May 2017

Medicines Use and Spending in the U.S.

A Review of 2016 and Outlook to 2021

Introduction

Growth in spending on medicines for 2016 slowed to less than half the rate seen in 2014 and 2015. The rate of growth, however, remained above inflation and continues to draw intense focus in public discourse. The discussion of drug pricing in particular continues to highlight issues of transparency and the complex interactions between stakeholders to determine not just "the price" of a drug, but "the price to whom". When examined through the lens of net spending and prices (after off-invoice discounts and rebates), drug spending and prices appear substantially lower, however, patients' out-of-pocket costs are influenced by different factors and remain commonly misunderstood.

The outlook suggests modest growth in medicine spending through 2021 but the challenges of balancing access and the cost of care in an era of innovative but more expensive treatments continues as a theme across the healthcare system.

In this report, we highlight different aspects regarding the use of medicines spanning overall spending, key market segments, volumes, patient cost exposure, as well as the outlook to 2021.

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Executive summary

Spending on medicines increased by 5.8% to $450Bn in 2016, growing at less than half the rate seen in the last two years, based on invoice prices. After adjusting for estimated rebates and other price concessions by manufacturers, which continued to rise in 2016, net spending was $323Bn, up 4.8% over 2015 levels. When adjusted for these concessions, as well as economic and population growth, medicine spending increased 2.6% in 2016 and has increased by an average of 1.1% per year since 2006, while the balance of medicines being used has shifted strongly to specialty medicines from traditional treatments. The surge of new medicines launched in the past few years paused in 2016 with fewer than half the new medicines launched than the prior two years, and a reduced level of spending on new medicines.

The usage of medicines by patients has continued to rise, as many have wider access to insurance and low cost generic medicines, while a minority of patients face substantial out-of-pocket costs and experience a dramatically different trend in their spending on medicines than other patients and the system overall.

The outlook for medicine spending through 2021 is for mid-single digit growth driven by further clusters of innovative treatments, offset by a rising impact from brands facing generic or biosimilar competition. Drug manufacturer responses to heightened market competition and scrutiny of drug pricing are expected to result in more modest levels of invoice (and net) price growth in the forecast period.

Spending and growth dynamics

Total spending on an invoice price basis reached $450Bn in 2016, up 5.8% from 2015. Spending adjusted for net prices reached $323Bn and grew by 4.8% in 2016. The net growth rate moderated significantly from 8.9% in 2015 (see Chart 1).

The increase in total spending in 2016 of $27.3Bn on an invoice price basis and $14.8Bn on a net basis, was driven by new brands and protected brands (see Chart 4).

A note on nomenclature:

In this report, "spending on medicines" and "invoice-price spending" refer to the amounts paid to distributors by their pharmacy or hospital customers. It does not relate directly to either the out-of-pocket costs paid by a patient, except where noted, nor does it refer to the amount health plans or Medicare pay for medicines, and does not include mark-ups and additional costs associated with dispensing or other services associated with medicines reaching patients. "Net-price spending" is *a proprietary derived* estimate of the amount received by pharmaceutical manufacturers after rebates, off-invoice discounts and other price concessions have been made by manufacturers to distributors, health plans and intermediaries. For a fuller explanation of methods to estimate net spending, see the Methodology section.

The average net price for brands already in the market is estimated to have increased by 3.5% in 2016, up from 2.5% in 2015, while remaining significantly lower than prior years. This reflects the heightened competition among manufacturers and more aggressive efforts by health plans and pharmacy benefit managers to limit price growth. Invoice price levels, prior to the impact of concessions, increased 9.2% in 2016 (see Chart 5).

Offsetting other growth elements is the impact of new competition for brands resulting from the expiry of patents or other forms of market exclusivity. Spending on such brands fell by $14.0Bn in 2016, about the same impact as in 2015, but much lower than the landmark year of 2012 when the comparable impact was $32.6Bn (see Chart 25)

Over 50% of positive spending growth in 2016 was from new brands that have been available for less than 24 months. Patients are seeking and receiving new treatments for cancer, autoimmune diseases, HIV, diabetes and other chronic conditions, driving $17.4Bn of new spending growth on an invoice price level, and an estimated $13.9Bn on a net basis, slightly lower than in the prior year but still significantly higher than historical levels (see Chart 6).

Spending on all generic medicines declined slightly in 2016 as the spike in price increases of older generics seen in 2013 and 2014 is no longer driving growth in 2016 (see Chart 4).

Medicine usage trends

Total prescriptions dispensed in 2016 reached 4,453 million, an increase of 1.9% which compares to increases of about 2 percent seen in earlier years. Notably, chronic prescriptions with 3-month duration have increased dramatically in the last two years and prescriptions grew by 3.3% when adjusting for prescription size. The largest drivers of prescription growth in 2016 were seniors, mostly due to population growth (see Chart 10). Younger patients have continued to increase per capita usage of medicines under the Affordable Care Act (ACA) exchanges.

The largest drivers of prescription growth were the most widely used medicines, with usage of hypertension treatments growing slightly faster than the market overall, and offset by declining use of pain medicines (see Chart 11). Usage of pain medicines, including both narcotic and non-narcotic treatments, declined by 1% as restrictions on prescribing and dispensing become increasingly common and impactful. Cholesterol treatments continue to be widely used but grew only modestly in 2016 (see Chart 12) and saw the rapid shift to generic usage for rosuvastatin (Crestor) following patent expiry. The cholesterol market also saw relatively limited uptake for the newest generation of treatments, PCSK9s (proprotein convertase subtilisin/kexin type 9), which dramatically lower "bad cholesterol" LDL but have been heavily restricted to their FDA approved uses by insurer formularies, reaching less than 0.25% of the current cholesterol market in terms of prescriptions.

An estimated 226,000 new patients were treated with hepatitis C medicines in 2016, down 23,000 from the prior year and bringing the total in the last three years to 645,000, potentially curing between 13-22% of the 3 to 5 million infected patients in the United States.

Out-of-pocket cost trends

Average patient out-of-pocket costs declined in 2016 as more patients received zero out-of-pocket cost prescriptions or paid lower costs or used generics, and a declining share paid rising costs (see Chart 14). Patient exposure to costs varies during the year, while an increasing number of patients are facing high costs and are reaching maximum out-of-pocket costs during the year. Coupons reduce patient costs for brands and one in five brand prescriptions in commercial insurance plans used a coupon in 2016 (see Chart 17). As list prices have risen, manufacturer out-of-pocket offsets for these coupons have also increased along with increasing patient cost exposure, typically reducing patient costs to a level similar to a standard copay.

The rising use of deductible plans, where patient copay is based on list prices, meant that 14% of brand prescriptions in commercial plans were paid during a deductible phase while those copays accounted for 39% of total brand out-of-pocket costs for patients in those plans (see Chart 18). Many patients are abandoning prescriptions at the pharmacy due to "sticker shock" and abandonment rates for brands are 2.5 times higher when a patient faces a deductible and sees the full cost of the medicine compared to patients who had a set copayment (see Chart 19).

Outlook to 2021

The outlook for U.S. spending growth on medicines has been revised significantly downward as a result of weaker than expected new product spending and a slowing of invoice price increases for branded products (See Chart 20). Average growth was projected in the 6-9% range prior to the autumn of 2016 but projections have been revised down to 4-7% through 2021. Price increases for branded products existing in the market were projected to continue historic growth in the 8-11% range but are now expected to grow more slowly at 7-10% on an invoice basis, while the outlook for net growth is unchanged at 2-5% as pricing remains under intense competitive and payer pressure (See Chart 21). The prospects for further innovative medicines becoming available over the next five years remain very bright despite a relatively small number of launches in 2016. The late phase pipeline holds 2,346 novel products and 40-45 New Active Substances are expected to be launched on average for each of the next five years. Oncology remains the area of greatest activity (see Chart 24).

Spending is forecast to reach $580-610Bn in 2021 on an invoice price basis, driven by innovation and offset by loss of exclusivity, including the impact of biosimilars. Spending on a net basis is expected to reach $375-405Bn growing at a more modest 2-5% to 2021.

Spending and growth dynamics

- Spending reached $450Bn, but growth slowed to 5.8% in 2016, less than half the 12.4% rate of 2015 on an invoice price basis.

- On a net basis spending grew only 4.8% and was 28% lower than invoice level at $323Bn.

- When adjusted for off-invoice discounts and rebates, population and economic growth, real net per capita drug spend grew 2.6% in 2016 and an average of 1.1% over the past ten years.

- Spending continues to shift from traditional to specialty medicines, which now account for $384 of the $895 per person per year spent on medicines.

- Spending growth has been driven by new brands and protected brand volume increases.

- Average invoice price increases slowed from 12.0% in 2015 to 9.2% in 2016 and net prices grew at 3.5%.

- New brands - those on the market for less than 24 months - contributed only $13.9Bn to growth in 2016, down from $17.3Bn in 2015 and $20.6Bn in 2014.

- New brands have significantly shifted to specialty therapies, but have not been driven by one single therapy area or product and the contribution to spending growth remains above historic levels despite a $1.9Bn decline in new brand spending for hepatitis C treatments.

- Growth continues in double digits for biologic drugs, driven by innovation, but growth is tempered by an increased impact from biosimilars.

U.S. medicines growth slowed by half in 2016 to 4.8% on a net basis

Chart 1: Total Spending on Medicines

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute
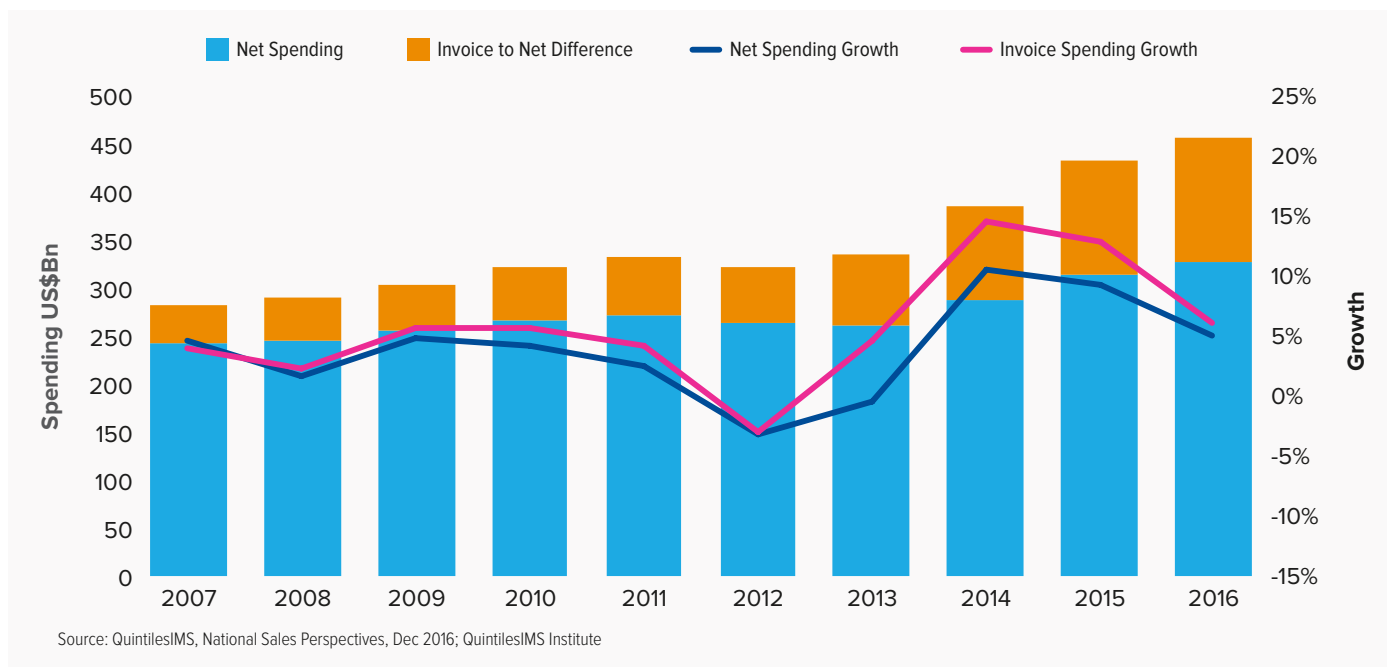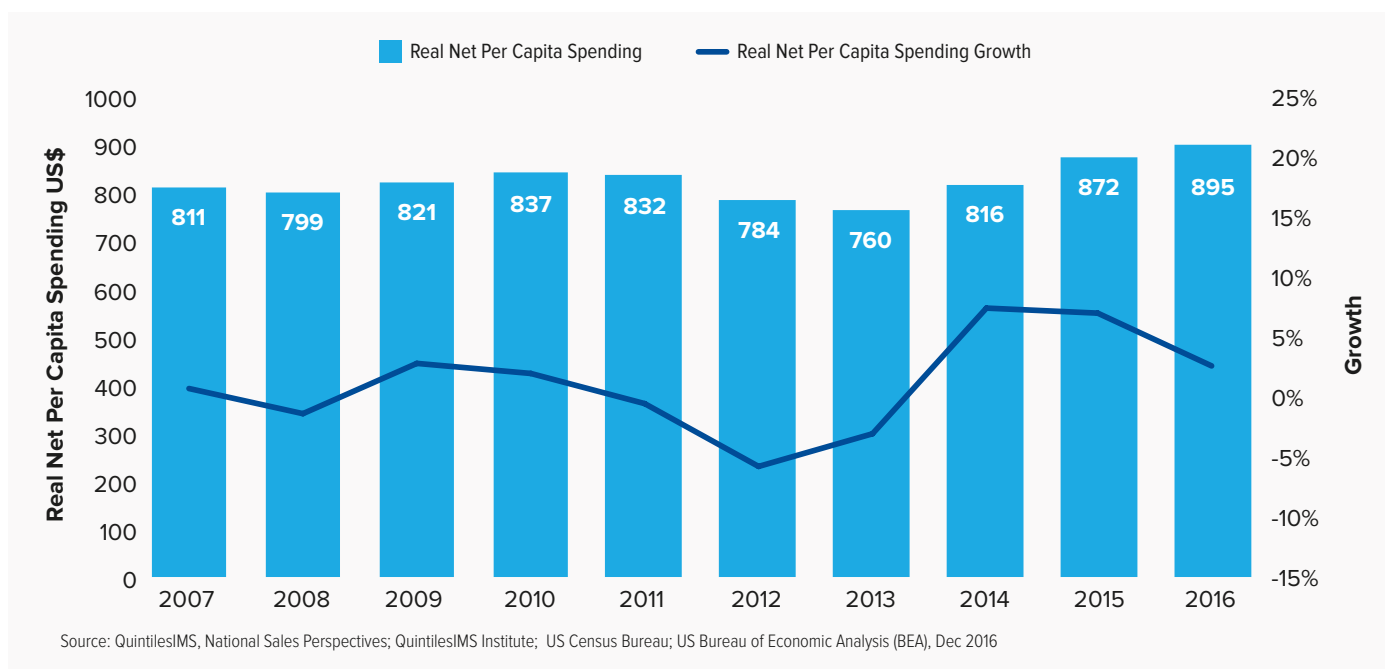
- Spending grew 4.8% net of off-invoice discounts and rebates, as invoice-level growth slowed to 5.8%.

- Discounts, rebates and other price concessions on brands reduced absolute invoice spending by an estimated 28% to $323.1Bn.

- Spending growth slowed in 2016 after two historically high years due to lower price increases for protected branded products, fewer new products launched and lower spending growth, specifically for hepatitis C treatments where spending declined in 2016.

- Net price increases averaged 3.5%, significantly lower than invoice price increases which averaged 9.2%, with 62% of growth from price on an invoice basis conceded after estimating net prices.

- On an invoice basis, spending has risen 67% since 2006, but just 42% on a net basis, with more than two-thirds of net growth occurring since 2013.

- After the historically high growth in 2014 and 2015, driven predominately by innovative new medicines, 2016 grew more slowly on a net basis than seven of the last ten years.

Chart notes:

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

Real net per capita drug spend has been relatively unchanged over the past decade

Chart 2: Real Net Per Capita Medicine Spending and Growth

Legend: ■ Real Net Per Capita Spending — Real Net Per Capita Spending Growth

Year	Real Net Per Capita Spending US$
2007	811
2008	799
2009	821
2010	837
2011	832
2012	784
2013	760
2014	816
2015	872
2016	895

Source: QuintilesIMS, National Sales Perspectives; QuintilesIMS Institute; US Census Bureau; US Bureau of Economic Analysis (BEA), Dec 2016
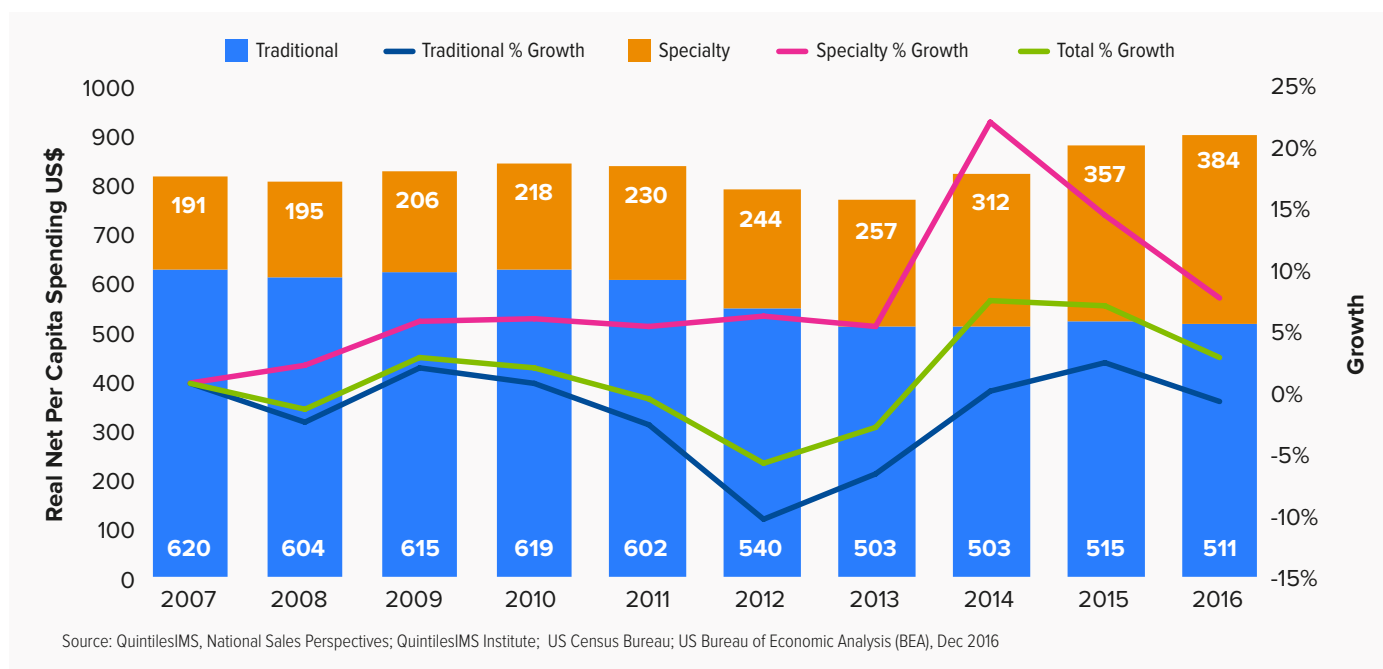
- Medicine spending including both pharmacy and medicines dispensed in hospitals, clinics and other non-retail settings, has increased an average of 1.1% per year since 2006 when it was $805 per person, and has risen only 11% in ten years to $895 in 2016.

- Spending increased 5.8% in 2016 on an invoice basis and 4.8% on a net basis, but after accounting for population, economic growth and estimates of off-invoice concessions by manufacturers, spending increased 2.6% over the prior year.

- While manufacturer net revenues, adjusted in this way, have increased only modestly over the past decade, patient exposure to costs has increased dramatically, more in line with list prices.

- Underlying these trends are complex and confidential negotiations between multiple stakeholders, setting price, rebate, and usage protocols intended to control the trend of overall medicine spend.

- As a result of the opaque system of pricing, it is difficult for many stakeholders to understand if they are achieving the same level of modest growth as seen for manufacturer's net revenues.

Chart notes:

"Invoice" values are QuintilesIMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. "Net" values denote company recognized revenue after discounts, rebates and other price concessions. Results are based on a comparative analysis of company reported net sales and IMS Health reported sales and prices at product level for branded products representing 79-93% of brand spending in the period displayed. Real Per capita adjustments based on data from U.S. Census Bureau and U.S. Bureau of Economic Analysis. Real per-capita spending reported in 2009.

Per capita spending on traditional medicines has declined and been replaced by specialty drugs

Chart 3: Real Net Per Capita Medicine Spending and Growth by Type

Source: QuintilesIMS, National Sales Perspectives; QuintilesIMS Institute; US Census Bureau; US Bureau of Economic Analysis (BEA), Dec 2016

- Specialty medicines have been an increasing share of medicine spending over the past decade, rising from 21.8% of spending in 2007 to 39.6% in 2016 on an invoice-price basis.

- Generally off-invoice discounts and rebates have been lower for specialty than for traditional medicines, resulting in a higher share of spending on a net basis. Specialty share of net spending rose from 23.6% in 2007 to 42.9% in 2016.

- The largest proportion of the new medicines launched in the last five years have been specialty drugs, and specialty share of spending has risen while traditional net medicine spending has declined by more than $100 per person over the past decade.

- For retail & mail, specialty medicines are 32.5% of spending and 1.9% of prescriptions, 1.3% of adjusted prescriptions.

- In non-retail settings, specialty medicines represent 58% of invoice spending and 2.6% of standard unit volumes.

- Across all settings, specialty medicines treat relatively few patients, and have costs far higher per patient than traditional medicines.

- Usage of specialty medicines is often less influenced by cost and instead due to extreme medical need, making it even more difficult to balance population health and overall cost concerns with the needs of an individual patient.

Chart notes:

Specialty and Traditional are proprietary definitions of QuintilesIMS, see Methodology section for more details.

Spending growth has slowed while new brands and protected brand volume growth drive most of the increase

Chart 4: Net Spending Growth by Product Type US$Bn

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute
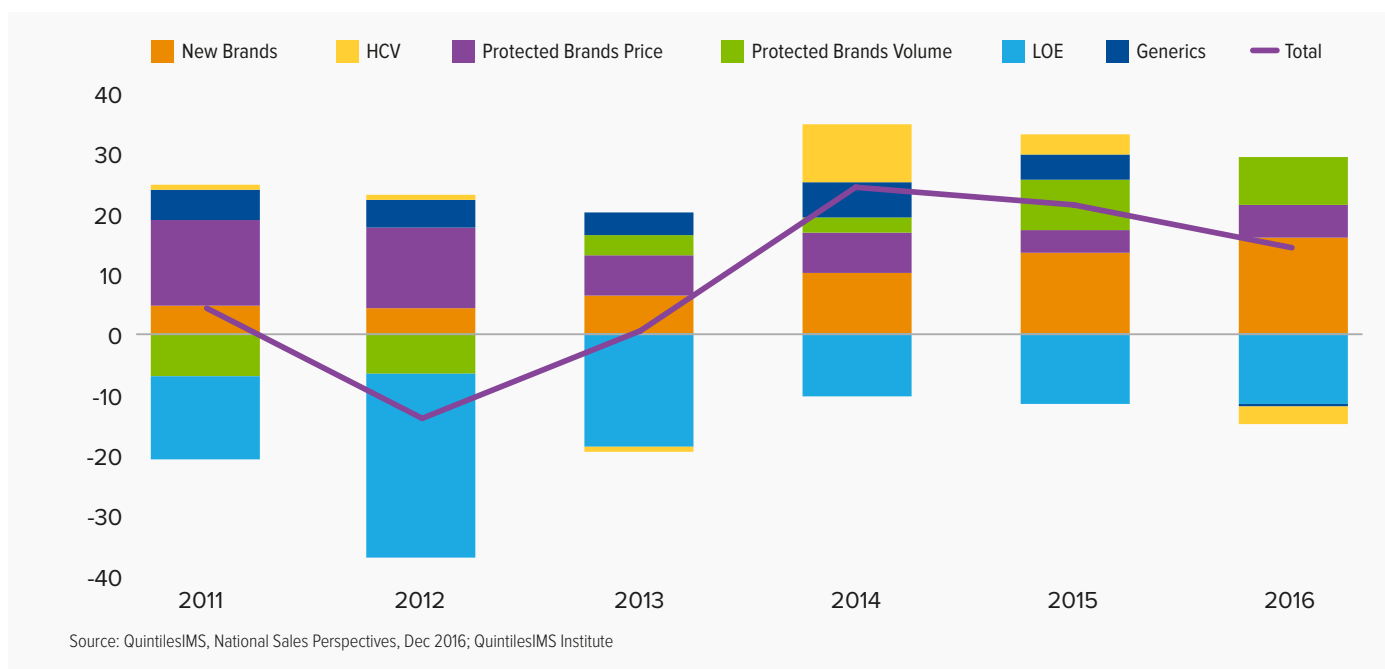
- The largest drivers of net spending growth in 2016 were the group of new brands on the market for less than 24 months.

- New branded products grew by $15.9Bn on a net basis even after a $1.9Bn decline by hepatitis C new brands.

- The dramatic rise and then plateau of hepatitis C spending represents a unique event in the history of medicine spending that distorts most of the recent trend and requires separate analysis (see Chart 13).

- Protected brands have historically had growth mostly due to invoice-price increases, with a much smaller contribution from incremental volume, however this has reversed since 2013 as newer medicines continue to grow on a volume basis.

- Net price growth in 2015 was reduced in aggregate by significant decreases in the net prices of hepatitis C drugs, and excluding hepatitis C products, average net price increases were 3.6% in 2015, almost unchanged to 3.5% in 2016.

- The impact of patent expiries has been largely unchanged for the last three years, offering limited offsetting reductions compared to prior years.

Chart notes:

New brands are protected branded products on the market less than 24 months during the year reported. Protected brands are products which are no longer "new" and have yet to reach patent expiry. Loss of Exclusivity (LOE) are brands which were once protected and have since lost patent protection.

Generics include both unbranded and branded generics. All segments exclude hepatitis C treatments. Hepatitis C spending growth is reported separately from the other segments in the chart as unusually there are declines in spending in both the new and protected segments for these drugs.

Net prices continued to increase more slowly than invoice prices

Chart 5: Protected Brand Invoice and Net Price Growth

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute
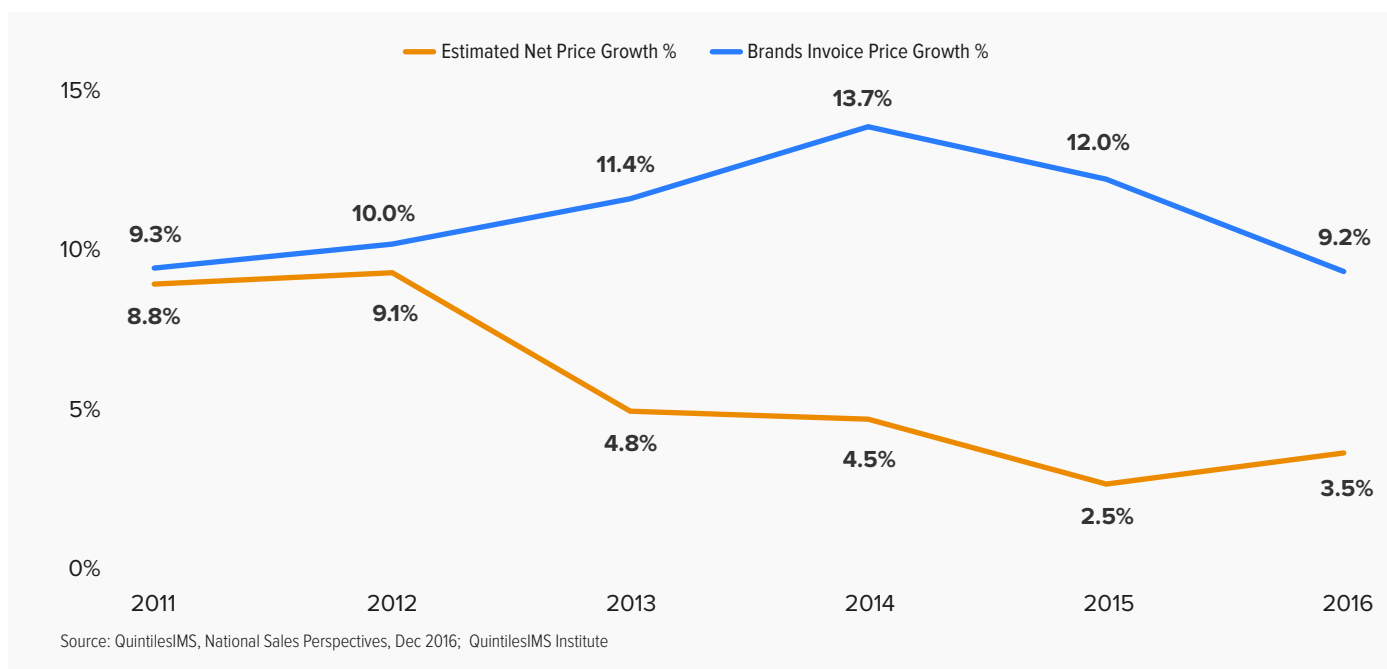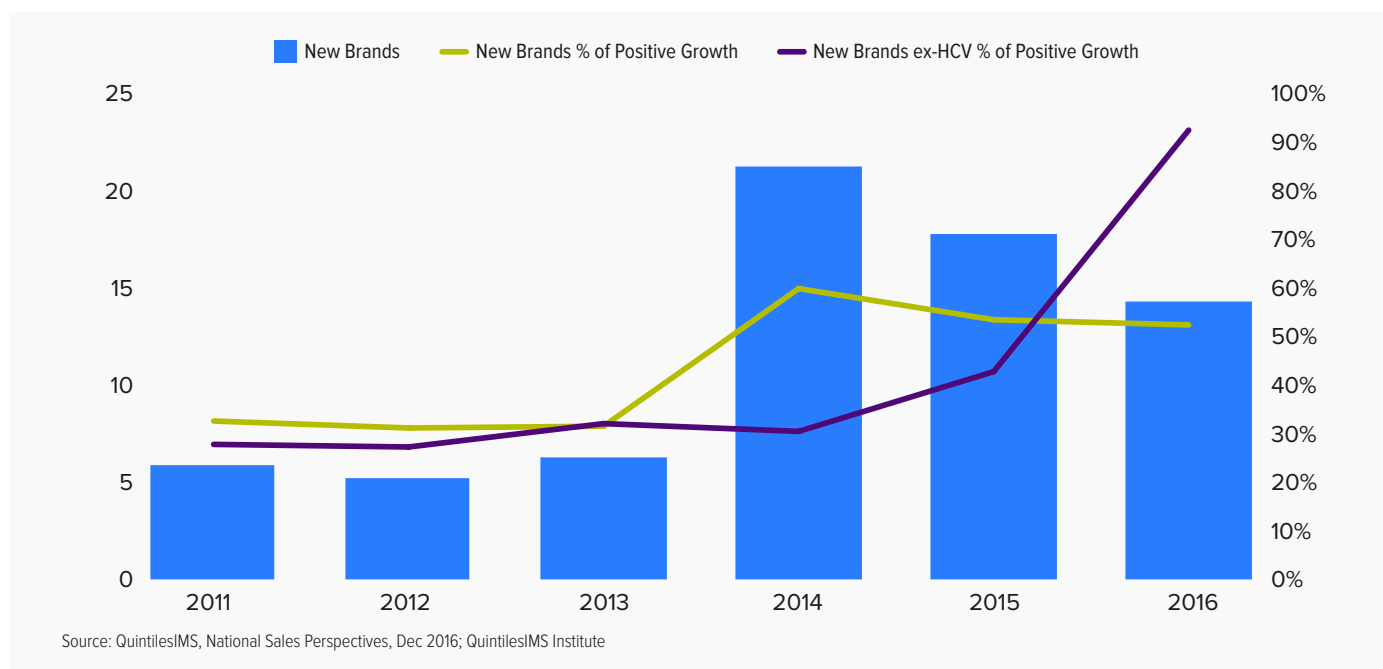
- Price increases for protected brands averaged 9.2% on an invoice-price basis while net price growth is estimated to have increased 3.5% in 2016 on average.

- Net price spending growth was driven by autoimmune, HIV and oncologic therapies while offset by large net price declines in hepatitis, MS and respiratory therapies.

- The increase in average net price growth from 2015 to 2016 reflects changes in the portfolio of large brands in the market and differential levels of price concessions.

- Discounts, rebates and other price concessions offset protected brands price growth by 62% in 2016.

- Brand invoice price growth also slowed this year, declining from 12% in 2015.

- Invoice price increases were lower than prior years on average, but above average increases were observed in many individual markets and had the most impact on invoice-level spending in autoimmune, cholesterol, nervous system disorders (e.g., epilepsy, Parkinson's), and erectile dysfunction.

- Net prices grew by 2.5% in 2015, revised from 2.8% in prior estimates due to changes in sampling and projection.

Chart notes:

"Invoice" values are QuintilesIMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. "Net" values denote company recognized revenue after discounts, rebates and other price concessions. Results are based on a comparative analysis of company reported net sales and IMS Health reported sales and prices at product level for branded products representing 79-93% of brand spending in the period displayed. All growth numbers calculated over same cohort of products in the prior year. See Methodology section for more details.

New treatments drove more than half of positive growth in net spending in 2016

Chart 6: New Brand Net Spending Growth US$Bn

Legend: New Brands · New Brands % of Positive Growth · New Brands ex-HCV % of Positive Growth

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute

- New brand spending growth slowed in 2016 primarily as hepatitis C new brand growth of $3.6Bn in 2015 shifted to a $1.9Bn decline in 2016, a $5.5Bn swing.

- Overall net new brand spending growth slowed only $3.4Bn to $13.9Bn as other areas of new brands spending growth improved from $13.6Bn in 2015 to $15.9Bn in 2016.

- Traditional medicines made up 57.4% of overall net spending, but accounted for just 39.2% of new brand growth.

- Specialty medicines, now accounting for 42.6% of net spending in 2016, drove 60.8% of new brand spending growth, driven by oncology, HIV and autoimmune. Spending was offset by a $1.9Bn decline in new hepatitis C brands, as some products were used by fewer patients and others gave way to hepatitis C treatments.

Chart notes:

New brands are defined as brands launched in the last twenty-four months and defined separately for each year. New brands share of positive growth are based on segments defined on Chart 4, however new brands includes hepatitis C treatments. New brands excluding hepatitis C treatments exclude HCV from both new brands and from other segments. Specialty and Traditional medicines are proprietary definitions by QuintilesIMS, see Methodology for more details.

Biologics growth continues, driven by innovation but seeing an increased impact from biosimilars

Chart 7: Biologics Net Spending US$Bn

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; QuintilesIMS Institute
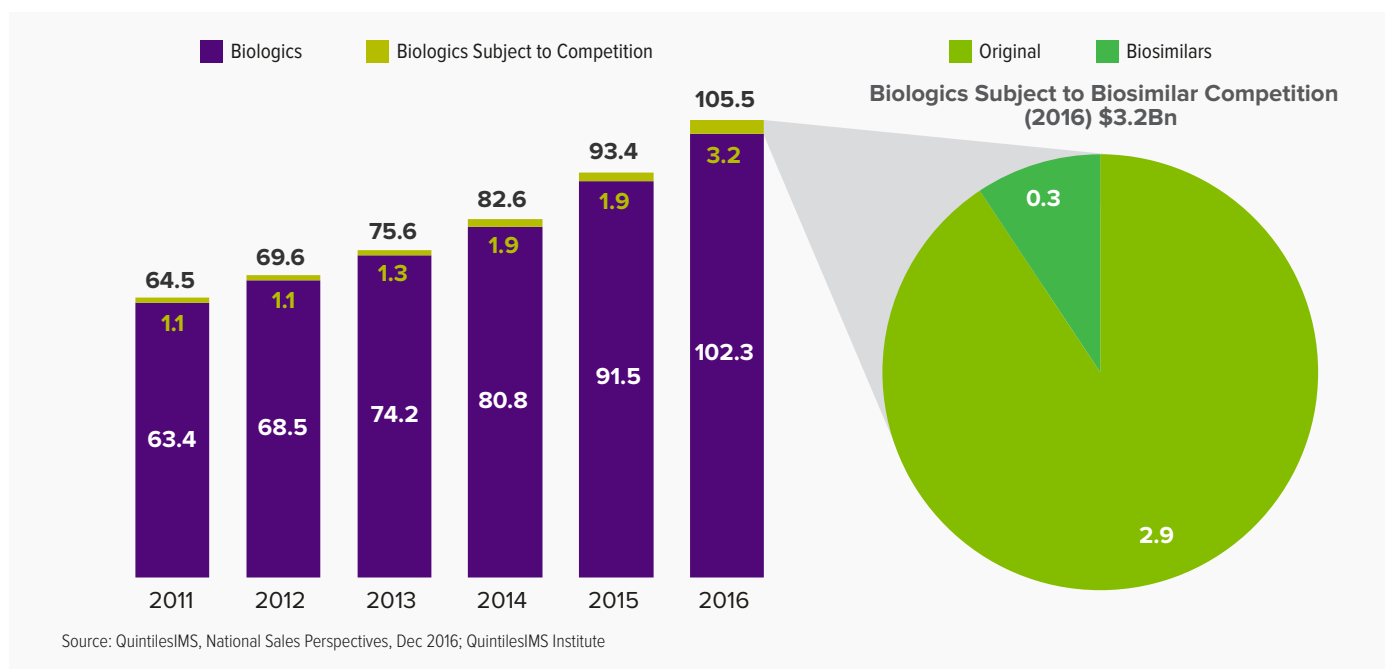
- Biologics grew by 13.0% in 2016, over 10% per year for the last five years as a variety of biologic treatments for autoimmune disorders, immunology and cancer came to the market.

- Biosimilars been slow to emerge since the creation of a biosimilar pathway in the Affordable Care Act in 2010.

- Filgrastim "biosimilars", Granix (approved as an original biologic in December 2012) and Zarxio (the first official approved biosimilar launched in September 2015), together have reached 42.6% of volume as of December 2016.

- An insulin glargine biosimilar, Basaglar, launched in December 2016 and has achieved a volume share of approximately 5% by the end of March 2017.

- The Basaglar uptake is notable, however, because it varies by the type of insurance a patient has, and in the parts of the market where insurers have preferred Basaglar to originator drug Lantus, it has achieved substantially higher shares, estimated at over 50%.

- These preferred formularies represent a small portion of the overall market but are expected to be more widely adopted in 2018 when Basaglar will be preferred in Medicare Part D plans, as well as other commercial plans.

Chart notes:

Biologics are defined by QuintilesIMS as clearly identifiable molecules of biologic origin, including but not limited to products created with recombinant DNA technology and without necessarily adhering to classifications by regulatory bodies which are sometimes inconsistent with this approach. Biosimilars are abbreviated biologic approvals made with reference to an original biologic and demonstrating similarity to the reference product. Non-original products approved outside the official biosimilar pathway have been noted as "biosimilar".

Medicine usage trends

- Adjusted dispensed prescriptions increased 3.3% compared to 2.0% growth without adjusting for prescription length.

- Patients 50 and over account for 70% of dispensed prescriptions in 2016 and 77% of the growth since 2011.

- Prescription growth in younger patients has been driven by higher per capita usage while population growth has resulted in higher usage by older patients.

- The biggest drivers of prescription growth were in large chronic therapy areas, while the largest decline was in pain management.

- Cholesterol treatments have shifted to generics and new PCSK9s have <0.25% of prescriptions.

- 23,000 fewer new patients received treatment for hepatitis C in 2016 while the overall number treated in the last three years reached 645,000.

Dispensed prescriptions increased over three percent in 2016, the highest rate since 2012

Chart 8: Adjusted Prescriptions Mn and Growth

Source: QuintilesIMS, National Prescription Audit; U.S. Census Bureau, Dec 2016
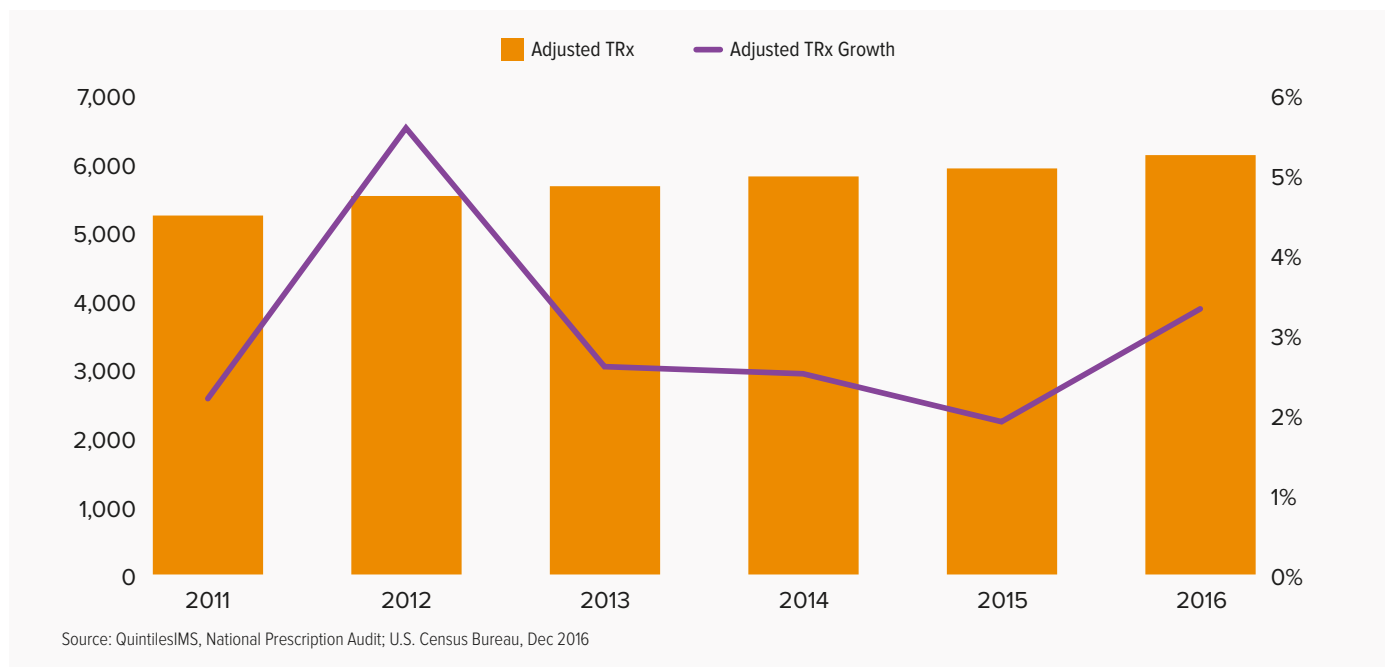
- Prescriptions increased at 3.3% in 2016, the highest rate of growth since 2012, when significant patent expiries and a strong flu season lifted demand.

- The increasing use of 90-day prescriptions is particularly notable as the rate of growth without adjusting for prescription length was 2.0%.

- Adjusted prescriptions exceeded 6.1Bn in 2016, up from 5.2Bn in 2011.

- The 884 million adjusted prescription increase since 2011 was driven by increased per capita usage of medicines, which contributed 680 million of the incremental prescriptions, while population grew by 3.9%, contributing 204 million prescriptions.

- The relatively weak flu season in 2016, less extra demand for generics from patent expiries and fewer changes in insurance coverage for patients relative to the prior two years, contributed to slower growth.

Chart notes:

Prescription counts are adjusted for length of prescriptions and re-aggregated, with prescriptions for 84 days supply or more factored by three, and those under 84 days unchanged. Patient age is reported anonymously along with other prescription information. Per capita estimates are based on overall U.S. population.

Patients 50 and over account for seventy percent of dispensed prescriptions and the majority of the growth since 2011

Chart 9: Adjusted Dispensed Prescriptions Mn by Patient Age

Source: QuintilesIMS National Prescription Audit; U.S. Census Bureau, Dec 2016
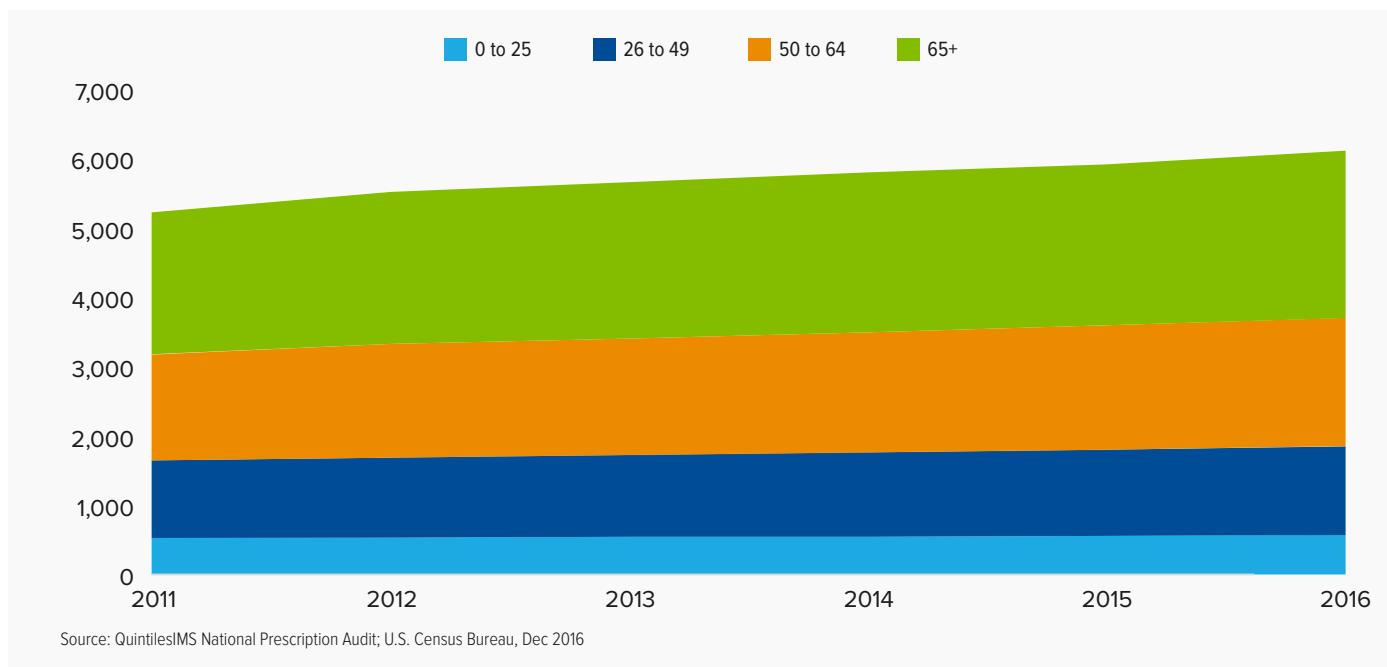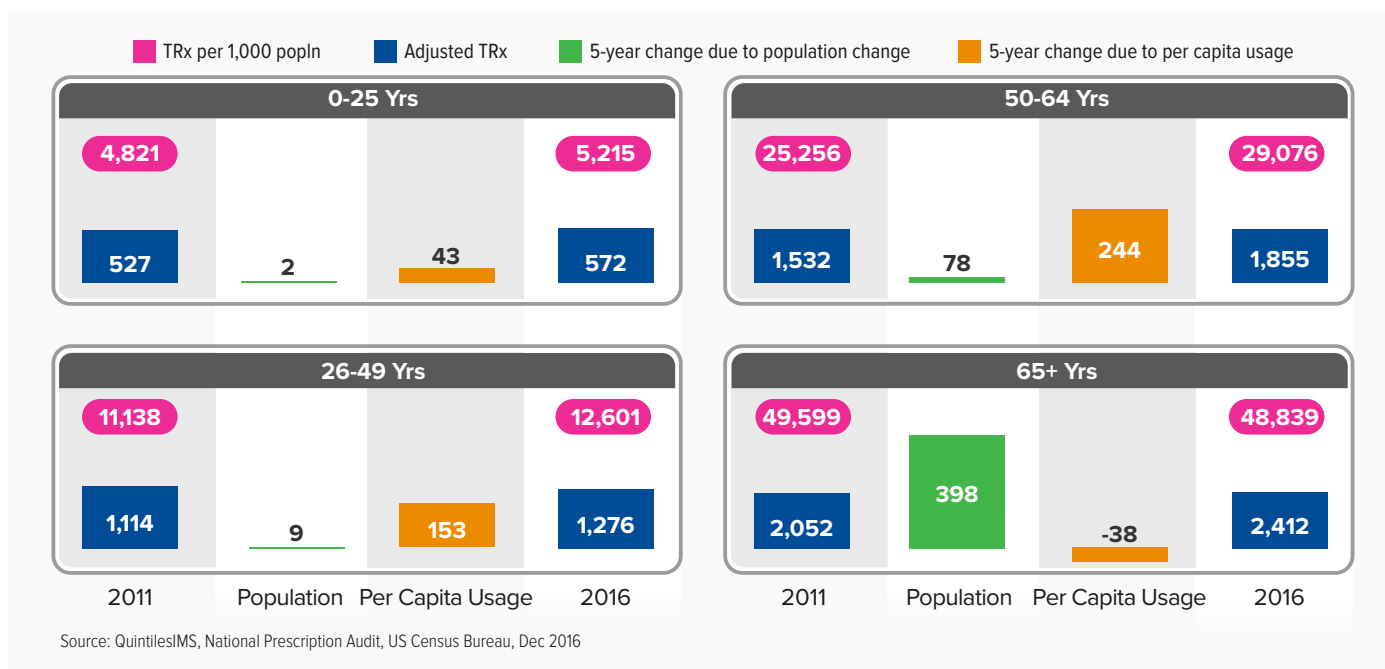
- Patients 50 and over accounted for 35% of the population in 2016, but received 70% of adjusted prescriptions in 2016.

- The U.S. added 12.3 million people to the population from 2011 to 2016, 91% of that increase was in the over 50 group, as patients are living longer, often healthier lives.

- Seniors over 50 drove 77% of prescription growth since 2011, as their per capita usage actually declined.

- Patients over 65 received 39% of prescriptions in 2016, and 41% of the increase since 2011.

- The over 65 age group account for 15% of the population in 2016 but 65% of the population increase since 2011.

- Patients over 65 years old averaged 49,559 prescriptions per 1,000 of population in 2011, falling to 48,839 prescriptions in 2016.

- An estimated 77% of prescriptions in the over 65 group are for chronic conditions, where a patient would be on therapy for 12 months, while 84% of over 65 prescriptions were for chronic treatments. The average over 65 year old patient would be receiving 4 concurrent prescription medicines.

- Medicine usage per 1,000 of overall U.S. population averaged 18,869 in 2016, up from 16,775 in 2011, increasing 2.4% per year on average and 12.5%, overall.

Chart notes:

Prescription counts are adjusted for length of prescriptions and re-aggregated, with prescriptions for 84 days supply or more factored by three, and those under 84 days unchanged. Patient age is reported anonymously along with other prescription information. Per capita estimates are based on overall U.S. population.

Prescription growth in younger patients is driven by usage, while growth in older patients is due to population

Chart 10: Adjusted Prescriptions by Age and Drivers

Legend: ■ TRx per 1,000 popln ■ Adjusted TRx ■ 5-year change due to population change ■ 5-year change due to per capita usage

0-25 Yrs
- 4,821 / 527
- Population: 2
- Per Capita Usage: 43
- 5,215 / 572

50-64 Yrs
- 25,256 / 1,532
- Population: 78
- Per Capita Usage: 244
- 29,076 / 1,855

26-49 Yrs
- 11,138 / 1,114
- Population: 9
- Per Capita Usage: 153
- 12,601 / 1,276

65+ Yrs
- 49,599 / 2,052
- Population: 398
- Per Capita Usage: -38
- 48,839 / 2,412

2011 | Population | Per Capita Usage | 2016

Source: QuintilesIMS, National Prescription Audit, US Census Bureau, Dec 2016

- Patients over 65 had declining per capita usage of prescriptions from 2011 to 2016 while driving most of the population growth in the country as "baby boomers" reached retirement age and many continue to live longer.

- Seniors aged 50-64 had the largest increase in prescription usage rates with their per capita usage rising from 25,256 per 1,000 of population to 29,076, and driving 244 million incremental prescriptions.

- Adults aged 26-64 accounted for 99% of the 402 million of incremental prescriptions from rising per capita usage, as both groups benefited significantly from Medicaid expansion and insurance exchanges under the ACA.

- Overall, the aging population is driving higher prescription usage. This is mainly occurring through population growth, with patients over 50 accounting for 682 million of the 884 million incremental prescriptions over the past five years, 70% of that from a rising share of the population, and 30% from higher usage, all from the 50-64 age group. Patients over 65 had declining usage.

Chart notes:

Prescription (TRx) counts are adjusted for length of prescriptions and re-aggregated, with prescriptions for 84 days supply or more factored by three, and those under 84 days unchanged. Patient age is reported anonymously along with other prescription information. Per capita estimates are based on overall U.S. population.

TRx growth due to population is determined by calculating excess prescriptions if population growth rate were applied to base TRx. Per capita usage is defined as additional TRxs over the 5 year period due to changes in the rate of per capita usage for the age group. Note that Population and Use are charted with consistent scale while Adjusted TRx and Per Capita TRx measures are not.

The largest prescription growth was in hypertension and mental health, with a decline in pain management

Chart 11: Adjusted Prescriptions and Growth by Therapy Class

Source: QuintilesIMS National Prescription Audit, Dec 2016
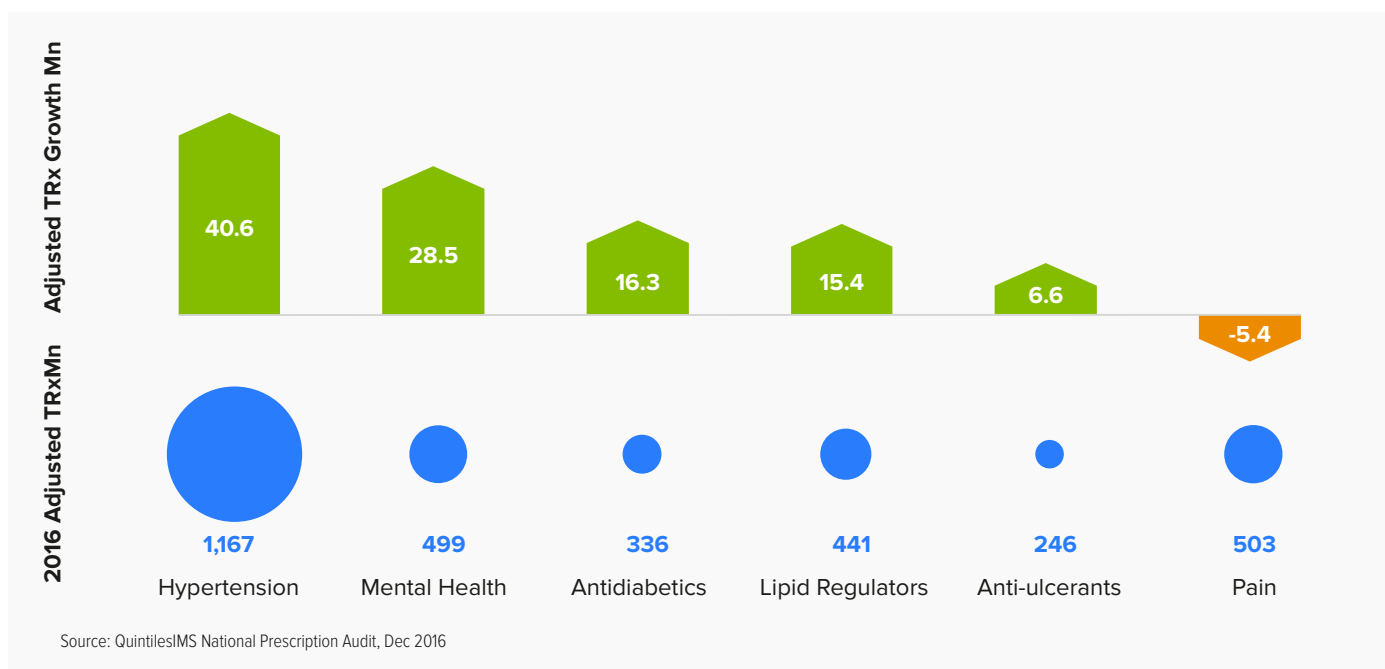
- Hypertension represents the largest therapy area by dispensed prescriptions, with 721 million prescriptions, 1.167 billion when adjusted for three month prescribing, and accounting for 19% of prescriptions in the country. Hypertension also increased by the largest amount in 2016, 40.6 million prescriptions, a 3.5% increase, only slightly faster than the market overall.

- Pain treatments were the second largest therapy area, with 460 million prescriptions, 503 million when adjusted for the smaller proportion of long-duration pain prescriptions, and declined 1% from 2015 as much of the country continues to implement dispensing volume controls on narcotic pain medicines.

- Mental health treatments, particularly more modern, second-generation anti-psychotics, have been widely used for decades, and the class has had relatively few new treatments. However recent patent expiries for products like aripiprazole (Abilify) have resulted in some incremental demand, as well as wider coverage of mental health services under the ACA.

- Growth for lipid regulators has been driven largely by generic medicines and only modest uptake of the newest treatments, the PCSK9s. Unadjusted prescriptions rose 4 million to 264 million in 2016, while widespread chronic use of cholesterol treatments is the norm and adjusted prescriptions rose 15.4 million to 441 million.

Chart notes:

Prescription counts are adjusted for length of prescriptions and re-aggregated, with prescriptions for 84 days supply or more factored by three, and those under 84 days unchanged. Therapy area definitions are proprietary to QuintilesIMS. Hypertension includes all types of hypertension treatments. Mental health includes antidepressants and antipsychotics. Antidiabetics includes all types of diabetes treatments. Lipid regulators includes all types of cholesterol treatments including statins, PCSK9s and other lipid regulating treatments. Pain medicines include narcotic and non-narcotic analgesics as well as muscle-relaxants and other topical pain treatments.

Cholesterol treatments have shifted to generics and new PCSK9s account for less than one percent of prescriptions

Chart 12: Statins & PCSK9 Unadjusted Dispensed Prescriptions Mn

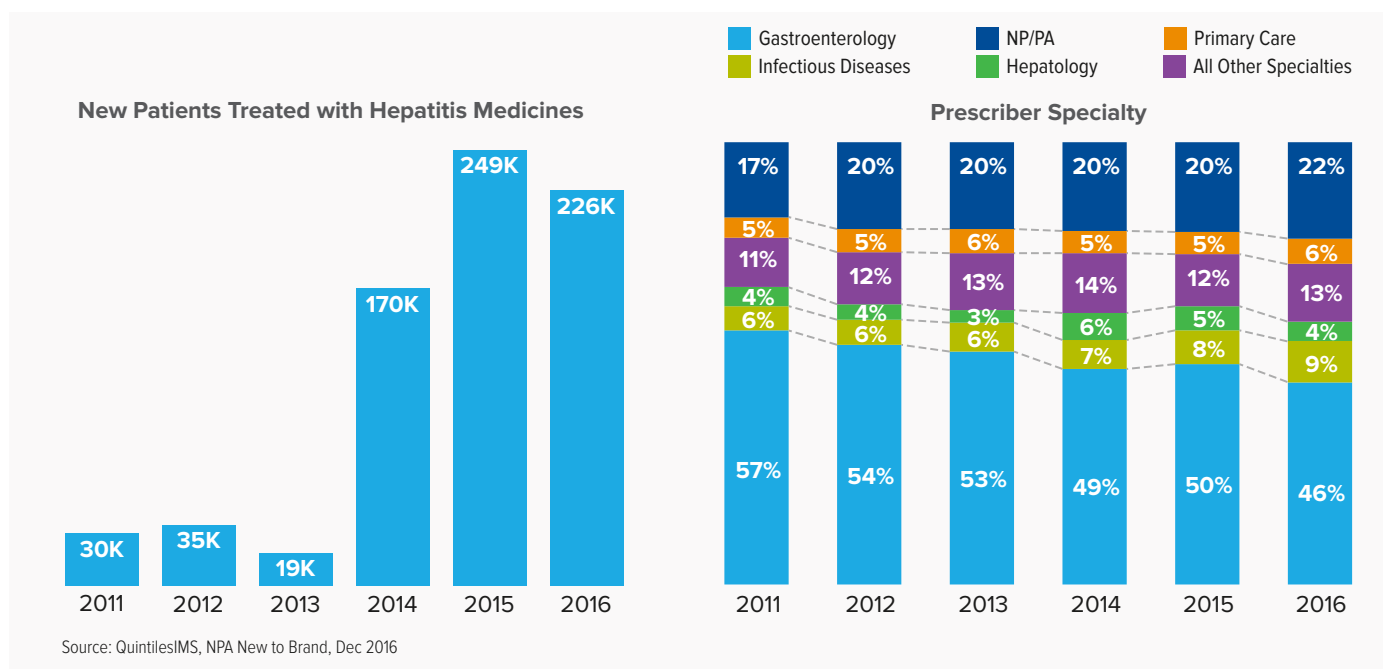Source: QuintilesIMS "SMART – Launch Edition", Dec 2016
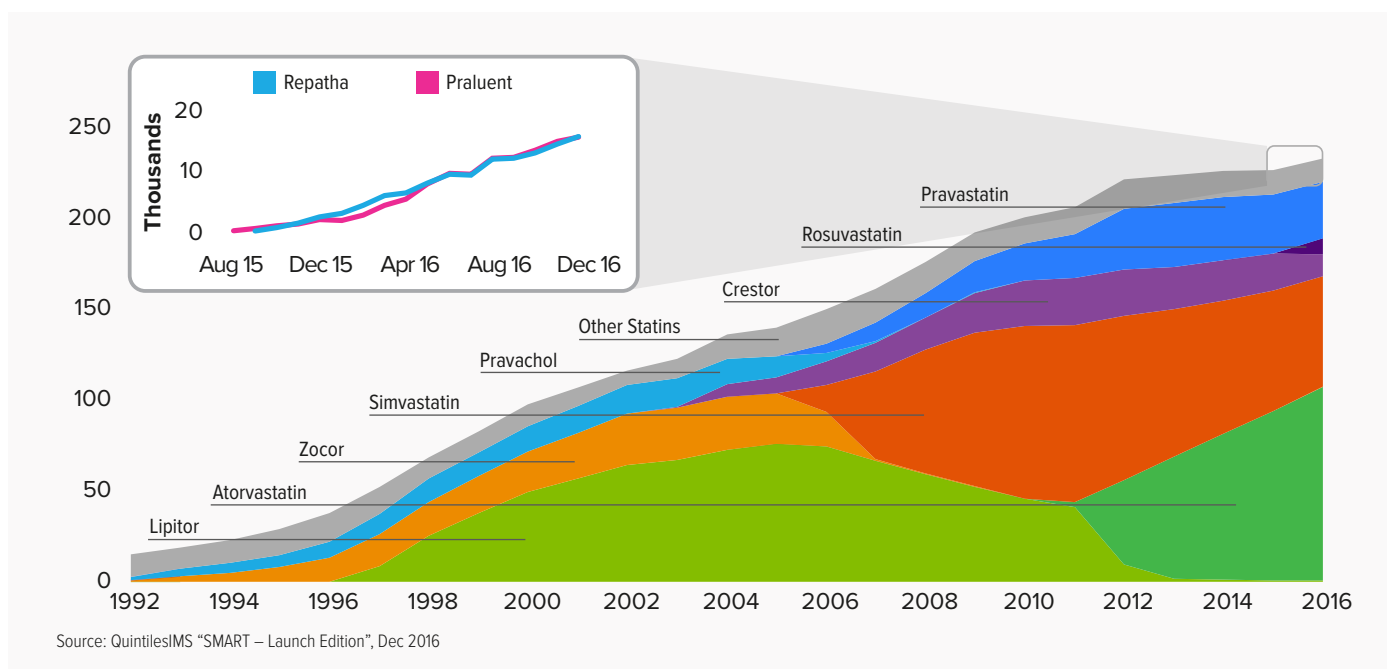
- Cholesterol prescriptions have increased by almost 10 times in 20 years, driven primarily by the introduction of atorvastatin (Lipitor) in 1997, and the dramatic reductions of cardiovascular and stroke events from the use of the class of drugs.

- The patent expiry of the 2nd leading product, simvastatin (Zocor), in 2006 led to a widespread shift in prescribing away from atorvastatin, which lasted until the 2011 patent expiry of Lipitor.

- Crestor, the other leading branded treatment until recently, lost patent protection in 2016 and rapidly converted to generic usage.

- The most recent introductions in treating cholesterol are the two new drugs using the PCSK9 mechanism which addresses very high LDL levels: alirocumab (Praluent) and evolocumab (Repatha).

- Both alirocumab and evolocumab have been used by relatively fewer patients, totaling fewer than 220,000 prescriptions in 2016, at least in part due to the strict conditions under which patients would be eligible for these newer drugs under insurer formularies.

- Key to these dynamics are the relative prices of treatments where older and generic statins average $0.05 to $0.50 per day, while newer generation PCSK9s have been reported as $14,000/year on a list-price basis.

- If patients were to face these costs because they were uninsured, or during a deductible or donut-hole, they would face a dramatic choice.

Chart notes:

"SMART – Launch Edition" includes brand and generic unadjusted dispensed prescriptions since 1992.

The rate in specialist prescribing has declined as fewer new patients received hepatitis C medicines in 2016

Chart 13: Patients Treated with Hepatitis Medicines

Legend: Gastroenterology, NP/PA, Primary Care, Infectious Diseases, Hepatology, All Other Specialties

New Patients Treated with Hepatitis Medicines

Year	Patients
2011	30K
2012	35K
2013	19K
2014	170K
2015	249K
2016	226K

Prescriber Specialty

	2011	2012	2013	2014	2015	2016
NP/PA	17%	20%	20%	20%	20%	22%
Primary Care	5%	5%	6%	5%	5%	6%
All Other Specialties	11%	12%	13%	14%	12%	13%
Hepatology	4%	4%	3%	6%	5%	4%
Infectious Diseases	6%	6%	6%	7%	8%	9%
Gastroenterology	57%	54%	53%	49%	50%	46%

Source: QuintilesIMS, NPA New to Brand, Dec 2016

- Fewer new patients received treatment for hepatitis C in 2016 than in the prior year, while the total number treated in the last three years reached an estimated 645,000 patients, with over 90% "cured".

- Estimates vary but have been in the range of 3-5 million infected patients in the U.S., with half undiagnosed. Despite the significant impact of newly cured patients, between 2.4 to 4.4 million infected patients remain.

- The recent increase in treated patients likely relates to the backlog of "warehoused" patients (diagnosed but previously untreated), curing between 13-22% of infected patients, though the exact ratio remains highly uncertain.

- The widely discussed high prices of these treatments is estimated to be 50% lower in 2016 after negotiated rebates, but the media coverage may have influenced some patients to avoid or delay seeking care.

- With 72% of treatments under the direction of a specialist of some kind, many patients would have had to pay two visit copays, one for a specialist and one for a primary care referral required by their insurer.

Chart notes:

New patients are defined as new to brand prescriptions for Daklinza, Incivek, Victrelis, Sovaldi, Olysio, Harvoni, Epclusa Technivie, Viekira Pak and Viekera XR. Patient estimates are adjusted based on company reports and QuintilesIMS estimates.

Patient out-of-pocket costs

- Average patient out-of-pocket costs declined as more patients received zero out-of-pocket cost prescriptions or paid lower costs or used generics.

- Patient exposure to costs varies during the year, while an increasing number of patients are reaching maximum out-of-pocket costs during the year.

- Coupons reduce patient costs for brands, and manufacturer out-of-pocket offsets have increased steadily along with patient cost exposure.

- One in five commercial branded prescriptions is filled using a copay assistance coupon, typically reducing patient costs to a level similar to a standard copay.

- Patients paying for their branded prescriptions in the deductible phase of their health plan accounted for 14% of branded prescriptions but paid 39% of the total out-of-pocket costs.

- Abandonment rates for brands are 2.5 times higher when the patient is in the deductible phase of their plan and sees the full cost of the medicine they have been prescribed.

Prescriptions dispensed at zero patient out-of-pocket cost reached thirty percent in 2016

Chart 14: Patient Out-of-Pocket Distribution and Average Costs

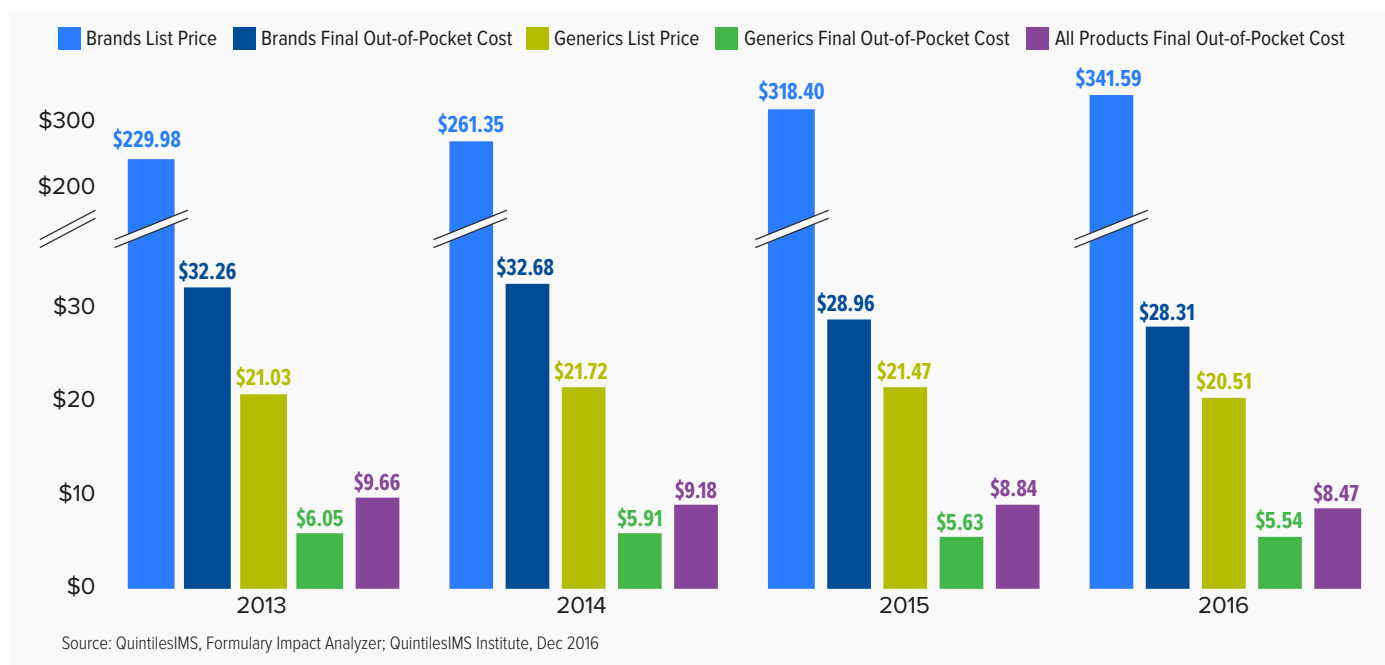Source: QuintilesIMS, Formulary Impact Analyzer; QuintilesIMS Institute, Dec 2016
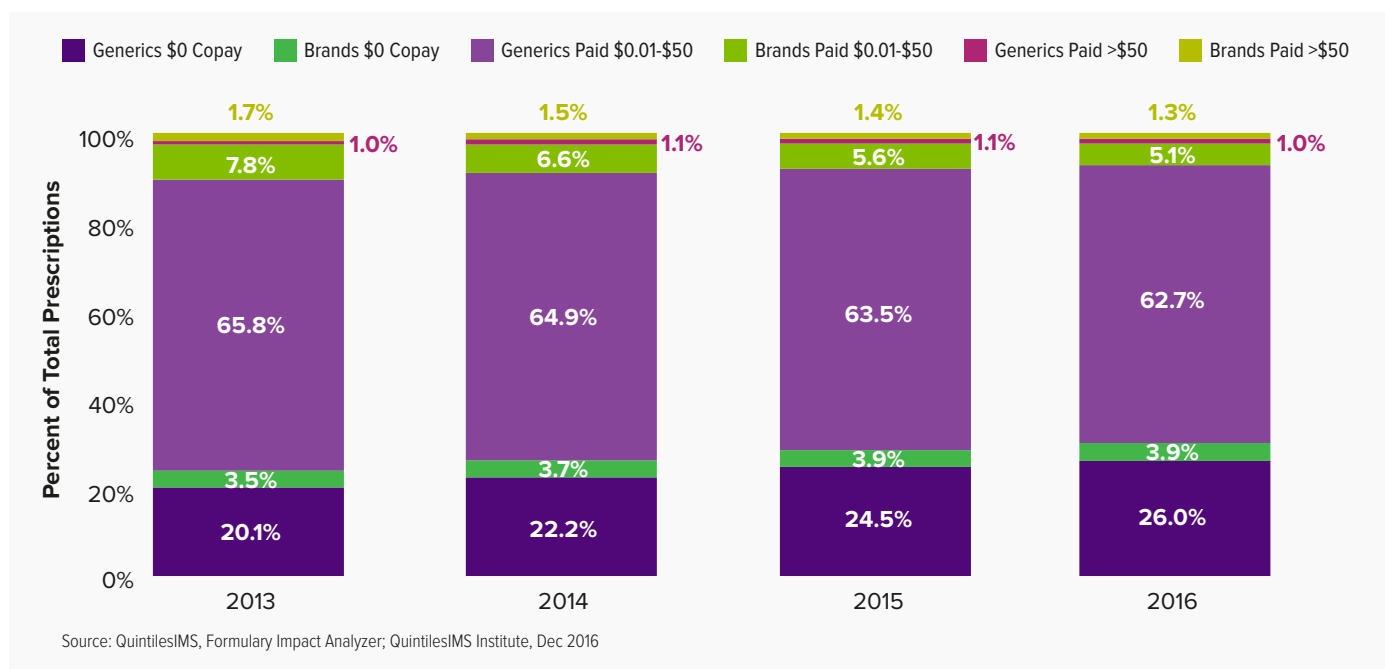
- Patient out-of-pocket costs are determined by their insurance plan and include a variety of provisions that can result in a zero out-of-pocket cost.

- Medicaid patients typically have zero out-of-pocket costs or often less than $10, while commercially insured patients would have a zero dollar copay for generics in some plans, or if they had surpassed an out-of-pocket maximum.

- All patients receive zero out-of-pocket costs for preventive treatments and for generic contraceptives under the Affordable Care Act.

- Under these various conditions of combined generics and brands, 29.9% of prescriptions have been dispensed at zero patient out-of-pocket cost including brands and generics, up 1.5% since 2015, all due to increased use of zero cost generics.

- The total share of prescriptions where patients paid some amount less than $50 declined by 1.3% to 67.8% in 2016.

- The proportion of claims with patient cost exposure greater than $50 also declined slightly from 2.5% to 2.3% in 2016.

Chart notes:

Cost exposure is calculated using paid and reversed claims, includes the impact of coupon if applicable and is normalized to 30 days.

Since 2013, average out-of-pocket costs for all brand and generic prescriptions has decreased by $1.19

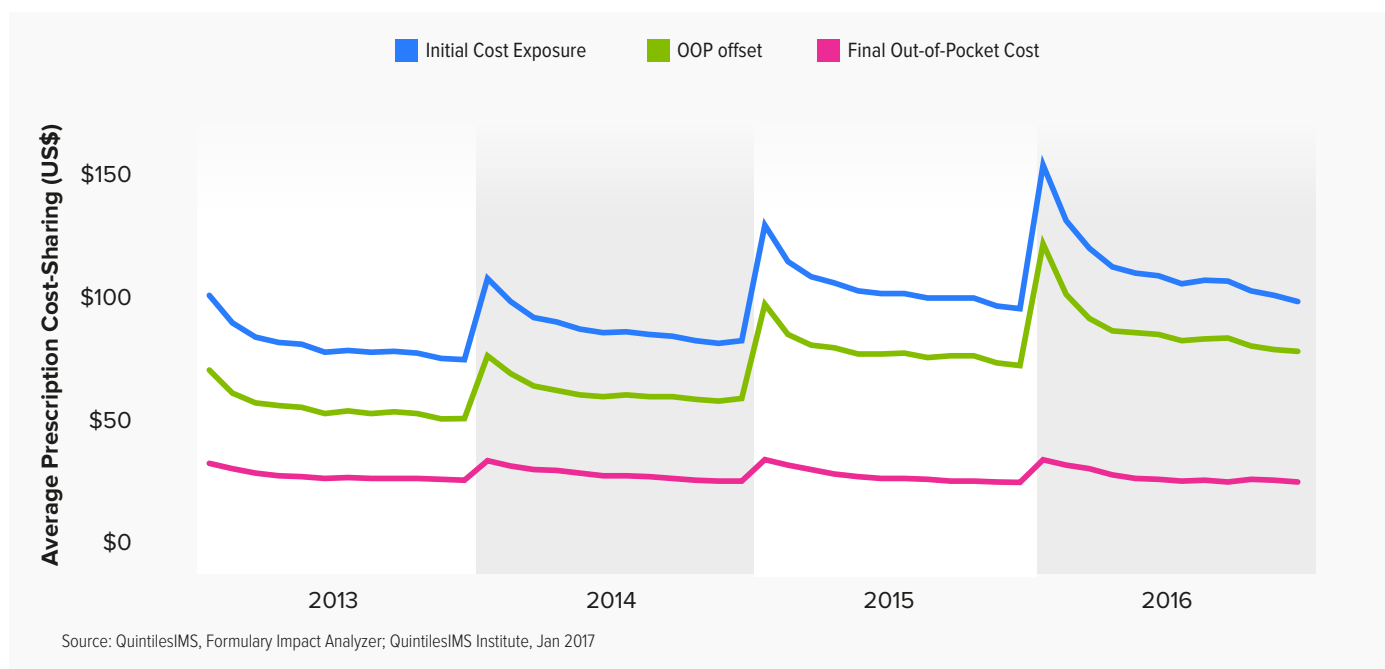**Chart 15: Patient Cost Exposure and Patient Out-of-Pocket Cost**

■ Brands List Price ■ Brands Final Out-of-Pocket Cost ■ Generics List Price ■ Generics Final Out-of-Pocket Cost ■ All Products Final Out-of-Pocket Cost

2013: $229.98 | $32.26 | $21.03 | $6.05 | $9.66
2014: $261.35 | $32.68 | $21.72 | $5.91 | $9.18
2015: $318.40 | $28.96 | $21.47 | $5.63 | $8.84
2016: $341.59 | $28.31 | $20.51 | $5.54 | $8.47

Source: QuintilesIMS, Formulary Impact Analyzer; QuintilesIMS Institute, Dec 2016

- Average patient out-of-pocket costs declined from $9.66 in 2013 to $8.47 in 2016, with 2016 brand costs declining to $28.31 from $32.36 in 2013 and generics dipping to $5.54 from a high of $6.05 in 2013.

- The list prices of brands continue to be far higher than the average paid by patients, as few patients are exposed to those costs in their insurance plans.

- The list price of branded products applies to patients in a deductible period or those with a standard benefit with a 'donut hole' in Medicare Part D, and could in theory apply for only part of the year, and then reduce as a result of the design of their insurance plan.

- List prices also apply for the uninsured or those whose insurance does not cover the brand in question.

- The average list price for brands averaged 12 times higher than the average out-of-pocket cost for patients in 2016 compared to 3 times higher for generics.

Chart notes:

Cost exposure is calculated using paid and reversed claims, includes the impact of coupon if applicable and is normalized to 30 days. List price is defined as the total amount to be paid to pharmacies by insurers and patients.

Coupons and manufacturer out-of-pocket offsets have increased steadily as patient cost exposure has increased

Chart 16: Patient Cost-Sharing and Manufacturer Out-of-Pocket Offsets for Branded Medicines in Commercial Plans

Source: QuintilesIMS, Formulary Impact Analyzer; QuintilesIMS Institute, Jan 2017

- As patient cost exposure has increased year over year, manufacturers have increased their out-of-pocket offsets through coupons and other savings programs, offsetting cost such that final patient out-of-pocket remains fairly stable.

- The effect of coupons or vouchers is to offset a significant amount of patient cost and, as they are paid for by manufacturers, they are referred to as out-of-pocket offsets.

- Manufacturers' out-of-pocket offsets are especially high in the first quarter of a calendar year, when some patients are in the deductible phase of coverage.

- Initial cost exposure is strongly linked to list prices, especially as more patients have insurance with deductibles.

- As a result, manufacturer out-of-pocket offsets increase over time as patients are exposed to higher costs — especially in deductibles.

Chart notes:

Averages are calculated among paid claims where a co-pay card is used as the secondary payer and normalized to 30 days. OOP = out-of-pocket

One in five patients fills a prescription using a copay assistance coupon, reducing costs on par with a standard copay

Chart 17: Branded Coupon Redemption Rate in Commercial Plans in Select Therapies

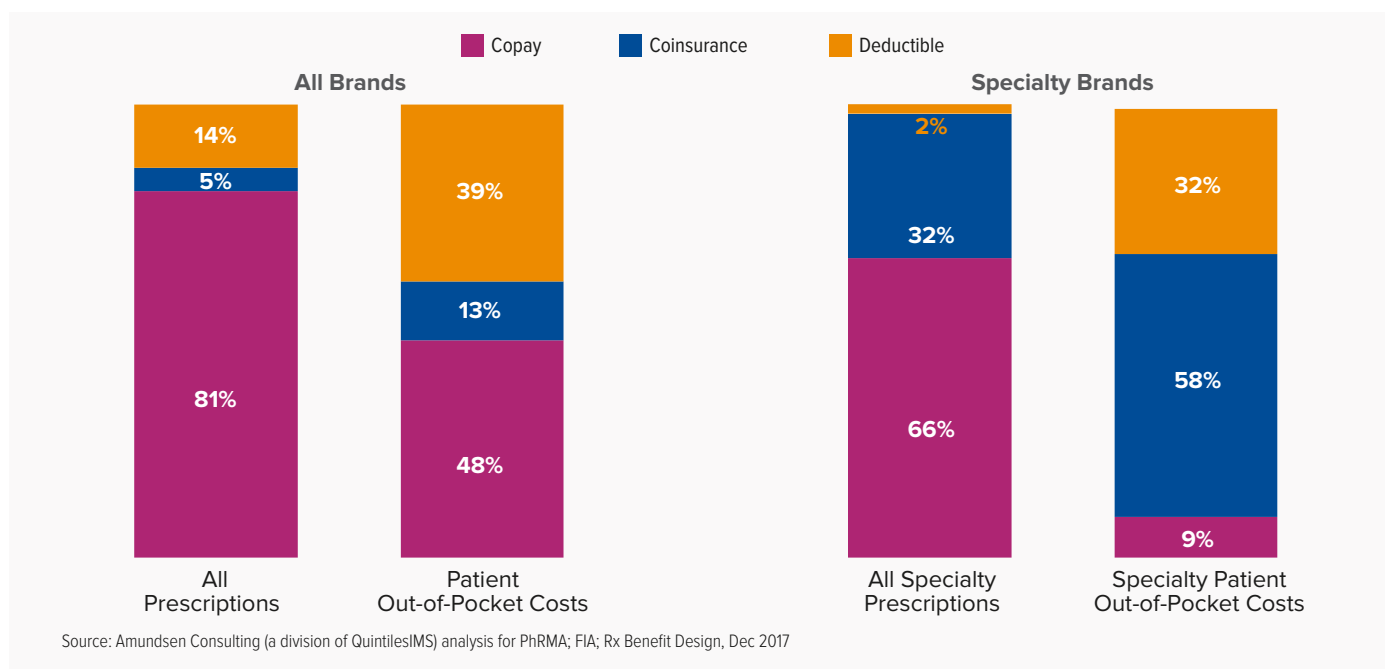Source: QuintilesIMS Formulary Impact Analyzer, Jan 2017
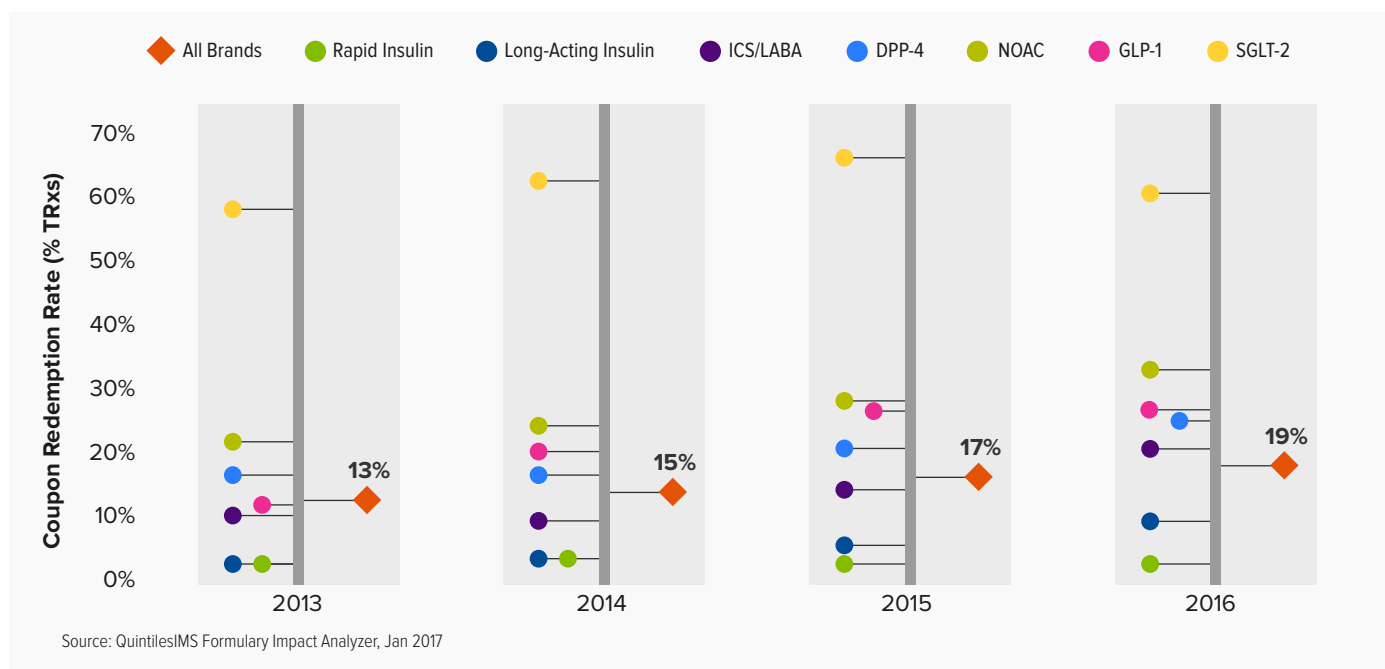
- Savings programs have increased in prevalence, accounting for one in five commercial brand claims in 2016.

- This varies significantly across therapy areas; some classes have less than 10% using coupons and others resulting in nearly 2/3rds of branded prescriptions in commercial plans using a coupon.

- There are several factors that drive the wider use of coupons including lack of insurer coverage in a formulary, coverage with coinsurance resulting in a significant cost or a high list price and a patient being in their deductible phase.

- Some newer therapy areas in diabetes, such as DPP-4, GLP-1 and SGLT-2, have significant coupon usage for all of these reasons.

- Novel Oral Anticoagulants (NOAC) launched in the past five years have seen rising coupon usage at least partly because of the wide availability of older generic options, and some insurers not placing the newer treatment options on a preferred formulary tier.

Chart notes:

ICS/LABA: treatments for Chronic Obstructive Pulmonary Disease (COPD) comprised of a combination of inhaled corticosteroid/long-acting beta-agonist inhalers

Patients in the deductible period paid for almost forty percent of out-of-pocket costs for branded prescriptions

Chart 18: Distribution of Prescriptions by Out-of-Pocket Costs for Branded Medicines in Commercial Plans

Legend: Copay · Coinsurance · Deductible

All Brands

Bar	Copay	Coinsurance	Deductible
All Prescriptions	81%	5%	14%
Patient Out-of-Pocket Costs	48%	13%	39%

Specialty Brands

Bar	Copay	Coinsurance	Deductible
All Specialty Prescriptions	66%	32%	2%
Specialty Patient Out-of-Pocket Costs	9%	58%	32%

Source: Amundsen Consulting (a division of QuintilesIMS) analysis for PhRMA; FIA; Rx Benefit Design, Dec 2017

- Patients' exposure to costs varies considerably and those with the greatest cost sharing bear substantially more costs than other patients.

- Together, deductibles and coinsurance set patient out-of-pocket costs based on list prices and 19% of commercial brand prescriptions are paid in this way, accounting for 52% of out-of-pocket costs.

- Specialty prescriptions are set based on list prices 34% of the time and that accounts for 91% of out-of-pocket spending by patients (data not shown).

- Patients with a deductible plan and paying for their prescriptions in the deductible period accounted for 14% of branded commercial scripts but paid 39% of the out-of-pocket costs for the group of patients.

- Patients with a specialty prescription in the deductible accounted for 2% of prescriptions but 32% of out-of-pocket costs.

- Insurance designs with traditional copays continue to account for a majority of prescription volumes and substantially insulate patients from costs.

- Brand commercial prescriptions with a copay were 81% of dispensed prescriptions but with set copay levels drove only 48% of out-of-pocket costs.
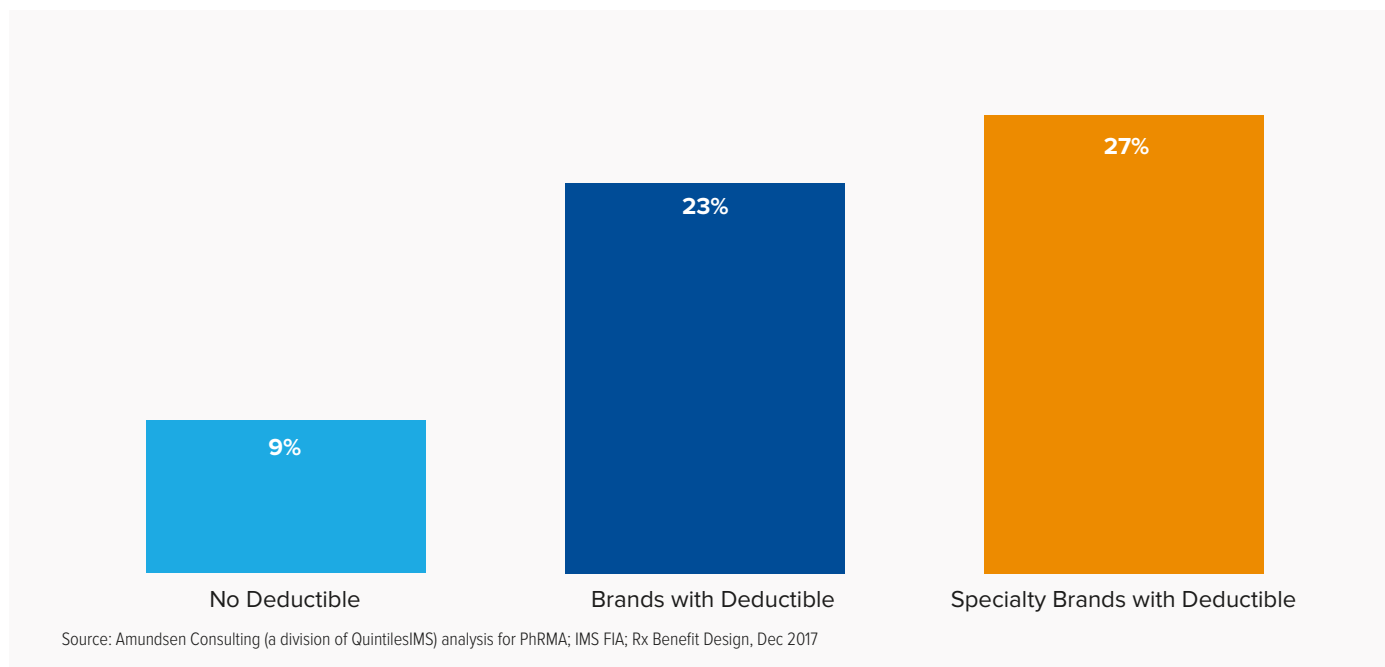
Chart notes:

Deductible includes prescriptions adjudicated entirely within the deductible and prescriptions for which the full cost of the medicine was less than the patient's copay, resulting in the patient paying the full amount out-of-pocket. Coinsurance includes prescriptions adjudicated where the patient's copay was a portion of the cost. Copay includes prescriptions where the patient's copay is equivalent to a set amount and is consistent across patients.

Full report available at: http://www.phrma.org/report/commercially-insured-patients-pay-undiscounted-list-prices-for-one-in-five-brand-prescriptions-accounting-for-half-of-out-of-pocket-spending-on-brand-medicines

Almost 1 in 4 prescriptions are abandoned by patients during their deductible phase

Chart 19: Abandonment Rates for Branded Medicines in Commercial Plans

Source: Amundsen Consulting (a division of QuintilesIMS) analysis for PhRMA; IMS FIA; Rx Benefit Design, Dec 2017

- The most common commercial insurance plans determine patient cost as either a set copay, a percentage level of coinsurance, or with a preliminary deductible.

- When patients' costs for medicines are under co-insurance or a copay, fewer than 1 in 10 patients with commercial insurance abandons those prescriptions at the pharmacy.

- Patients with a deductible pay the full cost of their medicines until a set level of costs have been accrued and then a copay or a percentage of coinsurance would apply, often followed by a cap or out-of-pocket maximum per year.

- When a patients' costs are in a deductible, prior to shifting to coinsurance or reaching an out-of-pocket maximum, they are 2.5 times more likely to abandon brand prescriptions (23% vs. 9%).

- Specialty medicines are even more likely to be abandoned, with 27% of patients failing to receive a medicine prescribed by their doctor and approved under their insurance.

Chart notes:

Abandonment is defined as prescriptions which were cancelled by the patient or not picked up at the pharmacy within 14 days of approval. Deductible includes prescriptions adjudicated entirely within the deductible and prescriptions for which the full cost of the medicine was less than the patient's copay, resulting in the patient paying the full amount out-of-pocket.

Full report available at:http://www.phrma.org/report/commercially-insured-patients-pay-undiscounted-list-prices-for-one-in-five-brand-prescriptions-accounting-for-half-of-out-of-pocket-spending-on-brand-medicines

Outlook to 2021

- The outlook for spending has been revised downward as expectations for new products and price increases have moderated.

- Invoice price growth for protected brands is projected to be between 7-10% down from 8-11% in the prior outlook.

- Net price growth for protected brands is forecast to be 2-5% through 2021.

- Launches of innovative medicines are expected to average 40-45 per year to 2021.

- Patient use of new treatments slowed in 2016 and is expected to slow further in 2017 before recovering to drive historically high levels of $15-17Bn of spending growth from 2018 to 2021.

- The late phase R&D pipeline remains robust and will ensure an ongoing high number of new brand launches by 2021, especially cancer treatments.

- The impact of losses of exclusivity are expected to be 50% greater in the next five years, including the impact of biosimilar introductions.

- Medicines spending growth slows in the near term due to fewer new products and lower price growth, but recovers to mid-single digit growth by 2021.

The outlook for spending has been revised downward as expectations for new products and price increases have moderated

Chart 20: U.S. Spending and Growth 2015-2021, US$Bn

Source: Market Prognosis, Sep 2016; QuintilesIMS Institute, Mar 2017
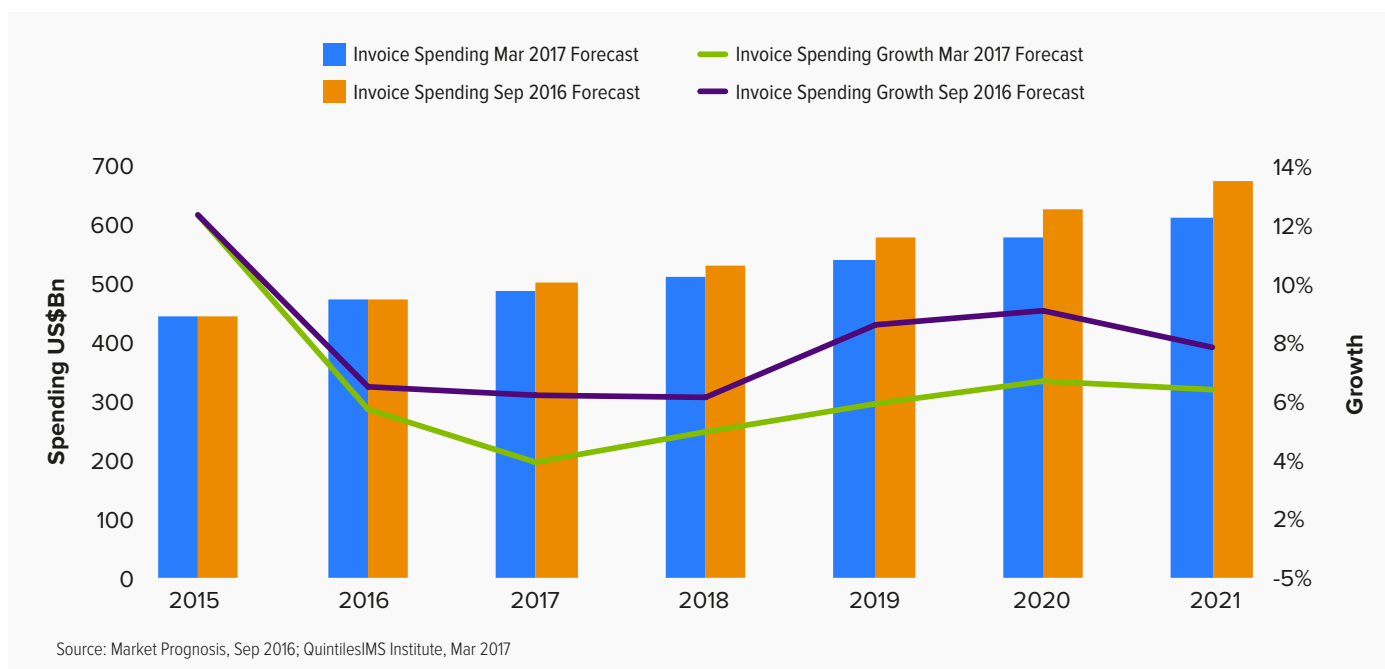
- As a result of lower expectations for invoice-price increases for brand products and a downward revision of new product expectations, the overall growth outlook has been revised downward by 2% to a CAGR of 4-7% from the previously estimated 6-9%.

- The U.S. will still see a 30% increase in spending over the next five years, compared to 39% in the past five years when growth averaged 5-8%.

- Price growth remains the subject of intense scrutiny and list price increases, which slowed dramatically in 2016, are projected to stay at lower levels through the forecast period.

- Spending growth in 2014 and 2015 were atypical relative to the long-term trend and were driven by wider use of hepatitis C treatments, less loss of exclusivity and higher price increases.

- New product growth is expected to be between $15-17Bn per year in 2018-2021 after only $9Bn in 2017 mostly due to an unusually low number of new medicine launched in 2016.

- The Affordable Care Act will continue to impact medicine spending over the next five years largely due to the impact expanded insurance coverage has on patient usage of medicines and the continuation of payment and delivery system reforms.

- Uncertainty looms over the healthcare system, however, as evidenced by the failed attempt to repeal and replace the ACA in March 2017.

Chart notes:

Chart compares Spending and Growth projected in the September 2016 and March 2017 updates of QuintilesIMS Market Prognosis. The September edition is based on mid-year actual data and March edition is based on year-end data. In addition to changes in baseline data, key events have been reinterpreted including brand price trends, expectations for new products, patent expiry impact and include a modest (<0.3%) revision in growth due to changed expectations around healthcare reform.

Net price growth for protected brands is forecast to be 2-5% through 2021

Chart 21: Protected Brand Invoice and Net Price Growth

Source: QuintilesIMS, National Sales Perspectives, QuintilesIMS Institute, Mar 2017
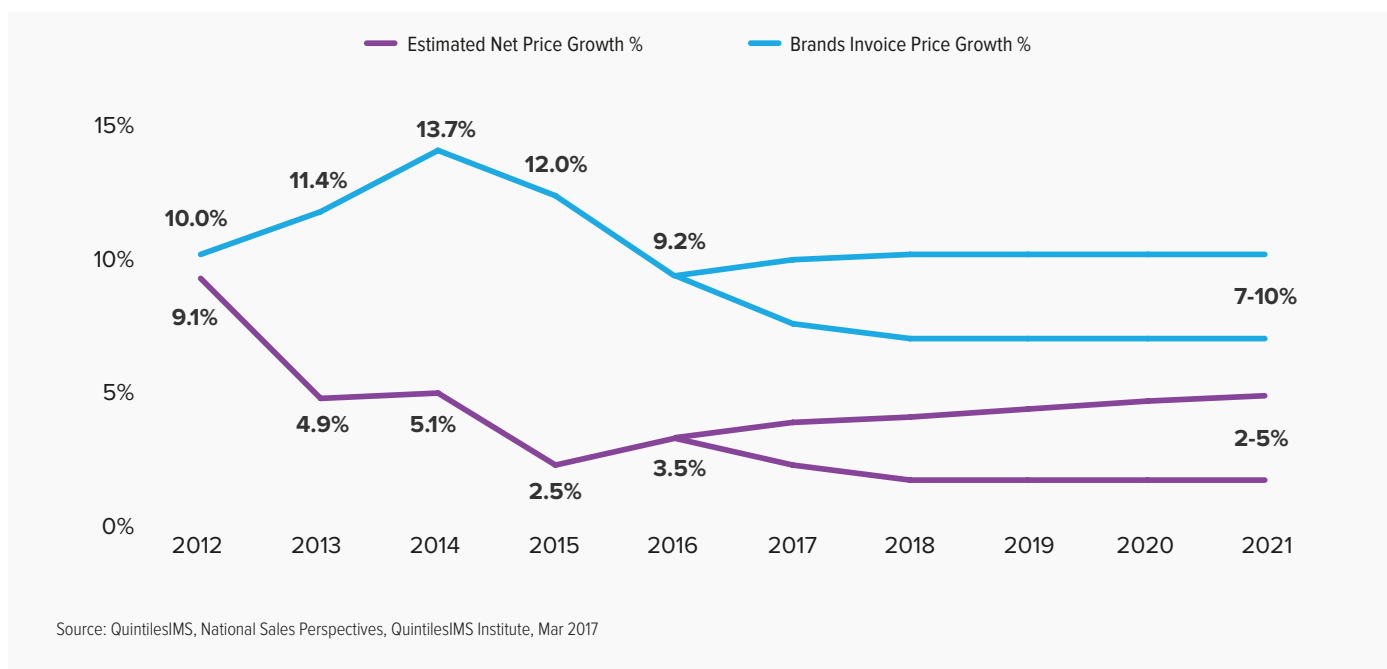
- Although price growth for protected brands averaged 9.2% for the year in 2016, the average increase in December 2016 was only 7.0% over the prior year, and it is still possible that invoice price trends could slow further below the projected 7-10% range.

- Net price growth is likely to remain in the 0-3% range as the structural drivers of low net price growth are expected to remain in effect including payer pressure and influence on prescribing.

- As public pressure on drug pricing has escalated, it is notable that list price increases have slowed significantly.

- Some products and therapy areas may be able to increase net prices to a greater or lesser extent, linked to the level of differentiation and/or competition in their markets.

- The lower level of net price growth and the continued gap between invoice and net price growth reflects the higher levels of off-invoice discounts, rebates, and price concessions since 2012.

- Increasingly, insurers and manufacturers have negotiated "price-protection" terms into contracts which drive higher rebates if list prices rise above agreed levels, and these terms have coincided with the period of higher levels of invoice price growth since 2012.

Chart notes:

"Invoice" values are QuintilesIMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. "Net" values denote company recognized revenue after discounts, rebates and other price concessions. Results are based on a comparative analysis of company reported net sales and IMS Health reported sales and prices at product level for branded products representing 79-93% of brand spending in the period displayed. All growth numbers calculated over same cohort of products in the prior year.

Launches of innovative medicines are expected to average 40-45 per year to 2021

Chart 22: New Active Substances (NAS) Launched in the U.S. 2007-2021

Source: QuintilesIMS LifeCycle New Product Focus, QuintilesIMS Institute, Mar 2017
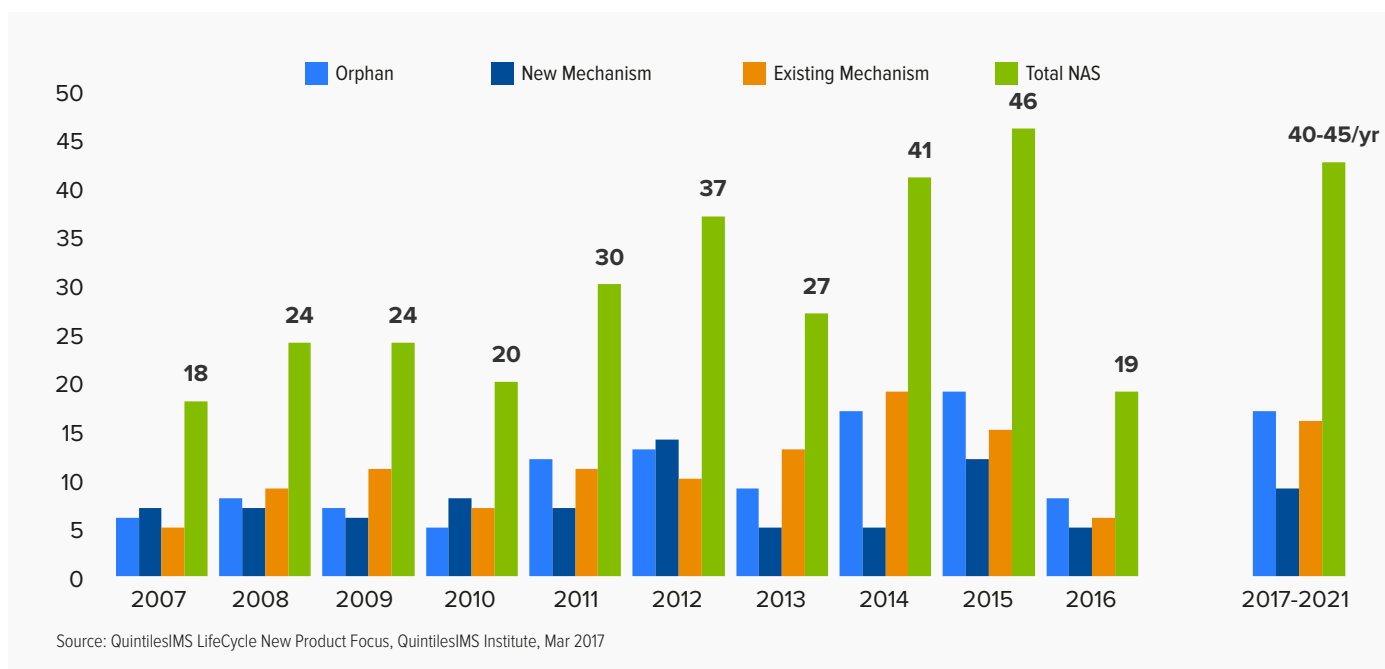
- Nineteen NASs were launched in 2016, fewer than half the number launched in either of the prior two years and lower than all but one of the last ten years.

- The FDA has noted that fewer applications were received in 2016. This in part was due to an increase in applications that were sent back for revision by the applicants and there were some drugs which were handled unexpectedly quickly, actually approving them in 2015.

- The level of year to year fluctuation in new drug launches is normal and does not necessarily suggest a substantial revision in the outlook for new medicines.

- Medicines are increasingly specialty and/or orphan drugs, and this trend is expected to continue with another 80-90 orphan drugs approved through 2021, compared to the 66 orphan drugs launched in the past five years.

- Two-thirds of all orphan drugs were for oncology indications, while the remaining indications targeted rare diseases, such as hemophilia B and cystic fibrosis.

- The outlook for new mechanisms and treatment options across a range of diseases remains robust as summarized in the December 2016 QuintilesIMS Institute report *Outlook for Global Medicines through 2021: Balancing Cost and Value.*

Chart notes:

A New Active Substance (NAS) is 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 refers to the first product with a new mechanism of action for its FDA approved indication. Existing Mechanism refers to subsequent products with existing mechanisms of action for an indication. Orphans are drugs with one or more orphan indications approved by the FDA at product launch. Products are not reclassified as orphan if they subsequently receive an approval for an orphan designated indication.

New brand spending growth expected to be $15-17Bn from 2018 through 2021

Chart 23: New Brand Invoice Spending Growth US$Bn

Source: QuintilesIMS, National Sales Perspectives, Dec 2016; Market Prognosis, Mar 2017
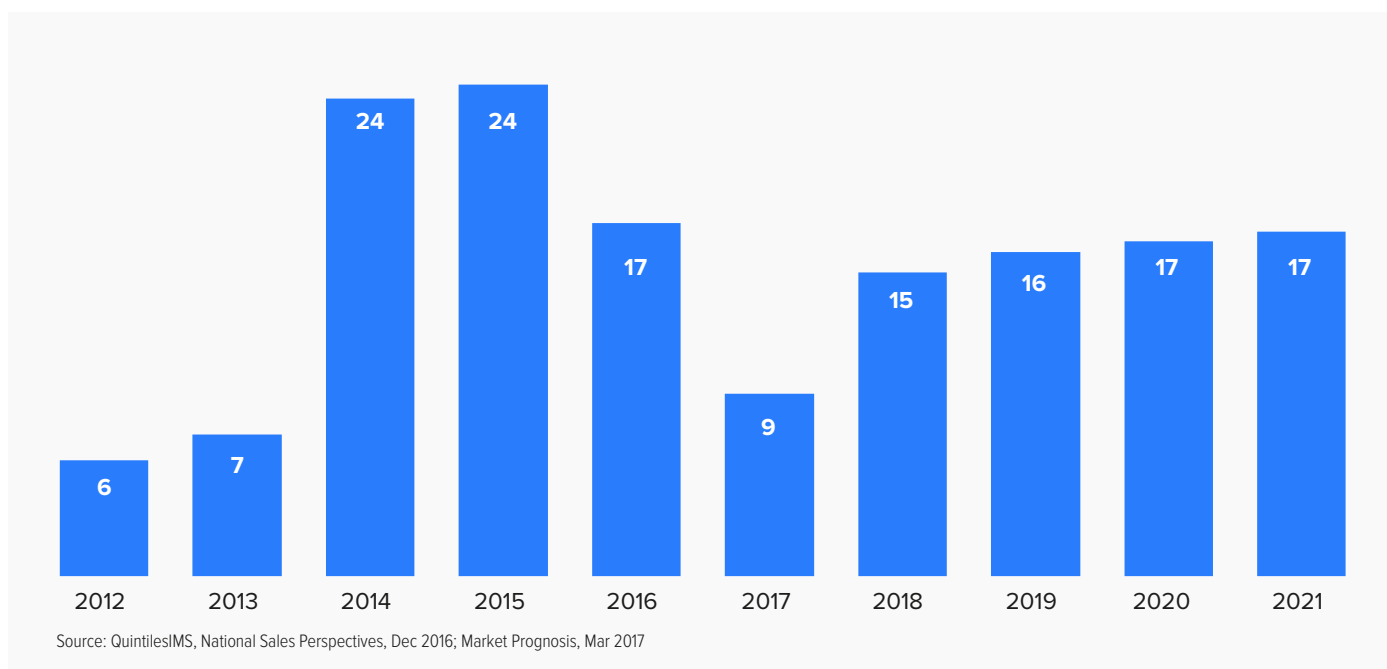
- New brand spending growth slowed in 2016 as recently launched hepatitis C treatments had lower sales.

- Growth from other previously launched new therapies continued relatively strong in 2016, however the dramatic reduction in the number of, and spending from, new drugs launched in 2016 is expected to result in a slowing contribution from new products in 2017.

- New medicine spending growth is expected to be driven by: newer generation immuno-oncology treatments, the rise of immunology treatments in a wider range of autoimmune disorders than previously, and a continued flow of orphan drugs.

- Medicines with limited differentiation from existing standards of care or competing new products are expected to face significant resistance from payers and will likely pay significant concessions in the form of rebates or patient copay assistance coupons, reducing these invoice-level projections by 1/3rd or more.

- The contribution to growth from new products is still expected to be substantially higher than it was prior to 2014, when the average annual contribution was $5-7Bn.

Chart notes:

Spending based on invoice prices. New brands are defined as brands launched in the last twenty-four months. Modeling of expected growth from new products based on Market Prognosis and based on a risk adjusted review of late-lifecycle pipeline.

The late phase R&D pipeline remains robust and will see an ongoing high number of new brand launches by 2021

Chart 24: Late Phase R&D Pipeline by Top Therapy Areas

Source: QuintilesIMS, LifeCycle R&D Focus, Dec 2016; QuintilesIMS Institute, Mar 2017
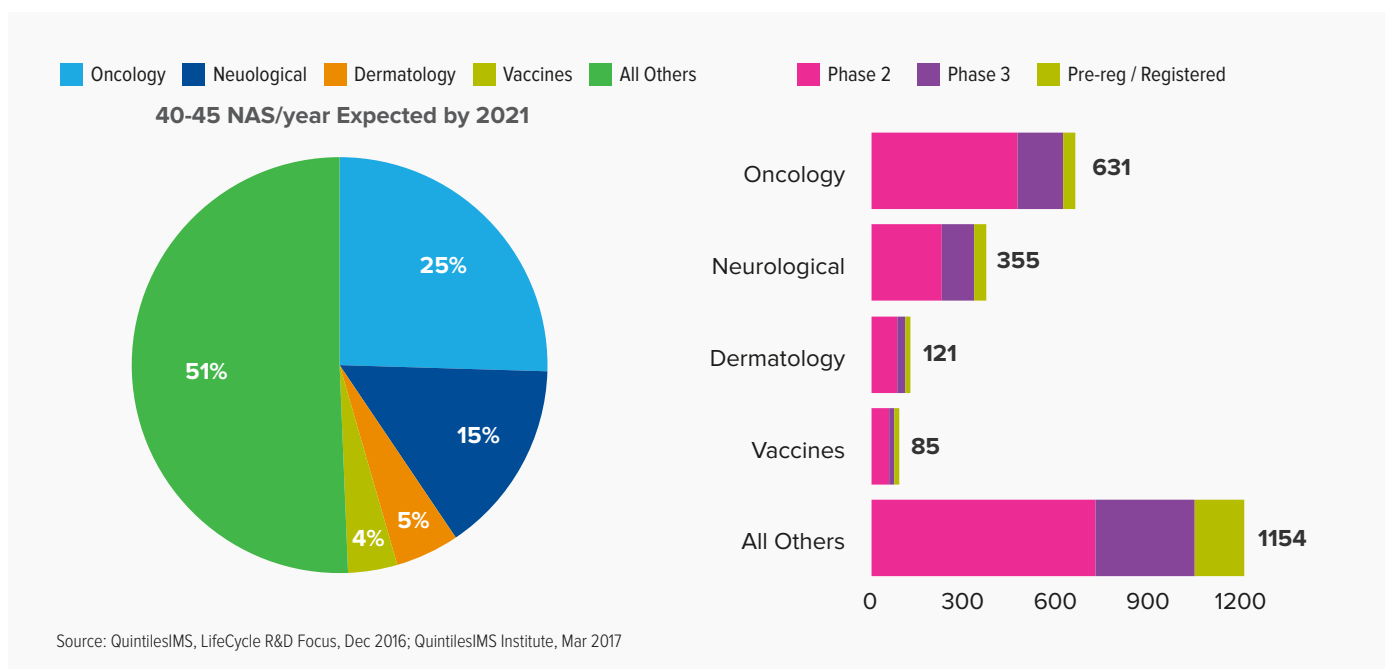
- The 2016 late phase pipeline includes 2,346 novel products, relatively unchanged from a year ago.

- Of over 630 distinct research programs in Phase II or later, 37% are in the specialty market.

- A quarter of the pipeline is comprised of oncology drugs, of which 25% are indicated for blood cancers.

- As more new cancer treatments reach the market, they are being adopted extremely rapidly, sometimes being subsequently superseded by even newer treatments within just a few years.

- The pace of development in cancer treatments is accelerating, not just because of the number of new medicines in research, but the combination regimens that may have greater effects than the individual drugs, and because of the continuous development of biomarkers and the potential to more appropriately target the right drug to the right patient with minimal waste and risk of non-response.

- Pain, Alzheimer's disease and epilepsy are the top three indications in the neurological pipeline, each addressing significant unmet needs but also raising the potential of significant policy and budget questions.

Chart notes:

Late phase pipeline is defined as active programs (activity in past 3 years) in Phase II through Registered. Pipeline products are categorized by their most-advanced indication, and additional indications for pipeline drugs still in earlier phases or for already marketed drugs are not counted.

A New Active Substance (NAS) is a new molecular or biologic entity or combination where at least one element is new.

CNS stands for central nervous system and includes the pain market.

Impact of losses of exclusivity are expected to be 50% greater in next five years including biosimilars

Chart 25: Lower Brand Spending Due to Loss of Exclusivity US$Bn

Source: QuintilesIMS Market Prognosis, National Sales Perspectives, QuintilesIMS Institute, Mar 2017
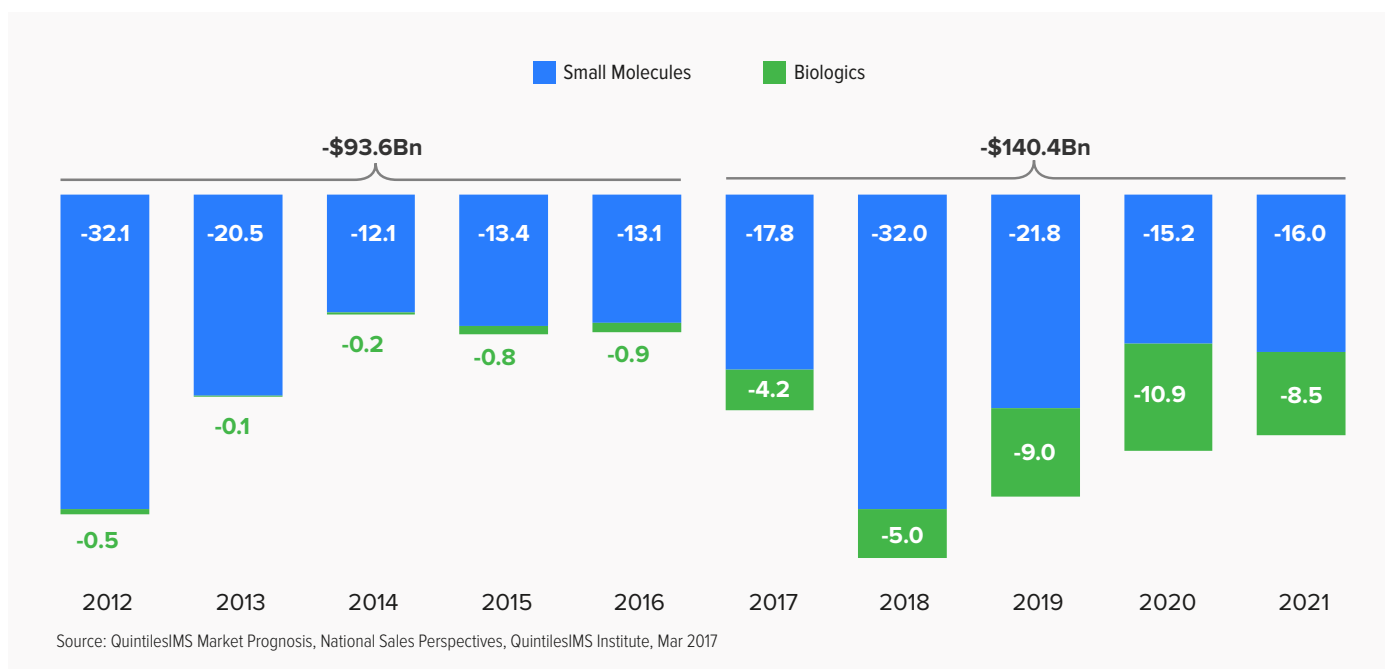
- The impact of patent expiries has been relatively unchanged for the past three years but is expected to increase sharply.

- The total impact of patent expiries is expected to be 50% higher in the next five years, however, excluding the impact of biosimilars the next five years will see $102.9Bn of impact compared to $91Bn in the last five years.

- Biosimilar impact is expected to be highly variable and each molecule will present different challenges to payers, providers, patients, originators and biosimilar manufacturers.

- The largest group of original biologics facing biosimilar competition are expected in 2019, including the largest selling branded medicine in 2017, adalimumab (Humira).

- Initial biosimilar uptake has been relatively muted, unlike a traditional generic, with limited impact on spending as discounts have also been modest in the 15-30% range.

- While the impact of each biosimilar is highly uncertain, one important and likely outcome will be the ability of payers to use the presence of biosimilars to better negotiate prices on the originator product and other competing brands.

Chart notes:

Lower brand spending based on invoice prices. Historic impacts from QuintilesIMS National Sales Perspectives, forecast impacts are modeled by projecting individual products sales growth to the point of patent expiry and then modeling expected impact based on historical analogues and actual data for in-progress events.

Net total spending growth will average 2-5% over the next five years

Chart 26: Total Spending on Medicines US$Bn

Source: QuintilesIMS Market Prognosis, QuintilesIMS Institute, Mar 2017
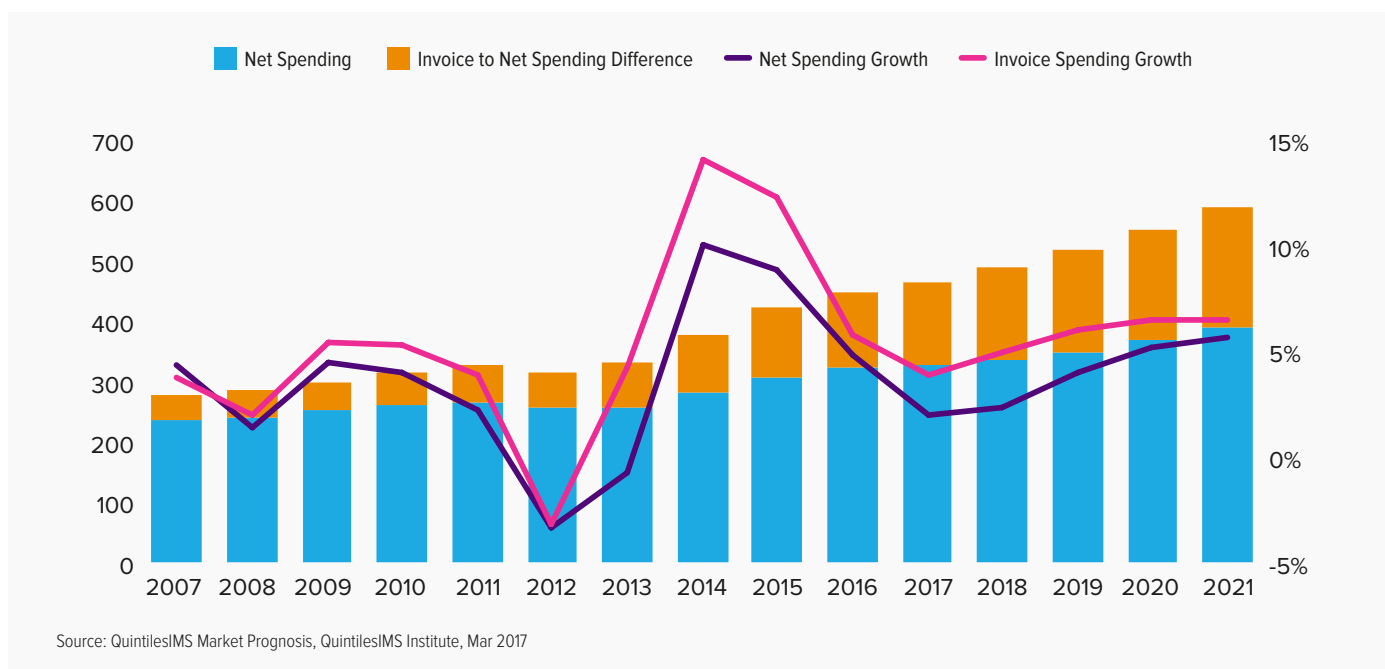
- Spending grew at only 5.8% on an invoice basis in 2016, slowing by more than half from 2015's 12.4%, and growing by only 4.8% after adjusting for off-invoice discounts and rebates.

- Slower price growth and weaker new products reduced the 2016 growth and are expected to contribute to slower 2017 growth before a recovering market rises to a 4-7% CAGR for the next five years.

- Net spending growth is expected to slow further in 2017, while the five year outlook will be for a 2-5% growth to 2021.

- The narrowing difference between invoice and net growth is largely due to the shift to specialty medicines, which typically have lower levels of off-invoice discounts and rebates, and as they reach a larger share of the market, will contribute to higher net growth, even as invoice-level growth remains moderate.

Chart notes:

Invoice spending is based on QuintilesIMS Health reported values from wholesaler transactions measured at trade/invoice prices and exclude off-invoice discounts and rebates that reduce net revenue received by manufacturers. Net spending reflects company recognized revenue after off-invoice discounts, rebates and price concessions are applied.

Notes on sources

QuintilesIMS regularly updates and restates historical data based on revised information from data suppliers and information in this report may not be consistent with prior editions.

This report is based on the QuintilesIMS services detailed in the panel below.

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. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

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

"SMART – Launch Edition" – is a service that allows users to study the market uptake and launch criteria, both of the marketplace and product, for branded and generic launches from 1992 to present-day.

"SMART – Generics Module" is an integrated solution that provides key metrics and dimensions necessary to measure performance in the generic markets. Additional studies pertaining to orphan and schedule status as well as regulatory pathway can be measured in the context of the NSP and NPA information sets.

Formulary Impact Analyzer (FIA) provides insight into what impact popular 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 switch house providing a comprehensive view of retailers and across geographies.

Market Prognosis is a comprehensive, strategic market forecasting publication that provides insight to decision makers about the economic and political issues that can affect spending on healthcare globally. It uses econometric modeling from the Economist Intelligence Unit to deliver in-depth analysis at a global, regional and country level about therapy class dynamics, distribution channel changes and brand vs. generic product spending.

LifeCycle™ **New Product Focus**™ is a comprehensive worldwide tracking service of historical product launches since 1982. It includes information about product launches in each country, including the indication and price at the time of the initial launch, and covers more than 300,000 launches.

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.
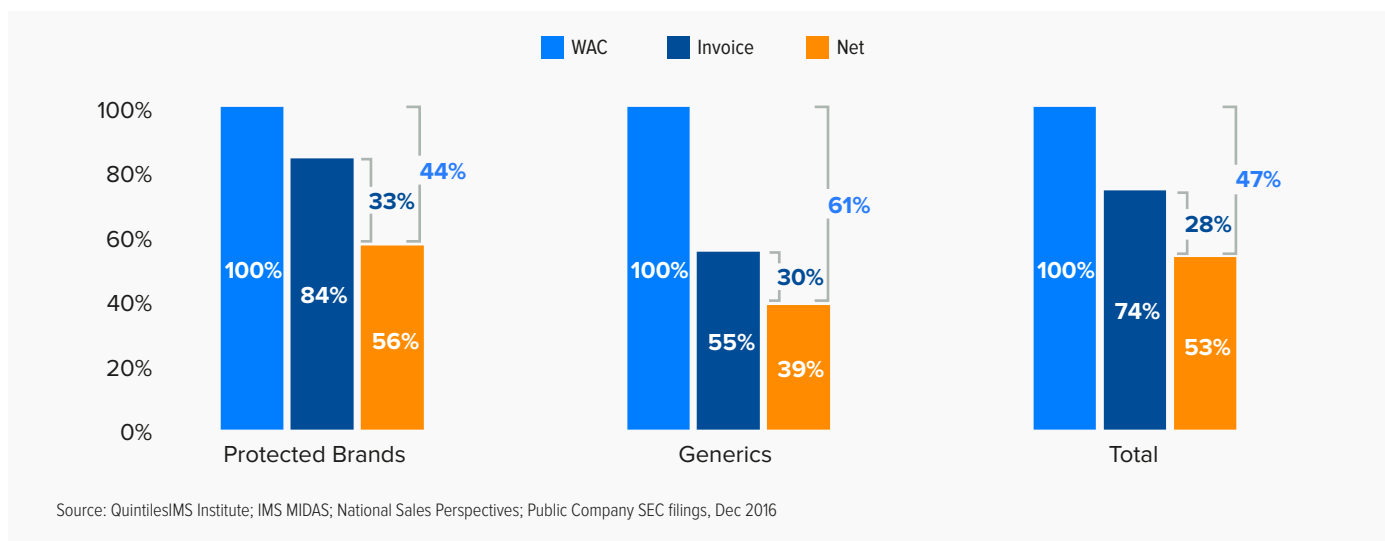
Methodology

The analysis covers the U.S. prescription-bound pharmaceutical market, including all channels of distribution (pharmacies, mail order, hospitals, clinics, etc).

Estimates of Net Pricing

WAC-based pricing is derived from list-prices of products as reported to QuintilesIMS. Invoice-based pricing is derived from QuintilesIMS proprietary information gathered from wholesalers and company direct sales. While QuintilesIMS invoice prices reflect supply-chain price concessions such as prompt-payment and volume discounts, they do not reflect the off-invoice discounts and rebates separately paid to insurers, or other price concessions paid to patients or other health system participants.

2016 Average Net Sales Adjustment By Product Type

Source: QuintilesIMS Institute; IMS MIDAS; National Sales Perspectives; Public Company SEC filings, Dec 2016

Estimated net price growth in this report are projected from a sample of large and mid-sized companies analyzed from 2011-2016. The sample includes between 225 to 299 product franchises, which represent between 79 to 93% of protected branded product sales in each of the years shown. Branded Products are included in the sample if their net sales amount is disclosed in financial filings with the Securities and Exchange Commission and if the volume of sales captured in QuintilesIMS Health audits is consistent with information provided directly by manufacturers in support of QuintilesIMS Health proprietary datasets. No confidential discounts or rebate information have been provided to the QuintilesIMS Institute for use in this study. Net prices are calculated by dividing publicly reported net sales values by volumes for the same products reported to IMS Health. Estimated brand net price growth for the total market is projected from the analysis sample to the total market. Net prices represent an estimate of the average manufacturer realized price, reflecting any reductions in net sales due to off-invoice discounts, rebates, co-pay assistance or other price concessions, and do not necessarily reflect the net costs paid by insurers, the federal government or patients, which all vary significantly and independently.

For generic companies, a sample of five large generic companies' generic portfolios were analyzed in aggregate consistent with their SEC filings, as specific generic product analyses are not possible.

Dispensed prescriptions adjusted for 90-day prescriptions

Prescriptions with >84 days supply to the patient are assumed to represent a 3-month prescription, and all other prescriptions are assumed to represent a 1 month prescription. Three-month prescriptions are factored by 3 to normalize prescriptions to 1-month durations.

Specialty pharmaceuticals

QuintilesIMS defines specialty medicines as those which treat chronic, complex or rare diseases, and which have a minimum of four out of seven additional characteristics related to the distribution, care delivery and/or cost of the medicines.

- Chronic diseases are long-lasting and often without direct cure, and treatments are intended to be used for more than 6 months.

- Complex diseases have both environmental and genetic components, meaning they may be hereditary and/or exacerbated by environmental factors (obesity, diet, etc.). Complex diseases can affect multiple organ systems and may be caused or be the cause of secondary diseases (e.g. diabetes can cause renal failure such that both are considered complex diseases).

- Rare diseases are defined as those with fewer than 200,000 new cases annually, equivalent to the U.S. definition of orphan diseases but not exclusively linked to the granting of an FDA orphan drug designation.

Additional product characteristics, where a product must exhibit 4 of the 7 to be considered specialty are:

- Costly: list price in excess of $6,000 per year

- Initiated/maintained by a specialist

- Requiring administration by another individual or health care professional (i.e. not self-administered)

- Requiring special handling in the supply chain (e.g. refrigerated, frozen, chemo precautions, biohazard)

- Requiring patient payment assistance

- Distributed through non-traditional channels (e.g. 'specialty pharmacy')

- Medication has significant side-effects that require additional monitoring/counselling (including, but not limited to REMS programs) and/or disease requires additional monitoring of therapy (e.g. monitoring of blood/cell counts to assess effectiveness/side effects of therapy)

Appendix

Top Therapeutic Classes by Prescriptions						
Dispensed Prescriptions Mn		2012	2013	2014	2015	2016
Total U.S. Market		4,154	4,235	4,325	4,368	4,453
1	Antihypertensives	691	701	705	706	721
2	Pain	480	477	481	468	460
3	Mental Health	335	348	364	376	395
4	Nervous System Disorders	346	357	368	376	387
5	Antibacterials	272	269	267	270	270
6	Lipid Regulators	266	264	263	260	264
7	Diabetes	186	193	201	211	224
8	Respiratory	157	162	169	176	181
9	Anti-Ulcerants	159	166	170	173	175
10	Thyroid Therapies	122	127	131	133	137
11	Dermatalogics	103	105	109	109	112
12	Hormonal Contraceptives	91	95	97	96	98
13	ADHD	76	80	83	87	91
14	Anticoagulants	76	77	78	78	79
15	Corticosteroids	60	62	65	68	71
16	GI Products	57	58	61	63	66
17	Other Cardiovasculars	51	50	49	48	48
18	Nasal Preps Topical	48	51	56	52	48
19	Ophthalmology	43	44	44	46	48
20	Benign Prostate Hyperplasia	36	37	40	41	45

Source: QuintilesIMS, National Prescription Audit, Dec 2016

Appendix notes:

Therapy areas are based on proprietary QuintilesIMS definitions. Includes prescription-bound products including insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Excludes OTC products. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Prescriptions are not adjusted for length of therapy; 90-day and 30-day prescriptions are both counted as one prescription.

Top Therapeutic Classes by Invoice Spending						
Invoice Spending US$Bn		**2012**	**2013**	**2014**	**2015**	**2016**
Total U.S. Market		317.8	331.5	378.5	425.3	450.0
1	Diabetes	22.3	25.6	33.7	43.9	51.5
2	Oncology	25.6	28.1	33.1	39.1	45.5
3	Autoimmune	15.2	18.3	23.5	30.2	37.2
4	Respiratory	21.1	19.9	21.4	23.8	26.0
5	Pain	17.9	18.9	21.0	20.4	19.7
6	Nervous System Disorders	11.6	13.2	14.6	16.9	19.0
7	HIV Antivirals	11.1	12.2	14.0	16.2	18.8
8	Multiple Sclerosis	9.1	11.9	15.0	17.7	18.7
9	Mental Health	22.3	21.2	21.2	19.8	17.2
10	Viral Hepatitis	2.9	1.9	12.2	18.8	15.7
11	Anticoagulants	9.3	7.2	8.5	9.9	12.5
12	Lipid Regulators	16.6	13.5	13.5	13.3	12.0
13	ADHD	10.5	10.3	10.5	11.2	11.2
14	Dermatologicals	7.6	8.8	9.4	10.7	11.0
15	Antihypertensives	13.3	12.6	12.0	10.3	9.5
16	Vaccines excl flu	6.0	6.1	6.9	8.5	8.7
17	Other Cardiovasculars	4.6	5.2	6.4	7.4	8.3
18	GI Products	4.1	4.8	5.7	7.0	8.1
19	Antibacterials	7.8	8.7	8.4	8.0	7.6
20	Sex Hormones	5.3	5.9	6.0	6.4	6.6

Source: QuintilesIMS, National Sales Perspectives, Dec 2016

Appendix notes:

Therapy areas are based on proprietary QuintilesIMS definitions. Includes prescription and insulin products sold into chain and independent pharmacies, food store pharmacies, mail service pharmacies, long-term care facilities, hospitals, clinics, and other institutional settings. Excludes OTC. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

Top Medicines by Prescriptions					
Dispensed Prescriptions Mn	2012	2013	2014	2015	2016
Total U.S. Market	4,154	4,235	4,325	4,368	4,453
1 levothyroxine	112	117	120	120	123
2 lisinopril	99	102	104	106	110
3 atorvastatin	55	68	81	93	106
4 acetaminophen/hydrocodone	136	129	119	97	90
5 metoprolol	82	84	85	86	88
6 amlodipine	69	75	78	81	87
7 metformin	68	73	77	80	87
8 omeprazole	67	72	75	77	76
9 albuterol	61	64	67	70	70
10 gabapentin	39	44	51	57	64
11 simvastatin	89	80	73	66	60
12 amoxicillin	53	54	54	56	58
13 sertraline	40	42	44	46	49
14 hydrochlorothiazide	51	50	49	49	49
15 losartan	28	34	39	44	48
16 alprazolam	49	50	49	49	48
17 fluticasone	41	45	50	49	46
18 furosemide	44	46	46	46	46
19 azithromycin	55	49	47	47	46
20 ibuprofen	36	38	40	42	44

Source: QuintilesIMS, National Prescription Audit, Dec 2016

Appendix notes:

Includes prescriptions and insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Excludes OTC. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Prescriptions are not adjusted for length of therapy; 90-day and 30-day prescriptions are both counted as one prescription. Table shows leading active-ingredients or fixed combinations of ingredients and includes both branded and generic products.

Top Medicines by Invoice Spending

Invoice Spending US$Bn		2012	2013	2014	2015	2016
Total U.S. Market		317.8	331.5	378.5	425.3	450.0
1	Humira	4.5	5.7	7.8	10.7	13.6
2	Harvoni	0.0	0.0	1.6	14.3	10.0
3	Enbrel	4.2	4.9	5.9	6.6	7.4
4	Lantus Solostar	2.3	3.3	4.8	5.8	5.7
5	Remicade	3.8	4.1	4.5	5.0	5.3
6	Januvia	2.6	2.9	3.5	4.2	4.8
7	Advair Diskus	4.6	5.0	4.7	4.7	4.7
8	Lyrica	1.9	2.4	3.1	3.8	4.4
9	Crestor	4.8	5.3	5.7	6.3	4.2
10	Neulasta	3.4	3.6	3.8	4.1	4.2
11	Copaxone	3.5	3.8	4.0	4.4	4.1
12	Rituxan	3.1	3.3	3.5	3.7	3.9
13	Tecfidera	0.0	1.0	2.9	3.5	3.7
14	Xarelto	0.3	1.1	2.1	2.8	3.6
15	Lantus	2.2	2.6	3.5	3.8	3.3
16	Eliquis	0.0	0.1	0.6	1.6	3.2
17	Truvada	2.1	2.1	2.4	2.8	3.1
18	Vyvanse	1.6	1.9	2.2	2.6	3.1
19	Avastin	2.6	2.7	2.9	3.1	3.1
20	Symbicort	1.2	1.5	2.2	2.7	3.0

Source: QuintilesIMS, National Sales Perspectives, Dec 2016

Appendix notes:

Spending is based on QuintilesIMS National Sales Perspectives and is not adjusted for estimates of off-invoice discounts and rebates.
Includes prescription and insulin products sold into chain and independent pharmacies, food store pharmacies, mail service pharmacies, long-term care facilities, hospitals, clinics, and other institutional settings. Excludes OTC. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Copaxone includes both 20mg and 40mg strengths.

Dispensing Location by Invoice Spending					
Invoice Spending US$Bn	**2012**	**2013**	**2014**	**2015**	**2016**
Total U.S. Market	317.8	331.5	378.5	425.3	450.0
Retail and Mail	227.4	237.2	272.9	307.1	322.7
Chain Stores	106.3	108.5	121.8	131.0	138.1
Mail Service	60.9	65.6	82.3	98.1	105.3
Independent	36.5	36.9	42.1	47.9	49.8
Food Stores	23.6	26.2	26.8	30.0	29.5
Non-Retail	90.4	94.3	105.6	118.2	127.3
Clinics	39.5	42.5	48.4	56.1	63.1
Non-Federal Hospitals	28.1	28.5	30.0	33.0	34.3
Long-Term Care	13.9	14.1	16.2	16.6	16.7
HMO	2.8	3.1	3.9	4.8	5.2
Home Health Care	2.7	2.8	3.4	3.8	3.9
Federal Facilities	2.5	2.4	2.7	2.6	2.9
Miscellaneous	0.9	0.9	1.0	1.2	1.3

Source: QuintilesIMS, National Sales Perspectives, Dec 2016

Appendix notes:

Spending is based on QuintilesIMS National Sales Perspectives and is not adjusted for estimates of off-invoice discounts and rebates. Includes prescription-bound products including insulin products and excluding other products such as OTC. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates.

Dispensed Prescriptions by Location Unadjusted for Prescription Length					
Dispensed Prescriptions Mn	**2012**	**2013**	**2014**	**2015**	**2016**
Total U.S. Market	4,154	4,235	4,325	4,368	4,453
Retail and Mail	3,822	3,868	3,939	3,988	4,066
Chain Stores	2,302	2,384	2,474	2,523	2,564
Independent	737	736	738	739	740
Food Stores	521	516	515	522	556
Mail Service	262	232	212	204	206
Non-Retail	332	367	386	380	387
Long-Term Care	332	367	386	380	387

Source: QuintilesIMS, National Prescription Audit, Dec 2016; QuintilesIMS Institute

Dispensed Prescriptions by Location Adjusted for Prescription Length					
Adjusted Dispensed Prescriptions Mn	**2012**	**2013**	**2014**	**2015**	**2016**
Total U.S. Market	5,265	5,379	5,505	5,598	5,769
Retail and Mail	4,929	5,008	5,114	5,212	5,376
Chain Stores	2,751	2,901	3,052	3,153	3,259
Independent	833	843	855	865	871
Food Stores	630	631	636	649	697
Mail Service	715	632	572	546	548
Non-Retail	337	371	391	385	393
Long-Term Care	337	371	391	385	393

Source: QuintilesIMS, National Prescription Audit, Dec 2016; QuintilesIMS Institute

Appendix notes:

Includes prescriptions and insulins dispensed through chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Adjusted prescription counts are adjusted for length of prescriptions and re-aggregated, with prescriptions for 84 days supply or more factored by three, and those under 84 days unchanged.

Dispensing by Payment Type for Retail Prescriptions

Dispensed Prescriptions Mn	2012	2013	2014	2015	2016
Retail Prescriptions	4,154	4,235	4,325	4,368	4,453
Commercial Third Party	57.0%	54.6%	52.9%	52.1%	51.3%
Medicare Part D	23.1%	25.5%	26.1%	26.3%	26.9%
Medicaid	11.2%	10.9%	12.4%	13.5%	14.1%
Cash	8.7%	9.0%	8.6%	8.1%	7.7%

Source: QuintilesIMS, National Prescription Audit; PayerTrak, Dec 2016

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.

Invoice Spending and Dispensing by Product Type

Invoice Spending US$Bn	2012	2013	2014	2015	2016
Total U.S. Market	317.8	331.5	378.5	425.3	450.0
Branded	71.6%	71.2%	71.8%	72.9%	74.2%
Unbranded Generic	16.3%	16.7%	17.1%	16.5%	15.0%
Branded Generic	12.2%	12.1%	11.0%	10.6%	10.8%

Dispensed Prescriptions Mn	2012	2013	2014	2015	2016
Total U.S. Market	4,154	4,235	4,325	4,368	4,453
Branded	15.9%	13.5%	12.2%	11.3%	10.5%
Unbranded Generic	77.8%	80.5%	82.1%	83.4%	84.6%
Branded Generic	6.3%	5.9%	5.6%	5.3%	4.9%

Source: QuintilesIMS, National Prescription Audit, Dec 2016; National Sales Perspectives, Dec 2016

Appendix notes:

Includes prescriptions and insulins dispensed by chain and independent pharmacies, food store pharmacies, mail service pharmacies, and long-term care facilities. Spending figures also include sales into hospitals, clinics, and other institutional settings. QuintilesIMS routinely updates its national audits, which may result in changes to previously reported market size and growth rates. Shares may not total 100% due to rounding.

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Murray Aitken is Executive Director for the QuintilesIMS Institute, which provides policy setters and decision makers in the global health sector with objective insights into healthcare dynamics. He assumed this role in January 2011. Murray previously held other roles within QuintilesIMS which he joined in 2001. Prior to QuintilesIMS, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

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Michael serves as Research Director for the QuintilesIMS Institute, setting the research agenda for the Institute and leading the development of reports and projects focused on the current and future role of biopharmaceuticals in healthcare in the U.S. and globally. He joined the company in 1999 and has held roles in consulting, service and marketing and assumed his current role in 2011. Michael holds a B.A. in History and Political Science from the University of Essex, Colchester, U.K. and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, U.K.

About the QuintilesIMS Institute

The QuintilesIMS Institute 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 QuintilesIMS'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 QuintilesIMS 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.