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A nationwide survey of community pharmacist contributions to polypharmacy in opioid-using and non-using cancer patients in Japan

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Summary

No nationwide study on polypharmacy in palliative care among Japanese community pharmacies has yet been conducted. We conducted an online questionnaire survey for community pharmacist members of The Japanese Society for Pharmaceutical Palliative Care and Sciences regarding their contributions to cancer patients who regularly used six or more drugs, including opioids, in service during the two-month period from October to November 2017. Of 579 community pharmacists, 83 responded to the survey (14.3%). Among them, 47.0% and 27.7% of respondents replied that more than 40% of opioid-using and non-using cancer patients were prescribed six or more regular medications, respectively. The proportion of patients with polypharmacy was marginally higher among opioid-using than non-using patients. Additionally, 31.3% and 22.9% of respondents replied that a low or moderate rate of opioid-using and non-using patients with polypharmacy received inappropriate prescriptions, respectively, including “unnecessary medications”, “adverse drug reactions” and “duplication of pharmacological effect”. The proportion of patients who received inappropriate prescriptions was significantly higher among opioid-using than non-using patients. Furthermore, 37.3% and 19.3% of respondents replied that pharmacist’s recommendations contributed to drug reduction in opioid-using and non-using patients with polypharmacy who received inappropriate prescriptions, respectively. The responders with higher confidence in palliative care showed more success rate for reducing inappropriate medications. Our findings suggest that opioid use can be associated with an increased risk of polypharmacy in cancer patients, and that recommendations by a population of community pharmacists can reduce inappropriate medications and improve adverse drug reactions in both opioid-using and non-using cancer patients with polypharmacy.

Keywords: Polypharmacy; Palliative care; Nationwide survey; Opioid; Pharmacist service;
Community pharmacists
Polypharmacy, defined as the inappropriate use of multiple medications by a patient, has been considered an important issue since the 1960s\(^1\). Although there is no clear consensus on the number of medications that constitute polypharmacy, many reports define it as the regular use of five or more, or six or more medications\(^2-8\). A systematic review of polypharmacy in long-term care facilities suggests that the prevalence, defined as the regular use of six or more medications, ranges between 46% and 69%\(^8\). Polypharmacy is potentially associated with inappropriate prescriptions\(^9-11\), and causes various problems such as drug-drug interactions, adverse drug reactions, increased medical expenses and decreased medication adherence\(^12\).

In Japan, Kojima et al. reported that polypharmacy, defined as using six or more regular medicines, is associated with an increase in adverse drug reactions\(^14\). Further, excessive polypharmacy, defined as the use of 10 or more medications, is reportedly associated with death\(^13\). Recent evidence suggests that deprescribing, a process of identifying and discontinuing inappropriate medications, can reduce inappropriate polypharmacy in elderly patients, although it is unclear whether this improves clinical outcomes\(^15,16\).

Community pharmacists help patients to optimize their use of medicines by conducting medication reviews\(^17,18\). An observational survey in a community medicine setting in Japan identified inappropriate prescriptions in 48% of elderly patients\(^19\). While the role of community pharmacists in Japan has traditionally been to dispense medications, revised recommendations by the Japan Pharmaceutical Association in 2012 encouraged community pharmacists to gradually undertake a more patient-centered role\(^20\). One outcome of this can be seen in the National Health Insurance Claims data for 2010–2015, provided by the Ministry of Health, Labour and Welfare in Japan, which reported an increase in medication reviews by community pharmacists involving consultations with a physician\(^21\). These data indicate that community pharmacists can conduct clinical drug evaluations in outpatients, and suggest that pharmacists should play an important role in intervening against polypharmacy.
Palliative care is a treatment for patients and their families to relieve and optimize symptoms due to terminally ill and quality of life. Patients receiving palliative care typically have multiple comorbid conditions and use multiple medications for symptomatic relief. They are therefore at substantial risk of polypharmacy, although many medications are actually needed to relieve the symptoms of the patients in palliative care. In the absence of a clearly defined clinical need, patients should be cautioned against the prescription of multiple drug combinations, particularly cancer patients and the elderly\textsuperscript{22).} For most community pharmacists in Japan, however, managing polypharmacy by identifying and discontinuing inappropriate medications has proven difficult. Moreover, evidence to support pharmacist service against polypharmacy in clinical practice settings in Japan is scarce. Of note, no nationwide study has yet investigated either the scale or prevention of polypharmacy in palliative care, despite the inherent risk of polypharmacy in this type of care. Indeed, we speculate that palliative care has among the highest risk of polypharmacy of any clinical field.

The Research Committee of the Japanese Society for Pharmaceutical Palliative Care and Sciences conducted a survey on polypharmacy among member pharmacists working in community pharmacies. The purpose of the present study was to gain insight into the current status of community pharmacist contributions and their effects on polypharmacy as their service in opioid-using and non-using cancer patients in Japan, whose experience with polypharmacy was expected to substantially differ.

**MATERIALS AND METHODS**

1) **Study design and data source**

The study was conducted under a cross-sectional design. The survey subjects were 579 community pharmacist members of the Japanese Society for Pharmaceutical Palliative Care.
and Sciences. The survey was conducted using a web-based questionnaire (supplementary document) in January and February, 2018, and asked the pharmacists about polypharmacy and their contributions to patients with cancer of any stage as their service in the convenience period of October and November, 2017. The research committee sent an email to all 579 community pharmacist members to explain the purpose of the questionnaire study. No reward was offered for participation, and completing the survey constituted voluntary work. The protocol was approved by the institutional review board of the Ethics Committee of Osaka University of Pharmaceutical Sciences (Approval No. 0046). A response was considered to indicate consent to participate.

2) Definitions

Although polypharmacy has been defined in a number of ways, we defined it here as the regular use of six or more medications according to “Total Drug Evaluation and Management Healthcare Reimbursement Fee”, the Japanese Medical Service Fee system. In this system, pharmacists are eligible to receive a healthcare reimbursement fee from Japan’s National Health Insurance system when they eliminate two or more drugs from a patient’s prescription of six or more regular medications, as prescribed through the Japanese National Healthcare system. The decision to advise that a particular medicine be eliminated and to classify a cancer patient as opioid-using or non-opioid-using was at the discretion of the responding pharmacist.

3) Data and statistical analysis

We excluded data from respondents who did not answer one or more questions. To compare opioid-using and non-using patients, bivariate analyses to examine differences in demographic characteristics and the chi-squared test to compare categorical variables. All
data were analysed using SPSS version 22.0 (SPSS Inc., Chicago, IL). A \( p \)-value < 0.05 and \( p \)-value < 0.10 was considered statistically and marginally significant, respectively.

**RESULTS**

**Response rates and subject background**

Of 579 community pharmacists, 83 responded to the survey (response rate 14.3%). As shown in Table 1, many respondents (83.1%) had more than 10 years of experience as a pharmacist, and slightly less than half of respondents (43.4%) had more than 19 years of experience. Among the respondents, 44.6% of the respondents had at least one board certification related to cancer therapy and palliative care, including Board-certified Pharmacists in Palliative Pharmacy accredited by the Japanese Society for Pharmaceutical Palliative Care and Sciences (14.5%). On a scale from 0–10, the median score for confidence in palliative care was 6. Approximately 90% of the respondents had attended at least one continuing education event related to palliative medicine in the preceding 12 months. The majority of respondents (78.3%) indicated that less than 40% of their patients were cancer patients, while a smaller proportion of respondents (14.4%) managed a higher ratio (more than 40%) of cancer patients.

**Pharmacist contributions to inappropriate prescriptions in opioid-using and non-using cancer patients with polypharmacy**

Polypharmacy, inappropriate prescriptions and community pharmacist contributions in opioid-using and non-using cancer patients are shown in Table 2. The median number of opioid-using and non-using cancer patients managed by the respondents in the two-month study period was 3 and 2, respectively.

Many responders (67.5%) found at least some opioid-using cancer patients prescribed six
or more regular medications (polypharmacy), and 27.7% of the respondents found more than 70% of cancer patients with polypharmacy. In the case of opioid non-using cancer patients, 41.0% of the respondents did not find any cancer patients with polypharmacy, and the percentage of the respondents who found more than 70% of cancer patients with polypharmacy was 13.2%. The proportion of cancer patients with polypharmacy was marginally higher among opioid-using than non-using patients.

When the pharmacists were asked about inappropriate prescriptions, 32.5% of the responders found inappropriate prescriptions in at least some opioid-using cancer patients with polypharmacy, and the percentage of the respondents who found more than 40% of cancer patients with inappropriate prescriptions was 9.6%. In the case of opioid non-using cancer patients with polypharmacy, 22.9% of responders found inappropriate prescriptions, but 60.2% of the responders did not find it. The rate of patients who received inappropriate medications did not statistically differ between the opioid-using and non-using patients. The three most common reasons for inappropriate prescriptions identified by pharmacists in the opioid-using and non-using patients were the same: “unnecessary medications”, “adverse drug reactions caused by medications” and “medication-mediated duplication of pharmacological effect”.

When the pharmacists were asked about drug reduction due to pharmacists’ recommendations, 37.3% of the respondents reduced the number of medications in at least some opioid-using cancer patients with polypharmacy, and the percentage of the respondents who reduced the number of medications in more than 40% of cancer patients with polypharmacy was 13.2%. In the case of opioid non-using cancer patients with polypharmacy, 19.3% of responders reduced the number of medications, but 47.0% of the responders did not. However, there was no statistical difference between the two groups. The most common reason for pharmacists’ recommendation to reduce inappropriate prescriptions was
“unnecessary medications” in both opioid-using and non-using patients. The second and third reasons differed between the groups.

When pharmacists were asked about the number of medications reduced due to pharmacist recommendations, the most common average number was one in both opioid-using and non-using cancer patients with polypharmacy. Some respondents reduced more than two medications. There was no statistical difference in the average number of medications reduced between opioid-using and non-using patients.

**Drugs reduced due to pharmacist recommendations for opioid-using and non-using cancer patients**

As shown in Table 3, the most common pharmacological category of drugs reduced due to pharmacist recommendations was “gastrointestinal medications” in both opioid-using and non-using cancer patients with polypharmacy. Other pharmacological categories included “antiemetics”, “analgesics”, “hypnotic sedatives” and “laxatives”, although the ranking was different between opioid-using and non-using cancer patients. The majority of these drugs fell into the following pharmacological categories: “benzodiazepine”, “dopamine receptor antagonist”, “nonsteroidal anti-inflammatory drug (NSAID)”, “histamine H₂ receptor blocker”, “gastric antacid”, “proton pump inhibitor”, “salt-based laxative” and “peroral stimulative laxative”.

**Improvement in adverse drug reactions due to pharmacist recommendations in opioid-using and non-using cancer patients**

As shown in Table 4, the three most common symptoms for adverse drug reactions reduced by pharmacist recommendations in opioid-using cancer patients with polypharmacy were “constipation”, “extrapyramidal symptoms”, and “sleepiness”. By contrast, the three
most common symptoms observed in non-opioid-using cancer patients with polypharmacy were “unsteady gait”, “hypoglycaemia”, and “gastrointestinal disorder”.

Factors associated with the successful reduction of inappropriate medications due to pharmacist recommendations

We further explored the factors related to successful reduction of inappropriate medications in cancer patient with polypharmacy. We detected “confidence score in palliative care” as a significant factor associated with the drug reduction. The responders with higher confidence score in palliative care showed more success rate for reducing inappropriate medications. However, there were no statistically significant differences in sex, years of pharmacist experience, pharmacy board certification and attendance at nationwide continuing education sessions related to palliative care per year (Table 5).

DISCUSSION

This is the first nationwide questionnaire survey-based study in Japan to gain insight community pharmacist contributions to cancer patients with polypharmacy in their service. While other studies have reported findings from medication reviews by community pharmacists from national insurance data21), pharmacist’s contributions have not been surveyed because the relevant data were not included in the national insurance data. Our present study helps clarify the incidence of polypharmacy and procedures to reduce this among both opioid-using and non-using cancer patients. Remarkably, more than half (approximately 57%) of respondents observed polypharmacy in their cancer patients and some of them (approximately 28%) reduced inappropriate medications prescribed to cancer patients with polypharmacy. Especially, community pharmacists with confidence in palliative
care could actively contribute to reduce inappropriate medications. Taken together with the results that more than 80% of the respondents had more than 10 years of pharmacist experience, these findings suggest that experienced community pharmacists with confidence in palliative care can provide a high rate of contributions to inappropriate prescriptions in their service. Although the survey was conducted among members of the Japanese Society for Pharmaceutical Palliative Care and Sciences who worked in community pharmacies, only 14.5% of respondents were Board-certified Pharmacists in Palliative Pharmacy. Likewise, another nationwide survey on the management of oral anticancer agents in community pharmacies reported that an average of zero or one to five medications were dispensed per week\(^2\). For most respondents, fewer than 40% of the patients they managed were cancer patients, and the number of cancer patients was not high. This low encounter rate with cancer patients may be related to pharmacists’ low rate of board certification, which may result in no association between the success rate for reducing inappropriate medications and the board certification or years of pharmacist experience.

To clarify the effects of opioid use on polypharmacy, inappropriate prescriptions and contributions of community pharmacist, we investigated differences in them between opioid-using and non-using cancer patients. Results showed that a large proportion of respondents observed polypharmacy (67.5% and 45.8%) and inappropriate prescriptions (32.5% and 22.9%) in both opioid-using and non-using cancer patients, respectively. Some respondents observed a high frequency of polypharmacy and inappropriate prescriptions in cancer patients. Although we could not calculate the prevalence of polypharmacy and inappropriate prescriptions in this study, the data appear to be consistent with those of previous studies\(^8,19,25-28\). Respondents observed a higher rate of polypharmacy among opioid-using than non-using patients. This finding is not surprising because opioid-using patients are commonly prescribed more medications due to the need for supportive
medications for opioids, such as antiemetics and laxatives. However, our results suggest that inappropriate prescriptions, such as unnecessary medications, medications that cause adverse drug reactions and duplicated pharmacological medications, can occur regardless of whether or not opioids are used. An increased number of concurrent medications resulting from the prescription of opioids and supportive medications for cancer pain is necessary for relieving the symptoms of the patient with cancer in palliative care, while it may increase the risk of inappropriate prescriptions\(^2\).

The present results suggest that some respondents (37.3% and 19.3%) deprescribed one or two inappropriate medications in opioid-using and non-using cancer patients with polypharmacy, respectively. In the Japanese Medical Service Fee system, community pharmacists are eligible to receive a dispensing fee from the National Health Insurance system when they avoid duplications and interactions between prescription drugs. This fee serves as a motivating factor for deprescribing inappropriate medicines. Nevertheless, the present findings suggest that opioid use might be a weak factor in increasing the deprescription of inappropriate medications. These findings suggest that a population of community pharmacists can actively identify and deprescribe inappropriate medications which accompany opioid prescriptions in cancer patients, such as unnecessary medications, those that cause adverse drug reactions and duplicated pharmacological medications.

The most common category of medications reduced by community pharmacists was gastrointestinal medications in both opioid-using and non-using patients. In contrast, the order of subsequent categories (i.e. antiemetics, analgesics, hypnotic sedatives and laxatives) differed between the two groups. Gastrointestinal medications are frequently used to prevent or treat gastrointestinal injury in cancer patients who are prescribed NSAIDs for cancer pain or other types of pain, combined with or without opioids. However, long-term and aimless treatment with gastrointestinal medications can lead these drugs to becoming inappropriate
medications in cancer patients, and can consequently be deprescribed as unnecessary medications by community pharmacist recommendation.

In contrast, the adverse drug reactions reduced by pharmacist recommendations differed between opioid-using (“constipation”, “extrapyramidal symptoms,” and “sleepiness”) and non-using patients (“wobbliness,” “delirium,” and “hypotension”). Opioids, corticosteroids, benzodiazepines and other psychosomatics potentially cause delirium and other adverse drug reactions. In general, concurrent use of antiemetics or hypnotic sedatives with opioids is associated with extrapyramidal symptoms or delirium and can worsen adverse drug reactions in opioid-using cancer patients. Several reports have shown that delirium can be improved in 20% to 49% of cases, even in advanced- or end-stage patients. In addition, histamine H2 receptor blockers are a risk factor for inducing delirium in patients with renal dysfunction, with pharmacists frequently deprescribing these drugs, as observed in the present results. The results of the present study therefore show that community pharmacists detected and solved constipation, extrapyramidal symptoms and sleepiness induced by polypharmacy in opioid-using cancer patients, indicating that pharmacists contribute greatly to the management of adverse drug reactions. These contributions were most evident in opioid-using cancer patients. The main reason that pharmacists reduced the use of antiemetics was likely to improve extrapyramidal symptoms. Furthermore, pharmacists may have reviewed the use of hypnotic sedatives and antipsychotics to manage sleepiness, wobbliness and delirium.

Although we defined polypharmacy as the regular use of six or more medications in this study, it is necessary to consider whether the increased number of medications the patient takes is related with the risk of polypharmacy (inappropriate use of too many medications). Furthermore, indiscriminate drug reduction does not necessarily prevent adverse drug reaction. In the present study, given that more than 80% of the respondents had more than 10
years of pharmacist experience, it is possible that these experienced community pharmacists with confidence in palliative care appropriately improved inappropriate prescriptions, which may include change of the regimen or adjust the dosages, rather than reduced the number of necessary medications for the patients. Such deeper contributions to inappropriate prescriptions may improve polypharmacy, resulting in prevention of adverse drug reactions.

Several limitations of our study warrant mention. First, response rate among all members of the Japanese Society for Pharmaceutical Palliative Care and Sciences was somewhat low, and respondents may have represented a population which was motivated to improve polypharmacy, and which was not representative of community pharmacists in Japan. Unfortunately, we could not get the data about the polypharmacy, inappropriate prescriptions and pharmacist contributions from non-responders. However, given more than 80% of the responders had more than 10 years of pharmacist experience, the population of non-responders may be not so experienced and motivated pharmacists, which can influence the present results as selection bias. To increase the response rate and to collect the answers from general population of community pharmacists, additional remind e-mails or letters/fax to respond the web-based questionnaire or paper-based questionnaire mailed to each community pharmacist might be needed. Second, evaluation was limited to a relatively short convenience period of two month’s clinical pharmacy service. Third, we did not attempt to validate participant responses regarding patient categorization or the decision to advise that a particularly medicine be eliminated. Rather, these were based on participant recall and participant discretion, respectively, albeit that the survey was conducted only several months after the service period, likely minimizing any recall bias. To validate these findings, we are now planning a multi-center prospective observational study.

Our findings suggest that opioid use can be associated with an increased risk of polypharmacy in cancer patients, and that recommendations by a population of community pharmacists
pharmacists can reduce inappropriate medications and improve adverse drug reactions in both opioid-using and non-using cancer patients with polypharmacy. Advances in cancer treatment, including outpatient chemotherapy, have accompanied changes in the roles of community pharmacists. In addition to dispensing medications for outpatients, the roles of community pharmacists have been expanded to home healthcare and palliative care. The present investigations for the current status of polypharmacy, inappropriate prescriptions and the contributions of community pharmacists in their service may help further promote to expand the roles of community pharmacists in palliative care.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Materials  The online version of this article contains supplementary materials.
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Table 1. Background characteristics of respondents

|                                      | n   | (%)  |
|--------------------------------------|-----|------|
| **Sex**                              |     |      |
| Male                                 | 42  | (50.6) |
| Female                               | 41  | (49.4) |
| **Pharmacist experience, years**     |     |      |
| 1 to 3                               | 1   | (1.2)  |
| 4 to 6                               | 4   | (4.8)  |
| 7 to 9                               | 9   | (10.8) |
| 10 to 14                             | 19  | (22.9) |
| 15 to 19                             | 14  | (16.9) |
| More than 19                         | 36  | (43.4) |
| **Pharmacy board certification**     |     |      |
| Yes                                  | 37  | (44.6) |
| No                                   | 46  | (55.4) |
|                                      |     |      |
| Board-certified Pharmacist in Palliative Pharmacy | 12  | (14.5) |
| **Confidence score in palliative care (no confidence, 0; full confidence, 10)** |     |      |
| Median                               | 6   |      |
| [Range]                              | [0–9] |      |
| **Attendance at nationwide continuing education sessions related to palliative care per year** |     |      |
| Zero                                 | 9   | (10.8) |
| 1 to 3                               | 65  | (78.3) |
| 4 to 6                               | 8   | (9.6)  |
| 7 to 9                               | 1   | (1.8)  |
| More than 9                          | 0   | (0)    |
| **Percentage of cancer patients among all patients managed by respondents** |     |      |
| Zero                                 | 6   | (7.2)  |
| Less than 40%                        | 65  | (78.3) |
| 40% to 69%                           | 5   | (6.0)  |
| 70% to 99%                           | 7   | (8.4)  |
| 100%                                 | 0   | (0)    |
Table 2. Pharmacists’ contributions to opioid-using and non-using cancer patients

|                                | Opioid-using | Opioid non-using | p value |
|--------------------------------|--------------|------------------|---------|
| **Number of patients managed by respondent** |              |                  |         |
| Median                         | 3            | 2                | 0.074   |
| [Range]                        | [0–30]       | [0–100]          |         |

| Percentage of cancer patients prescribed six or more regular medications | | | |
|---|---|---|---|
| Zero | 21 (25.3) | 34 (41.0) | 0.063 |
| Less than 40% | 17 (20.5) | 15 (18.1) | |
| 40% to 69% | 16 (19.3) | 12 (14.4) | |
| 70% to 99% | 10 (12.0) | 7 (8.4) | |
| 100% | 13 (15.7) | 4 (4.8) | |
| No response | 6 (7.2) | 11 (13.3) | |

| Percentage of inappropriate prescriptions among patients with polypharmacy | | | |
|---|---|---|---|
| Zero | 43 (51.8) | 50 (60.2) | 0.244 |
| Less than 40% | 19 (22.9) | 17 (20.5) | |
| 40% to 69% | 7 (8.4) | 2 (2.4) | |
| 70% to 99% | 1 (1.2) | 0 (0) | |
| No response | 13 (15.7) | 14 (16.9) | |

| Reasons prescriptions were considered inappropriate (multiple answers allowed) | | | |
|---|---|---|---|
| Unnecessary medications | 26 (31.3) | 17 (20.5) | |
| Adverse drug reactions caused by medications | 12 (14.5) | 7 (8.4) | |
| Medication-mediated duplication of pharmacological effect | 6 (7.2) | 5 (6.0) | |
| Medication-induced drug-drug interactions | 3 (3.6) | 3 (3.6) | |
| Other | 8 (9.6) | 2 (2.4) | |
Percentage of patients with polypharmacy with drug reduction due to pharmacist recommendations

| Percentage | N | (%)  | N | (%)  | P-value |
|------------|---|------|---|------|---------|
| Zero       | 36 | (43.4) | 39 | (47.0) | 0.159   |
| Less than 40% | 20 | (24.1) | 12 | (14.5) |         |
| 40% to 69%  | 2  | (2.4)  | 2  | (2.4)  |         |
| 70% to 99%  | 3  | (3.6)  | 0  | (0)    |         |
| 100%       | 6  | (7.2)  | 2  | (2.4)  |         |
| No response | 16 | (19.3) | 28 | (33.7) |         |

Reasons for pharmacist recommendations to reduce medications (multiple answers allowed)

| Reason                                    | N | (%)  | N | (%)  |
|-------------------------------------------|---|------|---|------|
| Unnecessary medications                    | 23 | (27.7) | 14 | (16.9) |
| Change in the drug form due to oral feeding difficulty | 20 | (24.1) | 5  | (6.0)  |
| Suggestions to avoid adverse drug reactions | 18 | (21.7) | 6  | (7.2)  |
| Medication-mediated duplication of the pharmacological effect | 11 | (13.3) | 7  | (8.4)  |
| Medication-induced drug-drug interactions | 4  | (4.8)  | 4  | (4.8)  |
| Other                                     | 8  | (9.6)  | 3  | (3.6)  |

Average number of medications reduced by pharmacist recommendations

| Average number | N | (%)  | N | (%)  | P-value |
|----------------|---|------|---|------|---------|
| 0              | 25 | (30.1) | 26 | (31.3) | 0.386   |
| 1              | 22 | (26.5) | 13 | (15.7) |         |
| 2              | 9  | (10.8) | 5  | (6.0)  |         |
| 3              | 0  | (0)    | 0  | (0)    |         |
| 4              | 0  | (0)    | 0  | (0)    |         |
| More than 4    | 3  | (3.6)  | 0  | (0)    |         |
| No response    | 24 | (28.9) | 39 | (47.0) |         |

N.D.: not determined
Table 3. Drugs reduced due to pharmacist recommendations in opioid-using and non-using cancer patients

| Pharmacological categories of drugs reduced by pharmacist recommendation | Drug type                  | Opioid-using | (% ) | Opioid non-using | (% ) |
|-------------------------------------------------------------------------|-----------------------------|--------------|------|------------------|------|
| Gastrointestinal medications                                           | n                           | 18 (21.7)    |      | 10 (12.0)       |      |
| Antiemetics                                                             | 15 (18.1)                   |              |      | 9 (10.8)        |      |
| Analgesics                                                              | 14 (16.9)                   |              |      | 6 (7.2)         |      |
| Hypnotic sedatives                                                      | 13 (15.7)                   |              |      | 5 (6.0)         |      |
| Laxatives                                                               | 12 (14.5)                   |              |      | 4 (4.8)         |      |
| Antipsychotics                                                          | 5 (6.0)                     |              |      | 2 (2.4)         |      |
| Other                                                                   | 4 (4.8)                     |              |      | 2 (2.4)         |      |

Drugs reduced under each pharmacological category

Gastrointestinal medications

| Histamine H\(_2\) receptor blocker | 6 (7.2) | Gastric antacid | 4 (4.8) |
|-------------------------------------|---------|-----------------|---------|
| Gastric antacid                     | 6 (7.2) | Proton pump inhibitor | 4 (4.8) |
| Proton pump inhibitor               | 6 (7.2) | blocke             | 3 (3.6) |
| Prostaglandin                       | 1 (1.2) | Other            | 3 (3.6) |
| Other                               | 5 (6.0) | –               |         |

Antiemetics

| Dopamine receptor antagonist      | 8 (9.6) | Dopamine receptor antagonist | 3 (3.6) |
|-----------------------------------|---------|-------------------------------|---------|
| Prokinetic agent                  | 5 (6.0) | Prokinetic agent               | 3 (3.6) |
| Antihistaminic agent              | 3 (3.6) | Antihistaminic agent           | 1 (1.2) |
| Other                             | 1 (1.2) | Other                         | 0 (0)   |

Analgesics

| Non-steroid anti-inflammatory drug | 3 (3.6) | Acetaminophen | 2 (2.4) |
|-----------------------------------|---------|---------------|---------|
| Opioid                             | 3 (3.6) |                |         |
| Non-steroid                        | 8 (9.6) |                |         |
| Category                          | Brand                     | Count | Percentage |
|----------------------------------|---------------------------|-------|------------|
| Anti-inflammatory drug           | Analgesic adjuvant        | 4     | (4.8)      |
|                                  | Acetaminophen             | 4     | (4.8)      |
| Hypnotic sedatives               | Benzodiazepine            | 13    | (15.7)     |
|                                  | Non-benzodiazepine        | 3     | (3.6)      |
| Laxatives                        | Salt-based laxative       | 6     | (7.2)      |
|                                  | Peroral stimulative laxative | 6   | (7.2)      |
|                                  | Enema                     | 1     | (1.2)      |
|                                  | Small intestine irritation laxative | 0 | (0) |
|                                  | Other                     | 0     | (0)        |
| Antipsychotics                   | Typical antipsychotic     | 5     | (6.0)      |
|                                  | Atypical antipsychotic    | 2     | (2.4)      |

*Note: The table includes counts and percentages for various categories of drugs, including analgesic adjuvants, hypnotic sedatives, laxatives, and antipsychotics.*
Table 4. Improved adverse drug reactions due to pharmacist recommendations in opioid-using and non-using cancer patients

| Adverse drug reaction       | Opioid-using n (%) | Opioid non-using n (%) |
|-----------------------------|--------------------|------------------------|
| Constipation                | 7 (8.4)            | Unsteady gait 3 (3.6)   |
| Extrapyramidal symptoms     | 6 (7.2)            | Hypoglycemia 2 (2.4)    |
| Sleepiness                  | 6 (7.2)            | Gastrointestinal disorder 2 (2.4) |
| Unsteady gait               | 4 (4.8)            | Delirium 1 (1.2)        |
| Nausea and vomiting         | 3 (3.6)            | Hypotension 1 (1.2)     |
| Delirium                    | 2 (2.4)            | Sleepiness 1 (1.2)      |
| Respiratory depression      | 2 (2.4)            | Constipation 1 (1.2)    |
| Renal dysfunction           | 1 (1.2)            | Electrolyte abnormalities 1 (1.2) |
| Electrolyte abnormalities    | 1 (1.2)            | –                      |
| Sleep disorder              | 1 (1.2)            | –                      |
| Gastrointestinal disorder   | 1 (1.2)            | –                      |
| Liver dysfunction           | 1 (1.2)            | –                      |
| Dysuria                     | 1 (1.2)            | –                      |
| Dysgeusia                   | 1 (1.2)            | –                      |
Table 5. Factors associated with the successful reduction of inappropriate medications due to pharmacist recommendations

|                              | Drug reduction | Drug reduction | p value |
|------------------------------|----------------|----------------|---------|
|                              | (-) n          | (+) n          |         |
| Sex                          |                |                |         |
| Male                         | 19             | 20             | 1.000   |
| Female                       | 15             | 16             |         |
| Pharmacist experience, years |                |                |         |
| 1 to 3                       | 1              | 0              | 0.518   |
| 4 to 6                       | 1              | 3              |         |
| 7 to 9                       | 3              | 6              |         |
| 10 to 14                     | 6              | 6              |         |
| 15 to 19                     | 9              | 5              |         |
| more than 19                 | 14             | 16             |         |
| Pharmacy board certification |                |                |         |
| Yes                          | 10             | 15             | 0.445   |
| No                           | 21             | 19             |         |
| Confidence score in palliative care (no confidence, 0; full confidence, 10) | | | |
| Zero                         | 0              | 0              | 0.007   |
| 1 to 3                       | 10             | 3              |         |
| 4 to 6                       | 20             | 14             |         |
| 7 to 9                       | 4              | 19             |         |
| Attendance at nationwide continuing education sessions related to palliative care per year | | | |
| Zero                         | 3              | 2              | 0.750   |
| 1 to 3                       | 28             | 30             |         |
| 4 to 6                       | 3              | 3              |         |
| 7 to 9                       | 0              | 1              |         |