

Deep Dive into the PIM and DDI Data

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Abstract

Through a contract funded by CMS, work was done to increase awareness and decrease the number of Medicare beneficiaries who have been prescribed a potentially inappropriate medication (PIM) and/or medications that could result in a drug on drug interaction (DDI). SAS 9® was used to analyze Part D claims data to track progress on improving rates as well as taking a deeper dive into the data to identify trends and opportunities for improvement. From baseline to re-measurement, Minnesota saw a relative improvement rate (RIR) of 29.3% for PIMs and 12.6% for DDIs. The nation saw RIRs of 15.4%, and 10.6%, respectively. Minnesota's PIM data showed that the biggest decrease was in the drug categories of narcotics. Compared to the actual Medicare population, there are a higher proportion of females being prescribed PIMs and DDIs. Specific counties in Minnesota were found to have worse rates of PIMs and DDIs. This paper will show the analysis done, the SAS® code used, and important findings.

Introduction

Under contract with Centers for Medicare & Medicaid Services (CMS), Stratis Health worked with health plans to reduce PIM and DDI rates in Minnesota. This work was done under contract with CMS, which ran from August 1, 2008, to July 31, 2011. The main themes of the contract were beneficiary protection, prevention, and patient safety. Tasks within the patient-safety theme included reducing nursing home pressure ulcers and physical restraints, hospital surgical care improvement project/heart failure, Methicillin-resistant *Staphylococcus aureus*, and drug safety. One goal of the drug safety work was to decrease the number of Medicare beneficiaries who are prescribed PIM and/or DDI. Another goal was to increase awareness and knowledge in the medical community about PIM and DDI.

CMS provided an analytic data set, pulled from Part D claims data, which had one record for each Medicare beneficiary that could be included in either the PIM or the DDI denominator. There were fields containing a 1 or 0 for numerator and denominator for both PIM and DDI. This data set also contained beneficiary information including race, gender, county, etc.

Potentially Inappropriate Medications in the Elderly

PIM Rates

The PIM quality measure is gathered through Part D claims data. The list of drugs used for this measure encompasses drugs found on the updated Beers list, Zhan's list, and in HEDIS® 2006 measures. The Beers list was developed by a group of 12 clinicians with expertise in geriatrics and led by Mark Beers, M.D. Released in 1991, the Beers list was initially created to help clinicians determine which medications should be avoided in nursing home patients as seniors in nursing homes are particularly at risk for suffering medication-related problems. Since then, the Beers list has been updated twice, with the most current revision released in 2003. Despite controversy, the Beers list has remained the most enduring list of drugs to be cautious of prescribing for the Medicare population. Certain medications on the list are either no longer the drugs of choice and should be replaced by better alternatives, or have no clinical justification. The Zhan criteria extends the Beers list to identify drugs that should always be avoided, are rarely appropriate, or have indications for use in elderly patients but are frequently misused. In 2006, the National Committee on Quality Assurance included drugs to avoid in the elderly as a HEDIS® measure for quality.

To be included in the PIM denominator, a Medicare beneficiary must be a Part D enrollee, 65 or older, have at least one prescription drug event (PDE) claim during the measurement period, and be enrolled for at least five months of the six-month measurement period. If a beneficiary dies during the measurement period, he or she is not included in the data. To be included in the numerator, a beneficiary must meet the denominator criteria and fill a prescription for at least one PIM during the measurement period. The PIM rate is calculated by dividing the numerator by the denominator. So, the PIM rate is calculated by taking the number of Part D enrollees with at least one PIM and dividing it by the total number of Part D enrollees over age 65 that had at least one PDE during the time frame.

The following is the SAS® code used to read in the CMS analytic data set and to calculate the numerator and denominator for the PIM rate.

```
DATA PartD;
    set partd1.partdanalytic_9sow_q10_mn;
    year='010110_063010';
run;
```

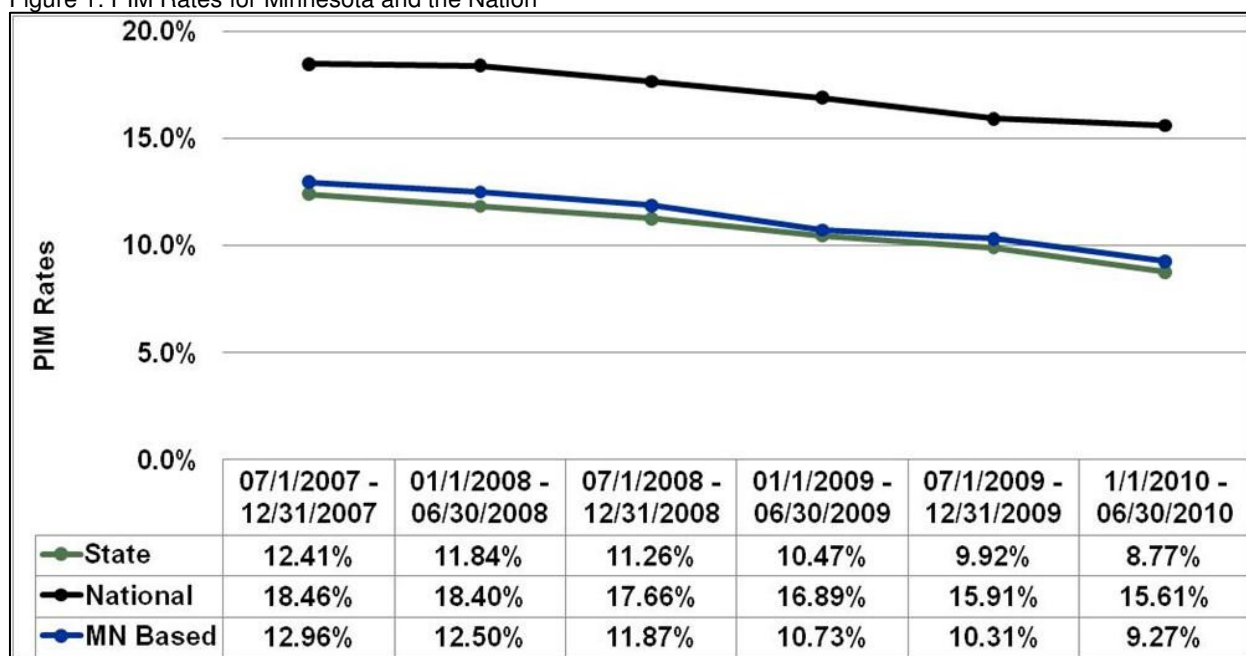
```

PROC MEANS data=partd NOPRINT;
  var PSNum1_1 PSDen1_1 PSNum1_2 PSDen1_2;
  output out=partd2.stateDDIandPIM_010110_063010
    sum=DDInum DDIden PIMnum PIMden;
run;

```

Figure 1 shows the Minnesota PIM rate compared with the National PIM rate. Lower is better. For the first two quarters of 2010, 8.77 percent of Minnesota's Part D enrollees over 65 were prescribed and filled a PIM prescription. Although Minnesota is below (better than) the national average, there is still room for improvement. When looking at the relative improvement rate, the state improved faster (-29.3 percent) than the national rate (-15.4 percent). This is comparing the last two quarters of 2007 with the first two quarters of 2010.

Figure 1: PIM Rates for Minnesota and the Nation



PIM Deep Dive

CMS also provided a PIM supplemental data set for further analysis. This data set contained a record for each PIM prescribed and filled, so multiple records for a beneficiary is likely. The data set also included a unique beneficiary ID, the national drug code (NDC) for each PIM prescribed, the prescription date, the prescriber ID, and the pharmacy provider ID. Another file used in analysis contained information about the drugs (e.g., NDC, brand name, generic name, category, etc.) that are considered to be a PIM.

The following is the SAS® code used to read in the CMS analytic data set, the supplemental data set, and a list of drugs considered to be a PIM. These three files were merged.

```

*Read in the supplemental data file for PIM*;
DATA PartDPIM;
  set partd1.pimsupplemental_9sow_q10_mn;
  year='010110_063010';
run;

*Read in the Part D analytic file for PIM and DDI*;
DATA partdselect;
  set partd1.partdanalytic_9sow_q10_mn;
  if PSNum1_2=1;
run;

*Merge Part D analytic file with PIM supplemental data*;
PROC SORT data=partdselect;
  by Bene_Clm_Num;
run;

```

```

PROC SORT data=PartDPIM;
    by Bene_Clm_Num;
run;

DATA PartDPIMmerged1;
    merge partdselect (in=ina) PartDPIM (in=inb);
    by Bene_Clm_Num;
    if ina=1 and inb=1;
run;

*Read in the NDC file*;
PROC IMPORT OUT= WORK.NDClst
    DATAFILE= "S:\9SOW\PS_DrugSafety\From_CMS_NDC_2007_CMS.xls"
    DBMS=EXCEL REPLACE;
    SHEET="HEDIS_DAE_PIM";
    GETNAMES=YES;
    MIXED=NO;
    SCANTEXT=YES;
    USEDATE=YES;
    SCANTIME=YES;
RUN;

*Merge PartDPIMmerged1 with NDC list*;
PROC SORT data=PartDPIMmerged1;
    by Product_Service_Id;
run;

PROC SORT data=NDClst;
    by Product_Service_Id;
run;

DATA PartDPIMmerged;
    merge PartDPIMmerged1 (in=ina) NDClst (in=inb);
    by Product_Service_Id;
    if ina=1 and inb=1;
run;

```

The following is the SAS® code used to calculate the frequencies of PIM by brand name.

```

*PIM frequencies by Brand Name*;
PROC SORT data=PartDPIMmerged out=PartDPIMmerged2 nodupkey;
    by contract_number bene_clm_num Brand_Name;
run;

PROC FREQ data=PartDPIMmerged2 order=freq;
    table Brand_Name / out=Brand_Name_freq;
run;

```

Figure 2 shows the top 10 PIM in Minnesota for the first two quarters of 2010. Most of these are the generic names as they show up as prescribed most often. For the drug class other, nitrofurantoin monohydrate/macrocrystals (Macrobid) is number one on the list, and nitrofurantoin macrocrystals (Macrochantin) is number seven. These drugs are commonly used to treat urinary tract infections in women. The concern is that they may cause renal impairment, especially with long-term use. There is also a risk of chronic pulmonary reactions, particularly in long-term usage. Other side effects include nerve damage, anemia, nausea, vomiting, vertigo, fever, and rash.

For the drug class skeletal muscle relaxants, Cyclobenzaprine Hydrochloride (Flexeril) is number two on the list, and methocarbamol (Robaxin) is number eight. The concern is that most muscle relaxants are poorly tolerated by elderly patients, causing anticholinergic adverse effects (dizziness, dry mouth, and constipation), sedation, and weakness. Due to the relaxant effects, there is an increased potential for falls and bone fractures.

For the drug class narcotics, acetaminophen-propoxyphene napsylate (Darvocet) is number three on the list, and Propacet 100 is number nine. The concern is that these drugs offer few analgesic advantages over acetaminophen. Also, there is an increased potential for falls and bone fractures due to the sedative effects on the central nervous system. These drugs also may cause confusion.

For the drug class oral estrogens, Premarin is number four on the list. The concern is no cardioprotective effect and a significant risk of carcinogenic effects (breast and endometrial cancer).

For the drug class antihistamines/antispasmodics, hydrOXYzine pamoate (Vistaril) is number five on the list, and dicyclomine hydrochloride (Bentyl) is number 10. The concern is that potent anticholinergic properties can cause sedation, weakness, blood pressure changes, dry mouth, problems with urination, and can lead to falls.

For the drug class belladonna alkaloids atropine SO4-diphenoxylate HCl (Lomotil, Lomocot, Lonox, Vi-Atro) is number six on the list. The concern is that effectiveness is uncertain and they are strongly anticholinergic. Use should be avoided, especially long-term use.

Figure 2: Top 10 PIM in Minnesota by Brand Name

Statewide - Minnesota 01/01/2010 - 06/30/2010 PIM Rate = 32472/370125 = 8.77%			
Brand Name	Bene Percent	Bene Count	Prescript Count
Nitrofurantoin Monohydrate/Macrocrystals	18.5%	7229	10655
Cyclobenzaprine Hydrochloride	16.2%	6332	10743
Acetaminophen-Propoxyphene Napsylate	12.8%	4979	10062
Premarin	10.7%	4191	10415
HydrOXYzine Pamoate	6.8%	2652	4368
Atropine SO4-Diphenoxylate HCl	5.2%	2013	4275
Nitrofurantoin Macrocrystals	4.8%	1884	4045
Methocarbamol	3.5%	1374	2620
Propacet 100	2.7%	1055	2109
Dicyclomine Hydrochloride	2.1%	825	1760

The following SAS® code calculates the frequencies of PIM by drug category.

```
*PIM frequency by drug category*;
PROC SORT data=PartDPIMmerged out=PartDPIMmerged3 nodupkey;
    by contract_number bene_clm_num category;
run;

PROC FREQ data=PartDPIMmerged3 order=freq;
    table category/out=PIMcategoryCount;
run;
```

Figure 3 shows the top 10 drug categories for PIM in Minnesota for the first two quarters of 2010.

Figure 3: Top 10 Drug Categories for PIM in Minnesota

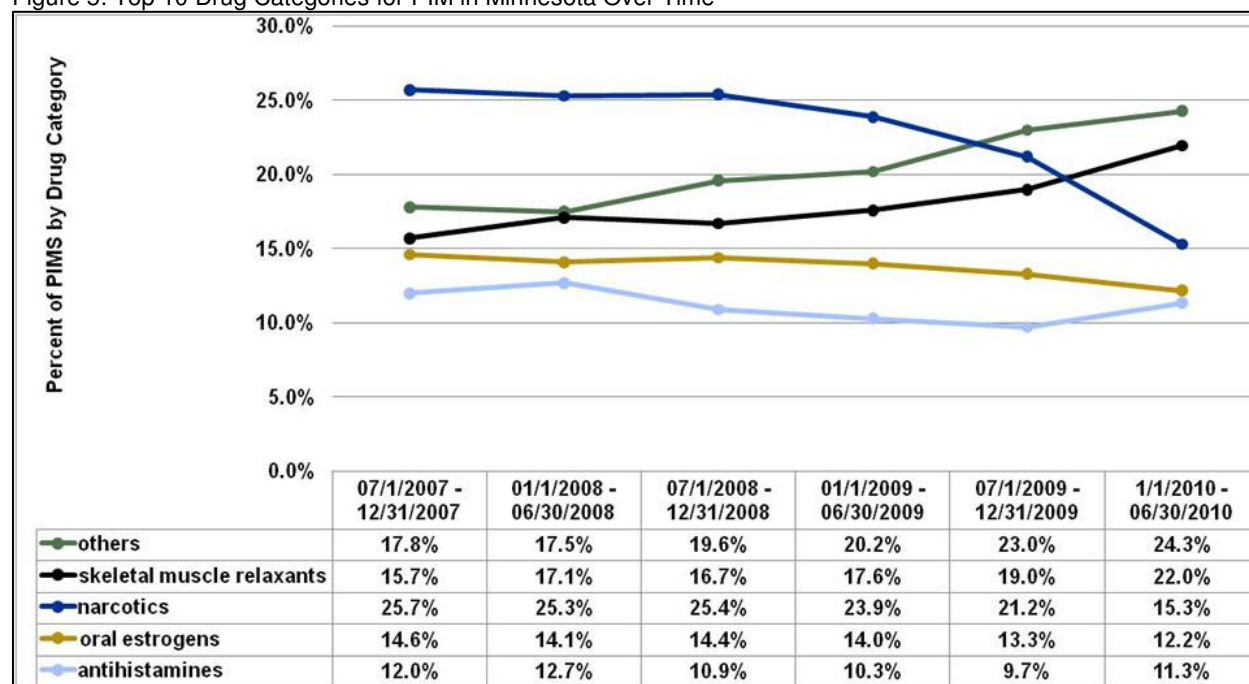
Statewide - Minnesota 01/01/2010 - 06/30/2010		
Drug Category	Bene Percent	Bene Count
others	24.3%	8610
skeletal muscle relaxants (including combinations)	22.0%	7779
narcotics (including combinations)	15.3%	5427
oral estrogens (including combinations)	12.2%	4314
antihistamines (including combinations)	11.3%	4017
belladonna alkaloids (including combinations)	5.7%	2034
amphetamines	2.9%	1042
gastrointestinal antispasmodics	2.2%	779
analgesics (including combinations)	1.3%	444
antiemetics	1.1%	391

Figures 4 and 5 show the top 10 drug categories for PIM in Minnesota from the last two quarters of 2007 to the first two quarters of 2010. The use of narcotics has decreased considerably in three years of data.

Figure 4: Top 10 Drug Categories for PIM in Minnesota Over Time

Statewide - Minnesota 01/01/2010 - 06/30/2010						
Drug Category	07/1/2007 - 12/31/2007	01/1/2008 - 06/30/2008	07/1/2008 - 12/31/2008	01/1/2009 - 06/30/2009	07/1/2009 - 12/31/2009	1/1/2010 - 06/30/2010
others	17.8%	17.5%	19.6%	20.2%	23.0%	24.3%
skeletal muscle relaxants (including combinations)	15.7%	17.1%	16.7%	17.6%	19.0%	22.0%
narcotics (including combinations)	25.7%	25.3%	25.4%	23.9%	21.2%	15.3%
oral estrogens (including combinations)	14.6%	14.1%	14.4%	14.0%	13.3%	12.2%
antihistamines (including combinations)	12.0%	12.7%	10.9%	10.3%	9.7%	11.3%
belladonna alkaloids (including combinations)	6.2%	5.6%	5.1%	5.5%	5.1%	5.7%
amphetamines	2.1%	2.0%	2.1%	2.4%	2.5%	2.9%
gastrointestinal antispasmodics	1.9%	2.0%	2.3%	2.4%	2.7%	2.2%
analgesics (including combinations)	1.0%	0.9%	1.0%	1.0%	1.0%	1.3%
antiemetics	0.9%	0.8%	0.8%	0.9%	0.9%	1.1%

Figure 5: Top 10 Drug Categories for PIM in Minnesota Over Time



One must remember that these are more than numbers, they reflect real people. The following is the SAS® code used to calculate the frequencies of PIM by the first name of the beneficiary.

```
DATA partdselect;
    set partd1.partdanalytic_9sow_q10_mn;
    if PSNum1_2=1;
run;

PROC FREQ data=partdselect order=freq;
    table Gender*FIRST_NAME/ out=PIMFIRST_NAMECount;
run;
```

Figure 6 shows the top five female and male first names prescribed a PIM in the first two quarters of 2010.

Figure 6: Top Five Female and Male First Names with At Least One PIM
32,472 Medicare beneficiaries with PIM

Females	Males
1,003 Mary	358 Robert
548 Patricia	308 Richard
467 Barbara	301 James
466 Dorothy	301 John
442 Carol	231 Donald

The following SAS® code calculates the frequencies of PIM by the beneficiary's gender and race.

```
PROC FREQ data=partdselect order=freq;
    table GENDER/out=PIMGENDERCount;
run;

PROC FREQ data=partdselect order=freq;
    table RACE/out=PIMRACECount;
run;
```

Figure 7 shows the frequency of PIM by gender and race for the first two quarters of 2010.

Figure 7: PIM frequencies by Gender and Race
32,472 Medicare beneficiaries with PIMs

Gender	Race
25,261 (77.8%) Female	31,064 (95.7%) White
7,211 (22.2%) Male	512 (1.6%) Black
	295 (0.9%) Asian
	281 (0.9%) Native American
	218 (0.7%) Other
	72 (0.2%) Hispanic
	30 (0.1%) Unknown

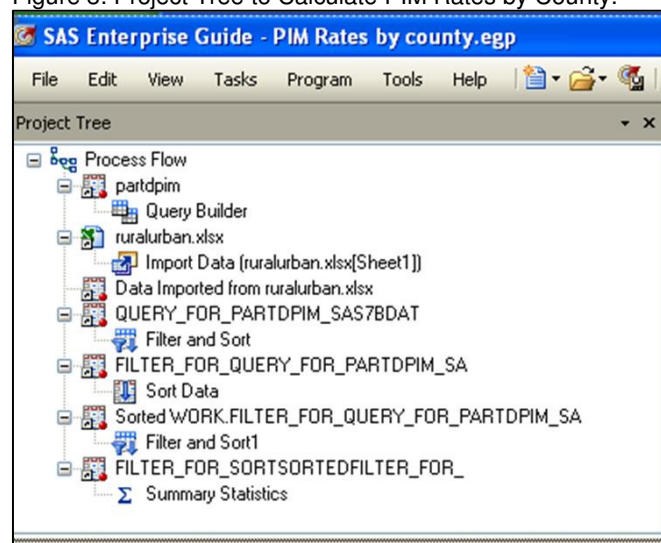
The PIM gender proportion is much different than the Medicare population in Minnesota, which is approximately 55 percent female. However, the PIM race proportion is about the same as the Medicare population in Minnesota, which is about 95 percent white.

The following SAS® code reads in the CMS analytic data set, including only the beneficiaries in which the PIM denominator is equal to 1. Because the Zip code in the data set is 10 digits, a new variable is created to allow for a five-digit Zip code.

```
DATA partd2.partdPIM;
    set partd1.partdanalytic_9sow_q10_mn;
    ZIPCODE5 = substr(ZIPCODE,1,5);
    if PSDen1_2=1;
run;
```

SAS Enterprise Guide® combines the newly formed data set with an existing data set that contains Minnesota Zip codes, corresponding county names, and rural/urban status. These tables are merged and the PIM numerator and denominator are calculated for each county in Minnesota. Figure 8 shows the project tree flow created in SAS Enterprise Guide®.

Figure 8: Project Tree to Calculate PIM Rates by County.



The following is a portion of the SAS® code that is generated from SAS Enterprise Guide®.

```
PROC MEANS DATA=WORK.SORTTempTableSorted
    FW=12
    PRINTALLTYPES
    CHARTYPE
        SUM
        N
    ;
    VAR PNum1_2 PSDen1_2;
    BY County;
    OUTPUT OUT=WORK.MEANSummaryStats(LABEL=
    "Summary Statistics for WORK.FILTER_FOR_SORTSORTEDFILTER_FOR_"
        SUM()=
        N()=
    / AUTONAME AUTOLABEL INHERIT;
RUN;
```

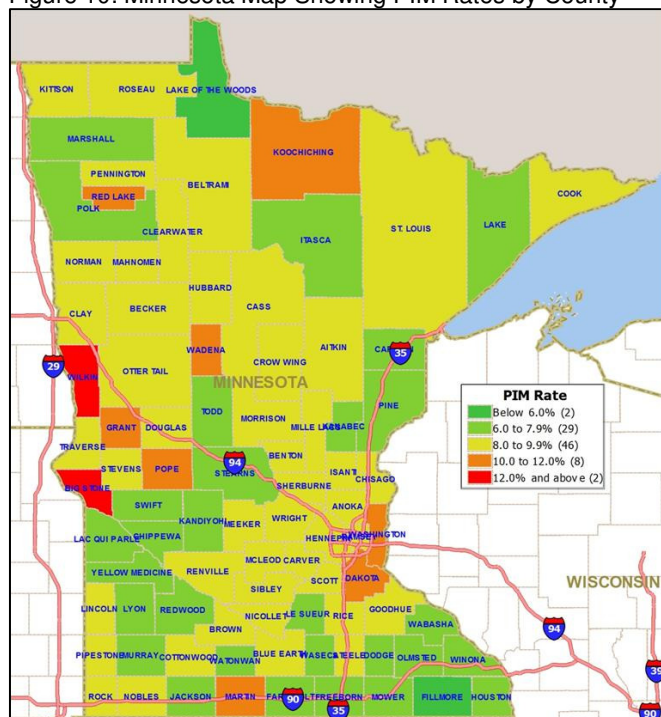
Figure 9 shows the five counties with the best PIM rates and the five counties with the worst PIM rates for the first two quarters of 2010. Remember that the actual state rate is 8.77 percent.

Figure 9: Top 5 Best PIM Rates and Worst PIM Rates by County

Best PIM Rates	Worst PIM Rates
Lake of the Woods 4.1%	Big Stone 12.8%
Fillmore 5.7%	Wilkin 12.6%
Olmsted 6.2%	Wadena 11.1%
Dodge 6.3%	Koochiching 11.0%
Lac Qui Parle 6.4%	Grant 10.5%

The PIM rates by county are brought into Maptitude, a mapping software, to generate a map of Minnesota. See Figure 10. The counties in yellow are about average. Orange and red counties are worse than average (e.g., Big Stone and Wilkin). Green counties are better than average (e.g., Lake of the Woods and Fillmore).

Figure 10: Minnesota Map Showing PIM Rates by County



The following SAS® code calculates the frequencies of PIM by the prescriber ID (i.e., National Provider Identifier (NPI)).

```
PROC FREQ data=PartDPIM order=freq;
    table Prescriber_Id /out=PIMPrescriberCount;
run;
```

The number of PIM prescribed by 10,995 different prescribers, ranged from one to 165 in the first two quarters of 2010.

- 10,342 prescribed 1 to 25 (3,703 prescribed 1)
- 546 prescribed 26 to 50
- 86 prescribed 51 to 75
- 13 prescribed 76 to 100
- 5 prescribed 101 to 125
- 2 prescribed 126 to 150
- 1 prescribed over 150 (1 prescribed 165)

The following SAS® code calculates the frequencies of PIM by the pharmacy ID (i.e., NPI).

```
PROC FREQ data=PartDPIM order=freq;
    table Service_Provider_Id /out=PIMPharmacyCount;
run;
```


The number of PIM prescriptions filled by 2,259 different pharmacies, ranged from one to 1,217 in the first two quarter of 2010.

- 2,049 filled 1 to 100 (614 filled 1)
- 181 filled 101 to 200
- 19 filled 201 to 300
- 5 filled 301 to 400
- 1 filled 401 to 500
- 0 filled 501 to 600
- 2 filled 601 to 700
- 1 filled 701 to 800
- 1 filled over 800 (1 filled 1,217)

Drug on Drug Interactions

DDI Rates

The DDI measure describes the percentage of Part D enrollees with claims for drugs that could potentially interact. It does not measure the effect or outcome of DDI. The effects from potential drug interactions vary in significance for each pair. The object drug is the drug in which effects or pharmacokinetics are impacted by subsequent administration of another drug. The precipitant drug triggers the change in effects or pharmacokinetics of another drug being administered. Drug interactions resulting in increased morbidity, mortality, and higher economic costs is a widely recognized public health issue.

To be included in the denominator, a Medicare beneficiary must be a Part D enrollee, have at least one PDE claim for one of the object or precipitant drugs selected for DDI during the measurement period, and enrolled for at least five months of the six-month measurement period. Although the DDI denominator includes beneficiaries under age 65, it is smaller than the PIM denominator because a beneficiary has to be prescribed either an object or precipitant drug during the measurement period. If a beneficiary dies during the measurement period, he or she is not included in the data. To be included in the numerator, a beneficiary must meet the denominator criteria and have at least one DDI during the measurement period. The DDI rate is calculated by dividing the numerator by the denominator. So, the DDI rate is calculated by taking the number of Part D enrollees with at least one DDI and dividing it by the total number of Part D enrollees that had at least one PDE for at least one of the object or precipitant drugs during the specific time frame.

The following is the SAS® code used to read in the CMS analytic data set and to calculate the numerator and denominator for the DDI rate.

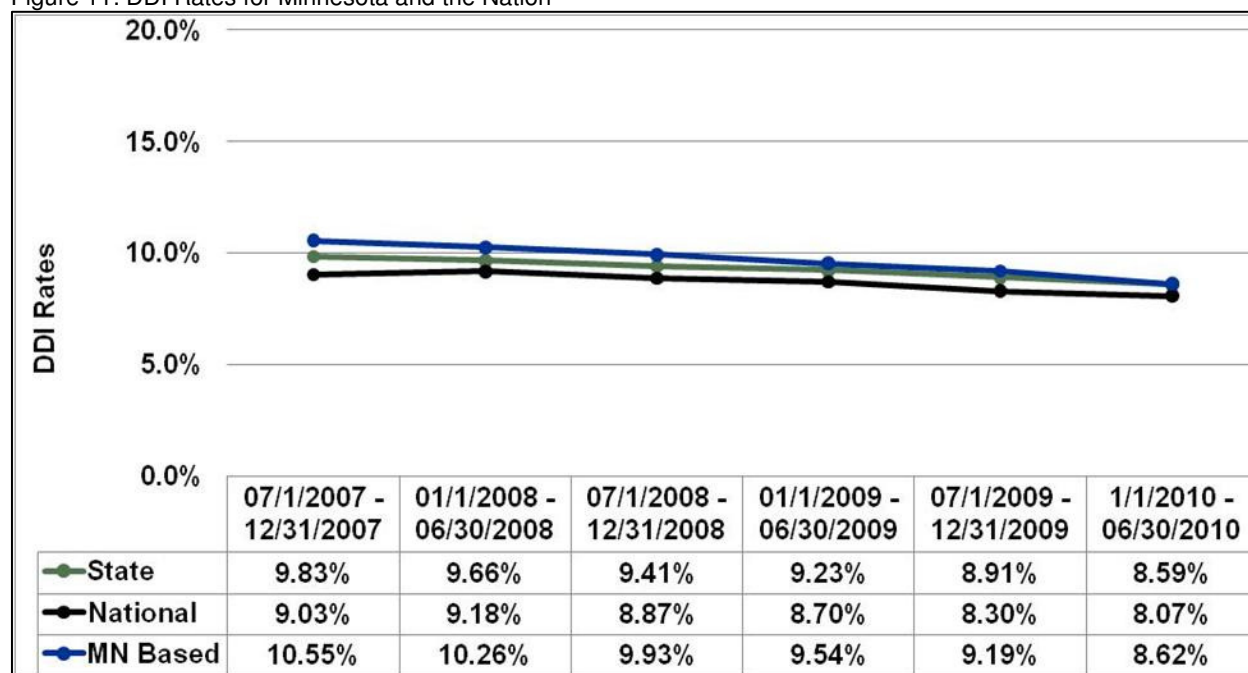
```
DATA PartD;
    set partd1.partdanalytic_9sow_q10_mn;
    year='010110_063010';
run;

PROC MEANS data=partd NOPRINT;
    var PSNum1_1 PSDen1_1 PSNum1_2 PSDen1_2;
    output out=partd2.stateDDIandPIM_010110_063010 sum=DDInum DDIden PIMnum PIMden;
run;
```

Figure 11 shows the Minnesota DDI rate compared with the National DDI rate. Again, lower is better. For the first two quarters of 2010, 8.59 percent of Part D enrollees with at least one precipitant or object drug PDE had at least one DDI.

Minnesota is doing slightly worse than the national average, so there is room for improvement. When looking at the RIR, the state, again, improved faster (-12.61 percent) than the national rate (-10.63 percent). Even better, the Minnesota-based health plans improved at a rate of -18.29 percent. This is comparing the last two quarters of 2007 with the first two quarters of 2010.

Figure 11: DDI Rates for Minnesota and the Nation



DDI Deep Dive

CMS also provided a DDI supplemental data set for further analysis. This data set contained a record for each DDI prescribed and filled, so multiple records for a beneficiary are common. The data set also included a unique beneficiary ID, the national drug code (NDC) for the object and precipitant drugs prescribed, the prescription dates, the prescriber ID for both drugs, and the pharmacy provider ID for both drugs. Another file used in analysis contained information about the drugs (e.g., NDC, brand name, generic name, drug category, etc.) that are considered to be either an object or precipitant drug involved in a DDI.

The following is the SAS® code used to read in the CMS analytic data set, the supplemental data set, a list of precipitant drugs, and a list of object drugs. These four files were merged.

```
DATA PartDDDI;
    set partd1.ddisupplemental_9sow_q10_mn;
    year='010110_063010';
run;

DATA partdselect;
    set partd1.partdanalytic_9sow_Q10_mn;
    if PSNum1_1=1;
run;

PROC SORT data=partdselect;
    by Bene_Clm_Num;
run;

*Merge Part D analytic file with DDI supplemental data*;
PROC SORT data=PartDDDI;
    by Bene_Clm_Num;
run;

DATA PartDDDImerged1;
    merge partdselect (in=ina) PartDDDI (in=inb);
    by Bene_Clm_Num;
    if ina=1 and inb=1;
run;
```

```

*Read in the NDC file-PRECIPITANT DDI*;
PROC IMPORT OUT= WORK.PrecDDI
    DATAFILE= "S:\9SOW\PS_DrugSafety\From_CMS_NDC_2007_CMS.xls"
    DBMS=EXCEL REPLACE;
    SHEET="DDI_PRECIPITANT";
    GETNAMES=YES;
    MIXED=NO;
    SCANTEXT=YES;
    USEDATE=YES;
    SCANTIME=YES;
RUN;

*Merge PartDPIMmerged1 with Precipitant NDC list*;
PROC SORT data=PartDDDImerged1;
    by Prec_NDC;
run;

PROC SORT data=PrecDDI;
    by Prec_NDC;
run;

DATA PartDDDImerged2;
    merge PartDDDImerged1 (in=ina) PrecDDI (in=inb);
    by Prec_NDC;
    if ina=1 and inb=1;
run;

*Read in the NDC file-Object DDI*;
PROC IMPORT OUT= WORK.ObjDDI
    DATAFILE= "S:\9SOW\PS_DrugSafety\From_CMS_NDC_2007_CMS.xls"
    DBMS=EXCEL REPLACE;
    SHEET="DDI_OBJECT";
    GETNAMES=YES;
    MIXED=NO;
    SCANTEXT=YES;
    USEDATE=YES;
    SCANTIME=YES;
RUN;

PROC SORT data=PartDDDImerged2;
    by Obj_NDC;
run;

PROC SORT data=ObjDDI;
    by Obj_NDC;
run;

DATA PartDDDImerged;
    merge PartDDDImerged2 (in=ina) ObjDDI (in=inb);
    by Obj_NDC;
    if ina=1 and inb=1;
    DDI_Prec_Obj_Brand_Name=Prec_Brand_Name||Obj_Brand_Name;
run;

```

The following is the SAS® code use to calculate the frequencies of DDI by precipitant and object drug brand names.

```

*DDI frequencies by Brand Name*;
PROC SORT data=PartDDDImerged out=PartDDDImerged3 nodupkey;
    by contract_number bene_clm_num DDI_Prec_Obj_Brand_Name;
run;

PROC FREQ data=PartDDDImerged3 order=freq;
    table DDI_Prec_Obj_Brand_Name /out=Brandcount;
run;

```

```

PROC SORT data=Brandcount;
  by DDI_Prec_Obj_Brand_Name;
run;

PROC SORT data=PartDDDImerged3;
  by DDI_Prec_Obj_Brand_Name;
run;

DATA Brandcount2 (keep=DDI_Prec_Obj_Brand_Name COUNT PERCENT prec_brand_name
Obj_brand_name);
  merge Brandcount (in=ina) PartDDDImerged3 (in=inb);
  by DDI_Prec_Obj_Brand_Name;
  if ina=1;
run;

PROC SORT data=Brandcount2 out=partd2.State_DDIxBrand_bene_fixed nodupkey;
  by prec_brand_name Obj_brand_name;
Run;

```

Figure 12 shows the top 10 DDI in Minnesota for the first two quarters of 2010. Again, most of these are the generic names as they show up as prescribed the most often. Examining the list by object brand name, many of the interactions are actually necessary and acceptable, if they are monitored. For the Warfarin/Jantoven (coumarin anticoagulants) interactions, levothyroxine sodium (thyroid hormone) with Warfarin is number one on the list. Levothyroxine sodium with jantoven is number three on the list. Amiodarone HCL (antiarrhythmics type III) with Warfarin is number seven on the list. Azithromycin (a macrolide antibiotic) with Warfarin is number five on the list. Ciproflaxin HCL (a flouroquinolone antibiotic) with Warfarin is number six on the list and Sulfamethoxazole/Trimethoprim (a sulfa drug) with Warfarin is number nine. The concern for each of these is an increased bleeding risk. There are no alternatives. As long as international normalized ratio (INR) is consistent, chronic use is acceptable. If the dose of either medication changes, regular INR should be taken until consistent. For antibiotic interactions, consider microbial identification and sensitivity testing before initiation. Use alternative antibiotic if possible.

For the Lisinopril (ACE inhibitor) interactions, triamterene/hydrochlorothiazide (Dyazide, Maxzide) (diuretic combinations) is number two on the list and spironolactone (aldactone) (potassium sparing diuretics) is number four. The concern is an increase in potassium levels. There are no alternatives, and heart failure guidelines actually recommend this combination. Potassium levels should be monitored when a patient starts these medications, doses change, or a medication is discontinued.

For Clonidine HCL (antiadrenergic antihypertensives) interactions, atenolol (beta blockers cardio-selective) (tenormin) is number eight on the list, and metoprolol tartrate (beta blockers cardio-selective) (Lopressor) is number 10. The concern is possible bradycardia (slow heart rate). Also, if the beta blocker is discontinued while Clonidine is continued, rebound hypertension may occur. There are alternatives, so this DDI could be avoided.

Figure 12: Top 10 DDI in Minnesota by Brand Name

Statewide - Minnesota 01/01/2010 - 06/30/2010 DDI Rate = 30146/350766 = 8.59%				
Precipitant Brand Name	Object Brand Name	Bene Percent	Bene Count	Prescript Count
LEVOTHYROXINE SODIUM	WARFARIN SODIUM	20.4%	10393	37946
TRIAMTERENE/HYDROCHLOROTHIAZIDE	LISINOPRIL	11.2%	5711	19024
LEVOTHYROXINE SODIUM	JANTOVEN	5.9%	3007	11487
SPIRONOLACTONE	LISINOPRIL	5.9%	2987	10460
AZITHROMYCIN	WARFARIN SODIUM	4.6%	2337	2786
CIPROFLOXACIN HCL	WARFARIN SODIUM	3.9%	2005	2545
AMIODARONE HCL	WARFARIN SODIUM	3.1%	1603	4631
ATENOLOL	CLONIDINE HCL	3.1%	1566	5698
SULFAMETHOXAZOLE/TRIMETHOPRIM DS	WARFARIN SODIUM	2.6%	1325	2176
METOPROLOL TARTRATE	CLONIDINE HCL	2.5%	1258	4724

The following is the SAS® code used to calculate the frequencies of DDI by drug categories.

```
*DDI frequency by drug category*;
PROC SORT data=PartDDDImerged out=PartDDDImerged2 nodupkey;
    by contract_number bene_clm_num Prec_Obj_Category;
run;

PROC FREQ data=PartDDDImerged2 order=freq;
    table Prec_Obj_Category/out=DDIcategoryCount;
run;
```

Figure 13 shows the top 10 drug categories for DDI in Minnesota for the first two quarters of 2010.

Figure 13: Top 10 Drug Categories for DDI in Minnesota

Statewide - Minnesota 01/01/2010 - 06/30/2010			
Precipitant Category	Object Category	Bene Percent	Bene Count
THYROID HORMONES	COUMARIN ANTICOAGULANTS	23.3%	8354
DIURETIC COMBINATIONS	ACE INHIBITORS	15.2%	5451
BETA BLOCKERS CARDIO-SELECTIVE	ANTIADRENERGIC ANTIHYPERTENSIVES	7.3%	2622
POTASSIUM SPARING DIURETICS	ACE INHIBITORS	7.3%	2602
AZITHROMYCIN	COUMARIN ANTICOAGULANTS	6.8%	2430
FLUOROQUINOLONES	COUMARIN ANTICOAGULANTS	6.4%	2288
DIURETIC COMBINATIONS	ANGIOTENSIN II RECEPTOR ANTAGONISTS	6.3%	2246
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)	COUMARIN ANTICOAGULANTS	4.5%	1617
ANTIARRHYTHMICS TYPE III	COUMARIN ANTICOAGULANTS	4.4%	1586
ANTI-INFECTIVE MISC. - COMBINATIONS	COUMARIN ANTICOAGULANTS	4.2%	1497

In an effort to again show that these numbers represent real people, the following is the SAS® code used to calculate the frequencies of DDI by the first name of the beneficiary.

```
DATA partdselect;
    set partd1.partdanalytic_9sow_q10_mn;
    if PSNum1_1=1;
run;

PROC FREQ data= partdselect order=freq;
    table Gender*FIRST_NAME/ out=DDIFIRST_NAMECount;
run;
```

Figure 14 shows the top five female and male first names prescribed a DDI in the first two quarters of 2010.

Figure 14: Top 5 Female and Male Names with At Least One DDI

30,146 Medicare beneficiaries with DDI

Females	Males
639 Mary	484 Robert
403 Dorothy	446 John
344 Patricia	422 James
301 Shirley	378 Richard
291 Betty	350 Donald

The following SAS® code calculates the frequencies of DDI by the beneficiaries' gender and race.

```
PROC FREQ data= partdselect order=freq;
  table GENDER/out=DDIGENDERCount;
run;

PROC FREQ data= partdselect order=freq;
  table RACE/out=DDIRACECount;
run;
```

Figure 15 shows the frequency of DDI by gender and race for the first two quarters of 2010.

Figure 15: DDI frequencies by Gender and Race

30,146 Medicare Beneficiaries with DDIs

Gender	Race
19,674 (65.3%) Female	28,725 (95.3%) White
10,472 (34.7%) Male	804 (2.7%) Black
	180 (0.6%) Other
	179 (0.6%) Asian
	175 (0.6%) Native American
	51 (0.2%) Hispanic
	32 (0.1%) Unknown

Although not as big a difference as PIM, the DDI gender proportion is different than the Medicare population in Minnesota, which is approximately 55 percent female. The DDI race proportion is similar to the Medicare population in Minnesota, which is also about 95 percent white.

The following SAS® code reads in the CMS analytic data set, includes only the beneficiaries in which the DDI denominator is equal to one. Since the Zip code in the data set is 10 digits, a new variable is created to allow for a five-digit Zip code.

```
DATA partd2.partdDDI;
  set partd1.partdanalytic_9sow_q10_mn;
  ZIPCODE5 = substr(ZIPCODE,1,5);
  if PSDen1_1=1;
run;
```

SAS Enterprise Guide® is used to combine this newly formed data with existing data that contains Minnesota Zip codes, corresponding county names, and rural/urban status. These tables are merged and the DDI numerator and denominator are calculated for each county in Minnesota.

Figure 16 shows the project tree flow created in SAS Enterprise Guide®.

Figure 16: Project Tree to Calculate DDI Rates by County.



The following is a portion of the SAS® code that is generated from SAS Enterprise Guide®.

```
PROC MEANS DATA=WORK.SORTTempTableSorted
  FW=12
  PRINTALLTYPES
  CHARTYPE
    SUM NONOBS ;
  VAR PSNum1_1 PSDen1_1;
  BY County;
  OUTPUT OUT=WORK.MEANSummaryStats(LABEL=
    "Summary Statistics for WORK.FILTER_FOR_QUERY_FOR_PARTDD_0000")
    SUM() =
  / AUTONAME AUTOLABEL INHERIT;
RUN;
```

Figure 17 shows the five counties with the best DDI rates and the five counties with the worst DDI rates for the first two quarters of 2010. Remember that the actual state rate is 8.59 percent.

Figure 17: Top Five Best DDI Rates and Worst DDI Rates by County

Best DDI Rates	Worst DDI Rates
Todd 7.5%	Stevens 14.6%
Morrison 7.6%	Houston 12.4%
Olmsted 7.6%	McLeod 11.5%
Carver 7.8%	Martin 11.4%
Watsonwan 7.9%	Nicollet 11.2%

The DDI rates by county are brought into Maptitude, a mapping software, to generate a map of Minnesota. See Figure 18. The counties in yellow are about average. Orange and red counties are worse than average (e.g., Stevens and Houston). Green counties are better than average (e.g., Todd, Morrison, Olmsted, Carver, and Watsonwan).

DDI Rate

- Below 6.0% (0)
- 6.0 to 7.9% (5)
- 8.0 to 9.9% (63)
- 10.0 to 11.9% (17)
- 12.0% and above (2)

```
PROC FREQ data=PartDDDImerged order=freq;
    table prec_prescriber_id /out=DDIPrecPrescriberCount;
run;

PROC FREQ data=PartDDDImerged order=freq;
    table obj_prescriber_id /out=DDIObjPrescriberCount;
run;
```

Figure 19: Number of Prescriptions for Precipitant and Object Drug Prescribers

9,402 Precipitant Prescribers	8,084 Object Prescribers
8,581 prescribed 1 to 50 (1782 prescribed 1)	7,223 prescribed 1 to 50 (1120 prescribed 1)
606 prescribed 51 to 100	637 prescribed 51 to 100
163 prescribed 101 to 150	162 prescribed 101 to 150
38 prescribed 151 to 200	48 prescribed 151 to 200
10 prescribed 201 to 250	10 prescribed 201 to 250
3 prescribed 251 to 300	3 prescribed 251 to 300
1 prescribed over 300 (1 prescribed 314)	1 prescribed over 300 (1 prescribed 311)

16

```

DATA PartDDDImerged (drop=category);
    merge PartDDDImerged2 (in=ina) ObjDDI (in=inb);
    by Obj_NDC;
    if ina=1 and inb=1;
    if prec_prescriber_id = obj_prescriber_id then same_prescriber="Yes";
    if prec_prescriber_id ne obj_prescriber_id then same_prescriber="No ";
run;

PROC FREQ data=PartDDDImerged order=freq;
    table same_prescriber/ out=DDIsame_prescriberCount;
run;

DATA diffprescriber;
    set PartDDDImerged;
    if same_prescriber="No ";
run;

*DDI frequency by same_prescriber*;
PROC FREQ data=diffprescriber order=freq;
    table prec_prescriber_id/ out=DDIsame_prec_prescriberCount;
run;

PROC FREQ data=diffprescriber order=freq;
    table obj_prescriber_id/ out=DDIsame_obj_prescriberCount;
run;

```

Analysis of the DDI supplemental data set showed that 111,611 (72.2 percent) DDI had the same prescribers for precipitant and object drug and 43,007 (27.8 percent) had different prescribers. For the group of DDI that had different prescribers, 7,488 precipitant prescribers ranged from one to 91 prescriptions and 6,225 object prescribers ranged from one to 131 prescriptions.

The following SAS® code looks at the top 10 DDI drug categories and calculates the number of same prescribers and different prescribers by drug category. This analysis was conducted to determine if there are any that have a higher number of instances of different prescribers.

```

DATA topprecobjcats;
    set PartDDDImerged;
    if Prec_Obj_Category = "THYROID HORMONES ... COUMARIN ANTICOAGULANTS" or
        Prec_Obj_Category = "DIURETIC COMBINATIONS ... ACE INHIBITORS" or
        Prec_Obj_Category = "BETA BLOCKERS CARDIO-SELECTIVE ... ANTIADRENERGIC
ANTIHYPERTENSIVES" or
        Prec_Obj_Category = "POTASSIUM SPARING DIURETICS ... ACE INHIBITORS" or
        Prec_Obj_Category = "AZITHROMYCIN ... COUMARIN ANTICOAGULANTS" or
        Prec_Obj_Category = "FLUOROQUINOLONES ... COUMARIN ANTICOAGULANTS" or
        Prec_Obj_Category = "DIURETIC COMBINATIONS ... ANGIOTENSIN II RECEPTOR
ANTAGONISTS" or
        Prec_Obj_Category = "NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS) ...
COUMARIN ANTICOAGULANTS" or
        Prec_Obj_Category = "ANTIARRHYTHMICS TYPE III ... COUMARIN ANTICOAGULANTS" or
        Prec_Obj_Category = "ANTI-INFECTIVE MISC. - COMBINATIONS ... COUMARIN
ANTICOAGULANTS";
run;

```

Figure 20 shows the top 10 drug categories for DDI in Minnesota for the first two quarters of 2010. The figure also shows the number having the same prescribers for the precipitant and object drugs, as well as the number having different prescribers. Noticeable differences compared with the entire data set, in which, 72.2 percent had same prescribers and 27.8 percent had different prescribers, include the following:

- AZITHROMYCIN/COUMARIN ANTICOAGULANTS (56.5 percent with different prescribers)
- FLUOROQUINOLONES/COUMARIN ANTICOAGULANTS (57.0 percent with different prescribers)
- NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)/COUMARIN ANTICOAGULANTS (43.2 percent with different prescribers)
- ANTIARRHYTHMICS TYPE III/COUMARIN ANTICOAGULANTS (48.1 percent with different prescribers)
- ANTI-INFECTIVE MISC. – COMBINATIONS/COUMARIN ANTICOAGULANTS (56.7 percent with different prescribers)

Figure 20: Top 10 Drug Categories for DDI in Minnesota with Number of Same and Different Prescribers

Statewide - Minnesota 01/01/2010 - 06/30/2010				
Precipitant Category	Object Category	Same Prescribers	Different Prescribers	MH Chi-square statistic (p-value)
THYROID HORMONES	COUMARIN ANTICOAGULANTS	6578 (66.1%)	3375 (33.9%)	701.29 (p<.0001)
DIURETIC COMBINATIONS	ACE INHIBITORS	4841 (80.8%)	1152 (19.2%)	
BETA BLOCKERS CARDIO-SELECTIVE	ANTIADRENERGIC ANTIHYPERTENSIVES	2187 (72.7%)	822 (27.3%)	
POTASSIUM SPARING DIURETICS	ACE INHIBITORS	2015 (68.0%)	947 (32.0%)	
AZITHROMYCIN	COUMARIN ANTICOAGULANTS	1116 (43.51%)	1449 (56.5%)	
FLUOROQUINOLONES	COUMARIN ANTICOAGULANTS	1067 (43.0%)	1416 (57.0%)	
DIURETIC COMBINATIONS	ANGIOTENSIN II RECEPTOR ANTAGONISTS	1995 (81.3%)	459 (18.7%)	
NONSTEROIDAL ANTI-INFLAMMATORY AGENTS (NSAIDS)	COUMARIN ANTICOAGULANTS	1024 (56.7%)	780 (43.2%)	
ANTIARRHYTHMICS TYPE III	COUMARIN ANTICOAGULANTS	976 (51.9%)	905 (48.1%)	
ANTI-INFECTIVE MISC. - COMBINATIONS	COUMARIN ANTICOAGULANTS	706 (43.3%)	926 (56.7%)	

The following SAS® code calculates the frequencies of DDI by the pharmacy ID (i.e. NPI) for the precipitant and object drug.

```
PROC FREQ data=PartDDDImerged order=freq;
    table prec_service_provider_id /out=DDIPrecPharmacyCount;
run;

PROC FREQ data=PartDDDImerged order=freq;
    table obj_service_provider_id /out=DDIobjPharmacyCount;
run;
```

Figure 21 shows the number of prescriptions for the pharmacies where the prescriptions for precipitant drugs and object drugs were filled. The number of prescriptions for the 1,943 different precipitant drug pharmacies ranged from one to 4,754 in the first two quarters of 2010. The number of prescriptions for the 1,937 different object drug pharmacies, ranged from one to 4,816 in the first two quarters of 2010.

Figure 21: Number of Prescriptions for Precipitant and Object Drug Pharmacies

1,943 Precipitant Pharmacies	1,937 Object Pharmacies
1825 filled 1 to 250 (264 filled 1)	1819 filled 1 to 250 (246 filled 1)
97 filled 251 to 500	97 filled 251 to 500
11 filled 501 to 750	11 filled 501 to 750
2 filled 751 to 1000	2 filled 751 to 1000
1 filled 1001 to 1250	0 filled 1001 to 1250
1 filled 1251 to 1500	2 filled 1251 to 1500
2 filled 1501 to 1750	2 filled 1501 to 1750
0 filled 1751 to 2000	0 filled 1751 to 2000
4 filled over 2000 (1 filled 4754)	4 filled over 2000 (1 filled 4816)

The following SAS® code categorizes each DDI into two groups. In one group, the pharmacy of the precipitant and object drugs is the same. In the other group, the two pharmacies are different. The code calculates the frequencies for each category. For the group in which the pharmacies are different, the code calculates the DDI frequencies by pharmacy ID (NPI) for both the precipitant and object drugs.

```
DATA PartDDDImerged (drop=category);
    merge PartDDDImerged2 (in=ina) ObjDDI (in=inb);
    by Obj_NDC;
    if ina=1 and inb=1;
    if prec_service_provider_id = obj_service_provider_id then same_pharmacy="Yes";
    if prec_service_provider_id ne obj_service_provider_id then same_pharmacy="No";
run;

*DDI frequency by same_pharmacy*;
PROC FREQ data=PartDDDImerged order=freq;
    table same_pharmacy/
        out=DDIsame_pharmCount;
run;
```

```

DATA diffpharmacy;
    set PartDDDImerged;
    if same_pharmacy="No ";
run;

PROC FREQ data=diffpharmacy order=freq;
    table prec_service_provider_id/ out=DDIsame_prec_pharmCount;
run;

PROC FREQ data=diffpharmacy order=freq;
    table obj_service_provider_id/ out=DDIsame_obj_pharmCount;
run;

```

Analysis of the DDI supplemental data set showed that 145,093 (93.8%) DDI had same pharmacies for precipitant and object drug, while 9,525 (6.2 percent) had different pharmacies. For the group of DDI that had different pharmacies, 1,400 precipitant pharmacies ranged from one to 407 prescriptions and 1,382 object prescribers ranged from one to 499 prescriptions. Because such a large percentage had same pharmacies, no analysis was done by drug category.

Conclusion

Using CMS data sets, significant discoveries were found in the PIM and DDI data. Although the Minnesota PIM rate is about half the national rate, there is still room for improvement, especially in long-term macrobid/macrodantin use, skeletal muscle relaxants, narcotics, and oral estrogens. Also, compared to the Medicare population in Minnesota, the proportion of females prescribed a PIM is much higher. Also, certain counties, such as Big Stone and Wilkin, have a much higher PIM rate than the rest of Minnesota. Also, certain prescribers prescribe more PIM and certain pharmacies fill more PIM prescriptions.

With the Minnesota DDI rate slightly higher than the national rate, there is, again, room for improvement. Compared with the Medicare population in Minnesota, the proportion of females prescribed DDI is much higher. Also, certain counties, such as Stevens and Houston, have a much higher DDI rate than the rest of Minnesota. Also, certain prescribers prescribe more DDI and certain pharmacies fill more DDI prescriptions. Compared with the entire data set where 72.2 percent had same prescribers, 27.8 percent had different prescribers, and certain drug combinations were found to have different proportions. Beneficiaries taking coumarin anticoagulants with azithromycin, flouroquinolones, or anti-infective misc. – combinations had different prescribers about 57.0 percent of the time.

Some suggestions for interventions include reviewing the patients' current medications and educating them on the medications, reconciling medications at transition points of the care continuum (i.e., hospital to home, home care or skilled care setting), and sharing information with the patients' physicians (e.g., current medication list, potential drug interactions, and potential for adverse drug reactions).

References

Source: BearingPoint, Inc. "Medication Measures for Part D Task 6 Technical Specifications"
http://www.nmmra.org/resources/Physician/112_1412.pdf

Acknowledgements

Stratis Health is a nonprofit organization founded in 1971 that leads collaboration and innovation in health care quality and safety, and serves as a trusted expert in facilitating improvement for people and communities.

Recommended Reading

<http://www2.thecarolinascener.org/drugsafety/drugsafety.aspx?tabid=2>
<http://www.stratishealth.org/providers/PrescriptionDrugSafetyResources.html>

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