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New Alert Override Codes for the Drug Utilization Review System Derived from Outpatient Prescription Data from a Tertiary Teaching Hospital in Korea

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Objectives: This paper proposes new alert override reason codes that are improvements on existing Drug Utilization Review (DUR) codes based on an analysis of DUR alert override cases in a tertiary medical institution. **Methods:** Data were obtained from a tertiary teaching hospital covering the period from April 1, 2012 to January 15, 2013. We analyzed cases in which doctors had used the 11 overlapping prescription codes provided by the Health Insurance Review and Assessment Service (HIRA) or had provided free-text reasons. **Results:** We identified 27,955 alert override cases. Among these, 7,772 (27.8%) utilized the HIRA codes, and 20,183 (72.2%) utilized free-text reasons. According to the free-text content analysis, 8,646 cases (42.8%) could be classified using the 11 HIRA codes, and 11,537 (57.2%) could not. In the unclassifiable cases, we identified the need for codes for "prescription relating to operation" and "emergency situations." Two overlapping prescription codes required removal because they were not used. Codes A, C, F, H, I, and J (for drug non-administration cases) explained surrounding situations in too much detail, making differentiation between them difficult. These 6 codes were merged into code J4: "patient was not taking/will not take the medications involved in the DDI." Of the 11 HIRA codes, 6 were merged into a single code, 2 were removed, and 2 were added, yielding 6 alert override codes. We could codify 23,550 (84.2%) alert override cases using these codes. **Conclusions:** These new codes will facilitate the use of the drug–drug interactions alert override in the current DUR system. For further study, an appropriate evaluation should be conducted with prescribing clinicians.

Keywords: Drug Utilization Review, Drug Interactions, Outpatient Care, Clinical Decision Support Systems, Contraindications

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I. Introduction

A Drug Utilization Review (DUR) system prevents drug side effects and helps reduce the use of problematic medicine and medical supplies by preventing the prescription and preparation of inappropriate drugs [1]. Although the United States implemented such a system in 1990, South Korea developed the DUR, and it was subsequently implemented in all recuperation centers in the country [2]. Korea's DUR system can be largely divided into inspection "within and between prescriptions." It contains various types of information, such as restrictions on combined intake, restrictions for certain age groups, restrictions for pregnant women, medicines prepared in low-content multiples, medicines suspended for safety reasons, and overlapping prescriptions with the same ingredients administered through the same injection routes [3]. In some cases, warning pop-ups appear during the prescription process, flagging restrictions on combined intake, restrictions for certain age groups, restrictions for pregnant women, and overlapping prescription drugs with the same ingredients. To proceed with such a prescription, a physician must provide a reason for prescription of the alerted medicine [4].

The prohibition on combined use is intended to prevent drug–drug interactions (DDIs) [5]. Patients can sometimes be prescribed more than 2 administered drugs during their treatments, which can cause DDIs. In a DDI, 2 administered drugs interact and change the absorption speed, protein-binding site, biotransformation, or excretion speed of one or both drugs [6]. Such changes manifest as additive, synergistic, or antagonistic reactions, and can cause severe side effects and toxicity. Although DDIs occur frequently [7,8], a considerable number can be prevented through use of a DUR system [9].

South Korea has the advantage that a single DUR system is used in all medical institutions and recuperation centers except in oriental medicine institutes. For the Korean DUR system to work effectively, it must be continually monitored and improved. However, there has been limited research on this system since 2010; in particular, no study has analyzed cases of alert overrides with overlapping prescription codes and reasons for override (i.e., free-text entry), even though these are the key elements of the DUR system. To fill this gap in the research, we examined all such cases among outpatients in a tertiary medical institution from the past 10 months and analyzed the current use of existing overlapping prescription codes and free-text exception reasons. Based on our findings, we were able to propose new alert override codes that improve upon the existing codes.

1. DUR System and Overlapping Prescription Codes

South Korea's DUR system involves 1) self-inspection within and cross-inspection between prescriptions, 2) prescription and preparation of medicines in accordance with the inspection results, and 3) entry of reasons and transmission completion. The first is a check for any prohibitions on combined use, ingredient overlap, restrictions for certain age groups, and restrictions for pregnant women within the same prescription. The second is a crosscheck of the information from self-inspection, which was automatically transmitted to the central server of the Health Insurance Review and Assessment Service (HIRA), with that of prescriptions of another medicine currently taken by the patient. The cross-inspection involves 1) comparison of prescriptions of medicines before preparation and 2) comparison of preparations for medicines already being taken. If a medicine prohibited from prescription is ultimately prescribed for medical and pharmaceutical reasons in a medical institution, the corresponding reason is entered into the system to complete the processing. When the reason is entered, the type and side effects of the relevant medicine must be explained to the patient, and the reason code or details must be input and sent to the HIRA. The reasons are entered differently depending on the inspection grades; they can be omitted if the inspection grade is A, but must be entered for grade B. For grade C, the drug must not be prescribed because it is prohibited, while for grade D, the reason entry is optional. Apart from inspection grades, there are 11 types of overlapping prescription codes already established, including A–C, F–K, and P. Overlapping prescription reasons related to combined use, age, or pregnancy can be entered as free text. The overlapping prescription codes, which were devised by the HIRA, are entered when

A: a patient must receive a prescription before exhausting the existing medicine or medical supplies due to a long-term business trip or travel;

B: specific ingredients cannot be sorted for separate prescriptions among existing prescribed medicines due to preparation in powder form;

C: a medicine is destroyed or altered for reasons not attributable to the patient (e.g., vomiting during drug intake);

F: the prescription and administration dates differ;

G: a medicine is administered weekly or monthly;

H: overlapping or combined drug use occurs by a change of only the method of intake or volume;

I: overlapping or combined medicine use occurs due to a change of only the number of administration dates;

J: a patient does not take the existing prescription or prepared medicine (voluntarily);

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K: a patient cannot reach the prescribing doctor or preparing pharmacists via phone;

L: a patient is not permitted to take the existing prescribed medicine (by the doctor); and

P: a medicine is administered pro re nata (PRN).

II. Methods

1. Study Material

This study examined all alert override cases in the DUR system among outpatients of a tertiary medical institution from April 1, 2012 to January 15, 2013. The data cover only cases in which an alert override occurred and do not contain any private or health-related patient or health professional information.

2. Code and Free-Text Analysis Methodology

While the alert override cases assigned an overlapping prescription code can be readily used in analysis, the free-text reasons comprise a large, diverse, and irregular body of free text including Korean and English text, meaningless symbols, and numbers. This makes automated analysis impossible. Therefore, all free-text data were classified manually by two researchers (JC, KBY) and evaluated by RWP. In this study, the exception processing codes of Grizzle et al. [10] and Ahn et al. [11] were referenced in classification. Grizzle et al. [10] developed 14 categories for overriding DDI alerts and prescribers classified their messages into the categories after excluding duplicated messages from ambulatory pharmacy dispensing records. Ahn et al. [11] was modified from the study of Grizzle et al. [10] and simplified according to the subject data.

3. Statistical Analysis Methods

This study did not require statistical evaluation, as the classification results were merely recorded. For data extraction and classification, MS-SQL 2012 (Microsoft, Redmond, WA, USA) was used.

III. Results

According to an analysis of the system log file of all outpatient DDIs in the target medical institution, there were 28,606 alert override cases. Among the 7,879 cases with overlapping prescription codes, we excluded 48 with missing data and 59 involving an unknown drug; this resulted in a 7,772 cases. Among the 20,727 free-text cases, we excluded 102 with missing data and 442 involving an unknown drug, thereby leaving 20,183 cases for analysis. In total, 27,955 cases were included in the analysis (Figure 1).

The most frequently appearing overlapping prescription code was F, at 2,519 cases (32.4%), followed by A, at 2,428 cases (31.2%). The least frequent code was K, which occurred only once (Table 1).

An analysis of the free-text reasons entered for alert override prescriptions revealed 15 classifications. The most frequently occurring reason was "prescribing a medicine to control a patient's symptom," with 5,665 cases (28.1%) followed by "meaningless/no meaning (e.g., ㅋㅋㅋ, aaa)," with 4,263 cases (21.1%). "Prescribing out of necessity" occurred

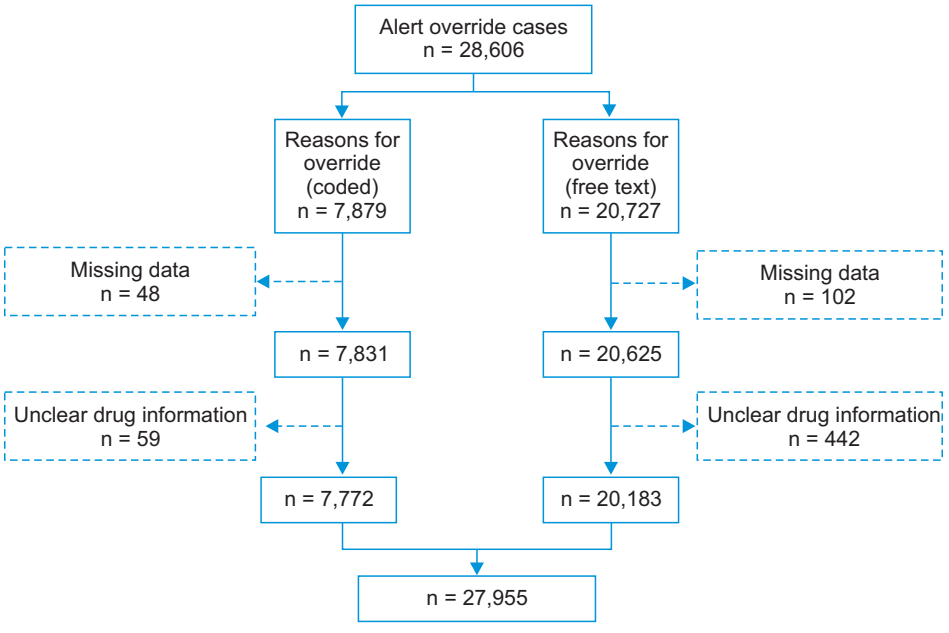

Figure 1. Data selection process.

Table 1. Frequency of overlapping prescription codes of the health insurance review and assessment service

Code	Reason	No. (%)
A	When a patient has to receive a prescription before exhausting the existing medicine or medical supplies due to a long-term business trip or travel	2,428 (31.2)
B	When specific ingredients cannot be sorted for separate prescriptions among existing prescribed medicines due to preparation in powder form	64 (0.8)
C	When medicine is destroyed or altered for reasons not attributable to the patient (e.g., vomiting during drug intake)	377 (4.9)
F	When the prescription and administration dates differ	2,519 (32.4)
G	When a medicine is administered weekly or monthly	490 (6.3)
H	When overlapping or combined drug use occurs due to a change of only the method of intake or volume	621 (8.0)
I	When overlapping or combined drug use occurs due to a change of only the number of administration dates	785 (10.1)
J	When a patient does not take the existing prescription or prepared drug (voluntarily)	79 (1.0)
K	When a patient cannot reach the prescribing doctor or preparing pharmacists via phone	1 (0.0)
L	When a patient is not permitted to take the existing prescribed medicine (by the doctor)	197 (2.5)
P	When a medicine is administered pro re nata (PRN)	211 (2.7)
Total		7,772 (100)

Table 2. Frequencies of override reasons in free text

	Reason	No. (%)
I	Meaningless/no meaning (ㅋㅋㅋ, aaa)	4,263 (21.1)
II	Can have combined use	124 (0.6)
III	Cannot have combined use (e.g., gargle medicines for external use).	1,936 (9.6)
IV	Instruction and prescription by a doctor	590 (2.9)
V	The drug can be taken because it has no side effects	1 (0.0)
VI	Prescribing out of necessity	3,719 (18.4)
VII	Prescribing a drug to control a patient's symptoms	5,665 (28.1)
VIII	Prescribing a drug according to the patient's demand	77 (0.4)
IX	Prescribing a drug after an explanation so that it is not taken at the same time	249 (1.2)
X	Prescribing a medicine after use of a drug is suspended or a medicine is changed	41 (0.2)
XI	Can be used because it is medicine for discharge	2,701 (13.4)
XII	Prescribing out of necessity before and after an operation or examination	290 (1.4)
XIII	A certain medicine has already been administered	29 (0.1)
XIV	Medicine has been taken previously	40 (0.2)
XV	Emergency situations	458 (2.3)
Total		20,183 (100)

in 3,719 cases (18.4%). For a number of cases, the reasons did not match any existing overlapping prescription codes, including 290 cases (1.4%) for "prescribing out of necessity before and after an operation or examination" and 458 cases (2.3%) of "emergency situations." Among these 15 classifications, 8,626 cases (42.8%) could be classified using the 11 HIRA codes; 11,537 cases (57.2%) could not. Notably, the need for new codes describing operations and emergency situations was identified when these unclassifiable cases were analyzed and classified (Table 2).

The results of the free-text classification were compared with the HIRA override prescription codes. This led to the identification of 6 new alert override codes (Table 3). Previous codes P and G were combined into J1. Previous

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Table 3. Frequency of alert override reasons using new classification system

	Suggested code	Reasons for override (code)		Reasons for override (free text)		Total no. (%)
		HIRA code	No. (%)	Free text	No. (%)	
Reasons for alert overrides						
PRN (as needed) or intermittent medication	J1	G, P	701 (9.0)	VI, IX	3,968 (19.7)	4,669 (16.7)
Prescriber provided clinical justification	J2			II, IV, V, VII, XIII, XIV	6,449 (32.0)	6,449 (23.1)
No PO drug	J3	L	197 (2.5)	III	1,936 (9.6)	2,133 (7.6)
Patient was not taking/will not take the medications involved in the DDI	J4	A, C, F, H, I, J	6,809 (87.6)	X, XI	2,742 (13.6)	9,551 (34.2)
Operation situation	J5		0 (0)	XII	290 (1.4)	290 (1.0)
Emergency situation	J6		0 (0)	XV	458 (2.3)	458 (1.6)
Prescriber provided no reason for override	-		0 (0)	I	4,263 (21.1)	4,263 (15.3)
Rarely used reasons	-	B, K	65 (0.8)		0 (0)	65 (0.2)
Patient requested it	-			VIII	77 (0.4)	77 (0.3)
Total			7,772 (27.8)		20,183 (72.2)	27,955 (100)

Code J1 was taken from the HIRA codes. Codes J2 and J4 were from Grizzle et al. [10] and Ahn et al. [11]. Codes J3, J5, and J6 were newly proposed in this study.

HIRA: Health Insurance Review and Assessment Service, PRN: pro re nata, DDI: drug–drug interaction.

code L was revised as J3. The 6 codes describing drug non-administration situations (A, C, F, H, I, and J) were thought to be overly descriptive of surrounding situations in which drugs were not being administered; thus, these 6 codes were combined into J4: "patient was not taking/will not take the medications involved in the DDI." The cases made up of meaningless symbols and characters were classified as "prescriber provided no reason for override" (n = 4,263, 21.1%) and were not included in the new classification system. Codes B (0.8%) and K (0%) were rarely used and thus were classified as "rarely used reasons" (n = 65, 0.8%); they were also not included in the new classification system.

Using the new classification structure, we reanalyzed the 20,183 alert override cases with free-text reasons. Of the free-text reasons, code J2 ("prescriber provided clinical justification") was the most frequent, with 6,449 cases (32.0%), followed by J1 ("PRN [as needed] or intermittent medication"), with 3,968 cases (19.7%). "Prescription according to patient request" (77 cases, 0.4%) was found to be too general and unclear, and thus was not included in the new system.

On the basis of the new classification, J4 was the most frequently occurring reason at 9,551 cases (34.2%), followed by J2, with 6,449 cases (23.1%), and then J1, with 4,669 cases (16.7%).

IV. Discussion

We analyzed and classified DUR alert override cases occurring among outpatients in a tertiary medical institution and codified the results to improve existing codes for overlapping prescription reasons, and based on our findings, we introduced a new coding system. The main purpose of the DUR system is to help physicians administer drugs safely and with minimal side effects. For the DUR system to be successfully implemented in accordance with this purpose, research on its effects and means of improvement is required in many areas, including strategy, cost, stability, and convenience. This study sought to identify appropriate methods of improvement by analyzing override reasons. Specifically, we analyzed the frequency of overlapping prescription codes and free-text reasons. In the process, the free-text content was classified into 15 different categories based on similarity of content as found by the researcher; these 15 categories were compared with the existing overlapping prescription codes, resulting in the creation of 6 new alert override codes.

This study utilized the entire set of DDI data on outpatients of a tertiary medical institution from April 1, 2012 to January 15, 2013. We minimized recall and selection biases by analyzing all prescription cases within the system log file,

and minimized the classification errors for all 20,183 cases involving free-text override reasons via manual evaluation and classification.

To create the new override reason codes, we consulted a previous study [11]; previous code P was revised and renamed J1; codes J2 and J4 were adopted from a previous study by Grizzle et al. [10]; and codes J3, J5, and J6 were created by the researcher. The main contribution of this study is the recommendation of an improved coding system for override reasons based on existing overlapping prescription codes and free-text reasons. Although one previous study [11] performed some analysis of overlapping prescription codes for hospitalized patients, there have been almost no studies that have conducted comparative analysis of these codes and free-text reasons. Therefore, the current study makes a meaningful contribution by conducting a systematic comparison of overlapping prescription codes and free-text reasons as the basis for developing an improved coding system.

In analyzing the overlapping prescription reason codes, the most frequent was F (32.4%), followed by A (31.2%). Code F ("when the prescription and administration dates differ") seems irrelevant to the prevention of DDIs caused by overlapping prescriptions.

Moreover, code A ("when a patient has to receive a prescription before exhausting the existing medicine or medical supplies due to a long-term business trip or travel") also seems irrelevant to the prevention of DDIs caused by overlapping prescriptions, as it seems a very reasonable reason for overlapping prescriptions from the patient's perspective. In contrast, codes B ("when specific ingredients cannot be sorted for separate prescriptions among existing prescribed medicines due to preparation in powder form") and K ("when a patient cannot reach the prescribing doctor or preparing pharmacists via phone") were very rarely used by the prescribing physician, and seem inappropriate from a researcher's perspective; they were thus classified as rarely used reasons (n = 65, 0.8%). Clinically irrelevant codes are known as the main source of alert fatigue [12] and most can be ignored [13,14].

Codes A, C, F, H, I, and J were thought to be overly descriptive of a situation wherein a drug is not being administered; thus, they are difficult to distinguish in practice. To prevent confusion among physicians, we merged these codes into a new code, J4: "patient was not taking/will not take the medications involved in the DDI."

According to the analysis of the free-text cases that could not be classified using existing codes, we noted many occurrences of "prescription relating to operation" and "emergency situations." This led to our creating two additional codes (J5 and J6). The most frequently occurring reason among the free-text cases was "prescribing a medicine to control a patient's symptoms," with 5,665 cases (28.1%); this reason was mapped onto J2. The second most frequently occurring reason was "meaningless/no meaning (e.g., ㅋㅋㅋ, aaa)" with 4,263 cases (21.1%). However, such cases were difficult to codify; therefore, they were processed as "prescriber provided no reason for override" (n = 4,263, 21.1%). "Prescribing out of necessity" also frequently occurred, at 3,719 cases (18.4%), and was subsequently mapped onto code J1.

We considered establishing code G ("when a medicine is administered weekly or monthly") as a separate item but decided to merge it with J1 because it was rarely used (6.3%) and the code itself means that the medicine is administered rarely. Ultimately, the analysis of the existing 11 overlapping prescription codes resulted in 6 codes being merged into a single code, 2 codes being deleted, and 2 codes being created, resulting in 6 new alert override codes. When this new set of codes was applied to the cases, we found that 23,550 (84.2%) of the total 27,955 cases could be codified.

This study had the following limitations. First, this was a case study of DUR alert override reasons from a single tertiary medical institution over a period of approximately 10 months. This could have resulted in selection bias. Second, we excluded prescriptions for hospitalized patients; if prescription patterns differ between inpatients and outpatients, the results of this study may not reflect the actual clinical environment. Third, the prescription analysis was limited to drugs prescribed over a certain period of time within the same hospital, and the number of alerts in this study cannot be considered to reliably represent all DDI cases. Finally, our own subjective standards may have influenced the codifying of the free-text, the mapping of the existing codes and free-text reasons onto new codes, and the deletion of existing codes.

These new codes will facilitate the use of drug–drug interactions alert override in the current DUR system. For further studies, an appropriate evaluation should be conducted with prescribing clinicians and the reason "meaningless/no meaning (e.g., ㅋㅋㅋ, aaa)" in free text needs to be identified.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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References

1. Choi NK, Park BJ. Strategy for establishing an effective Korean drug utilization review system. J Korean Med Assoc 2010;53(12):1130-8.
2. Choi JS, Kim DS. A case study of implementation of concurrent drug utilization review system at a general hospital. J Korean Inst Ind Eng 2013;39(1):20-9.
3. Strom BL, Kimmel SE, Hennessy S. Pharmacoepidemiology. 5th ed. Chichester: Wiley-Blackwell; 2012.
4. Jeon HL, Park JH, Kim DS, Choi BC. Review of the Drug Utilization Review program of United States 47 States and suggestion of policy. Health Soc Welf Rev 2014;34(3):192-221.
5. Kim DS, Park JH, Jeon HL, Park CM, Kang HA. The effect of Korean Prospective Drug Utilization Review Program on the prescription rate of drug-drug interactions. Health Policy Manag 2014;24(2):120-7.
6. Brunton L, Chabner B, Knollmann B. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York (NY): McGraw-Hill; 2011.
7. Rodrigues AD. Drug-drug interactions. 2nd ed. New York (NY): Informa Healthcare; 2008.
8. Hines LE, Murphy JE. Potentially harmful drug-drug interactions in the elderly: a review. Am J Geriatr Pharmacother 2011;9(6):364-77.
9. Hansten PD, Horn JR. Drug interactions analysis and management. 6th ed. St. Louis (MO): Wolters Kluwers Health; 2011.
10. Grizzle AJ, Mahmood MH, Ko Y, Murphy JE, Armstrong EP, Skrepnek GH, et al. Reasons provided by prescribers when overriding drug-drug interaction alerts. Am J Manag Care 2007;13:573-8.
11. Ahn EK, Cho SY, Shin D, Jang C, Park RW. Differences of reasons for alert overrides on contraindicated coprescriptions by admitting department. Healthc Inform Res 2014;20(4):280-7.
12. Ahearn MD, Kerr SJ. General practitioners' perceptions of the pharmaceutical decision-support tools in their prescribing software. Med J Aust 2003;179(1):34-7.
13. Magnus D, Rodgers S, Avery AJ. GPs' views on computerized drug interaction alerts: questionnaire survey. J Clin Pharm Ther 2002;27(5):377-82.
14. Glassman PA, Simon B, Belperio P, Lanto A. Improving recognition of drug interactions: benefits and barriers to using automated drug alerts. Med Care 2002;40(12):1161-71.