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Declining Medicine Use and Costs: For Better or Worse?

A Review of the Use of Medicines in the United States in 2012

Introduction

In 2012, both the per capita use and cost of medicines declined. The "cost curve" for medicines – if not for other elements of the U.S. healthcare system – was bent. For some, this will be good news and a harbinger of more efficient use of our healthcare resources. For others, this decline may indicate undertreatment and imbalance between prevention and care. Whichever the perspective, this year's review of the utilization and cost of medicines – and their role in the overall healthcare system – brings forward important issues, especially as we sit on the eve of arguably the most transformative period in healthcare.

In this year's report, we have brought together our review of 2012 from several perspectives: the utilization of healthcare services overall, including medicines; total system spending on medicines at an aggregate and segmented level; patient out-of-pocket costs for medical and pharmacy benefits including retail prescription copays; and transformations in disease treatment resulting from newly approved medicines.

It's clear the U.S. is in a state of flux. As implementation of the Affordable Care Act brings fundamental change to healthcare access, delivery systems and payment structures, the landscape will continue to change in the next 5 years and beyond. Understanding the underlying drivers will be essential as we navigate the waters ahead – and assess whether change is for better or worse.

The study was produced independently by the IMS Institute for Healthcare Informatics as a public service, without industry or government funding. The contributions to this report of Michael Kleinrock, Steve Gubernick, Bill McClellan, Shiraz Hasan, Naomi Sacks and dozens of others at IMS Health are gratefully acknowledged.

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Executive Summary

In 2012, utilization of healthcare services declined nationally and contributed to a reduction in the overall cost of medicines. The drivers of these declines are many and complex and point to the paradox that while drug costs are actually falling for many patients, their exposure to healthcare costs is increasing. These issues are affecting patients differently depending on the type of insurance coverage they have, and which diseases they suffer from. Millions are paying less for medicines due to patent expiries, while others with rare diseases may be able to use transformative and breakthrough medicines, but may also be exposed to very high costs for those treatments.

- **Changes in the Utilization of Healthcare and Medicines**

  Overall per capita utilization of healthcare and medicines declined slightly in 2012 with important variations by the age of patients and the point of care. Medicine use declined slightly as patients made fewer office visits and continued to reduce their retail drug use. Prescriptions dispensed to 19-25 year olds declined slightly in 2012, after having been the only group to show an increase in 2011, following the provision of the ACA allowing them to stay on their parents' health insurance. Seniors continued to have the highest rates of prescriptions per person even with some small declines in usage in 2012.

- **Healthcare Costs and Spending on Medicines**

  Overall healthcare spending is growing more rapidly than spending on medicines and is expected to continue to do so, at least through 2017. Total spending on medicines on a real per capita basis declined by 3.5% in 2012, as a result of declining use of branded drugs, greater availability of lower-cost generics, lower levels of price increases, and reduced spending on new medicines. Nominal pharmaceutical spending reached $325.8 billion in 2012, a decline of 1.0%.

- **Patient Payment for Healthcare and Medicines**

  Patients with insurance are paying higher deductibles and higher copays or co-insurance, and those with newer kinds of health plans have much greater visibility and responsibility for the overall costs of their care. Deductibles and out-of-pocket costs have more than tripled for insured patients in the last five years, while costs for the subset with consumer-driven health plans are seven times higher. Despite overall increases in out-of-pocket costs, prescription drug costs for most patients are actually declining, with 72% of all prescriptions costing patients $10 or less and only 3% of prescriptions costing more than $70. There remain wide variations in the out-of-pocket costs faced by patients with different types of insurance.

- **Transformations in Disease Treatment**

  There were 28 New Molecular Entities launched in 2012, including nine new cancer treatments, the most in over a decade and including a breakthrough for very common skin cancers. Seven orphan drugs also became available to patients including treatments for Gaucher's disease, cystic fibrosis, chronic myeloid leukemia, and multiple myeloma. The next decade promises a much faster approval process for truly breakthrough drugs gaining FDA's new Breakthrough Therapy Designation. Several drugs have already benefited from the rapid review and approval procedures in early 2013. Further breakthrough products to treat hepatitis C, multiple sclerosis, cystic fibrosis and a number of cancers are expected in the next few years.

- **Usage and Spending in Major Therapy areas**

  Patent expiries provided savings in a number of therapy areas, while new medicines drove spending in more specialty therapy areas. The top 5 classes in 2012, based on spending, were oncologics ($25.9Bn), mental health ($23.5Bn) respiratory agents ($22.1Bn), antidiabetics ($22.0Bn), and pain ($18.2Bn). Absolute spending growth gains were highest for antivirals (excluding HIV), multiple sclerosis, ADHD, HIV antivirals and autoimmune diseases. Antivirals excluding HIV, the therapy area that includes flu vaccines and newer treatments for Hepatitis C virus, grew by more than 20%, driven by breakthrough therapy telaprevir (Incivek®).

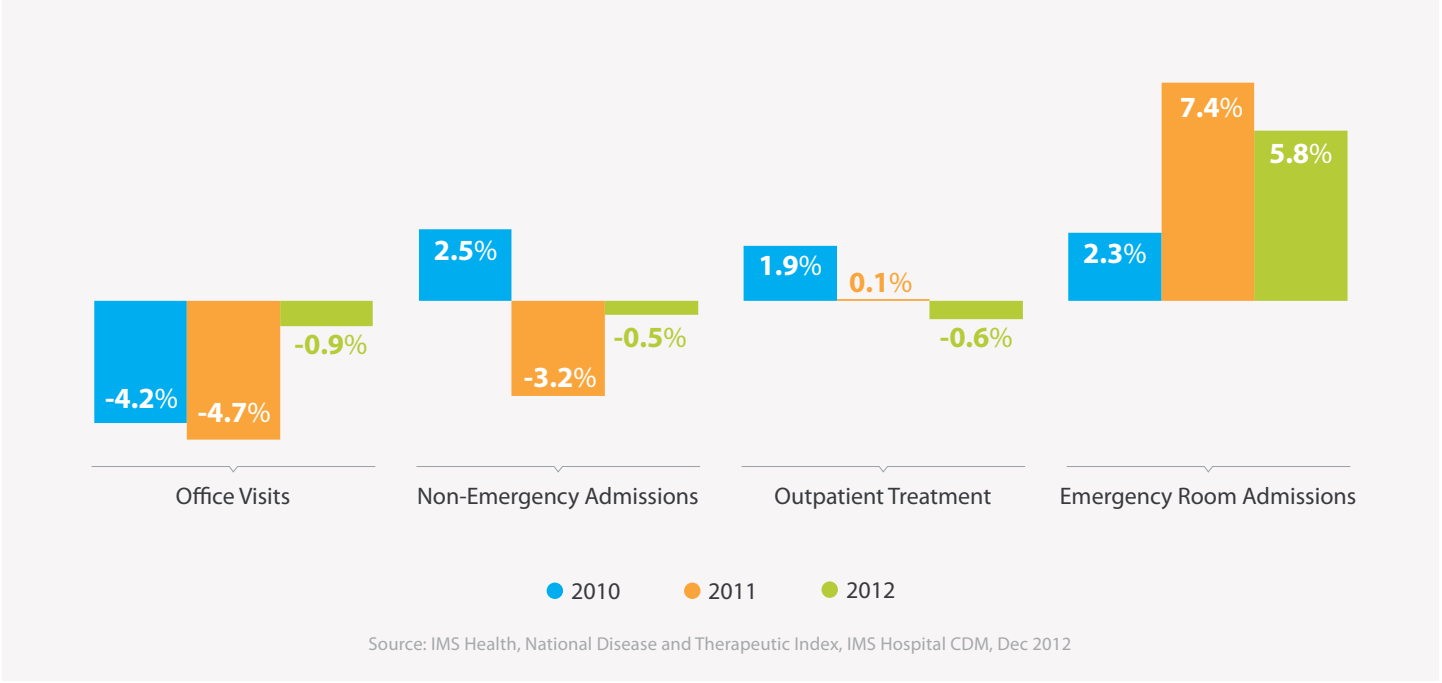
Changes in the Utilization of Healthcare and Medicines

Overall per capita utilization of healthcare and medicines declined slightly in 2012 with important variations by the age of patients and the point of care.

- Patient office visits, non-emergency hospitalizations and per capita use of medicines all continued to decline in 2012.
- Patient office visits declined by 0.9% in 2012, a moderation of the declines in the prior two years.
- Non-emergency hospital admissions declined by 0.5%, a smaller decline than in 2011.
- Emergency room admissions, while a relatively small number, increased by 5.8% in 2012.
- There were 1.2% more prescriptions filled in 2012, but a 0.1% decline on a per capita basis. Most therapy areas had small nominal increases in prescriptions in 2012, while those with the greatest reductions in usage were concentrated in the five with the largest declines including allergy, cough and cold.
- The cough, cold and flu season in 2011-2012 was weaker than in the previous year, contributing the most to the lower per capita usage of medicines for those under 18 and those 26 to 49.
- The use of prescriptions by 19-25 year olds declined slightly in 2012, after having been the only group with increasing usage in 2011 following the provision of the ACA allowing them to stay on their parents' health insurance.
- Seniors remained the largest users of medicines per person, but had small declines in per capita usage of medicines.

Fewer patients made office visits, while ER visits increased

Percent change in Hospital Admissions & Office Visits



Source: IMS Health, National Disease and Therapeutic Index, IMS Hospital CDM, Dec 2012

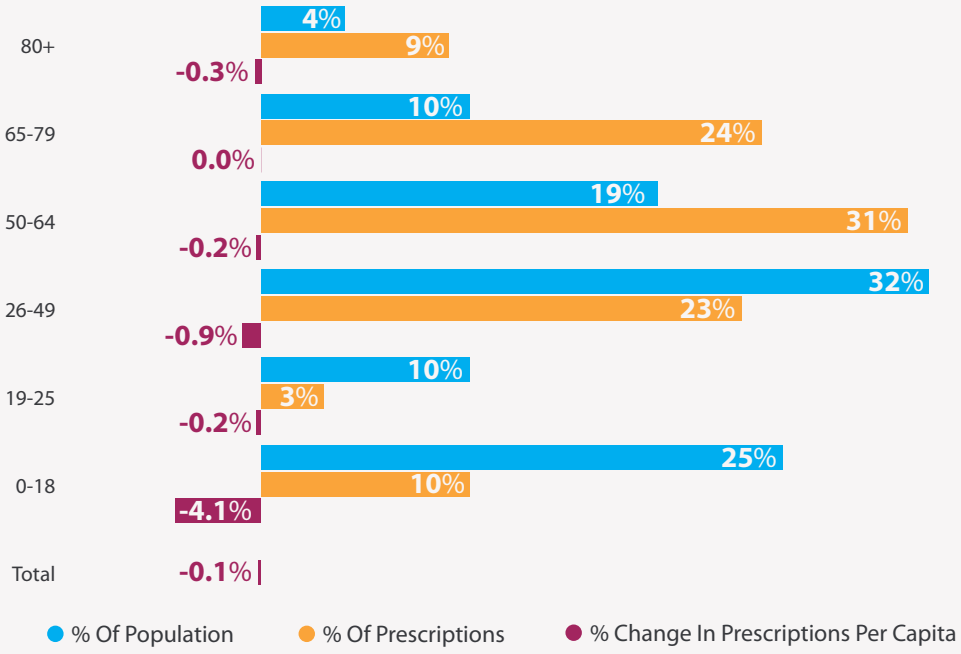
- The lowest-cost medical interventions are visits to doctors' offices, which continued to decline in 2012, though much more slowly than the prior two years.
- Non-emergency hospital admissions declined again in 2012, though also more slowly.
- Outpatient treatment also declined.
- Patient admissions to hospitals via emergency departments are relatively small in number, but increased at a dramatically higher rate in the last two years, driven by increased ER visits from the insured population.

Chart notes:

Hospital admissions data are projected from charges submitted by a statistically significant sample of over 20% 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.
Office visits projected using a national sample of over 4,100 office-based doctors each reporting for 2 days per quarter. The margin of error for office visits is +/- 3.9%.

Patients' use of medicines declined by 0.1% in 2012, driven by the largest population group, adults aged 26-49

Percent Population, Prescriptions & Per Capita Change in Dispensed Prescriptions by Age



Source: IMS Health, Vector One® National, Dec 2012; U.S. Census Bureau

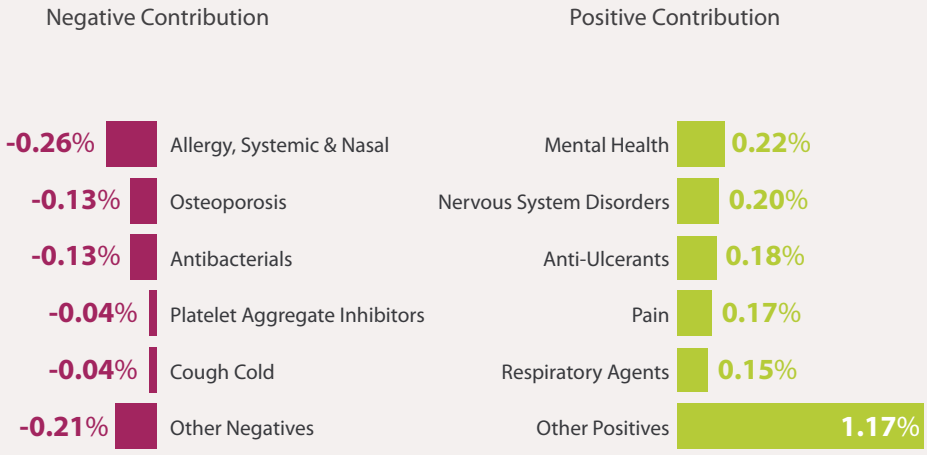
- Americans' use of medicines per person declined by 0.1% in 2012, up from 2011 when usage declined by 1.1%.
- Seniors remained the largest users of medicines with those over 50 using 64% of prescriptions, while only making up 33% of the population.
- The cough, cold and flu season from November 2011 to April 2012 was weaker than in the previous year contributing the most to the lower per capita usage of medicines, and particularly those under 18 as well as the 26 to 49-year-old group.
- The use of prescriptions by 19-25 year olds declined slightly in 2012, after having been the only group to see increasing usage in 2011 following the provision of the ACA allowing them to stay on their parents' health insurance.
- Changes in per capita use of prescription drugs could indicate either appropriate disease management or concerning trends in self-rationing by patients and could contribute positively or negatively to healthcare cost trends in the future.

Chart notes:

Dispensed prescriptions in retail pharmacies, excluding mail order and long-term care pharmacies. Prescriptions are normalized to reflect consistent prescription sizes. Prescriptions can be of different durations and this has been shown to vary significantly and to change over time. Increasing numbers of 3-month prescriptions over time result in fewer prescriptions. This analysis adjusts all prescriptions to the national average number of extended units per prescription.

Prescriptions increased by 1.2% in 2012, as therapy areas with increased utilization outweighed those with declines

Therapy Areas by Largest Positive and Negative Contribution to Growth



Source: IMS Health, National Prescription Audit, Dec 2012

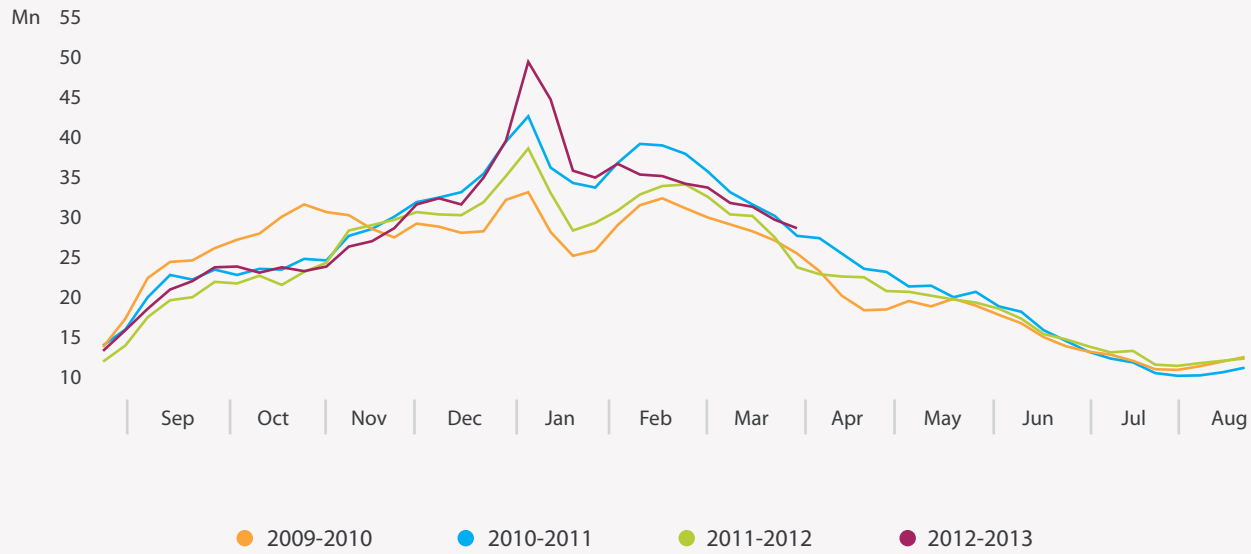
- Dispensed prescriptions grew at 1.2%, but declined by 0.1% on a per capita basis.
- On a nominal basis, therapy areas with positive contributions to dispensed prescriptions outweighed declining areas more than two to one.
- Therapy areas associated with declining costs, such as mental health, pain and respiratory agents saw increasing volume.
- 2012 was characterized by a mild allergy season and prescription allergy medicines also continued to decline because of high quality over-the-counter versions of many treatments.
- A weaker cough, cold and flu season in the 2011-2012 season was partly offset by a stronger season in 2012 into early 2013.

Chart notes:

Therapy areas are based on proprietary IMS Health definitions. Cough Cold includes prescription-bound cough and cold treatments.
Mental health includes antipsychotics and antidepressants. Nervous system disorder treatments include therapies for epilepsy and Parkinson's disease.
Respiratory agents include treatments for both asthma and COPD – Chronic Obstructive Pulmonary Disease.

The flu season is a relatively small part of prescription volume but variations year to year can be substantial

U.S. National Respiratory Illness Estimates



Source: IMS FAN, Apr 2013

- Cough, cold and flu medicines typically represent as much as 5% of prescription demand, but seasonal variations often cause a disproportionate impact on prescription trends.
- The 2011-2012 flu season was less severe than the prior year, primarily in January and February 2012.
- The 2012-2013 flu season was more severe than any season since the H1N1 season in 2009-2010.
- The 2009-2010 H1N1 pandemic flu, similar to other pandemic outbreaks, started earlier, having a sustained impact beginning in the autumn of 2009.
- The last three years have been characterized by relatively less severe flu strains.
- The 2012-2013 season peaked in the first week of January and did not disproportionately impact prescription trends in 2012.

Chart notes:

Chart indicates millions of people estimated to be sick with respiratory illness weekly.

Estimates are based on surveys and predictive modeling and correlate strongly with future demand for prescription and OTC medicines for cough, cold and flu symptoms.

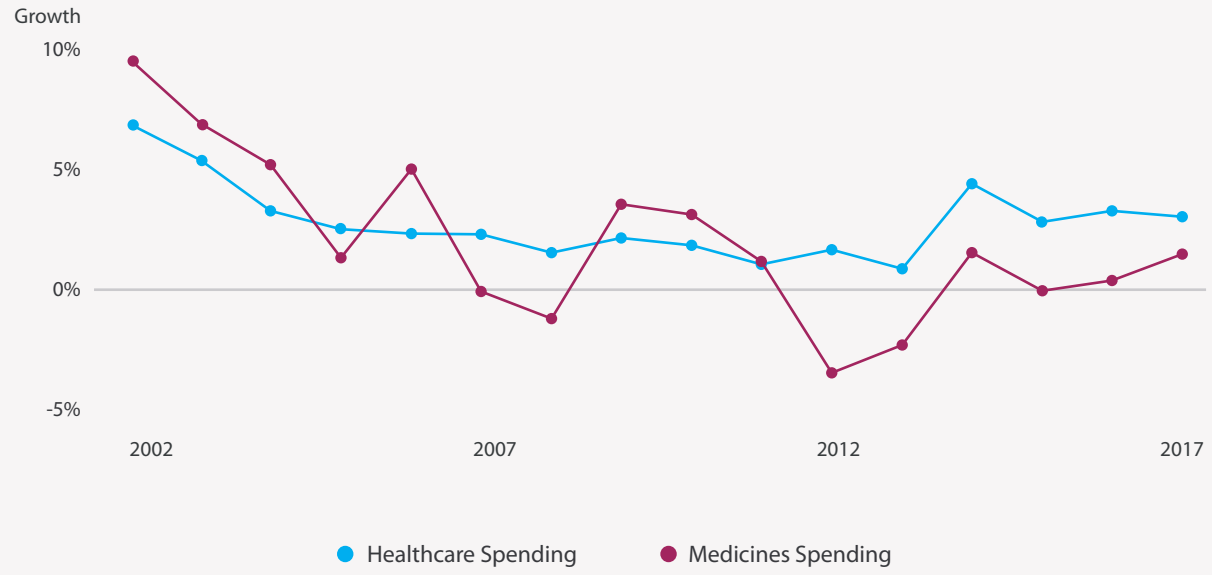
Healthcare Costs and Spending on Medicines

Total spending on medicines on a real per capita basis declined by 3.5%, as a result of declining use of branded drugs, greater availability of lower-cost generics, lower levels of price increases, and reduced spending on new medicines.

- Overall healthcare spending is growing more rapidly than spending on medicines and is expected to continue to do so at least through 2017.
- Nominal spending on pharmaceuticals reached $325.8 billion in 2012, a decline of 1.0%.
- Healthcare costs for the privately-insured-under-65 population continue to be concentrated, with 1% of patients accounting for 26% of healthcare costs and 5% accounting for 51%.
- Spending on branded products declined by $11.4 billion to $230.2 billion in 2012.
- Lower volume for branded products contributed to $3.9 billion in lower spending, offset by unadjusted price increases of $15.7 billion, estimated to be $13.2 billion after adjusting for incremental rebates and discounts.
- Losses of patent exclusivity led to $28.9 billion lower spending on affected medicines, taking the 5-year total "patent dividend" to $75 billion.
- Spending on new brands slowed slightly but still added $10.8 billion to spending.
- In 2012, generics reached 84% of dispensed prescriptions, and spending in this segment grew by $8 billion.
- Overall spending on medicines continued to be concentrated in traditional small-molecule pills dispensed through retail pharmacies, even as growth in this segment was outpaced by biologics, specialty drugs, injectables, and institutional channels, which accounted for as much as 31% of total spending.

Spending on medicines declined by 3.5% in 2012 and is expected to continue below overall healthcare spending through the next five years

Real Per Capita Spending Growth 2002-2017



Source: CMS National Health Expenditures Jul 2012; IMS Health, National Sales Perspectives, Dec 2012; U.S. Census Bureau Jan 2013; Economic Intelligence Unit Nov 2012; IMS Market Prognosis Apr 2013

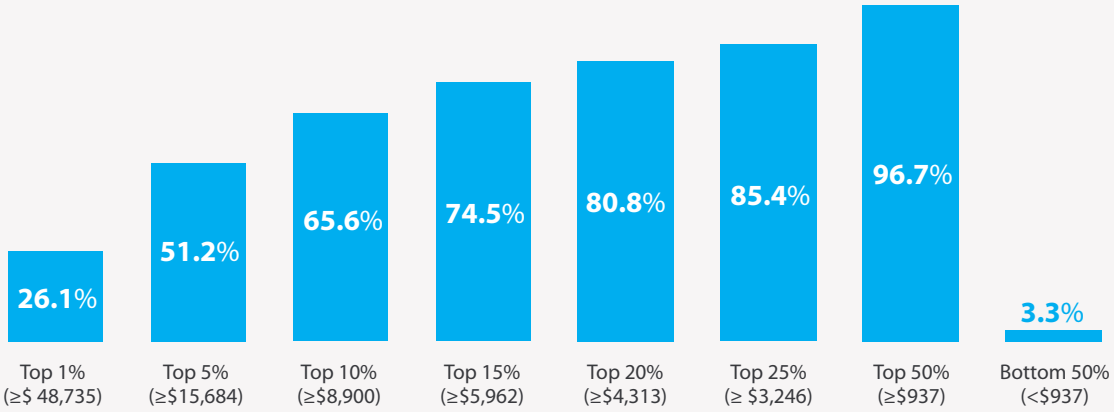
- On a real per capita basis, spending on prescription medicines declined by 3.5% in 2012. The decline was 1.0% on a nominal basis.
- Lower levels of growth in spending in recent years reflect broad dynamics of lower volume growth, increased use of generics, loss of patent protection for major branded products and less spending on new drugs.
- For most of the last 10 years, spending on prescription medicines has grown more slowly than overall healthcare.
- The periods from 2002-2004 and 2009-2010 included substantial groups of innovative medicines which became more broadly used and drove spending.
- In 2006, the introduction of the Medicare Part D program drove significant incremental medicine usage.

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 channels 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.

A minority of patients account for the vast majority of healthcare costs

Percent of Health Plan Members Ranked by Healthcare Spending ($)



Source: IMS PharMetrics, Jun 2012

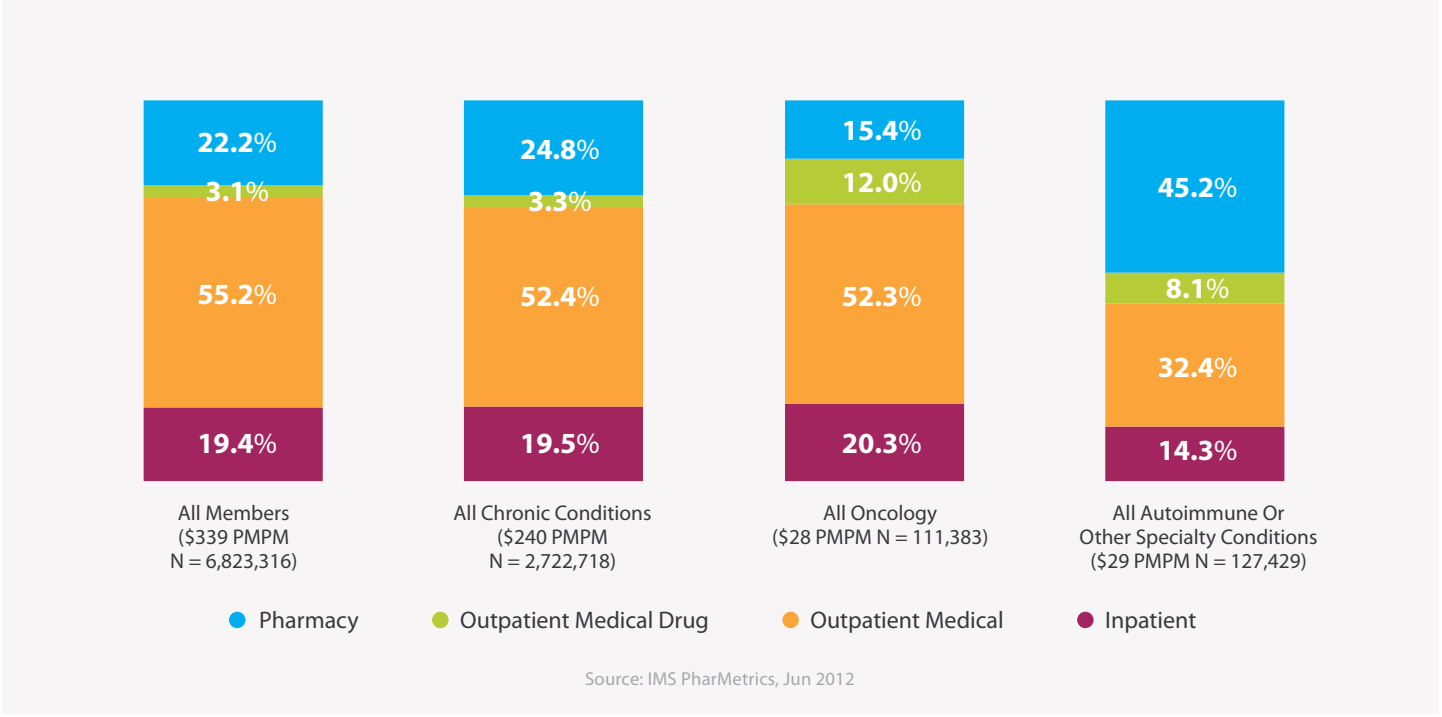
- One percent of privately insured health plan members accounted for 26.1% of all spending in the first half of 2012, up from 25.6% in 2010.
- A similar increase was seen in the top 5% and 10% as concentration of healthcare costs for the most expensive patients continues to increase.
- More than 51% of the total spending was for only 5% of all health plan members.
- Slightly more than 3% of expenditures went to treat the bottom 50% of all members, who had average annual spending of less than $937 per member.
- Spending distribution nearly mirrored the overall U.S. population, where AHRQ also reports that 3% of spending was driven by the bottom 50%, while 22% of spending was driven by the top 1%.
- Patients with lower overall healthcare costs, tend to have more of their costs concentrated in pharmacy benefits.
- These patients benefited substantially from the increasing availability of lower cost generics in recent years as a result of patent expiries.

Chart notes:

Spending distribution reflects spending for all health plan members, including members with no service use and no spending in the analysis year. Spending reflects the commercially insured population for those under 65 years old. Updated analysis first included in IMS Institute for Healthcare Informatics report: "Healthcare Spending Among Privately Insured Individuals Under Age 65" February 2012.

The majority of costs are for outpatient medical services, but this varies substantially by disease

Percent of Health Plan Members Healthcare Spending ($)



Source: IMS PharMetrics, Jun 2012

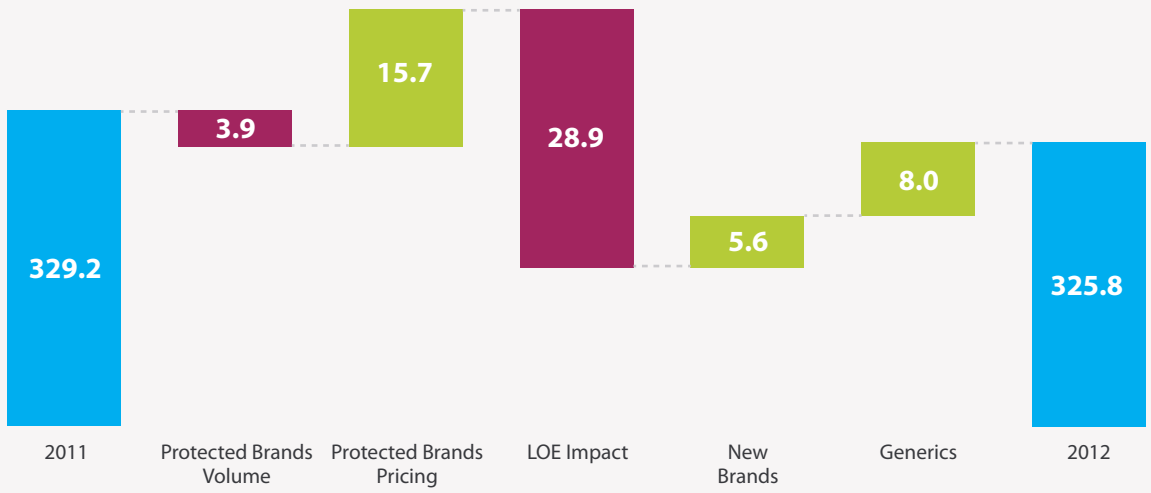
- Treatment patterns were outpatient driven among members with chronic or oncology conditions, and pharmacy driven for members with autoimmune and other specialty conditions.
- For members with chronic conditions, 56% of all spending was for outpatient services, of which 3% was for medical drug therapy.
- Outpatient services comprised 64% of all spending for members being treated for cancer with 12% of all spending for medical drug therapy.
- Inpatient spending represented a smaller share of all spending for members with autoimmune and other specialty conditions, while outpatient spending was 41% and medical drug therapy 8% of all spending.
- Pharmacy spending was 45% of all spending for members with autoimmune and other specialty conditions, up from 39% in 2010.

Chart notes:

Outpatient Medical Drug includes injected or infused drug therapy administered in a facility, office, or home health setting. $PMPM is spending per member per month. Spending reflects the commercially insured population for those under 65 years old. Updated analysis first included in IMS Institute for Healthcare Informatics report: "Healthcare Spending Among Privately Insured Individuals Under Age 65" February 2012.

Overall medicine spending, including inpatient usage, changed from 5 major segments

Components of Change in Total Spending US$Bn



Source: IMS Health, National Sales Perspectives, Dec 2012

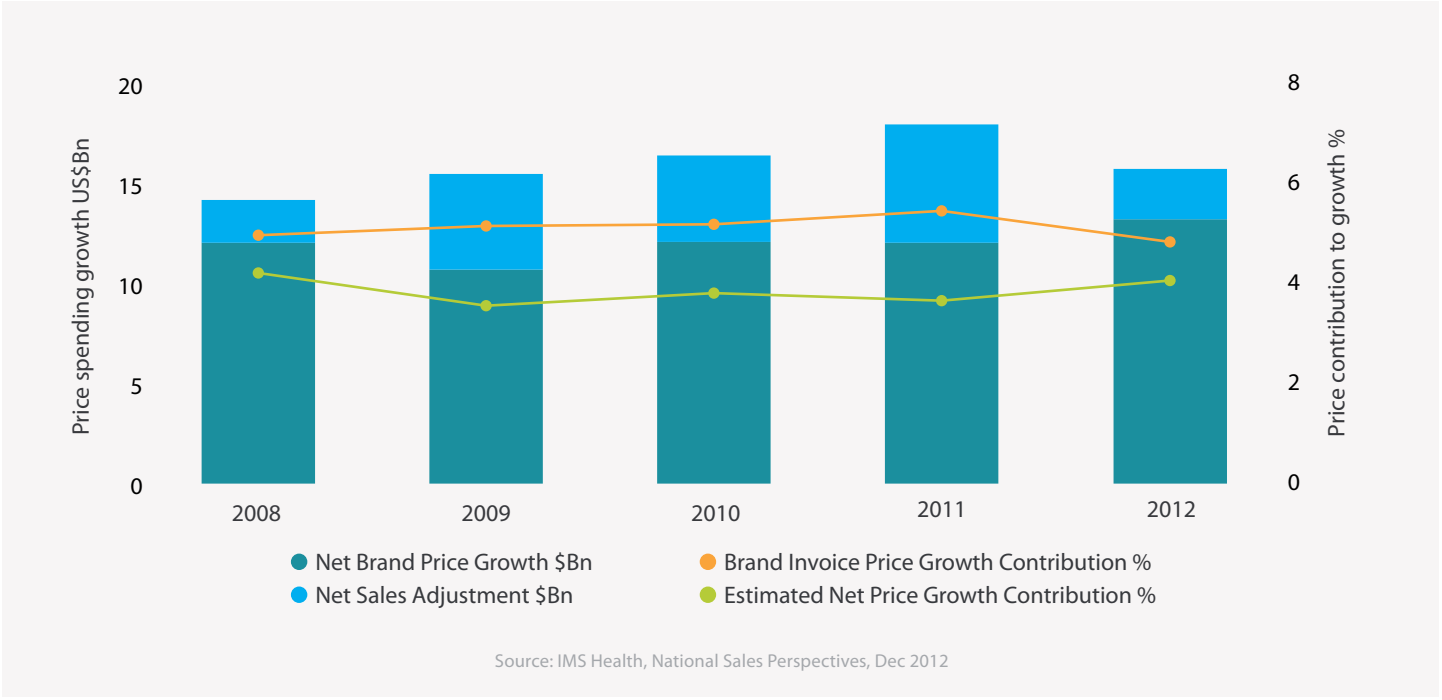
- Total spending on medicines decreased from $329.2Bn in 2011 to $325.8Bn in 2012.
- The decline in the volume of protected branded products reduced spending in 2012 by $3.9Bn compared to 2011.
- Increases in the pricing of protected branded products – without consideration to off-invoice discounts or rebates – raised spending by $15.7Bn.
- Brands losing patent protection or exclusivity, in 2012 or previously, resulted in a reduction in spending of $28.9Bn.
- Spending growth for new brands was $5.6Bn in 2012 compared to $6.4Bn in 2011.
- Spending on generics – including both volume and price effects – increased by $8.0Bn in 2012 compared to 2011.

Chart notes:

Segments are mutually exclusive and reflect the change in spending between 2011 and 2012 in billions of dollars. Protected brands (brands that have not reached patent expiry) have been split based on growth through pricing dynamics and volume (absent pricing dynamics). New Brands segment includes all new products launched in 2011 and 2012. Generics segment includes unbranded generics and branded generics. LOE – Loss of Exclusivity – includes branded products that lost patent exclusivity during 2012 or previously.

Net pricing increases for brands contributed an estimated 4.1% to spending growth in 2012

Protected Brand Price Spending Growth



Source: IMS Health, National Sales Perspectives, Dec 2012

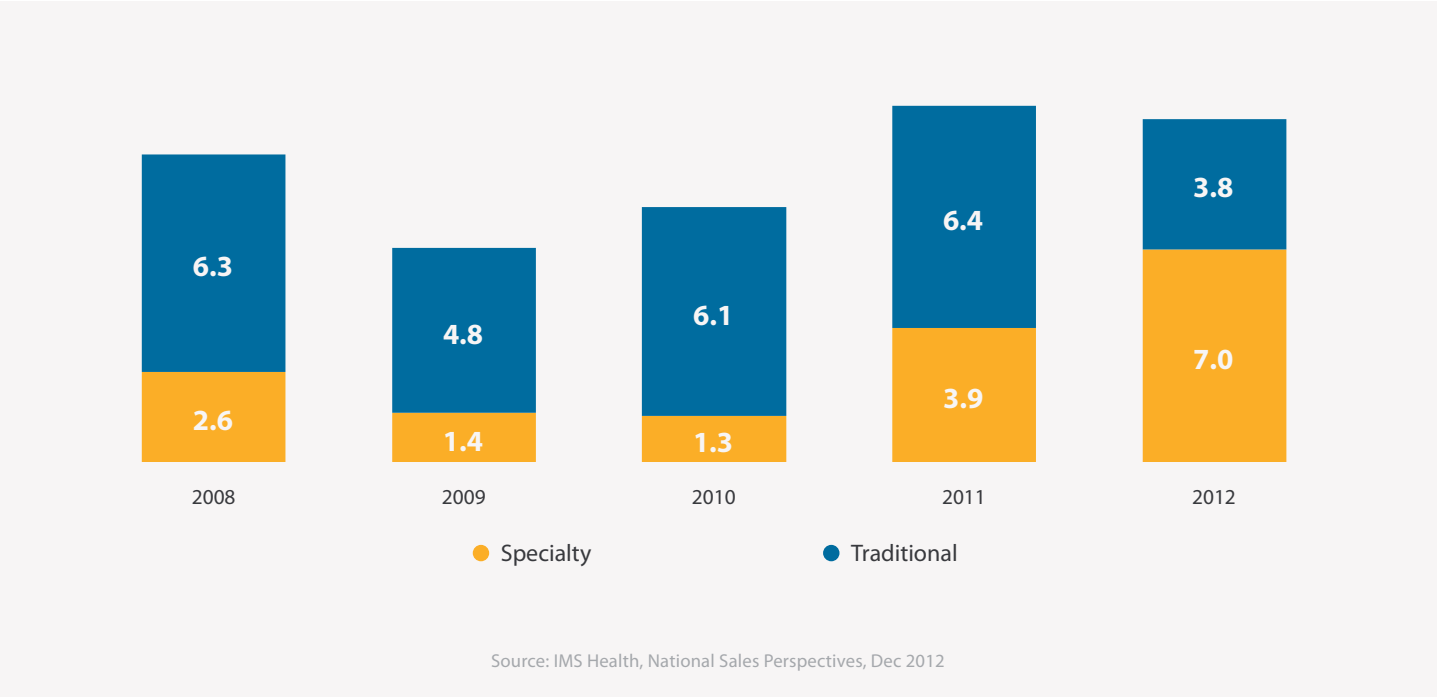
- Spending on protected brands increased by $15.7Bn in 2012 due to invoice price changes, compared to $17.9Bn in the prior year.
- Growth of spending due to protected brand invoice pricing contributed to overall spending growth by 4.8% in 2012, compared to 5.5% in 2011.
- Protected brands invoice price increases averaged 9.2% in 2012, down from 9.6% in 2011.
- Levels of off-invoice discounts and rebates declined dramatically as brands that lost patent protection had $28.9Bn of lower spending and ceased their previous levels of discounts or rebates.
- When adjusted for changes in the aggregate level of rebates and discounts, net price growth of an estimated $13.2Bn contributed 4.1% to spending growth in 2012.
- Trends for net pricing for protected brands are expected to remain consistent through the next five years.

Chart notes:

Protected brands include brands before loss of exclusivity; new brands on the market for less than 24 months are excluded. Price spending growth is dollar growth driven by invoice price changes and excludes the impact of rebates and contract pricing agreements. Price contribution to growth is contribution to market growth and does not reflect a price growth rate. Estimated net price growth is based on a comparison of company reported net sales and IMS reported sales at invoice prices from wholesaler transactions.

New brand spending continues to rebound, driven by a significant group of new specialty medicines

New Brand Spending US$Bn



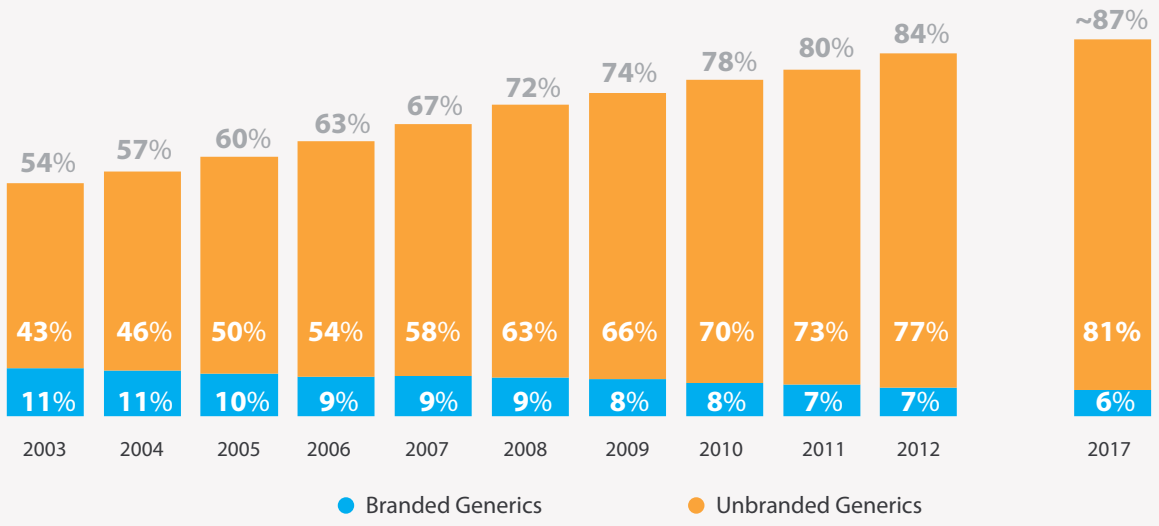
Source: IMS Health, National Sales Perspectives, Dec 2012

- Total drug spending on products that have been available to patients for less than 24 months rose to $10.8Bn up from $10.3Bn in 2011, well above the low in 2009 of $6.2Bn.
- Spending on new specialty medicines increased dramatically, with almost two-thirds of 2012 total new brand spending driven by specialty products.
- The five largest drivers of new specialty product spending were telaprevir (Incivek®) for hepatitis C, aflibercept (Eylea®) for wet age-related macular degeneration, and denosumab (Xgeva®) for bone metastases in cancer, fingolimod (Gilenya®) for multiple sclerosis and ipilimumab (Yervoy®) for inoperable or metastatic melanoma.
- Spending on new medicines represented 5.1% of total brand spending, with $7.0Bn from specialty medicines launched in 2011 or 2012.
- There were 28 New Molecular Entities (NME) launched in 2012 including 16 specialty medicines.
- Overall there were 39 NMEs approved by the FDA in 2012, the most in over a decade and a significant number late in the year, which means they will likely be launched in 2013.

Chart notes:
New brands defined as brands launched in the prior 24 months including products which are New Molecular Entities (NME) as well as other branded medicines. Numbers rounded in chart above. New molecular entities include both small-molecules and biologic medicines.
Chart has been adjusted to reflect estimated spending for recently launched products where they are understood to be under-reported by IMS.

Generics share of prescriptions reached 84% in 2012 and will likely rise to 87% by 2017

Percent Share of Prescriptions



Source: IMS Health, National Prescription Audit, Dec 2012

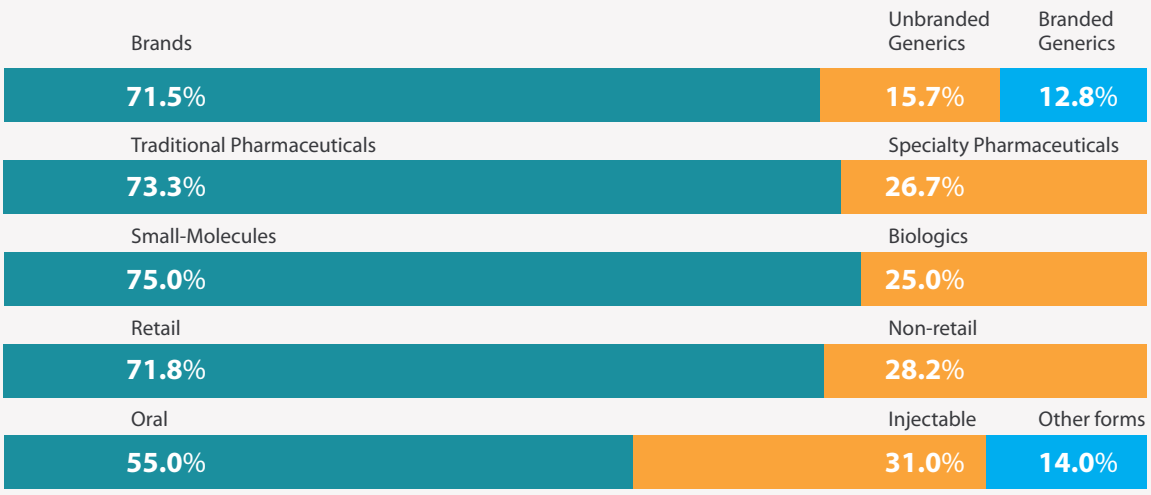
- Patent expiries for products used by millions of patients have contributed to a 30% rise in the generic share of prescriptions over the last ten years.
- The next five years include a smaller number of expiries and further genericization of drug usage is not expected beyond 87%.
- Generics are now dispensed 95% of the time when a generic form is available, up 1% from 2011.
- Generics contributed $8.0Bn to spending growth in 2012.
- Generics now make up 28% of total spending.
- Branded generic medicines have been facing competition in recent years from unbranded generics, and share of prescription volume has steadily declined.

Chart notes:

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. Generics include branded and unbranded generic medicines. Prescription counts are not adjusted for length of therapy.
90-day and 30-day prescriptions are both counted as one prescription.

Spending continues to be concentrated on traditional small-molecule pills from pharmacies

2012 Medicines Spending Segmentation Comparison



Source: IMS Health, National Sales Perspectives, Dec 2012

- Spending on branded drugs totaled $235Bn, or 71.5% of total spending, with branded and unbranded generics accounting for 28.5%.
- Traditional medicines were 73.3%, while specialty reached 26.7% and includes a variety of treatments for serious diseases including cancer, autoimmune diseases, HIV and multiple sclerosis.
- Small-molecule products were 75% of spending.
- Oral forms of medicines remained the most common form, while injectables were 31% of spending.
- Retail channels accounted for 71.8% of the total and included an increasing amount of injectable medicines that patients are able to self-administer.

Chart notes:

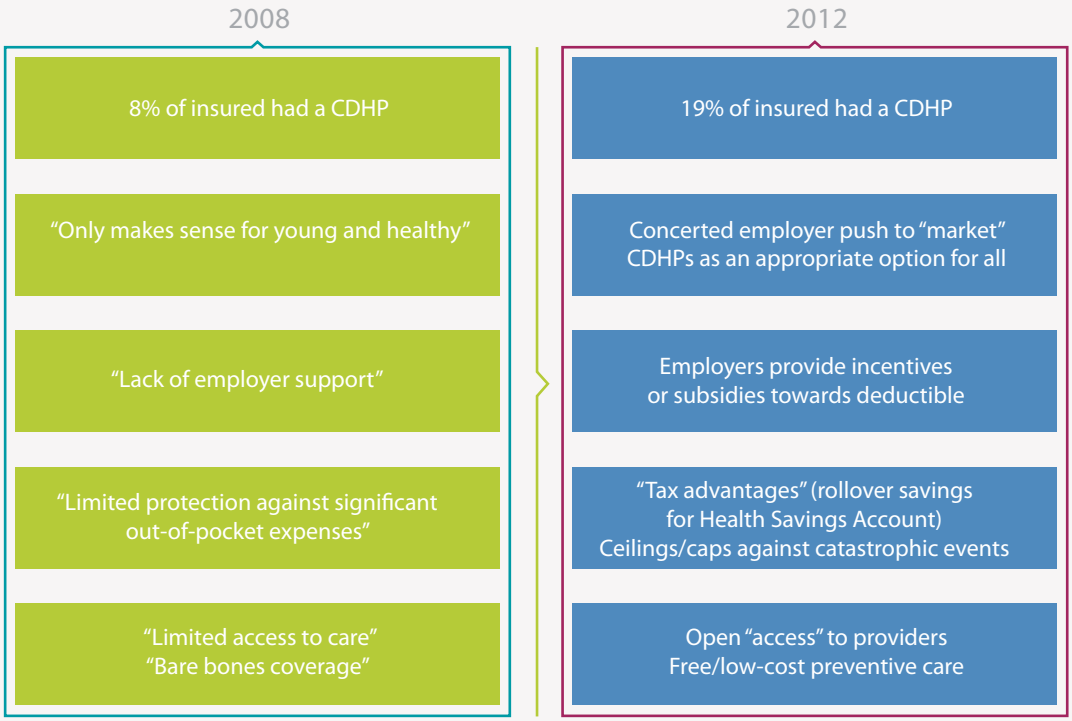
Each bar represents total spending in nominal dollars using a distinct segmentation of overall spending; the percentage refers to the segments' share of the total. Brands are those products with current or former patent protection or other forms of market exclusivity. Specialty, Traditional, and Biologics segments are based on proprietary IMS Health definitions.

Patient Payment for Healthcare and Medicines

Patients with insurance are paying higher deductibles and higher copays or co-insurance, and those with newer kinds of health plans have much greater visibility and responsibility for the overall costs of their care.

- Consumer-driven health plans, typified by high deductibles and 20% or more co-insurance after reaching a deductible, once only attractive to younger healthier workers are now much more commonly chosen by employers and employees and 19% of insured patients now have such plans.
- Many traditional insurance plans now also carry a high deductible, and patients face a much higher portion of costs than in the past.
- Deductibles and out-of-pocket costs have more than tripled for insured patients in the last five years, while costs for the subset with consumer-driven health plans have gone up seven times.
- Despite overall increases in out-of-pocket costs, prescription drug costs for most patients are actually declining, with 72% of all prescriptions costing patients $10 or less and only 3% of prescriptions costing more than $70.
- There are wide variations in the out-of-pocket costs faced by patients with different types of insurance.

Consumer-driven health plans have changed substantially in the last five years, contributing to a significant rise in enrollment



n=2,121 Firms; 3,173,121 Enrollees

Source: Kaiser/HRET Survey of Employer-Sponsored Health Benefits, 2012

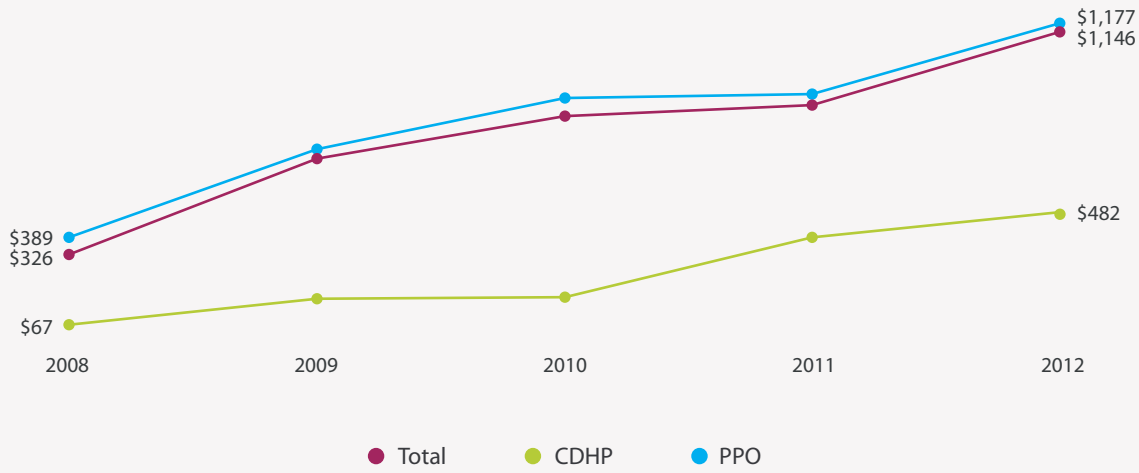
- Over the past five years, approximately 20 million Americans have switched from traditional preferred provider organization (PPO)/health maintenance organization (HMO) health plans to consumer-driven health plans (CDHPs). In the latter plans, patients bear more of the costs of their care either directly through deductibles of $1,000 or more or through co-insurance where they pay a fixed percentage of costs.
- In addition to the shift to CDHPs, the design of a typical PPO plan has changed over the past 5 years. A PPO plan now largely resembles a CDHP, and may include deductibles over $1,000 and co-insurance of more than 20% for medicines.
- Historically, the inherent financial risk of CDHPs meant they made sense only for young and healthy people. Employers, prompted by rising healthcare costs, have been making a concerted effort to shift more beneficiaries to these plans.

Chart notes:

A Consumer-Driven Health Plan (CDHP) is a high-deductible health plan coupled with a personal health account that enrollees can use to pay health care expenses not covered by insurance.

Patient out-of-pocket costs have risen three times higher than they were 5 years ago, and seven times higher in consumer-driven health plans

Average Patient Annual Out-of-Pocket Costs by Plan Type, 2008-2012 (per patient, including deductible, copay & co-insurance)



Source: IMS PharMetrics Plus, June 2012

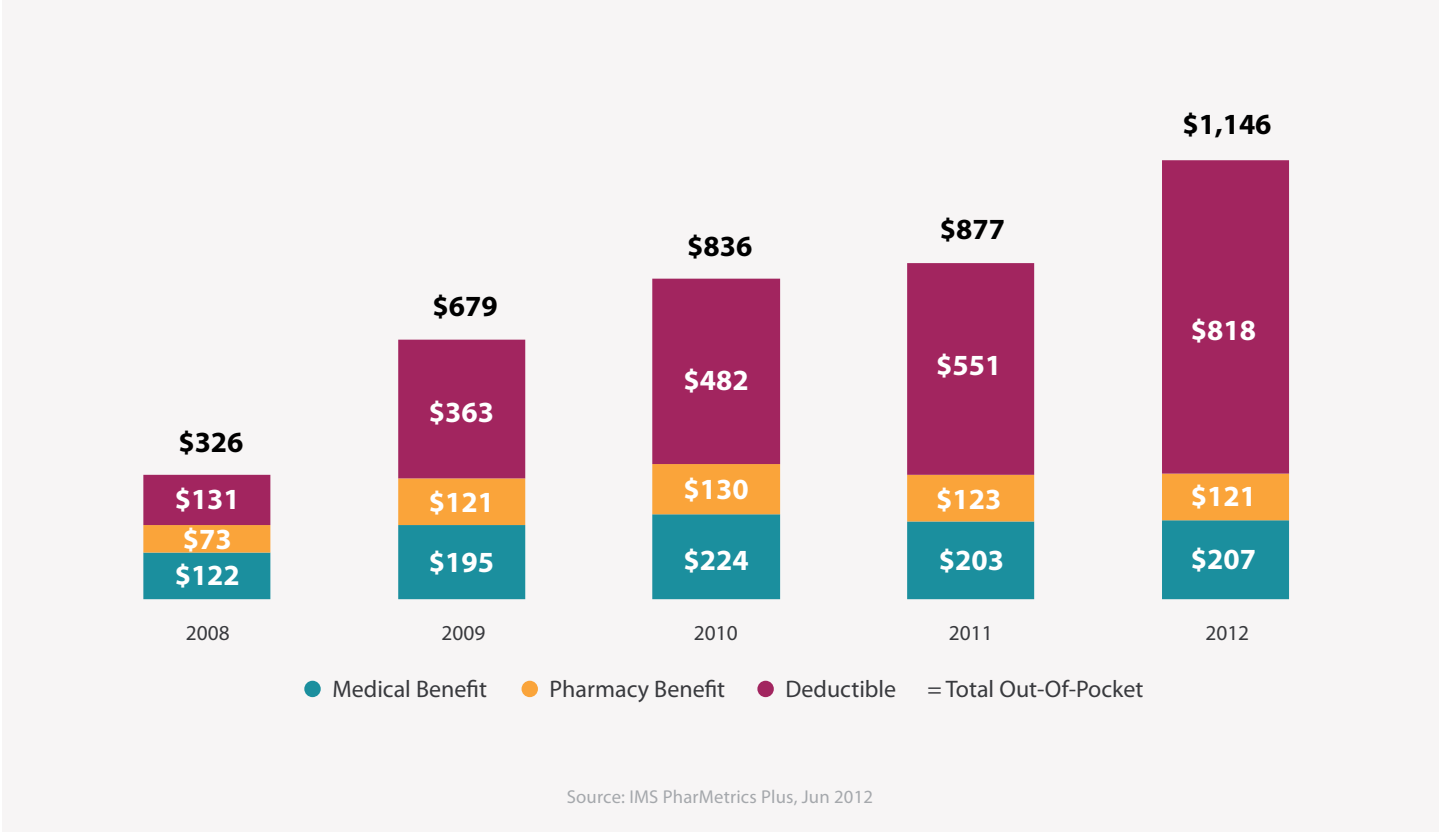
- Patient out-of-pocket cost increases have been seen in both PPO plans and CDHPs.
- Payers have been shifting more of the burden of insurance and prescription drug costs to patients.
- Patients with CDHPs are typically younger and healthier so those who do use healthcare average a lower overall out-of-pocket cost.
- Rising copays or co-insurance are linked to increased abandonment and poorer adherence while conversely, patients who pay less out of pocket are less likely to abandon medication and more likely to stay on therapy.
- While average out-of-pocket costs are rising, individual patients have very different exposure to these costs due to their illnesses, their insurance coverage, and their healthcare choices including medicines.
- Patients with CDHPs have seen rising costs, perhaps because of changes in the mix of patients who are enrolling in these plans as well as changes in benefit designs.

Chart notes:

Annual 2012 out-of-pocket costs approximated using data from the first and second quarters of 2012. Sample size for this analysis: n = 17,926 (2008), n = 23,548 (2009), n = 29,214 (2010), n = 44,602 (2011), n = 62,082 (2012). Dataset matched by patient gender and age. CDHP = consumer-driven health plan; PPO = preferred provider organization (plan). IMS PharMetrics Plus is representative of the commercially insured under-65 population.

Deductibles have driven most of the increases in patient out-of-pocket costs, impacting patient decisions for all types of healthcare

Average Annual Out-of-Pocket Costs for Deductibles, Copay and Co-insurance Spend 2008-2012



Source: IMS PharMetrics Plus, Jun 2012

- Pharmacy copays and co-insurance were $121 of the out-of-pocket spending by insured patients in 2012 down from $123 in 2011.
- Medical benefit copays and co-insurance increased slightly in 2012 to $207.
- Deductibles increased dramatically in 2012 to $818, an increase of $267 or 48%, in the commercially insured under-65 population.
- Patients' exposure to rising out-of-pocket costs may be having an effect on their utilization of healthcare services.

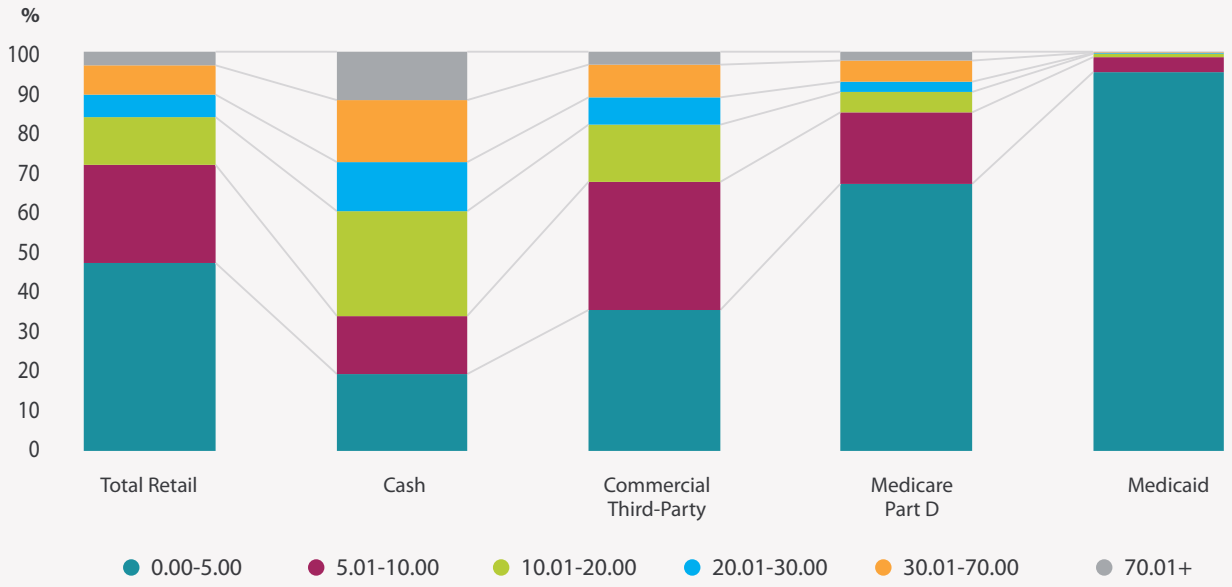
Chart notes:

Annual 2012 out-of-pocket costs approximated using data from the first and second quarters of 2012. Sample size for this analysis: n = 17,926 (2008), n = 23,548 (2009), n = 29,214 (2010), n = 44,602 (2011), n = 62,082 (2012). Dataset matched by patient gender and age.

IMS PharMetrics Plus is representative of the commercially insured under-65 population.

Prescription drug out-of-pocket costs vary widely by payment type

Percent of Retail Dispensed Prescriptions by Out-of-Pocket Costs US$ (2012)



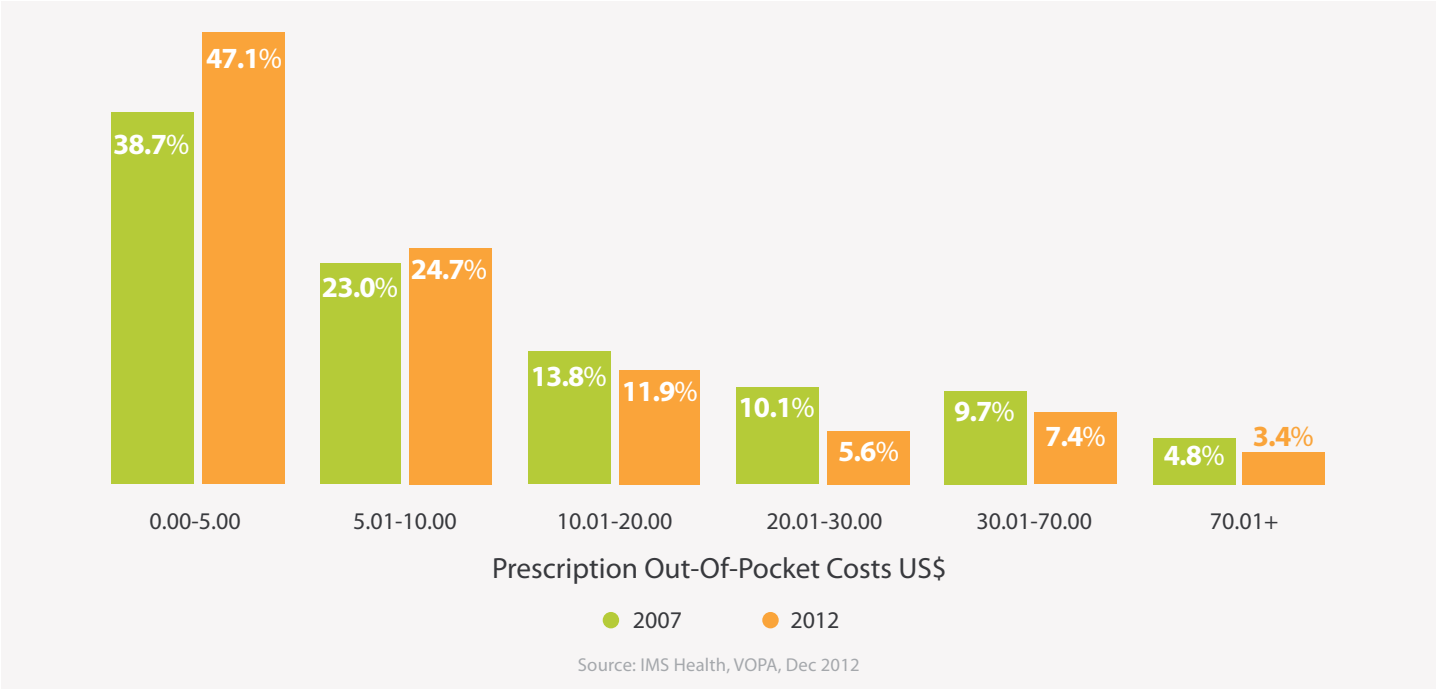
Source: IMS Health, VOPA, Dec 2012

- The average copay for nearly 72% of all retail dispensed prescriptions was $10 or less.
- Medicare Part D prescriptions were substantially lower cost with 84% costing patients less than $10 and only 7% costing more than $30.
- Medicaid prescriptions cost beneficiaries very little, with 95% costing less than $5 and 99% less than $10.
- Commercially insured patients face a higher medicine copayment costs than other insured patients, partly due to their copayments for branded medicines which are typically $20 or more.
- Patients who pay cash, perhaps because of the costs they face, are a relatively small proportion of overall prescription volume.
- It is not possible to consistently measure whether some patients have been paying cash even while they have insurance, though this is understood to be the case in a small number of circumstances where pharmacy discounts and loyalty schemes and manufacturer coupons may offer a better price for that patient.

Chart notes:
Out-of-pocket costs at retail pharmacies for patients with private insurance, Medicare Part D, Medicaid or cash payment.

More patients are paying less than $10 for their prescriptions than five years ago

Percent of Retail Dispensed Prescriptions by Out-of-Pocket Costs US$



Source: IMS Health, VOPA, Dec 2012

- Average out-of-pocket costs have been declining from increasing use of generics, typically costing less than $10 for a prescription.
- Fewer prescriptions are being dispensed in all cost ranges above $10.
- Substantial numbers of products have become available as generics during this period and fewer new medicines have been approved.
- The percentage of prescriptions dispensed with a patient out-of-pocket cost less than $10 increased from 62% to 72% in the last five years.
- Of the 3.5Bn prescriptions dispensed in retail pharmacies in 2012, 72% or 2.5Bn had an out-of-pocket cost of less than $10.
- Higher out-of-pocket costs are typically associated with biologic medicines and other specialty drugs which account for 3% of total retail dispensed prescriptions.

Chart notes:
Out-of-pocket costs at retail pharmacies for patients with private insurance, Medicare Part D, Medicaid or cash payment.

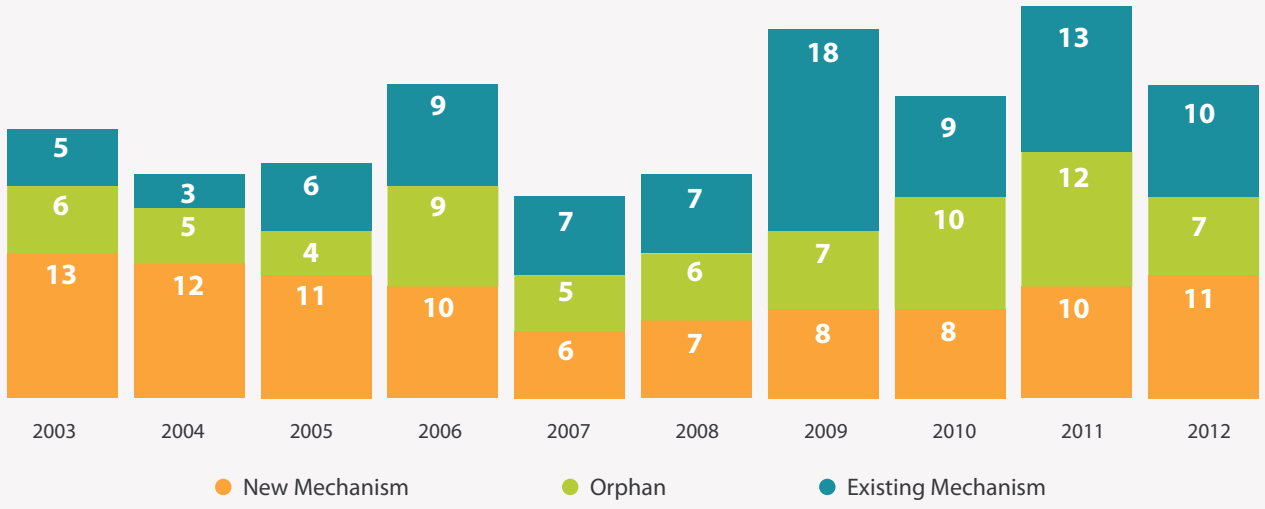
Transformations in Disease Treatment

Many NMEs focused on small or strictly defined patient populations became available in 2012.

- There were 28 New Molecular Entity launches in 2012, down from 35 in 2011.
- Orphan drugs, FDA approvals for rare diseases affecting less than 200,000 people, were launched for Gaucher's disease, cystic fibrosis, chronic myeloid leukemia, and multiple myeloma.
- There were nine new cancer treatments launched, the most in over a decade, including a breakthrough for very common skin cancers.
- 2012 launches also included ten medicines with easier dosing including once-daily formulations of diabetes drugs, an inhalable form of an antipsychotic drug, and a short 3-day topical treatment for one of the most common forms of skin condition that can result in skin cancer if untreated.
- Researchers discovered that previous exposure to JC virus was the primary cause of fatalities associated with the multiple sclerosis treatment natalizumab (Tsyabri®), originally launched in 2006, and can now administer a blood test to prevent patients from suffering from progressive multifocal leukoencephalopathy (PML) a rare and usually fatal viral brain disease.
- A synthetic alternative to biologic erythropoiesis-stimulating agent (ESA) medicines, peginesatide (Omontys®) was launched in April 2012, but was recalled in early 2013 due to unexpected safety issues.
- FDA began 2013 by granting Breakthrough Therapy Designations which could lead to extremely rapid clinical progress and availability of medicines within just a couple of years.
- Breakthrough products to treat Hepatitis C, multiple sclerosis, cystic fibrosis, and a number of cancers, are expected in the next few years.

Medicines with novel mechanisms launched in 2012 maintain momentum of upturn in the number of new product launches

New Molecular Entities Launched in the U.S. 2003-2012



Source: IMS Institute for Healthcare Informatics, Mar 2013

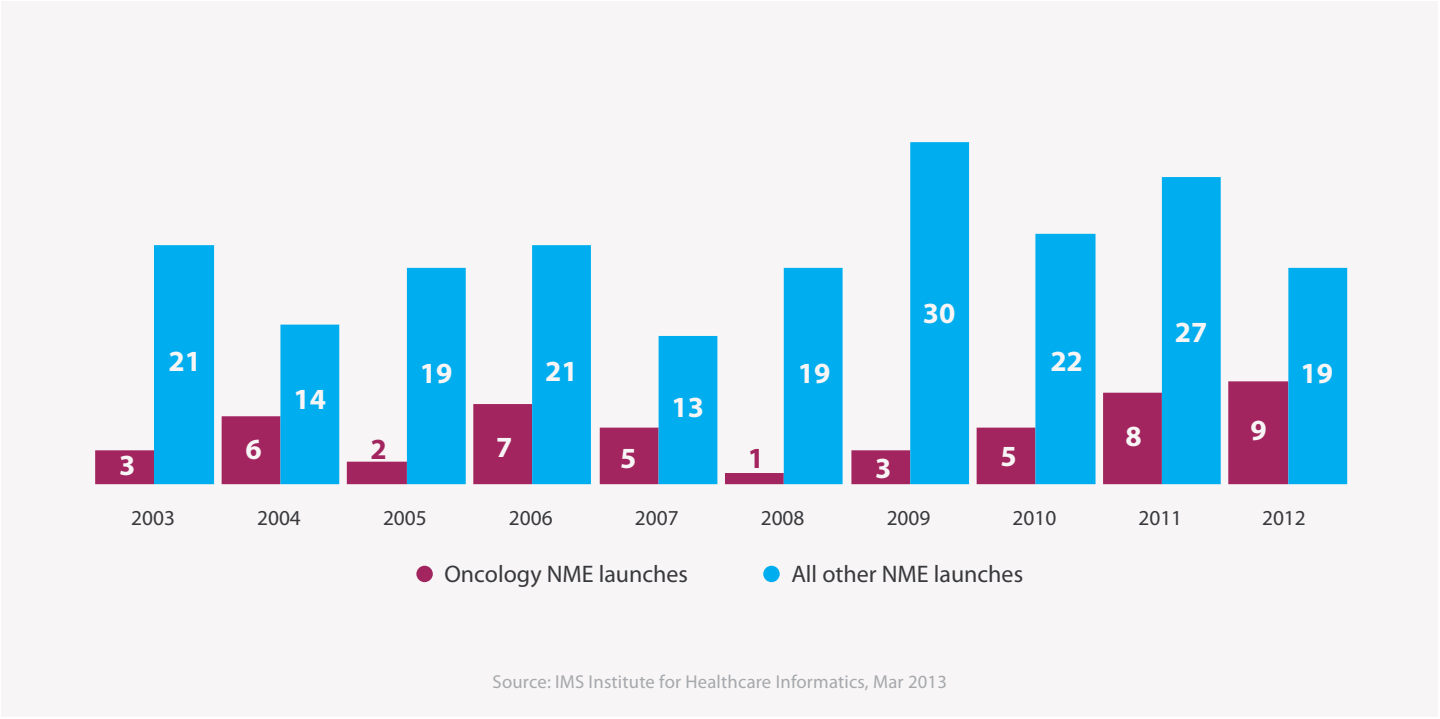
- 28 New Molecular Entities were launched in 2012, 18 of which had novel mechanisms or orphan indications, three fewer than 2011 but part of the largest number of FDA approvals since the late 1990s with 39 approvals. Some of these approvals occurred late in December meaning they will launch in 2013.
- Medicines with new mechanisms of action in their therapy areas were launched in greater numbers versus prior years, many of which represented significant breakthroughs.
- There were 7 launches of orphan disease medicines for rare diseases affecting less than 200,000 people and for which few therapies are effective.

Chart notes:

New Molecular Entity (NME): A novel molecular or biologic entity or combination where at least one element is novel. NME 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.

The 9 New Molecular Entities to treat cancers launched in 2012 is the most in a decade

New Molecular Entities Launched in the U.S. 2003-2012



Source: IMS Institute for Healthcare Informatics, Mar 2013

- 52% of R&D activity has been focused in cancer for most of the last decade and the increase in the number of launches is a reflection of those historic investments.
- The 9 oncology NMEs launched in 2012 is the most in a decade and a continuing increase over the low-point with only one launch in 2008.
- New treatments include vismodegib, a breakthrough therapy for one of the most common forms of skin cancer, basal-cell carcinoma.
- New treatments included new medicines and additional uses for existing treatments in breast cancer, renal cell carcinoma, colorectal cancer, chronic myeloid leukemia, myeloma, prostate cancer, non-small cell lung cancer, and soft tissue sarcomas.

Chart notes:

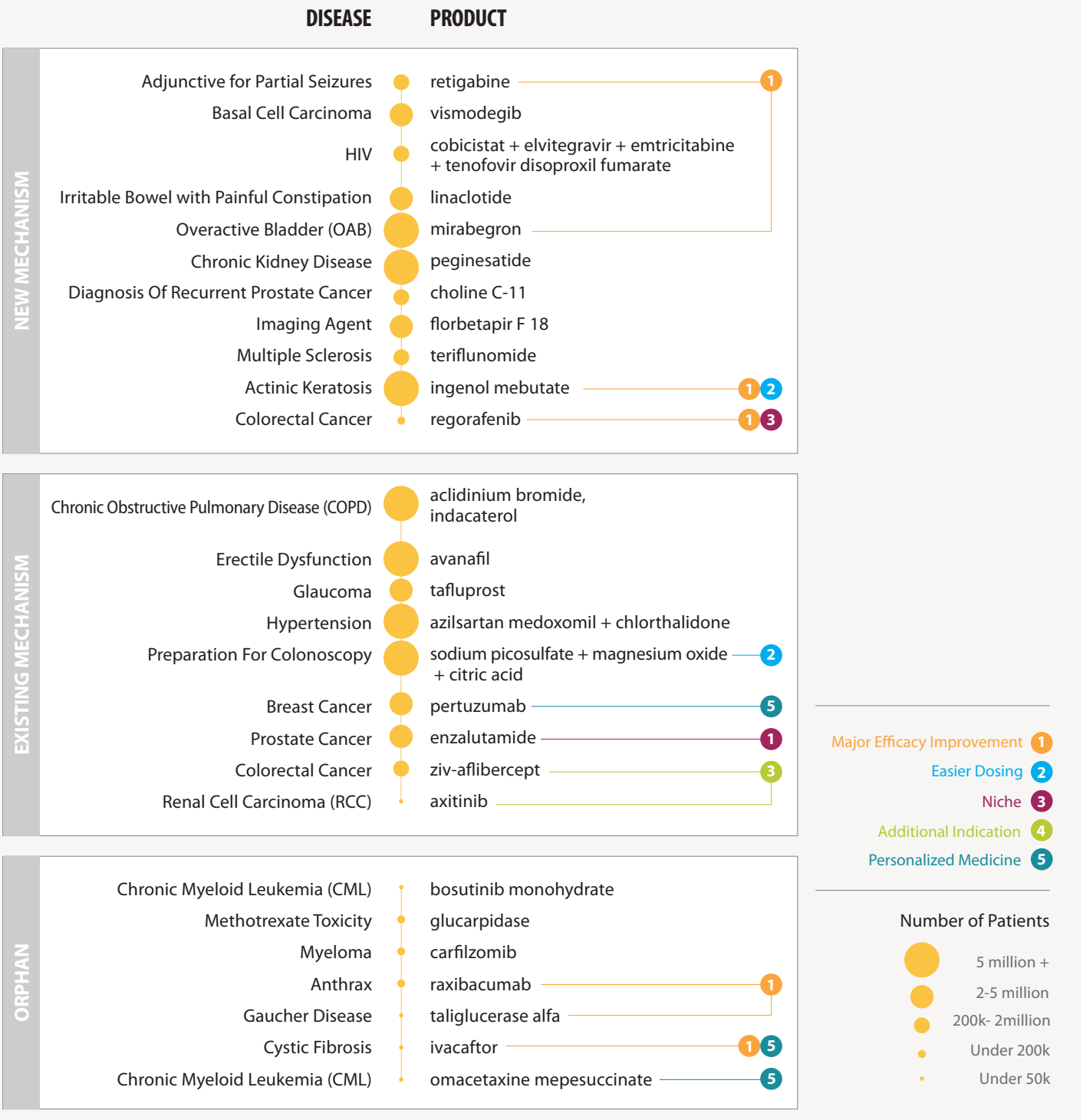
New Molecular Entity (NME): A novel molecular or biologic entity or combination where at least one element is novel.

NME launches in the U.S. by year of launch, regardless of timing of FDA approval.

Oncology NME launches include therapeutic oncology treatments, and exclude supportive care and diagnostics.

A large number of breakthroughs were launched to treat diseases affecting a few thousand to several million people

New Molecular Entity Launches in 2012



2012 saw many new formulations and additional uses of existing medicines, especially easier dosing options

Other New Medicine Launches in 2012

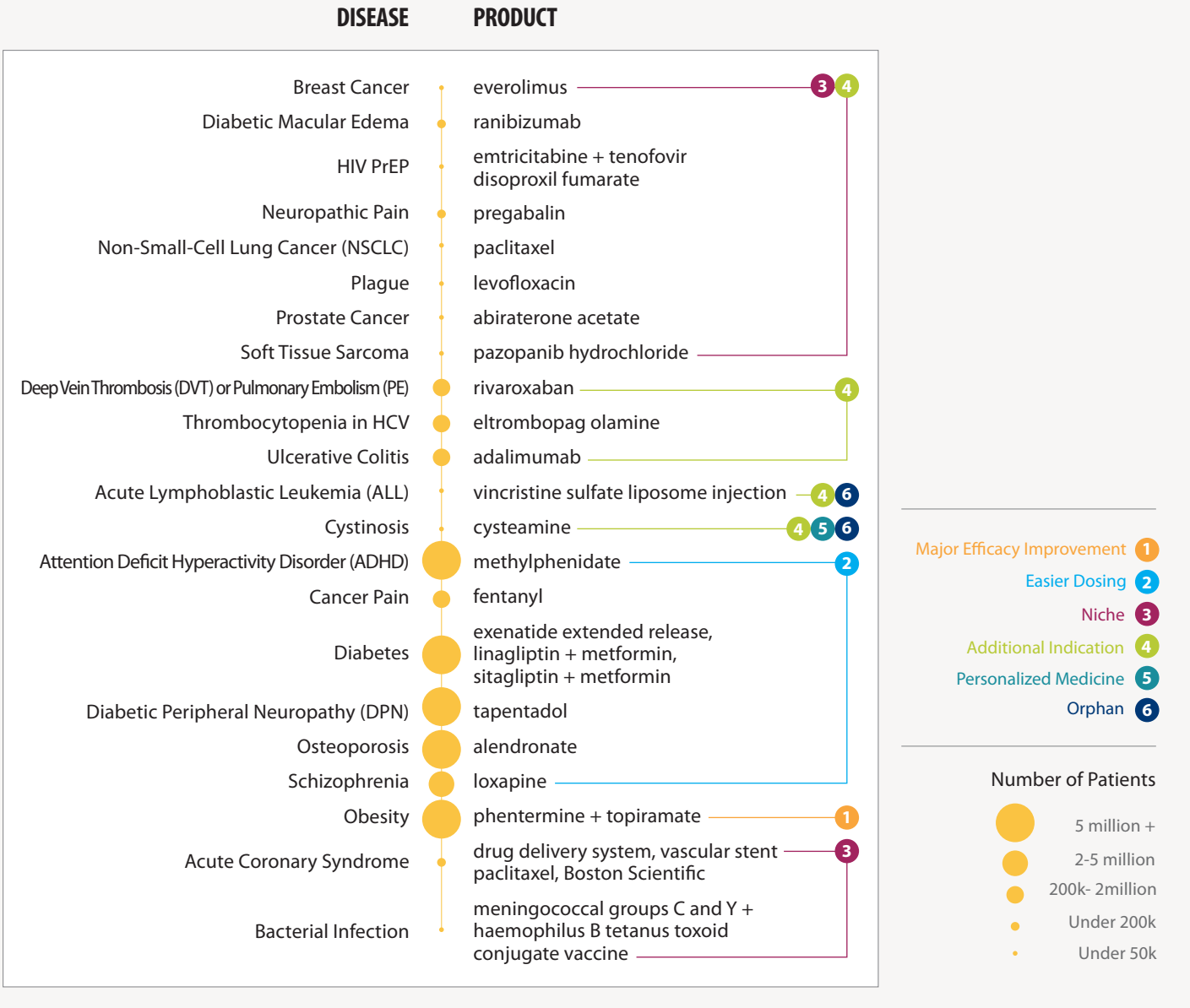


Chart notes:

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

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

Niche indicates smaller patient populations where orphan status was not granted by FDA.

HIV PrEP - pre-exposure prophylaxis.

Some key breakthrough therapies were approved or became available for the first time in 2012

New medicines launched last year brought improved efficacy, safety and convenience for diseases affecting patient populations as small as a few hundred with a rare genetic variant of cystic fibrosis to millions battling the most common forms of skin cancer.

Among the most notable developments were:

Cystic fibrosis: ivacaftor (Kalydeco™). Cystic Fibrosis (CF) is a progressive lung disease caused by mutations that affect ion transport by the cystic fibrosis transmembrane regulator (CFTR) protein. Until 2012, the standard of care for cystic fibrosis entailed treating the symptoms of CF. The introduction of ivacaftor (Kalydeco™) brings a functional cure for 4 to 5% of the approximately 30,000 CF patients in the United States (those having two copies of the G551D mutation), and it will significantly improve life expectancy of this subset of patients. Ivacaftor FDA breakthrough designations in January 2013 as monotherapy and for a combination therapy with investigational compound VX-809.

Rheumatoid arthritis: tofacitinib (Xeljanz®). Approved at the end of 2012, this is the first of a new class of therapies for this indication. Unlike the dominant rheumatoid arthritis treatments, TNF-inhibitors, tofacitinib works by inhibiting a type of signaling protein, JAK (janus associated kinases) which are implicated in a variety of immune diseases and cancers, suggesting there may be multiple additional uses for this drug and others like it.

Basal-cell carcinoma: vismodegib (Erivedge®). This is the first therapy for the most common type of skin cancer. The Erivance BCC trial showed response rates of 43% in patients with locally advanced basal-cell carcinoma and 30% in patients with metastatic basal-cell carcinoma. An editorial in the New England Journal of Medicine hailed vismodegib as the "greatest advance yet seen for this disease [basal cell carcinoma]". The hedgehog pathway targeted by vismodegib, is implicated in multiple cancer types leaving open the possibility of new therapeutic uses in the future.

Irritable bowel syndrome with constipation: linaclotide (Linzess™). This condition affects 7-15% of the U.S. population but prior to 2012, the lone FDA-approved treatment on the market was indicated for women only. In addition to being indicated for both sexes, linaclotide is taken once daily and also contributes to reduction of intestinal pain.

HIV: emtricitabine and tenofovir disoproxil fumarate (Truvada®). In July 2012, FDA approved the use of this product for for Pre-Exposure Prophylaxis (PrEP) to reduce the risk of sexually transmitted HIV in people who are not infected with the virus. The annual treatment cost of $13,000 is likely to limit the usage to those with the financial means and who are at risk due to their sexual behavior.

The four drug combination, or "Quad" of elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate, (STRIBILD™). This once-daily treatment of HIV in adults who have never received HIV treatment is expected to bring the convenience of a one-tablet a day regimen and fewer psychiatric side effects than other three-in-one HIV medications; however drug drug interactions (DDIs) with cobicistat (the "booster" in STRIBILD™) may limit its use somewhat, particularly in patients also infected with hepatitis C.

Notable safety related issues:
Researchers discovered that previous exposure to JC virus was the primary cause of fatalities associated with multiple sclerosis treatment natalizumab (Tysabri®), originally launched in 2006. FDA has now approved a blood test that can be administered to detect the JC virus and avoid the risk of patients suffering from progressive multifocal leukoencephalopathy (PML) a rare and usually fatal viral brain disease.

A synthetic alternative to biologic erythropoiesis-stimulating agent (ESA) medicines, peginesatide (Omontys®), was launched in April 2012, but was recalled in early 2013 due to unexpected safety issues.

Treatment will continue to be transformed by a range of new medicines that are likely to emerge from clinical trials in the next few years

The next few years are expected to bring a number of safer, more narrowly targeted and highly effective therapies for a wide range of diseases, some reaching patients far faster than ever before.

Breakthrough FDA designations

Enacted as part of the 2012 FDA Safety and Innovation Act (FDASIA), FDA's Breakthrough Therapy Designation can expedite the development and review time for a potential new medicine "to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies." With this new designation, medicines can progress rapidly from their first human trials to full approval in just a couple of years, compared to the normal 8-10 year timeframe. In addition to two of these designations granted to Cystic Fibrosis drug ivacaftor (Kalydeco®), additional designations were granted for ibrutinib and LDK378, and FDA is currently reviewing another eleven applications.

"Smart Bomb" for breast cancer

In February 2013, the FDA approved Kadcyla™ (trastuzumab emtansine) an antibody-drug conjugate consisting of the monoclonal antibody trastuzumab (Herceptin®) linked to the cytotoxic agent mertansine (DM1), and has been called a "smart bomb" for the targeted delivery of the cytotoxic agent only to tumor cells expressing HER2 genes.

The next wave of multiple sclerosis treatments

The FDA approved oral treatment dimethyl fumarate (Tecfidera™) which could deliver significant efficacy improvements over current standards of care for multiple sclerosis. It activates teh Nrf-2 pathway which is understood to play an important role in neuroprotection.

The next hope in type-II diabetes treatment

In March 2013, FDA approved the first of the newest class of type-II diabetes agents, SGLT-2 inhibitors, with Janssen's canagliflozin (Invokana™), which blocks the reabsorption of glucose and could be an important addition to the options for type-II diabetes management.

All-oral regimens in hepatitis C

Approvals are expected in late 2013 for the first once-daily protease inhibitor (simeprevir) and the first nucleotide (sofosbuvir) to treat Hepatitis C virus (HCV). The first of the all-oral regimens for genotype-1 HCV (about 70% of HCV cases) are expected to receive approval in the second half of 2014. As a result of the availability of these new therapies, the spending on medicines for HCV is expected to increase dramatically, which may help to lower overall healthcare costs by reducing the number of patients eventually suffering some of the worst complications such as liver failure, liver cancer or the need for transplants.

Prescription drugs for obesity

Lorcaserin (Belviq®), approved in July 2012 and expected to launch in the 2nd quarter of 2013, is the first novel active substance for obesity treatments approved in over a decade. It acts on serotonin and appetite receptors. It was approved shortly after a combination product phentermine + topiramate (Qsymia™) which is a combination of a stimulant and an additional use for a migraine medicine.

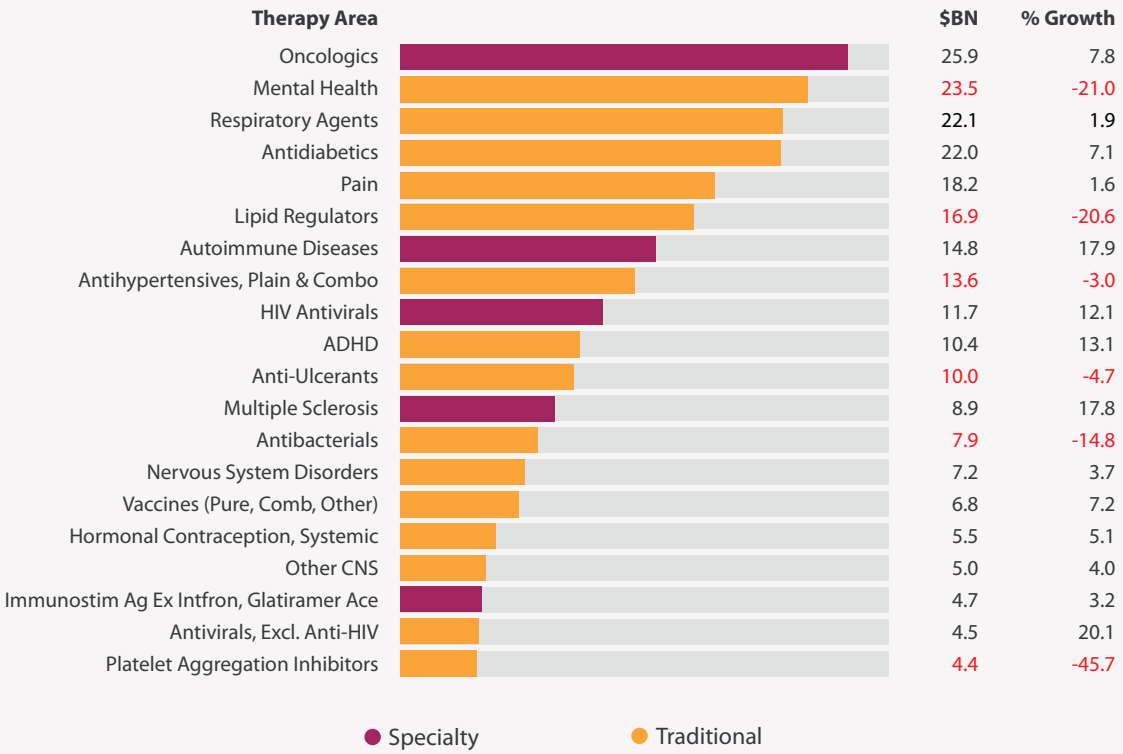
Usage and Spending in Major Therapy Areas

Patent expiries provided savings in a number of therapy areas while new medicines drove spending in specialty therapy areas.

- The top 5 classes in 2012, based on spending, were oncologics ($25.9Bn), mental health ($23.5Bn), respiratory agents ($22.1Bn), antidiabetics ($22.0Bn), and pain ($18.2Bn).
- Absolute spending growth gains were highest for antivirals (excluding HIV), multiple sclerosis, ADHD, HIV antivirals, and autoimmune diseases.
- Antivirals excluding HIV, the therapy area that includes flu vaccines and newer treatments for Hepatitis C virus, grew by more than 20% driven by breakthrough therapy Incivek®.
- Oncologics spending was $25.9Bn in 2012, up 7.8% from innovative new targeted therapies and offset by patent expiries.
- Spending on mental health declined by $6.2Bn to $23.5Bn in 2012 mainly from patent expiries.
- Respiratory treatments reached $22.1Bn, up $0.4Bn, with savings from the patent expiries and generic competition offsetting increased spending on branded medicines.
- Antidiabetes spending grew by $1.5Bn, driven by insulins and further uptake of newer generation therapies. 13 million patients were treated with diabetes medicines.
- Pain spending in 2012 reached $18.2Bn, up 1.6%, relatively slow growth for these widely used medicines.

Over one-third of spending was concentrated in the top 5 therapies

Spending in Leading Therapy Areas



Source: IMS Health, National Sales Perspectives, Dec 2012

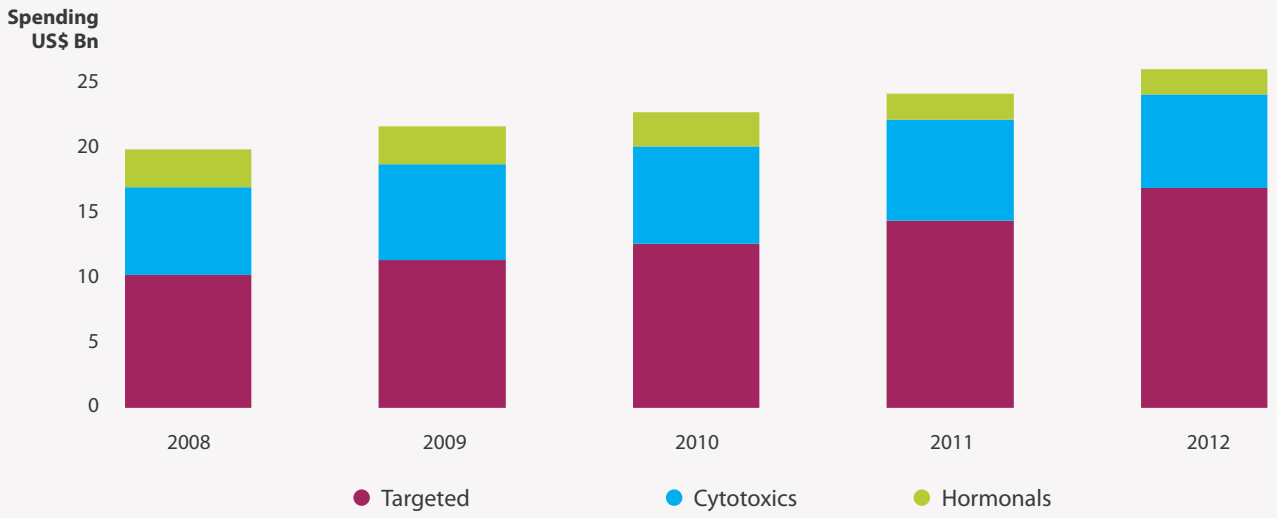
- The top 5 classes in 2012, based on spending, were oncologics ($25.9Bn), mental health ($23.5Bn), respiratory agents ($22.1Bn), antidiabetics ($22.0Bn), and pain ($18.2Bn).
- Absolute spending growth gains were highest for antivirals (excluding HIV), multiple sclerosis, ADHD, HIV antivirals, and autoimmune diseases.
- Spending was up more than 20% antivirals excluding HIV, the category that includes flu vaccines and newer treatments for hepatitis C virus.
- Oncologics grew by less than 8% (up from 6.3% in 2011), as new treatments became available to more patients and the savings from patent expiries from prior years were fully realized.
- Spending in four classes, mental health, lipid regulators, antibacterials, and platelet aggregation inhibitors declined by more than 10%, all driven by patent expiries.

Chart notes:

Specialty, Traditional and therapy area definitions based on proprietary IMS Health definitions. Spending measured at the price paid to wholesalers or manufacturers by retail and non-retail channels and excluding off-invoice discounts and rebates that lower net prices received by manufacturers.

Oncologics spending reached $25.9Bn in 2012

Oncology Spending by Area



Source: IMS Health, National Sales Perspectives, Dec 2012

- Oncologics led all classes in spending in 2012, at $25.9Bn.
- Spending grew by nearly $1.9Bn, which was higher than the $1.4Bn of growth in 2011.
- Recovery in growth has been driven by new brands launched within the last two years, which contributed $1.4Bn of growth for the second straight year.
- Patent expiries and resulting lower cost generics resulted in $744Mn of lower brand spending in 2012, less than half the impact seen in 2011 when patent expiries drove a decline of $1.7Bn in brand spending.
- Targeted agents grew by $2.5Bn, higher than the $1.8Bn in 2011, but mostly driven by launches in 2011 rather than contribution from 2012 launches.
- Hormonal therapies, typically for breast and prostate cancer, reduced spend by $60Mn after letrozole became generically available in 2011.

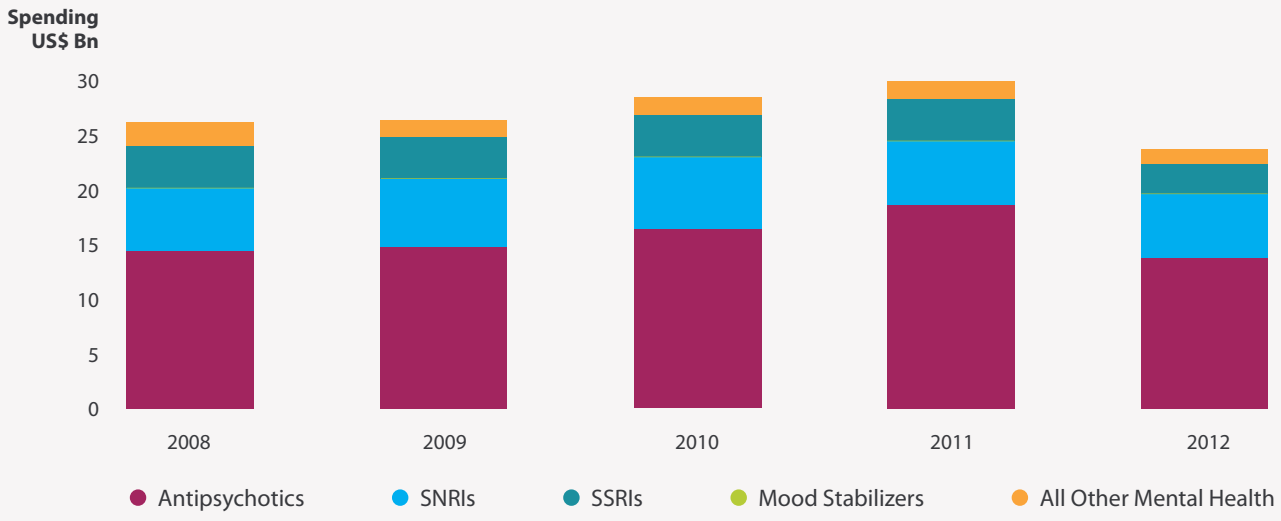
Chart notes:

Therapy areas are based on proprietary IMS Health definitions.

Spending growth defined as dollar growth driven by price, volume, new products and mix changes.

Spending on mental health declined by $6.2Bn to $23.5Bn in 2012 mainly from patent expiries

Mental Health Spending by Area



Source: IMS Health, National Sales Perspectives, Dec 2012

- Mental health was the second largest area of spending on medicines in 2012, with $23.5Bn in 2012, down from $29.7Bn in 2011.
- Spending declined due to patent expiries in antipsychotic and antidepressant therapy areas during 2012.
- Antipsychotic medicines olanzapine (Zyprexa®), quetiapine (Seroquel®) and ziprasidone (Geodon®) lost protection and faced generic competition, losing $6.7Bn in sales. Spending in 2012 on generics of these three molecules totaled $984Mn.
- Escitalopram (Lexapro®), an antidepressant in the selective serotonin reuptake inhibitor area (SSRI) lost protection and $2.2Bn in sales, replaced by $1.1Bn in spending on generics.

Chart notes:

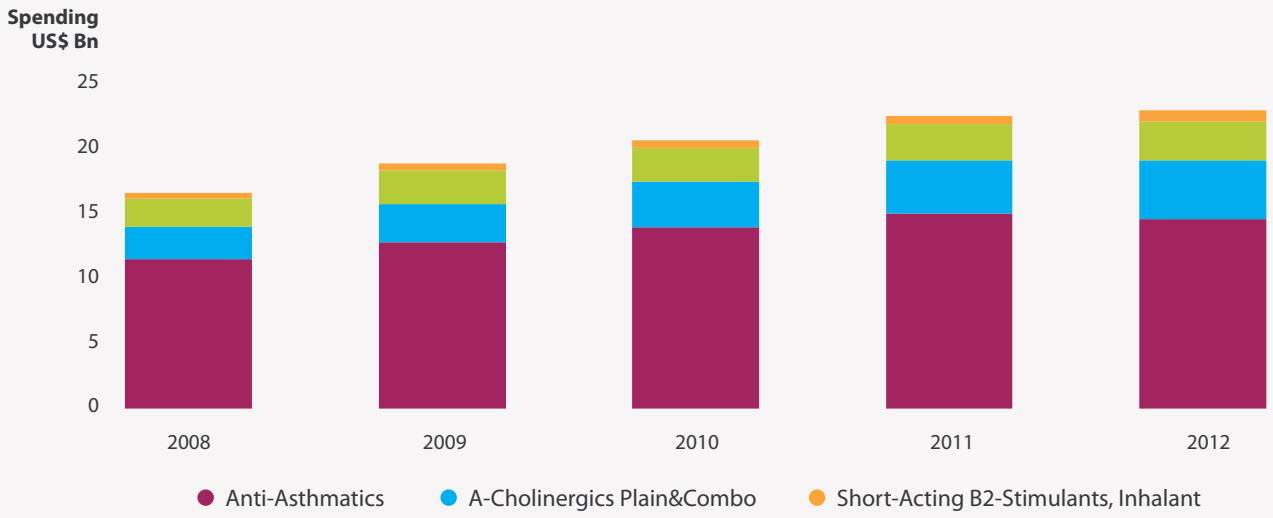
Therapy areas are based on proprietary IMS Health definitions. Mental health includes treatments for depression and psychoses including bipolar disorder, schizophrenia, and other forms of mania. Antipsychotics include "typical" and "atypical" antipsychotics.

SNRI – Serotonin–norepinephrine reuptake inhibitor. SSRI – Selective serotonin reuptake inhibitor.

Mood stabilizers – include lithium, carbamazepine, lamotrigine, divalproex, and other similar medicines

Asthma and COPD accounted for $22.1Bn in spending

Respiratory Spending by Area



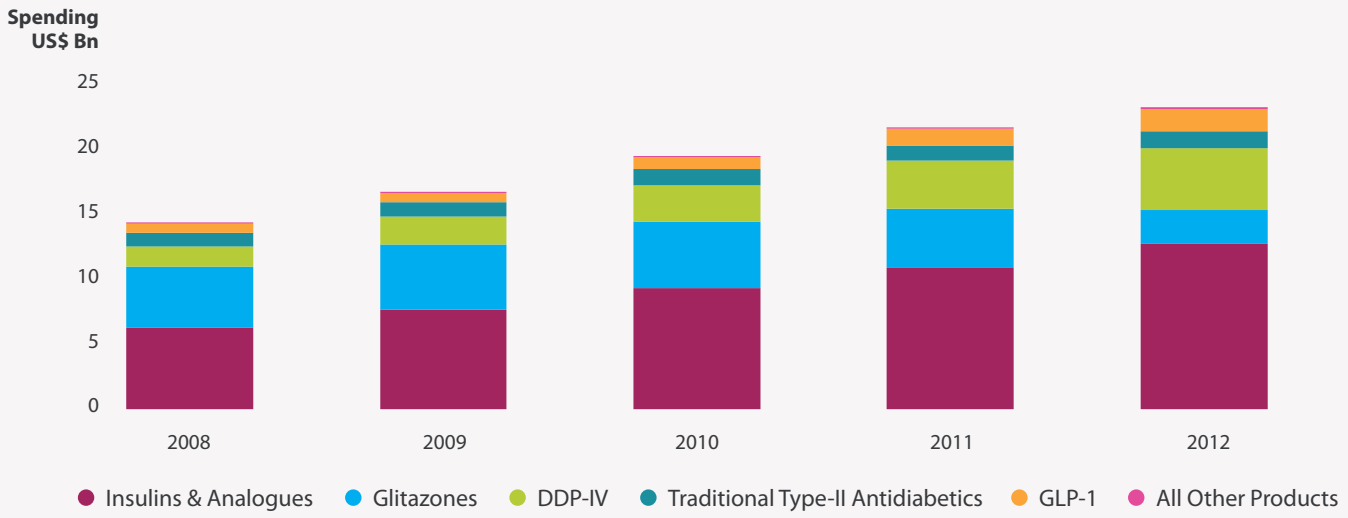
Source: IMS Health, National Sales Perspectives, Dec 2012

- Respiratory agent spending was $22.1Bn in 2012. Spending growth was $420.8Mn in 2012, down from $1.8Bn in 2011 due to generic montelukast entering the market.
- Anti-asthmatics made up two-thirds of the spending within the respiratory classes in 2012, at $14Bn.
- Leading therapies in the anti-asthmatic therapy area included combination product fluticasone/salmeterol (Advair® Diskus®), which is approved for use for both asthma and COPD.
- Asthma treatment montelukast (Singulair®), lost patent protection in 2012 and spending declined by $1.2Bn as a result of lower spending on the brand and the transition to generics.
- Anticholinergic agents used in the treatment of COPD contributed $462Mn in growth versus $531Mn in 2011. Leading therapies in this class included tiotropium bromide inhalation powder (Spiriva® Handihaler®) and albuterol and ipratropium inhalation (Combivent®).

Chart notes:
Therapy areas are based on proprietary IMS Health definitions.
COPD – Chronic Obstructive Pulmonary Disease.

Increased diabetes spending was driven by insulins and DPP-IVs

Antidiabetes Spending by Area



Source: IMS Health, National Sales Perspectives, Dec 2012

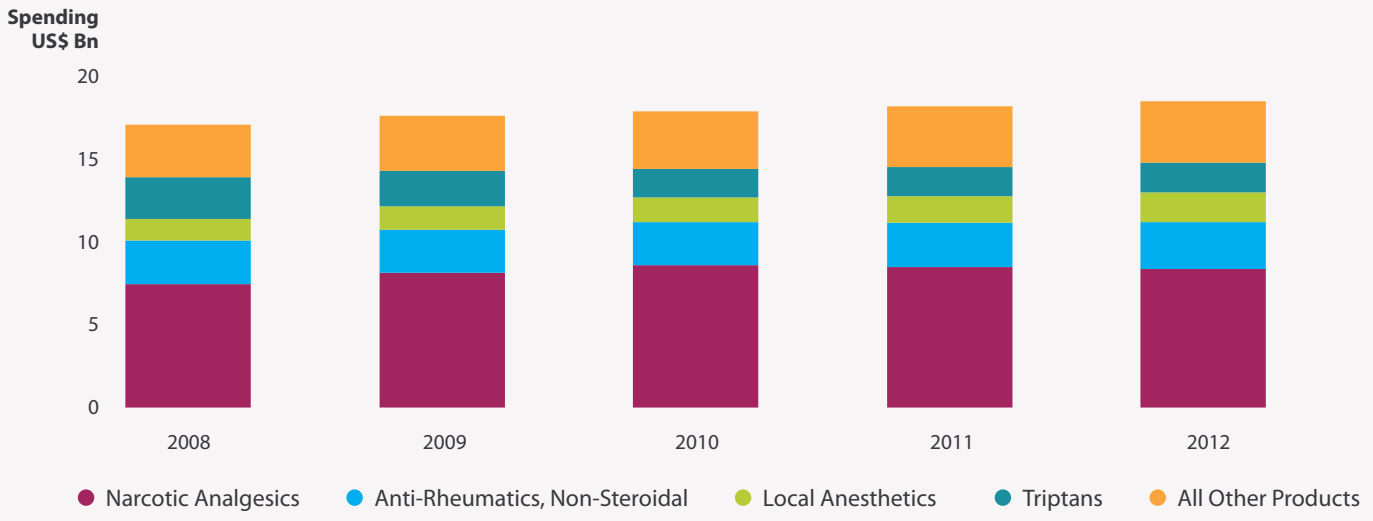
- Diabetes spending reached $22.0Bn, as growth decreased slightly at $1.5Bn in 2012, down from $2.1Bn in 2011.
- Patients filled 173Mn prescriptions in 2011, up 0.5% over 2010.
- Spending for human insulins and synthetic analogues increased by $1.8Bn in 2012 led by insulin glargine (Lantus®).
- DPP-IV therapies contributed $1.0Bn to increased spending.
- GLP-1 therapies exenatide (Byetta®) and liraglutide (Victoza®) and newly launched long-acting formulation of exenatide (Bydureon™) together had spending growth of $426Mn.
- Concerns about cardiovascular complications have limited the use of glitazone therapies since 2007, while patent expiry and generic competition were the key driver of lower spending on pioglitazone (Actos®) products in 2012.

Chart notes:

Therapy areas are based on proprietary IMS Health definitions. DPP-IV - Dipeptidyl peptidase-4 inhibitors block glucagon and reduce blood glucose levels.
GLP-1 –Glucagon-like peptide-1 are a type of incretin mimetic that simulate natural metabolic hormones in type-II diabetics.
All Other Products include multi-therapy combinations and other therapies used in diabetes

Pain spending in 2012 reached $18.2Bn, up 1.6%

Pain Spending by Area



Source: IMS Health, National Sales Perspectives, Dec 2012

- Pain spending reached $18.2Bn, growing by $289Mn in 2012.
- The largest spending increase was in local anesthetics, associated with price increases and a mild recovery in elective surgeries.
- Narcotic Analgesics dropped by $86.7Mn since 2011 largely from the continuing impact on usage from the reformulation of oxycodone (OxyContin®) into an abuse-resistant form in June 2010.
- Narcotic pain medicines are used for both chronic and episodic pain following surgery.

Chart notes:

Therapy areas are based on proprietary IMS Health definitions. Includes medicines for pain including anesthesia products, NSAIDS (non-steroidal anti-inflammatories), Narcotic analgesics, non-narcotic analgesics and anti-migraine medicines including triptan and non-triptan migraine medicines.

Notes on sources

This report is based on the IMS services detailed in the panel 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.

NPA Market Dynamics (NPA-MD)™ is a national-level prescription offering that links NPA with de-identified patient-level data that tracks patients over time and enables analysis such as whether a patient's prescription was new, switched from another medicine, or added to an existing regimen in the last year. Diagnoses, compliance and persistence, as well as ethnicity analytics are among other analyses that are possible.

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.

IMS MIDAS™ is an analytics platform used to assess worldwide healthcare markets. It aggregates IMS's global audits and normalizes to international standards of product naming, company ownership, currency exchange rates, volume metrics and product segmentations, and estimates of price levels at different points in the supply chain. Segmentations include therapy classes, forms, dosages, and those related to brands, generics and patent protection.

IMS Market Prognosis™ is a comprehensive, strategic market forecasting publication that provides insight to decision makers about the economic and political issues which 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.

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.

Vector One®: National (VONA) is a nationally syndicated database that provides nationally projected counts of patient-based prescription activities including measures of new starts, switching, and continuances.

Vector One®: Payer (VOPA) is a nationally syndicated database that provides estimates of projected patient activities by drug and the payers who help patients subsidize the costs of the medication. VOPA provides both product plan shares as well as measures of patient out-of-pocket costs (OPC).

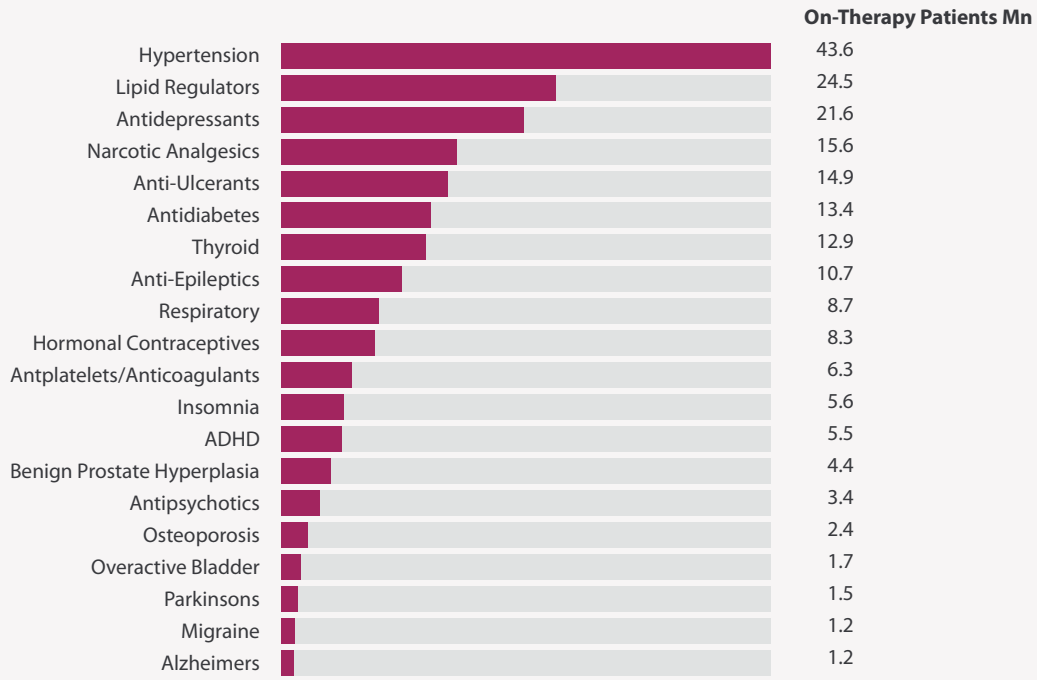
PharMetrics is a closed-source de-identified longitudinal patient database that is derived from the activities as provided by plans and payers. Patient membership eligibility is accounted for within the source which ensures complete longitudinal activity per patient. The PharMetrics database captures activity from 15Mn patients per year with 70Mn cumulative unique patients available for analysis.

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 legacy PharMetrics data with Health Intelligence Company's participating plan claims data. Health Intelligence Company is the operating entity of Blue Health Intelligence.

FAN: The Flu/Cold/Respiratory Activity Notification program (FAN®) measures the total affected population with upper respiratory illness at both a national level and regional level down to 135 geographic markets within the U.S. FAN provides flu status levels for each regional market area reflecting seasonal severity and illness spread rate throughout the season.

On-Therapy Patients - 2012

Treated Patients in Selected Therapies



Source: IMS Health, NPA Market Dynamics, Dec 2012

Appendix notes:

Hypertension includes plain and combo ace inhibitors, angiotensin II inhibitors, renin inhibitors, beta blockers and calcium channel blockers.

Lipid regulators include all cholesterol lowering drugs.

Antidepressants include SSRIs, SNRIs and newer generation products.

Narcotic analgesics include codeine, morphine, propoxyphene and other synthetic narcotics. On-therapy patients reflect those patients on therapy as of December 2012. Narcotics are estimated to be used by as many as 75Mn unique patients per year, though only 15-16Mn are on therapy at any one time.

Anti-ulcerants is limited to the proton pump inhibitors (PPI).

Antidiabetes includes human insulins & analogues, oral antidiabetics and newer generation diabetes treatments including glitazones, GLP-1 analogues and DPP-IV inhibitor classes.

Thyroid includes natural & synthetic thyroid hormonal preparations.

Anti-epileptics include drugs for seizure disorders, some of which are also used for pain indications.

Respiratory agents include maintenance products for asthma & COPD.

Insomnia includes melatonin agonists and other non-barbiturate sleep aids.

Antiplatelets/anticoagulants include oral antiplatelets such as Plavix®, and anticoagulants such as warfarin.

ADHD (Attention Deficit Hyperactivity Disorder) includes medications such as Ritalin® and newer generation psychotherapeutic agents.

Benign prostate hyperplasia (BPH) includes alpha blockers and other agents.

Antipsychotics includes typical and atypical antipsychotics.

Osteoporosis includes biphosphonates, calcitonins, bone density regulators and bone formation agents, but not hormonal therapies.

Overactive bladder includes antispasmodics for urinary incontinence.

On-therapy patients are defined as those who have received a dispensed prescription in prior months and for which the amount of medicine and dosage prescribed has not been exhausted.

Therapy areas are based on proprietary IMS Health definitions.

Patients treated in these 20 leading chronic therapy areas represent 52% of spending and 52% of prescriptions in 2012.

Top Therapeutic Classes by Prescriptions

Dispensed Prescriptions Mn		2008	2009	2010	2011	2012
Total U.S. Market		**3,870**	**3,953**	**3,997**	**4,028**	**4,078**
1	Antihypertensives, Plain & Combo	653	654	657	653	656
2	Pain	439	449	459	465	472
3	Mental Health	293	301	309	320	329
4	Antibacterials	272	275	271	274	268
5	Lipid Regulators	238	249	255	255	255
6	Other CNS	173	179	184	188	189
7	Antidiabetics	166	169	172	173	174
8	Respiratory Agents	147	152	153	153	159
9	Anti-Ulcerants	139	146	147	150	157
10	Nervous System Disorders	128	135	142	148	156
11	Thyroid Preps	104	105	107	110	114
12	Hormonal Contraception, Systemic	94	93	91	90	91
13	ADHD	58	62	67	73	78
14	Vitamins & Minerals	68	73	78	77	76
15	Corticosteroids, Plain	49	51	53	55	58
16	Nasal Preps, Topical	40	41	44	46	49
17	Corticosteroid, Topical, Plain & Combo	41	43	44	44	45
18	Other Cardiovasculars	50	47	46	45	44
19	Sex Hormones (Androgens, Oestrogens, Progestogens)	41	39	38	36	37
20	Vitamin K Antagonists	35	36	36	34	34

Source: IMS Health, National Prescription Audit, Dec 2012

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 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.

Updated March 22, 2013

Top Medicines by Prescriptions

Dispensed Prescriptions Mn		2008	2009	2010	2011	2012
Total U.S. Market		**3,870**	**3,953**	**3,997**	**4,028**	**4,078**
1	hydrocodone/paracetamol	125.5	129.4	132.1	136.7	135.3
2	levothyroxine sodium	98.8	100.2	103.2	104.7	107.5
3	lisinopril	77.2	83.0	87.6	88.8	90.8
4	simvastatin	68.0	84.1	94.4	96.8	86.1
5	metoprolol	79.7	76.9	76.6	76.3	78.1
6	amlodipine	46.0	52.1	57.8	62.5	66.0
7	omeprazole	35.8	45.6	53.5	59.4	65.7
8	metformin	51.6	53.8	57.0	59.1	61.6
9	salbutamol	50.1	54.5	55.1	56.9	61.5
10	atorvastatin	58.5	51.7	45.3	43.3	54.9
11	azithromycin	51.9	54.7	53.6	56.2	54.5
12	amoxicillin	51.3	52.8	52.4	53.8	52.0
13	alprazolam	43.3	45.3	47.7	49.1	49.2
14	hydrochlorothiazide	48.5	47.9	47.8	48.1	47.7
15	zolpidem	39.1	42.7	43.7	44.6	43.8
16	furosemide	44.4	43.8	43.6	42.3	41.9
17	fluticasone	24.2	28.0	32.8	36.7	41.4
18	sertraline	33.7	34.8	36.2	37.6	39.2
19	citalopram	22.6	27.3	32.2	37.8	38.9
20	gabapentin	22.5	25.7	29.6	33.4	38.0
21	tramadol	23.3	25.5	28.0	33.9	37.3
22	oxycodone/paracetamol	33.5	36.0	36.3	37.3	36.6
23	prednisone	27.1	27.8	28.7	33.7	34.0
24	warfarin	34.9	35.7	35.6	33.9	33.8
25	ibuprofen	28.5	30.3	31.1	32.6	33.4

Source: IMS Health, National Prescription Audit, Dec 2012

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.

Active ingredient names use international naming standards (e.g. paracetamol is called acetaminophen in the U.S.). 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.

Updated March 22, 2013

Top Medicines by Non-Discounted Spending

Non-Discounted Spending $Bn	2008	2009	2010	2011	2012
Total U.S. Market	**285.7**	**300.7**	**316.5**	**329.2**	**325.8**
1 Nexium®	5.9	6.3	6.5	6.4	6.0
2 Abilify®	3.0	4.0	4.6	5.3	5.9
3 Crestor®	2.1	3.0	4.0	4.6	5.1
4 Advair® Diskus®	4.4	4.7	4.9	4.8	4.9
5 Cymbalta®	2.4	2.8	3.2	3.8	4.7
6 HUMIRA®	2.1	2.5	3.1	3.7	4.6
7 Enbrel®	3.1	3.3	3.5	3.8	4.3
8 Remicade®	3.0	3.2	3.3	3.5	3.9
9 Copaxone®	1.4	1.7	2.4	3.2	3.6
10 Neulasta®	3.0	3.0	3.0	3.3	3.5
11 Singulair®	3.5	3.7	4.2	4.8	3.3
12 Rituxan®	2.4	2.6	2.8	3.0	3.2
13 Plavix®	4.8	5.6	6.4	7.1	3.0
14 Atripla®	1.4	1.9	2.3	2.6	2.9
15 Spiriva® Handihaler®	1.4	1.7	2.1	2.5	2.8
16 Oxycontin®	2.3	2.9	3.1	2.9	2.8
17 Januvia®	1.2	1.5	1.8	2.2	2.7
18 Avastin®	2.5	3.0	3.1	2.7	2.7
19 Lantus®	1.8	1.9	2.0	2.1	2.3
20 Truvada®	1.1	1.4	1.7	2.0	2.3
21 atorvastatin	-	-	-	0.5	2.3
22 Lantus® SoloSTAR®	0.4	0.7	1.1	1.6	2.2
23 Epogen®	3.0	3.2	3.3	2.8	2.2
24 Diovan®	1.6	1.7	2.0	2.0	2.1
25 Lyrica®	1.5	1.6	1.7	1.8	2.0

Source: IMS Health, National Sales Perspectives, Dec 2012

Appendix notes:

Prescription-bound products including insulins and excluding other products such as OTC. Table shows leading products by 2012 spending as reported in IMS's National Sales Perspectives Audit. Products which were leading products in prior years (e.g. Lipitor) are not shown if their 2012 ranking is outside the top 25. Generic atorvastatin includes generics by all manufacturers. IMS routinely updates its market audits, which may result in changes to previously reported data. Off-invoice discounts and rebates are not reflected and are understood to be significant for some products, resulting in substantial differences between IMS-reported spending and company-reported sales after accounting for off-invoice discounts and rebates.

Updated March 20, 2013

Dispensing by Payment Type

Dispensed Prescriptions Mn	2008	2009	2010	2011	2012
Total U.S. Market	**3,870**	**3,953**	**3,997**	**4,028**	**4,078**
Commercial Third-Party	65.1%	62.9%	61.6%	61.3%	58.6%
Medicare Part D	19.0%	19.9%	19.8%	20.6%	23.7%
Medicaid	7.5%	8.3%	9.6%	9.5%	9.4%
Cash	8.3%	8.9%	9.0%	8.6%	8.3%

Source: IMS Health, National Prescription Audit, VONA, Dec 2012

Appendix notes:

Medicare Part D reflects only retail pharmacy prescriptions. Mail order delivery of Medicare Part D prescriptions are not distinguished from other Commercial Third-Party.

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

Medicaid includes both Fee for Service and Managed Medicaid.

Updated February 17, 2012

Dispensing Locations

Non-Discounted Spending $Bn	2008	2009	2010	2011	2012
Total U.S. Prescription Market	**285.7**	**300.7**	**316.5**	**329.7**	**325.8**
Retail Channels	**203.5**	**215.0**	**227.0**	**236.2**	**233.6**
Chain Stores	99.7	105.4	108.2	112.5	109.9
Mail Service	46.5	51.0	59.4	63.8	65.7
Independent	36.9	37.4	38.1	38.3	36.3
Food Stores	20.4	21.2	21.3	21.6	21.6
Institutional Channels	**82.1**	**85.7**	**89.5**	**93.5**	**92.3**
Clinics	33.0	34.8	36.9	38.8	39.5
Non-Federal Hospitals	26.8	27.6	28.2	28.8	28.1
Long-Term Care	13.7	13.9	14.8	15.2	14.0
Federal Facilities	3.8	4.1	4.0	4.3	4.4
Home Health Care	2.5	2.6	2.5	2.7	2.6
HMO	1.3	1.7	2.1	2.7	2.8
Miscellaneous	0.9	1.0	1.0	1.0	1.0

Dispensed Prescriptions Mn	2008	2009	2010	2011	2012
Total U.S. Market	**3,870**	**3,953**	**3,997**	**4,028**	**4,078**
Retail Channels	**3,563**	**3,637**	**3,678**	**3,699**	**3,747**
Chain Stores	2,048	2,130	2,174	2,213	2,230
Independent	770	756	749	741	739
Food Stores	482	489	490	484	514
Mail Service	262	262	265	261	263
Institutional Channels	**307**	**316**	**319**	**329**	**330**
Long-Term Care	307	316	319	329	330

Source: IMS Health, National Sales Perspectives, National Prescription Audit, Dec 2012

Appendix notes:

Report reflects prescription-bound products including insulins and excluding other products such as OTC. IMS routinely updates its market audits, which may result in changes to previously reported market size and growth rates. Prescriptions include 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.

Updated March 19, 2013

Top Therapeutic Classes by Non-Discounted Spending

Non-Discounted Spending $Bn	2008	2009	2010	2011	2012
Total U.S. Market	**285.7**	**300.7**	**316.5**	**329.2**	**325.8**
1 Oncologics	19.7	21.5	22.6	24.0	25.9
2 Mental Health	26.0	26.1	28.2	29.7	23.5
3 Respiratory Agents	16.0	18.1	19.8	21.7	22.1
4 Antidiabetics	13.6	15.8	18.4	20.5	22.0
5 Pain	16.8	17.3	17.6	17.9	18.2
6 Lipid Regulators	18.1	18.6	19.8	21.3	16.9
7 Autoimmune Diseases	8.6	9.7	11.0	12.5	14.8
8 Antihypertensives, Plain & Combo	14.7	15.4	15.6	14.0	13.6
9 HIV Antivirals	7.1	8.2	9.4	10.4	11.7
10 ADHD	5.5	6.7	7.9	9.2	10.4
11 Anti-Ulcerants	14.2	14.1	12.4	10.5	10.0
12 Multiple Sclerosis	4.1	5.0	6.1	7.6	8.9
13 Antibacterials	10.1	10.4	10.1	9.3	7.9
14 Nervous System Disorders	12.3	8.1	6.9	6.9	7.2
15 Vaccines (Pure, Comb, Other)	5.0	4.7	5.7	6.4	6.8
16 Hormonal Contraception, Systemic	4.5	4.7	4.9	5.2	5.5
17 Other CNS	4.3	4.5	4.8	4.8	5.0
18 Immunostim AG Ex Intfron, Glatiramer Ace	4.1	4.1	4.2	4.6	4.7
19 Antivirals, Excl. Anti-HIV	3.9	4.8	3.3	3.8	4.5
20 Platelet Aggregation Inhibitors	5.7	6.5	7.4	8.2	4.4

Source: IMS Health, National Sales Perspectives, Dec 2012

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

Updated February 17, 2012

Authors

Murray Aitken

Executive Director, IMS Institute for Healthcare Informatics

Murray Aitken is executive director, IMS Institute for Healthcare Informatics, 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 was senior vice president, Healthcare Insight, leading IMS's thought leadership initiatives worldwide. Before that, he served as senior vice president, Corporate Strategy from 2004 to 2007. Murray joined IMS in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS, 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 writes and speaks regularly on the challenges facing the healthcare industry. He is editor of HealthIQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive.

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.

Michael Kleinrock

Director, Research Development

Michael serves as Research Director for the IMS Institute, setting the research agenda for the institute, leading the development of reports and projects focused on the current and future role of biopharmaceuticals in healthcare in the U.S. and globally.

Each year Michael leads the development of IMS' perspectives included in its annual "Year in Review" presentations as well as its review of the future outlook for the global pharma market. Michael writes and speaks regularly on these and other topics and he is sought after for his unique and pragmatic perspectives, backed by rigorous analysis and research, on issues of interest to pharmaceutical companies, financial analysts, trade groups, policy advocates and regulatory agencies.

Michael joined IMS in 1999 and held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team which in 2011 became the IMS Institute for Healthcare Informatics.

Michael holds a BA in History and Political Science from the University of Essex, Colchester, UK, and an MA in Journalism and Radio Production from Goldsmiths College, University of London, UK.

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'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 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:

Demonstrating 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.

IMS INSTITUTE FOR HEALTHCARE INFORMATICS

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