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The Use Of Generic Drugs In Prevention Of Chronic Disease Is Far More Cost-Effective Than Thought, And May Save Money

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ABSTRACT In this article we highlight the important role that medication therapy can play in preventing disease and controlling costs. Focusing on coronary artery disease, we demonstrate that prevention, with the appropriate use of generic medications, appears far more cost-effective than previously documented, and it may even save on costs. For example, an earlier study estimated that reducing blood pressure to widely established clinical guidelines in nondiabetic patients cost an estimated \$52,983 per quality-adjusted life-year if a brand-name drug was used. However, we estimate that the cost is just \$7,753 per quality-adjusted life-year at generic medication prices. As the nation attempts to find strategies to improve population health without adding to the unsustainably high cost of care, policy makers should focus on ensuring that patients have access to essential generic medications.

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Chronic disease accounts for the overwhelming majority of US health care costs.¹ Appropriate medical management of chronic disease can improve health outcomes and reduce downstream health care costs.² Patients with chronic diseases are frequently managed with ongoing pharmacologic therapy. Better delivery of cost-effective pharmaceutical care may be one important approach to containing cost while maintaining high-quality care.

Over the next three years, increasing numbers of patents for commonly prescribed chronic disease medications are expected to expire, and many classes of drugs will soon have highly effective generic alternatives that provide low-cost options for chronic disease management. Yet these low-cost generic options are often overlooked in analyses of the cost-effectiveness of chronic disease management.

Published analyses of cost-effectiveness generally are based on the cost of brand-name drugs. As a result, an exhaustive review of a registry of published cost-effectiveness analyses of preven-

tive therapies concluded that although appropriate preventive drug therapy offers meaningful health benefits, it does so at great cost to society.³ These conclusions were based entirely on the cost of brand-name medications.

A highly publicized 2008 study by Richard Kahn and colleagues, which was endorsed by both the American Heart Association and the American Diabetes Association, offers another example.⁴ The authors used brand-name medication costs in their analysis of the cost-effectiveness of strategies to prevent adverse outcomes associated with cardiovascular disease and diabetes in the United States. They concluded that up to 244 million quality-adjusted life-years could be gained over thirty years in the United States with appropriate preventive care, but that "most prevention activities are expensive when considering direct medical costs."^{4(p576)}

In this article we examine the cost-effectiveness of generic medications for chronic disease prevention. First, we describe recent and forthcoming instances in which drugs have come off patent and generic equivalents have come on the

market. By 2012 these developments will produce a full range of generic options in many therapeutic categories.

Next, using cardiovascular disease as an example, we explore more carefully the potential cost savings of generic drug use. We used the study by Kahn and colleagues as a basis for this work, substituting reasonable generic alternatives and their associated prices in the analysis. We surveyed the cost-effectiveness literature to identify published thresholds that demarcate when preventive cardiovascular medications save costs. The exercise allowed us to explore whether the use of generics can reduce overall health care outlays while improving cardiovascular outcomes. We found that the broad adoption of generic medications, when clinically appropriate, offers a clear way to improve the value of health care.

Availability Of Generic Medications

Pharmaceutical manufacturers produce medications whose patent rights enable them to maintain a monopoly on production for a restricted period of time. This monopoly enables manufacturers to recoup the costs associated with the discovery of useful medications. Because the process of developing and testing medications takes such a long time, the government allows a twenty-year monopoly and specifies the process for generic entry into the marketplace under the Drug Price Competition and Patent Term Restoration Act of 1984 (usually referred to as the Hatch-Waxman Act). These brand-name medica-

tions, sold under monopoly, are the primary source of profits for drug manufacturers.

Once a patent expires, other manufacturers can market generic versions of the original drug, and the price for the medication drops enormously.⁵ Thus, the cost of pharmaceutical therapies should decrease over time, unless much more efficacious brand-name medications continuously replace older ones, and patients are switched to these new drugs.

Such is not the case today. Great advances in understanding the physiological basis of disease in the 1960s gave way to pharmacological advances of the 1970s and 1980s. Many of these medications have now “gone generic,” and still others will follow over the next few years. The best example is Lipitor, the highest-revenue-producing medication in the United States. The Lipitor patents, held by Pfizer, lapse in 2011.⁶ In 2012 the second-largest-revenue-generating medication, Plavix, goes generic.⁶

Exhibit 1 shows the value of medications that become available as generics between 2010 and 2013. At the same time, the pipeline for non-biologic medications that could become “blockbuster” sellers appears relatively dry, and many new brand-name agents are only third- or fourth-tier selections for physicians.

The result is that many key classes of pharmacotherapy, excluding the so-called specialty or biologic drugs, will soon have acceptable generic alternatives. Although some physicians have complaints about generics’ quality, the scientific literature indicates no inferiority of clinical efficacy.⁷ Increasingly, clinical guidelines are encouraging more frequent screening and earlier treatment for chronic disease, leading more patients, particularly in an aging population, to require more frequent chronic medication therapy. So, in a health care system strapped for resources, physicians will increasingly use generics, and patients will have to expect that most of their medications will be generic.

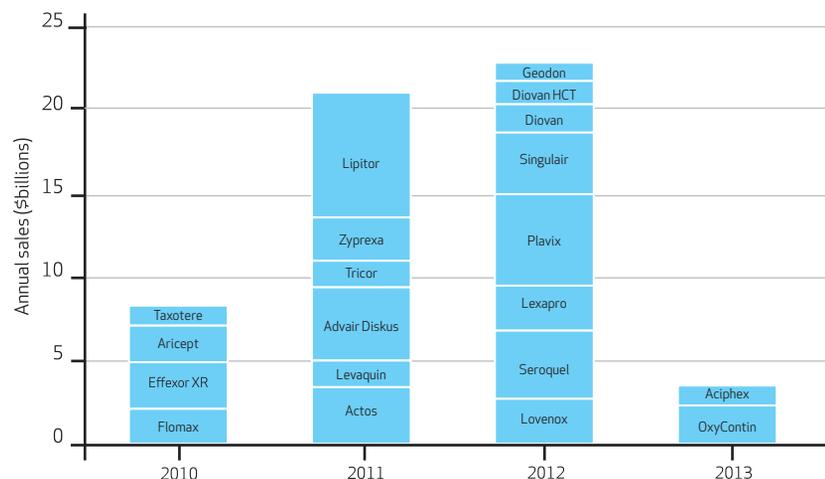
The Cost Of Drug Therapy To Prevent Cardiovascular Disease

Prevention of cardiovascular disease, the most common cause of death in the United States, is central to any policy discussion about overall health care costs. Approximately eighty million Americans have some form of cardiovascular disease, and related annual health care costs in the United States are more than \$475 billion.⁸

Preventing cardiovascular disease can be largely accomplished with low-cost generic medications. National guidelines for the management of hypertension and diabetes recommend generic medications as first-line therapy for

EXHIBIT 1

Expected Patent Expirations For Medications With Annual Sales Greater Than \$1 Billion, 2010-13



SOURCES IMS Health, Goldman Sachs.

most patients.^{9,10} Guidelines for the treatment of high cholesterol are agnostic as to the choice of statins, as long as patients reach their cholesterol management goals.¹¹

Most large pharmacy chains have lists of generic medications that can be purchased for five dollars or less a month—generally less than fifty dollars annually in total costs per medication. All of these lists include first-line medications to prevent cardiovascular disease in the management of hypertension (thiazide diuretics, angiotensin-converting enzyme inhibitors, and beta-blockers), diabetes (biguanides and sulfonylureas), and hypercholesterolemia (older statins). Exhibit 2 lists major drug classes to prevent cardiovascular disease, and available generic drugs in those classes.

One additional consideration is that combination medications, which simplify therapy by combining two distinct treatments (for example, a diabetes drug combined with a blood pressure medication), can lead to greater use of brand-name medications and increased medication costs, because brand-name medications often are components of combination medications.

CURRENT PRICES In their assessment of the cost of preventing cardiovascular disease, Kahn and colleagues used person-specific data from a representative database in the United States to assess potential candidates for nationally recommended preventive activities. The authors then applied a mathematical model to simulate the effect of each preventive activity on the cost and health burden of cardiovascular disease over thirty years.

The cost inputs used in the model did not accurately reflect medication prices in the marketplace. The cost of statin therapy to lower low-density lipoprotein cholesterol in low-risk patients to a stated goal was quoted at \$1,082 annually; statin costs for higher-risk patients were estimated at \$1,543 per year. However, many patients can be adequately treated with generic statins at a fraction of that cost.

Similarly, in the 2008 analysis, annual treatment with an angiotensin-converting enzyme inhibitor was estimated at \$1,238 a year for both diabetic and nondiabetic patients, and medication costs for glucose control in diabetic patients were estimated at \$3,150 a year. Again, medication management could cost far less with the use of generics. Angiotensin-converting enzyme inhibitors—an important class for the management of hypertension—are available generically at very low cost. Metformin is recommended as a first-line therapy for most diabetics, and sulfonylurea agents, as an appropriate second-line therapy for most diabetics. Both of these are available at very low cost.

RECALCULATING COSTS WITH GENERIC PRICES

The study by Kahn and colleagues specifically identified annual cost inputs for medications, physician visits, and lab tests for each preventive activity.⁴ By adjusting the annual medication costs to reflect current generic prices, without altering any of the other health care costs, we recalculated the cost per quality-adjusted life-year of each preventive intervention, assuming prescribing decisions consistent with widely accepted guidelines.

To estimate current medication costs, we used the Centers for Medicare and Medicaid Services' federal upper limit prices, which represent the highest amount Medicaid can be charged for generic medications.¹² We identified the most commonly prescribed drug on the federal upper limit list for each class in this analysis, and we assigned an annual cost by calculating the mean of the available doses on the federal upper limit list and adding two dollars a month for a dispensing fee (Exhibit 3).¹³ To manage cholesterol in high-risk patients, we assumed that the highest dose of pravastatin would be used.

After the cost inputs for the populations of patients modeled by Kahn and colleagues are updated, preventive care using generics appears far more cost-effective than was previously described in Kahn's original study (Exhibit 3).

EXHIBIT 2

Generic Availability In Major Drug Classes Used To Prevent Cardiovascular Disease

Disease and drug class (example)	Generic availability in class
DIABETES	
Sulfonylureas (glyburide, glipizide)	Yes
Biguanides (metformin)	Yes
Thiazolidinediones (pioglitazone)	No
Meglitinides (repaglinide)	No
Others (Byetta, Januvia)	No
CHOLESTEROL MANAGEMENT	
Statins (simvastatin, pravastatin)	Yes
Fenofibrates	Yes
Niacin	Yes
Bile-acid sequestrants (cholestyramine)	Yes
HYPERTENSION MANAGEMENT	
Beta-blockers (atenolol, metoprolol)	Yes
Angiotensin-converting enzyme inhibitors (lisinopril, captopril)	Yes
Calcium channel blockers (amlodipine, diltiazem)	Yes
Thiazide diuretics (hydrochlorothiazide)	Yes
Alpha blockers (clonidine, doxazosin)	Yes
Aldosterone antagonists (spironolactone)	Yes
Loop diuretics (furosemide)	Yes
Angiotensin receptor blockers (losartan)	Yes
Anti-platelets (clopidogrel)	No ^a
Anti-platelets (aspirin)	Yes
Nitrates (isosorbide dinitrate)	Yes

SOURCE See Note 6 in text. ^aPatent expires in 2012.

EXHIBIT 3

Recalculated Costs Of Generic Treatment Versus Brand-Name Treatment

Intervention	Medication costs per year used in 2008 study (\$)	Total costs per year used in 2008 study (\$)	Cost-effectiveness reported in 2008 study (\$ per QALY)	Generic medication costs per year, FUL pricing (\$)	Recalculated total costs per year, generic pricing (\$)	Recalculated cost-effectiveness, generic pricing (\$ per QALY)
Lower LDL to <160 in low-risk people	1,082	1,281	272,061	129	328	47,225
Lower LDL to <130 in high-risk people	1,543	1,816	83,327	152	425	1,7084
Lower LDL to <100 in people with CAD	1,543	2,140	39,130	152	749	9,636
Lower blood pressure in nondiabetics	1,238	1,582	52,983	45	389	7,753
HbA1C control in diabetics	3,150	3,564	48,759	130	543	1,022
Lower blood pressure in diabetics	1,238	1,582	25,317	45	425	3,131
Lower LDL in diabetics	1,543	2,140	67,199	152	278	19,231
Reduce fasting glucose to < 100 mg/dL	524	732	17,428	70	278	7,306

SOURCE See Notes 4 and 12 in text. **NOTES** QALY is quality-adjusted life-year. FUL is federal upper limit. LDL is low-density lipoprotein. CAD is coronary artery disease. HbA1C is a hemoglobin test used to measure glucose levels.

For example, reducing blood pressure to widely established clinical guidelines⁹ in non-diabetic patients costs \$7,753 per quality-adjusted life-year with generic medication versus \$52,983 described in the study by Kahn and colleagues. Reaching American Diabetes Association goals for glucose control would cost only \$1,022 per quality-adjusted life-year with generic pricing compared with \$48,759 reported in the 2008 study (Exhibit 3).

Cost-Saving Thresholds In The Published Literature

To quantify better the cost-savings potential of preventive use of generic medications, we reviewed cost-effectiveness studies of preventive therapy (details are provided in the online Appendix).¹⁴

We found that overall, there is substantial variation in the reported cost thresholds where medication therapy to prevent cardiovascular disease becomes cost saving (see Appendix Exhibit).¹⁴ However, generic therapies appear to be extremely cost-effective and potentially cost saving at current prices. Many cost-effectiveness studies of prevention suggest that generic medications can save lives and reduce costs, because their price is less than some published thresholds for cost savings. Cost savings result when the use of generic therapies reduce downstream complications and the use of health services that outweigh the cost of the medications themselves.

Discussion

THE IMPORTANCE OF GENERIC MEDICATIONS Preventive cardiovascular pharmaceutical care, using generic medications, has the potential to both save lives and reduce overall costs for the health care system. As the nation struggles to find strategies to improve population health without adding to the unsustainably high cost of care, policy makers should focus on ensuring that patients have access to essential generic medications. Not all chronic conditions can be managed sufficiently with generics alone. However, we believe that the example of cardiovascular disease is instructive as policy makers prioritize efforts to expand coverage while reducing costs.

Payers and pharmacy benefit managers have attempted to move patients to generic medications for years, to lower costs for employers and individuals. Virtually all payers have implemented a tiered pharmacy benefit structure that charges patients more for brand-name than generic medications,¹⁵ which has led to greater use of generic drugs.¹⁶ Strategies such as requiring prior authorization for certain drugs and step therapy, which requires that patients start with the most cost-effective and safest drug therapy before moving to costlier medications, have been widely implemented, reducing unnecessary use of expensive brand-name medications.¹⁷

Generic substitution laws have been implemented in all states to simplify generic use, although variations in those laws lead to varied rates of generic adoption.¹⁸ Specifically, states that require patient consent prior to generic substitution have lower generic substitution rates

Policies to improve access to essential generic medications should be central to implementation of health reform

than those states that do not require consent.¹⁸

CONTINUED RESISTANCE Despite these efforts, some physicians and patients remain resistant to the use of generics and harbor suspicions about them.^{19,20} A recent survey of physicians suggests that approximately one-fourth of respondents expressed concern about the efficacy and safety of generic drugs.¹⁹

Similarly, although patients broadly recognize that generics offer greater value than brand-name medications and endorse greater generic use for the US population generally, only a minority prefer to use generics themselves.²⁰ As a result, one recent study demonstrated that nearly 5 percent of all prescriptions written were designated “dispense as written” by either physicians or patients, which suggests that they demanded the brand-name therapy. The cost of dispense-as-written requests was estimated at more than \$7 billion annually in the United States.²¹

Beyond generic substitution, patients may be more resistant to therapeutic interchange, where a generic medication is substituted for a similar, but not identical, brand-name product to treat the same condition. Some of these perceptions may be related to effective marketing campaigns from brand-name drug makers. Prevailing perceptions by patients and providers highlight an important opportunity for payers and policy makers to target educational campaigns to promote generic acceptability.

We should note that physicians also have a fiduciary role to play. A recent analysis of medical ethics²² suggests that physicians have a responsibility to reduce health care costs wherever possible. Certainly, the use of generic med-

ications is part of that responsibility. Educating physicians about the use of generics will no doubt also allay patients’ concerns.

RELEVANCE TO HEALTH REFORM Efforts to implement health reform aim to both expand coverage and contain costs. Policies to improve access to essential generic medications should be central to that effort. Provisions in the health reform legislation to fill the Medicare Part D coverage gap, or so-called doughnut hole, have begun to take effect. However, policies that discount brand-name medications and do not promote access to generic medications seem counter-intuitive and may not encourage cost-effective medication use or adherence to therapy.²³

As we consider approaches to restructure fundamentally the way we pay for health care through accountable care organizations, providers and policy makers will increasingly be responsible for determining how to invest precious resources to improve health. Accordingly, we must not lose sight of the importance of affordable chronic disease therapy.

Accountable care organizations will have the responsibility to encourage the use of generics. They, patients, and arguably the public at large will benefit from reduced prescription drug prices, while also improving adherence to essential medications and reducing costs related to complications of chronic disease. Physicians must develop better lines of communication with retail pharmacies and pharmacy benefit managers so that they can assist in identifying more cost-effective generic options for patients.

Policy options that limit use of the dispense-as-written designation or that eliminate the need for patient consent prior to generic substitution could have a dramatic effect on generic use. Additionally, the implementation of electronic prescribing should encourage the greater use of generics. Better real-time decision support will be an important tool to use in identifying patient cost-sharing requirements and encouraging doctors to initiate generic options.

Patient and physician education about generics and the use of financial incentives to promote their use should also be considered. No matter who holds the financial risk for illness, using generic medications to prevent, forestall progression of, and treat chronic disease has to be a key part of patient management in a more cost-effective health care system. ■

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NOTES

- 1 Hoffman C, Rice D, Sung HY. Persons with chronic conditions: their prevalence and costs. *JAMA*. 1996;276(18):1473–9.
- 2 Fireman B, Bartlett J, Selby J. Can disease management reduce health care costs by improving quality? *Health Aff (Millwood)*. 2004; 23(6):63–75.
- 3 Cohen JT, Neumann PJ, Weinstein MC. Does preventive care save money? Health economics and the presidential candidates. *N Engl J Med*. 2008;358(7):661–3.
- 4 Kahn R, Robertson RM, Smith R, Eddy D. The impact of prevention on reducing the burden of cardiovascular disease. *Circulation*. 2008; 118(5):576–85.
- 5 Frank RG, Salkever DS (Harvard University; University of Maryland, Baltimore County). Generic entry and the pricing of pharmaceuticals [Internet]. Cambridge (MA): National Bureau of Economic Research; 1997 May [cited 2011 Jun 24]. (NBER Working Paper No. w5306). Abstract available from: <http://ssrn.com/abstract=225370>
- 6 Food and Drug Administration. Orange book: approved drug products with therapeutic equivalence evaluations [Internet]. Rockville (MD): FDA; [cited 2011 Jun 15]. Available from: <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>
- 7 Kesselheim AS, Misono AS, Lee JL, Stedman MR, Brookhart MA, Choudhry NK, et al. Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. *JAMA*. 2008;300(21):2514–26.
- 8 Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation*. 2010;121(7): e46–215.
- 9 Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19): 2560–72.
- 10 American Diabetes Association. Standards of medical care in diabetes—2010. *Diabetes Care*. 2010;33:S11–61.
- 11 Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation*. 2002;106(25):3143–421.
- 12 Centers for Medicare and Medicaid Services. Federal upper limits [Internet]. Baltimore (MD): CMS; [cited 2010 Feb 27]. Available from: http://www.cms.hhs.gov/Reimbursement/05_FederalUpperLimits.asp
- 13 Centers for Medicare and Medicaid Services. Medicaid prescription reimbursement information by state—quarter ending March 2009 [Internet]. Baltimore (MD): CMS; [cited 2011 Jun 15]. Available from: <http://www.cms.hhs.gov/Reimbursement/Downloads/reimbursementchart1q2009.pdf>
- 14 To access the Appendix, click on the Appendix link in the box to the right of the article online.
- 15 Kaiser Family Foundation, Health Research and Educational Trust. Employer health benefits: 2010 annual survey [Internet]. Menlo Park (CA): KFF; 2010 [cited 2011 Feb 21]. Available from: <http://ehbs.kff.org/pdf/2010/8085.pdf>
- 16 Huskamp HA, Deverka PA, Epstein AM, Epstein RS, McGuigan KA, Frank RG. The effect of incentive-based formularies on prescription-drug utilization and spending. *N Engl J Med*. 2003;349(23): 2224–32.
- 17 Carlton RI, Bramley TJ, Nightengale B, Conner TM, Zacker C. Review of outcomes associated with formulary restrictions: focus on step therapy. *Am J Pharm Benefits*. 2010 Feb:50–8.
- 18 Shrank WH, Choudhry NK, Agnew-Blais J, Federman AD, Liberman JN, Liu J, et al. State generic substitution laws can lower drug outlays under Medicaid. *Health Aff (Millwood)*. 2010;29(7): 1383–90.
- 19 Shrank WH, Liberman JN, Fischer MA, Girdish C, Brennan TA, Choudhry NK. Physician perceptions about generic drugs. *Ann Pharmacother*. 2011;45(1):31–8.
- 20 Shrank WH, Cox E, Fischer MA, Mehta J, Choudhry NK. Patient perceptions of generic medications. *Health Aff (Millwood)*. 2009;28(2): 546–56.
- 21 Shrank WH, Liberman JN, Fischer MA, Avorn J, Kilabuk E, Chang A, et al. The consequences of requesting “dispense as written.” *Am J Med*. 2011;124(4):309–17.
- 22 National Partnership for Women and Families. Patient charter for physician performance measurement, reporting, and tiering programs: ensuring transparency, fairness and independent review [Internet]. Washington (DC): The Partnership; [cited 2010 Feb 27]. Available from: <http://www.rwjf.org/files/research/disclosurepatientcharter.pdf>
- 23 Shrank WH, Choudhry NK. Time to fill the donuts: health reform and Medicare Part D. *N Engl J Med*. 2011;364(7):598–601.

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In this issue of *Health Affairs*, William Shrank and coauthors find that the use of generic medications to treat patients with chronic disease is highly cost-effective and may even be cost saving. The findings contradict previous analyses of the preventive use of drugs, which considered the use of much more expensive brand-name medications.

The authors conducted their study as part of the CVS Caremark Harvard Partnership to Improve Medication Adherence. They share an interest in maximizing the value of prescription drugs, and they concluded that “using the least expensive among similarly effective medications seemed like a good place to promote more cost-effective medication use,” Shrank says.

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