Program Outcomes

Evaluating, Measuring, and Identifying
Patient Care Benefits and Cost Reduction

Kansas Medical Assistance Programs
Retrospective Drug Utilization Review
Provider Education and Intervention Program

Increased Risk of Serotonin Syndrome
Mailed November 2010

Prepared by Health Information Designs
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HEALTH INFORMATION DESIGNS

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Executive Summary

This *Outcomes Assessment* report prepared for the Kansas Medical Assistance Programs shows the expected improvements in beneficiary health and cost savings from using retrospective drug utilization review and provider education to effect appropriate prescribing and utilization and, in turn, prevent adverse drug reactions and reduce costs in a targeted beneficiary population.

Program Summary

Drug interactions can lead to serious adverse drug events. One such interaction is the duplicate prescribing of serotonergic drugs, which can lead to an increased risk of serotonin syndrome. In an effort to improve clinical outcomes and reduce drug expenditures and related health care costs, Kansas Medical Assistance Programs beneficiaries found to have an increased risk of serotonin syndrome were identified, and educational intervention letters were mailed to their prescribers in November 2010. The selected beneficiaries were then evaluated 6 months after the prescriber letters were mailed to determine the impact of the intervention letters.

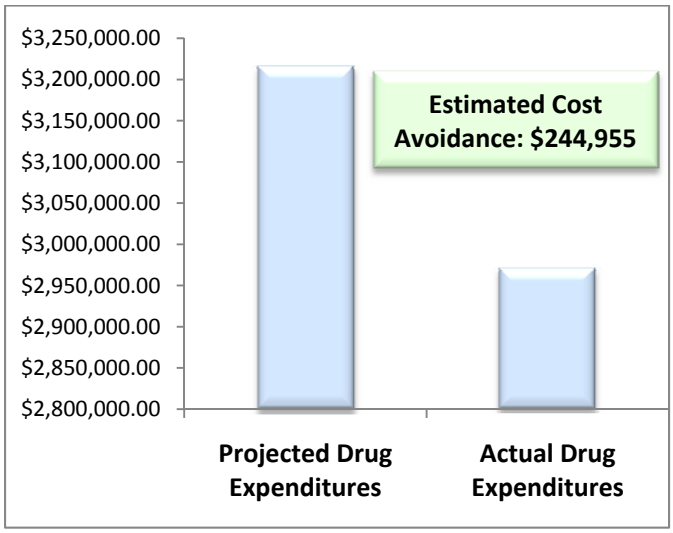
Changes in Criteria Exceptions

At the 6-month evaluation post intervention, appropriate utilization was significantly improved in the target population. Six months after letters were mailed to the prescribers, 595 of the original 677 beneficiaries had at least one claim for any drug and could be evaluated. **Of those remaining 595 beneficiaries, 45.2% of those who were previously at an increased risk for serotonin syndrome were no longer found to be using the same therapies that put them at risk for serotonin syndrome**. Based on improved utilization, it is clinically probable that serious adverse outcomes—such as emergency room visits or hospitalizations due to serotonin syndrome—were avoided and overall drug utilization was significantly reduced.

PRE-Intervention (November 2010)	POST-Intervention (May 2011)		
Beneficiaries with Letter Mailed to Prescriber	**Beneficiaries with Any Drug Claim**	**Beneficiaries with Same Criteria Exception**	**% Decrease in Criteria Exceptions**
677	595	326	45.2%

Cost Avoidance for Kansas Medical Assistance Programs

Actual drug expenditures for the post intervention period were compared to projected drug expenditures. For the 6-month post-intervention period, actual drug expenditures for the intervention population were $2,971,310 compared to the projected cost of $3,216,266, **an estimated cost avoidance of $244,955 for the 6 months following the mailing of intervention letters**.



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Background

Health Information Designs (HID), in coordination with HP Enterprise Services (HPES), currently performs retrospective drug utilization review (RetroDUR) for Kansas Medical Assistance Programs' fee-for-service population. The total number of unique beneficiaries enrolled in the traditional Medicaid fee-for-service population in State Fiscal Year (SFY) 2011 (July 1, 2010 – June 30, 2011) was 292,522, with an average of 158,846 beneficiaries per month. Prescription claims for approximately 51,000 beneficiaries were processed each month in SFY 2011.

Drug interactions and adverse drug events can be a resulting complication of treating patients with medications. The risk for adverse drug events may be increased when the patient is taking multiple medications and may be complicated further when the patient is seeing multiple providers.

Serotonin syndrome is a potentially life-threatening adverse drug event that causes the body to have too much serotonin. It often occurs when two drugs that affect the body's level of serotonin are taken together[1]. This drug interaction causes too much serotonin to be released or remain in the brain. Symptoms of serotonin syndrome can include: agitation, diarrhea, hallucinations, nausea, vomiting, rapid changes in blood pressure and an increased heart rate. Severe, untreated serotonin syndrome can be deadly, however, with treatment symptoms typically resolve within 24 hours.

Beneficiary Identification and Prescriber Intervention

In an effort to promote appropriate prescribing and reduce adverse drug events, HID identified beneficiaries with an increased risk of serotonin syndrome and mailed educational letters to their prescribers. When more than one prescriber was attributed to pertinent claims on a patient profile, letters were mailed to all relevant prescribers. Informing prescribers of a patients' complete drug and diagnosis history, including medications prescribed by other providers, may help to reduce drug interactions and adverse drug events.

While the intervention letter itself only addressed the risk of serotonin syndrome, HID included a patient profile with up to two additional alert messages regarding drug therapy issues and a 6-month history of drug claims and diagnoses along with the letter. Prescribers had the opportunity to review the entire beneficiary drug and diagnosis history, including medications prescribed by other providers, and make changes to therapies based upon this information. For this reason, whenever intervention letters are sent to prescribers, the impact on total drug utilization should be measured. Therefore, total drug utilization in the targeted population was evaluated for 6 months before and after intervention letters were mailed to determine any change in drug cost.

[1] Sternbach H. The Serotonin Syndrome. *Am J Psychiatry*. 1991: 148:705.

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Analysis Methodology

Each month HID evaluates Kansas Medical Assistance Programs pharmacy claims data against thousands of proprietary criteria. The criteria are developed and maintained by HID clinical pharmacists who review package insert updates as well as medical literature to develop the criteria.

Criteria Evaluated

The following criteria were reviewed for the intervention letters mailed in November 2010.

High Dose Alerts:

- Serotonergic antidepressants may be over utilized, increasing the risk for serotonin syndrome.

Drug-Drug Interactions:

- The concurrent use of agents with serotonergic properties increases the risk of developing serotonin syndrome.
- The concurrent use of a selective serotonin reuptake inhibitor and tramadol or tramadol-containing products may result in serotonin syndrome and increased risk of seizures.
- Concomitant use of venlafaxine and metoclopramide may cause serious extrapyramidal symptoms (EPS) and serotonin syndrome.
- Concomitant use of venlafaxine and selective triptans may cause rapid CNS serotonin accumulation. Monitor the patient for signs and symptoms of serotonin syndrome.
- The concurrent use of SSRIs or SNRIs and triptans may increase the risk of serotonin syndrome.
- Tapentadol should be prescribed with caution in patients taking serotonergic drugs due to the risk of developing potentially life-threatening serotonin syndrome.

Therapeutic Duplication:

- Therapeutic duplication of serotonergic antidepressant agents may be occurring. Concomitant use of these drugs may cause additive adverse effects.
- Duplicate therapy with serotonin reuptake inhibitors may be occurring. Concomitant use of these drugs may cause additive adverse effects.
- Therapeutic duplication of fluoxetine products may be occurring. Prozac/Prozac Weekly/Sarafem (fluoxetine) and Symbyax (olanzapine/fluoxetine) both contain the selective serotonin reuptake inhibitor fluoxetine.
- Therapeutic duplication of serotonin-norepinephrine reuptake inhibitors may be occurring. Concomitant use of these drugs may cause additive adverse effects.

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Beneficiary Selection

A total of 935 beneficiaries met the criteria for increased risk of serotonin syndrome. The drug history profile for each beneficiary was reviewed by a clinical pharmacist to determine if the beneficiary should be selected for intervention. Beneficiaries were not selected for intervention after the profile review for multiple reasons, including the following:

- A recent dose change from the same prescriber
- A recent change in therapy from the same prescribers
- Multiple strengths of a medication from the same prescriber

After beneficiaries were selected for intervention, educational intervention letters—along with a complete drug and diagnosis history profile listing all pharmacy and available diagnosis claims data for the past 6 months—were mailed to the appropriate prescribers. (Prior to mailing, generated letters undergo a quality assurance (QA) process. Some letters are not mailed due to various reasons, including missing or invalid prescriber addresses.)

Beneficiaries Reviewed	Beneficiaries Selected for Intervention	Beneficiaries Actually Intervened	Letters Generated	Letters Deleted in QA process	Letters Mailed
935	741	677	1,017	159	858

Once a beneficiary was selected for intervention, the criteria were suppressed by the DUR system for that beneficiary for 6 months.

Prescriber Response Tabulation

The intervention letter and drug history profile included a response form, which allowed the prescriber to provide feedback and enabled HID to determine whether any action would be taken in response to the letter. The response form includes standard responses printed on the form that allow the prescriber to check a box for the response that best fits their intended action as well as space for written in comments from the prescriber.

The prescribers were encouraged to return the response forms using the self-addressed stamped envelope included with the intervention letter or via fax. HID tracked all response forms returned as well as all written-in comments from prescribers for evaluation. See the Results section for these numbers.

Evaluation of Changes in Criteria Exceptions

In an effort to determine the impact of the intervention letters independent of prescriber responses, beneficiary claims were evaluated 6 months after letters were mailed. Since the letters were mailed in November 2010, the 6-month follow up was performed in May 2011. HID first determined how many of the initially-selected beneficiaries continued to have Medicaid benefits and still had active eligibility by determining how many had any claim for any drug in May 2011. Following that, HID determined who still met the same criteria for increased risk of serotonin syndrome in May 2011. See the Results section for these numbers.

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Estimated Cost Avoidance and Changes in Drug Utilization

To determine the impact of the intervention letters on overall drug expenditures, total drug utilization (claims for all drugs) in the targeted population was evaluated 6 months before and 6 months after intervention letters were mailed. For those beneficiaries selected for intervention in November 2010, HID determined the total drug expenditures for June 2010 – November 2010 (pre-intervention period) and December 2010 – May 2011 (post-intervention period). HID then compared drug expenditures and utilization in the targeted population for the pre- and post- intervention time frames with a comparison group to determine the estimated impact of the intervention letters.

The comparison group consisted of fee-for-service beneficiaries who were identified using the same criteria, but whose prescribers did not receive an intervention letter because they did not hit the intervention criteria in the same month that intervention letters were mailed.

For a beneficiary to be included in the analysis for either the intervention or comparison groups, he or she had to have at least one claim for any drug in the month at the beginning of the pre-intervention period (June 2010) and the month at the end of the post-intervention period (May 2011).

Estimated cost avoidance and projected drug expenditures were determined for the intervention group by using the percent change from pre-to post-intervention in both groups, using the following equations:

Estimated Cost Avoidance = Intervention Group Pre-Intervention Cost X ((% Change Comparison Group - % Change Intervention Group)/100)

Projected Drug Expenditures = Estimated Cost Avoidance + Post-Intervention Drug Expenditures

The same equations were used to determine the estimated claims avoided. See the Results section for changes in drug utilization and expenditures.

Limitations

One limitation resulted from the fact that no eligibility data was available to determine whether beneficiaries continued to be eligible for Medicaid for the full 6 months before and after intervention letters were mailed. Therefore, as a means to test for Medicaid eligibility when calculating cost avoidance, HID determined how many beneficiaries had any claim for any drug during the first month of the pre-intervention period and the last month of the post-intervention period. Those beneficiaries who did not have claims in both months were not included in the follow up analysis. It is possible that some patients may have been excluded from the follow up analysis that continued to have Medicaid eligibility but had no recent pharmacy claims.

A similar eligibility process was applied to the changes in criteria exceptions. Since the change in criteria exceptions only dealt with the month the letter was mailed and 6 months after the letter was mailed, drug claims during the month of the 6-month follow up were examined to determine eligibility.

The reduction in drug utilization and expenditures could be effected by multiple factors; it would be impossible to attribute the changes in utilization and expenditures to one thing—including the intervention letters. The comparison group is used to evaluate these factors, as many of them affect the entire Medicaid fee-for-service population.

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Results

Prescriber Responses to Intervention Letters

A total of 235 coded responses were received from prescribers who were sent an intervention letter, for a response rate of 27.4%. Out of the 235 coded responses, there were 13 response forms that had additional written comments. Coded responses are in the table below, followed by examples of written comments.

Response	Number
Benefits of the drug outweigh the risk	53
Prescriber unaware of other prescribers	7
Beneficiary no longer under this prescribers care	20
Reviewed information and continuing therapy without change	67
Prescriber will modify drug therapy	21
Tried to modify drug therapy, beneficiary is non-cooperative	2
Beneficiary has not been seen recently	8
Beneficiary was never under prescribers care	8
Has appointment to discuss therapy	11
Prescriber did not write prescription attributed to them	20
Tried to modify therapy, symptoms reoccurred	1
Prescribed medication while covering for other MD or in the ER	9
Response form returned blank	8
Total Responses	***235***

Prescriber Comments

The following statements are samples of comments received from providers via the response forms:

"Only seen as inpatient"

"I have just assumed care of this patient"

"Patient has been advised to discontinue tramadol at this time"

"Thank you for your help"

"Will hold amitriptyline"

"Will watch for any problems"

"I am aware of the interactions. Thank you"

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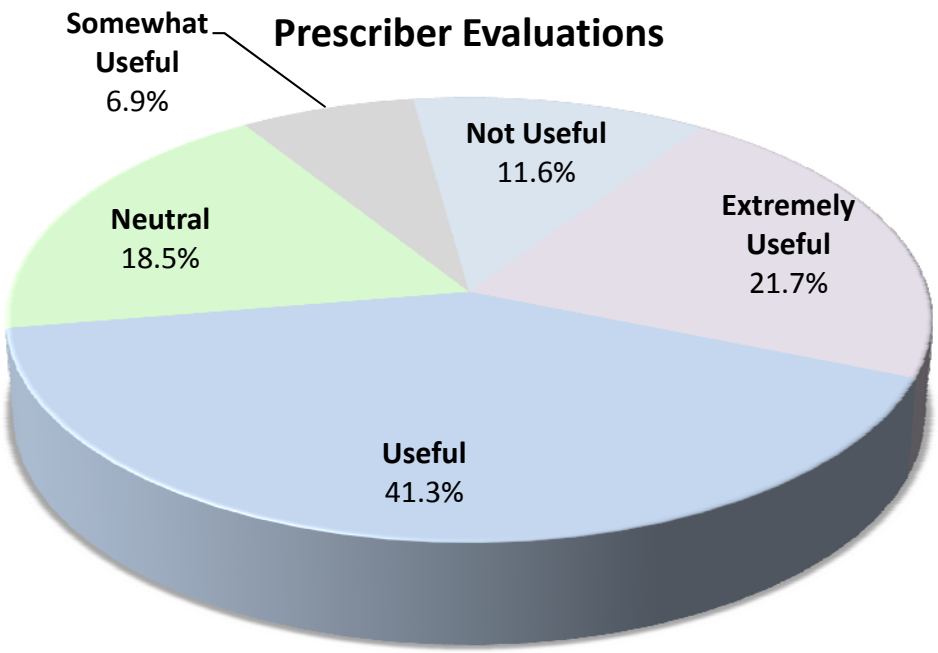
Prescriber Feedback on Intervention Letters

In addition to being able to provide information about their course of action following receipt of the intervention letter, prescribers are also able to provide additional feedback on intervention letters. Out of the 235 coded responses received, 189 provided additional feedback. A total of 63.0% of feedback responses ranked the letters as 'Useful' or 'Extremely useful'. A chart showing the percentage of responses in each evaluation category is shown below:



Changes in Criteria Exceptions

A total of 677 beneficiaries were selected for intervention based on the criteria for increased risk of serotonin syndrome. Six months after letters were mailed to the prescriber, 595 of the original 677 beneficiaries had at least one claim for any drug and could be evaluated. Of those 595 beneficiaries, 326 (54.8%) were found to hit the same criteria in the follow up period, meaning they had the same therapy problem post-intervention that their prescriber received a letter regarding. ***The remaining 269 beneficiaries (45.2%) were found to no longer have the same therapy problem that their prescriber received a letter regarding.***

Criteria	PRE-Intervention (November 2010)	POST-Intervention (May 2011)		
	Beneficiaries with Letter Mailed	Beneficiaries with Any Drug Claim	Beneficiaries with Same Criteria Exception	% Decrease in Criteria Exceptions
High Dose Alert	2	2	1	50.0%
Drug-Drug Interactions	546	478	251	47.3%
Therapeutic Duplication	129	115	74	35.5%
Totals	***677***	***595***	***326***	**45.2%**

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Total Drug Utilization and Estimated Cost Avoidance in Targeted Population

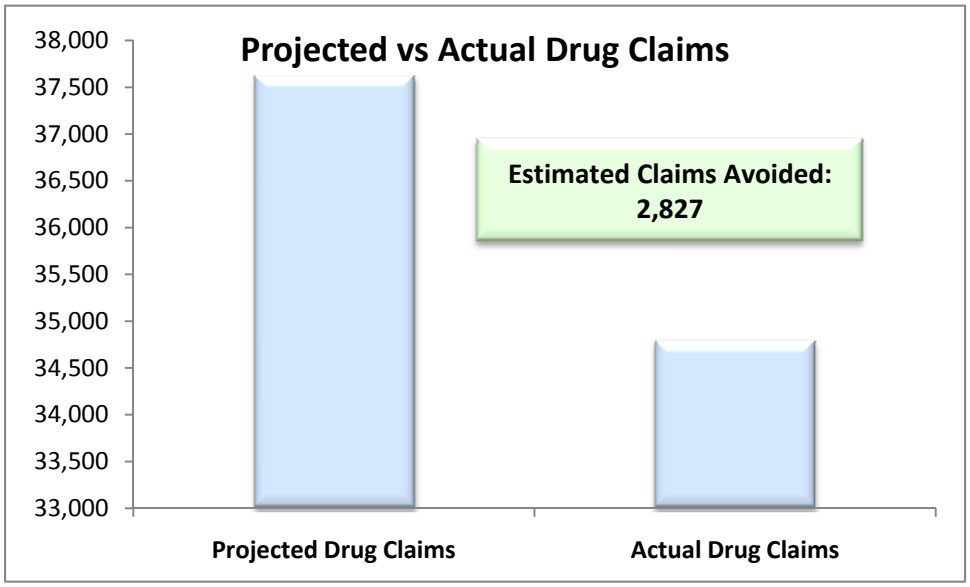
For the intervention and comparison group beneficiaries who had claims for any drug during the beginning of the pre-intervention and end of the post-intervention periods, HID evaluated total drug expenditures and claims for the 6 months prior to, and 6 months after, letters were mailed [2].

		Drug Expenditures	Drug Claims
Intervention Group	**Pre-Intervention**	$2,951,916	35,548
	Post-Intervention	$2,971,310	34,784
	Difference	$19,395	-764
	% Change	0.653%	-2.196%
Comparison Group	**Pre-Intervention**	$2,282,699	29,288
	Post-Intervention	$2,507,108	31,135
	Difference	$224,409	1,847
	% Change	8.951%	5.932%

Intervention Group: *531 beneficiaries*

Comparison Group: *476 beneficiaries*

Projected Intervention Group Post-Intervention Cost:	**$3,216,266**
Estimated Cost Avoidance:	**$244,955**
Projected Intervention Group Post-Intervention Claims:	**37,611**
Estimated Claims Avoided:	**2,827**



[2] Calculation amounts may vary slightly due to rounding

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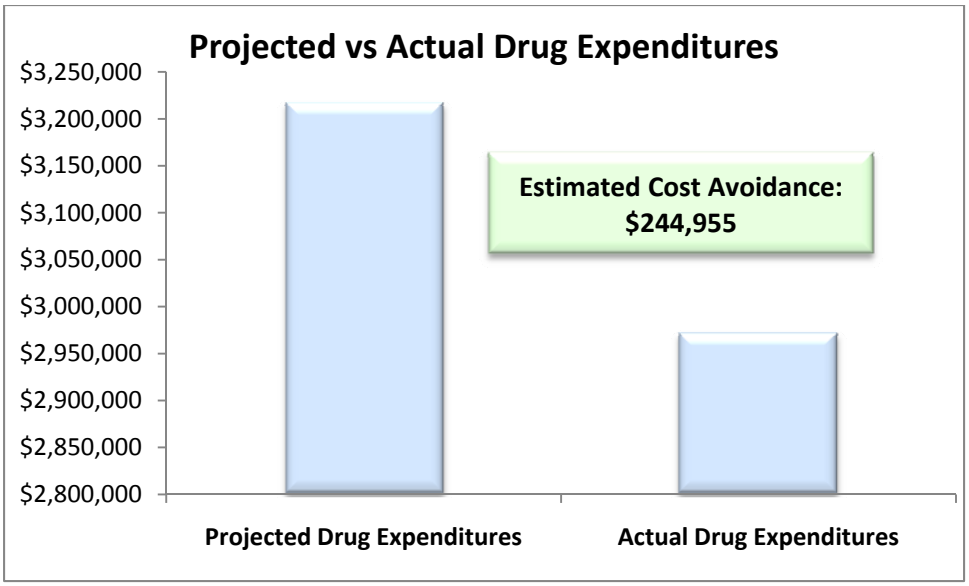

Results Discussion

Within the targeted beneficiary population, improvements in medication utilization were noted. Six months after intervention letters were mailed, a population of 595 patients had enough data available to evaluate. Of these patients, all of whom met criteria for increased risk of serotonin syndrome prior to the mailing of prescriber letters, 45.2% no longer met the same criteria 6 months after the letters were mailed.

All drug claims data and some diagnosis data is available for analysis. Any diagnosis data available is processed along with the pharmacy claims data to provide as complete a drug and diagnosis history as possible for each beneficiary. Medical data that includes the cost associated with hospitalization, doctor visits, and emergency room visits is not analyzed as part of the RetroDUR program. However, it is suspected by reducing the risk for drug interactions that may cause serotonin syndrome, other medical associated costs due to adverse drug reactions would be reduced in addition to the reduction in drug expenditures.

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Conclusion

The prescribing and utilization of serotonergic agents improved after intervention letters were mailed to prescribers for targeted beneficiaries. For beneficiaries with data available for follow up 6 months after letters were mailed, 45.2% of them no longer met the same criteria. Claims data for 6 months before and after intervention letters were mailed was evaluated and compared, showing a cost avoidance of drug expenditures of over $240,000 in the 6-month time period following the mailing of the intervention letters.

Claims data for 6 months before and after intervention letters were mailed was evaluated and compared, showing *a cost avoidance of drug expenditures of over $240,000 in the 6-month time period following the mailing of the intervention letters.*

Prescribers were encouraged to return response forms to indicate their intended action following the receipt of the intervention letter and patient profile. The response rate was 27.4%; 235 response forms were returned indicating the prescribers intended action and 189 feedback forms were returned. Prescriber feedback showed 63.0% of the feedback responses ranked the intervention letters as 'Extremely Useful' or 'Useful'.

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