Author's response to reviews

Title: Drug Utilization and Cost in a Medicaid Population: A Simulation Study of Community vs. Mail Order Pharmacy

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Author's response to reviews: see over
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RE: Drug Utilization and Cost in a Medicaid Population: A Simulation Study of Community vs. Mail Order Pharmacy (MS: 1737966039129947)

Dear Dr. Saltman:

We thank the helpful comments from the two reviewers and guidance from the editors. We have considered all these comments in the revised version of the manuscript.

Find below our response to the reviewers’ comments. Changes in the manuscript have been highlighted in blue color throughout the text of the manuscript.

Thank you for your consideration

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Review comments on: "Drug Utilization and Cost in a Medicaid Population: A Simulation Study of Community vs. Mail Order Pharmacy"

Thank you very much for the comments and suggestions from the Reviewers. Detailed answers to those comments and suggestions are provided below and have been incorporated in the revised version of the manuscript.

Reviewer: Cindy P. Thomas

We appreciate the comments and suggestions provided by Dr. Thomas. We have revised the manuscript to account for those comments and suggestions.

Major Compulsory

1. I am concerned with some of the model assumptions. It appears that the model assumes that the choice of drugs (and cost per product) would be the same for mail versus retail purchases. Several of the references listed by the authors (and a new one in March 2007 Jnl of Managed Care Pharmacy) show empirically that mail order use is different from retail, in terms of generic use rates, prices, and types of drugs purchased. Generic rates for instance are lower for mail, as cost sharing is lower, and many insured members specifically choose mail order to purchase more expensive drugs.

Model Assumptions: Choice of drugs

Yes, thank you, these differences were accounted for using the following strategies. First, the choice of drugs in the model was different for mail and for community pharmacy. We started with a large sample of claims used in community pharmacy. We selected from that sample a sub-sample of claims that were more appropriate for mail order pharmacy.

Second, the sub-sample selection criteria aimed to solve three main issues: a) exclusion of claims of drugs for chronic diseases that were used for acute conditions; b) inclusion of claims of drugs for acute diseases that were used for chronic conditions; and c) selection of claims of drugs used for chronic diseases that could be used for both chronic and acute conditions.

Third, the assumptions of the model restricted the sub-sample to those community pharmacy claims that were more appropriate for mail order (i.e. the patient had utilized the drug for at least 90 days, the patient maintained a minimum MPR of 0.5, mail order begins with the second fill). These strategies were used to put both mail-order pharmacy and community pharmacy on the same plane.

Finally, the baseline sample included all medications suitable for mail order, regardless of their classification and therapeutic category. To assess the validity of the criteria used to
select these drugs, a sub-analysis was performed in relation to those drugs classified by the Ohio State Medicaid program as drugs for chronic use.

Model Assumptions: Cost per product

Dr. Thomas indicated that “3. The discussion is long but I would take the results and discussion further to make the policy point: what would be the optimal design or potential product cost differences to assure neutral results (mail and retail same cost) or true savings through use of mail order?”

We thank Dr. Thomas for her suggestion. Following Dr. Thomas’ suggestion we rephrased our statement related to cost estimation. The objective has been more appropriately rewritten as follow:

“to estimate the mail order cost reduction required to become cost neutral in comparison with community pharmacy.”

We also included the following sentence in the discussion section of the manuscript:

“Information about the unit cost of mail order in Medicaid is not available therefore, we assumed that the cost would be the same in mail and in community pharmacy regarding the estimation of the breakeven point; that is the cost reduction required in mail order to become cost neutral in comparison with community pharmacy. The results of our study indicate that mail order cost should be reduced in 5.4% to become cost neutral in comparison with community pharmacy.”

Also, drug cost management tools are implemented to some extent differently at mail pharmacies. The study does not take this into account.

We included Dr. Thomas’s comment as one of the limitations of the study:

“Additionally, the study does not account for drug cost management tools that are implemented to some extent differently at mail and community pharmacies.”

At the very least, I would include a sensitivity analysis to show how different results would be under various other cost assumptions, and different drug use patterns.

Thank you, this was the purpose of performing several sub-analyses and also an extensive sensitivity analysis changing the model assumptions that may affect drug use patterns.

Sub-analyses were performed in relation to drugs for chronic conditions, dual-eligible patients, and the subset of dual-eligible patients using drugs for chronic conditions. Multivariate sensitivity analysis was performed in relation to the baseline model by varying the point where mail order filling was initiated, the minimum acceptable MPR
for a CDT being eligible for mail order, and the minimum day supply utilized in community pharmacy for a CDT being eligible for mail order.

Changes in drug use patterns affected the cost results. We did not include different mail order cost assumptions in the sensitivity analysis because the study does not evaluate the cost of mail order pharmacy, but the breakeven point were mail order becomes neutral with community pharmacy.

2. The model is based on actual retail MPR. The authors assume that MPR is the same in mail versus retail, which I am not sure is the case.

The model assumes that the MPR associated with mail order pharmacy is the same as that observed in community pharmacy. Nevertheless, mail order could increase the MPR given that patients have more medication available when 90-day supplies (vs. the 30-day supplies used in community pharmacy) are dispensed.

To clarify the differences in adherence between mail and community pharmacy we included the following sentence in the discussion section of the manuscript:

“Future studies should also evaluate if the increase in utilization associated to mail order pharmacy could improve medication adherence and if adherence rates vary in different groups of Medicaid beneficiaries.”

3. The discussion is long but I would take the results and discussion further to make the policy point: what would be the optimal design or potential product cost differences to assure neutral results (mail and retail same cost) or true savings through use of mail order?

We included a discussion of the breakeven point as suggested by Dr. Thomas in the discussion section of the manuscript.

“Information about the unit cost of mail order in Medicaid is not available therefore, we assumed that the cost would be the same in mail and in community pharmacy regarding the estimation of the breakeven point; that is the cost reduction required in mail order to become cost neutral in comparison with community pharmacy. The results of our study indicate that mail order cost should be reduced in 5.4% to breakeven with the cost in community pharmacy.”
4. Table 4: Please describe in text or appendix what calculations let to the result of 35.3 as the average incremental utilization effect. An Explicit description of the model and results would help the reader understand this analysis.

We included an explicit description of the model and results as follow:

“The final sample of 680,277 CDTs yielded a mean of 640.0± 515.0 day supply in community pharmacy and the model for mail order resulted in 675.0±518.0 day supply (Table 4). The mean difference was estimated at 35.3 days supply (95% confidence interval of the mean difference = 32.5-35.3).

The mean cost in community pharmacy of the CDTs included in the sample was $1,395.63 ± $5,982.19 and the model for mail order resulted in a mean cost of $1,471.62 ± $6,349.17. The mean drug product cost difference was estimated at $75.99 (95% confidence interval of the mean difference = $75.97-$77.00).”

Minor Essential

1. Sub-analyses: How does MPR differ between the different groups of Medicaid beneficiaries?

The analysis of MPR differences between the different groups of Medicaid beneficiaries is an interesting question that we plan to evaluate in future research. Dr. Thomas’s comment has been included as one of the areas for future research.

“Future studies should also evaluate if the increase in utilization associated to mail order pharmacy could improve medication adherence and if adherence rates vary in different groups of Medicaid beneficiaries.”

Table 3: does aged, blind and disabled include duals also? The category must in fact be blind and disabled, with aged all in the duals category.

We followed the Ohio Medicaid classification. ABD category includes aged, blind and disabled, and excludes dual eligible. Dual eligible does not sub-classify beneficiaries in ABD. Beneficiaries included in the category ABD are excluded from the dual eligible category.

2. What are examples of acute drugs used for long term use? (page 6)

Examples of acute drugs used for long term use include:
- Antibiotics for treatment of mycoplasma (e.g. doxycycline) or acne (e.g erythromycin)
- Nonbenzodiazepines for treatment of insomnia, approved for short term use (e.g. eszopiclone – Lunesta; zolpidem- Ambien)

Additionally, the model also accounted for drugs that could have long-term or short-term use, for example:
- fluticasone propionate and salmeterol xinafoate (Advair Diskus) is used for long-term control of asthma and short-term control of Chronic obstructive pulmonary disease associated with bronchitis
- esomeprazol magnesium (Nexium) is approved for short term use for healing of erosive esophagitis and for long term for maintenance of healing of erosive esophagitis.
Reviewer: Anders Ekedahl

We appreciate very much the comments and suggestions made by Mr. Ekedahl. Detailed answers to those comments and suggestions are provided below and have been incorporated in the revised version of the manuscript.

Minor Essential Revisions

1 It is not clear to me what the authors define as drug utilization - drug purchases or drug use – please define!

We included the following definition in the methods section of the revised version of the manuscript:

“Drug utilization is defined in this study as the day supply of drug product reimbursed by the Ohio Medicaid program.”

An additional comment has been included in the methods section related with this issue.

“The MPR was estimated using the number of days supply reimbursed by Ohio Medicaid according with the information available in the claims data.”

2 Increased wastage - is mentioned in the Background but is not discussed at all.
3 Wastage - what assumptions are made about wastage in modeling? It seems as the model does not include an assumption on wastage - please comment

The model estimates the increase in utilization, but does not estimate what percentage of that increase represents wastage.

Following Mr. Ekedahl’s suggestion we included in the discussion section the following sentence:

“Future research is needed to examine therapy discontinuation and estimation of drug wastage, resulting from medications that were not used because of tolerability issues, medication changes, ineffectiveness, and wastage attributed to other factors such as mail mishaps, spoilage, and patient failure to pickup rates, and an analysis of the impact of mail order pharmacy utilization on patient health outcomes.”
4 References - 6 references are made to drug discontinuation. However - a search on Google on "drug discontinuation" gave me 1 240 000 hits, and on PubMed 14 312 hits. On what grounds are the 6 references chosen - and the 14 306 other references in the scientific literature discarded?

We did also find a large number of references on the topic of compliance. We selected a convenient sample of articles to illustrate the issue of lack of compliance with different drug therapies (myocardial infarction, HIV, Chlamydia, renal transplantation).

Reference nr 18 is used to validate the claim that discontinuation is frequent - on what grounds?

The survey conducted by Ying et al. (1993) showed that 57% of long-term medication patients changed their medication therapy– change in dosage, change in schedule or medication. Of those patients who had changes in drug regimens, 39% had their medication changed. Moreover, patients’ reasons for running out of medications before receiving their next refill included mail delay (16%) and not allowing enough lead time when requesting a refill (79%).

5 In Background the authors states that "patients that have better adherence to drug therapy could be more inclined to select mail order pharmacy" - However, no reference or data supporting this view is presented, neither can I find that this is discussed. Please support with data/references and discussion.

Mr. Ekedahl highlighted an important issue. Unfortunately, to the authors’ knowledge, there are no studies available that assessed patient adherence to drug therapy in mail order vs. community pharmacy. We agree with Mr. Ekedahl this could be considered a limitation of the study. We included a new sentence in the discussion section indicating that:

“Future studies should also evaluate if the increase in utilization associated to mail order pharmacy could improve medication adherence and if adherence rates vary in different groups of Medicaid beneficiaries.”

Table 7. Several abbreviations in the table that are not explained.

We appreciate the comment. We have included the following information at the bottom of Table 7:

“AWP = average wholesaler price; FUL = Federal Upper Limit; MAC = maximum allowable cost.”