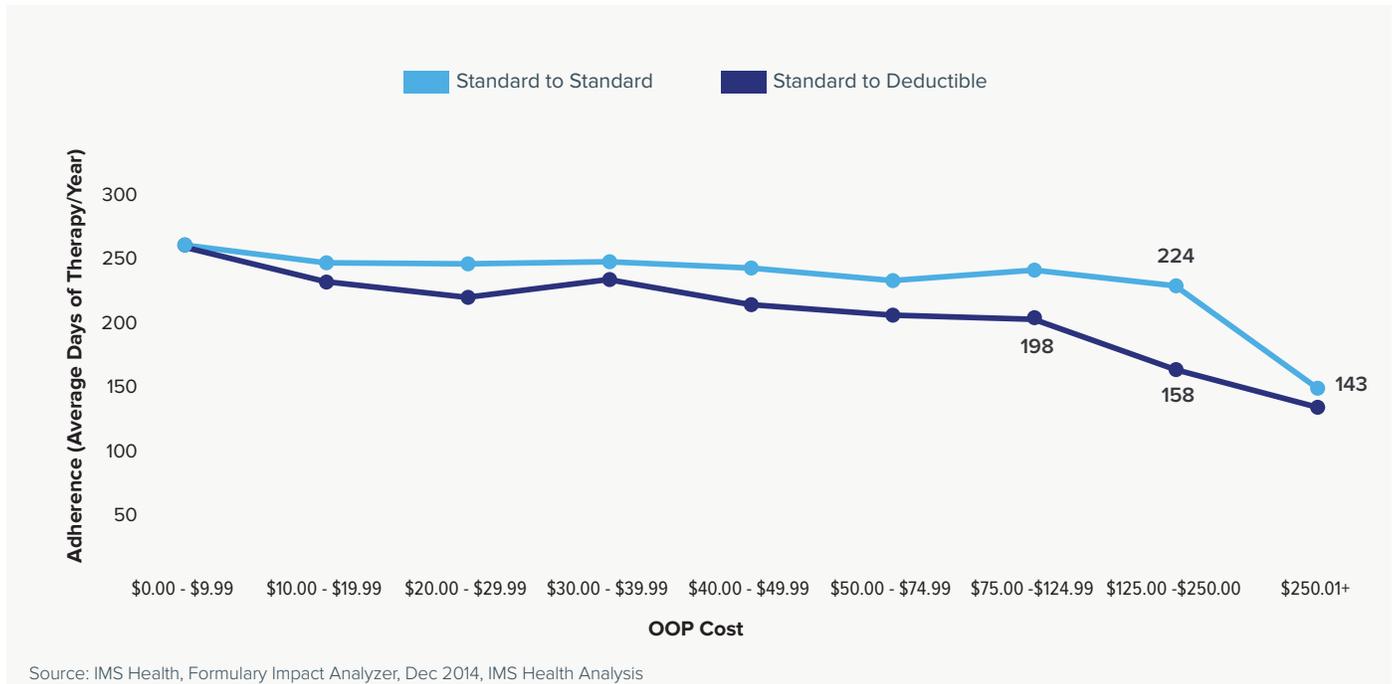


- Twenty percent of employees have a health plan with a high deductible.
- High deductibles have become a more common feature of insurance plans, but 93% of employer-sponsored plans have an annual out-of-pocket maximum expenditure \$6,350 or lower.
- The 7% of employees without an annual out-of-pocket maximum are potentially exposed to very high costs.

Chart notes:
HDHP/SO High deductible health plan with a savings option; OOP out-of-pocket maximum.

Deductibles have had a proven negative effect on patient adherence particularly when out-of-pocket costs are over \$125 per prescription

Average Continuing Adherence for Patients Changing Insurance Type (DPP-IVs)



- Patient exposure to cost pressures is a key factor potentially impacting patient adherence to planned treatments.
- Patients who have started treatment can be said to have passed a hurdle and are understood to be less likely to be non-adherent than new patients.
- Patients also demonstrate cost sensitivity when switched from a standard plan to one with a deductible.
- Lower adherence is seen at every out-of-pocket level for patients with a deductible, worsening after costs exceed \$30, and most when costs exceed \$125.
- Standard insurance patients showed a substantial decline in adherence if their out-of-pocket cost exceeded \$250.
- Overall, patients who changed to a plan with a deductible averaged 25 fewer days of therapy than those with standard insurance.

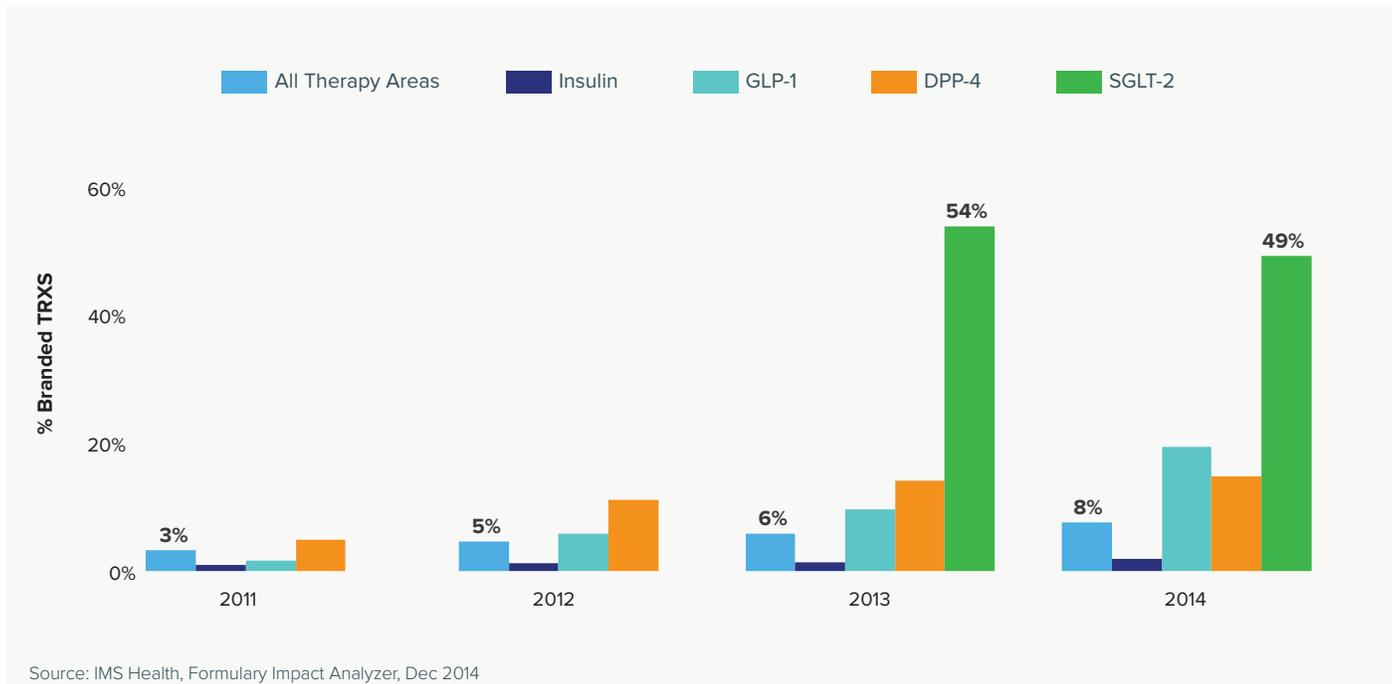
Chart notes:

A cohort of patients with traditional insurance in 2013 were tracked into 2014. One subset continued on traditional insurance with a deductible less than \$200/year, and another subset switched to an insurance plan with a deductible greater than \$200/year.

OOP cost is the mode out-of-pocket cost per patient for their DPP-IV (Dipeptidyl peptidase-4) diabetes medicines.

Coupons offset costs for some patients and are widely used in some classes of medicines

Brand Co-Pay Card Penetration for Commercial Claims by Year



- The overall number of prescriptions where patients used a co-pay card have now reached 8% of all branded prescriptions.
- Diabetes includes both very low coupon usage for insulins and very high usage for the newest class of diabetes drugs, SGLT-2s.
- Manufacturers commonly provide coupons when their brand is not covered on a formulary.
- Increasingly, coupons are being used around the launch of an innovative brand to eliminate barriers for patients considering new medicines.
- Some specialty classes such as multiple sclerosis and rheumatoid arthritis have 70% usage of coupons with terms that reduce out-of-pocket spend to nominal levels such as \$5.

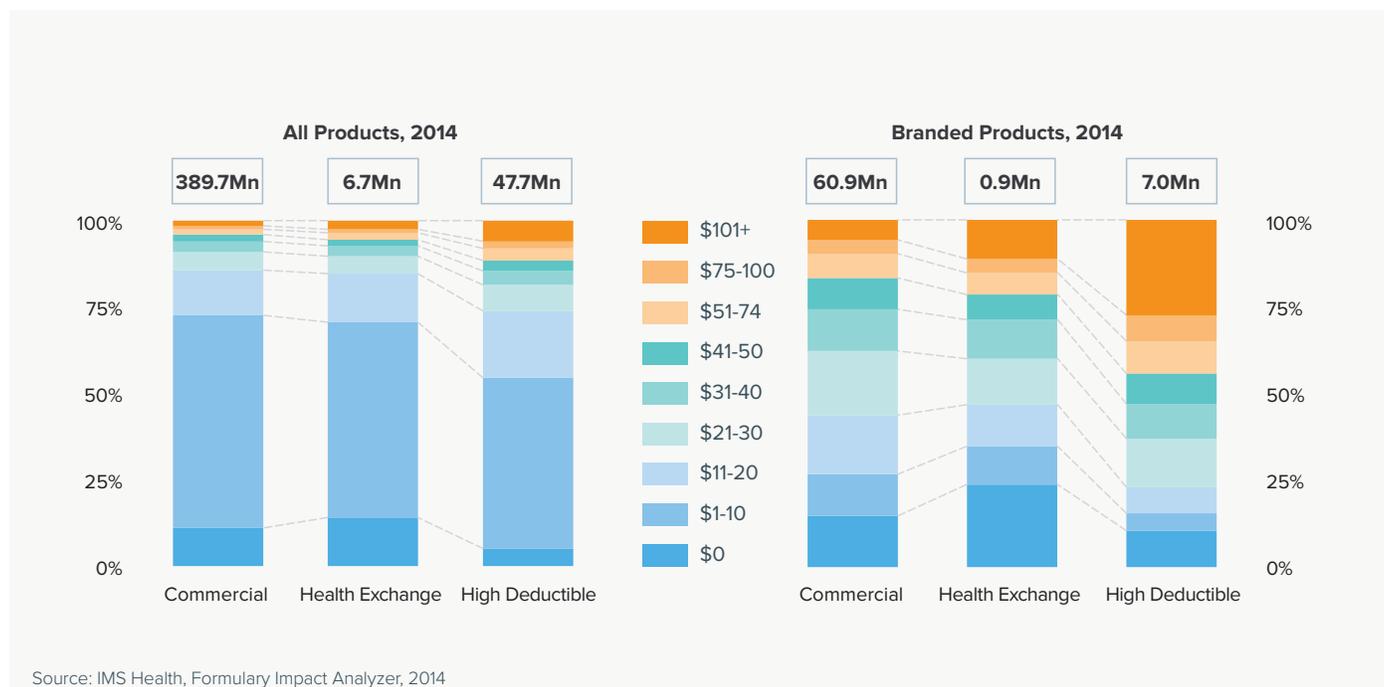
Chart notes:

GLP-1: Glucagon-like peptide-1; SGLT-2: Sodium-glucose linked transporter; DPP-IV: Dipeptidyl peptidase-4.

Claims where a known coupon program/vendor is the primary or secondary payer are counted as co-pay card redemptions. Coupons are identified using the IMS Health Model Type designation and Plan Names. Values for all therapy areas were calculated across all branded products in the data, including the diabetes markets that are also broken out by sub-class.

Co-pay distribution in insurance plans differs dramatically by type of insurance

Distribution of Commercial Prescriptions by Plan Type and Cost Sharing



- Health Insurance Exchange plans (HIX) have been associated with high out-of-pocket costs for the consumers, but almost 25% of branded claims in HIX plans have a co-pay of \$0, and only 2% of all claims in HIX are over \$100.
- Different cost-sharing designs of HIX plans mean that some patients with subsidies have reduced their out-of-pocket exposure, often to less than \$50.
- Nearly 80% of branded claims across all insurance types have out-of-pocket costs less than \$50.
- High deductible and HIX patients have more claims over \$100 than those with traditional employer insurance.
- Over 10% of all prescriptions had zero out-of-pocket costs, either as a result of ACA preventive care provisions, having reached a deductible or as a result of the HIX income-based subsidies.

Chart notes:

HIX – Health Insurance Exchange plans are identified as having a majority portion of claims within a HIX plan.

HDHP – High Deductible plans are identified by observed change over time from deductibles to co-pays/co-insurance and eventually zero out-of-pocket for patients in the same plan.

Commercial insurance excludes HIX and HDHP and are characterized by costs that are consistently co-pay/coinsurance

Out-of-pocket costs include co-pay offsets through coupons.

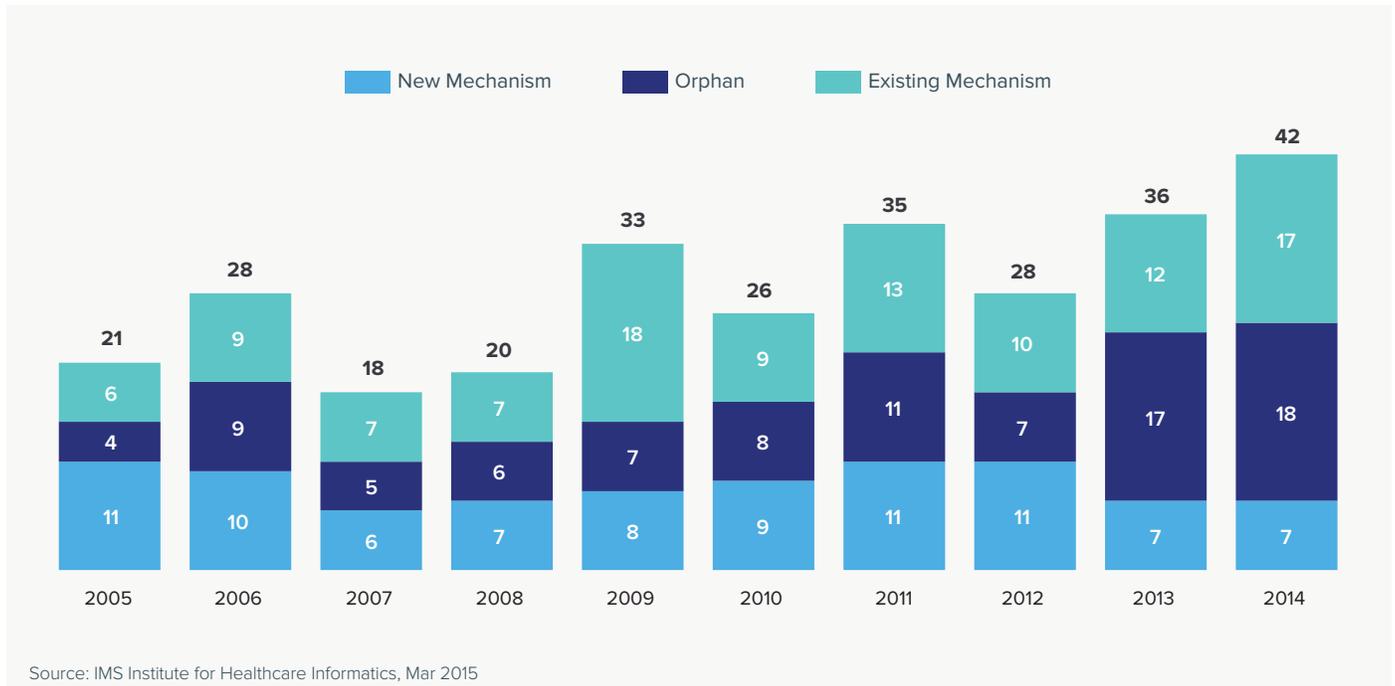
Transformations in disease treatment

More new medicines were launched in 2014 than in any year since 2001 and included 23 breakthrough therapies and orphan drugs.

- There were 42 New Active Substance (NAS) launches in 2014, the most since 2001 when there were 47 launched.
- Manufacturers have shifted their R&D priorities over the past decade to focus increasingly on specialty drugs, driving specialty sales to 33% of medicine spending in 2014 compared to 19% in 2004.
- More than half of new drugs in 2014 were orphan or other specialty drugs; others include new treatment options for type 2 diabetics and the first diagnostic for Alzheimer's disease.
- In the last five years, 61 orphan drugs were launched, the largest number in any five-year period since the passage of the Orphan Drug Act in 1983.
- Of the 29 new non-NAS 2014 launches, a third were medicines with easier dosing, including the first non-biologic single injection for osteoarthritis, once-daily formulations of diabetes drugs, an inhalable antipsychotic, and three new immunotherapeutic allergy products which can be taken at home rather than in a doctor's office.
- Notable clusters of innovation in 2014 included Breakthrough designated products launched, including the first Breakthrough biologic; an infectious disease cluster spurred by an FDA incentive program; and two major oncologic immunotherapy advances.
- Aided by expedited approval pathways and FDA incentive programs for rare and infectious diseases, a robust late-phase pipeline with more than 530 distinct research programs is expected to maintain the high number of launches seen in the past five years into the future.
- The first applications for biosimilars were submitted to the FDA in 2014 and are expected to make new options available to patients.

The 42 innovative products launched in 2014 is the most since 2001

New Active Substances (NAS) launched in the U.S. 2005-2014



- Forty-two NASs were launched in 2014, 25 of which had new mechanisms or orphan indications.
- For a second year in a row, launches were strengthened by the highest number of orphan launches on record.
- In the last five years, 61 orphan drugs were launched, including 18 in 2014, compared with 31 total from 2005 to 2009.
- Six of the nine NAS drugs receiving Breakthrough Therapy Designations were orphans, emphasizing a push towards making life-saving treatments quickly available to patients where treatment may not exist.

Chart notes:

New Active Substance (NAS): A new molecular or biologic entity or combination where at least one element is new. NAS launches in the U.S. by year of launch, regardless of timing of FDA approval.

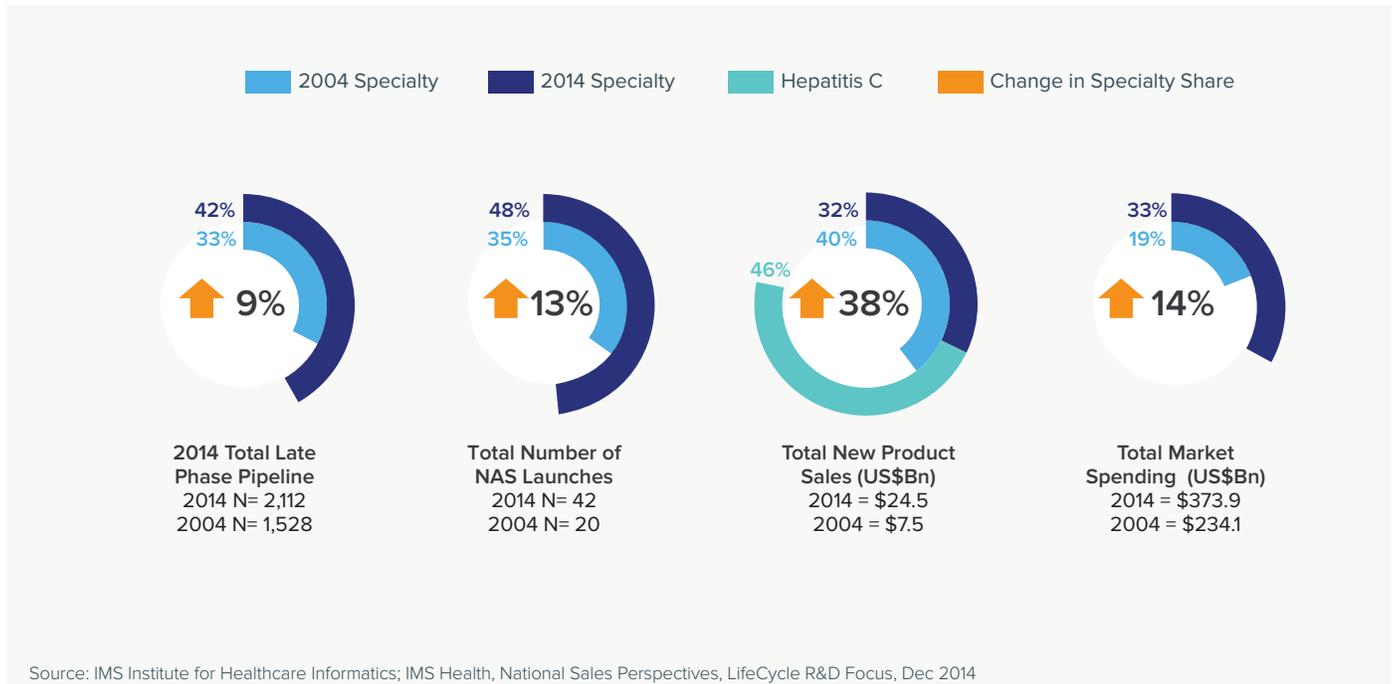
New mechanism: First product with a new mechanism of action for its FDA approved indication.

Existing mechanism: Subsequent products with an existing mechanism of action for an indication.

Orphan: Drugs with one or more orphan indications approved by FDA at launch.

Increasing numbers of launches and growth in spending on specialty products in 2014 were driven by growing R&D focus on specialty medicines over the past decade

Specialty Share of Pipeline, Launches, New Product Sales, and Total Market



- The specialty products share of the R&D pipeline has increased 9% in the past decade, driven by drugs targeting cancer, nervous system disorders, infectious diseases, diabetes and respiratory disorders.
- While the share of specialty launches has only minimally increased in the past 10 years, the total number has doubled from 7 in 2004 to 20 specialty drugs launched in 2014.
- New product spending has increasingly come from specialty products and 2014 included the extraordinary level of increased spending on hepatitis C products, which accounted for \$11.3Bn (46%) of the \$24.5Bn in new product sales.
- The share of spending for specialty drugs has increased dramatically over the past decade and they now account for a third of medicine spending, a trend expected to continue as 42% of the late-stage pipeline are specialty drugs.

Chart notes:

Late phase pipeline is defined as active programs (activity in past 3 years) in Phase II through Registered.

New Products are defined as New Active Substances (NASs) launched in the specified year.

New Products Sales are defined as brands launched in the prior 24 months including products which are NASs, as well as other branded medicines. Total Market Spending is defined as the total U.S. market in the specified year. Specialty therapies are defined by IMS Health as products that are often injectable, high-cost, biologic or requiring cold-chain distribution. They are mostly used by specialists, and include treatment for cancer and other serious chronic conditions, and often involve complex patient follow-up and monitoring.

There were a wide range of new launches for larger disease populations, offering efficacy improvements or easier dosing

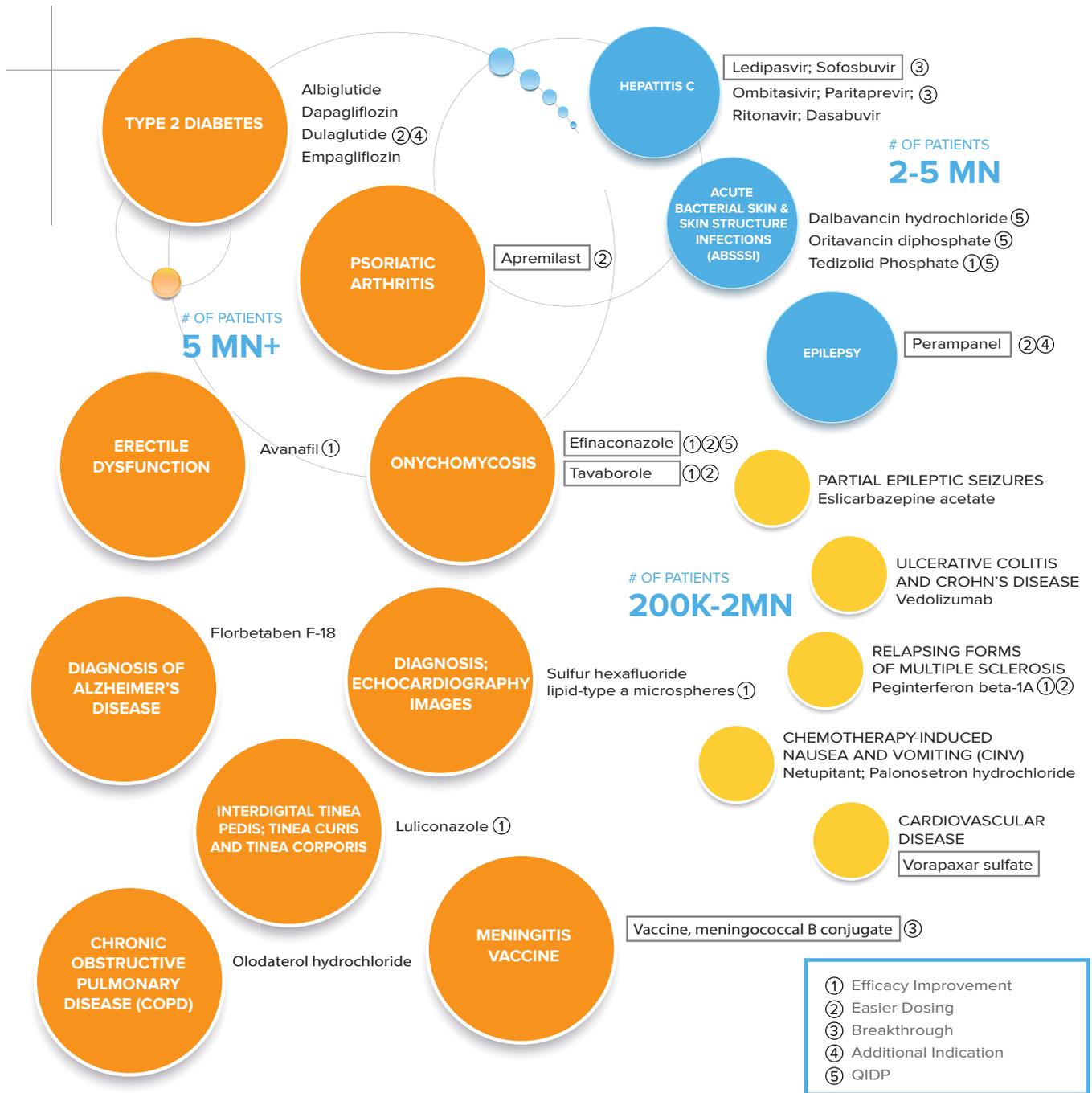


Chart notes:
See next page.

Eighteen orphan drugs launched in 2014, including nine treatments for diseases afflicting fewer than 10,000 patients

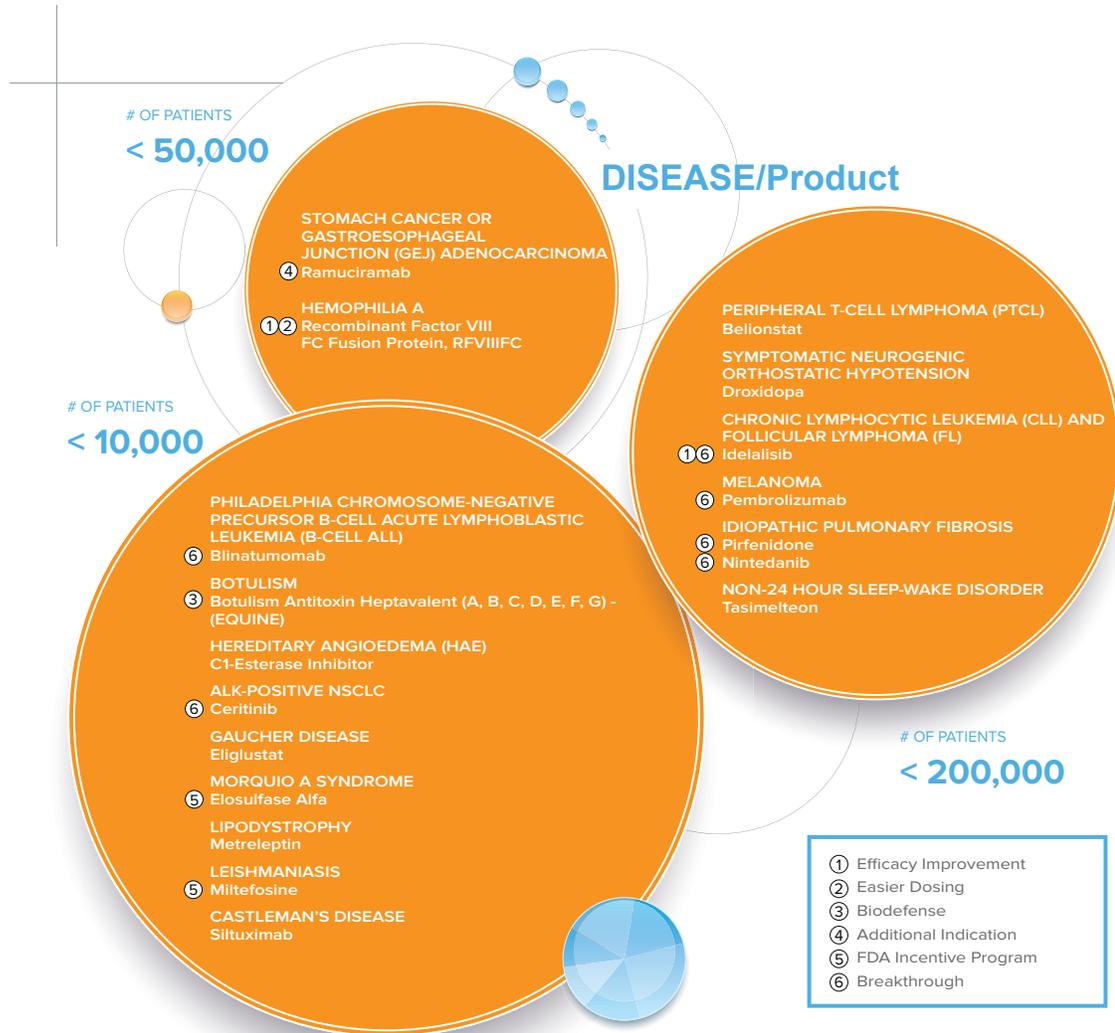


Chart notes:

Patient population estimates based on published literature and intended to represent the total disease population for which the medicine is indicated.

FDA Orphan drug designations are granted for major improvements for patient populations under 200,000.

Breakthrough represents drugs which received the FDA's Breakthrough Therapy Designation for demonstrating through preliminary clinical evidence that the drug may offer substantial improvement in safety or effectiveness in the treatment of a serious condition.

FDA incentive programs:

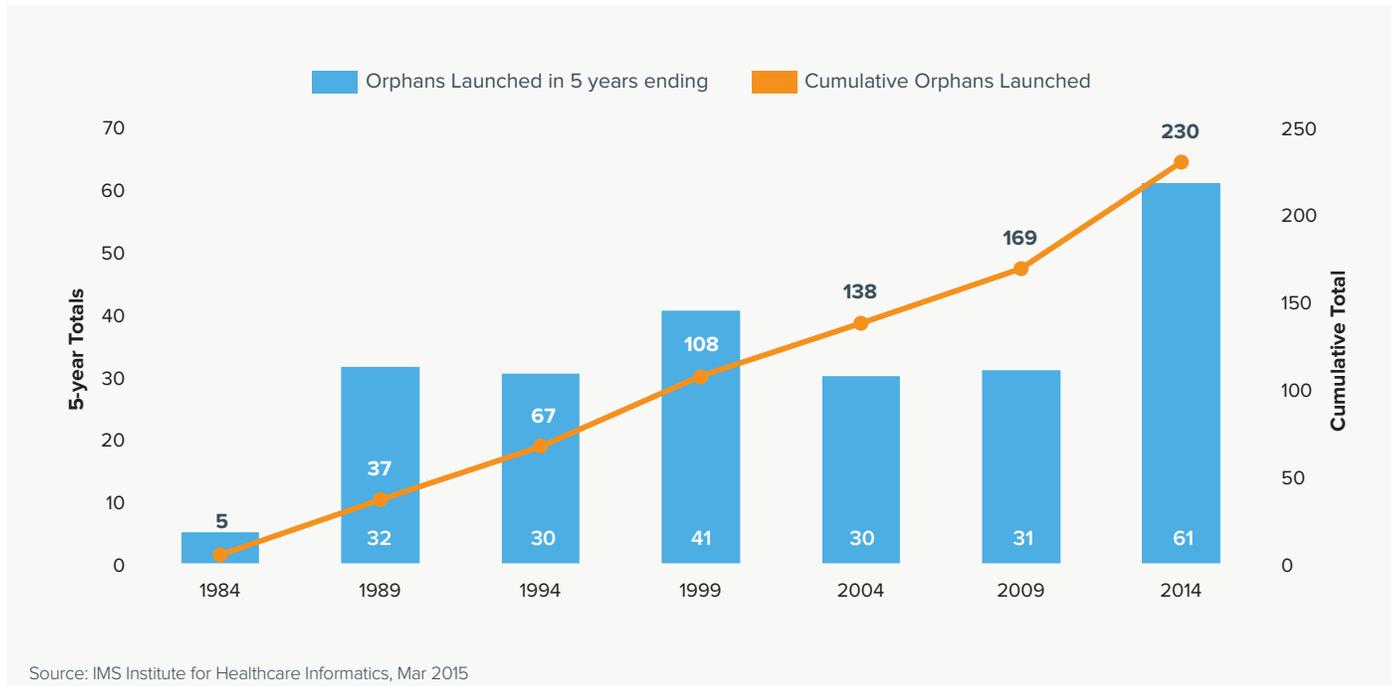
Qualified Infectious Disease Program (QIDP) (efinaconazole, dalbavancin hydrochloride, oritavancin diphosphate, tedizolid phosphate);

Neglected Tropical Diseases Program (miltefosine);

Rare Pediatric Disease Priority Review Voucher (elosulfase alfa).

The total number of orphan drugs launched since 1983 reached 230 in 2014

Number of Orphan Drugs Launched in the U.S. 1983-2014



- More new orphan drugs launched in the last five years than in any other 5-year period since the passage of the Orphan Drug Act in 1983.
- More than half (35) of the 61 orphan drugs launched in the last five years were launched in the last two years.
- Orphan drugs are increasingly focused on even smaller populations, with over 40% of orphans launched in the last 2 years treating fewer than 10,000 patients.
- Ten first-in-class products launched in 2014 had orphan designations and were evenly split between the ultra-orphan (fewer than 10,000 patients) and the larger population orphan drugs treating 50,000 to 200,000 patients.
- Treatments for rare cancers are the most common orphan drugs accounting for 27 of the 61 products launched over the past 5 years.
- The rarest conditions that are now able to be treated include homozygous familial hypercholesterolemia (HoFH), idiopathic pulmonary arterial hypertension (PAH), Gaucher’s disease, and multiple hemophilias all with fewer than 10,000 patients.

Chart notes:

Orphans: Drugs with one or more orphan indications approved by FDA at launch.

Population estimates for orphans are derived from Institute research, the composite of consensus incidence/prevalence, from the FDA, developer, or main disease advocacy group.

There were 29 new brands based on existing medicines which brought easier dosing to a variety of treatments

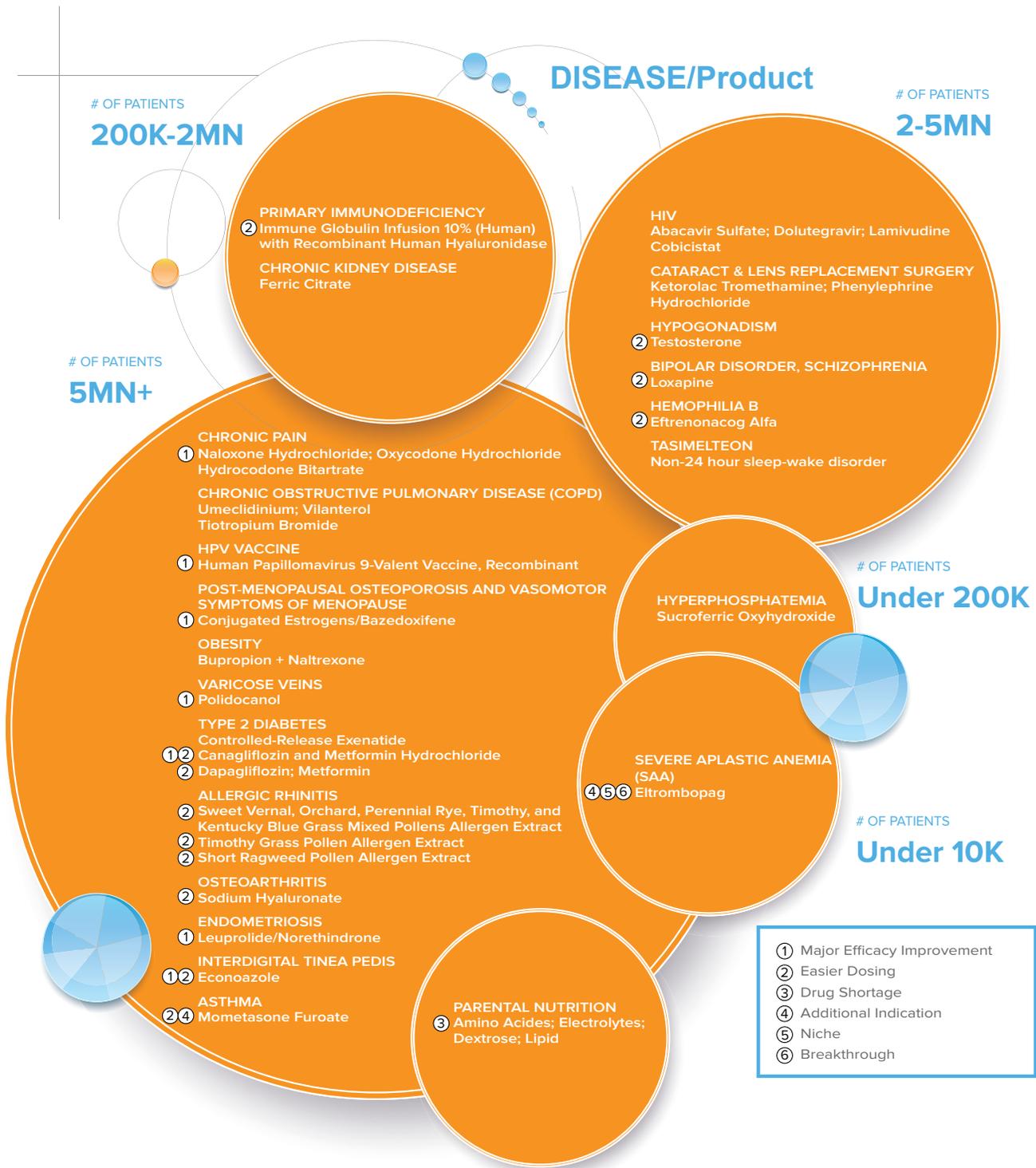


Chart notes:

Patient population estimates based on published literature and intended to represent the total disease population for which the medicine is indicated.

Medicines Use and Spending Shifts. Report by the IMS Institute for Healthcare Informatics.

FDA incentive programs were successful at driving development of treatments targeting high-need populations

Notable Aspects in R&D in 2014

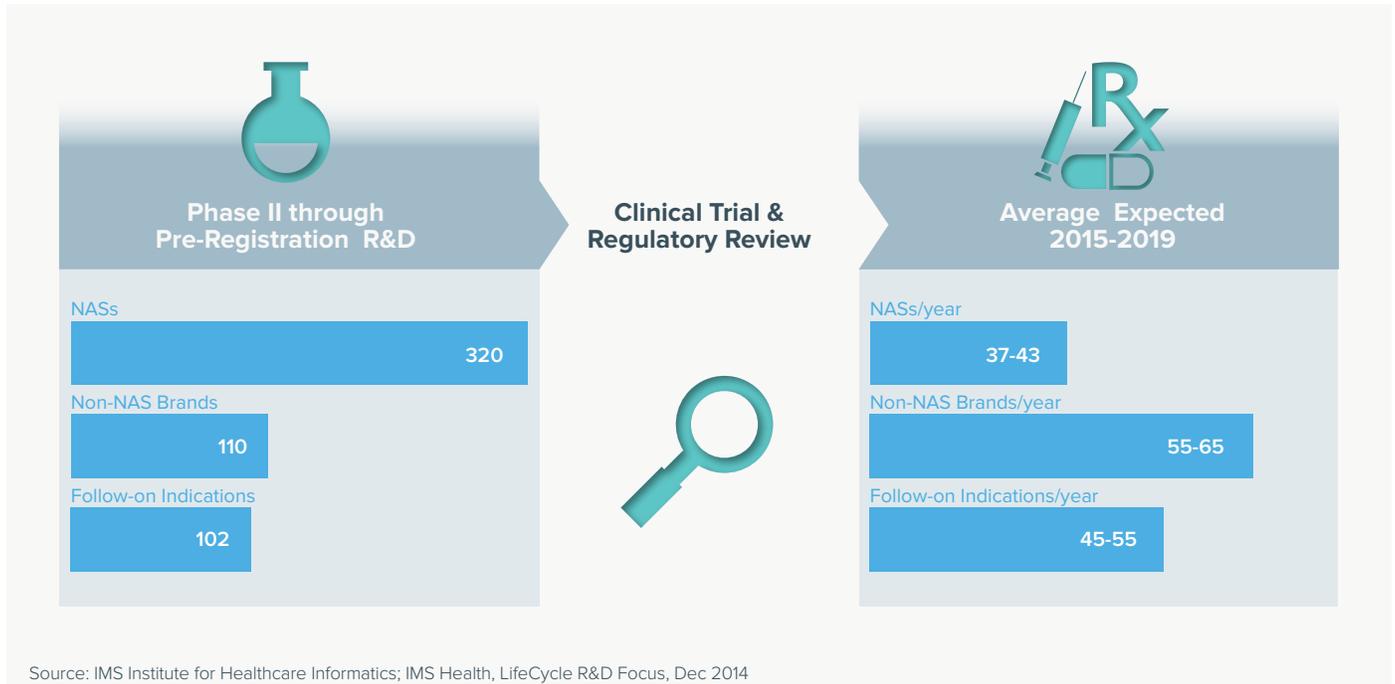
Breakthrough Therapies: In 2014, over 40 Breakthrough Therapy Designations were approved and ten drugs with the designation were launched, making lifesaving drugs quickly available to the most vulnerable patient populations. Seven of the ten were orphan drugs, and the non-orphan drugs (meningitis vaccine, hepatitis C) serve large populations and provide cures for potentially fatal diseases. Drugs deemed breakthroughs are often launched within a month of approval to provide new therapies to patient populations as quickly as possible. The number of Breakthroughs is expected to continue to increase in the next year, based on the 22% increase in the number of designation requests by sponsors. Greater numbers of both original and supplemental applications will be approved in 2015 than in the early years of the program.

Infectious and Neglected Diseases: Few antibacterial products have been developed in recent years, but following new incentive programs, five new products were launched in 2014, four receiving Qualified Infectious Disease Program (QIDP) designation. As a part of the Generating Antibiotic Incentives Now (GAIN) Act of 2012, QIDP seeks to address the issue of antimicrobial-resistance by providing incentives for new infectious disease treatments. Three of the QIDP drugs target acute bacterial skin and skin structure infections (ABSSSI), while the other products target fungal infections. Also launched was a treatment for the rare tropical disease leishmaniasis, through the Tropical Disease Priority Review Voucher program. Ranking among the top 5 drug classes in clinical trials, antibacterials and antibiotics will provide more options to combat antimicrobial-resistant infections through development of drugs that target infectious and neglected diseases, making an impact nationally and globally.

Oncology Immunotherapy Advances: Two new therapies targeting T-cells were launched in 2014. The first PD-1 blocker, pembrolizumab (Keytruda), impedes the PD-1 pathway and allows T-cells to attack cancer cells. The first BiTE treatment – Bi-specific T-Cell Engager – blinatumumab (Blincyto) links T-cells with tumor cells, recruiting the immune system to destroy tumor cells. Pembrolizumab is approved for metastatic melanoma, and Blinatumumab is approved for Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukemia (Ph+ ALL). The approach of utilizing the host's own immune system to fight cancer demonstrates great potential for application to many other indications, as evidenced by a deep pipeline for these treatments.

New medicines will continue to emerge from a healthy late-stage pipeline, encouraged by new FDA incentives

Late Stage R&D Pipeline and Expected Launches by Product Type



- There are over 532 distinct research programs in late stage (phase II and greater) for the U.S. market, 60–65% of which will likely make it to market.
- Based on historic approval rates and time to launch, launch trajectory is expected to peak in the next 24 months and remain elevated through the next 5 years.
- The pipeline continues to be driven by innovation, supplemented by many new drug delivery methods and additional indications.
- Cancer, autoimmune and infectious disease indications lead the NAS group, specifically non-small cell lung cancer (12), rheumatoid arthritis, breast cancer and bacterial infection (9 each), followed by 8 more drugs in the hepatitis C cluster of innovation.
- Follow-on indications are also led by cancer with 49 (48%) follow-on indications in late stage pipeline, followed by autoimmune (11), cardiovascular (7) and respiratory (5) indications.
- FDA incentive programs such as Breakthrough Therapy designations and infectious disease programs enhance the pipeline, along with a slow and steady movement in the number of biosimilars coming to market.

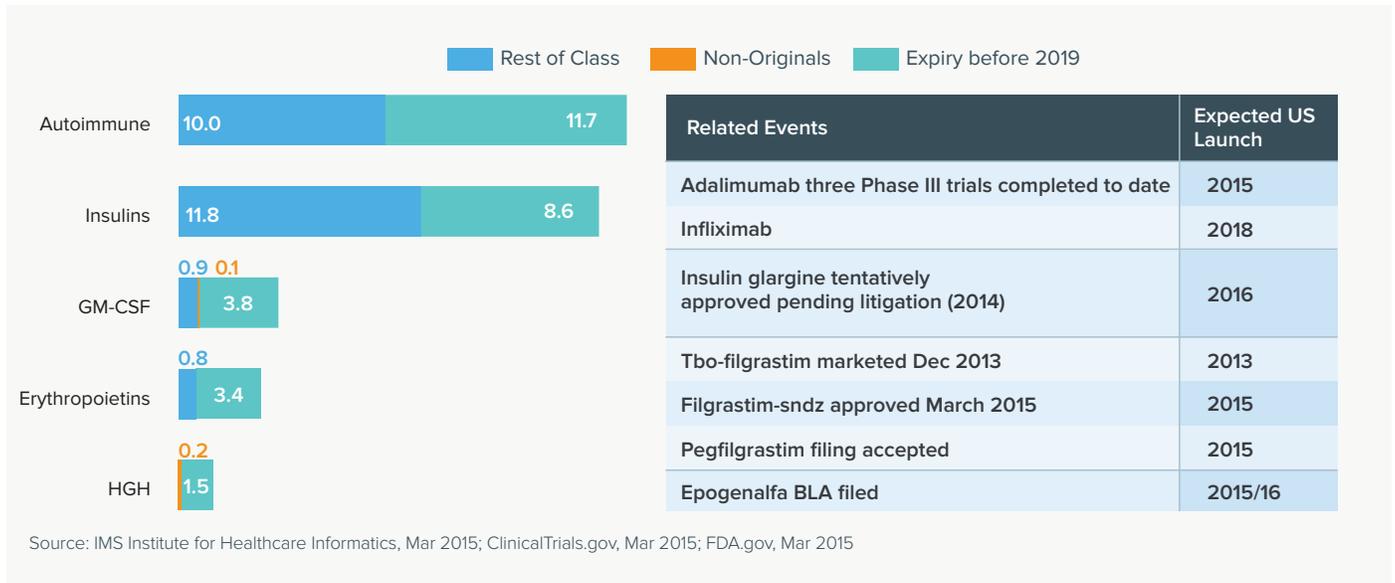
Chart notes:

New Active Substance (NAS): A new molecular or biologic entity or combination where at least one element is new. NAS launches in the U.S. by year of launch, regardless of timing of FDA approval. Non-NAS: Products that are drug delivery systems, line extensions, biosimilars, and other non-NAS products. Follow-on indications: Subsequent products with an existing approved and marketed mechanism of action.

Probability of success is derived from historic success rates applied to products in late-phase (Phase II, III, Pre-Registration), confirmed through time through phase analyses using IMS LifeCycle R&D Focus.

The first biosimilar applications were filed in 2014, five years after legislation created the biosimilar pathway

2014 Spending on Biologic Molecules in Classes with Current Non-Original Biologics and Upcoming Losses of Exclusivity (US\$Bn)



- The biosimilars pathway, established by the 2009 Biologics Price Competition and Innovation Act (BPCIA), matured in 2014 with the first applications and approvals through the pathway.
- Prior to the BPCIA pathway, only two non-original products were developed and approved in the U.S., Omnitrope (somatropin) via the 505(b)(2) pathway in 2006 and Granix (tbo-filgrastim) as an original biologic (BLA) in 2013.
- There are a number of non-original products in Phase III trials or pending with FDA including insulin glargine, pegfilgrastim (the longer acting form of filgrastim) and epoetin alfa, some of which will be filed via the biosimilar pathway, the 505(b)(2) pathway or as original biologics.
- The first non-original insulin glargine in the U.S. was approved in August 2014 via the 505(b)(2) pathway, as a tentative approval pending resolution of patent litigation which could delay launch until at least 2016.
- The first biosimilar of filgrastim, filgrastim-sndz, was approved in March 2015 through the BPCIA pathway by the FDA for the same indications as its reference product but was not deemed substitutable, which may limit its adoption by physicians.
- Epoetin alfa may also face non-original competition in the near future as the first BLA was submitted in late 2014 and other Phase III trials reached completion, but all of the applicants may face patent litigation that could delay their launches.

Chart notes:

GM-CSF: Granulocyte macrophage colony-stimulating factor incl. filgrastim, tbo-filgrastim, filgrastim-sndz. HGH: Human Growth Hormones, somatropin.

Section 505(b)(2) of the 1984 Hatch-Waxman Act allows sponsors to obtain approval of NDAs containing investigations of safety and effectiveness that were not conducted by or for the applicant, but for which the FDA has issued an approval.

Notes on Sources

This report is based on the IMS Health services detailed below. Analyses exclude OTC products and focus on prescription-bound products (including insulins which are available without prescription). Spending is reported at wholesaler invoice prices and does not reflect off-invoice discounts and rebates.

IMS National Sales Perspectives (NSP)[™] measures spending 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.

IMS National Prescription Audit (NPA)[™] is a suite of services that provides the industry standard source of national prescription activity for all products and markets.

IMS National Disease and Therapeutic Index (NDTI)[™] is a database of de-identified patient contacts with office-based physicians projected from a panel of physicians in the U.S. who report on all patient contacts for two consecutive workdays each quarter. Information collected includes patient demographics, diagnosis and treatment information, and physician demographics.

PharMetrics Plus[™] is a closed-source de-identified longitudinal patient database that captures a patient plan experience through his/her pharmacy, medical provider, and hospital. Patient membership eligibility is accounted for within the source which ensure complete longitudinal activity per patient. PharMetrics Plus captures activities from a membership of approximately 60Mn lives per year. PharMetrics Plus integrates IMS Health legacy PharMetrics data with Health Intelligence Company's participating plan claims data. Health Intelligence Company is the operating entity of Blue Health Intelligence.

IMS Xponent[®] is a suite of services that provides near census level coverage of dispensed prescription information at a prescriber and insurance plan level.

IMS Xponent Prescribing Dynamics[™] combines Xponent data with longitudinal tracking of anonymous patient data to analyze the treatment decisions and patterns at a prescriber level.

IMS PayerTrak[™] provides retail prescriptions by insurance plan and segments those plans into types of insurance including Medicare Part D, Medicaid (including Fee for Service and Managed Medicaid plans), Commercial Third Party insurance, and Cash (prescriptions without insurance).

IMS Charge Data Master (CDM) is a projected estimate of Hospital admissions from charges submitted by a statistically significant sample of nearly 10% of all acute care hospitals in the U.S. Results are generally comparable to the National Hospital Discharge Survey 2009 from the Centers for Disease Control and Prevention (CDC). Admissions include inpatient and outpatient visits (hospital visits more or less than 24 hours respectively). Visits begin in the emergency room or elsewhere and include same-day surgeries, rehabilitation and reoccurring treatments such as chemotherapy. All payment types are included, such as Medicare, Medicaid, Commercial Third-Party, Cash, Tricare, Workman's Compensation and Charity.

IMS Healthcare Organization Services (HCOS)[™] is an organizational and affiliation reference for hospitals, long-term care and alternate care sites, medical group practices, outpatient surgery centers, diagnostic imaging centers, and home health agencies and the doctors associated with them. Organization data can be aligned and integrated with IMS Health professional, prescription and/or medicine spending data. The approximately 640,000 facilities includes single ownership relationships and multiple purchasing, distribution, academic and alliance relationships.

IMS Formulary Impact Analyzer (FIA) provides insight into what impact utilization-control measures enforced by managed care organizations have had on prescription volumes including the dynamics that affect patient behavior in filling and/or refilling prescriptions. Formulary measures include tiered co-pay benefit designs, prior authorization restrictions, and often result in non-preferred prescriptions being rejected or switched at the pharmacy. FIA offers visibility to claims rejected for other reasons such as contraindications as well as those attempted to be refilled too soon. FIA sources include national and regional chains, independent pharmacies and a claims coordination switch company providing a comprehensive view of retailers and across geographies.

IMS LifeCycle[™]R&D Focus[™] is a global database for evaluating the market for medicines, covering more than 31,000 drugs in R&D and over 8,900 drugs in active development worldwide. It includes information about the commercial, scientific and clinical features of the products, analyst predictions of future performance, and reference information on their regulatory stage globally.

Appendix

| Top Therapeutic Classes by Prescriptions | | | | | | |
|--|--------------------------|--------------|--------------|--------------|--------------|--------------|
| Dispensed Prescriptions Mn | | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | | 3,990 | 4,017 | 4,158 | 4,240 | 4,327 |
| 1 | Antihypertensives | 652 | 649 | 691 | 701 | 705 |
| 2 | Mental Health | 481 | 495 | 511 | 523 | 537 |
| 3 | Pain | 462 | 470 | 482 | 478 | 480 |
| 4 | Antibacterials | 271 | 274 | 272 | 269 | 267 |
| 5 | Lipid Regulators | 255 | 255 | 266 | 264 | 263 |
| 6 | Antidiabetes | 173 | 174 | 186 | 193 | 201 |
| 7 | Nervous System Disorders | 142 | 148 | 157 | 168 | 179 |
| 8 | Anti-Ulcerants | 147 | 150 | 159 | 166 | 170 |
| 9 | Respiratory | 153 | 153 | 157 | 162 | 169 |
| 10 | Thyroid Therapies | 110 | 113 | 122 | 127 | 131 |
| 11 | Dermatologicals | 102 | 102 | 103 | 105 | 109 |
| 12 | Hormonal Contraceptives | 91 | 90 | 91 | 95 | 97 |
| 13 | ADHD | 67 | 73 | 76 | 80 | 83 |
| 14 | Anticoagulants | 74 | 73 | 76 | 77 | 78 |
| 15 | Corticosteroids | 53 | 55 | 60 | 62 | 65 |
| 16 | GI Products | 55 | 55 | 57 | 58 | 61 |
| 17 | Nasal Preps Topical | 44 | 46 | 48 | 51 | 56 |
| 18 | Other Cardiovasculars | 52 | 51 | 51 | 50 | 49 |
| 19 | Ophthalmology | 38 | 42 | 43 | 44 | 44 |
| 20 | Sex Hormones | 44 | 43 | 45 | 45 | 43 |

Source: IMS Health, National Prescription Audit, Jan 2015

Appendix notes:

Therapy areas are based on proprietary IMS Health definitions. Report reflects prescription-bound products including insulins and excluding other products such as OTC.

IMS Health routinely updates its market audits, which may result in changes to previously reported market size and growth rates.

Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities.

Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

| Top Therapeutic Classes by Non-Discounted Spending | | | | | | |
|--|--------------------------|--------------|--------------|--------------|--------------|--------------|
| Non-Discounted Spending US\$Bn | | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | | 315.7 | 328.7 | 319.6 | 330.5 | 373.9 |
| 1 | Oncology | 22.6 | 24.1 | 25.6 | 27.9 | 32.6 |
| 2 | Antidiabetes | 18.6 | 20.8 | 21.9 | 24.7 | 32.2 |
| 3 | Mental Health | 31.1 | 32.2 | 25.1 | 23.8 | 23.1 |
| 4 | Autoimmune | 11.3 | 13.0 | 15.1 | 17.9 | 22.2 |
| 5 | Respiratory | 19.8 | 21.7 | 21.5 | 20.4 | 22.0 |
| 6 | Pain | 17.6 | 17.9 | 18.0 | 18.8 | 20.4 |
| 7 | HIV Antivirals | 9.4 | 10.4 | 11.4 | 12.5 | 14.3 |
| 8 | Multiple Sclerosis | 6.1 | 7.7 | 8.9 | 11.1 | 13.8 |
| 9 | Lipid Regulators | 19.8 | 21.3 | 16.5 | 13.6 | 13.7 |
| 10 | Viral Hepatitis Products | 1.0 | 2.0 | 2.9 | 1.9 | 12.3 |
| 11 | Antihypertensives | 15.6 | 14.0 | 13.2 | 12.5 | 12.0 |
| 12 | ADHD | 7.9 | 9.2 | 10.3 | 9.9 | 10.1 |
| 13 | Nervous System Disorders | 6.9 | 6.9 | 7.0 | 8.1 | 9.5 |
| 14 | Dermatologicals | 6.3 | 6.9 | 7.7 | 8.9 | 9.5 |
| 15 | Anti-Ulcerants | 12.4 | 10.5 | 9.8 | 10.1 | 9.3 |
| 16 | Anticoagulants | 12.4 | 13.6 | 9.5 | 7.4 | 8.5 |
| 17 | Antibacterials | 10.2 | 9.3 | 7.9 | 8.6 | 8.0 |
| 18 | Vaccines excl flu | 4.9 | 5.6 | 6.0 | 6.1 | 6.8 |
| 19 | Other Cardiovasculars | 3.6 | 4.2 | 4.7 | 5.2 | 6.3 |
| 20 | Ophthalmology | 4.3 | 4.9 | 5.0 | 5.6 | 6.3 |

Source: IMS Health, National Sales Perspectives, Dec 2014

Appendix notes:

Therapy areas are based on proprietary IMS Health definitions. Report reflects prescription-bound products including insulins and excluding other products such as OTC. IMS Health routinely updates its market audits, which may result in changes to previously reported market size and growth rates.

| Top Medicines by Prescriptions | | | | | | |
|--------------------------------|---------------------------|--------------|--------------|--------------|--------------|--------------|
| Dispensed Prescriptions Mn | | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | | 3,990 | 4,017 | 4,158 | 4,240 | 4,327 |
| 1 | levothyroxine | 103.2 | 104.7 | 112.2 | 116.9 | 119.9 |
| 2 | acetaminophen/hydrocodone | 132.1 | 136.7 | 136.4 | 129.5 | 119.2 |
| 3 | lisinopril | 87.6 | 88.8 | 99.1 | 101.8 | 103.7 |
| 4 | metoprolol | 76.6 | 76.3 | 82.6 | 83.7 | 85.3 |
| 5 | atorvastatin | 45.3 | 43.3 | 55.5 | 68.1 | 80.7 |
| 6 | amlodipine | 57.8 | 62.5 | 69.1 | 74.8 | 78.3 |
| 7 | metformin | 57.0 | 59.1 | 67.8 | 73.1 | 76.9 |
| 8 | omeprazole | 53.5 | 59.4 | 66.6 | 71.7 | 75.0 |
| 9 | simvastatin | 94.4 | 96.8 | 89.3 | 80.5 | 72.8 |
| 10 | albuterol | 55.1 | 56.9 | 61.2 | 63.6 | 67.1 |
| 11 | amoxicillin | 52.4 | 53.8 | 52.8 | 54.3 | 54.5 |
| 12 | fluticasone | 34.8 | 38.4 | 42.1 | 45.3 | 50.8 |
| 13 | gabapentin | 29.6 | 33.4 | 38.6 | 43.9 | 50.7 |
| 14 | alprazolam | 47.7 | 49.1 | 49.5 | 49.7 | 49.4 |
| 15 | hydrochlorothiazide | 47.8 | 48.1 | 51.2 | 50.0 | 49.1 |
| 16 | azithromycin | 53.6 | 56.2 | 54.6 | 48.7 | 47.0 |
| 17 | furosemide | 43.6 | 42.3 | 44.1 | 45.9 | 46.5 |
| 18 | sertraline | 36.2 | 37.6 | 39.7 | 42.0 | 44.2 |
| 19 | tramadol | 28.0 | 33.9 | 39.3 | 41.9 | 44.2 |
| 20 | losartan | 11.2 | 19.2 | 27.6 | 33.8 | 39.5 |

Source: IMS Health, National Prescription Audit, Jan 2015

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

Table shows leading active-ingredients or fixed-combinations of ingredients, and includes those produced by both branded and generic manufacturers. Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities.

Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

| Top Medicines by Non-Discounted Spending | | | | | | |
|--|--------------------|--------------|--------------|--------------|--------------|--------------|
| Non-Discounted Spending US\$Bn | | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | | 315.7 | 328.7 | 319.6 | 330.5 | 373.9 |
| 1 | Sovaldi | 0.0 | 0.0 | 0.0 | 0.1 | 7.9 |
| 2 | Abilify | 4.6 | 5.3 | 5.7 | 6.5 | 7.8 |
| 3 | Humira | 3.1 | 3.7 | 4.5 | 5.6 | 7.2 |
| 4 | Nexium | 6.5 | 6.4 | 5.9 | 6.2 | 5.9 |
| 5 | Crestor | 4.0 | 4.6 | 5.0 | 5.4 | 5.8 |
| 6 | Enbrel | 3.5 | 3.8 | 4.2 | 4.7 | 5.5 |
| 7 | Advair Diskus | 4.9 | 4.8 | 4.8 | 5.2 | 4.8 |
| 8 | Remicade | 3.3 | 3.5 | 3.8 | 4.1 | 4.5 |
| 9 | Lantus SoloSTAR | 1.1 | 1.6 | 2.2 | 3.1 | 4.5 |
| 10 | Copaxone | 2.4 | 3.2 | 3.5 | 3.7 | 3.9 |
| 11 | Neulasta | 3.0 | 3.3 | 3.4 | 3.6 | 3.8 |
| 12 | Rituxan | 2.8 | 3.0 | 3.1 | 3.3 | 3.5 |
| 13 | Januvia | 1.8 | 2.2 | 2.6 | 2.9 | 3.5 |
| 14 | Lantus | 2.0 | 2.1 | 2.2 | 2.6 | 3.4 |
| 15 | SPIRIVA HandiHaler | 2.1 | 2.5 | 2.7 | 3.0 | 3.3 |
| 16 | Lyrica | 1.7 | 1.8 | 2.0 | 2.5 | 3.1 |
| 17 | Atripla | 2.3 | 2.6 | 2.8 | 2.9 | 3.0 |
| 18 | Avastin | 3.1 | 2.7 | 2.6 | 2.7 | 2.9 |
| 19 | Tecfidera | 0.0 | 0.0 | 0.0 | 0.9 | 2.6 |
| 20 | Truvada | 1.7 | 2.0 | 2.2 | 2.3 | 2.5 |

Source: IMS Health, National Sales Perspectives, Dec 2014

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

| Dispensing Locations by Non-Discounted Spending | | | | | |
|---|--------------|--------------|--------------|--------------|--------------|
| Non-Discounted Spending US\$Bn | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | 315.7 | 328.7 | 319.6 | 330.5 | 373.9 |
| Retail And Mail | 226.8 | 236.3 | 229.2 | 236.8 | 268.6 |
| Chain Stores | 108.1 | 112.6 | 110.6 | 115.2 | 124.0 |
| Mail Service | 59.4 | 63.9 | 60.9 | 63.1 | 79.9 |
| Independent | 38.1 | 38.3 | 36.5 | 36.7 | 41.9 |
| Food Stores | 21.3 | 21.5 | 21.2 | 21.8 | 22.8 |
| Non-Retail | 88.9 | 92.4 | 90.4 | 93.7 | 105.2 |
| Clinics | 36.7 | 38.6 | 39.5 | 42.2 | 48.1 |
| Non-Federal Hospital | 28.0 | 28.2 | 28.1 | 28.4 | 30.2 |
| Long-Term Care | 14.7 | 15.2 | 13.9 | 14.0 | 16.2 |
| HMO | 2.1 | 2.6 | 2.8 | 3.1 | 3.9 |
| Home Health Care | 2.5 | 2.7 | 2.7 | 2.7 | 3.2 |
| Federal Facilities | 3.9 | 4.2 | 2.5 | 2.4 | 2.7 |
| Miscellaneous | 1.0 | 1.0 | 0.9 | 0.9 | 1.0 |

Source: IMS Health, National Sales Perspectives, Dec 2014

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

| Dispensed Prescriptions by Dispensing Locations Unadjusted for Prescription Length | | | | | |
|--|--------------|--------------|--------------|--------------|--------------|
| Dispensed Prescriptions Mn | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | 3,990 | 4,017 | 4,158 | 4,240 | 4,327 |
| Retail and Mail | 3,671 | 3,688 | 3,828 | 3,874 | 3,942 |
| Chain stores | 2,172 | 2,207 | 2,305 | 2,388 | 2,477 |
| Independent | 748 | 740 | 738 | 737 | 738 |
| Food stores | 487 | 482 | 522 | 517 | 516 |
| Mail service | 264 | 260 | 262 | 233 | 212 |
| Non-Retail | 319 | 329 | 330 | 366 | 385 |
| Long-term care | 319 | 329 | 330 | 366 | 385 |

Source: IMS Health, National Prescription Audit, Jan 2015

| Dispensed Prescriptions by Dispensing Locations Adjusted for Prescription Length | | | | | |
|--|--------------|--------------|--------------|--------------|--------------|
| Adjusted Dispensed Prescriptions Mn | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | 4,893 | 4,990 | 5,271 | 5,385 | 5,506 |
| Retail and Mail | 4,571 | 4,657 | 4,936 | 5,015 | 5,117 |
| Chain stores | 2,455 | 2,549 | 2,756 | 2,906 | 3,054 |
| Independent | 825 | 826 | 834 | 844 | 855 |
| Food stores | 570 | 574 | 631 | 632 | 636 |
| Mail service | 721 | 708 | 715 | 633 | 572 |
| Non-Retail | 322 | 333 | 335 | 370 | 389 |
| Long-term care | 322 | 333 | 335 | 370 | 389 |

Source: IMS Institute for Healthcare Informatics; IMS Health, National Prescription Audit, Jan 2015

Appendix notes:

90-day prescriptions are defined as those with more than 84 days supply and represented 7% of unadjusted retail TRx in 2010, rising to 10.9% in 2014; Prescriptions for 90 days have been adjusted to estimate 30 day prescriptions in all dispensing locations.

| Dispensing by Payment Type | | | | |
|-------------------------------------|--------------|--------------|--------------|--------------|
| Dispensed Prescriptions Mn | 2011 | 2012 | 2013 | 2014 |
| Retail Channel Prescriptions | 3,429 | 3,566 | 3,641 | 3,731 |
| Commercial Third-Party | 58.4% | 56.0% | 54.9% | 53.1% |
| Medicare Part D | 21.5% | 23.1% | 24.9% | 25.7% |
| Medicaid | 12.8% | 12.1% | 11.7% | 13.3% |
| Cash | 7.3% | 8.7% | 8.5% | 7.8% |

Source: IMS Health, National Prescription Audit; PayerTrak, Jan 2015

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

PayerTrak provides payer-type segmentation for retail prescriptions only.

Medicaid includes both Fee for Service and Managed Medicaid.

| Non-Discounted Spending and Dispensing by Product Type | | | | | |
|--|--------------|--------------|--------------|--------------|--------------|
| Spending US\$Bn | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | 315.7 | 328.7 | 319.6 | 330.5 | 373.9 |
| Brands | 75.7% | 74.5% | 71.6% | 70.8% | 71.7% |
| Unbranded Generics | 12.5% | 13.7% | 16.3% | 17.1% | 17.3% |
| Branded Generics | 11.7% | 11.8% | 12.0% | 12.0% | 11.1% |
| Dispensed prescriptions Mn | 2010 | 2011 | 2012 | 2013 | 2014 |
| Total U.S. Market | 3,990 | 4,017 | 4,158 | 4,240 | 4,327 |
| Brands | 22.8% | 20.3% | 16.1% | 13.8% | 12.4% |
| Unbranded Generics | 69.7% | 72.6% | 77.6% | 80.2% | 81.9% |
| Branded Generics | 7.5% | 7.1% | 6.3% | 6.0% | 5.6% |

Source: IMS Health, National Sales Perspectives, Dec 2014; National Prescription Audit, Jan 2015

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC.

Includes all prescriptions dispensed through retail pharmacies - including independent and chain drug stores, food store pharmacies and mail order as well as long-term care facilities.

Prescription counts are not adjusted for length of therapy. 90-day and 30-day prescriptions are both counted as one prescription.

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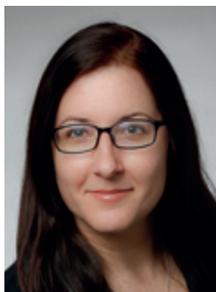
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About the Institute

The IMS Institute for Healthcare Informatics leverages collaborative relationships in the public and private sectors to strengthen the vital role of information in advancing healthcare globally. Its mission is to provide key policy setters and decision makers in the global health sector with unique and transformational insights into healthcare dynamics derived from granular analysis of information.

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 patient care. With access to IMS Health's extensive global data assets and analytics, the Institute works in tandem with a broad set of healthcare stakeholders, including government agencies, academic institutions, the life sciences industry and payers, to drive a research agenda dedicated to addressing today's healthcare challenges.

By collaborating on research of common interest, it builds on a long-standing and extensive tradition of using IMS Health information and expertise to support the advancement of evidence-based healthcare around the world.

Research Agenda

The research agenda for the Institute centers on five areas considered vital to the advancement of healthcare globally:

The effective use of information by healthcare stakeholders globally to improve health outcomes, reduce costs and increase access to available treatments.

Optimizing the performance of medical care through better understanding of disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

Understanding the future global role for biopharmaceuticals, the dynamics that shape the market and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.

Researching the role of innovation in health system products, processes and delivery systems, and the business and policy systems that drive innovation.

Informing and advancing the healthcare agendas in developing nations through information and analysis.

Guiding Principles

The Institute operates from a set of Guiding Principles:

The advancement of healthcare globally is a vital, continuous process.

Timely, high-quality and relevant information is critical to sound healthcare decision making.

Insights gained from information and analysis should be made widely available to healthcare stakeholders.

Effective use of information is often complex, requiring unique knowledge and expertise.

The ongoing innovation and reform in all aspects of healthcare require a dynamic approach to understanding the entire healthcare system.

Personal health information is confidential and patient privacy must be protected.

The private sector has a valuable role to play in collaborating with the public sector related to the use of healthcare data.

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