Association between cost-sharing and drug prescribing in Korean elderly veterans with chronic diseases
A real-world claims data study

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Abstract
This study aimed to investigate the relationship between cost-sharing and drug prescribing and its appropriateness in Korean elderly veterans with chronic conditions. This is a cross-sectional study using real-world claims data. Veterans with primary hypertension or dyslipidemia were compared with two controls with higher levels of cost-sharing. Study subjects (age ≥65 years) were selected through stratified random sampling and matching the individual attributes. The primary outcome was the annual amount of drugs prescribed per patient, and the secondary outcomes included several other measures investigating multifaceted aspects of drug prescribing, medical institution utilization behavior, and prescribing appropriateness. Gamma regression models or logistic regression models were employed. Veterans were prescribed 59%–74% more drugs (exp(β) = 1.59 [95% confidence interval [CI] = 1.55–1.64] ~ 1.74 [1.70–1.79]) compared to the National Health Insurance (NHI) patients. This was attributed mainly to longer prescribing days (44%) and slightly more prescriptions (6%–7%) than NHI patients. Veterans spent 14%–15% higher medication costs. Veterans were less likely to visit multiple medical institutions by estimates of 0.77 (0.76–0.79) ~ 0.80 (0.79–0.82). Similar but smaller differences were observed between veterans and medical aid (MedAid) patients. The veteran patients showed a more than 50% increased risk of therapeutic duplication than the other two controls (adjusted odds ratio [ORs] = 1.47 [1.37–1.57] ~ 1.61 [1.50–1.72]). Inappropriate drug prescribing was also more common in veterans than the two controls (adjusted ORs = 1.20 [1.11–1.31] ~ 1.32 [1.22–1.43]). In Korean elderly veterans with chronic illnesses, a level of cost-sharing was associated with having more prescribed medicines, and increased inappropriate prescribing.

Abbreviations: ADE = adverse drug event, APS = aged patient sample, CI = confidence interval, HIRA = Health Insurance Review & Assessment Service, ICD-10 = International Classification of Diseases and Related Health Problems 10th Revision, MedAid = medical aid, NHI = National Health Insurance, OR = odds ratio, PIM = potentially inappropriate medication, STROBE = STrengthening the Reporting of OBservational studies in Epidemiology, SD = standard deviation.

Keywords: cost-sharing, drug prescribing, elderly, prescribing appropriateness, veterans

1. Introduction
Since the idea of a price signal to consumers at the time of use was proposed,\(^1\) many healthcare systems have introduced a variety of cost-sharing schemes to contain pharmaceutical spending.\(^2,3\) Including the RAND experiments,\(^4,5\) existing evidence demonstrated that the level of cost-sharing might be negatively associated with healthcare consumption.\(^6–11\) At the same time, doubts have long been demonstrated that raising copayment to drug utilization may result in negative outcomes in patient health
and higher consumption in more expensive services.[6–8] Existing studies have been dedicated to proving if the excessive levels of copayment could reduce the utilization of essential medications.[6–11] It has been rarely addressed in the other way what the impact of lifting the copayment barrier is on medication utilization, for example, inappropriate medication use.

Inappropriate medication use could pose a threat to patient safety. Previous studies have demonstrated an association between potentially inappropriate medication (PIM) use in the Beers Criteria and poor health outcomes, including hospitalization, falls, and mortality.[12–14] A meta-analysis using 13 cohort studies concluded that PIM use was associated with a 1.6-fold increased mortality in the elderly.[14] The incidence of adverse drug events is more common in older people than their younger counterparts due to age-related changes in pharmacokinetics and pharmacodynamics.[15,16] Polypharmacy can lead to unnecessary therapeutic duplication and harmful drug combinations.[17,18]

South Korea has run a National Health Insurance (NHI) system that includes the entire population.[19] Koreans are covered either by a NHI which is a standard healthcare program or by a medical aid (MedAid) which provides for low-income households. Korean healthcare system features a weak gatekeeping of primary care providers, a relatively high burden of private expenditure, and high drug consumption.[16–21] Overall, NHI patients pay 30% of the total costs for insured pharmaceuticals in outpatient care.[22] MedAid patients pay a fixed copayment, which is 0 – 0.5USD per prescription for insured pharmaceuticals in the outpatient setting.[23] There are few administrative barriers in patient access to medical institutions except that patients have to pay higher shares of total costs for the upper-level medical institutions to get prescriptions from 30% in clinics to 60% in tertiary hospitals.[22] Outpatient cost-sharing is lower for MedAid patients in general.[23] Thus far, MedAid patients have been likely to utilize more healthcare resources than NHI patients in the outpatient setting.[24,25]

In addition, there is a healthcare program for veterans that allows them an additional reduction in copayment. Korean government operates 6 veterans hospitals providing medical services primarily for veterans and about 322 ministry-commissioned clinics or hospitals.[26] Veterans are eligible to receive an additional exemption from 50% to 100% of their co-pay. In other words, veterans only pay 0%–15% of the copayments for services or medicines that the NHI or MedAid patient has to pay.[26] There are no legal limits for veterans to access other kinds of medical institutions but it could take more administrative work for them to get copay exemption.[26] This study aimed primarily to investigate the relationship between cost-sharing and medication prescribing in Korean elderly veterans. Secondly, this study aimed to interpret drug use by examining the multifaceted aspects of drug prescribing and to assess the relationship between cost-sharing and prescribing appropriateness in Korean elderly veterans.

2. Methods

2.1. Study design

This is a cross-sectional study and followed the STrengthening the Reporting of OBservational studies in Epidemiology guideline.[27] This study compared drug prescribing and its appropriateness between veteran patients and 2 cost-sharing groups in two disease cohorts. Elderly veteran patients were defined as the lowest copayment group and were compared with two matched controls, respectively. Two control groups were NHI patients (a standard copayment group) and MedAid patients (the second-lowest copayment group).

2.2. Data sources and study subjects

The administrative claims databases of the Health Insurance Review & Assessment Service were searched to identify the study population of elderly veterans (≥65 years old). Two cohorts of veterans were constructed by including elderly veterans who had at least one prescription with a diagnosis of primary hypertension or dyslipidemia in an outpatient setting between January 1, 2014, and December 31, 2015. Two diseases were selected because they were the two most common chronic conditions in the Korean elderly.[28] The chronic conditions were defined with diagnostic codes of I10 as primary hypertension; E78 as dyslipidemia in the 6th Korean Standard Classification of Diseases and Causes of Death, an official Korean version of the International Classification of Diseases and Related Health Problems 10th Revision.[29] Of the identified elderly veterans, those with complications were excluded because it was difficult to evaluate the clinical need for medications only with claims data. Diagnostic codes representing complications were hypertensive heart diseases (I11), hypertensive renal diseases (I12), hypertensive heart and renal diseases (I13), and secondary hypertension (I15). Women were excluded because of the extremely small population of elderly veteran patients (<1%).

Comparative NHI or MedAid patients were identified by employing the aged patient sample (APS). The APS is distributed annually by the Health Insurance Review & Assessment Service and contains the claims data of 20% of the population aged 65 years and older.[30] After excluding women and veterans from the APS, the same process of identification as veterans was carried out.

To enhance the efficiency in analysis, a proportional stratified random sampling (5%) was carried out in the veterans and NHI population. Owing to the small size of the MedAid population, 100% of MedAid patients were included. Attributes considered in the stratified random sampling were age, Elixhauser comorbidity score, region, and data year. Elixhauser comorbidity score was computed with 31 comorbidity groups[31] using both in- and outpatient claims data. The region was divided into three categories which were Seoul, six metropolitan cities, and ten provinces. Data year indicated 2014 or 2015, the year when data for services or prescribing medications were claimed.

To balance between groups, an exact match process was conducted using four available covariates which were age (± 1 year), Elixhauser score, region, and data year. Finally, four matched cohorts were established for analysis. Two veteran-NHI cohorts included each of 8009 patients with primary hypertension and each of 7943 with dyslipidemia. Two veteran-MedAid cohorts included each of 8633 patients with primary hypertension and each of 8657 with dyslipidemia.

2.3. Outcomes

The primary outcome was the annual amount of drugs prescribed per patient. A unit for each medication is designated in the Korean pharmaceutical reimbursement list and generally defined depending on the formulation of the product, for example, 1 tablet, 1 capsule, and so forth. Medications in oral formulations were included for analysis. Others such as injections or those for external uses were excluded because units for them were not always comparable across patients.

Secondary outcomes included variables demonstrating several other aspects of drug prescribing, medical institution utilization behavior, and appropriateness of drug prescribing. Variables in drug prescribing included the annual number of prescriptions per patient, annual total prescribing days per patient, a number of drug items per prescription and annual costs prescribed for a patient (annual drug costs per patient). A number of medical institutions involved in prescribing a patient’s medication during 1-year for a patient was measured for investigating medical institution utilization behavior. If there were duplicate visits to the same medical institution, it was counted once.

 Appropriateness of drug prescribing was defined in 2 ways; therapeutic duplication and PIM. Therapeutic duplication was defined if there was a repetition of the Anatomical Therapeutic Chemical code at the 4th level (e.g., A10BA biguanides, A10BB
sulfonylureas, etc.), which represents the identical chemical subgroup in the same prescription. Therapeutic duplication between more than 2 prescriptions covering the same period was also checked. PIMs were detected using American Geriatrics Society 2015 Updated Beers Criteria.[32]

2.4. Statistical analysis

Descriptive analyses were carried out for all variables. To compare the basic characteristics between veterans and each comparative group, Wilcoxon rank-sum tests were performed for the continuous variables that were not distributed normally; chi-squared tests were performed for the categorical variables. To quantify the differences between veterans and each comparative group in outcomes presenting positively skewed distribution, multivariable gamma regression with a log-link function was performed with adjustment for age and number of operations. The results from the gamma regression were presented as the exponential of coefficients (exp [β]) and 95% confidence interval (CI). For binary outcomes measuring the appropriateness of drug use, logistic regression was carried out to quantify the risk of therapeutic duplications or inappropriate prescribing in elderly veterans compared either to the NHI or MedAid group. Multivariable logistic regression was conducted with adjustment for age, the number of operations, and the number of drug items per prescription. The results from the logistic regression were presented as the odds ratio (OR) and 95% CI. The analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC) and P value <.05 was considered significant.

2.5. Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of Yeungnam University (protocol code 7002016-E-2016-004, June 29, 2016). All data were provided after the authority fully anonymized and the ethics committee waived the requirement for informed consent.

3. Results

3.1. Study subject demographics

Tables 1 and 2 list the basic demographics of the patients for four matched cohorts. In all comparison cohorts, veteran patients were slightly younger than the NHI or MedAid patients (P < .05) and had more operations (P < .05). No significant differences in other characteristics were noted.

3.2. Drug prescribing compared to NHI patients (a standard copayment group)

Table 3 displays the results from regression analyses. Compared to the NHI patients, the veteran patients had 1.59 ~1.74 times

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Table 1

| Variable                  | Primary hypertension | Dyslipidemia |
|---------------------------|----------------------|--------------|
|                          | Veteran patients     | NHI patients |
| Age, mean ± SD           | (N = 8009)           | (N = 8009)   |
| 71.6 ± 6.1$              | 71.9 ± 5.9$          | 71.2 ± 5.7$  |
| Elixhauser score, mean ± SD | 4.2 ± 2.1            | 4.2 ± 2.1    |
| 1.0 ± 1.6$               | 0.9 ± 1.4$           | 1.1 ± 1.8$   |
| Resident area, N (%)      | Seoul                | 1775 (22.2)  |
|                          | Six metropolitan cities | 2248 (28.1) |
|                          | Ten provinces        | 3986 (49.8)  |
| Year, N (%)               | 2014                 | 3960 (49.4)  |
|                          | 2015                 | 4049 (50.6)  |

NHI = National Health Insurance, SD = standard deviation.
*P < .05.
$P < .01.

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Table 2

| Variable                  | Primary hypertension | Dyslipidemia |
|---------------------------|----------------------|--------------|
|                          | Veteran patients     | NHI patients |
| Age, mean ± SD           | (N = 8633)           | (N = 8633)   |
| 71.5 ± 6.0$              | 71.9 ± 5.9$          | 71.2 ± 5.8$  |
| Elixhauser score, mean ± SD | 4.5 ± 2.3            | 4.5 ± 2.3    |
| 1.1 ± 1.7$               | 1.0 ± 1.7$           | 1.2 ± 1.8$   |
| Resident area, N (%)      | Seoul                | 1940 (22.5)  |
|                          | Six metropolitan cities | 2506 (29.0) |
|                          | Ten provinces        | 4187 (48.5)  |
| Year, N (%)               | 2014                 | 4243 (49.1)  |
|                          | 2015                 | 4390 (50.9)  |

MedAid = medical aid, SD = standard deviation.
*P < .05.
$P < .01.
higher prescribed medications (\(\beta = 1.59\) [95% CI = 1.55–1.64] – 1.74 [1.70–1.79]). They had 44% longer prescribing days (\(\beta = 1.44\) [1.41–1.47] in primary hypertension, 1.44 [1.41–1.46] in dyslipidemia), had 6%–7% higher number of prescriptions (\(\beta = 1.06\) [1.04–1.09] – 1.07 [1.05–1.09]) and had slightly more drug items per prescription (\(\beta = 1.14\) [1.12–1.17] – 1.15 [1.12–1.18]). They were less likely to visit multiple medical institutions by estimates of 0.77 (0.76–0.79) – 0.80 (0.79–0.82). The relevant absolute numbers are displayed in Table S1, Supplemental Digital Content 1, http://links.lww.com/MD/H349.

3.3. Drug prescribing compared to medical aid patients (the second-lowest copayment group)

Table 4 displays the results from regression analyses. Compared to the MedAid patients, the veteran patients had 1.26 – 1.29 times higher prescribed medications (\(\beta = 1.26\) [1.23–1.29] – 1.29 [1.26–1.33]). Those with dyslipidemia were issued slightly fewer prescriptions (\(\beta = 0.98\) [0.96–0.99]), while those with primary hypertension were not different from the MedAid patients in terms of the number of prescriptions (\(\beta = 0.98\) [0.96–1.00]). Veterans had 24% – 25% longer prescribing days (\(\beta = 1.24\) [1.21–1.26] – 1.25 [1.22–1.27] and fewer drug items per prescription by estimates of 0.92 [0.91–0.93]). Spending on medications were not different from the MedAid patients (\(\beta = 1.00\) [0.97–1.02] – 1.01 [0.98–1.03]). Veterans were less likely to visit multiple medical institutions by estimates of 0.88 [0.87–0.90] – 0.94 [0.92–0.95]). The relevant absolute numbers are displayed in Table S2, Supplemental Digital Content 2, http://links.lww.com/MD/H350.

3.4. Inappropriate prescribing compared to two control groups

As shown in Figure 1, the veteran patients with two chronic diseases had higher odds of having medications in therapeutic duplication compared to the NHI (adjusted ORs = 1.47 [1.37–1.57] – 1.52 [1.41–1.63]) or MedAid patients (adjusted ORs = 1.52 [1.42–1.63] – 1.61 [1.50–1.72]). The veteran patients with two chronic diseases also had higher odds of having medications potentially inappropriate for the elderly compared to the NHI (adjusted ORs = 1.25 [1.15–1.33] – 1.32 [1.22–1.43]) or MedAid patients (adjusted ORs = 1.20 [1.11–1.31] – 1.27 [1.17–1.37]). The risk pattern of having inappropriate prescribing was similar in two chronic conditions.

4. Discussion

The present study investigating how cost-sharing is associated with drug prescribing and its appropriateness in Korean elderly veterans with chronic illnesses yielded four key findings. First, elderly veterans who paid the lowest copayments were prescribed significantly more medicines compared to NHI elderly patients, that is, standard copayment patients. They also were prescribed more medicines compared to MedAid elderly patients, that is, the second-lowest copayment group, but the differences were smaller. Compared to NHI patients, veteran

| Outcome variable | Primary hypertension | | | Dyslipidemia | | |
|------------------|----------------------|---|---|------------------|---|---|
|                  | Exp (β) (95% CI)     | P value | Exp (β) (95% CI) | P value |
| Primary outcome  | Annual amount of drugs prescribed per patient | 1.29 (1.26–1.33) | <.001 | 1.26 (1.23–1.29) | <.001 |
| Secondary outcomes: drug prescribing | Annual number of prescriptions per patient | 0.98 (0.96–1.00) | .119 | 0.98 (0.96–0.999) | .040 |
|                  | Annual total prescribing days per patient | 1.24 (1.21–1.26) | <.001 | 1.25 (1.22–1.27) | <.001 |
|                  | Number of drug items per prescription | 0.92 (0.91–0.93) | <.001 | 0.92 (0.91–0.93) | <.001 |
| Secondary outcome: drug costs | Annual drug costs per patient | 1.01 (0.98–1.03) | .653 | 1.00 (0.97–1.02) | .789 |
| Secondary outcome: medical institution utilization behavior | Annual number of medical institutions prescribing for a patient | 0.94 (0.92–0.95) | <.001 | 0.88 (0.87–0.90) | <.001 |

Q = confidence interval; Reference group = National Health Insurance patients.

### Table 3

Comparison of drug prescribing and costs between veterans and National Health Insurance patients.

| Outcome variable | Primary hypertension | | | Dyslipidemia | | |
|------------------|----------------------|---|---|------------------|---|---|
|                  | Exp (β) (95% CI)     | P value | Exp (β) (95% CI) | P value |
| Primary outcome  | Annual amount of drugs prescribed per patient | 1.29 (1.26–1.33) | <.001 | 1.59 (1.55–1.64) | <.001 |
| Secondary outcomes: drug prescribing | Annual number of prescriptions per patient | 1.07 (1.05–1.09) | <.001 | 1.06 (1.04–1.09) | <.001 |
|                  | Annual total prescribing days per patient | 1.44 (1.41–1.47) | <.001 | 1.44 (1.41–1.46) | <.001 |
|                  | Number of drug items per prescription | 1.02 (1.01–1.03) | <.001 | 1.03 (1.02–1.04) | <.001 |
| Secondary outcome: drug costs | Annual drug costs per patient | 1.15 (1.12–1.18) | <.001 | 1.14 (1.12–1.17) | <.001 |
| Secondary outcome: medical institution utilization behavior | Annual number of medical institutions prescribing for a patient | 0.80 (0.79–0.82) | <.001 | 0.77 (0.76–0.79) | <.001 |

Q = confidence interval; Reference group = Medical Aid patients.
patients had significantly longer prescription days and slightly larger numbers of prescriptions, which contributed to having higher prescription drugs. The narrower gaps between veterans and MedAid patients in prescribing outcome variables were expectable because the levels of cost-sharing of the two populations were more similar.

Second, in contrast to medication prescribing, elderly veterans visited fewer medical institutions. Korean elderly veterans utilized fewer medical institutions and the reasons for that have been rarely investigated. A recent qualitative study demonstrates that Korean veterans prefer veteran medical facilities as they can receive full benefits with a minimum administrative process.[33] Further exploration of other potential barriers affecting veterans’ behavior in choosing healthcare facilities is needed.

Third, there were potential safety issues in elderly veterans’ medication use. Elderly veterans were more likely to be prescribed inappropriate drugs, which can potentiate either the risks of adverse drug reactions or inefficiency in health resources use. Elderly veterans had a 1.5~1.8 higher odds of being prescribed therapeutically duplicate medications and a 1.2~1.5 higher odds of being prescribed PIMs for the elderly. A body of evidence suggests that therapeutic duplication and PIMs are notably associated with preventable adverse drug reactions,[17,34] and the considerably high prevalence odds of such inappropriate prescriptions in our study population is alarming.

Given the long prescription days found in the present analysis, the following presents one of the presumed etiological mechanisms that account for therapeutically duplicated prescriptions: low copayment decreases the sense of price at the time of use and, consequently, increases the number of prescriptions for long days; but unexpected allergies or clinical inefficiency may force a patient to search another prescription. Over-prescribed medicines might be associated with adverse drug events if the medications were used, or with increased waste if they were thrown away. Clinical decision-making for prescribing medications is primarily made by prescribers. In this regard, the mechanism described above is formed by patients and their prescribers together. Notably, it has been known that prescribers can also be influenced by how much their patients pay drug costs out-of-pocket.[35,36] Undoubtedly, prescribers can also be affected by various factors other than cost-sharing and it is worthy of a further investigation whether there are any facility-oriented factors affecting medication utilization.

Thus far, decreasing the level of copayment has been considered a way to increase the welfare for the elderly, because international experience strongly suggests a negative relationship between cost-sharing and health outcomes in a vulnerable population.[6–8] The present study, however, demonstrated that a low level of cost-sharing could increase harmful inefficiency of drug prescribing which is closely linked to drug utilization. Our findings suggest that the elderly adults with low levels of cost-sharing are considered as a target population whose drug prescribing should be intensively monitored.

To improve the internal validity, influences of the illness condition were minimized by identifying the study population who were diagnosed with specific chronic diseases, and two comparable groups were constructed as controls through matching potential confounding factors. Similar patterns of prescribing inappropriateness were shown in two chronic conditions, which enhances the external validity of our findings.

The results of the present study must be regarded with the following limitations. Firstly, there were some limitations commonly seen in claims data analysis. It was impossible to include covariates reflecting prescribers’ individual characteristics, and
patients’ clinical status such as laboratory test results (blood pressures, lipid levels, etc.) or health behaviors such as exercise or diets. Amid this situation, we excluded patients with complications whose clinical need for medications was not easily evaluated only with claims data. Although we excluded them based on diagnosis codes, it might be unable to exclude all relevant subjects because diagnosis codes in claims data might be inaccurate. In addition, short-term data did not allow us to consider the length of health conditions for each patient or to evaluate patients’ needs whether there are any differences between veterans and other patients. Secondly, only oral formulations were included for analysis to control for bias due to different dosages across medications. In addition, this study included data from outpatient settings and patients with two simple chronic diseases, and employed multiple outcome variables showing various facets of drug prescribing. Nevertheless, possible bias due to different dosages across medications may not be completely eliminated. Thirdly, the annual utilization could be underestimated because the utilization can be partly measured for some subjects who newly had a diagnosis during the study period. This happened in all cost-sharing groups but we failed to ensure if it distributed evenly across groups. Fourthly, the inappropriateness of drug use could be underestimated because two relevant variables were measured only in a binary form. Further investigation differentiating patients having one or multiple PIMs will be helpful to distinguish population at a greater risk. Lastly, there are some limitations that can constrain external validity of the study. The present study included male elderly and the study findings may not be applicable to female elderly. The present results may not be generalizable to other disease conditions, particularly to acute illnesses.

5. Conclusions
In older patients with one of two major chronic illnesses, a lower level of cost-sharing was associated with having more prescribed medicines, and increased inappropriate prescribing. This not only has negative effects on the health budget but may also threaten patient safety. The central factor in higher prescribed medications was the long length of prescription days, which would be linked to improper prescribing behavior. It is suggested that the elderly adults with low levels of cost-sharing would be a primary target population whose medication prescribing should be intensively monitored. However, this study did not examine the direct relationship between cost-sharing and patient safety, and further studies are needed to draw more definitive conclusions.

Author contributions
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