Do Newer Prescription Drugs Pay For Themselves? A Reassessment Of The Evidence

Reanalysis of an important study on drug pricing suggests that the health cost–reducing effects of newer drugs might have been overstated.

by Yuting Zhang and Stephen B. Soumerai

ABSTRACT: Citing evidence from studies conducted by Frank Lichtenberg, some health policy advocates have argued that, on average, use of new prescription drugs reduces total health care costs. While recognizing that the cross-sectional research design cannot guard against many biases that could overstate the results, we replicated the original study results and examined the findings’ sensitivity to different analytical approaches. Using the same data, we were able to replicate the original results; however, the original findings are not maintained under plausible alternative assumptions. More rigorous research on specific drugs and conditions is necessary before one can claim that newer drugs lower total health care costs. [Health Affairs 26, no. 3 (2007): 880–886; 10.1377/hlthaff.26.3.880]

Prescription drug spending in the United States has risen from $50 billion in 1990 to $219 billion in 2006; in 2006 it accounted for 13 percent of total health care spending. Use of newer drugs, which tend to be more expensive, accounts for a large proportion of this spending growth. In response to this trend, both public and private payers have established drug cost containment policies to discourage the use of new, more costly drugs. However, the use of certain new and effective drugs may reduce total health system costs, resulting in reduced use of other more expensive health care services. If these savings can more than offset the increase in drug costs, there might be net cost savings to society (the so-called drug-offset effect).

Importance of drug-offset effects. Whether newer medications can “pay for themselves” through the offset effect has important implications for private and public health policies. Such evidence may assist payers in deciding whether newer, more costly drugs should be covered and, if so, how to structure the benefit.

Some countries use drug-offset evidence to decide whether or not to permit a premium price for a new drug to treat a particular condition. For example, the Australian Pharmaceutical Benefits Pricing Authority (PBPA) pays a higher price for new drugs if manufacturers can provide evidence that they are more
cost-effective than existing agents. Relevant evidence of cost-effectiveness includes savings on nondrug health services.

Cost offsets also can affect the appraisal of new drugs' effectiveness and treatment guidelines. For example, the British National Institute for Health and Clinical Excellence (NICE) specifically requires economic evaluations of newer versus older drugs to provide recommendations of coverage in the National Health Service (NHS), to maximize health gains in the context of overall health care spending.5

Evidence of drug-offset effects. Since the drug-offset effect has important policy implications, gathering robust evidence is critical. Previous studies have used two approaches to investigate these effects: disease-level and aggregate-level analysis. The most common strategy is a case-by-case, disease-level approach to evaluate whether use of a new drug can reduce use of other medical services relative to an existing drug. For example, rigorous systematic reviews have concluded that some drugs, including low-molecular-weight heparin and inhaled corticosteroids, result in drug-offset effects when used by specific groups of patients.6

The second approach for studying drug-offset effects is the aggregate-level approach: to evaluate whether, on average, newer drugs produce those effects. This is the approach taken in a series of papers by Frank Lichtenberg.7 He has concluded that, on average, the use of newer drugs reduces total health care costs in the United States. These results have been widely disseminated in numerous research papers and government reports that have influenced pharmaceutical policies.8 A 2002 Congressional Budget Office (CBO) report to the president concludes that Lichtenberg's 2002 study “makes perhaps the strongest case that greater use of prescription drugs can lead to declines in nondrug health services.”9 This work has also been cited to promote the economic benefits of new drugs in reports to the U.S. Department of Commerce on policies affecting drug prices and access controls.10

Given the importance of the findings, it is critical to understand whether the reported conclusions of the studies on which they are based are valid and robust. Both of Lichtenberg's studies used a publicly available data set from the Medical Expenditure Panel Survey (MEPS), a large, nationally representative survey of U.S. adults.11 Thus, it is possible to replicate the results and examine whether the underlying assumptions are valid. We first highlight several features of the Lichtenberg studies' research design that could undermine their stated conclusions. We report the results of replicating Lichtenberg's findings using his reported methods, and we examine the sensitivity of the findings to underlying methodological assumptions.

Summary of the Original Lichtenberg Papers

Lichtenberg used data from the 1996 MEPS to study the relationship between the age of the active ingredient in a prescription and health care use and spending. He defined drug age as the number of years prior to 1996 that the active ingredient was first approved by the Food and Drug Administration (FDA). He then estimated how drug age affects health care spending, using linear regression models for all prescription drugs, by controlling for a person's demographic and economic characteristics. His estimates implied that, on average, replacing a fifteen-year-old drug with a five-and-one-half-year-old drug would save $72 in nondrug health care spending and cost $18 more in drug spending, for a drug-offset effect of $54.12 Lichtenberg's second paper on this topic added data from the 1997 and 1998 MEPS and treated the medical condition rather than the prescription as the unit of observation.13 This paper reported a larger drug-offset effect of $111.

Study designs. Lichtenberg's first paper used a cross-sectional study design, where a sample of subjects was studied at a single point in time (1996). The nature of the MEPS data cannot provide information about the order of events. For example, a patient might have specific drugs initiated during a hospital
stay, in which case the medications could not have “caused” the costs of the hospitalization (in fact, the hospitalization “caused” the costs of the drug). Moreover, the attribution of offset effects to use of newer drugs might be exaggerated as a result of uncontrolled variables (that is, selection bias). For example, wealthier people, those with better drug coverage, or those with lower existing health care spending might be more likely to purchase newer, more costly drugs. To mitigate selection biases, Lichtenberg’s second paper sought to control for some individual-specific confounders that are constant over time (such as education and race) by using three years of MEPS data. However, the analysis failed to control for prior health status and other omitted variables that vary over time, such as changes in health insurance or choice of physicians. Because of these limitations, Lichtenberg’s estimates might be seriously biased and might not represent causal effects of new drugs.

**Replication and reanalysis of previous results.** Acknowledging these fundamental design limitations, we nevertheless examined whether Lichtenberg’s results are consistent under plausible alternative assumptions. Using the same data (1996–1998 MEPS) and methodologies as in Lichtenberg's original papers, we were able to replicate the reported results for prescription drugs, hospitalization, office visits, and home health care. We then tested the sensitivity of the findings to more plausible alternative assumptions. Specifically, as detailed below, we updated for missing data on drug ages, recalculated prescription drug spending data associated with diseases, controlled for additional covariates, and conducted robustness checks using alternative model specifications.

**Study Methods**

**Step 1: updating data on ages of prescription drugs.** In the drug-age file there are 62,507 unique national drug codes (NDCs), of which 45 percent have an FDA approval year set at 1900. This coding occurred because observations with missing approval dates were set to 1900. We obtained the approval dates for drugs with missing ages using information from the FDA.

**Step 2: calculating drug spending associated with medical conditions.** In the MEPS pharmacy data, each monthly prescription is a unique unit of observation, whether for the same or a different drug. In the first Lichtenberg paper, the cost of prescription drugs associated with a particular condition was calculated by multiplying mean drug spending within a condition by the number of unique drugs associated with that condition. However, counting the number of unique drugs does not accurately represent the total cost of drugs associated with conditions, because the same drug might be recorded multiple times to reflect multiple monthly dispensings. To obtain accurate total drug costs associated with a condition, we multiplied mean drug spending within a condition by the total number of prescriptions, instead of the number of unique drugs used in the original analyses.

**Step 3: controlling for severity of illness.** Although no cross-sectional analysis can fully control for selection biases, severity of illness is certainly a key factor that must be accounted for in studies of use and cost. An older and sicker patient might be more likely to use older medications and be hospitalized more often, not because of the age of the drug but because of prior severity of illness. Thus, failing to control for illness severity can bias the results. Ed Miller and colleagues found that controlling for the number of unique medications taken by a patient substantially reduces the cost-offset effects of new cardiovascular drugs. After reviewing Lichtenberg’s refutation of this paper and recent research on the validity of severity-of-illness indicators, we decided to control for the number of unique medications taken by a patient.

**Step 4: testing alternative model specifications.** Because health care expenditures are often highly skewed, with a high proportion of people having zero spending, simple linear regression models might not fit the data well. Thus, we analyzed two alternative specifications: a generalized linear model with a
log link function and gamma distribution, and a two-part nonlinear model, which consists of a logistic model to estimate the probability of utilization and an ordinary least squares model to estimate spending given utilization.

**Study Results**

Exhibit 1, column 1 reports the results from the replication, which are the same as the original Lichtenberg results. They are presented here as a comparison for our reanalysis. Updating drug age (step 1) resulted in an increase in drug costs of $28, $10 higher than the original results (Exhibit 1, column 2). This first correction reduced the original estimates of drug-offset effects by one-sixth.

Correcting the calculation of drug spending associated with each condition (step 2) greatly increased the drug spending estimates. Newer drugs were determined to be about 3.2 times more costly than in the estimates reported in Lichtenberg's original papers. On average, drug spending increased $57 for every unit of drug age (measured by the logarithm of drug age in the study), compared to $18 in Lichtenberg's original papers (Exhibit 1, column 3). This step again greatly reduced drug-offset effects.

After we adjusted for severity of illness and used the alternative nonlinear model (steps 3 and 4 above), the estimated offset effects were only 20 percent of those originally reported by Lichtenberg (Exhibit 1, column 4).

In summary, using Lichtenberg's original methods, we replicated the same drug-offset effects in the original reports. However, after

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**EXHIBIT 1**

Estimated Effects Of Newer Drug Use On Prescription Drug Spending And Spending On Other Types Of Health Services

<table>
<thead>
<tr>
<th>Spending category</th>
<th>Replication of original analysis</th>
<th>Updated drug-age data</th>
<th>Correct cost of Rx</th>
<th>Alternative specifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitals</td>
<td>–81** (17.05)</td>
<td>–74** (19.05)</td>
<td>–91** (21.19)</td>
<td>–61** (21.18)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>–18** (3.37)</td>
<td>–16** (3.70)</td>
<td>–17** (4.02)</td>
<td>–14** (4.02)</td>
</tr>
<tr>
<td>Office visit</td>
<td>–25** (2.93)</td>
<td>–19** (3.25)</td>
<td>–21** (3.58)</td>
<td>–12** (3.56)</td>
</tr>
<tr>
<td>Emergency room</td>
<td>–4** (1.13)</td>
<td>–3** (1.29)</td>
<td>–4** (1.41)</td>
<td>–3** (1.42)</td>
</tr>
<tr>
<td>Home health care</td>
<td>–17** (5.65)</td>
<td>–18** (6.66)</td>
<td>–11** (6.95)</td>
<td>–6** (6.96)</td>
</tr>
<tr>
<td>Total nondrug spending ($)</td>
<td>–139** (19.26)</td>
<td>–131** (21.66)</td>
<td>–145** (23.91)</td>
<td>–96** (23.82)</td>
</tr>
<tr>
<td>Prescription drug spending ($)</td>
<td>18** (0.55)</td>
<td>26** (0.70)</td>
<td>57** (1.98)</td>
<td>73** (1.69)</td>
</tr>
<tr>
<td>Difference (drug-offset effect) ($)</td>
<td>–121** (0.55)</td>
<td>–103** (0.70)</td>
<td>–88** (1.98)</td>
<td>–23** (1.69)</td>
</tr>
</tbody>
</table>

**SOURCE:** Authors’ regression analysis using 1996–1998 Medical Expenditure Panel Survey (MEPS) data.

**NOTES:** The coefficients shown above show the estimated effect on spending of a one-unit change in drug age. Positive values indicate that spending will increase in response to a newer drug; negative values indicate that spending will decrease. The drug-offset effect is the difference between drug spending and nondrug spending. As in the original studies by Frank Lichtenberg, we estimated multiple equations simultaneously and used an individual fixed-effect model controlling for time and condition dummies. Positive standard errors are in parentheses. Replication results are approximately the same as the original results in F.R. Lichtenberg, “Benefits and Costs of Newer Drugs: An Update,” NBER Working Paper no. 8996 (Cambridge, Mass.: National Bureau of Economic Research, 2002), except for outpatient spending. These data should not be used to estimate an offset effect; they only demonstrate the sensitivity of the original results to several more plausible assumptions. **p < 0.05**
including corrected data and alternative model specifications, the large reported drug-offset effects did not persist (Exhibit 2).

**Discussion**

To date, Lichtenberg’s papers are the only published evidence regarding whether, on average, newer drugs result in lower total health care costs. However, because of the limitations of the data source and research design, it is impossible to address all of the potential selection biases, especially whether the use of a given medication precedes, is contemporaneous with, or follows nondrug health care costs in a given year. Therefore, neither the original papers nor our reanalysis represents adequate evidence that newer drugs cause overall reductions in use of nondrug services. Despite the limitations of this analysis, the idea that specific therapeutic advances can offset other medical spending is plausible in both theory and practice. It is important to emphasize that development of new medications can still provide net benefits to society, even in the absence of a cost offset. Some medications might have important nonpecuniary advantages relative to older drugs, such as higher life expectancy, better health outcomes, or reduced sick days, even if they do not reduce overall costs.

On the other hand, some new drugs might be associated with higher potential costs without offering measurable economic and clinical benefits. For example, new medications are often associated with higher promotion costs. Some new chemical entities might be minor variations of older agents without offering measurable clinical benefits, such as esomeprazole (Nexium) versus omeprazole (Prilosec). Others might be less effective than their older counterparts; for example, calcium-channel blockers are less effective than diuretics for uncomplicated hypertension.

Lichtenberg’s work has been disseminated widely to promote policy changes. Our evaluation questions the validity of the original findings and offers some research implications. To obtain high-quality evidence, researchers should take advantage of policy interventions and longitudinal data that assess the outcome after exposure to drug treatment. While some cost containment policies, such as cost sharing and prior authorization of new drugs, can re-

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**EXHIBIT 2**

**Estimated Change In Spending From Use Of Newer Medications In Original Lichtenberg Study, Replication Of Original Results, And Reanalysis (Steps 1–4) Using More Plausible Assumptions**

<table>
<thead>
<tr>
<th>Spending change (dollars)</th>
<th>Prescription drugs</th>
<th>Nondrug items</th>
<th>Drug-offset effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-150</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Original</td>
<td>Replication</td>
<td>Step 1</td>
<td>Step 2</td>
</tr>
</tbody>
</table>

**SOURCE:** The original results are from Table 1 in F.R. Lichtenberg, “Benefits and Costs of Newer Drugs: An Update,” NBER Working Paper no. 8996 (Cambridge, Mass.: National Bureau of Economic Research, 2002). The results of the replication and reanalysis are from the data in Exhibit 1.

**NOTES:** Exhibit shows the sensitivity of the original findings to each assumption and does not represent actual estimates of a drug-offset effect. For details on the original, replication, and reanalysis steps, see text.
duce drug spending, their effects on total system costs remain largely unknown. Therefore, more research on such policy experiments can keep pace with policy implementation and lead to less biased estimates of cost offsets. For example, Medicare drug coverage and accompanying cost controls (which frequently seek to reduce the use of new and expensive drugs) provide an excellent opportunity to conduct longitudinal studies of the effects of new drugs on the costs of other medical services (for example, do policies that restrain use of the newest antidepressants lead to greater incidence of side effects, reduced medication adherence, and increased hospitalization?).

Evidence on the existence of drug-offset effects is important for policy decisions such as drug pricing and coverage. We need robust evidence to guide policy making. However, the previous evidence of drug-cost offsets at the aggregate level is not reliable. Furthermore, it is unlikely that any aggregate analysis of new versus old drugs can yield valid estimates of cost offsets. Instead, policymakers need the result of more (and more-rigorous) longitudinal research to evaluate whether specific medications or drug classes improve outcomes and lower overall costs.

NOTES
8. As of 22 June 2006, according to Google Scholar, this work has been cited eighty-six times in peer-reviewed journal articles. The terms “Lichtenberg” and “newer drugs” resulted in fifty-six hits in government Web sites, according to a Google government search.
10. “Foreign Government Pharmaceutical Price and Access Controls,” Submission by the Pharmaceutical...


12. Lichtenberg, “Are the Benefits of Newer Drugs Worth Their Cost?”


14. We are grateful to Frank Lichtenberg for sharing these data.


19. These costs are those associated with a one-unit increase in the age of a drug (measured by loga-

20. Of the two model specifications tested, a generalized linear model fits the data better, so we present findings for this model instead of the two-part model.

21. We also did a specification check by adding in interactions between condition and drug age. The results imply different drug-offset effects across medical conditions and raise further questions about the validity of aggregate analysis.


