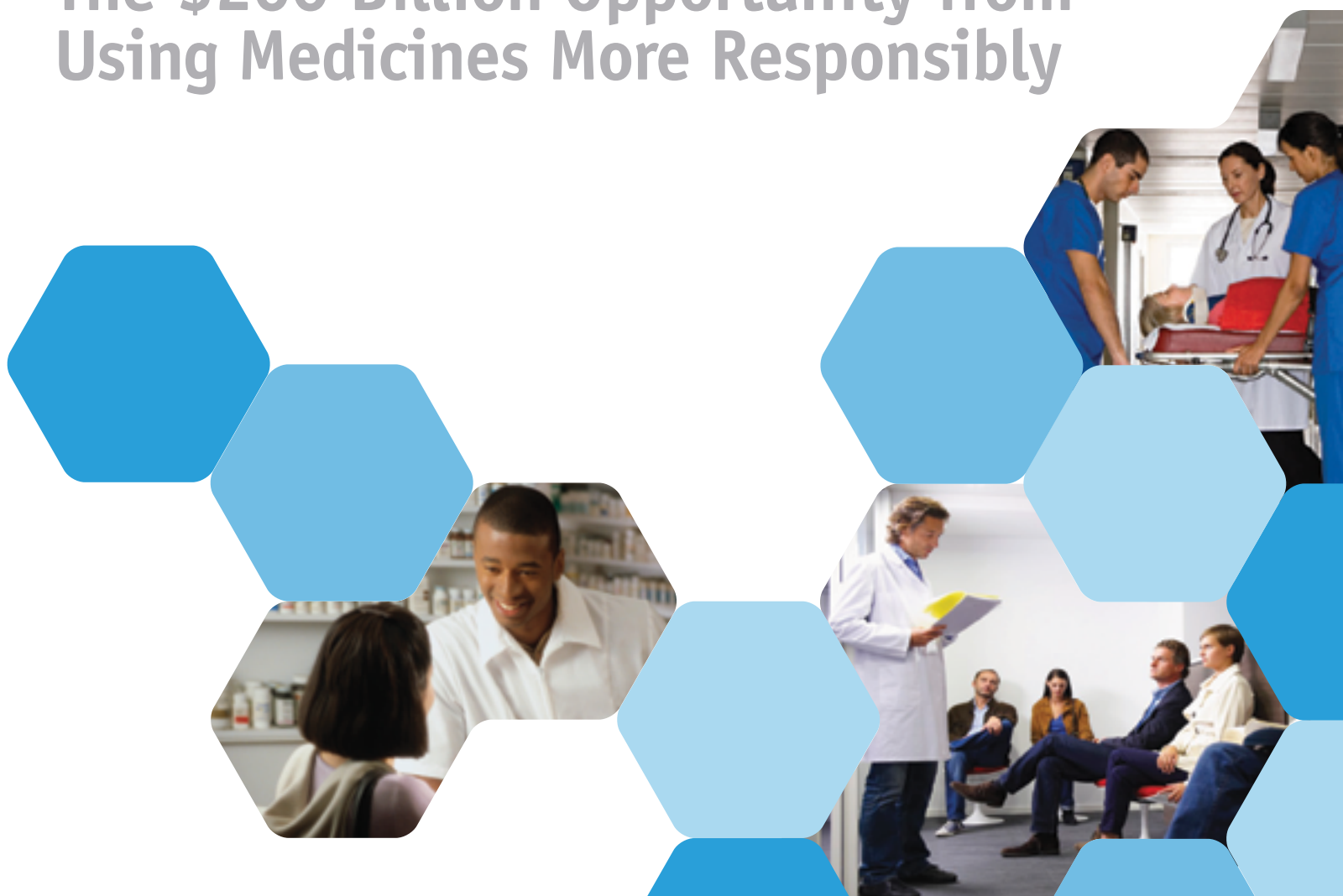


June 2013

Avoidable Costs in U.S. Healthcare

The \$200 Billion Opportunity from
Using Medicines More Responsibly



Introduction

Considerable research on healthcare system inefficiencies and strategies to address them has been undertaken in the U.S. based on a widespread recognition of the urgency of cost containment. Each year since 2008, a different institution has quantified avoidable costs and potential savings across a myriad of healthcare issues. Their results have yielded a wide range of values—each significant, but varying considerably.^{1,2,3} For example, in 2008, NEHI (formerly the New England Health Institute) identified \$680 billion in avoidable costs;⁴ in 2010, Thomson Reuters set the amount at \$3.6 trillion;⁵ and in 2011, Donald Berwick and Andrew Hackbarth pointed to \$476 billion to \$992 billion in avoidable costs.⁶

These studies sustain an ongoing discourse about both the magnitude of the problem and possible interventions. Given the cost and difficulty of obtaining accurate and up-to-date data, most research draws from and improves on previous efforts. This report, with its focus on use of medications in the healthcare system, offers an innovative perspective in three respects:

- It applies a consistent lens – the use of medicines – to assess medication value in the context of wasteful spending in the healthcare system.
- It leverages the latest information, including proprietary data gathered by the IMS Institute for Healthcare Informatics, to account for changes in healthcare costs, including costs for medications and for outpatient, inpatient, and emergency room care.
- It provides actionable priorities for various healthcare stakeholders, including physicians, patients, pharmacists, payers, policymakers and the pharmaceutical industry.

This study focuses on the U.S. healthcare system, but the analysis draws on the global Responsible Use of Medicines report issued by the IMS Institute in October 2012.⁷ It is intended to advance the national dialogue on optimizing healthcare delivery and cost, and to shift the discourse from medicine costs to the value of pharmacotherapy in reducing overall healthcare expenditures.

The study was produced independently by the IMS Institute for Healthcare Informatics as a public service, without industry or government funding.

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Executive Summary

Wasteful spending in the U.S. healthcare system is a widely acknowledged and seemingly intractable problem. The country is still recovering from a long economic downturn, and imperatives to reduce the increase in costs across all areas of the healthcare system are increasingly prominent in discussions about the distribution of limited dollars.

Healthcare costs caused by improper and unnecessary use of medicines exceeded \$200 billion in 2012, according to IMS Institute for Healthcare Informatics estimates. This amount is equal to 8% of the nation's healthcare spending that year, and would be sufficient to pay for the healthcare of more than 24 million currently uninsured citizens.

These avoidable costs arise when patients fail to receive the right medications at the right time or in the right way, or receive them but fail to take them. This report examines avoidable costs in six "opportunity" areas involving different diseases and care situations: nonadherence, delayed evidence-based treatment practice, misuse of antibiotics, medication errors, suboptimal use of generics, and mismanaged polypharmacy.

This study finds that even though avoidable costs are significant, encouraging progress is being made in addressing some of the challenges that drive wasteful spending in many parts of the healthcare system. Medication adherence among large populations of patients with three of the most prevalent chronic diseases – hypertension, hyperlipidemia and diabetes – has improved since 2009 by about 3%. The proportion of patients diagnosed with a cold or the flu – both viral infections that do not respond to antibiotics – who inappropriately received antibiotic prescriptions has fallen from 20% to 6% since 2007. And, for diseases where lower-cost generic medications are available, use of generics reached 95% in 2012. A large number of pilot programs and initiatives have, in recent years, advanced the understanding of the underlying causes of improper prescription and use of drugs, and have led to the development of new techniques and approaches to address the issue.

Such improvements are possible only through collaboration among multiple healthcare stakeholders: providers, pharmacists, patients, payers, pharmaceutical manufacturers and policymakers. The report's case studies demonstrate that the most effective and innovative approaches being taken to address any of the six areas of avoidable costs cannot be planned or implemented singlehandedly. In addition, healthcare informatics — the use of technology and analytical approaches to harness the value of data — is a key driver of improvements.

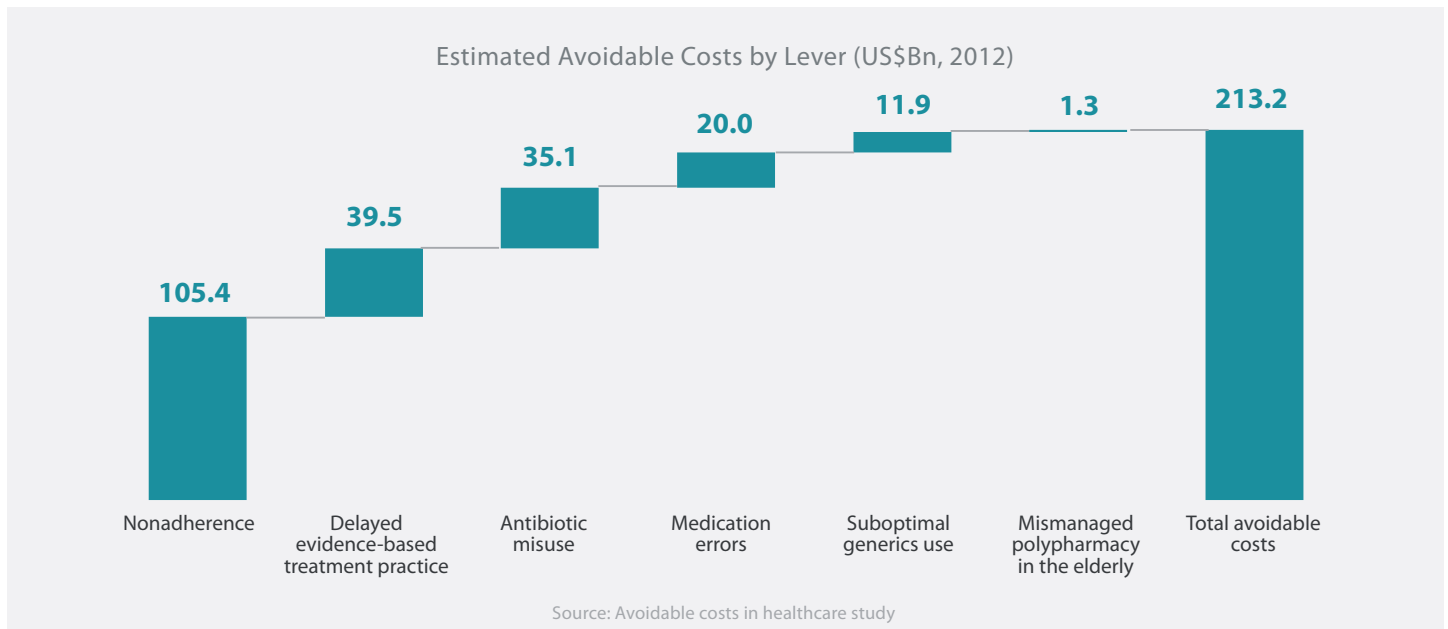
This report identifies actions that all healthcare stakeholders can take to address the avoidable costs currently incurred by the U.S. healthcare system due to medications not being used according to the best evidence-based clinical practice. These priorities represent the best thinking in the six areas of opportunity identified, and in many cases are consistent with the direction and intention of elements of the Patient Protection and Affordable Care Act.

Advancing Responsible Medicine Use in the United States: A \$200 Billion Opportunity

Responsible use of medicines can eliminate at least \$213 billion in avoidable costs by addressing six key areas, or “levers” of opportunity illustrated in Exhibit 1: nonadherence, delayed evidence-based treatment practice, antibiotic misuse, medication errors, suboptimal generic use, and mismanaged polypharmacy.

In 2012, more than \$2.7 trillion was spent on healthcare in the U.S.,⁸ so \$213 billion represents nearly 8% of the nation’s healthcare spending that could be avoided. That amount equals the funding required to pay for the healthcare of more than 24 million people who are currently uninsured. Over the next several years, the use of medicines is expected to increase due to expansion of insurance coverage, rising incidence and prevalence of chronic disease and population aging. This places an even greater importance on ensuring those medicines are being used appropriately.

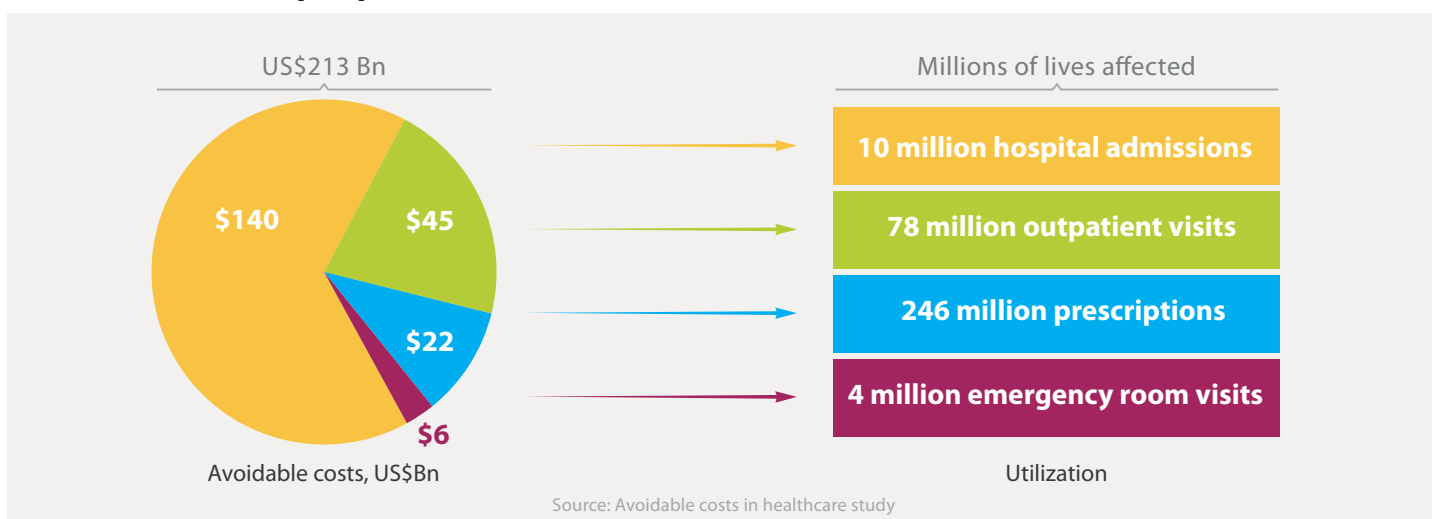
Exhibit 1: Avoidable U.S. healthcare costs add up to \$213 billion



Avoidable healthcare costs are incurred across all sites of care. Exhibit 2 shows that two thirds of the total estimated avoidable costs, or \$140 billion, relate to ten million hospitalizations, while \$45 billion of avoidable costs are associated with 78 million outpatient visits. An additional \$22 billion is incurred in avoidable pharmacy costs related to 246 million prescriptions, and four million avoidable emergency room visits cost \$6 billion. Along with these significant costs, the inappropriate use of medicines also imposes an enormous burden on the U.S. healthcare system overall, including patients and caregivers.

The avoidable healthcare cost figures are based on estimates and assumptions with a degree of uncertainty. Therefore avoidable costs are estimated in the range of \$140-295 billion and are based on a sensitivity analysis of lever-specific measures, such as the level of nonadherence or the risk of complications resulting from nonadherence and delayed evidence-based treatment.

Exhibit 2: \$213 billion includes unnecessary healthcare utilization and scripts and affects millions of people



The findings of this analysis are consistent with a previous assessment of global avoidable healthcare costs undertaken by the IMS Institute for Healthcare Informatics. Through a global modeling approach, the cost burden attributable to the U.S. was estimated at \$222 billion in 2011, with a similar cost distribution between the same six levers of opportunity, although based on a slightly different set of diseases. This report is developed specifically for the U.S. healthcare system and takes advantage of the greater availability of information on healthcare utilization and costs in the U.S. available both from IMS and published research.

The methodology and information sources used in this report are limited in various ways. One of the constraints of this analysis is the use of healthcare claims data derived from a commercially insured, under-65 patient cohort. These patients do not represent morbidity patterns in the overall U.S. population; additionally, healthcare costs are also understood to differ across payment sources. Medication costs, where used in the calculation of avoidable costs, reflect ex-manufacturer prices and do not include off-invoice discounts and rebates. Finally, some of the information based on peer-reviewed publications is dated and may not reflect trends and events in 2012. Limitations specific to avoidable cost estimates for each lever are listed in greater detail in the Appendix.

Medication nonadherence and delayed evidence-based treatment practice are the key contributors to avoidable costs, accounting for 68% of the total. The definitions for each lever are adapted from the IMS Institute's global report on the Responsible Use of Medicines and include disease-specific and non-disease-specific attributes. The definitions are as follows:

Medication nonadherence. This occurs when patients do not take their medicines appropriately or at all. Nonadherence can result in costly complications that are often more expensive than the medicines and worsen health outcomes. The diseases assessed for nonadherence are hypercholesterolemia, hypertension, diabetes type 2, osteoporosis, HIV and congestive heart failure (CHF).

Delayed evidenced-based treatment practice. This occurs when medicines are not delivered to patients at a time that would be most valuable in terms of health outcome and cost effectiveness. Screening and diagnostic capabilities could support timely medicine use for highly prevalent diseases and ensure that patients receive medicines to prevent or delay relatively costlier complications. The diseases assessed for delayed treatment are hepatitis C, diabetes type 2, atrial fibrillation, and coronary heart disease (CHD).

Misuse of antibiotics. This occurs due to misdiagnosis or inappropriate decisions by prescribers and dispensers to provide patients with antibiotics. Ease of access, low cost, and misperceptions about antibiotics' potency against severe diseases contribute to their misuse and overuse, particularly against viral infections. This problem often results in downstream avoidable costs through hospitalizations, promotion of antimicrobial resistance, and, consequently, more expensive treatment.

Medication errors. These occur across four processes—prescribing, preparation/dispensing, administration, and monitoring—and often result in costly complications. Healthcare professionals are not always supported in reporting errors, nor do they necessarily have access to training and tools to help them improve their performance.

Suboptimal use of generics. This occurs if there is an unexploited opportunity for greater use of safe, less costly generics in the market once patented drugs have lost their legal protection. The opportunity varies by therapy class. While generics are already used almost exclusively in many areas, in others, brands are still prescribed and dispensed despite the availability of therapeutically equivalent, lower-cost generics.

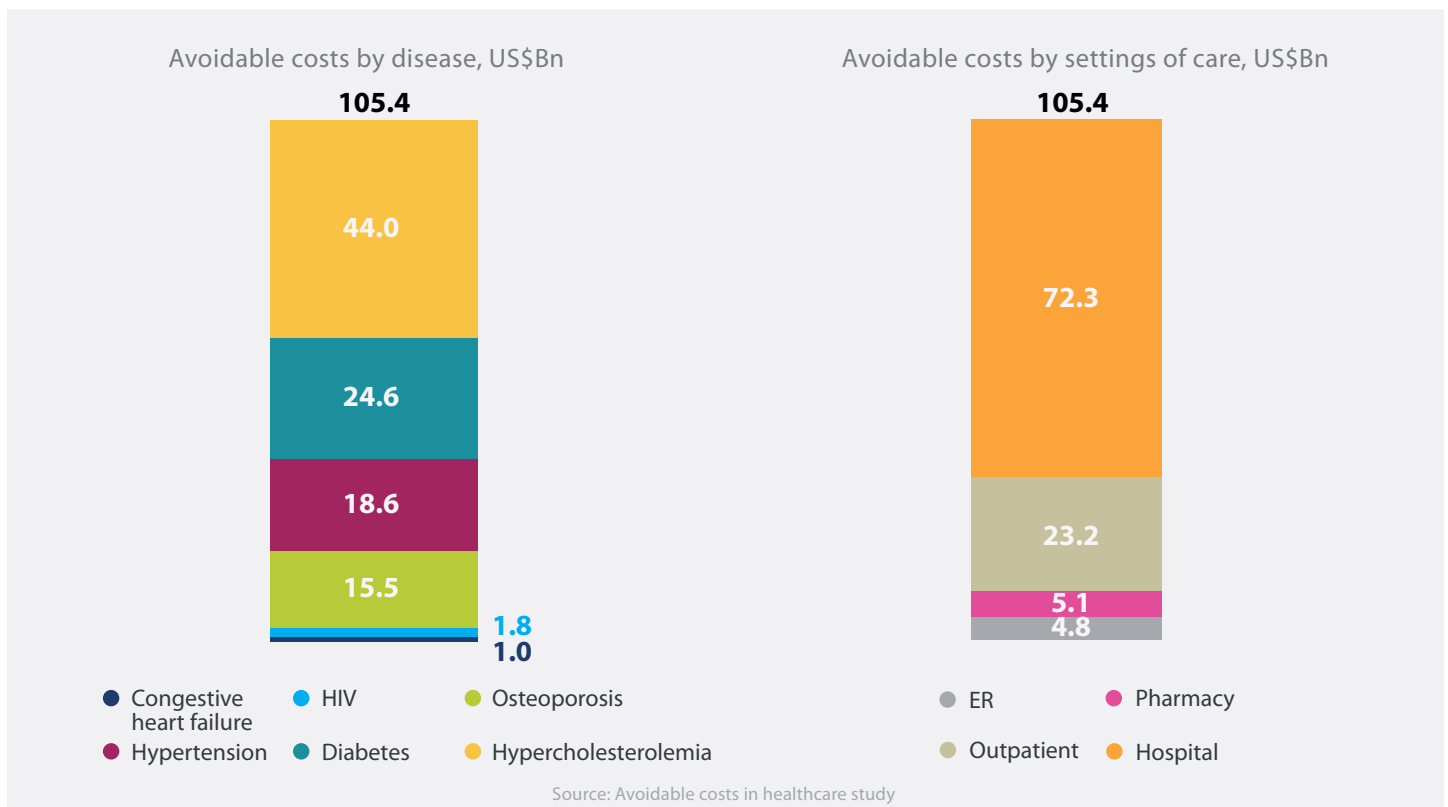
Mismanaged polypharmacy. This occurs when healthcare professionals do not, or cannot, adequately oversee patients who take multiple medicines concurrently. The risk of costly and adverse events increases with age, particularly when patients are over 60 years old, and when patients take more than five medicines concurrently.

In this study, avoidable costs are quantified based on a customized modeling approach for each of these six levers. The methods are explained in detail in the Appendix. The estimated avoidable costs are defined as the difference between healthcare utilization costs incurred for patients suffering complications, resulting from suboptimal medicines use, and patients with the same disease who experienced no complications. The underlying assumption is that suboptimal medication use specifically puts patients at risk, leads to harmful health outcomes and results in avoidable healthcare utilization. The final estimate is expressed as a monetary range to reflect the uncertainty of the parameters used in the approach.

Medication Nonadherence

- The avoidable cost opportunity from nonadherence is \$105 billion, with a range of \$68 billion to \$146 billion.
- Among the six diseases analyzed in the study, hypercholesterolemia and diabetes have the biggest impact on avoidable costs.
- Despite the substantial avoidable costs incurred in different settings of care, there are encouraging signs that secondary nonadherence is improving for three of the most prevalent chronic diseases.
- The lower cost of widely used medicines after the loss of patent protection, as well as the growing number of effective interventions by pharmacists, healthcare professionals and payers, are driving these improvements in adherence.

Exhibit 3: Avoidable costs due to nonadherence



Underlying reasons for nonadherence

There are many reasons why patients in the U.S. fail to adhere to recommended medication regimens. For years, cost was a dominant driver of nonadherence, but this is increasingly less of a factor for chronic conditions treated with cheaper, off-patent medicines. For example, prices of oral medicines for diabetes have decreased by more than half, on average, since 2001. Medicines for hypercholesterolemia and hypertension have seen similar declines.⁹

In other cases, non-economic factors are key contributors to medication nonadherence. Among patients with diabetes, hypertension, and hypercholesterolemia, it has been demonstrated that a lack of information about the longer-term effects of the diseases contributes to non-adherence.^{10,11,12,13,14} In addition, fear of drug side effects contributes to nonadherence. Health and cultural beliefs sometimes play a role as well. For example, among African Americans, suspicion and mistrust of the medical system have been identified as factors associated with medication nonadherence. Substance abuse also has been identified as contributing to non-adherence in some populations.¹⁵ Among HIV/AIDS patients, the toxicity of the drugs makes some patients less likely to comply with drug recommendations.¹⁶ Low levels of health literacy, social support, and mental health status also are associated with nonadherence, while patient-provider relationships characterized by provider cultural competence, patient trust, and shared treatment decisions are associated with higher adherence levels.^{17,18,19,20}

Estimated avoidable costs

This study focuses on six chronic conditions that have previously been assessed for avoidable costs. These conditions—hypercholesterolemia, diabetes, hypertension, osteoporosis, HIV and CHF—result in high morbidity in the U.S. and are major drivers of healthcare costs. More than half of the population is affected by these diseases, and many people with the diseases experience co-morbidities, as well. The growing burden of obesity and diabetes are increasing the risk of cardiovascular disease.²¹ CVD and osteoporosis are expected to become even more prevalent, given the increasing aging of the population. Adherence to prescribed therapies for patients with these diseases can prevent or delay the onset of complications, reduce hospitalization risks, and decrease healthcare costs.

Among the six diseases examined in this analysis of nonadherence, the two diseases with the highest avoidable costs are hypercholesterolemia with \$44 billion and diabetes with \$24.6 billion per year, according to Exhibit 3. Hypertension and osteoporosis carry an annual avoidable cost of \$18.6 billion and \$15.5 billion respectively, followed by almost \$2 billion for HIV and \$1 billion for congestive heart failure. Of the \$105 billion wasted due to medication therapy nonadherence in 2012, 69% is spent on hospitalizations.

Quantification approach

This analysis is disease-focused and based on research showing that nonadherent patients have a higher likelihood of experiencing complications that result in additional healthcare service utilization, defined as additional emergency room visits, hospitalizations, pharmacy scripts, and outpatient professional, facility and home health visits. The analysis is based on the specific complications described in Table 1. This focus on a specific and limited number of diseases and complications implies that the cost estimates are conservative and underestimate the true avoidable cost value.

Table 1: Selected complications resulting from nonadherence

Disease	Complication as a result of nonadherence
Hypercholesterolemia	Acute myocardial infarction ²²
Diabetes	Stroke ²³
Hypertension	Acute myocardial infarction ²⁴
Osteoporosis	Bone-related fractures among lower adhering patients ²⁵
HIV	Complications from nonadherence based on Hepatitis C data as proxy measure ²⁶
Congestive heart failure (CHF)	All complications resulting in additional inpatient, outpatient, emergency room and pharmacy utilization, calculated as incremental difference between nonadherent and adherent CHF patients ²⁷

This analysis covers two distinct types of nonadherence – primary and secondary nonadherence – and also takes into account the impact of patent expirations on medicine costs.

Primary nonadherence occurs when a new medication is prescribed for a patient, but the patient does not obtain the medication, or an appropriate alternative, within an acceptable period of time after it was prescribed.²⁸ Recent figures from IMS Health show that among patients taking medicines for CHF, those receiving a prescription for the first time have a fill rate of only 75%.²⁹ In other words, 25% of patients who have been diagnosed and given a prescription have not actually picked up the prescription. For patients with osteoporosis, the first prescription fill rate is only 63%.³⁰ Many existing measures of avoidable costs do not account for primary nonadherence, and therefore are likely to underestimate the problem. This factor is not well studied because of historic difficulties in tracking prescriptions written by physicians but not filled by patients.³¹

Secondary nonadherence occurs when patients do not refill their prescriptions on time, do not take medications as prescribed or discontinue their medications altogether.³² The magnitude of secondary nonadherence is better understood and measured more extensively than primary nonadherence.^{33,34} However, secondary nonadherence estimates often have two disadvantages: they are based on small patient samples in narrowly defined settings of care, or are outdated. Secondary nonadherence measures used in this analysis range from 32% for oral diabetes therapies to 40% for cholesterol medications, and are based on 2011 administrative data covering over 2 million patients.³⁵

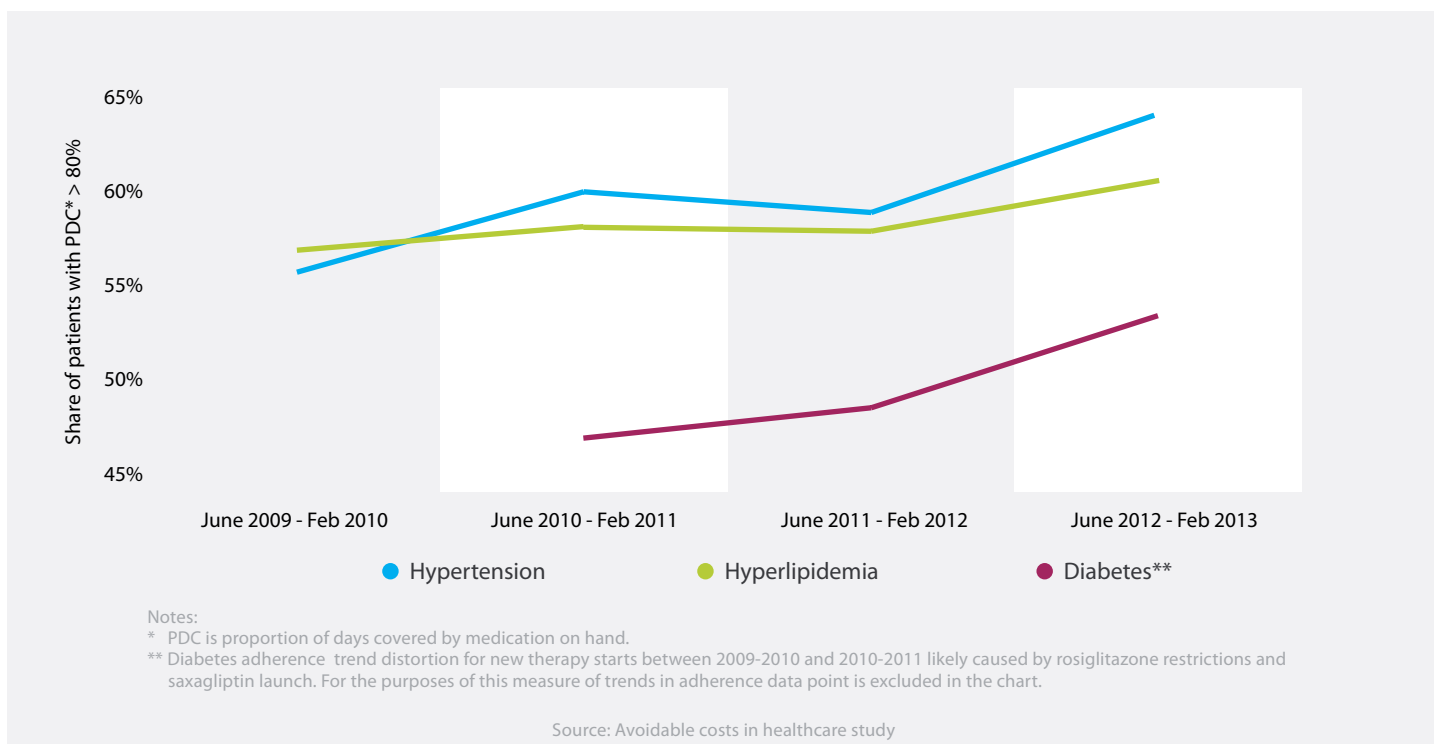
Existing studies rarely account for the impact of patent expiries on medicine costs. They typically use outdated information on drug prices, and therefore often find that the higher medication spending associated with greater adherence exceeds reductions in non-medication spending.^{36,37,38,39} However, recent and ongoing patent expirations, as well as generic prescribing increases, have led to lower prescription medication costs for many patients. Ongoing research that takes into account prescription drug market changes and links that data to adherence rates is needed. Existing studies have a number of problems that limit their application. Most are heterogeneous in sources used and outcomes measured, and cite results from earlier studies to demonstrate the magnitude in present-day context. These studies do not reflect changes in medication price, drug availability and healthcare treatment patterns, nor changes in levels of adherence over time.

This study leverages, where possible, IMS Health data for 2012 values, which take into account the latest costs of treatment and estimates of recent primary and secondary nonadherence rates based on large samples of provider prescribing and patient fill/refill data, as well as health plan claims data.

Medication adherence is improving

The encouraging news is that medication adherence is improving among patients with widespread chronic diseases. Adherence among patients with diabetes, hypertension and hyperlipidemia has increased 3% to 7% since 2009, as illustrated in Exhibit 4. This trend also is evident at the therapeutic subclass level and for medicines with similar mechanisms of action within each therapy class.

Exhibit 4: Historical trends in adherence to chronic disease therapies among new patients since 2009

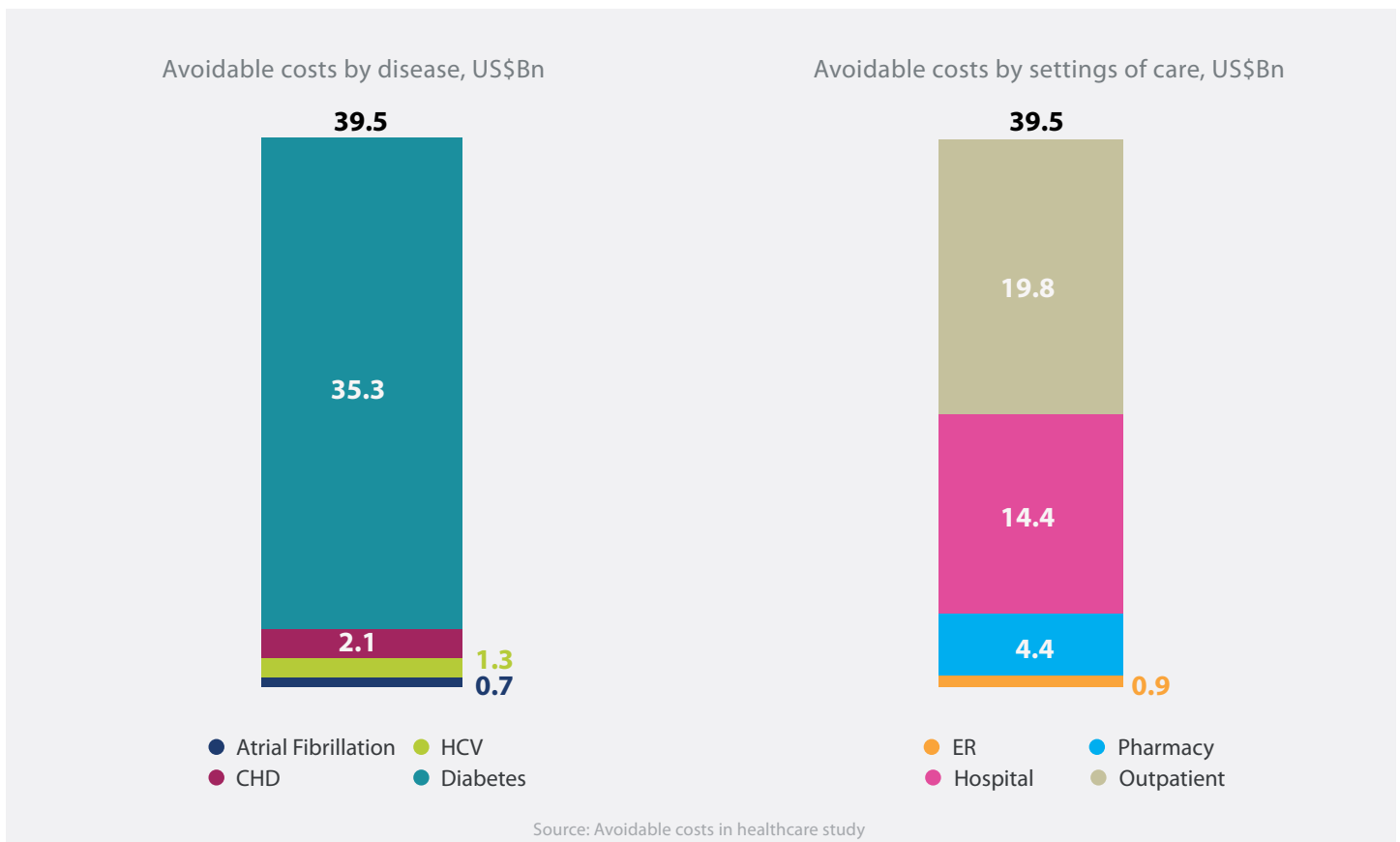


Adherence improvements are associated with two factors. The first is the lower cost of medications for major chronic diseases. The loss of patent protection of widely used medicines has resulted in the availability of low-cost generic alternatives, making therapy affordable for more patients. The second factor is the growing number of interventions by various healthcare stakeholders and at different junctures of the healthcare system aimed at keeping patients on therapy. The body of knowledge about promoting adherence is growing. Also, the scale of these interventions is greater as technology enables more patients to be reached and high-risk patients to be identified and proactive intervention approaches developed. This encouraging news should provide impetus to invest further in adherence interventions and critically examine their effectiveness.

Delayed Evidence-Based Treatment Practice

- The avoidable cost opportunity from delayed evidence-based treatment is \$39 billion, with a range of \$19 billion to \$64 billion.
- Among the four diseases analyzed, diabetes has the largest impact, representing 90% of avoidable spending.
- A substantial part of avoidable costs is incurred through outpatient and inpatient care as a result of higher or premature morbidity.
- Providing patient treatment at the right time requires a better understanding and systematic tracking of the reasons for delayed evidence-based medicine use.

Exhibit 5: Avoidable costs due to delayed evidence-based treatment practice



Underlying reasons for delayed evidence-based treatment practice

The primary reasons for delayed medicine use include lack of diagnosis, inappropriate prescribing that ignores evidence-based clinical guidelines, and the costs of drugs to patients. Among those with chronic hepatitis C, lack of diagnosis is the primary driver of delayed treatment, even though diagnosis and treatment have been demonstrated to prevent costly complications, especially among at-risk populations such as people who use injectable drugs and patients co-infected with HIV.^{40,41,42,43} For patients with atrial fibrillation, warfarin can prevent ischemic strokes, but it also may cause major episodes of bleeding that can result in death. This risk inhibits clinicians from immediately prescribing warfarin. While new oral therapies are now also available, their cost and the need to balance the benefits and disadvantages of treatment options for each patient are additional deterrents to therapy initiation. Failure to prescribe appropriately may be the fault of the healthcare provider, but patients also play an active role in timely diagnosis, treatment initiation and the follow-up use of non-prescription medications such as aspirin. Patient influences include the patient-provider relationship, beliefs and attitudes towards the healthcare system, and recognition of disease symptoms.

Estimated avoidable costs

This study focuses on four diseases: diabetes type 2, coronary heart disease (CHD), hepatitis C (HCV), and atrial fibrillation (AF). These four diseases affect more than one in ten people in the U.S., with diabetes prevalence estimated at 8.3%, CHD prevalence at 6.0%, HCV prevalence at 1.2% to 2%, and AF prevalence at more than 1%. Prevalence rates are considerably higher among older adults; diabetes and CHD prevalence is estimated at 26.7% and 19.8%, respectively, among those age 65 and older, and heart disease is the leading cause of death among men and women in the U.S.^{44,45,46,47,48} Well-defined treatment paradigms supported by evidence-based clinical guidelines exist for patients with these diseases. The guidelines reflect evidence of the positive impact of appropriate, timely treatment on slowing or preventing the development of costly and debilitating complications. The Appendix provides a full list of guidelines and supporting evidence.

Diabetes is identified here as the disease most heavily affected by delayed evidence-based treatment, accounting for \$35 billion of the \$39 billion in avoidable healthcare costs estimated for the four diseases in the analysis, as illustrated in Exhibit 5. Medication treatment delays are associated with \$2 billion of wasteful spending on complications of coronary heart disease, and \$1 billion on complications of Hepatitis C virus infections. Almost half, or \$20 billion, of these avoidable costs are incurred through outpatient care, \$14 billion are spent on hospitalizations and \$4 billion on medications.

Quantification approach

This analysis is focused on appropriate pharmacologic treatment and pharmacologic quality of care indicators. Current prevalence measures are used to estimate the number of patients with each disease. Then, estimates of the percentage of patients who have been subject to treatment delays are documented, as reported in peer reviewed published literature and public surveys. Peer reviewed literature also is used to estimate the risks of complications and adverse events that result from treatment delays. IMS Health data is used to estimate the costs associated with those complications and adverse events.

Table 2 below lists evidence-based treatment for each disease, as well as the complications that can develop when that treatment is delayed.

Table 2: Delayed evidence-based treatment and resulting complication by disease

Disease	Type of delayed evidence-based treatment	Resulting complications
Hepatitis C	Diagnosis and initiation of treatment	Liver transplants, cirrhosis, chronic liver disease ^{49,50,51,52}
Coronary heart disease (CHD)	Aspirin therapy initiation for patients with CHD within 1 week of diagnosis	Myocardial infarctions ^{53,54,55}
Diabetes	Angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin receptor blockers (ARB) therapy for diabetes patients with proteinuria	Chronic kidney disease ^{56,57,58,59}
Atrial fibrillation (AF)	Warfarin therapy for patients 65 and older who have AF for more than 48 hours	Stroke ^{60,61,62,63,64}

While quality measures for quantifying delays in use of medications exist, aggregate national-level estimates of the avoidable costs associated with these delays are not available. Nevertheless, evidence on the prevalence of delayed use of medications suggests that the scale of the problem is not negligible. For example, one study in 2006 found that pharmacologic care guidelines were followed only 61.9% of the time.⁶⁵ This finding supports earlier findings of underuse of guideline-recommended pharmacotherapy for patients with common and costly chronic conditions, including diabetes.⁶⁶

For hepatitis C, estimates of treatment rates are low, at 20%, despite indications that avoidable costs increase if delivery of medication is delayed.⁶⁷ These rates are associated with the two most common forms of treatment, pegylated interferon and ribavirin, which can prevent or delay disease progression and the associated economic burden of advanced disease.⁶⁸ Among patients with coronary heart disease, diabetes, and atrial fibrillation, the use of available low-cost medicines also is suboptimal. Among CHD patients, outpatient use of aspirin for secondary prevention of cardiovascular disease is estimated at approximately 24%.⁶⁹ Among diabetic patients with proteinuria, studies have reported treatment rates of approximately 50%.^{70,71} Proteinuria is a sign of chronic kidney disease (CKD), which can result from diabetes, high blood pressure, and diseases that cause inflammation in the kidneys.⁷² Among patients with AF, the National Stroke Association has reported that “while most AF-related strokes could be prevented with blood thinners, up to two-thirds of AF patients who had strokes are not prescribed these medications.”^{73,74} Also, only 50% of AF patients who meet criteria for use are prescribed warfarin.⁷⁵

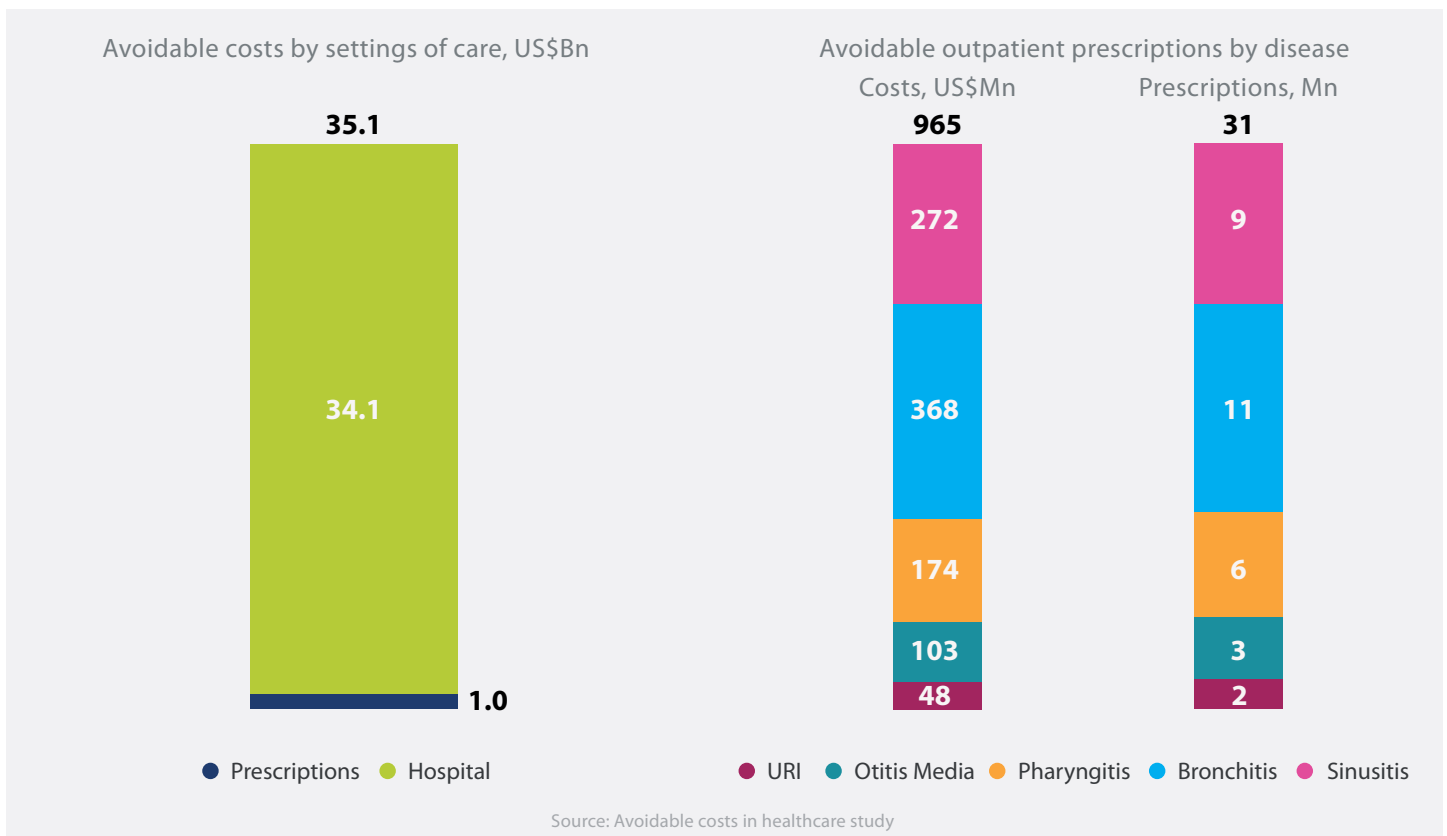
Existing literature describes suboptimal treatment of patients across these four diseases, but there is little or no available evidence on the economic impact. This study offers a new perspective on the value of tracking and measuring the consequences of delayed medication use. Although it is possible to track a given complication back to the lack of appropriate medication treatment, few institutions do this. It is a difficult undertaking that requires providers to determine when the delay started or track events backwards from the complication if it is known that the patient was not given the appropriate medicine on time. Additionally, making causal inferences from delayed medicine use to complications is a challenge for clinicians, since there may be other reasons for the complication. Complications can occur even when patients receive medicine therapy on time.

Keeping these challenges in mind, yet recognizing that this is a crucial issue that requires further understanding, the goal of this approach is to drive a discussion about the health outcomes and economic consequences of suboptimal care within the healthcare system. This analysis suggests that the reasons for delayed evidence-based medicine use are poorly understood, not systematically tracked, and stand in the way of providing patient treatment at the right time.

Misuse of Antibiotics

- The avoidable cost opportunity from antibiotic misuse is \$35 billion, with a range of \$27 billion to \$42 billion.
- Inappropriate use of antibiotics is driven by various systemic and human factors, and continues to exacerbate antibiotic resistance which in turn contributes to substantial avoidable healthcare costs.
- There are encouraging signs that efforts to use antibiotics responsibly are paying off, particularly in declining prescriptions for the common cold and flu.

Exhibit 6: Avoidable costs due to antibiotics misuse



Underlying reasons for misuse of antibiotics

Prescriptions for viral infections and broad spectrum use are still common. The CDC estimated in 2012 that antibiotics were prescribed 68% of the time during acute respiratory tract infection visits, and of those, 80% were unnecessary according to CDC guidelines. A large number of factors underlie the inappropriate use of antibiotics. These factors vary in intensity and applicability, and have proved difficult to disentangle in research.^{76,77}

Among the leading reasons for the continued misuse of antibiotics is the physician's perception that the patient, or, commonly the parent of a sick child, is expecting a prescription and that the easiest way to ensure patient satisfaction is to provide a prescription.⁷⁸ Physicians may also face additional demand side pressures, such as a patient's ability to pay, clinical pressures (e.g. addressing long waiting times by treating patients quickly with an antibiotic to meet their expectations), litigation concerns, etc.⁷⁹ The inappropriate use of broad spectrum antibiotics is common for adults with acute respiratory tract infections and is also linked to the increasing problem of *C. difficile*. The latter is not only the most common identifiable cause of healthcare-associated infectious diarrhea in acute and chronic care facilities, but also is an increasingly resistant microbe.⁸⁰ Antibiotic misuse and overuse occurs due to misaligned incentives and measurement tools, such as guidelines that suggest immediate provision of broad spectrum antibiotics.⁸¹

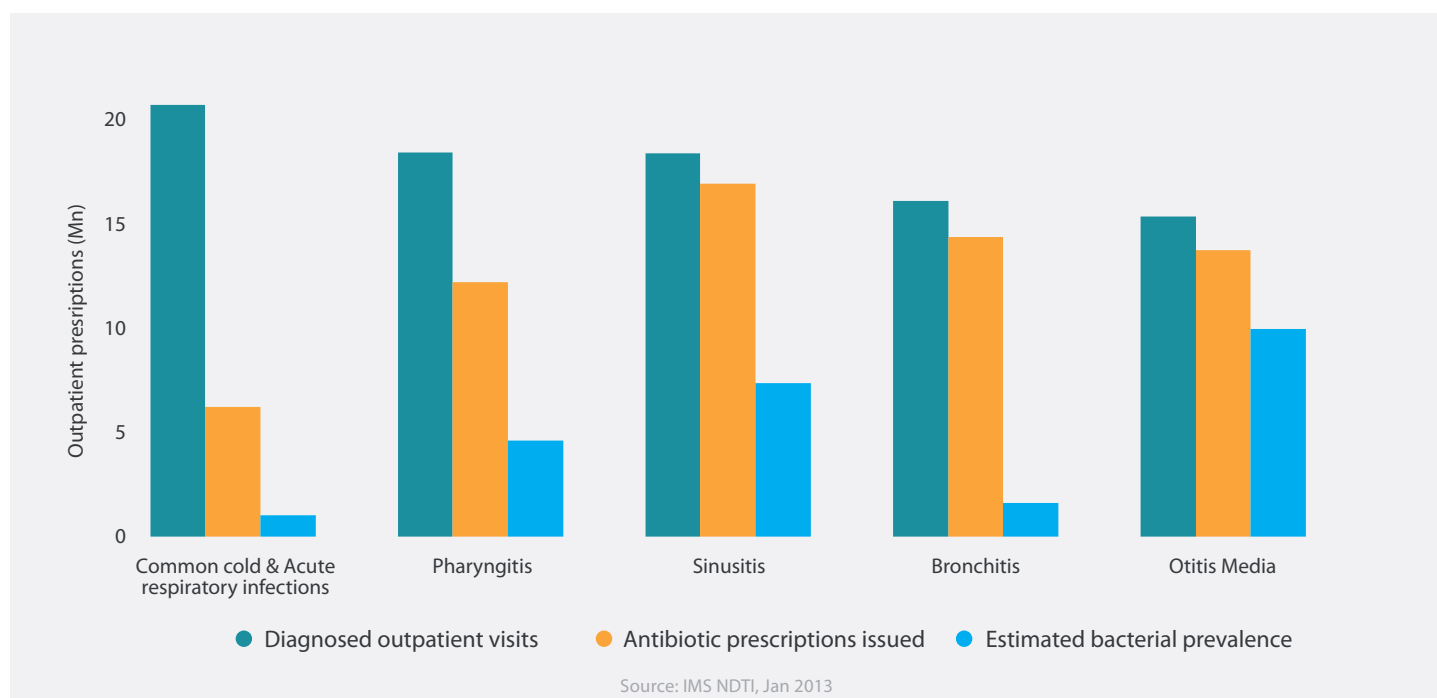
While resistance to antibiotics is a natural biologic phenomenon, there is a clear correlation between the rate of antibiotic use and level of resistance.^{82,83} The inappropriate use of antibiotics, characterized by both misuse and overuse by healthcare professionals and patients, has been long acknowledged as the key contributor to the development of antibiotic resistance.^{84,85} Misuse is exemplified in use of broad spectrum antibiotics, as well as the high rate of prescribing of antibiotics for viral infections.^{86,87,88,89}

Estimated avoidable costs

Avoidable costs due to inappropriate use of antibiotics are estimated to total \$35 billion annually. Exhibit 6 shows that most of that amount – \$34 billion – is incurred through inpatient care. This burden is a result of antibiotic resistant infections which are much costlier to treat than antibiotic susceptible infections. Direct costs are incurred through longer medical treatment, expensive second- and third-line antibiotic therapies, and screening and diagnostics to detect and prevent the spread of resistant bacterial strains.⁹⁰

The cost of excessive antibiotics prescribed in outpatient settings is \$1 billion. The bulk of these unnecessary prescriptions are issued for bronchitis, sinusitis and pharyngitis; however, the rate of antibiotic prescribing substantially exceeds the rate of bacterial infection for these diagnoses, according to Exhibit 7.

Exhibit 7: Antibiotic misuse for upper respiratory tract infections in 2012



Quantification approach

Existing efforts to quantify the impact of antibiotic misuse have focused on the setting of care. In the inpatient setting, costs are commonly defined as the added cost of treating a patient with an antibiotic resistant infection relative to a patient with an antibiotic susceptible infection. The most widely cited cost estimate for the inpatient setting is \$24 billion to \$38 billion in 2009 dollars, a national-level extrapolation by Susan D. Foster of the Alliance for Prudent Use of Antibiotics in 2010.^{91,92} By contrast, in the outpatient setting, estimates from the early 2000s indicate that the costs of excess antibiotic prescriptions for predominantly viral infections could reach between \$726 million and \$1.1 billion.^{93,94,95}

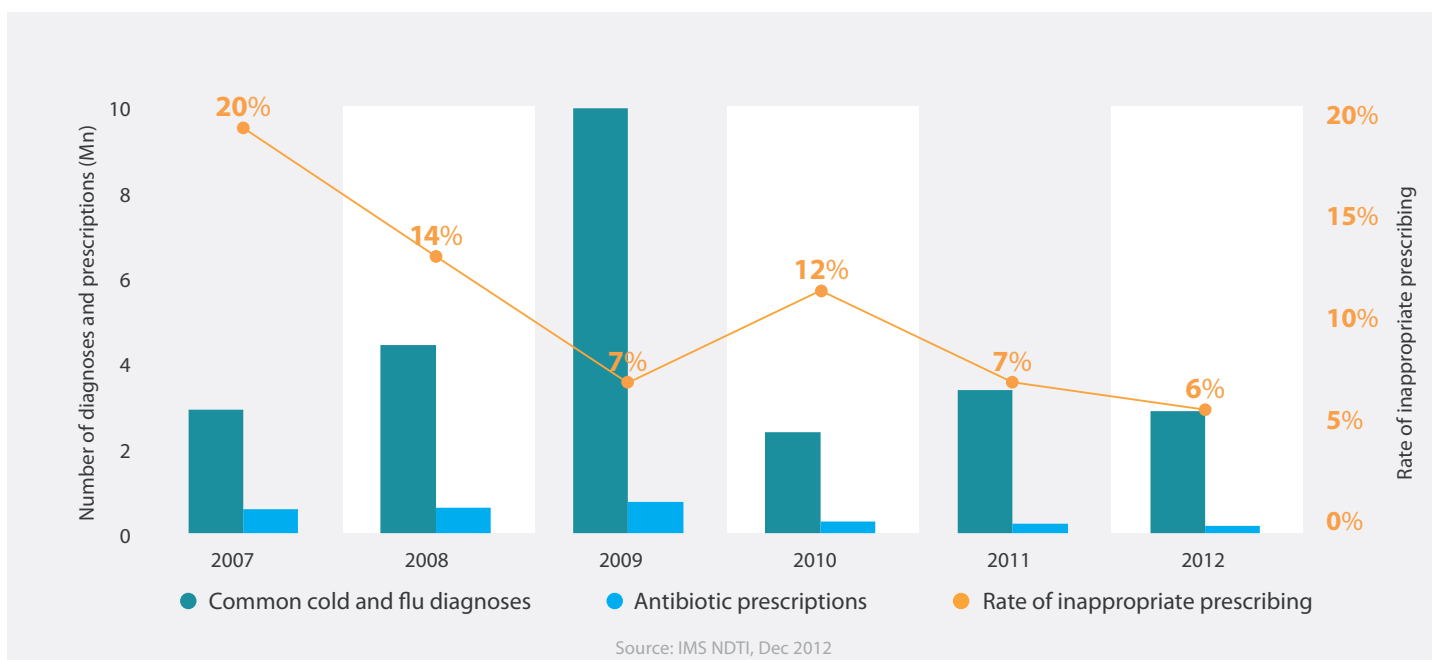
This study follows established methodologies to provide updated avoidable costs. Inpatient and outpatient costs are assessed separately, following Foster's methodology on the inpatient side, and using IMS Health prescription data to provide cost estimates of unnecessary prescriptions in the outpatient setting. On the inpatient side, we are able to update existing estimates to 2012 cost levels. On the outpatient side, we applied a new analysis leveraging previous research⁹⁶ and the most recent available estimates from IMS Health proprietary data of diagnosed visits for respiratory conditions and the frequency in which antibiotics are prescribed.⁹⁷

Given that previous estimates date from the early 2000s, this analysis substantially adds to the understanding of the magnitude of antibiotic prescribing for upper respiratory tract infections. Other contributors, such as the wider effects of high antibiotic use in livestock and agriculture on human resistance to antibiotics, have not been included in this analysis.⁹⁸

More responsible antibiotic prescribing for the common cold and flu

Despite continuing antibiotic misuse, an encouraging trend is emerging in the prescribing of antibiotics for the common cold and flu. Since 2007, the proportion of patients diagnosed with a cold or the flu – both viral infections that do not respond to antibiotics – who inappropriately received antibiotic prescriptions has declined from 20% to 6%, as shown in Exhibit 8.⁹⁹ This signals the positive impact of efforts to increase awareness about increasing pathogen resistance and to adopt a more responsible use of antimicrobial therapies.

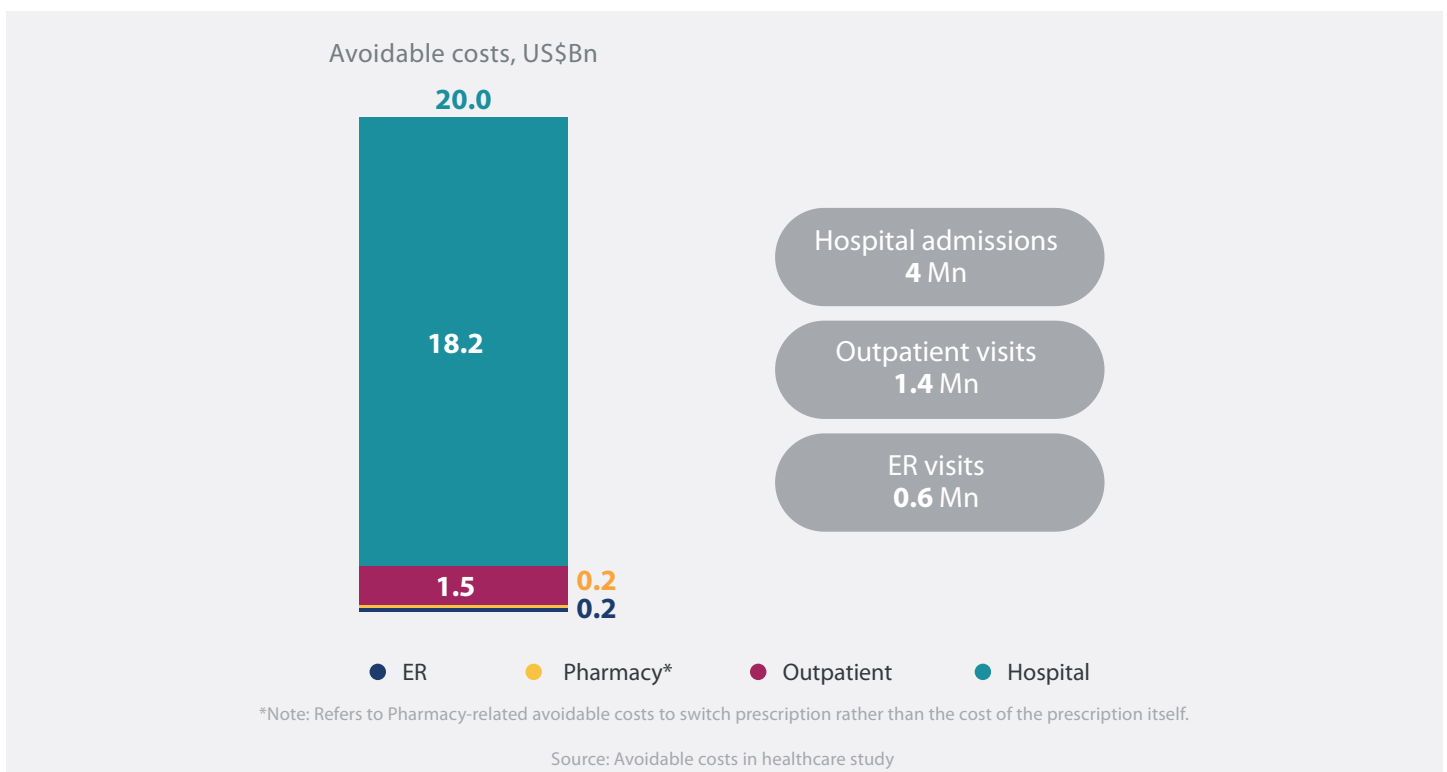
Exhibit 8: Antibiotic prescriptions for the common cold and flu are declining



Medication Errors

- The avoidable cost opportunity from medication errors is \$20 billion, with a range of \$15 billion to \$28 billion.
- Medication errors occur at every step of medicines use - administration, prescribing, dispensing and monitoring - and contribute to substantial morbidity and costs to the health system.
- Medication errors resulting in avoidable costs are concentrated in the inpatient care setting and impact approximately 4 million avoidable hospital admissions.
- In the outpatient setting, medication errors result in 1.4 million avoidable office visits.

Exhibit 9: Avoidable costs due to medication errors



Underlying reasons for medication errors

Medication errors result from faults in the administration, prescribing, dispensing, and monitoring of medicines. Incorrect dosage, omission of administration, and timing of administration have been reported as consistent errors.¹⁰⁰ Insulin and warfarin are the most common medications resulting in hospitalizations due to adverse drug events (ADEs) caused by incorrect administration.¹⁰¹ In hospitals, prescribing errors make up approximately 25% of medication errors. These errors are related to illegible handwriting, incorrect dosage, overprescribing, and miscommunication about prescriptions during a transition in care. In the outpatient setting, 45% of preventable ADEs result from inadequate prescription monitoring.¹⁰² In emergency departments, leading causes for medication errors are not following procedures and protocols and poor communication, with contributing factors of distractions, emergency situations, and workload levels.¹⁰³ ADE rates are generally the highest among children up to age 5 and among adults older than 60. Older adult patients account for 49% of annual ADEs that result in hospitalizations, while children had a higher annual incidence of ADEs of all types.¹⁰⁴ Approximately 45% of emergency room visits by children are due to unintentional overdoses, and approximately 35% are due to allergic reactions.¹⁰⁵

As the healthcare system becomes increasingly complex and the pressure increases for cost reduction, transparency, and accountability in the delivery of care, medication errors become more apparent. They reflect the enormous challenges in the continuity of care when patients experience multiple “handoffs”—transitions of care from one group of healthcare providers to another. Complex and variegated processes involving different organizations, departments or stakeholders result in a greater likelihood of miscommunication of pertinent medical information among incompatible systems, particularly for patients with complex health problems.^{106,107} As a result of disruptions and interruptions in care, medication errors often increase in fast-paced healthcare environments, such as in the emergency department and the operating room.¹⁰⁸

Estimated avoidable costs

ADEs represent a substantial financial impact on the healthcare system, with previous estimates indicating that preventable medication errors cost approximately \$21 billion per year.¹⁰⁹ Research studies indicate that at least 25% of all ADEs are preventable, with nearly 3.8 million instances of preventable ADEs annually in the inpatient setting, and 3.3 million in the outpatient setting.¹¹⁰ While both types of errors are cause for concern, preventable ADEs in the outpatient setting tend to be less severe and cost less.¹¹¹

Avoidable health costs due to medical errors reached \$20 billion in 2012, with \$18 billion spent on 4 million inpatient care admissions and \$1.5 billion spent on 1.4 million outpatient visits, according to Exhibit 9. Avoidable pharmacy-related and emergency room costs were lower at \$158 million and \$153 million, respectively.

Quantification approach

Many studies articulating the reasons why medication errors occur are from the mid-2000s. It was during this period that the use of electronic prescribing methods—or e-prescribing—began to increase. This suggests that medication error measures in the existing literature may be outdated and warrant new research.

No evidence links the cost of medication errors to the error-prone processes (e.g., prescribing, dispensing, etc.). Since the literature on ADEs indicates dichotomous rates for avoidable costs based on setting, this study stratifies inpatient and outpatient costs and applies a methodology to generalize those costs to the total population. The rate of avoidable ADEs in the inpatient setting was obtained from the NEHI and Massachusetts Technology Collaborative study conducted in 2008.¹¹² The rates were generalized nationally and applied to the total annual number of discharges from U.S. hospitals. Many studies focus on an isolated or targeted impact of medication errors and ADEs, or both, such as inpatient versus outpatient incidents, or rates versus cost. By contrast, this study aggregates all of the most recent figures relevant to medication errors in order to provide a total avoidable cost estimate.

Suboptimal Use of Generics

- The avoidable cost opportunity from underutilization of generics is \$12 billion, with a range of \$10 billion to \$13 billion.
- 85 million prescriptions could be prescribed and dispensed using low-cost, safe generic alternatives instead of unprotected brands.
- Although the U.S. has already achieved a higher level of generic utilization than any other country, there is still room for increasing generic efficiency within many therapy classes.

Exhibit 10: Avoidable costs due to generic underutilization



Underlying reasons for suboptimal use of generics

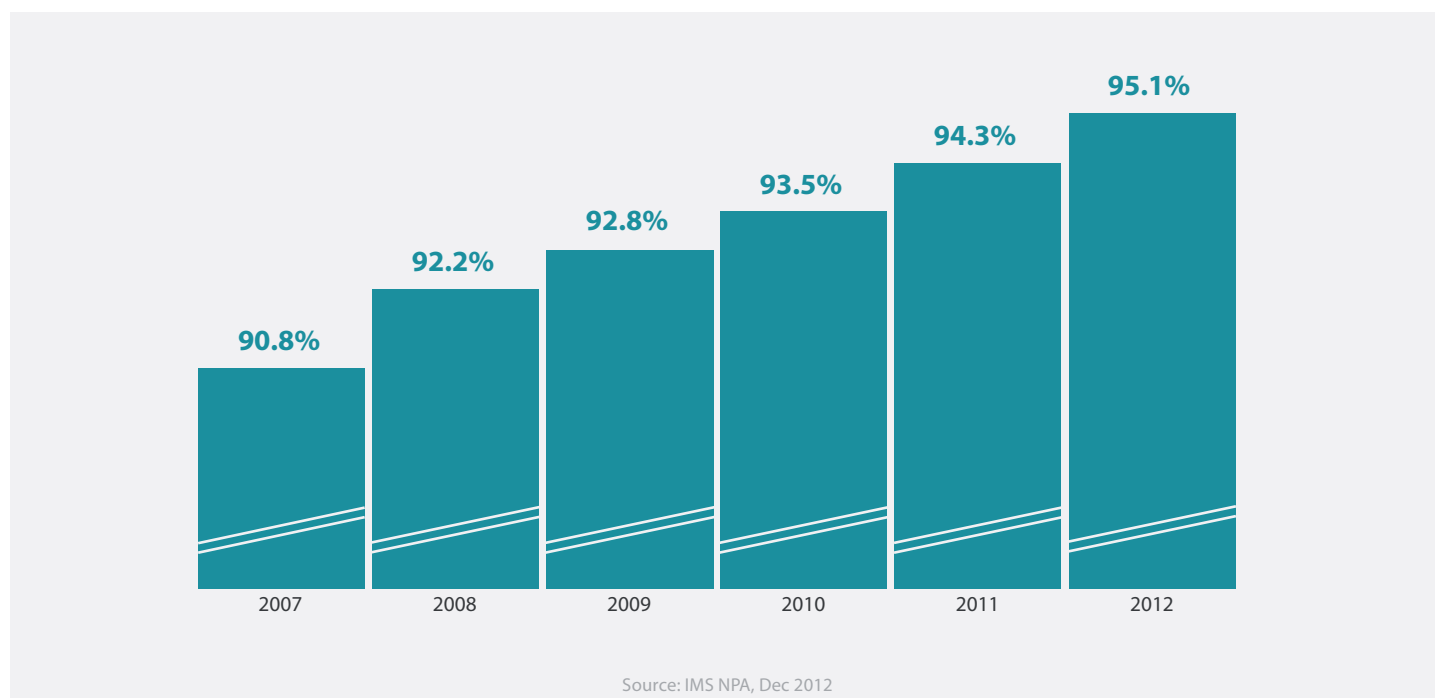
A large number of medications in the U.S. are available with safe, low-cost generic versions of off-patent branded products with the same active ingredients. Generic substitution refers to the prescribing and dispensing of a generic product instead of a branded product, when both contain the same molecule in the same form. Generic substitution is different from therapeutic substitution where switching occurs between medications within the same therapy area and with similar mechanisms of action.

Physician and patient factors are important influences on generic drug therapy initiation. Patient mistrust of generic medications or in the healthcare system is a barrier to generics use.¹¹³ Many physicians also hold negative views about generic medications.¹¹⁴ Pharmacy benefit plans and mail-order pharmacies often steer patients toward generic medications once the first prescription has been filled, but they have little effect on initial prescriptions.¹¹⁵

Clinical practice guidelines by professional physician organizations and research articles in peer-reviewed journals reveal that concerns about generic substitution primarily lie in central nervous system (CNS) therapy areas such as antipsychotics, antidepressants, anti-epileptics and drugs for Attention Deficit Hyperactivity Disorder (ADHD), as well as thyroid and contraceptive pharmacotherapies. There are two main reasons for low generic use in these classes: first, despite bioequivalence, the precise optimal dose can vary across different products with the same active ingredient¹¹⁶, and second, substitution can lead to poor compliance in these therapy areas. Both sub-optimal dosing and non-compliance can lead to dangerous or highly undesirable outcomes, such as breakthrough seizures in anti-epileptics¹¹⁷ or pregnancy on contraceptives.¹¹⁸

After the loss of exclusivity of major brands, patients are converted to the newly available generics and the brands experience market share erosion (e.g., Lipitor® & Plavix® recently).¹¹⁹ During this conversion period generic utilization is not always optimal. Also, certain therapy areas may hold limited commercial incentives for generic manufacturers to invest in developing and manufacturing generic drugs.

Recent IMS Health data indicate that 84% of prescriptions in the U.S. were filled with generics in 2012, including both branded and unbranded generics.¹²⁰ This overall generic utilization rate covers all prescription drugs, including those available only as brands. When looking at the rate of utilization of medications for which generic versions are available for the same molecule and form, also known as generic efficiency, patients were dispensed the generic alternative 95% of the time in 2012.¹²¹ This is a utilization increase of 4% in the past five years, according to Exhibit 11.

Exhibit 11: U.S. generic efficiency reached 95% in 2012**Estimated avoidable costs**

Assuming that a maximum generic efficiency of 98% could be achieved in most therapy classes where generics are available, the avoidable cost is \$10 billion. If a maximum efficiency of 99% were achieved, the avoidable cost would increase to \$13 billion. Exhibit 10 shows the average cost reductions that could be achieved through such increase in generic efficiency. These estimates exclude any potential savings from CNS therapy areas, thyroid preparations and oral contraceptives. This approach provides the most complete estimate of the additional value of achieving high generic efficiency at the therapy class level and molecule form level where usage is currently lower than 98%. Our analysis shows that achieving even incremental gains toward higher generic efficiency can result in substantial cost savings.

Generic use is recognized widely as a means of health expenditure control. The U.S. has achieved an unparalleled level of generic utilization and reduction of therapeutic drug costs, compared with any other country. National spending data from 2011 show that American consumers, taxpayers, federal and state governments, insurers and other payers have been saving an average of more than \$1 billion every two days. According to IMS Health research, utilization of generic medicines saved the U.S. healthcare system \$193 billion in 2011.^{122,123} Optimizing generic use will be crucial in controlling spending, considering the Medicaid expansion and aging baby boomer generation.

Quantification approach

While a generic efficiency of 100% is rarely possible, therapy classes such as antihypertensives, analgesics, antibiotics and antidiabetics already are in excess of 98% generically efficient. In this report, potential health system savings from increased generic efficiency are calculated for therapy areas where generic efficiency is currently below 98%. The calculation estimates potential savings based on the availability of low-cost and safe generics, assuming no changes in utilization and using the latest available information for the cost difference between branded and generic medications.

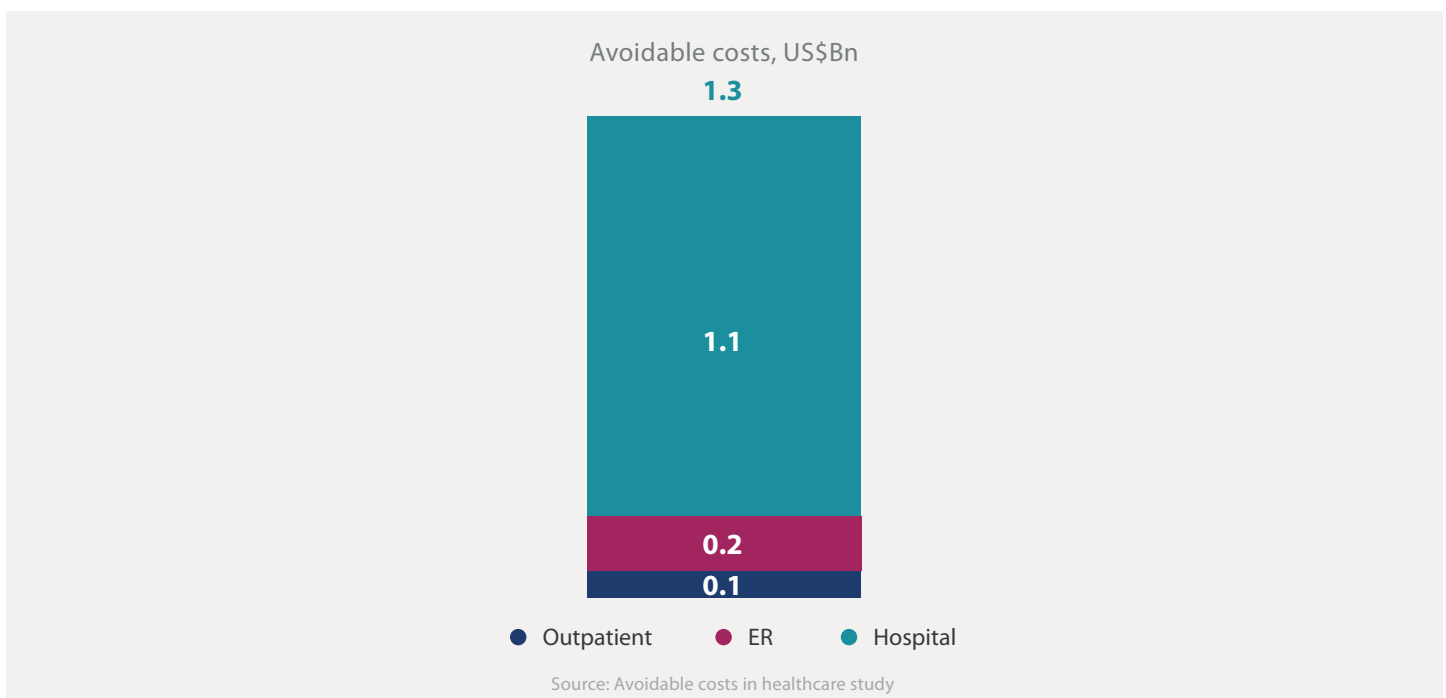
The analysis considers the potential substitution of no-longer-protected brands (off-patent brands) with available generic alternatives. CNS therapies, thyroid preparations, and oral contraceptives are excluded from analysis, and the total avoidable cost does not include increased efficiency in these areas, due to concerns about generic substitution or clinical practice guidelines discouraging the use of generics. In 2012, branded medications in these categories made up 3% of brand spending and 9% of brand prescriptions in the U.S.

Generic efficiency in 2012 was calculated for each therapy class as the ratio of generic prescriptions to the sum of generic and off-patent brand prescriptions. This estimate is based on monthly branded and generic prescriptions at molecule and form level and excludes from the calculation months in which generic alternatives were not available, e.g. if the branded product was still protected in some months during 2012.

Mismanaged Polypharmacy in Older Adults

- The avoidable cost opportunity from polypharmacy mismanagement among older adults is \$1.3 billion, with a range of \$900 million to \$1.7 billion.
- Most of these costs are incurred through inpatient care and emergency room visits and hospitalizations due to complications and adverse drug events.
- The growing share of older adults of the overall U.S. population makes polypharmacy an increasingly relevant challenge.

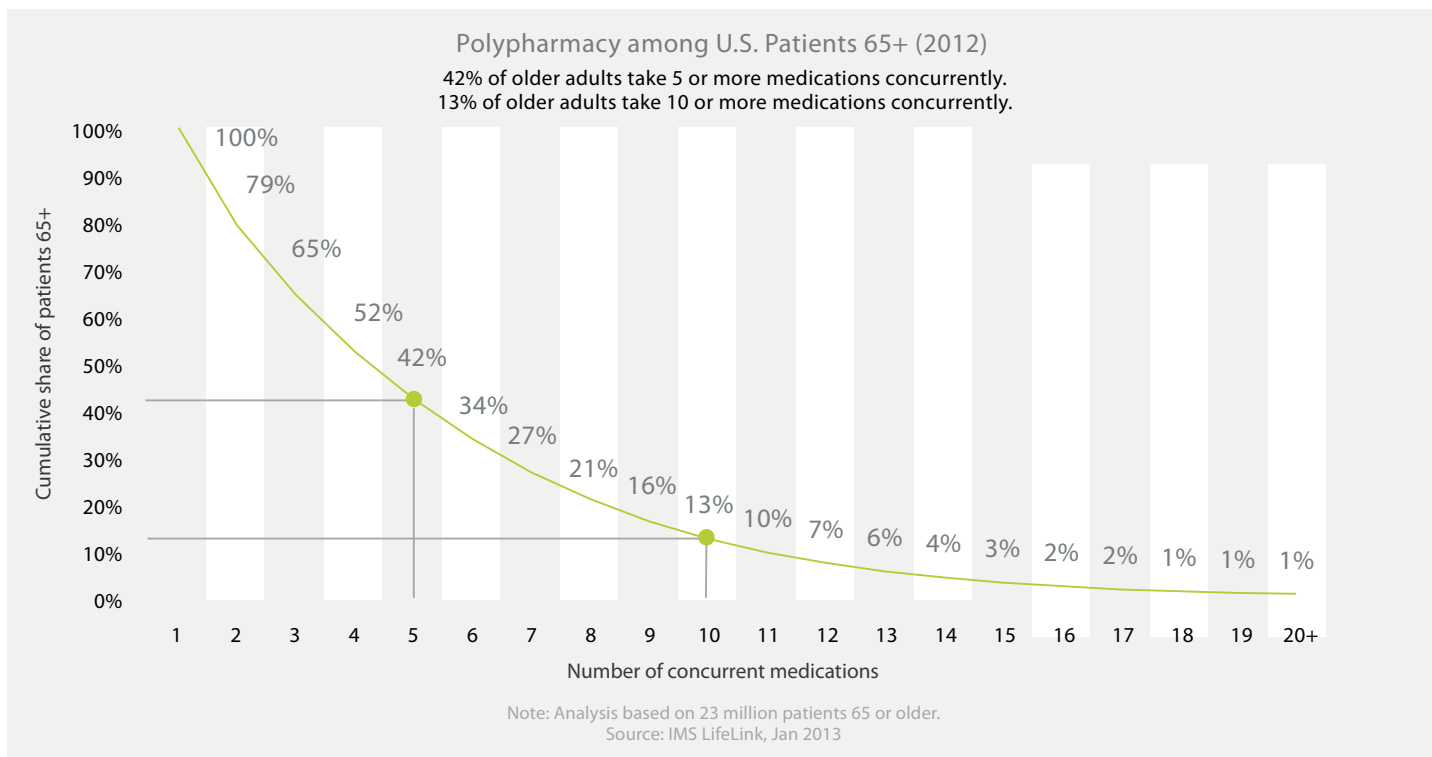
Exhibit 12: Avoidable costs due to mismanaged polypharmacy



Underlying reasons for mismanaged polypharmacy

Evidence suggests that polypharmacy is a challenge among older patients. According to the CDC, 80% of people ages 65 and over have at least one, and 50% two or more, chronic conditions.¹²⁴ IMS Health prescription data in Exhibit 13 indicate that 42% of patients 65 and older took five or more prescription drugs in 2012, and the average number of drugs taken increases from five at age 65 to seven at age 85.¹²⁵

Exhibit 13: 42% of older adults in the U.S. have polypharmacy



Complex medication regimens carry the risk of drug interactions and cause adverse reactions. Among older adults, additional factors that may lead to mismanaged polypharmacy and adverse events include increased frailty and the higher likelihood of co-morbidities and errors in self-administration of medications. The likelihood of an adverse event increases among older patients whose medications are not carefully tracked and managed.¹²⁶ Mismanaged polypharmacy in older adults is a risk also due to body composition, metabolic and absorption changes that occur with advancing age.

The majority of adverse events among older adults involve patients using five or more concurrent medications, and two-thirds of adverse events are attributable to only four medication classes (either alone or in combination): warfarin (33%), insulins (14%), oral antiplatelet agents (13%), and oral hypoglycemic agents (13%).¹²⁷

As the number of older adults in the U.S. population continues to rise – those age 65 and over are projected to increase from 40 million in 2010 to 71 million by 2030¹²⁸ – polypharmacy management among this particularly vulnerable group will grow in importance.

Estimated avoidable costs

Polypharmacy with an adverse event may occur if a rational decision has been made to prescribe a medicine when the risks are outweighed by potential clinical benefits. However, avoidable ADEs in this research refer to unexpected ADEs that result from mismanaged polypharmacy with no designated healthcare professional keeping track of the patient's medicines prescribed by different physicians. In these situations, patients experience avoidable ADEs and incur substantial expenditures. Avoidable costs from mismanaged polypharmacy include unnecessary medication costs from overprescription, costs for physician and emergency department visits, and costs for hospitalizations due to adverse events, as well as the costs of additional medication needed to treat them.

Mismanaged polypharmacy among older adults resulted in at least \$1.3 billion of avoidable healthcare costs in 2012. The vast majority, or \$1.1 billion, was spent on inpatient treatment (see Exhibit 12), with the remainder spent on emergency room and outpatient visits.

Quantification approach

Supporting evidence on how mismanaged polypharmacy results in costly adverse events has been assessed with a focus on older adults.^{129,130} However, there are no existing estimates of the costs associated with ADEs that result from mismanaged polypharmacy among older adults independent of medication errors.

This is believed to be the first report to quantify total medical costs associated with mismanaged polypharmacy. Since these costs have not been estimated previously, a new algorithm was developed to estimate avoidable costs based on existing evidence of the challenge and risks. The calculation focuses on older adults in the U.S., and considers existing literature on the prevalence of mismanaged polypharmacy and risks of adverse events driving additional healthcare utilization. Estimates in this study reflect current costs for hospitalizations, physician visits, and emergency department visits, representing a more comprehensive look at the total costs involved.

Case Studies of Recent and Innovative Interventions

In the course of this study it became clear that a large number of efforts are underway to address the underlying causes of avoidable spending and improve medication use. Novel interventions, critical assessments of established solutions and pioneering models of stakeholder cooperation are emerging, and in some cases, thriving. On the following pages are six representative examples of interventions and activities in the private and public sector. Each of these case studies covers more than a single area of suboptimal medicine use.

These case studies illustrate new and effective solutions designed to make tangible improvements in patient health outcomes while reducing the cost of care. They are collaborative working solutions that target high-risk patients with chronic diseases and provide proper incentives to all stakeholders.

CASE STUDY 1

CareFirst's Patient-Centered Medical Home achieved \$40 million in savings through chronic disease management by primary care providers.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

Launched in January 2011 across Maryland, the District of Columbia and Northern Virginia, CareFirst's Patient-Centered Medical Home (PCMH) program is designed to address the shortage of Primary Care Physicians (PCP), reduce healthcare costs, and improve care coordination quality for members, primarily those with chronic illnesses.¹³¹ The goal is to provide PCPs a more complete view of their patients' needs and the services they receive from other providers.

CareFirst's PCMH program involves 80% of primary care physicians and nurse practitioners in the region. The program provides incentives in the form of higher reimbursement, fees for creating and maintaining customized patient care plans, and bonus payments for achieving better cost and quality outcomes. Through internet access and a web-based tool, providers are able to maintain a detailed online member health record and care plan. Registered nurses, community-based local care coordinators and CareFirst regional staff also are members of the teams that engage with patients, gather and analyze comprehensive data on CareFirst patient populations, and identify opportunities for care improvement and cost savings.

In the two years since CareFirst launched the PCMH program, nearly 3,600 primary care providers in 283 PCMH Medical Care Panels (groups of primary care physicians, nurse practitioners, community pharmacists) and one million CareFirst patients have joined the program, making it the largest of its type in the country.

Outcomes

In its first year the program achieved savings of \$40 million¹³² by reducing unnecessary hospital admissions and ER visits by patients with chronic diseases. The best performing healthcare providers reduced their patients' overall health costs 4.2% from the level of expected costs in 2011, while general cost savings for all other providers averaged 4% higher than expected in 2011. Provider reimbursement increased 20%, in addition to a 12% increase paid to all participants who remained in good standing in the PCMH program. The cost of care for all CareFirst members attributed to PCMH participants was 1.5% lower than had been projected for 2011.

Key lessons learned and relevance to the avoidable cost opportunity

- Proper incentives for primary care health professionals, especially those in small practices, promote a sharper focus on high-risk patients with chronic conditions and enable better outcomes through more efficient care.
- Health information technology can be applied and managed through web-based tools without imposing a cost and infrastructure burden on small practices.
- Healthcare utilization and outcomes data, when analyzed and monitored proactively, can inform delivery of care changes leading to greater efficiency.

CASE STUDY 2

Centers for Medicare and Medicaid Services' medication therapy management programs demonstrate positive impact on chronic disease outcomes and healthcare costs.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

Medication therapy management (MTM) programs target high-risk, high-cost Medicare Part D patients with a variety of chronic medical conditions, and strive to optimize therapeutic outcomes while reducing the risk of adverse events through improved medication use. They represent a multi-stakeholder effort to improve chronic care quality and management, and to reduce costs. Pharmacists and various healthcare professionals working within a Part D MTM program provide customized patient care by conducting annual one-on-one comprehensive medication reviews (CMRs) and quarterly targeted medication reviews (TMRs), developing personal medication lists and medication-related action plans. They also reach out to physicians and other healthcare professionals on behalf of patients to resolve medication-related problems.¹³³

CMS set out to identify the impact of 2010 Part D MTM programs on Medicare beneficiaries' adherence, medication use, drug therapies and resource utilization associated with hospital and emergency room (ER) visits, medications and costs. The evaluation¹³⁴ focused specifically on high-cost, high-risk beneficiaries with two diseases: congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD). These patients were expected to benefit significantly from MTM program interventions.

Outcomes

The impact on patients' health was identified in claims data within a six-month outcome period. Additional analyses considered the impact of MTM programs in the context of organizations of different sizes and varying approaches to CMR implementation, as well as the managed versus fee-for-service types of Medicare Part D plans.

According to the study findings, patients enrolled in MTM programs experienced significant improvement in the quality of their drug regimens. MTM programs consistently helped improve adherence and discontinue the use of high-risk medications for both CHF and COPD patients. Comprehensive medication reviews demonstrated a positive impact across most outcomes for patients who received them. Patients who received CMR experienced significant improvements in the quality of their drug regimens, while those who did not incurred on average about \$1,034 more in inpatient costs during the study period.

The programs' impact on other drug therapy outcomes, hospital and ER visits, and other resource utilization, including costs, was less consistent. At the overall level for both Part D plans and Medicare Advantage Part D plans, the study found significant cost savings associated with all-cause hospitalizations, but not for COPD- or CHF-specific hospitalizations. Given that MTM programs target improvements in medication therapy across all chronic conditions of any participating patient, the interventions were very likely successful in improving outcomes related to conditions other than CHF and COPD.

Another interesting finding identified larger cost savings for COPD patients than for CHF patients, most of whom were already adherent to their medications. Finally, apart from lowering inpatient and emergency room costs, the analysis suggested that MTMs may generate additional Medicare Part D cost savings through the promotion of cost-effective medications, including generics, and by identifying treatment duplication.

Key lessons learned and relevance to the avoidable cost opportunity

- Medication therapy management programs need to be appropriately targeted at patients and chronic diseases for an optimal balance of health outcomes improvement and cost effectiveness.
- Medication therapy management impact depends on a variety of factors, so the programs need to be applied as a tool requiring customization.

CASE STUDY 3

Thrifty White's community pharmacy programs improve adherence to chronic disease therapies by fostering pharmacist engagement with patients.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

In 2011 Thrifty White, a Minnesota-based, 89-store drug chain with pharmacies across six Midwest states, introduced various programs aimed at giving pharmacists more time to engage with patients and play a role in improving health outcomes. Pharmacists usually have limited time for each patient, since their primary function is to fill prescriptions. This often results in little or no interaction with patients beyond the dispensing of medications.

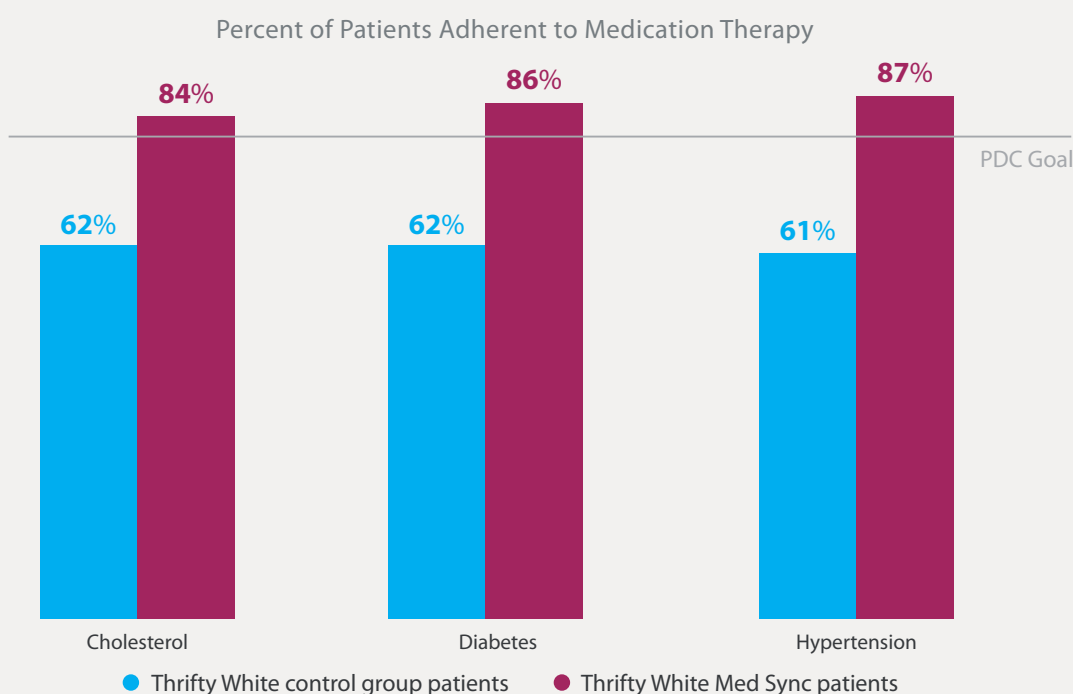
Through MedSync, patients with chronic diseases receive automated phone calls with reminders to pick up refills or alert the pharmacy about a prescription medication change. In a program called Ready Refill, prescriptions are prepared in robotically dependent, central-fill facilities without compromising safety or accuracy, and can be delivered to a patient's home or workplace. A majority of patients choose to pick up medications at the pharmacy, where pharmacists provide counseling, discuss potential adverse effects, and conduct comprehensive medication reviews or other medication therapy management services.¹³⁵

Additional Thrifty White initiatives designed to improve adherence include HealthyPackRx Compliance Packaging for multi-dose prescriptions. Individual packets provided to patients simplify the way they take medications and reduce the risk of medication errors.

Outcomes

According to Thrifty White/Virginia Commonwealth University Study results in Exhibit 14, one year after these programs began, adherence among patients in the program increased up to 26% across three chronic diseases.

Exhibit 14: Thrifty White's Med Sync program increased medication adherence



Note: Patients are considered adherent with a proportion of Days Covered (PDC) of 80% or greater.

Source: Thrifty White/Virginia Commonwealth University study, 2012

These results are based on a population of 3,300 patients enrolled in the MedSync program and 45,000 patients receiving standard pharmacy services from Thrifty White. Depending on the drug class, patients enrolled in the program had 3.4 to 6.1 times greater odds of remaining adherent, compared with patients outside the program. Conversely, control patients had a 52% to 73% greater likelihood of becoming non-persistent, compared with patients enrolled in MedSync. As of 2012, nearly 17,000 patients with an average of four concurrent drug therapies for chronic conditions had enrolled in the MedSync program.¹³⁶

Key capabilities enabling this intervention included:¹³⁷

- Technology for automated filling of prescription medications, automated reminder calls to patients, video conferencing between pharmacies to receive expert advice from an available pharmacist at a different location.
- Incentives to motivate and empower pharmacists to adopt the new patient service model and participate in the program, with a long-term plan and clearly defined objectives and benefits.
- Training programs offered to other pharmacies and healthcare stakeholders who can benefit from the approach and the lessons learned.

Thrifty White is also implementing an intervention program for patients in assisted living and home care settings aimed at screening polypharmacy, identifying medication errors and improving adherence. In addition, the pharmacy chain is collaborating with local hospitals to develop medication adherence solutions during transitions of care.

Key lessons learned and relevance to the avoidable cost opportunity

- Empowering pharmacists to actively work with patients to customize or improve medication therapy regimens has a tangible and positive effect on patient adherence.
- Technology can be used to help free up pharmacists' time, reduce medication fill errors, and identify patients at risk for nonadherence.

CASE STUDY 4

The National Consumers League's Script Your Future campaign challenges multi-stakeholder teams to develop creative, collaborative solutions to nonadherence.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

The National Consumers League (NCL) is spearheading the largest consumer-facing campaign in the U.S. aimed at improving medication adherence among chronically ill patients and their families.^{138,139} The Script Your Future campaign involves all healthcare stakeholders - healthcare professional groups, government agencies, adherence researchers, and consumer, insurance, business, and pharmaceutical organizations. While the program was created assuming that no one solution by a single stakeholder group can sufficiently address nonadherence, Script Your Future centers on patients and patient empowerment. The campaign encompasses public education and marketing efforts at national and regional levels, research and targeted outreach initiatives, and other activities in six pilot cities.

NCL intervention efforts surround consumers with messages about the importance of adherence and its impact on the entire family. The campaign also provides tools and information about improving communications between patients and healthcare professionals specifically targeting adherence. One such tool is a wallet card, available in multiple languages, with questions that patients should ask during doctor and pharmacy visits in order to understand the severity of their condition, the benefits and importance of their medication regimen, and the steps they can take to improve their health.

A major 2013 campaign event is the Medication Adherence Team Challenge – a project that challenges student pharmacists, as well as faculty and students preparing for other healthcare professions, to develop creative approaches that raise awareness about medication adherence. The program encourages interdisciplinary student teams from pharmacy, medicine, nursing, and other health professions to tackle the problem of poor adherence.

Outcomes

Since 2011, the campaign has attracted more than 130 public and private healthcare stakeholder organizations and institutions, including the U.S. Surgeon General. Notably, the campaign partnered with the Million Hearts™ initiative, the Centers for Disease Control and Prevention, and the Office of the National Coordinator for Health IT.

To date, the campaign has disseminated more than 450,000 wallet cards and 40,000 posters in multiple languages to consumers and healthcare professionals nationwide at pharmacies, community centers, work places, clinic offices, health fairs, and local events. In 2012 alone, the program introduced 30,000 healthcare professionals to Script Your Future materials to be used during patient visits. The campaign's website has registered more than 70,000 visits and thousands of adherence-tool downloads. The 2013 Team Challenge enrolled more than 85 schools and over 1,700 participating students. Through the 2013 campaign intervention, more than 12,000 patients were counseled as part of an effort that has reached a total of at least 3 million people.¹⁴⁰

The impact of the campaign on adherence will be formally evaluated in 2014, but benchmark surveys have been conducted at national and pilot city level with over 3,000 patients. Key findings reveal that communication about adherence between patients and healthcare professionals needs to improve, and that the most useful solutions are question lists, reduced co-pays, automatic prescription refills and seven-day pill boxes.

Key lessons learned and relevance to the avoidable cost opportunity

- **Multi-stakeholder healthcare teams provide novel solutions that no individual stakeholder group can create or implement singlehandedly.**
- **Successful adherence interventions resonate with patients when they reflect personal goals, adapt to something relevant, and enable behavior change.**
- **A new generation of healthcare professionals is enthusiastic about actively engaging patients in their own care.**

CASE STUDY 5

Walgreens becomes the first retail chain to lead an accountable-care organization and expands chronic disease diagnosis and management services.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

In April 2013 Walgreens announced an expansion of chronic disease diagnosis and management services at more than 300 in-store clinics in 18 states.¹⁴¹ Nurse practitioners and physician assistants will offer patients with asthma, diabetes and high cholesterol services that include testing and diagnosis of the chronic condition, prescribing medication therapy, providing referrals for additional testing, and managing the disease. Walgreens also is the first pharmacy to establish an accountable-care organization (ACO). The pharmacy chain is partnering with Advocare and its physicians to provide care to more than 500,000 patients in southeastern Pennsylvania and New Jersey, and is participating in two other ACOs with physician groups in Florida and Texas.

Walgreens' in-store clinics already provide a broad range of healthcare services, especially screening and immunizations. The ACO model further advances the sharing of information about pharmacy and in-store clinic services with physicians and payers, and enables better coordination of care. It also helps eliminate the duplication of services, improve treatment outcomes, reduce costs and increase patient satisfaction.

Walgreens considers pharmacists and the staffs of its in-store clinics to be an extension of healthcare in the community. The pharmacy chain intends to close existing gaps in primary care through links to physicians and healthcare information technology.¹⁴² Services to be provided include blood pressure and blood glucose monitoring, screenings, smoking cessation programs and immunizations. Some of these services can be conducted entirely at pharmacies, while others will be handled by partnering physicians. Through ACOs, Walgreens aims to improve connections between primary care physicians and its pharmacies during transitions of care.

Outcomes

Early indications show that Walgreens' ACOs are having a significant impact. In the first four months of existence, the ACO organizations, which manage healthcare for approximately 50,000 patients, demonstrated hospital readmission levels at half the national average. More importantly, Walgreens ACOs are achieving a fundamental transformation of physician perceptions about pharmacies and the benefits of this new kind of partnership.

The new options for accessing primary care health professionals may attract patients looking for convenience and cost savings. Care costs at in-store clinics are lower than identical services performed in doctors' offices and emergency rooms. Walgreens' chronic disease management services have the potential to address some of the anticipated primary care workforce problem that will result when millions of newly insured people enter the U.S. healthcare system.

Key lessons learned and relevance to the avoidable cost opportunity

- Pharmacies are capable of, and have been taking on, greater responsibility to provide more primary care services.
- Through aligned incentives for all healthcare partners, ACOs are moving healthcare delivery away from a fragmented, fee-for-service model to a shared, collaborative coordination of care.
- Shared benefits and savings within multi-stakeholder ACOs can change the notion that healthcare services are a zero-sum game for physicians and pharmacies.

CASE STUDY 6

CVS Caremark's Pharmacy Advisor program improves medication adherence and increases therapy initiation rates.

Levers

- Improved adherence
- Evidence-based clinical practice
- Managed polypharmacy
- Optimal generics use
- Fewer medication errors
- Rational antibiotic use

Stakeholders:

- Payers
- Providers
- Patients
- Pharmacists
- Policy Makers
- Pharma Companies

Intervention

In the belief that face-to-face and one-on-one time with a pharmacist is an effective solution to improve health outcomes and care, especially for patients with chronic conditions, CVS Caremark launched Pharmacy Advisor®.¹⁴³ The program engages members who are diagnosed with chronic conditions when they are most receptive to messages about their prescribed therapy – face-to-face when members choose to fill prescriptions at the pharmacy or by phone from the Pharmacy Advisor Call Center when members choose home delivery. These integrated tactics drive behavior change over time and lead to better clinical outcomes. In addition to improving medication adherence, the program saves money and enhances the quality of treatment. The program also closes gaps in care and directs members with chronic conditions to existing disease management programs where they can obtain additional support.

Pharmacy Advisor® was launched in 2011 with a focus on diabetes. In 2012 the program was expanded to include chronic cardiovascular care, with the specific goal of improving medication adherence for four conditions: high blood pressure, high cholesterol, coronary artery disease (CAD) and congestive heart failure (CHF). The program was expanded in 2013 to include support for patients with asthma, breast cancer, chronic obstructive pulmonary disease (COPD) and osteoporosis.

Outcomes

A research study published in Health Affairs in January 2012¹⁴⁴ found that the Pharmacy Advisor program focusing on diabetes increased both patient medication adherence and physician initiation of prescriptions. The research highlighted the essential role of pharmacists in monitoring patient adherence, improving outcomes and reducing overall costs. Face-to-face counseling can be two to three times more effective than other forms of communication between pharmacists and patients in increasing medication adherence. The study also indicated that face-to-face counseling led to a 3.9% improvement in medication adherence, and an increase of 2.1% in overall medication adherence rates among Pharmacy Advisor patients. Participating employers saved more than \$600,000 through healthcare cost avoidance with the intervention group, achieving a return on investment of \$3 for every \$1 spent on additional counseling. Results from the Pharmacy Advisor pilot demonstrate higher therapy initiation rates for concomitant therapies for diabetes, such as statins, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), which are commonly prescribed to diabetes patients for kidney protection.¹⁴⁵ Contacts by pharmacists with patients and their doctors significantly increased therapy initiation rates, closing these common “gaps in care” by as much as 39% for the full sample and 68% for the group counseled face-to-face at the CVS/pharmacy locations.

Key lessons learned and relevance to the avoidable cost opportunity

- A positive correlation exists between face-to-face interactions of pharmacists and patients and medication adherence.
- Appropriately designed and adequately funded intervention programs can lead to better medication adherence and cost savings.
- Expanded advisory services focusing on chronic diseases should be encouraged.

Priorities for Promoting Responsible Medication Use

These case studies demonstrate that the opportunity for reduction of avoidable costs through synergies and collaboration is significant. Based on the featured case studies, on broader observations of the healthcare system, and on investigations by the IMS Institute and dialogues with stakeholders, a list of priorities for improving medication use has emerged.

The U.S. health system is undergoing dramatic changes initiated by and accelerating with the passage of the Patient Protection and Affordable Care Act (PPACA). Eliminating inefficiencies and wasteful spending in the U.S. healthcare system, while improving the quality of care and treatment outcomes, are priorities of the healthcare reform. The legislation is giving impetus to new, multi-stakeholder alliances and innovative approaches to medicine use challenges and the resulting avoidable healthcare costs.

Changes are happening along three dimensions of healthcare – structure, delivery and financing. These three categories provide a functional framework for defining priorities that address suboptimal medication use through the six levers discussed in this report, and are consistent with the intent and direction of the PPACA legislation.

Structural changes represent the expansion of access to healthcare coverage to tens of millions of people currently uninsured or who have only limited coverage options available. Structural changes include state-level exchanges and the expansion of federal programs, individual and employer coverage requirements, premium and cost-sharing subsidies and tax changes.

Delivery of care changes center on the patient and creating connections between all settings of care. Team-based, holistic care models are preferred to fragmented, episodic services. A major component of healthcare delivery reform is preventive healthcare, which will become cost-free to patients. New organizational models enabling these changes include integrated delivery networks, accountable care organizations and patient-centered medical homes.

Financing changes include incentives for improved health outcomes and coordinated or integrated care, as well as penalties for hospital readmissions. Established and emerging new rules seek to balance benefits and patient costs in health insurance plans, and to eliminate the maximum allowable lifetime payment for the care of an individual patient.

Priorities for addressing avoidable costs require alignment and collaboration of multiple stakeholders

Improve Adherence
Apply Evidence-Based Treatment
Reduce Medication Errors
Use Antibiotics Responsibly
Manage Polypharmacy
Use Generics Optimally

◆ Optimal medication use levers
+ Healthcare stakeholders

Priorities regarding access and structural changes											
◆	◆		◆		◆	◆	◆	◆			
						◆	◆				
◆	◆							◆	◆	◆	◆
	◆								◆	◆	
◆	◆							◆	◆	◆	◆
◆	◆							◆	◆	◆	◆
◆	◆					◆	◆				
Priorities related to financing and reimbursement changes											
◆	◆	◆	◆	◆	◆			◆	◆	◆	◆
		◆			◆			◆	◆	◆	◆
◆								◆	◆	◆	
◆	◆					◆		◆	◆	◆	◆
◆								◆	◆	◆	◆
◆								◆	◆	◆	◆

Note: The patient stakeholder group includes also patient advocates and caregivers. Healthcare professionals include physicians, nurses, physician assistants, nurse practitioners and healthcare administrators. Payer stakeholders include private insurance companies, government payer agencies and employers.

Patients
Providers
Pharmacists
Payers
Policy Makers
Manufacturers

Improve Adherence
Apply Evidence-Based Treatment
Reduce Medication Errors
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◆ Optimal medication use levers

+ Healthcare stakeholders

Priorities related to delivery of care changes											
◆	◆	◆	◆	◆	◆	Identify best practices through guidelines, protocols and pathways adopted by integrated delivery networks, including Accountable Care Organizations and Patient-Centered Medical Homes, in order to accelerate knowledge-sharing and adoption of high-quality care standards.	+	+	+	+	
◆	◆	◆			◆	Develop best practices for team case management in transitions of care after hospital discharge.	+	+	+		
◆	◆					Expand healthcare access options for chronic disease diagnosis and management through the use of physician-led interprofessional teams.	+	+	+	+	
◆			◆	◆	◆	Engage patients as key partners in therapeutic and cost decisions.	+	+	+	+	+
◆			◆			Expand public health literacy and education campaigns under the impetus of preventive healthcare and the essential healthcare benefit. Increase patient awareness about expanded or free diagnostic and preventive healthcare services.	+	+	+	+	+
	◆		◆			Promote appropriate use of rapid diagnostic tests by pharmacists and encourage adoption of rapid diagnostic testing standards.	+	+	+	+	+
			◆			Increase flu vaccination rates in order to reduce opportunities for infections and inappropriate antibiotics use.	+	+	+	+	

Priorities related to healthcare information technology utilization											
◆	◆	◆			◆	Maximize incentives and improve standards for meaningful use of electronic health records and electronic prescribing in order to enable information-sharing between healthcare stakeholders and across settings of care.	+	+	+	+	
◆	◆	◆			◆	Coordinate care and manage costs through implementation of healthcare IT systems and best practices within increasingly complex and integrated healthcare delivery organizations.	+		+		
◆	◆	◆			◆	Leverage healthcare IT to maintain continuity in patients' medical and medication therapy records during healthcare coverage changes.	+		+		
	◆	◆	◆		◆	Incorporate evidence-based clinical practice guidelines into electronic prescribing decision support tools.	+		+	+	
◆	◆	◆			◆	Encourage implementation and reward use of Medication Therapy Management as a tool to improve medication regimens for high-risk patients.	+	+	+	+	
◆						Regularly assess the effectiveness of interventions aimed at improving patient adherence to medications. Define and apply best practices for designing and implementing such interventions for optimal balance between investment and outcomes.	+	+	+	+	

Patients
Providers
Pharmacists
Payers
Policy Makers
Manufacturers

Conclusion

There are many things U.S. healthcare stakeholders can do to promote the responsible use of medicines, to improve health outcomes and ultimately reduce avoidable healthcare costs. Most of these actions require the involvement of multiple healthcare stakeholders. Considering the priority actions outlined above, the magnitude of the improvement opportunity in terms of avoidable costs, and the timing and investment required by each action, five guiding principles surfaced which need to be pursued aggressively in order to accelerate progress.

1. Consistent focus on high-risk patients who are most vulnerable to suboptimal medicines use and require the costliest healthcare interventions: risk factors, morbidity and health outcomes can help determine the areas of greatest need.
2. Steadfast engagement with patients as responsible and capable partners: pharmacists are particularly well positioned to create and maintain relationships through frequent and direct communication with patients about responsible use of medicines.
3. Rigorous assessment of impact and ROI in the design and implementation of interventions for optimum avoidable cost reduction: smart resource allocation is the key to long-term success.
4. Continuous measurement and accountability for interventions impact on cost reduction and health outcomes: sustainability and scalability of multi-stakeholder partnership depend on effective solutions.
5. Alignment of compensation models with new healthcare delivery models: cost reductions from optimal medicines use need to be shared by participating stakeholders.

Reaching some level of consensus and alignment based on measured and proven success models is a necessary step to advance the collective effort to further unlock the opportunity identified in this report.

References Cited

- 1 Mark, S., Sounders, R., Stuckhardt, L., McGinnis, M. (2012). Best care at lower cost: The path to continuously learning health care in America. Retrieved from <http://www.iom.edu/Reports/2012/Best-Care-at-Lower-Cost-The-Path-to-Continuously-Learning-Health-Care-in-America.aspx>
- 2 Kelley, R. (2009). Where can \$700 billion in waste be cut annually from the U.S. healthcare system? Retrieved from <https://healthleadersmedia.com/content/241965.pdf>
- 3 Keckley, P., & Freeman, A. (2011). The hidden costs of U.S. health care for consumers: A comprehensive analysis. Retrieved from http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/US_CHS_HiddenCostsofUSHealthCareforConsumers_032111.pdf
- 4 Delaune, J., & Everett, W. (2008). Waste and inefficiency in the U.S. health care system - Clinical care. New England Health Institute. Retrieved from http://www.nehi.net/publications/27/clinical_care_a_comprehensive_analysis_in_support_of_system_wide_improvements
- 5 Kelly, B., Fabius, R. (2010). A path to eliminating \$3.6 trillion in wasteful healthcare spending. Thomson Reuters. Retrieved from http://healthcare.thomsonreuters.com/thought-leadership/testimony/WP_6_15_10.pdf
- 6 Berwick, D., & Hackbarth, A. (2012). Eliminating waste in U.S. health care. *Journal of the American Medical Association*, 307(14), 1513-1516. doi:10.1001/jama.2012.362
- 7 IMS Institute for Healthcare Informatics. (2012). Advancing the responsible use of medicines: Quantifying avoidable health system costs. Retrieved from <http://www.responsibleuseofmedicines.org>
- 8 Keehan, S. P., Cuckler, G. A., Sisko, A. M. (2012). National health expenditure projections: Modest annual growth until coverage expands and economic growth accelerates. *Health Affairs*, 31(7), 1600-1612. doi: 10.1377/hlthaff.2012.0404
- 9 IMS Institute analysis. (2012). IMS Health MIDAS data 2001-2012
- 10 Moskowitz, D., Thom, D., Hessler, D., Ghorob, A., Bodenheimer, T. (2013). Peer coaching to improve diabetes self-management: Which patients benefit most? *Journal of General Internal Medicine*. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23404203>
- 11 Triplitt, C. (2010). Improving treatment success rates for type 2 diabetes: Recommendations for a changing environment. *The American Journal of Managed Care*, 16(7), 195-200
- 12 Gonzalez, J. S., Peyrot, M., McCarl, L. A., et al. (2008). Depression and diabetes treatment nonadherence: A meta-analysis. *Diabetes Care*, 31(12), 2398-2403. doi: 10.2337/dc08-1341
- 13 Gonzalez, J. S., Esbitt, S. (2010). Depression and treatment nonadherence in type 2 diabetes: Assessment issues and an integrative treatment approach. *Epidemiologia e Psichitria Sociale*, 19(2), 110-115
- 14 Bhattacharya, G. (2012). Self-management of type 2 diabetes among African Americans in the Arkansas Delta: A strengths perspective in social-cultural context. *Journal of Health Care for the Poor and Underserved*, 23(1), 161-178. doi: 10.1353/hpu.2012.0035
- 15 Bailey, J. E., Hajjar, M., Shoib, B., Tang, J., Ray, M., Wan, J. (2012). Risk factors associated with antihypertensive medication nonadherence in a statewide Medicaid population. *The American Journal of the Medical Sciences*
- 16 Robison, L. S., Westfall, A. O., Mugavero, M. J., et al. (2008). Short-term discontinuation of HAART regimens more common in vulnerable patient populations. *AIDS Research and Human Retroviruses*, 24(11), 1347-1355
- 17 Huynh, A. K., Kinsler, J. J., Cunningham, W. E., Sayles J. N. (2013). The role of mental health in mediating the relationship between social support and optimal ART adherence. *AIDS Care*.
- 18 Gaston, G. B. (2013). African-Americans' perceptions of health care provider cultural competence that promote HIV medical self-care and antiretroviral medication adherence. *AIDS Care*.
- 19 Kalichman, S. C., Cherry, C., Kalichman, M. O., et al. (2013). Randomized clinical trial of HIV treatment adherence counseling interventions for people living with HIV and limited health literacy. *Journal of Acquired Immune Deficiency Syndrome*, 63(1), 42-50. doi: 10.1097/QAI.0b013e318286ce49
- 20 Saha, S., Korthuis, P. T., Cohn, J. A., Sharp, V. L., Moore, R. D., Beach, M. C. (2013). Primary care provider cultural competence and racial disparities in HIV care and outcomes. *Journal of General Internal Medicine*, 28(5), 622-629. doi: 10.1007/s11606-012-2298-8
- 21 Heidenreich, P. A., Trogon, J. G., Khavjou, O. A., et al. (2011). Forecasting the future of cardiovascular disease in the United States. *Circulation*, 123, 933-944. doi: 10.1161/CIR.0b013e31820a55f5

- 22 Sokol, M., McGuigan, K., Verbrugge, R., Epstein, R. S. (2005). Impact of medication adherence on hospitalization risk and healthcare cost. *Medical Care*, 43(6), 521-530
- 23 Ho, P. M., Bryson, C., Rumsfeld, S. (2009). Medication adherence: Its importance in cardiovascular outcomes. *Circulation*, 119(23), 3028-3035. doi: 10.1161/CIRCULATIONAHA.108.768986
- 24 Sokol, M., McGuigan, K., Verbrugge, R., Epstein, R. S. (2005). Impact of medication adherence on hospitalization risk and healthcare cost. *Medical Care*, 43(6), 521-530
- 25 Halpern, R., Becker, L., Iqbal, S. U., Kazis, L. E., Macarios, D., Badamgarav, E. (2011). The association of adherence to osteoporosis therapies with fracture, all-cause medical costs, and all-cause hospitalizations: A retrospective claims analysis of female health plan enrollees with osteoporosis. *Journal of Managed Care Pharmacy*, 17(1), 25-39
- 26 Mitra, D., Davis, K., Beam, C., Medjedovic, J., Rustgi, V. (2010). Treatment patterns and adherence among patients with chronic hepatitis C virus in a U.S. managed care population. *International Society for Pharmacoeconomics and Outcomes Research*, 13(4), 479-486. doi: 10.1111/j.1524-4733.2009.00691479-486
- 27 Roebuck, M., Liberman, J., Gemmill-Toyama, M., Brennan, T. A. (2011). Medication adherence leads to lower health care use and costs despite increased drug spending. *Health Affairs*, 30(1), 91-99. doi: 10.1377/hlthaff.2009.1087
- 28 Halpern, R., Becker, L., Iqbal, S. U., Kazis, L. E., Macarios, D., Badamgarav, E. (2011). The association of adherence to osteoporosis therapies with fracture, all-cause medical costs, and all-cause hospitalizations: A retrospective claims analysis of female health plan enrollees with osteoporosis. *Journal of Managed Care Pharmacy*, 17(1), 25-39.
- 29 IMS National Disease and Therapeutic Index Survey and National Prescription Audit (December 2012)
- 30 IMS National Disease and Therapeutic Index Survey and National Prescription Audit (December 2012)
- 31 Solomon, M., & Majumdar, S. R. (2010). Primary non-adherence of medications: Lifting the veil on prescription-filling behaviors. *Journal of General Internal Medicine*, 25(4), 280-281. doi: 10.1007/s11606-010-1286-0
- 32 Shin, J., McCombs, J. S., Sanchez, R. J., et al. (2012). Medicines adherence: Involving patients in decisions about prescribed medicines and supporting adherence. *The American Journal of Managed Care*, 18(8), 426-434
- 33 Choudhry, N. K., Shrank, W. H., Levin, R. L., et al. (2009). Measuring concurrent adherence to multiple related medications. *American Journal of Managed Care*, 48(3), 196-202. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2873865/>
- 34 Chan, D. C., Shrank, W. H., Cutler, D., et al. (2010). Patient, physician, and payment predictors of statin adherence. *Medical Care*, 48(3), 196-202. doi: 10.1097/MLR.0b013e3181c132ad
- 35 IMS Health RxQuality™, 2011.
- 36 Thompson, D., Hylan, T. R., McMullen, W., Romeis, M. E., Buesching, D., Oster, G. (1998). Predictors of a medical-offset effect among patients receiving antidepressant therapy. *The American Journal of Psychiatry*, 155(6), 824-827
- 37 Stuart, B., Shoemaker, S., Dai, M., Davidoff, A. (2013). Regions with higher Medicare part D spending show better drug adherence, but not lower Medicare costs for two diseases. *Health Affairs*, 32(1), 1120-1126. doi: 10.1377/hlthaff.2011.0727
- 38 Stein, M. B., Cantrell, C. R., Sokolm, M. C., Eaddy, M. T., Shah, M. B. (2006). Antidepressant adherence and medical resource use among managed care patients with anxiety disorders. *Psychiatric Services*, 57(5), 673-680
- 39 Hepke, K. L., Martus, M. T., Share, D. A. (2004). Costs and utilization associated with pharmaceutical adherence in a diabetic population. *The American Journal of Managed Care*, 10(2), 144-151
- 40 Centers for Disease Control and Prevention. (2012). Hepatitis C information for the public. Retrieved from <http://www.cdc.gov/hepatitis/c/cfaq.htm>
- 41 Liu, S., Cipriano, L. E., Holodniy, M., Owens, D. K., Goldhaber-Fiebert, J. D. (2012). New protease inhibitors for the treatment of chronic hepatitis C: A cost-effectiveness analysis. *Annals of Internal Medicine*, 156(4), 279-299. doi: 10.1059/0003-4819-156-4-201202210-00005
- 42 Campos, N. G., Salomon, J. A., Servoss, J. C. (2007). Cost-effectiveness of treatment for hepatitis C in an urban cohort co-infected with HIV. *American Journal of Medicine*, 120(3), 272-279. doi: 10.1016/j.amjmed.2006.06.036
- 43 Martin, N. K., Vickerman, P., Miners, A., et al. (2012). Cost-effectiveness of hepatitis C virus antiviral treatment for injection drug user populations. *Hepatology*, 55(1), 49-57. doi: 10.1002/hep.24656

- 44 Centers for Disease Control and Prevention. (2011). Prevalence of coronary heart disease—United States 2006–2010. Retrieved from http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6040a1.htm?s_cid=mm6040a1_w
- 45 National Center for Health Statistics. (2011). Health, United States with special features on death and dying. Retrieved from <http://www.cdc.gov/nchs/data/hsr/hsr10.pdf>
- 46 Centers for Disease Control and Prevention. (2010). National diabetes fact sheet 2011. Retrieved from http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf
- 47 Division for Heart Disease and Stroke Prevention. (2010). Atrial fibrillation fact sheet. Retrieved from http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm
- 48 Chak, E., Talal, A. H., Sherman, K. E., Schiff, E. R., Saab, S. (2011). Hepatitis C virus infection in USA: An estimate of true prevalence. *Liver International*, 31(8), 1090–1101. doi: 10.1111/j.1478-3231.2011.02494
- 49 American Cancer Society. (2012). Cancer facts and figures 2012. Retrieved from <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-031941.pdf>
- 50 Centers for Disease Control and Prevention. (2012). CDC division of viral hepatitis - May is hepatitis awareness month. Retrieved from <http://www.cdc.gov/hepatitis/HEPAwarenessMonth.htm>
- 51 Khoury, E. I., Klimack, W. K., Wallace, C., Razavi, H. (2011). Economic burden of hepatitis C-associated diseases in the United States. *Journal of Viral Hepatitis*, 19(3), 153–160. doi: 10.1111/j.1365-2893.2011.01563
- 52 Centers for Disease Control and Prevention. (2009). Hepatitis C FAQs for the public. Retrieved from <http://www.cdc.gov/hepatitis/c/cfaq.htm>
- 53 Vandvik, P. O., Lincoff, A. M., Gore, J. M., et al. (2012). Primary and secondary prevention of cardiovascular disease: Antithrombotic therapy and prevention of thrombosis, 9th edth: American college of chest physicians evidence-based clinical practice guidelines. *Chest*, 141(2), e637S–e668S. doi: 10.1378/chest.11-2306.
- 54 Hall, S., & Lorenc, T. (2010). Secondary prevention of coronary artery disease. *American Family Physician*, 81(3), 289–296
- 55 Centers for Disease Control and Prevention. (2012). Heart disease fact sheet. Retrieved from http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm
- 56 Winkelmayer, W. C., Zhang, Z., Shahinfar, S., et al. (2006). Efficacy and safety of angiotensin II receptor blockade in elderly patients with diabetes. *Diabetes Care*, 29(10), 2210–2217
- 57 Winkelmayer, W. C., Fischer, M. A., Schneeweiss, S., Wang, P. S., Levin R., Avorn, J. (2005.) Underuse of ACE inhibitors and angiotensin II receptor blockers in elderly patients with diabetes. *American Journal of Kidney Diseases*, 46(6), 1080–1087
- 58 Rosen, A. B. (2006). Indications for and utilization of ACE inhibitors in older individuals with diabetes. *Journal of General Internal Medicine*, 21(4), 315–319
- 59 Cooke, C. E., & Fatodu, H. (2006). Physician conformity and patient adherence to ACE inhibitors and ARBs in patients with diabetes, with and without renal disease and hypertension, in a Medicaid managed care organization. *Journal of Managed Care Pharmacy*, 12(8), 649–655
- 60 National Stroke Association. (2012). Stroke risk reduction atrial fibrillation. Retrieved from <http://www.stroke.org/site/PageServer?pagename=afib>
- 61 Bajpai, A., & Savelieva, I. (2007). Epidemiology and economic burden of atrial fibrillation. *Circulation*, 4(1), 14–17
- 62 Centers for Disease Control and Prevention. (2010). Atrial fibrillation fact sheet. Retrieved from http://s/www.stoptheclot.org/Afib/CDC%20reference%20document%20fs_atrial_fibrillation.pdf
- 63 Fuster, V., Ryden, L. E., Cannom, D. S., et al. (2011). 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*, 123(10), e269–367. doi: 10.1161/CIR.0b013e318214876d
- 64 Mercaldi, C., Siu, K., Sander, S. D., et. al. (2012). Long-term costs of ischemic stroke and major bleeding events among Medicare patients with nonvalvular atrial fibrillation. *Cardiology Research and Practice*, 2012. doi: 10.1155/2012/645469

- 65 Shrank, W. H., Asch, S. M., Adams, J., et al. (2006). The quality of pharmacologic care for adults in the United States. *Medical Care*, 44(10), 936-945. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17001265>
- 66 McGlynn, E. A., Asch, S. M., Adams, J., et al. (2003). The quality of health care delivered to adults in the United States. *The New England Journal of Medicine*, 34(8), 2635-2645. doi: 10.1056/NEJMsa022615
- 67 Centers for Disease Control and Prevention. (2012). Unpublished data.
- 68 Gordon, S. C., Pockros, P. J., Terrault, N. A., et al. (2011). Disease burden in patients with chronic hepatitis C virus (HCV) infection in a United States (US) private health insurance claims database analysis from 2003 to 2010. 62nd Annual Meeting of the American Association for the Study of Liver Diseases, San Francisco (Nov 6-9). Retrieved from http://www.natap.org/2011/AASLD/AASLD_48.htm
- 69 Stafford, R., Monti, V., Ma, J. (2006). Underutilization of aspirin persists in US ambulatory care for the secondary and primary prevention of cardiovascular disease. *US Cardiology*, 3(1), 1-7
- 70 Winkelmayr, W. C., Fischer, M. A., Schneeweiss, S., Wang, P. S., Levin R., Avorn, J. (2005.) Underuse of ACE inhibitors and angiotensin II receptor blockers in elderly patients with diabetes. *American Journal of Kidney Diseases*, 46(6), 1080-1087
- 71 Rosen, A. B. (2006). Indications for and utilization of ACE inhibitors in older individuals with diabetes. *Journal of General Internal Medicine*, 21(4), 315-319
- 72 National Kidney and Urologic Diseases Information Clearinghouse. (2010). Proteinuria. Retrieved from <http://kidney.niddk.nih.gov/kudiseases/pubs/proteinuria/>
- 73 Bungard, T. J., Ghali, W. A., Teo, K. K., McAlister, F. A., Tsuyuki, R. T. (2000). Why do patients with atrial fibrillation not receive warfarin? *Archives of Internal Medicine*, 160(1), 41-46
- 74 National Stroke Association. (2012). Stroke risk reduction atrial fibrillation. Retrieved from <http://www.stroke.org/site/PageServer?pagename=afib>
- 75 Baczek, V. L., Chen, W. T., Kluger, J., Coleman, C. I. (2012). Predictors of warfarin use in atrial fibrillation in the United States: A systematic review and meta-analysis. *BMC Family Practice*, 13(5)
- 76 Infectious Disease Society of America, Spellberg, B., Blaser, M., et al. (2011). Combating antimicrobial resistance: Policy recommendations to save lives. *Clinical Infectious Diseases*, 52(5), 397-428
- 77 Hicks, L. A., Taylor, M. S., Hunkler, R. J. (2013). US outpatient antibiotic prescribing, 2010. *New England Journal of Medicine*, 368, 1461-1462. doi: 10.1056/NEJMc1212055
- 78 Mangione-Smith, R., Elliot, M. N., Stivers, T., McDonald, L. L., Heritage, J. (2006). Ruling out the need for antibiotics: Are we sending the right message?. *Archives of Pediatrics & Adolescent Medicine*, 160(9), 945-952
- 79 Mangione-Smith, R., Elliot, M. N., Stivers, T., McDonald, L. L., Heritage, J. (2006). Ruling out the need for antibiotics: Are we sending the right message? *Archives of Pediatrics & Adolescent Medicine*, 160(9), 945-952
- 80 Dubberke, E., & Wertheimer, A. I. (2009). Review of current literature on the economic burden of *Clostridium difficile* infection. *Infection Control and Hospital Epidemiology*, 30(1), 57-66
- 81 Carlet, J., & Pittet, D. (2013). Access to antibiotics: A safety and equity challenge for the next decade. *Antimicrobial Resistance and Infection Control*, 2(1), 1-4. doi:10.1186/2047-2994-2-1
- 82 Kaplan, W., & Liang, R. (2004). Priority medicines for Europe and the world. Retrieved from http://whqlibdoc.who.int/7DD3FEA0-C209-4625-AC61-1B33E0561233/FinalDownload/DownloadId-7CDAD06A7AAEF7611D1606EE37D42907/7DD3FEA0-C209-4625-AC61-1B33E0561233/hq/2004/WHO_EDM_PAR_2004.7.pdf
- 83 Hicks, L. A., Chien, Y. W., Taylor T. H., Haber, M., Klugman, K. P. (2011). Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996-2003. *Clinical Infectious Diseases*, 53(7), 631-639. doi: 10.1093/cid/cir443
- 84 Davies, J., & Dorothy, D. (2010). The origins and evolution of antibiotic resistance. *Microbiology and Molecular Biology Reviews*, 74(3), 417-433. doi: 10.1128/MMBR.00016-10

- 85 Centers for Disease Control and Prevention. (2011). Office-related antibiotic prescribing for persons aged 14 years—United States, 1993-1994 to 2007-2008. *Morbidity and Mortality Weekly Report*, 60(34), 1153-1156
- 86 Spellberg, B., Blaser, M., Guidos, R. J., et al. (2011). Combating antimicrobial resistance: Policy recommendations to save lives. *Clinical Infectious Diseases*, 52(5), 397-428. doi: 10.1093/cid/cir153
- 87 White, A. R. (2011). Effective antibacterials: At what cost? The economics of antibacterial resistance and its control. *Journal of Antimicrobial Chemotherapy*, 66(9), 1948-1953. doi: 10.1093/jac/dkr260
- 88 Steinman, M. A., Gonzales, R., Linder J. A., Landefeld, C. S. (2003). Changing use of antibiotics in community-based outpatient practice, 1991-1999. *Annals of Internal Medicine*, 138(7), 525-33. doi:10.7326/0003-4819-138-7-200304010-00008
- 89 Grijalva, C. G., Nuorti, J. P., Griffin, M. R. (2009). Antibiotic prescription rates for acute respiratory tract infections in U.S. ambulatory settings. *Journal of the American Medical Association*, 30(7), 758-66. doi: 10.1001/jama.2009.1163
- 90 Foster, S. D. (2010). *The Economic Burden Of Antibiotic Resistance - Evidence From Three Recent Studies*. 2010 Annual Conference on Antimicrobial Resistance, Bethesda, Feb (1-3). Retrieved from http://www.tufts.edu/med/apua/news/events_65_4102135958.pdf Accessed January 2013
- 91 Roberts, R. R., Hota, B., Ahmad, I., et al. (2009). Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: Implications for antibiotic stewardship. *Clinical Infectious Diseases*, 49(8), 1175-1184. doi: 10.1086/605630
- 92 Foster, S. D. (2010). *The Economic Burden Of Antibiotic Resistance - Evidence From Three Recent Studies*. 2010 Annual Conference on Antimicrobial Resistance, Bethesda, Feb (1-3). Retrieved from http://www.tufts.edu/med/apua/news/events_65_4102135958.pdf
- 93 Gonzales, R., Malone, D. C., Maselli, J. H., Sande, M. A. (2001). Excessive antibiotic use for acute respiratory infections in the United States. *Clinical Infectious Diseases*, 33(6), 757-762
- 94 Centers for Disease Control and Prevention. (2011). Facts about antibiotic resistance. Retrieved from <http://www.cdc.gov/getsmart/antibiotic-use/fast-facts.html>
- 95 Centers for Disease Control and Prevention. (2011). Office-related antibiotic prescribing for persons aged 14 years—United States, 1993-1994 to 2007-2008. *Morbidity and Mortality Weekly Report*, 60(34), 1153-1156
- 96 Gonzales, R., Malone, D. C., Maselli, J. H., Sande, M. A. (2001). Excessive antibiotic use for acute respiratory infections in the United States. *Clinical Infectious Diseases*, 33(6), 757-762
- 97 IMS National Drug and Therapeutic Index, Jan 2013.
- 98 Mathew, A. G., Cissell, R., Liamthong, S. (2007). Antibiotic resistance in bacteria associated with food animals: A United States perspective of livestock production. *Foodborne Pathogens and Disease*, 4(2), 115-133
- 99 IMS National Drug and Therapeutic Index. Dec 2012
- 100 McBride-Henry, K., & Foureur, M. (2006). Medication administration errors: Understanding the issues. *Australian Journal of Advanced Nursing*, 23(3), 33-41
- 101 Budnitz, D. S., Polluck, D. A., Weidenback, K. N., Mendelsohn, A. B., Schroeder, T. J., Annest, J. L. (2006). National surveillance of emergency department visits for outpatient adverse drug events. *Journal of the American Medical Association*, 296(15), 1858-1866
- 102 Thomsen, L. A., Winterstein, A. G., Sondergaard, B., Hauqbolle, L. S., Melander, A. (2007). Systematic review of the incidence and characteristics of preventable adverse drug events in ambulatory care. *Annals of Pharmacotherapy*, 41(9), 1411-1426
- 103 Pham, J. C., Story, J. L., Hicks, R. W., et al. (2011). National study on the frequency, types, causes, and consequences of voluntarily reported emergency department medication errors. *Journal of Emergency Medicine*, 40(5), 485-492. doi: 10.1016/j.jemermed.2008.02.059
- 104 Budnitz, D. S., Polluck, D. A., Weidenback, K. N., Mendelsohn, A. B., Schroeder, T. J., Annest, J. L. (2006). National surveillance of emergency department visits for outpatient adverse drug events. *Journal of the American Medical Association*, 296(15), 1858-1866
- 105 Cohen, A. L., Budnitz, D. S., Weidenbach, K. N., et al. (2008). National surveillance of emergency department visits for outpatient adverse drug events in children and adolescents. *Journal of Pediatrics*, 152(3), 416-421. doi: 10.1016/j.jpeds.2007.07.041

- 106 Crane, J., & Crane, F. G. (2006). Preventing medication errors in hospitals through a systems approach and technological innovation: A prescription for 2010. *Hospital Medicine Journal Watch*, 84(4), 3-8
- 107 Frydenberg, K., & Brekke, M. (2012). Poor communication on patients' medication across health care levels leads to potentially harmful medication errors. *Scandinavian Journal of Primary Health Care*, 30(4), 234-40. doi: 10.3109/02813432.2012.712021
- 108 Westbrook, J. I., Woods, A., Rob, M. I., Dunsmuir, W. T., Day, R. O. (2010). Association of interruptions with an increased risk and severity of medication administration errors. *Archives of Internal Medicine*, 170(8), 683-690
- 109 New England Healthcare Institute. (2010). Preventing medication errors: A \$21 billion opportunity. Retrieved from www.nehi.net/bendthecurve/sup/documents/Medication_Errors_%20Presentation.ppt
- 110 New England Healthcare Institute. (2010). Preventing medication errors: A \$21 billion opportunity. Retrieved from www.nehi.net/bendthecurve/sup/documents/Medication_Errors_%20Presentation.ppt
- 111 Massachusetts Technology Collaboration, & New England Healthcare Institute. (2008). Saving lives, saving money: The imperative for CPOE in Massachusetts. Retrieved from http://www.nehi.net/publications/8/saving_lives_saving_money_the_imperative_for_computerized_physician_order_entry_in_massachusetts_hospitals
- 112 Massachusetts Technology Collaboration (MTC) & NEHI. (2008). Saving Lives, Saving Money: The Imperative for CPOE in Massachusetts. Retrieved from http://www.nehi.net/publications/8/saving_lives_saving_money_the_imperative_for_computerized_physician_order_entry_in_massachusetts_hospitals
- 113 Sewell, K., Andreae, S., Luke, E., Safford, M. M. (2012). Perceptions of and barriers to use of generic medications in a rural African American population, Alabama, 2011. *Preventing Chronic Disease*, 9. doi: <http://dx.doi.org/10.5888/pcd9.120010>
- 114 Shrank, W. H., Liberman, J. N., Fischer, M. A., Girdish, C., Brennan, T. A., Choudhry, N. K. (2011). Physician perceptions about generic drugs. *Annals of Pharmacotherapy*, 45(1), 31-38. doi: 10.1345/aph.1P389
- 115 Shrank, W. H., Liberman, J. N., Fischer, M. A., Girdish, C., Brennan, T. A., Choudhry, N. K. (2011). Physician perceptions about generic drugs. *Annals of Pharmacotherapy*, 45(1), 31-38. doi: 10.1345/aph.1P389
- 116 Desmarais, J. E., Beauclair, L., Marquese, H. C. (2011). Switching from brand-name to generic psychotropic medications, a literature review. *CNS Neuroscience and Therapeutics*, 17(6), 750-760. doi: 10.1111/j.1755-5949.2010.00210
- 117 Steinhoff, B. J., Runge, U., Witte, O. W., et al. (2009). Substitution of anticonvulsant drugs. *Therapeutics and Clinical Risk Management*, 5(3), 449-457
- 118 American Congress of Obstetricians and Gynecologists. (2010). Brand versus generic oral contraceptives. Retrieved from http://www.acog.org/Resources_And_Publications/Committee_Opinions/Committee_on_Gynecologic_Practice/Brand_Versus_Generic_Oral_Contraceptives
- 119 IMS National Prescription Audit, Dec 2012.
- 120 IMS National Prescription Audit, Dec 2012.
- 121 IMS National Prescription Audit, Dec 2012.
- 122 IMS Institute for Healthcare Informatics. (2011) and (2012). Use of medicines in the United States. Retrieved from http://www.imshealth.com/ims/Global/Content/Insights/IMS%20Institute%20for%20Healthcare%20Informatics/IHII_Medicines_in_U.S_Report_2011.pdf
- 123 IMS Institute for Healthcare Informatics. (2012). Generic drug savings in the U.S. Retrieved from <http://www.gphaonline.org/sites/default/files/IMS%20Study%20Aug%202012%20WEB.pdf>
- 124 Centers for Disease Control and Prevention. (2011). Healthy aging - At a glance. Retrieved from <http://www.cdc.gov/chronicdisease/resources/publications/AAG/aging.htm>
- 125 IMS LifeLink, Jan 2013
- 126 Ginsberg, G., Hattis, D., Russ, A., Sonawane, B. (2005). Pharmacokinetic and pharmacodynamic factors that can affect sensitivity to neurotoxic sequence in elderly individuals. *Environmental Health Perspectives*, 113(9), 1243-1249. doi: 10.1289/ehp.7568
- 127 Budnitz, D. S., Lovegrove, M. C., Shehab, N., Richards, C. L. (2011). Emergency hospitalizations for adverse drug events in older Americans. *The New England Journal of Medicine*, 365(21), 2002-2012. doi: 10.1056/NEJMsa1103053
- 128 Administration on Aging. (2010). Projected future growth of the older population. Retrieved from http://www.aoa.gov/aoaroot/aging_statistics/future_growth/future_growth.aspx

- 129 Sarkar, U., Lopez, A., Maselli, J. H., Gonzales, R. (2011). Adverse drug events in U.S. adult ambulatory medical care. *Health Services Research*, 46(5), 1517-1533. doi: 10.1111/j.1475-6773.2011.01269.x
- 130 Budnitz, D. S., Lovegrove, M. C., Shehab, N., Richards, C. L. (2011). Emergency hospitalizations for adverse drug events in older Americans. *The New England Journal of Medicine*, 365(21), 2002-2012. doi: 10.1056/NEJMsa1103053
- 131 CareFirst BlueCross BlueShield. (2012). CareFirst BlueCross BlueShield announces first-year patient-centered medical home results. Retrieved from https://member.carefirst.com/wps/portal/%21ut/p/c5/04_SB8K8xLLM9MSSzPy8xBz9CP0os3hLbzN_Q09LYwN3VxNjA08zP98QQ0sXA4MAM6B8JJk8v1uQq4FnYICIX4iRr5G7twFJug2C3c0MPE2CLb09zAONDNyNCOgOB7kWv-0o8lJMB8kb4ACOBvp-Hvm5qfoFuaERBpkB6QD54kJX/dl3/d3/L2dJQSEvUUt3QS9ZQnZ3LzZfOU52TzFJOTMwT0RIMTBJTThVQUhSUjEwQTY%21/?WCM_GLOBAL_CONTEXT=/wcmwps/wcm/connect/content-member/carefirst/memberportal/medianews/popup/medianews20120607
- 132 Overland, D. (2012). CareFirst patient-centered medical home saved \$40M. *Fierce Health Payer*. Retrieved from <http://www.fiercehealthpayer.com/story/carefirst-patient-centered-medical-home-saved-40m/2012-06-13>
- 133 National Association of Chain Drug Stores. (2010). Pharmacies: Improving health, reducing costs. Retrieved from <http://www.maine.gov/legis/opla/healthreformpharmacies.pdf>
- 134 Marrujo, G., Dixit, A., Perloth, D., Montesinos, A., Rusev, E., Packard, M. (2013). Medication therapy management in a chronically ill population: Interim report, 2013. Retrieved from <http://innovation.cms.gov/Files/reports/MTM-Interim-Report-01-2013.pdf>
- 135 National Association of Chain Drug Stores. (2010). Pharmacies: Improving health, reducing costs. Retrieved from <http://www.maine.gov/legis/opla/healthreformpharmacies.pdf>
- 136 David, P. (2012). Thrifty white: An Rx innovator. Chain Drug Review. Retrieved from <http://www.chaindrugreview.com/inside-this-issue/news/11-05-2012/thrifty-white-an-rx-innovator>
- 137 Personal communication with Robert Narveson, CEO and President of Thrifty White, March 2013.
- 138 National Consumers League. (2013). Script your future. Retrieved from <https://scriptyourfuture.org/about/challenge>
- 139 Bosworth, H. B., & The National Consumers League. Medication adherence: Making the case for increased awareness. Retrieved from http://scriptyourfuture.org/wp-content/themes/cons/m/Script_Your_Future_Briefing_Paper.pdf
- 140 Personal communication with Rebecca Burkholder, Vice President of Health Policy at the National Consumers League, May 2013.
- 141 Appleby, J. (2013). Walgreens becomes 1st retail chain to diagnose, treat chronic conditions. Kaiser Health News. Retrieved from <http://www.kaiserhealthnews.org/Stories/2013/April/04/walgreens-primary-care-services.aspx>
- 142 Personal communication with Ron Weinert, Vice President Healthcare Solutions at Walgreens, May 2013.
- 143 CVS Caremark. (2013). Our pharmacy advisor program. Retrieved from <http://www.cvscaremarkfyi.com/blogs/our-pharmacy-advisor-program>
- 144 Brennan, T. A., Dollear, T. J., Hu, M., et al. (2012). An integrated pharmacy-based program improved medication prescription and adherence rates in diabetes patients. *Health Affairs*, 31(1), 120-129. doi: 10.1377/hlthaff.2011.0931
- 145 Personal communication with Dr. Troyen Brennan, Executive Vice President and Chief Medical Officer at CVS Caremark.

Authors



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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.



Silvia Valkova

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Silvia is a researcher and project manager at the IMS Institute for Healthcare Informatics, leading the development of reports and analyses focused on biopharmaceuticals and healthcare in the U.S. and globally. Silvia's primary and secondary market research experience spans clinical biopharmaceutical innovation, pipeline development, launch, loss of exclusivity, generic competition, and the regulatory environment. She has focused particularly on aspects of return on R&D investment, the pace of progress and quality of pipeline products as well as the nuances of patent protection and generic penetration globally.

Silvia joined IMS in 2007 and worked in the Market Insights and Thought Leadership teams which in 2011 became the IMS Institute.

Prior to IMS, Silvia was a translator and project manager for seven years, translating texts about biopharmaceuticals, reproductive health and consumer marketing from Spanish, German and Bulgarian. Silvia holds a Master of Science degree in Health Research and Communication from Temple University.

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:

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

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

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

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

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

Guiding Principles

The Institute operates from a set of Guiding Principles:

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

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

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

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

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

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

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

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