Medication Adherence for 90-Day Quantities of Medication Dispensed Through Retail and Mail Order Pharmacies

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Objectives: To examine relative medication adherence of patients filling 90-day supplies of maintenance medications using retail and mail order channels. It was hypothesized that adherence rates would not differ across the 2 channels.

Study Design: A cross-sectional retrospective analysis was conducted using de-identified pharmacy claims data from a large pharmacy benefit manager (PBM) database over a 2-year period (January 2008 to August 2010). Patients who were continuously eligible for at least 12 months during this time frame, with benefit plan designs that allowed filling of 90-day supplies either at retail or by mail order pharmacy, were selected.

Methods: Adherence was measured by medication possession ratio (MPR) within a 1-year period. Propensity score matching was employed to minimize differences between the Retail-90 group and Mail Order-90 group.

Results: Overall, patients filling 90-day prescriptions for 9 therapeutic groups (antiasthmatics and bronchodilators, antidepressants, antidiabetics, antihyperlipidemics, antihypertensives, beta blockers, calcium channel blockers, diuretics, and thyroid agents) at retail pharmacies demonstrated a propensity score–matched average MPR that was statistically higher than for patients filling prescriptions via mail order (77.0% vs 76.0%). There were no significant differences in MPR (post-matching) between 90-day retail and mail order channels for individual therapeutic groups, except for antidiabetics (80.2% vs 83.1%).

Conclusions: On a propensity-matched basis, patients who fill maintenance prescriptions at retail have a slightly, but statistically significantly, higher MPR than patients who fill their prescriptions by mail.

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For author information and disclosures, see end of text.

Patient adherence to medication therapy is an important aspect in the management of chronic diseases. Studies show that medication nonadherence is associated with increased hospitalizations and mortality for patients with chronic diseases, such as diabetes and coronary artery disease.[1-3] Despite the adverse effects of poor medication adherence, it is estimated that on average, 50% of patients do not take their medication as prescribed.[4]

Medication nonadherence carries a significant financial burden as well, estimated to be $100 billion for hospitalizations alone,[5] impacting patients, employers, and health plans. However, these excess costs can be prevented. A study by Sokol et al[6] found that medication adherence rates of 80% and higher are associated with decreased total medical costs for diabetes, high cholesterol, and hypertension. Furthermore, Balkrishnan et al[7] showed that for diabetes every 10% increase in medication adherence could help cut medical costs by 8.6%.

Many more Americans are using prescription drugs,[8] a trend that is likely to continue as the US population ages[9] and as the prevalence of chronic conditions increases.[10] As a result, health plan sponsors have been seeking ways to improve adherence and impact overall healthcare costs.

Mail order pharmacy is one channel for dispensing 90-day supplies of maintenance medications that pharmacy benefit managers (PBMs) have been using to help control prescription costs and increase generic utilization.[11,12] Mail order pharmacy provides patients with the convenience of having medication delivered to their homes, while incurring lower costs through a reduced copayment incentive.[12] Some studies indicate use of mail order pharmacy may also contribute toward greater medication adherence.[13,14] While patients using mail order pharmacy generally have access to a toll-free number for medication questions, they lose the ability to have a face-to-face interaction with a pharmacist,[11] particularly when filling by mail order is mandatory rather than optional.

Retail pharmacies also offer fulfillment of 90-day supplies of medication.[15] This was implemented in an effort not only to compete with mail order pharmacy, but also to offer patients increased options for 90-day prescription fulfillment.[15] Retail pharmacies, as a channel for fulfillment of maintenance prescriptions, offer several advantages over mail order pharmacy. First, patients seem to prefer filling their prescriptions at retail pharma-

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Take-Away Points

Given that patient adherence to medication therapy is necessary in the management of chronic diseases, it is important to investigate adherence levels for patients using different distribution channels.

- Our study demonstrated that fulfillment of 90-day prescriptions at retail pharmacies resulted in medication adherence that is comparable to that of mail order.
- Retail pharmacy has the added advantage of providing pharmacist-led care, including face-to-face interaction with patients for medication management, which could improve health and well-being of patients, ultimately leading to cost savings.

cies compared with mail order, as demonstrated by higher utilization rates for retail pharmacies, regardless of incentive to use mail order.[16] Second, this allows patients who prefer to fill their prescriptions at retail pharmacies the added convenience of doing so for all of their 30-day and 90-day medication needs. Third, retail pharmacies offer patients the opportunity to have face-to-face consultations with a pharmacist to address any concerns they may have about their medications. Finally, pharmacists are provided with an opportunity to proactively counsel patients on the importance of taking their medicines as prescribed, which has been demonstrated to improve adherence rates.[17]

The objective of this study was to compare medication adherence of patients who fill 90-day quantities of maintenance medications through retail versus mail order channels. We limited our analysis to prescriptions of 90-day quantities, rather than 30-day quantity fills, because maintenance-drug patients using this quantity of refills are likely to be stabilized with respect to medication and dosing regimen.[18] To our knowledge, this is the first study to compare medication adherence between the 2 delivery channels for 90-day prescriptions. We hypothesize that patients filling 90-day prescriptions at retail pharmacies will have adherence rates similar to those of patients employing mail order pharmacy.

METHODS

Patient Population

This retrospective cross-sectional analysis used de-identified demographic and pharmacy claims data obtained from a large PBM database covering the 2-year period from January 1, 2008, to August 31, 2010. All patients who were continuously eligible for at least 12 months during this time and had a pharmacy benefit plan design that allowed for prescription fulfillment of 90-day supplies at either a retail pharmacy or by mail order with equal copays were considered for inclusion. Equivalence of benefits was determined by analyzing the distribution of patient cost sharing by client year, distribution channel, and drug type (generic, preferred, non-preferred), excluding claims where the patient payment amount was equal to the drug cost.

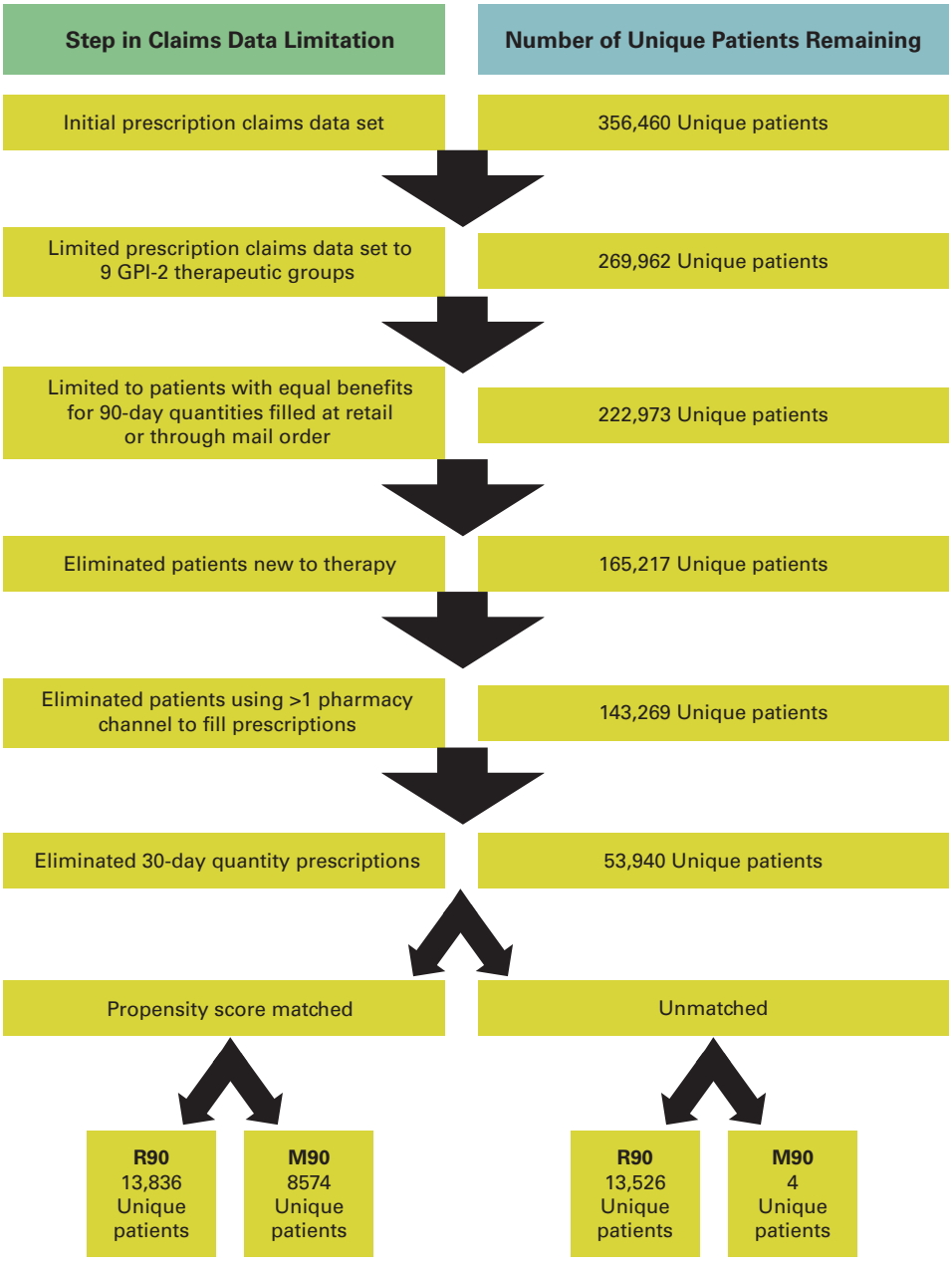
The analysis was limited to those patients who had at least 1 pharmacy claim for a 90-day supply for any of the following therapeutic groups within the study period: antiasthmatics and bronchodilator agents, antidepressants, antidiabetics, antihyperlipidemics, antihypertensives, beta blockers, calcium channel blockers, diuretics, and thyroid agents. All drugs within each therapeutic group were included, regardless of dosage form. Therapeutic group was identified via the first 2 digits of the generic product identifier (GPI) associated with each pharmacy claim (respective GPI-2s: 44, 58, 27, 39, 36, 33, 34, 37, and 28). We limited our analysis to patients who were not new to therapy (identified by the presence of a prescription fill in the previous 6 months). Patients filling both 30-day and 90-day supplies for the same therapeutic group and those filling only 30-day supplies were excluded from this analysis. If a patient filled a prescription for more than 1 therapeutic group, they were included in each of the respective groups.

Patients were grouped based on the pharmacy channel used to obtain their 90-day supply of medication. Patients who exclusively used a retail pharmacy for a single therapeutic group were placed into the "Retail-90" group. Patients who exclusively used mail order services for a single therapeutic group were placed into the "Mail Order-90" group. Patients who used both mail order services and retail pharmacies for a single therapeutic group were excluded (n = 21,948) in order to eliminate any potential variation caused by using both channels. Patients filling prescriptions for 90-day supplies at retail for 1 therapeutic group, but filling 90-day prescriptions through mail order for a different therapeutic group, would be included in both the Retail-90 and the Mail Order-90 group for each respective therapeutic group. Construction of the study groups is shown in the **Figure**.

Measures

We used the medication possession ratio (MPR) to calculate medication adherence for a 1-year period separately for each of the 9 therapeutic groups. MPR was calculated as the number of actual adherent days divided by 365, where actual adherent days is the total days' supply of medication a patient had available in a 365-day period starting with the index date of the initial prescription filled for each therapeutic group. If a patient had any prescription refills beyond 365 days following the first fill, those prescriptions were excluded from the analysis. If a patient had a refill toward the end of the 365-day period, the number of days' supply of that refill exceeding 365 days from the first fill was subtracted from the number of actual adherent days so that the maximum MPR could not exceed

Figure. Patient Selection Flow Chart



GPI indicates generic product identifier; M90, Mail-order-90; R90, Retail-90.

100%. If a patient filled a prescription for more than 1 type of medication within a particular therapeutic group, then the days' supplies of each medication were added together and divided by 365. In such cases, patients need not be adherent to every medication, as a single MPR was computed for all drugs within that particular class. Overall MPR represents the average MPR at the patient level. When a patient used medications from more than 1 therapeutic group, the group-specific MPRs were averaged to obtain a single MPR measure for that patient.

Statistical Analysis

Risk scores were developed from national drug codes in the pharmacy claims records using the Medicaid Rx (MRX) model of the University of California, San Diego Chronic Illness and Disability Payment System (CDPS), version 5.2 (The Regents of the University of California). (MRX is a pharmacy-based risk assessment model originally designed for a Medicaid population. The MRX model assigns each member to 1 or more of 45 medical condition categories based on the prescription drugs used by each member and to 1 of 11

Table 1. Population Characteristics

	All Patients		Unmatched/Excluded		Propensity Score Matched	
	Retail-90	Mail Order-90	Retail-90	Mail Order-90	Retail-90	Mail Order-90
Unique patients	45,362	8578	31,526	4	13,836	8574
Average age, y (SD)	65.2 (14.1)	61.4 (12.3)	65.6 (14.6)	24.5 (22.8)	64.2 (13.0)	61.4 (12.3)
Male, %	44.7	46.4	43.6	75.0	47.2	46.4
Average risk score (SD)	2.09 (1.08)	1.89 (1.00)	2.11 (1.11)	2.99 (3.63)	2.05 (1.03)	1.89 (1.00)

SD indicates standard deviation.

age/sex categories. Based on the medical conditions and age/sex categories, the model predicts the overall medical costs for each member. However, recalibration of the CDPS model was not performed in this study because relative risk scores are assigned within therapeutic groups and not across the entire population.)

Propensity score matching was then used to minimize differences between the Retail-90 and Mail Order-90 groups at the therapeutic group level in terms of age-sex and risk score bands. A logistic regression model was applied with outcome variables representing Retail-90 versus Mail Order-90 channel status and independent variables including multiple age-sex bands and pharmacy risk score bands. We used a sample matching algorithm of the propensity score based on a "greedy" algorithm.[19] A 1-to-1 match was performed at the therapeutic group level for the Retail-90 group and for the Mail Order-90 group. The matching process yielded an equal number of patients in the Retail-90 group and Mail Order-90 group for each of the 9 therapeutic groups. Unmatched patients were excluded from the analysis. **Table 1** shows characteristics of all patients (before matching), matched patients, and those who were left unmatched (excluded) through this process. Propensity score matching was performed using bands and not continuous variables. However, population characteristics for age, gender (percent male), and risk score for patients pre- and post-propensity score matching can be found in **Appendix 1**. Results for χ^2 comparison between the groups for age-sex and risk bands can be seen in **Appendix 2**. All statistical analyses were performed using SAS statistical software, version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Patients in the Retail-90 group used drugs from an average of 1.13 different therapeutic groups during the study period compared with 1.83 for patients in the Mail Order-90 group, resulting in 13,836 unique patients across the 9 therapeutic groups in the Retail-90 group and 8574 in the Mail Order-90 group (see Table 1). Before matching, the Retail-90 and Mail Order-90 groups had significant differences (at the P <.0001 level) in age-sex and risk bands across each of the 9 therapeutic groups. After propensity score matching was applied, patients in the 2 groups were found to not have significant differences in terms of age-sex and risk bands (P >.99 for all therapeutic groups).

Propensity score–matched results indicate that across the 9 therapeutic groups analyzed in this study, unique patients who chose to obtain 90-day supplies of medication through a retail pharmacy had an overall average adherence rate that was higher (77.0% vs 76.0%) than for patients who chose to use mail order pharmacy for 90-day prescription fulfillment. This overall MPR difference was statistically significant (P = .0067). There were no significant differences in MPR (post-matching) between retail and mail order channels for the individual therapeutic groups evaluated in this study, except for antidiabetics (80.2% vs 83.1%). These results are shown in **Table 2**.

Results by MPR range (<50%, 50%-79%, and ≥80%) for the propensity score–matched therapeutic groups are presented in **Table 3**.

DISCUSSION

In the aggregate, our findings show that adherence rates for patients who choose to fulfill 90-day prescriptions through retail pharmacies compare favorably to those of patients using mail order. This finding is representative of patients using prescription drugs in the 9 therapeutic groups studied and with propensity-matched characteristics shown in Table 1. However, this study finding is not necessarily representative of patients using drugs in other therapeutic groups or of a commercial population.

Many factors may impact levels of adherence for prescriptions filled through different dispensing channels, although additional research is needed to fully assess their significance.

Table 2. MPR Pre- and Post-Propensity Matching: Retail-90 Versus Mail Order-90

	Pre-Matching MPR, % (SD)				Post-Matching MPR, % (SD)		
Therapeutic Group	Retail-90	Mail Order-90	*P*	Total, n	Retail-90	Mail Order-90	*P*
Antiasthmatics and bronchodilator agents	66.4 (.30)	68.1 (.31)	.2501	1120	67.2 (.29)	68.1 (.30)	.6286
Antidepressants	72.5 (.27)	72.3 (.28)	.8367	2942	71.5 (.27)	72.3 (.28)	.4121
Antidiabetics	81.4 (.25)	83.1 (.25)	.0307	2336	80.2 (.26)	83.1 (.25)	.0048
Antihyperlipidemics	77.3 (.25)	77.6 (.26)	.4808	7478	76.7 (.26)	77.6 (.26)	.1233
Antihypertensives	79.5 (.25)	79.0 (.25)	.2753	7034	79.0 (.25)	79.0 (.25)	.9851
Beta blockers	79.5 (.24)	77.3 (.26)	.0006	3622	78.9 (.24)	77.3 (.26)	.0519
Calcium channel blockers	80.1 (.25)	78.8 (.25)	.1207	2108	79.3 (.24)	78.9 (.25)	.6616
Diuretics	75.7 (.26)	75.4 (.27)	.6890	2154	73.9 (.27)	75.4 (.27)	.1956
Thyroid agents	80.7 (.24)	80.2 (.24)	.4570	2600	80.8 (.23)	80.2 (.24)	.4738

MPR indicates medication possession ratio; SD, standard deviation.

Retail pharmacies have the added advantage of offering patients the opportunity to interact face-to-face with a pharmacist on-site, as well as immediate prescription fulfillment.

A face-to-face interaction with a pharmacist can provide the framework for building a trusting relationship between the patient and pharmacist. This can present the pharmacist with opportunities to counsel patients on the importance of adherence to medication therapy, as well as address any medication-related issues. Several published studies have demonstrated that pharmacist counseling and medication management improve adherence levels.[20,21]

Retail pharmacies can fill 90-day prescriptions quickly. Except for patients enrolled in automatic refill programs, patients who rely on mail order must anticipate several days' delay in receipt and so must remember to reorder well before running out of medication. In addition, any increased processing time or delay in mail delivery could prevent the patient from receiving medication when needed, potentially jeopardizing adherence.

Our study showed antidiabetics were the only therapeutic group in which adherence was found to be higher in the Mail Order-90 channel compared with Retail-90. Other published studies have found improved adherence in mail order relative to retail pharmacy for particular therapeutic drug classes. With respect to antidiabetics, a study by Devine et al[14] assessing adherence rates for patients switching from retail to mail order also demonstrated higher adherence through mail order. However, their study was not limited to prescriptions of 90-day quantities. A study done by Duru et al in a population enrolled in a fully integrated health system demonstrated that patients with diabetes receiving newly prescribed antidiabetics, antihypertensives, or antihyperlipidemics through mail order are more likely

Table 3. Percentage of Propensity Score–Matched Patients by MPR Range in Therapeutic Group

	Retail-90			Mail Order-90		
Therapeutic Group	<50%	50%-79%	≥80%	<50%	50%-79%	≥80%
Antiasthmatics and bronchodilator agents	41.3	18.8	40.0	40.2	16.6	43.2
Antidepressants	32.5	22.6	44.9	32.9	20.1	47.0
Antidiabetics	23.3	16.0	60.7	20.2	12.3	67.5
Antihyperlipidemics	24.6	20.5	54.9	24.2	19.8	56.0
Antihypertensives	21.6	20.3	58.1	22.0	19.3	58.6
Beta blockers	21.6	21.6	56.8	25.3	18.5	56.2
Calcium channel blockers	21.3	21.1	57.6	23.1	17.8	59.1
Diuretics	29.3	21.3	49.4	27.4	20.7	51.9
Thyroid agents	18.9	21.2	59.8	20.5	19.5	60.1

MPR indicates medication possession ratio.

to be adherent compared with patients dispensed medications through a retail pharmacy.[13] Patients who primarily used mail order in the Duru study were more likely to have a financial incentive to use mail order compared with patients who primarily employed community pharmacies. Unlike a significant fraction of benefit designs,[22] Duru does not indicate that the former group was subject to mandatory mail order, which Liberman et al found to correlate with reduced persistence during the patient's first year of therapy.[23] Additional studies are needed to better understand factors which may contribute to this result.

Limitations

Our study had several limitations. First, in addition to cost share, a variety of factors may affect a person's decision to obtain 90-day prescriptions through retail versus mail order pharmacy (when that choice is available), as well as adherence to medication therapy. Factors not controlled for in this study which may affect a person's choice of pharmacy for filling 90-day prescriptions include patient income, race, education, setting (urban, suburban, or rural), and distance from a retail pharmacy. We were unable to adjust our findings for motivation-driven patient self-selection of dispensing channel. Because this analysis used prescription claims to measure adherence, it is not possible to confirm whether filled prescriptions were taken as instructed, whether instructions remained unchanged, whether patients were instructed to use "pill splitting" to achieve a desired dosage, whether medication samples were obtained, or whether prescriptions were obtained through pharmacy "$4 generic" cash programs. Our method of risk scoring based on prescription claims may not fully capture comorbidity or severity of illness. We were unable to determine whether the patients in this study were enrolled in automatic refill dispensing programs, which may increase adherence.

CONCLUSIONS

On a propensity-matched basis, patients who fill maintenance prescriptions at retail have a statistically significantly higher MPR than patients who fill their prescriptions via mail. Although the study demonstrated statistical significance in adherence for retail compared with mail, these findings may or may not be clinically significant, which was beyond the scope of the current study. The retail setting may present advantages related to quality of care and patient convenience. However, additional studies are needed to better understand factors which may contribute to this result.

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Appendix 1. Population Characteristics: All Patients Prior to Propensity Score Matching

	Average Age			Male, %			Average Risk Score		
Therapeutic Group	Retail-90	Mail Order-90	*P*	Retail-90	Mail Order-90	*P*	Retail-90	Mail Order-90	*P*
Antiasthmatics and bronchodilator agents	57.2	54.9	<.0001	40.9	41.6	.7932	1.99	1.85	.0226
Antidepressants	59.9	58.5	<.0001	30.1	28.1	.1356	2.21	2.10	.0006
Antidiabetics	67.1	62.7	<.0001	50.6	55.3	.0033	2.60	2.39	<.0001
Antihyperlipidemics	67.3	63.8	<.0001	51.8	55.9	<.0001	2.17	1.98	<.0001
Antihypertensives	67.1	63.6	<.0001	51.6	54.4	.0027	2.14	1.99	<.0001
Beta blockers	68.9	64.8	<.0001	49.2	51.4	.0849	2.29	2.10	<.0001
Calcium channel blockers	71.1	66.4	<.0001	45.1	48.5	.0418	2.30	2.16	.0001
Diuretics	69.6	65.8	<.0001	42.8	42.4	.8226	2.36	2.26	.0073
Thyroid agents	65.0	62.5	<.0001	20.8	20.8	.9800	2.06	1.84	<.0001

Appendix 2. Population Characteristics: Propensity Score–Matched Patients

	Average Age			Male, %			Average Risk Score		
Therapeutic Group	Retail-90	Mail Order-90	*P*	Retail-90	Mail Order-90	*P*	Retail-90	Mail Order-90	*P*
Antiasthmatics and bronchodilator agents	55.6	54.9	.5588	41.4	41.4	.9999	1.82	1.82	.9289
Antidepressants	59.3	58.5	.0807	28.1	28.1	.9999	2.12	2.10	.5488
Antidiabetics	63.9	62.7	.0143	55.4	55.3	.9667	2.42	2.39	.4794
Antihyperlipidemics	64.9	63.9	<.0001	55.8	55.8	.9999	2.00	1.98	.4427
Antihypertensives	64.4	63.6	.0023	54.3	54.4	.9617	2.00	1.99	.5767
Beta blockers	65.9	64.8	.0028	51.4	51.4	.9736	2.10	2.10	.9067
Calcium channel blockers	67.6	66.4	.0234	48.3	48.6	.8958	2.13	2.16	.6002
Diuretics	67.0	65.9	.0265	42.6	42.3	.8962	2.26	2.26	.9842
Thyroid agents	63.6	62.5	.0279	20.7	20.8	.9614	1.82	1.84	.5741