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The Relationship Between Prescription Patterns and Symptom-Based Subtypes of Depression Using Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF) Specific Problems Scales in Korean Clinical Sample

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We derived five heterogeneous subtypes for 473 Korean depressive disorder patients through a latent profile analysis using the specific problems scale of the Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF), which we used in a previous study (Choi, 2019). In this study, we attempted to confirm the clinical usefulness of specific problem scales by comparing the drug prescription patterns of the five derived subtypes: mild, helpless, somatic, avoidant with anxiety, and irritable with anxiety. Through retrospective medical records of 473 patients with depressive disorder, we investigated their demographic variables, hospitalizations, and prescriptions during the initial, third, and sixth months of treatment. There was a significant difference among the groups in the number of antidepressants prescribed initially and in the third months of treatment. Additionally, we noted differences in antipsychotics prescription in months three and six and sedative/hypnotics prescription in month six. The study results confirmed that the subtypes of depressive disorder based on specific problem scales of the MMPI-2-RF were associated with prescription patterns and clinical course. This finding suggests that subtyping based on multidimensional symptoms, not just the main symptoms of depression, may be useful in establishing a focused treatment plan tailored to the individual characteristics of patients in the initial phase of treatment.

Keywords: depression, symptom-based subtypes, specific problems scale of MMPI-2-RF, latent profile analysis, prescription patterns

Depressive disorders, which include multiple heterogeneous clinical features, are classified into subtypes based on various criteria. Historically, researchers and clinicians have attempted to classify the subtypes based on the heterogeneous aspects of depressive disorder, such as the specifier of the disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM), severity, family history, and age of onset (American Psychiatric Association, 2013; Savitz & Drevets, 2009; Sharpley & Bitsika 2013). In recent years, subtypes classification has included data-driven approaches because of the advantages of using various indicators to explore real and heterogeneous subgroups within depressive disorders (Ten Have et al.,2016; Van Loo, De Jonge, Romeijn, Kessler & Schoevers, 2012). Latent cluster analysis or latent profile analysis using various symptom dimensions as indicators is also referred to as a person-centered approach rather than a variable-centered approach because it subtypes based on the similarities and differences within

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patients with depressive disorder.

Previous studies that analyzed symptom patterns through a person-centered approach mainly derived latent clusters based on diagnostic criteria or depression scales, such as the Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAM-D), and Center for Epidemiologic Studies-Depression Scale (CES-D) (Van Loo et al., 2012; Ten Have et al., 2016; You et al., 2011). These studies had the advantage of classifying subgroups based on the typical symptoms of depressive disorder. However, the limitation was that they did not reflect the patterns of various atypical symptoms of depressive disorder. Patients with depressive disorder also often have anxiety or somatic symptoms, irritability, or aggression, which are not included in the DSM specifiers.

The Minnesota Multiphasic Personality Inventory-2 (MMPI-2), widely used in clinical settings as an assessment tool, covers various psychopathologies (Butcher et al. 2001). A reconstructed version with improved psychometric stability and construct validity has been launched, thereby increasing its usefulness in research and clinical evaluation (Ben-Porath & Tellegen, 2008; Han, Moon, Lee & Kim, 2011). Among the subscales of the reconstructed version that can be used directly with the 338-item Minnesota Multiphasic Personality Inventory-2 Restructured Form (MMPI-2-RF) or converted from MMPI-2, the 23 specific problem scales have the advantage of allowing the identification of detailed symptoms in various dimensions. Because the 23 specific problem scales measure detailed symptoms without overlapping each other in various dimensions, they have the advantage of identifying symptom patterns of a wide range of dimensions in addition to the severe level of accompanying symptoms indicated by the comorbid diagnosis. It includes somatic/cognitive, internalizing, externalizing, and interpersonal scales; therefore, it can be a useful tool for grouping patients with a depressive disorder based on the patterns of various symptom dimensions.

To classify patients with a depressive disorder based on multi-dimensional symptoms, we conducted a latent profile analysis (LPA) of 473 patients with depressive disorders using the MMPI-2-RF specific problems scales as indicators in a previous study (Choi, 2019[1]). As a result, we adopted a classification model with five classes (or groups): "mild group", "helpless group", "somatic group", "avoidant group with anxiety", and "irritable group with anxiety". The mild group (22.6%) showed a low level of symptoms in all dimensions and had lower comorbidity. The helplessness group (23.9%) had high hopelessness and self-doubt but a lower level of other somatic/cognitive symptoms or externalizing symptoms. This group is similar to the group classified as having typical depression (Rodgers et al., 2014a) or moderate depression without anxiety (Ten Have et al., 2016). In the somatic group (27.9%), we observed elevated somatic/cognitive domain symptoms, whereas passivity and social avoidance on interpersonal scales were not as high as those of the helplessness group. It is understood as a group showing a tendency to experience depression as somatic symptoms, a subtype frequently reported in previous studies (Carragher, Adamson, Bunting & McCann, 2009; Lee et al, 2014). The avoidance group with anxiety (19.0%) showed high overall symptoms on all internalizing scales, especially high passivity and social avoidance on interpersonal scales. There was also a high rate of co-occurrence of anxiety disorders in this group. The irritable group with anxiety (6.6%) showed high externalizing symptoms such as aggression and activation, in addition to overall high internalizing symptoms, and had a high rate of alcohol use disorder. Both groups were similar to depression with anxiety reported in previous studies (Ten Have et al., 2016; You et al., 2011). However, since the MMPI-2-RF-specific problem scales, including externalizing problems, were used as indicators, it was possible to divide the anxious group into avoidant and irritable groups. Figure 1 shows the plot of the five-class model. Appendix 1 illustrates the fit indices of the competing latent class models in this study and Appendix 2 summarizes the comorbid diagnoses of the four classes. The five-class model contained one mild group, two moderate groups, and two severe groups in terms of criticality. It also derived groups of heterogeneous patterns with similar severity levels but with symptoms in different domains. In other words, we suggest that subtyping using the specific problem scales of the MMPI-2-RF effectively captures heterogeneous the aspects of depression.

1) Choi, J. Y. (2019). Symptom-based subtypes of depression: latent profile analysis with specific problems scales in MMPI-2-RF. *Korean Journal of Clinical Psychology, 38*, 287-299. https://doi.org/10.15842/kjcp.2019.38.3.002.

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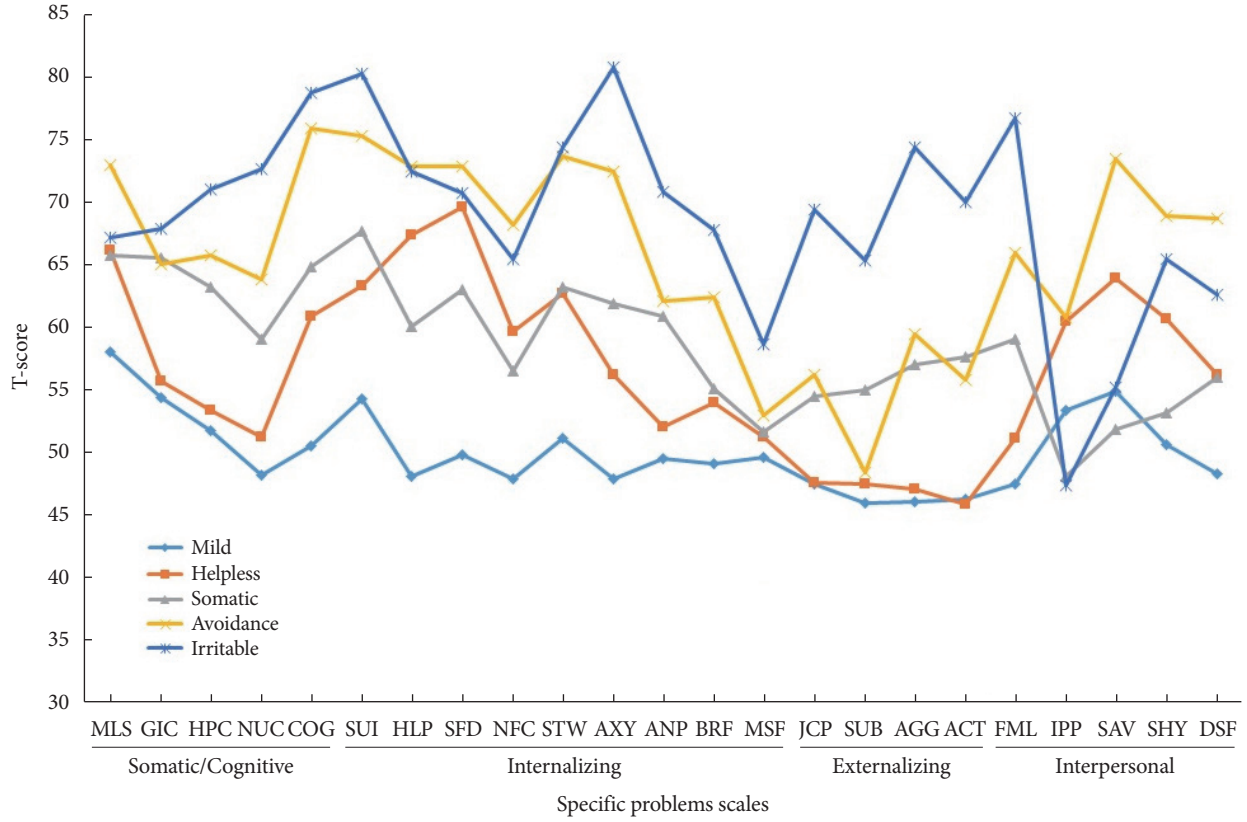

Figure 1. *Latent profiles plot of the 5-class model.*
Note. MLS = Malaise; GIC = Gastrointestinal Complaints; HPC = Head Pain Complaints; NUC = Neurological Complaints; COG = Cognitive Complaints; SUI = Suicidal/Death Ideation; HLP = Helplessness; SFD = Self-Doubt; NFC = Inefficacy; STW = Stress/Worry; AXY = Anxiety; ANP = Anger Proneness; BRF = Behavior-Restricting Fears; MSF = Multiple Specific Fears; JCP = Juvenile Conduct Problems; SUB = Substance Abuse; AGG = Aggression; ACT = Activation; FML = Family Problems; IPP = Interpersonal Passivity; SAV = Social Avoidance; SHY = Shyness; DSF = Disaffiliativeness.

Comparing the prescription patterns according to subtypes is expected to support the clinical usefulness of the classification using the specific problem scales of the MMPI-2-RF as indicators. A few previous studies classified depressive disorder into subtypes based on symptoms and compared the clinical course of the disease, but most of them analyzed subtypes based on typical symptoms of depression using criteria for depressive disorder or depression scales (Alexandrino-Silva et al., 2013; Lamers et al., 2010; You et al., 2011; Ulbricht, Rothschild & Lapane, 2015). Few studies have compared drug prescription patterns to data-driven subtypes of depressive disorder based on personality characteristics rather than symptoms (Hori et al., 2017).

Therefore, this study aimed to confirm any significant differences in the pattern of actual prescribing by clinical judgement according to these multipledimensional symptom-based subtypes using MMPI-2-RF specific scales. It is expected that patients in the mild group, with the lowest severity of depression, are more likely not to receive an antidepressant in the initial treatment, and the two high-severity groups, the avoidant and irritable groups, would likely receive more antidepressants in combination with antipsychotics. In addition, even at the same severity level, it is expected that the prescription patterns of the helpless and somatic symptom groups were different and that the prescription rates of antipsychotic drugs were different between the avoidant and irritable groups. We also examined whether the medications corresponded to the Korean Medication Algorithm for Depressive Disorders revised in 2017 by the Korean Society for Affective Disorders and the Korean College of Neuropsychopharmacology (Seo et al., 2017). In the Korean Medication Algorithm for Depressive Disorders, antidepressant monotherapies are recommended as first-line treatment for non-

psychotic depression. The combination of antidepressants and atypical antipsychotics is recommended for psychotic depression, mixed feature, and anxious distress. In addition, when the initial treatment is ineffective, the method of adding antidepressants and antipsychotics is selected rather than changing antidepressants as the severity increases.

For this study, we retrospectively analyzed medical records to identify the medications prescribed to patients with each of the five subtypes of depression. The analysis of medical records included a comparison of differences in medication selection (e.g., antidepressants, antipsychotics, mood stabilizers, augmentation drugs, anxiolytics, and sedative/hypnotics) across the subtypes in the initial and the secondary treatment strategies, and an assessment of any differences in the duration of treatment.

Methods

Participants and Procedure

For this study, we collected medical records from the same sample reported by Choi (2019). The medical records retrospectively include psychological assessment data, types of medication, and maintenance periods of drug treatment for outpatients and inpatients who visited the Department of Mental Health and Medicine at the University Hospital from March 2014 to December 2016, and those who provided informed consent and responded to a series of questionnaires. Additionally, we collected data on demographic variables, including sex, age, and years of education. Psychological assessments, including the MMPI-2-RF and BDI, were usually conducted within 1 to 4 weeks after the first consultation with a psychiatrist. During the follow-up, the psychiatrist recorded the diagnosis after psychological assessment. Data on medication prescriptions were collected during initial treatment. On December 31, 2019, when we collected the study data, the rate of treatment maintenance was 19.5%, and the average follow-up period was 640.45 days.

We studied 473 patients, excluding cases of suspected involvement in the brain's organic damage and medical condition, or those diagnosed with intellectual disability, past mania or hypomania, or suspected schizoaffective disorder. The age range of the participants was 18–80 years, with an average age of 39.56 years (standard deviation, 16.79), among whom 217 were men (45.9%) and 256 were women (54.1%). A total of 395 patients (83.5%) were diagnosed with major depressive disorder, 30 (6.3%) with persistent depressive disorder, and 40 (8.5%) with unspecified depressive disorders.

We conducted this study as a retrospective medical record analysis of patients who had provided written informed consent after reading the manual for usage of research data. This study was approved by the Institutional Review Board (IRB) of the hospital.

Lists of Drugs used by Patients

We divided the drug list proposed by the Korean Medication Algorithm for Depressive Disorders into initial, three-month, and six-month periods of treatment. The list of drugs is presented in Table 1.

Table 1. *List of Prescribed Drugs*

Antidepressant	Escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
	Desvenlafaxine, duloxetine, milnacipran, venlafaxine
	Bupropion
	Mirtazapine
	Moclobemide
	Tianeptine
	Agomelatine
	TCA (amitriptyline, clomipramine, imipramine, etc)
Antipsychotics	Amisulpiride, aripiprazole, blonanserin, clozapine, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone, typical antipychotics
Mood stabilizers	Carbamazepine, lamotrigine, lithium, valproate
Augmentation drugs	Buspirone, gabapentin, ketamine, pindolol, psychostimulant, thyroid hormone, topiramate
Anxiolytics & hypnotics	Alprazolam, Clonazepam, Lorazepam, Diazepam, Clobazam, Bromazepam
	Stilnox, triazolam, etc.

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Measures

Specific Problems Scales in the Minnesota Multiphasic Personality Inventory–2 Restructured Form (MMPI–2–RF)

Clinicians have developed the MMPI-2-RF to improve the overall psychometric properties of the MMPI-2, which assesses symptoms and diagnostic possibilities in clinical populations (Ben-Porath & Tellegen, 2008). The published MMPI-2-RF Korean version has acceptable reliability and validity (Han et al., 2011). The MMPI-2-RF consists of nine validity scales, three higher-order (H-O) scales, nine restructured clinical (RC) scales, 23 specific problems (SP) scales, two interest scales, and the revised Personality Psychopathology-Five (PSY-5) scales. In this study, we used 23 specific problem scales as indicators for latent profile analysis (LPA). The somatic and cognitive sets of specific problem scales include malaise (MLS), gastrointestinal complaint (GIC), head pain complaint (HPC), neurological (NUC), and cognitive complaint (COG). Internalizing scales included suicidal/death ideation (SUI), helplessness (HLP), self-doubt (SFD), inefficacy (NFD), stress/worry (STW), anxiety (AXY), anger proneness (ANP), behavior-restricting fear (BRF), and multiple specific fear (MSF). Externalizing scales included juvenile conduct problems (JCP), substance abuse (SUB), aggression (AGG), and activation (ACT). Interpersonal problem scales included family problems (FML), interpersonal passivity (IPP), social avoidance (SAV), shyness (SHY), and disaffiliativeness (DSF). The validation study in the Korean clinical sample indicated an adequate internal consistency of .63-.80 for the specific problem scales (Han et al., 2011).

Beck Depression Inventory

This scale was originally developed by Beck, Steer, and Brown (1996) to assess the degree of depression and was standardized in Korea by Lee and Song (1991). The scale consists of 21 items measured on a three-point Likert scale. The internal consistency of the Korean version was .78, and the test-retest reliability was .75. The internal consistency in the present study was .92. We used the BDI score to compare the degree of depression among subtypes.

Data Analyses

First, to compare the demographic characteristics between the five subtypes derived from LPA, we used the MMPI-2-RF specific problems scale as an indicator, as in the previous study (Choi, 2019). We used the chi-square test, ANOVA, and Bonferroni post-test to analyze the severity of depression measured by BDI, hospitalization rate, duration of hospitalization, and rate of follow-up maintenance after three months, six months, and at the time of analysis. We performed a chi-square test to assess drug prescription patterns according to the period for each depression subtype, antidepressant prescription rates, combined treatment, and types of drugs divided into initial, three-month, and six-month periods. SPSS 25.0 (IBM Corp., Armonk, NY, USA) was used for the analysis

Results

Demographic and Clinical Course of the Subtypes

Analysis of the demographic data revealed a statistically significant difference in age and sex between the groups according to the clinical type of depression, but no significant difference in years of education. The proportion of women in the mild group (66.4%), helpless group (55.8%), and somatic group (59.8%) was high but low in the avoidant group with anxiety (33.3%) and irritable group with anxiety (41.9%). The mean age of the groups was as follow: mild (47.27), helpless (41.60), somatic (39.93), irritable group with anxiety (32.94), and avoidant group with anxiety (29.58). There were no significant differences in hospitalization rates or duration between the groups at the three-month follow-up, six-month follow-up, and overall follow-up periods. At the three-month follow-up, 66.44% ($n = 319$) of the total patients ($N = 473$) continued treatment, and at the six-month follow-up, 50.3% ($n = 238$) of the total patients continued treatment. The demographic and clinical characteristics of the subtypes are presented in Table 2.

Prescription Patterns of the Subtypes

First, a significant difference in the initial antidepressant prescription was observed between the groups in the initial antidepressant prescription. In the mild (31.8%), somatic (34.8%), and avoidant group with anxiety (32.2%), the rate of not prescribing antidepressants was high from the initial visit. In contrast, in the irritable group with anxiety, the prescription rate of two or more antidepressants from the initial visit was 19.4%. The initial prescriptions of the subtypes are presented Table 3.

Table 2. *Comparison of Subtypes on Demographic and Clinical Characteristics (N = 473)*

	Class 1 Mild group	Class 2 Helpless group	Class 3 Somatic group	Class 4 Avoidant group with anxiety	Class 5 Irritable group with anxiety	χ^2/F	Bonferroni
Component ratio	107 (22.6)	113 (23.9)	132 (27.9)	90 (19.03)	31 (6.6)		
Age[a]	47.27 (15.54)	41.6 (18.30)	39.93 (15.42)	29.58 (13.44)	32.94 (13.50)	17.36***	1 > 3, 4.5/2 > 4/ 3 > 4
Sex: women[b]	71 (66.4)	63 (55.8)	79 (59.8)	30 (33.3)	13 (41.9)	25.83***	
Education (years)[a]	12.14 (3.41)	12.32 (3.19)	14.6 (4.88)	13.17 (3.01)	13.16 (2.69)	1.34	
BDI : *M* (*SD*)[a]	19.98 (10.06)	30.30 (9.44)	29.14 (10.21)	38.62 (11.12)	42.17 (9.27)	48.36***	1 < 2, 3, 4, 5/ 2 < 4, 5/3 < 4,5
Admission (%)[b]	31.00 (29.00)	26.00 (23.00)	27.00 (20.50)	14.00 (15.60)	7.00 (22.60)	4.45	
Admission (days)[a]	20.90	26.23	20.07	25.21	25.71	0.96	
at 3rd month treatment retention rate[b]	68.00 (63.60)	75.00 (66.40)	87.00 (65.90)	68.00 (75.60)	21.00 (67.70)	3.64	
at 6th month treatment retention rate[b]	50.00 (46.70)	57.00 (50.40)	60.00 (45.50)	54.00 (60.00)	17.00 (54.80)	5.43	
Present treatment maintenance[b]	20.00 (18.70)	24.00 (21.20)	20.00 (15.20)	23.00 (25.60)	5.00 (16.10)	4.19	

Values are presented as a mean (standard deviation) or number (%).
[a]By ANOVA, [b]By chi-square test, ***$p < .001$.

Table 3. *Comparison of Subtypes on Initial Prescription Pattern (N = 473)*

	Mild group	Helpless group	Somatic group	Avoidant group with anxiety	Irritable group with anxiety	χ^2
Antidepressant no use	34 (31.80)	26 (23.00)	46 (34.80)	29 (32.20)	7 (22.60)	15.79*
Antidepressant 1 kind	70 (65.40)	78 (69.00)	77 (58.30)	51 (56.70)	18 (58.10)	
Antidepressant 2 kinds	3 (2.80)	9 (8.00)	9 (6.80)	10 (11.10)	6 (19.40)	
Antipsychotics use	1 (0.90)	0	0	1 (1.10)	1 (3.20)	5.35
Mood stabilizer use	0	0	0	0	0	
Adjunctive drug use	1 (0.90)	0	0	0	1 (3.20)	7.87
Anxiolytics Sedative/hypnotics use	53 (49.50)	68 (60.20)	83 (62.90)	55 (61.10)	18 (58.10)	4.97

Values are presented as a number (%).
*$p < 0.05$.

Second, there were statistically significant differences in the prescriptions of antidepressants and antipsychotics between each clinical group for patients who continued treatment for three months. The mild (16.2%) and somatic (14.9%) groups showed higher rates of not prescribing antidepressants even after three months of treatment. In contrast, the rate of prescription of two or more antidepressants increased in the following order: irritable group with anxiety (38.1%), avoidant group with anxiety (23.5%), and helpless group (22.7%). At treatment initiation, antipsychotics prescriptions comprised 0.6% of the total but increased to 45.5% after three months of treatment. After three months of treatment, the antipsychotics prescription rate was high in the irritable group with anxiety (61.9%) and the avoidant group with anxiety (55.9%), followed by the helpless (48.0%), somatic (40.2%), and mild (33.8%) groups. The 3rd month prescriptions of the subtypes are presented Table 4.

Lastly, there were significant differences in the prescription rates of antipsychotics and anxiolytics combined with sedative/hypnotics in patients after six months. Regarding the prescription of antipsychotics at the six-month follow-up visit, the prescription rate was higher in the avoidant group with anxiety (61.1%) and the irritable group with anxiety (64.7%) than other groups. A moderate rate occurred in the helpless (50.9%) and somatic groups (50.0%), whereas it was low in the mild group (30.0%). Regarding treatment with anxiolytics and sedative/hypnotics at six months of treatment, the prescription rate in the irritable group with anxiety (94.1%) was very high, followed by the avoidant group with anxiety (75.9%) and the somatic group (75.0%). This rate was rela-

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Table 4. *Comparison of Subtypes on 3rd Month Prescription Pattern (N=319)*

	Mild group	Helpless group	Somatic group	Avoidant group with anxiety	Irritable group with anxiety	χ^2
Antidepressant no use	11 (16.20)	4 (5.30)	13 (14.90)	6 (8.80)	1 (4.80)	22.29*
Antidepressant 1kind	44 (64.70)	54 (72.00)	60 (69.00)	43 (63.20)	12 (57.10)	
Antidepressant 2 kinds	13 (19.10)	17 (22.70)	14 (19.10)	16 (23.50)	8 (38.10)	
Antidepressant 3 kinds	0	0	0	3 (4.40)	0	
Antipsychotics use	23 (33.80)	39 (48.00)	35 (40.20)	38 (55.90)	13 (61.90)	10.14*
Mood stabilizer use	3 (4.40)	3 (4.00)	6 (6.90)	5 (7.40)	2 (9.50)	1.65
Adjunctive drug use	5 (7.40)	4 (5.30)	3 (3.40)	3 (4.40)	1 (4.80)	1.30
Anxiolytics Sedative/hypnotics use	42 (61.80)	48 (64.00)	87 (72.40)	68 (73.50)	21 (85.70)	6.43

Values are presented as a number (%).
*$p < 0.05$.

Table 5. *Comparison of Subtypes on 6th Month Prescription Pattern (N=238)*

	Mild group	Helpless group	Somatic group	Avoidant group with anxiety	Irritable group with anxiety	χ^2
Antidepressant no use	6 (12.00)	7 (12.30)	7 (11.70)	3 (5.60)	1 (5.90)	11.13
Antidepressant 1kind	34 (68.00)	33 (57.90)	40 (66.70)	31 (57.40)	10 (58.80)	
Antidepressant 2 kinds	9 (18.00)	17 (29.80)	13 (21.70)	18 (33.30)	5 (29.40)	
Antidepressant 3 kinds	1 (2.00)	0	0	2 (3.70)	1 (5.90)	
Antipsychotics use	15 (30.00)	29 (50.90)	30 (50.00)	33 (61.10)	11 (64.70)	12.14*
Mood stabilizer use	1 (2.00)	4 (7.00)	4 (6.70)	5 (9.30)	1 (5.90)	2.44
Adjunctive drug use	2 (4.00)	1 (1.80)	3 (5.00)	2 (3.70)	0	1.62
Anxiolytics Sedative/hypnotics use	29 (58.00)	34 (59.60)	45 (75.00)	41 (75.90)	16 (94.10)	12.46*

Values are presented as a number (%).
*$p < 0.05$.

tively low in the helpless (59.6%) and mild (58.0%) groups. The 6th month prescriptions of the subtypes are presented Table 5.

Discussion

The purpose of this study was to verify the clinical usefulness of the MMPI-2-RF in the initial evaluation of patients with depressive disorder by confirming whether the pattern of medication prescription differed according to the subtype of depression derived based on the MMPI-2-RF specific problem scales. The types of prescribed drugs differed among the five symptom-based subtypes. We found no statistically significant difference between the subtypes of depression in the maintenance of outpatient treatment.

Specifically, among the groups, we observed a difference in the selection of antidepressants for the initial treatment according to the clinical evaluation of the practitioner. In the mild and somatic groups, the proportion of prescribed antidepressants was not high. In contrast, in the irritable group with anxiety, the prescription rate of the two types of antidepressants from the initial treatment onwards was the highest, followed by the avoidant group with anxiety. Considering the differences in the severity of depression measured by BDI and the increasing levels of depression observed in order of the mild, the somatic and helpless, the avoidant and irritable groups, we observed a correlation between the prescription of antidepressants from the initial treatment onward and the severity of depression. In addition, the helpless group, which was characterized by typical depressive symptoms, received more initial antidepressant prescriptions than the somatic group, which showed a similar level of severity, and the avoidant group with higher levels of depression as measured by the BDI. In the initial treatment, the less severe the depression and the less typical depressive symptoms, the fewer antidepressants were prescribed.

At the three-month follow-up visit, there were significant differ-

ences in the prescriptions of antidepressants and antipsychotics for patients among the groups. At three months, although there was no significant difference between the subtypes in the duration of treatment, a large proportion of patients in the mild and somatic groups were not prescribed antidepressants at all. In addition, the rate of prescribing two or more antidepressants was higher in the irritable group with anxiety. Prescriptions included SSRIs, such as escitalopram, serotonin–norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine, and other antidepressants such as bupropion or mirtazapine. The more severe and irritable the depression, the higher the frequency of prescriptions for two or more antidepressants. Practitioners selected and prescribed primary antidepressants (escitalopram and venlafaxine) for severe episodes as recommended by the Korean Medication Algorithm for Depressive Disorders. In particular, the rate of prescription for antipsychotics at the three-month follow-up visit increased overall, with the rate being highest in the irritable group with anxiety and the avoidant group with anxiety. We noted that antipsychotics controlled patients' symptoms in both the irritable and avoidant groups with anxiety, considering that the severity of depression was high and accompanied by anxiety-related symptoms. This finding is consistent with the Korean Medication Algorithm for Depressive Disorders, which in severe episodes, recommends antidepressant treatment alone or in combination with antipsychotics (Seo et al., 2017).

The antidepressant prescription rate for patients receiving treatment for six months did not differ among the types of depression. Rather, there were differences among the subtypes of prescription antipsychotics, anxiolytics, and sedative/hypnotics. In particular, the prescription rate of anxiolytics and sedative/hypnotics was overwhelmingly high (94.1%) in the irritable group with anxiety among patients in treatment for six months. Patients in the irritable group had externalizing problems such as drug abuse, aggression, and a tendency for excitability. These characteristics may be related to the high prescription rates of anxiolytics and sedative/hypnotics in this group. Subtyping with the MMPI-2-RF specific problem scales helped discriminate the irritable group requiring more combination therapy with antipsychotics and sedatives from the depression group accompanying anxiety, which has been considered a typical subtype of depression

Despite experiencing relatively high depression and anxiety-related symptoms, patients in the avoidant group with anxiety did not show externalizing behavior problems. These problems appear primarily as social avoidance and interpersonal passiveness, particularly in men and younger age groups (Choi, 2019). Researchers reported that men have a lower serotonin-based antidepressant response than women (Sramek et al., 2016) and may benefit more from cognitive behavioral therapy (López-López et al., 2019; Health Quality Ontario, 2019; Churchill et al., 2013). In this subtype, psychotherapeutic approaches such as cognitive-behavioral therapy, including exposure in addition to drug treatment, could be more useful. Meanwhile, in the somatic group, it may be helpful to use a physical control method such as respiratory training or a muscle relaxation method in addition to drug treatment (Van Dessel et al., 2014).

In patients with mild depressive symptoms, we expected the rate of discontinuation of treatment at three months or six months to be high, but there was no significant difference between the subtypes of depression. At three months of treatment, 66.4% (319) of the total (473) patients continued treatment, and 33.26% discontinued treatment, which was similar to the discontinuation rate of acute treatment (30–40%) in previous studies (Bull et al., 2002; Lin et al., 1995; Maddox, Levi & Thompson, 1994; Olfson, Marcus, Tedeschi & Wan, 2006). At six months of treatment, 50.3% (238) of the total (473) patients continued treatment. This finding is similar to the drug compliance rate for treating depression (49.1%) (Gauthier et al., 2017). Regarding the discontinuation of treatment for each type of depression, clinicians should consider various other variables such as compliance issues, economic or primary support groups, the degree of interest in treatment, side effects of drug treatment, and the patient-therapist relationship. However, the reasons for such treatment discontinuation could not be identified in this study. In future studies, an accurate comparison of progress will be possible only when the reasons for discontinuation between the groups are identified.

Our previous study (Choi, 2019) derived five subtypes with different severity and symptom patterns through a person-centered approach using the MMPI-2-RF specific problems scales for depressive disorder patients. The current research confirmed that the patterns of actual medication prescriptions differed according

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to the derived subtypes through medical record investigation. To summarize, first, the ratio of antidepressant prescription and combination therapy was different depending on the severity of depression. Second, even within the same severity level, the helpless group showing typical depressive patterns had more depression prescriptions from the first treatment to three and six months than the somatic group. Third, among the groups with anxiety, the irritable group with externalizing problems required more antidepressants and a combination of antipsychotics and sedatives than the avoidant group.

These findings suggest that using the profile of the MMPI-2-RF specific problem scales in the initial evaluation of patients with depression may be helpful in medication planning. Clinicians treating patients with a mild profile on the specific problem scales or symptoms in the somatic/cognitive domain may first defer from drug treatment. Both the mild and helpless groups were more likely to have alleviated symptoms with antidepressants alone. On the other hand, avoidant and irritable groups with anxiety may benefit from combining two or more antidepressants, antipsychotics, anxiolytics, and sedative/hypnotics at treatment initiation.

The strengths of this study are as follows; First, to distinguish between the heterogeneous types of depressive disorder, we identified the subtypes through a person-centered approach rather than a variable-centered approach. We retrospectively analyzed the natural clinical course according to this classification. Second, based on the evaluation time point, we divided the treatment into early, middle, and late treatments and continuously reviewed the prescription patterns for each type of drug, as recommended by the Korean Medication Algorithm for Depressive Disorders. Finally, we suggested a more effective drug type and treatment strategy to follow after the initiation of treatment according to the data-driven depression subtype based on the MMPI-2-RF specific problems scales.

The study also has some limitations. First, in some cases, the study participants completed MMPI-2-RF without a drug prescription; however, in other cases, they completed a questionnaire after starting medication. Therefore, the MMPI-2-RF profile may reflect the effect of medication. Second, we considered the natural clinical course of the disease in term of drug prescriptions from the therapist's perspective. Changes in patient symptoms were not considered objective indicator. In future studies, it is necessary to check whether symptoms improve in patients after a certain medication according to the subtype. Furthermore, if it can be confirmed whether there is a change in subtypes after treatment, classification based on the MMPI-2-RF special problem scales can be used as an indicator of treatment outcome. Third, since this study was conducted on patients who visited one hospital, it is difficult to generalize the results to all patients with depressive disorders. It is necessary to check whether the subtypes derived through the data-driven approach can be reliably reproduced using other samples.

In conclusion, the current study suggests that using this classification model based on multidimensional symptoms may help clinicians better understand the patients at the initiation of treatment and develop more tailored treatment strategies. Clinicians may benefit from using the specific problem scale of the MMPI-2-RF, which allows detailed assessment of multidimensional symptoms rather than focusing only on symptoms that meet the criteria for diagnosing depression or the problem most suitable for the patient.

Author contributions statement

M.S. Gim, Associate Professor at Inje University, collected and analyzed the data and prepared the manuscript. J.Y. Choi, Associate Professor at Inha University, supervised the study plan and assisted with the analysis. Both authors participated in the revision of the manuscript and approved the final submission.

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Appendix 1. *Fit Information for Latent Profile Analysis Models with 1-6 Class (N = 473) (Choi, 2019)*

Model	Log-likelihood Values	AIC	BIC	SSA BIC	LMRa-LRT *p*-value	Entropy	BLRT *p*-value	Smallest Class Proportion
1	-42883.724	85859.449	86050.767	85904.771	N/A	N/A	N/A	N/A
2	-41963.185	84066.371	84357.508	84135.339	1828.706 ($p = 0.0008$)	0.872	< 0.0001	46.7%
3	-41667.458	83522.916	83913.870	83615.530	587.481 ($p = 0.0198$)	0.877	< 0.0001	25.6%
4	-41503.352	83242.704	83733.478	83358.965	326.006 ($p = 0.6025$)	0.865	< 0.0001	23.04%
5	-41381.102	83046.205	83636.796	83186.112	242.857 ($p = 0.2920$)	0.878	< 0.0001	6.6%
6	-41293.719	82919.438	83609.991	83082.991	173.592 ($p = 0.3005$)	0.882	< 0.0001	9.7%

Note. AIC = Akaike information criterion; BIC = Bayesian information criterion; SSABIC = Sample size adjusted Bayesian information; LMRa-LRT = Lo-Mendell-Rubin adjusted likelihood ration test; BLRT = Bootstrapped likelihood ratio test.

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Appendix 2. *Comparison of Clinical Characteristics (N = 473) (Choi, 2019)*

Variables	Class 1 Mild group n (%)	Class 2 Helpless group n (%)	Class 3 Somatic group n (%)	Class 4 Avoidant group with anxiety n (%)	Class 5 Irritable group with anxiety n (%)	χ^2/F
MDD	82 (76.6)	100 (88.5)	112 (84.8)	79 (87.8)	30 (96.8)	10.98*
PDD	8 (7.5)	4 (3.5)	9 (6.8)	9 (10.0)	0 (0.0)	5.90
Psychotic feature	12 (11.2)	7 (6.2)	6 (4.5)	10 (11.1)	3 (9.7)	5.42
Comorbidity	38 (35.5)	44 (38.9)	77 (58.3)	51 (56.7)	25 (80.6)	31.41***
Anxiety disorder	6 (5.6)	7 (6.2)	9 (6.8)	10 (11.1)	4 (12.9)	3.85
PTSD	4 (3.7)	12 (10.6)	9 (6.8)	9 (10.0)	6 (19.4)	9.25
Alcohol use disorder	5 (4.7)	2 (1.8)	19 (14.4)	4 (4.4)	9 (29.0)	34.09***
Somatic symptom	5 (4.7)	5 (4.4)	8 (6.1)	5 (5.6)	0 (0.0)	2.14
Personality disorder	10 (9.3)	10 (8.8)	20 (15.2)	18 (20.0)	5 (16.1)	7.49

Note. MDD = Major depressive disorder; PDD = Persist depressive disorder; PTSD = Posttraumatic stress disorder; Somatic symptom = Somatic symptom disorder.
*$p < .05$, **$p < .001$.