Is Newer Always Better?
Re-evaluating the benefits of newer pharmaceuticals

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Benefits and costs of newer drugs

- Prescription drug expenditures growing rapidly
  - In part due to higher-priced “newer” drugs

- Overall benefit from this expenditure depends on numerous factors:
  - Health & quality of life improvements
  - Reduced side-effects
  - Convenience
  - “Offsets” of other costs both within and outside of health sector
Evidence on drug offset effects

- Two main research approaches:
  - **Randomized trial data:**
    - Neumann et al. (2000): Cost-effectiveness studies find some drugs are cost-effective
  - **Aggregate survey and administrative data:**
    - Lichtenberg (2001, 2007): Found higher cost of newer drugs was offset by lower non-drug expenditures
    - This result has been widely cited and debated
Are The Benefits Of Newer Drugs Worth Their Cost? Evidence From The 1996 MEPS

The newer the drug in use, the less spending on nondrug items.

by Frank R. Lichtenberg

ABSTRACT: This study analyzes data on prescribed medicines from the 1996 Medical Expenditure Panel Survey (MEPS) to examine the association between the use of newer medicines and morbidity, mortality, and health spending. We find that people consuming newer drugs were significantly less likely to die by the end of the survey and were significantly less likely to experience work-loss days than were people consuming older drugs. Our most notable finding, however, is that use of newer drugs tends to lower all types of nondrug medical spending, resulting in a substantial net reduction in the total cost of treating a given condition.
The use of evidence on drug offset effects

“Lichtenberg also found that while the use of newer medicines increased drug costs, overall healthcare spending decreased when newer drugs were used primarily due to decreased hospital use.”

- “Pricing and Value”, Pfizer Website
Newer research on drug offset effects

Further work has consistently found no evidence of drug offset effects:

- **Duggan (2005):** No evidence of an offset from newer antipsychotic agents for schizophrenia

- **Miller et al. (2006):** Used same data source as Lichtenberg to investigate cardiovascular diseases. After including a number of control variables, they find no offset effects

- **Zhang and Soumerai (2007):** Replicated Lichtenberg’s 2007 paper, conclude the study design is poor and the results are not robust
Replication data and variables

● **Goal:**
  - Assess the original Lichtenberg (2001) paper

● **Data:**
  - Drug Utilization and Expenditures: 1996 Medical Expenditure Panel Survey
  - Drug Age: Mosby’s GenRx, Drugs@FDA database

● **Variables:**
  - Dependent Variables: drug expenditure per prescription and yearly non-drug expenditure
  - Control Variables: Income of individual, sex, condition fixed effects (~500), condition duration, race, insurance status, age of person, education
Comparison of replication results

- Original replication results – effect of log(drug age)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Model</th>
<th>Estimate</th>
<th>SE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of Rx</td>
<td>Lichtenberg</td>
<td>-18.00</td>
<td>0.184</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Replication</td>
<td>-17.92</td>
<td>0.186</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total non-Rx Costs</td>
<td>Lichtenberg</td>
<td>71.09</td>
<td>15.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Replication</td>
<td>67.81</td>
<td>23.37</td>
<td>0.004</td>
</tr>
</tbody>
</table>

- Lichtenberg concludes:
  - “This reduction of $71.09 in non-drug spending is much greater than the $18 increase in prescription cost, so using a newer drug results in a substantial net reduction in total cost”
Three main concerns and potential fixes

- **Dataset**
  - AHRQ has released an updated dataset
  - Proposed fix: update the dataset

- **Model Appropriateness**
  - L01 uses cost in a linear regression, but large literature suggests this may be inappropriate
  - Proposed fix: use a log-transformed model (\ln\text{cost}+1)

- **Outcomes are not directly comparable**
  - Drug expenditures are per prescription; however, non-drug expenditures are annual
  - Proposed fix: perform analysis on a single condition
The result: offset effects disappear

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<th>SE</th>
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</thead>
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<tr>
<td>Total non-Rx Costs</td>
<td>67.81</td>
<td>23.37</td>
<td>0.004</td>
</tr>
<tr>
<td>Proposed Fix 1: Update the dataset</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total non-Rx Costs</td>
<td>0.21</td>
<td>25.36</td>
<td>0.993</td>
</tr>
<tr>
<td>Result: Offset effect disappears</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proposed Fix 2: Use a log-transformed outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total non-Rx Costs</td>
<td>-0.01</td>
<td>0.01</td>
<td>0.496</td>
</tr>
<tr>
<td>Result: Offset effect disappears</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proposed Fix 1 and 2 together</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total non-Rx Costs</td>
<td>-0.06</td>
<td>0.01</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Result: Offset effect reverses</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Method for alternative approach

<table>
<thead>
<tr>
<th>Limitation of L01</th>
<th>Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumes an additional log year would have same effect over entire drug lifespan</td>
<td>Defined “newer” at the drug class level</td>
</tr>
<tr>
<td>Assumes treatment effect to be constant across all conditions</td>
<td>Focused on one condition: hypertension</td>
</tr>
<tr>
<td>Model did not account for characteristics of health expenditures</td>
<td>Used a GLM with log-link to help account for outliers</td>
</tr>
</tbody>
</table>
Analysis of Hypertension

- We defined “newer” drugs for hypertension based on clinical guidelines
  - Older: diuretics and beta-blockers
  - Newer: CCBs, ACE-I's, alpha-blockers, ARBs

- Combinations: explicitly modeled

- Temporality: only modeled those that started drug prior to survey year
Use of GLM model

- Model for total expenditure:
  - Includes both hypertension drug costs and non-drug costs for complications of hypertension

- Expectation in the GLM model is:

  \[ E[ y_i | X_i ] = \exp(X_i \beta) \]

- We included a range of control covariates and used data from 1998-2002
Finding: Newer drugs are more expensive

- Predicted hypertension drug expenditures:

<table>
<thead>
<tr>
<th>Drug Use</th>
<th>Drug Age</th>
<th>Expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>Older</td>
<td>$248</td>
</tr>
<tr>
<td></td>
<td>Newer</td>
<td>$453</td>
</tr>
<tr>
<td>Combination</td>
<td>Older only</td>
<td>$411</td>
</tr>
<tr>
<td></td>
<td>Old &amp; New</td>
<td>$665</td>
</tr>
<tr>
<td></td>
<td>Newer only</td>
<td>$814</td>
</tr>
</tbody>
</table>

- Unsurprisingly, using newer drugs and combinations led to higher predicted expenditures
Finding: No evidence of an offset effect

- Predicted total expenditures:

<table>
<thead>
<tr>
<th>Drug Use</th>
<th>Drug Age</th>
<th>Total</th>
<th>Additional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>Older</td>
<td>$769</td>
<td>$521</td>
</tr>
<tr>
<td></td>
<td>Newer</td>
<td>$903</td>
<td>$450</td>
</tr>
<tr>
<td>Combination</td>
<td>Older only</td>
<td>$823</td>
<td>$412</td>
</tr>
<tr>
<td></td>
<td>Old &amp; New</td>
<td>$1,505</td>
<td>$840</td>
</tr>
<tr>
<td></td>
<td>Newer only</td>
<td>$1,615</td>
<td>$801</td>
</tr>
</tbody>
</table>

- These results contradict very strong clinical trial evidence, so are likely seriously confounded
Discussion

● Main Contributions
  ■ Interpret previous results with caution
  ■ Research methods in this area need improvement
  ■ Even in a model for only one condition, there are serious methodological problems

● Limitations
  ■ Model is likely not balancing unobservable characteristics (however, this is the point)
  ■ Costs are not everything
Acknowledgements

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Thank You!