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ORIGINAL REPORT

Investigation of Racial Disparities in Early Supportive Medication Use and End-of-Life Care Among Medicare Beneficiaries With Stage IV Breast Cancer

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ABSTRACT

Purpose

Early supportive care may improve quality of life and end-of-life care among patients with cancer. We assessed racial disparities in early use of medications for common cancer symptoms (depression, anxiety, insomnia) and whether these potential disparities modify end-of-life care.

Methods

We used 2007 to 2012 SEER-Medicare data to evaluate use of supportive medications (opioid pain medications and nonopioid psychotropics, including antidepressants/anxiolytics and sleep aids) in the 90 days postdiagnosis among black and white women with stage IV breast cancer who died between 2007 and 2012. We used modified Poisson regression to assess the relationship between race and supportive treatment use and end-of-life care (hospice, intensive care unit, more than one emergency department visit or hospitalization 30 days before death, in-hospital death).

Results

The study included 752 white and 131 black women. We observed disparities in nonopioid psychotropic use between black and white women (adjusted risk ratio [aRR], 0.51; 95% CI, 0.35 to 0.74) but not in opioid pain medication use. There were also disparities in hospice use (aRR, 0.86; 95% CI, 0.74 to 0.99), intensive care unit admission or more than one emergency department visit or hospitalization 30 days before death (aRR, 1.28; 95% CI, 1.01 to 1.63), and risk of dying in the hospital (aRR, 1.59; 95% CI, 1.22 to 2.09). Supportive medication use did not attenuate end-of-life care disparities.

Conclusion

We observed racial disparities in early supportive medication use among patients with stage IV breast cancer. Although they did not clearly attenuate end-of-life care disparities, medication use disparities may be of concern if they point to disparities in adequacy of symptom management given the potential implications for quality of life.

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INTRODUCTION

Cancer and its treatment are associated with a range of physiologic and psychosocial symptoms.[1-7] Research suggests that minority patients with cancer may receive inadequate symptom management. Studies have documented racial/ethnic disparities in outcomes related to symptom burden and severity,[8,9] adequacy of pain treatment,[10-12] and patients' perceived unmet need for supportive services, including psychologic services.[13] Disparities persist even as supportive care is increasingly recognized as a vital component of high-quality cancer care.[14,15]

Adequacy of cancer-related symptom control has important implications for patients' quality of life (QOL) and well-being.[3,14-21] Data from a randomized controlled trial suggested that early use of supportive care may influence health care use at the end of life. Specifically, patients who received early supportive care integrated with standard oncologic care were less likely than patients who received standard oncologic care alone to receive chemotherapy within 14 days of death and were more likely to transition to hospice before death.[22] One plausible hypothesis for the relationship among early palliative care, hospice use, and less-intensive end-of-life care is that in providing decisional support, supportive/palliative care providers may

assist both oncologists and patients in planning for the end of life. Such discussions may facilitate the transition from active treatment to hospice services and improve the quality of end-of-life care.[22]

Several studies have demonstrated that black patients are less likely than white patients to use hospice,[23] which has been linked with enhanced patient and caregiver QOL,[24,25] prolonged survival,[26,27] and increased concordance with patients' preferred place of death.[28,29] Studies have also demonstrated that black patients are more likely to receive intensive interventions at the end of life,[30] which are of questionable benefit in terms of lengthening life of patients with terminal illness, and may be detrimental to patients' QOL.[24,31]

Early integration of supportive care services may be a promising strategy for improving patients' QOL as well as the quality of their care at the end of life. The objectives of this study were twofold. Within a cohort of patients with stage IV breast cancer who died during the study period, we explored early use of medications to treat common breast cancer symptoms (pain, depression/anxiety, and insomnia) and assessed whether use varied by race. Second, we evaluated racial disparities in hospice use and end-of-life care measures and examined the role of supportive medication use in attenuating potential racial disparities in end-of-life care, should they exist.

METHODS

Data Source

We used the National Cancer Institute SEER database linked with Medicare fee-for-service claims from 2006 to 2012. The SEER program consists of population-based cancer registries and represents 28% of the population with cancer. SEER data are merged with Medicare claims data of patients age 65 years and older and then linked with the National Death Index to obtain date and cause of death.[32] This study was conducted in accordance with a SEER-Medicare data use agreement and received exemption from the institutional review board at the University of North Carolina at Chapel Hill.

Cohort

We identified patients with a first diagnosis of breast cancer during 2007 to 2011 who were age 65 years or older and who were alive at diagnosis and not missing month of diagnosis (n = 104,629). We further excluded those not continuously enrolled in fee-for-service Medicare Parts A and B for 6 months before and 3 months after diagnosis (n = 40,875). We excluded patients who were not enrolled in a stand-alone Medicare Part D plan for 3 months before and after diagnosis (n = 30,105) as well as men (n = 263) and women with end-stage renal disease (n = 220). Finally, we excluded women with stage 0 to III disease (n = 31,767), those without a recorded date of death (n = 321), those who died within 90 days after diagnosis (n = 108), and those enrolled in a health maintenance organization in the 3 months before death (n = 23). The study was limited to women with stage IV disease at initial diagnosis because SEER does not contain information about disease recurrence. Furthermore, because of the small proportion of nonblack minorities in the sample (n = 64), we restricted the study to black and white patients. The final cohort comprised 883 decedents.

Outcomes

Supportive Treatment Use. We assessed patients' use of supportive medications, including opioid pain medications and nonopioid psychotropic medications (antidepressants and nonbenzodiazepine sleep aids) within 90 days after cancer diagnosis. We measured any use of supportive medications and use of each category of medications (opioid pain medications and nonopioid psychotropics). We were unable to capture benzodiazepines, which were not covered by Medicare Part D until 2013. A complete list of included medications is provided in the Appendix Table A1 (online only). We selected these treatments as a potential claims-based indicator for patients' engagement with supportive care with the hypothesis that patients who received symptomatic treatment early in the course of the postdiagnosis period were more likely to receive comprehensive supportive care, including end-of-life care planning, later in the care trajectory.

End-of-Life Care. We created indicators of four end-of-life care measures that were based on those developed and measured in administrative data.[33,34] These were hospice use before death (both any use and use of ≤ 3 days among users), in-hospital death, receipt of chemotherapy within 14 days of death, and high-cost health care utilization (intensive care unit [ICU] admission, more than one emergency department [ED] visit, more than one hospitalization) in the last 30 days of life. We created a composite indicator of occurrence of any of these three outcomes because each individual outcome was relatively rare in the present sample.

Independent Variable

The main independent variable in the analysis was race (black or white) as reported in the SEER-Medicare data.

Covariates

Covariates were age and marital status at diagnosis; year of diagnosis; US region; the extent of urbanization at patients' residences (obtained from the Area Resource File); and 2000 census tract–level measures of socioeconomic status (SES), including high school completion rate and median income. We assessed comorbid illness by using the Klabunde modification of the Charlson comorbidity index.[35] Cancer-directed treatment (surgery, radiation, chemotherapy, endocrine therapy) was identified by using inpatient, outpatient, and pharmacy claims. We also controlled for patients' history of any inpatient or outpatient mental health diagnosis (International Classification of Diseases, Ninth Revision, codes 290.0 to 319.99) and prior use of supportive medications.

Statistical Analysis

We examined the distribution of patient characteristics, supportive medication use, and end-of-life care between racial groups by using χ^2 tests for categorical variables and *t* tests for continuous variables. We used modified Poisson regression[36] to assess the relationship between race and receipt of early supportive medications and end-of-life care by controlling for relevant patient characteristics. Indicators of supportive medication use and interactions of race and supportive medication use were then added to the end-of-life care models. We present adjusted risks and adjusted risk ratios (aRRs) with 95% CIs.

Accounting for SES

The Institute of Medicine defines racial health care disparities as differences in treatment not justified by differences in health status or preferences.[37] Analytically, this definition of disparities controls for differences in health status and, if available, preferences for care but recognizes the mediating role of SES and SES-related factors and excludes these from the model. This approach acknowledges that adjusting for SES-related factors may mask the effect of race on care.[38-40]

In accordance with the Institute of Medicine definition of health care disparities, our primary models adjusted for clinical characteristics, namely age, year of cancer diagnosis, medical comorbidity, and receipt of cancer-directed therapy. The supportive medication models also included indicators of mental health and supportive medication use history. We did not adjust for census tract–level measures of SES in the primary models. We also did not adjust for other potential mediators of disparities, namely geographic factors (US region of residence and metropolitan versus nonmetropolitan residence) and marital status.[40] However, because an understanding of where disparities in care might arise is important, we conducted sensitivity analyses to assess whether differences in census tract–level SES, marital status, or geography attenuated observed disparities in supportive medication use and end-of-life care.

Finally, we conducted additional sensitivity analyses that limited the sample to women who died as a result of breast cancer because women with rapidly progressing cancer may have supportive care needs and experiences that are distinct from women with competing health concerns.

RESULTS

The sample included 883 women (85.2% white, 14.8% black). Clinical and demographic characteristics of the study sample by race are shown in Table 1. Black women had a higher comorbidity burden and were more likely to be single and to have a lower SES than white women. All women had similar patterns of cancer-directed therapy. With regard to prior supportive treatment use, no difference was found in prediagnosis use of opioids (22.1 *v* 22.7 for black and white women, respectively), but black women were significantly less likely to have used nonopioid psychotropics in the months preceding a breast cancer diagnosis (13% *v* 23%).

Bivariate Analysis

Unadjusted analyses did not reveal statistically significant racial differences in women's early use of any supportive medications (Table 2). Within specific medication groups, black women were as likely as white women to receive opioid pain medications; however, they were half as likely to receive nonopioid psychotropics (32% white, 16% black; $P < .001$).

Racial differences also were found in hospice use, with black women 11% less likely to use hospice than white women (risk of hospice use, 71% white, 60% black; $P < .05$; Table 3). Black women were also 16% more likely to die in the hospital (risk of terminal hospitalization, 22% white, 36% black; $P < .001$) and 11% more likely to have an ICU admission or more than one hospitalization or ED visit in the final 30 days of life (risk of admission, 29% white, 40% black; $P < .05$). Because few women in the sample received chemotherapy in the last 14 days of life or entered hospice within 3 days of death, we excluded these outcomes from the final models.

Primary Analysis

In the primary models that adjusted for clinical characteristics, racial differences in any supportive medication use, and use of opioid pain medications remained insignificant. However, disparities in use of nonopioid psychotropic medications persisted, with black women having a 44% decreased risk of using these medications (aRR, 0.56; 95% CI, 0.39 to 0.80). The results of the adjusted medication use models are shown in Table 2.

We also observed racial disparities in end-of-life care. Black women had a 60% increased risk of dying in the hospital (aRR, 1.60; 95% CI, 1.22 to 2.09) and a 14% decreased risk of entering hospice (aRR, 0.86; 95% CI, 0.74 to 0.99). The relationship between race and risk of having an ICU admission or more than one ED visit or hospitalization in the last 30 days of life was also significant after adjustment, with black women having a 30% increased risk of use of these services (aRR, 1.30; 95% CI, 1.02 to 1.65). The results of the adjusted end-of-life care models are shown in Table 3. In adjusted (and unadjusted) models, use of nonopioid psychotropic medications was not statistically significantly associated with hospice use, dying in the hospital, or health care utilization in the last 30 days of life overall or by racial subgroup (Table 4).

Table 1. Clinical and Demographic Characteristics of Sample by Race

Characteristic	White (%)	Black (%)	*P*
No. of patients	752	131	
Demographic characteristic			
Age at cancer diagnosis			.05
65-70 years	24	33	
71-76 years	23	28	
77-82 years	24	21	
≥ 83 years	30	20	
Marital status at diagnosis			
Married/partnered	27	8	**< .001**
Nonmarried/partnered	69	82	
Unknown	4	9	
Median household income in census tract of residence			
$5,299-$26,469	21	49	**< .001**
$26,470-$36,165	26	23	
$36,166-$50,838	—	—	
$50,839-$200,014	28	—	
Unknown	—	0	
Proportion of residents with no high school degree in census tract of residence			
0.53-8.88	28	—	**< .001**
8.89-15.91	27	15	
15.92-27.06	—	—	
27.07-79.92	21	49	
Unknown	—	0	
Residence			
Metropolitan county	79	87	**.04**
Nonmetropolitan county	21	13	
US region			
Northeast	28	18	**< .001**
Midwest	16	14	
West	32	22	
South	25	47	
Clinical characteristic			
Year of cancer diagnosis			
2007	24	22	.82
2008	21	22	
2009	22	19	
2010	17	21	
2011	16	16	
Charlson comorbidity index			
0	73	63	**.03**
1	19	22	
≥ 2	8	15	
Cancer treatment (any), % yes	85	84	.74
Surgery	25	22	.46
Radiation	35	33	.65
Chemotherapy	45	39	.20
Endocrine therapy	61	58	.51
Previous mental health diagnosis, % yes	18	15	.39
Previous supportive medication use (any), % yes	37	29	.08
Previous opioid use, % yes	23	22	.88
Previous nonopioid psychotropic use, % yes	23	13	**.02**

NOTE. Values in bold are statistically significant. Percentages that reflect counts < 11 and percentages that would allow counts < 11 to be derived by using other information in the table were suppressed (—) to protect patient identity.

Sensitivity Analyses

In models that adjusted for census tract–level measures of SES and indicators of marital status and geographic location in addition to clinical characteristics, racial disparities in the use of supportive medications were similar to those demonstrated in the primary

Table 2. Unadjusted and Adjusted Associations of Race With Supportive Medication Use

	Risk (95% CI)				Risk Ratio (95% CI)	
	Unadjusted		Adjusted		Black *v* White	
Supportive Medication Use	White	Black	White	Black	Unadjusted	Adjusted
Any supportive medications	0.69 (0.66 to 0.73)	0.64 (0.56 to 0.73)	0.49 (0.42 to 0.58)	0.46 (0.39 to 0.56)	0.93 (0.81 to 1.06)	0.94 (0.83 to 1.07)
Opioid pain medications	0.61 (0.57 to 0.64)	0.60 (0.52 to 0.69)	0.45 (0.36 to 0.56)	0.47 (0.38 to 0.57)	0.98 (0.84 to 1.14)	0.97 (0.84 to 1.13)
Nonopioid psychotropic medications	0.32 (0.28 to 0.35)	0.16 (0.11 to 0.24)	0.32 (0.11 to 0.90)	0.18 (0.06 to 0.51)	**0.51 (0.34 to 0.76)**	**0.56 (0.39 to 0.80)**

NOTE. Risks for black and white patients were calculated at the reference values of the covariates, which were as follows for each covariate: age (≥ 83 years), year of cancer diagnosis (2011), cancer treatment received (none received), comorbidity score (≥ 2), previous mental health diagnosis (no diagnosis), and previous use of supportive medications (no use). Risk ratios in bold are statistically significant. The following covariates were included in the adjusted models: age, marital status, year of cancer diagnosis, cancer treatment received, comorbidity score, previous mental health diagnosis, and previous use of supportive medications.

models (data not shown). Racial disparities in end-of-life care were also consistent with those demonstrated in the primary models, although the relationships between race and risk of hospice use and risk of having an ICU admission or more than one ED visit or hospitalization became marginally statistically significant.

In an analysis restricted to women who died as a result of breast cancer (n = 607), disparities in supportive medication use were again similar to those demonstrated in the primary models. The disparity in risk of hospice use did not persist in this restricted sample, and the relationship between race and risk of having an ICU admission or more than one ED visit or hospitalization was marginally statistically significant. Of the 276 women in the sample who did not have breast cancer recorded as the cause of death, nearly one half (n = 131) did not have another cause of death recorded. Among those who did, diseases of the heart (n = 37) and miscellaneous malignant cancer (n = 23) were most common.

DISCUSSION

In the primary analyses, we observed no racial disparities in women's early use of any supportive medications or opioid pain medications. However, we did find a racial disparity in women's use of nonopioid psychotropic medications to treat depression, anxiety, and insomnia. Specifically, compared with similar white women, black women had a 44% decreased risk of using these medications. We also observed disparities in end-of-life care. Black women were at decreased risk of entering hospice and increased risk of having an ICU admission or more than one ED visit or hospitalization in the last 30 days of life and of dying in the hospital. Use of nonopioid psychotropics was not associated with end-of-life care measures; thus, it does not seem to mediate the observed relationship between race and end-of-life care.

This study is the first to our knowledge to demonstrate potential disparities in the use of supportive medications for treatment of common symptoms of cancer, namely depression, anxiety, and insomnia, although others have demonstrated racial disparities in self-reported unmet supportive care needs.[13] Potential disparities in use of medications to treat cancer-related symptoms may be attributable to cost-related barriers.[41] However, the addition of SES variables to the present medication use models did not attenuate disparities in nonopioid psychotropic use. This may be due to potential misclassification of individual-level SES from using area-level SES measures, which often capture complementary contextual dimensions of SES.[42,43] An alternative explanation for the lack of effect of SES on disparities in nonopioid psychotropic medication use is that observed disparities are not purely related to the cost of medications. Previous research on disparities in use of mental health services suggested that lower use of services among minorities may be due to cultural or attitudinal factors around mental health.[44-46] Still, minorities' lower access to general and specialty care are likely to contribute to disparities in cancer symptom management.[47]

Suboptimal pain treatment among minorities has been demonstrated consistently in previous studies and has been partly explained by cultural differences in pain-related attitudes.

Table 3. Unadjusted and Adjusted Associations of Race With End-of-Life Care Measures

	Risk (95% CI)				Risk Ratio (95% CI)	
	Unadjusted		Adjusted		Black *v* White	
End-of-Life Care Measure	White	Black	White	Black	Unadjusted	Adjusted
Any hospice use	0.71 (0.68 to 0.74)	0.60 (0.52 to 0.69)	0.44 (0.27 to 0.73)	0.38 (0.23 to 0.62)	**0.85 (0.73 to 0.98)**	**0.86 (0.74 to 0.99)**
Terminal hospitalization	0.22 (0.19 to 0.25)	0.36 (0.29 to 0.45)	0.27 (0.17 to 0.43)	0.43 (0.27 to 0.68)	**1.63 (1.25 to 2.12)**	**1.60 (1.22 to 2.09)**
ICU admission, more than one ED visit, or more than one hospitalization in last 30 days of life	0.29 (0.26 to 0.32)	0.40 (0.32 to 0.49)	0.28 (0.20 to 0.37)	0.36 (0.26 to 0.50)	**1.38 (1.08 to 1.75)**	**1.30 (1.02 to 1.65)**

NOTE. Risks for black and white patients were calculated at the reference values of the covariates, which were as follows for each covariate: age (≥ 83 years), year of cancer diagnosis (2011), cancer treatment received (none received), comorbidity score (≥ 2), previous mental health diagnosis (no diagnosis), and previous use of supportive medications (no use). Estimated risk ratios in bold are statistically significant. The following covariates were included in the adjusted models: age, marital status, year of cancer diagnosis, cancer treatment received, and comorbidity score.
Abbreviations: ED, emergency department; ICU, intensive care unit.

Table 4. Adjusted Associations of Nonopioid Psychotropic Medication Use and End-of-Life Care Measures Overall and Stratified by Race

End-of-Life Care Measure	Risk Ratio and (95% CI), Medication Users *v* Non-Users		
	Full Sample (n = 883)	White (n = 752)	Black (n = 131)
Any hospice use	1.02 (0.93 to 1.13)	1.02 (0.92 to 1.13)	0.87 (0.59 to 1.29)
Terminal hospitalization	0.94 (0.73 to 1.23)	0.96 (0.71 to 1.30)	1.19 (0.64 to 2.21)
ICU admission, one or more ED visits, or one or more hospitalizations in last 30 days of life	1.13 (0.91 to 1.40)	1.12 (0.88 to 1.42)	1.60 (0.97 to 2.67)

NOTE. Reference category is nonuse of medications. The following covariates were included in the models: age, marital status, year of cancer diagnosis, cancer treatment received, and comorbidity score.
Abbreviations: ED, emergency department; ICU, intensive care unit.

Physician-related factors, including underestimation of minority patients' pain and beliefs about minority groups, also contribute to disparities in pain treatment.[47] Of note, we did not observe a racial disparity in use of opioid pain medications in the present sample. Several possible reasons exist for the seeming inconsistency of our findings with previous research. First, we measured pain treatment as a binary indicator of any opioid pain medication use. Other studies of disparities in analgesic use have used more-nuanced measures of pain management that capture the appropriateness of prescribed drugs and dosing and patient adherence.[48-50] Second, many studies of disparities in cancer pain management have used patients' symptom reports rather than or in addition to an examination of medication use.[50-52] Thus, the lack of disparity in opioid use in the present study is not necessarily indicative of a lack of disparity in adequacy of pain management; however, the data were not sufficient to capture the latter outcome.

All of the present analyses revealed that black women were more likely to die in the hospital. This finding is consistent with previous research on racial disparities in end-of-life care.[53] We also found that black women were less likely to use hospice and more likely to have an ICU admission or more than one ED visit or hospitalization in the 30 days before death. However, these findings were inconsistent across primary and sensitivity analyses. Supportive medication use did not attenuate observed end-of-life care disparities possibly because pharmacologic symptom management is an insufficient indicator of patients' engagement with supportive care. The single outpatient palliative care intervention to date that has demonstrated an effect on end-of-life care consisted of multiple components, including symptom management, patient and family coping, and illness understanding and education.[19,54] This prior intervention, however, was tested among patients with advanced lung cancer, which has a different prognosis and trajectory than advanced breast cancer. An alternative explanation is that disparities in risk of hospice use and dying in the hospital may be explained by factors other than early use of supportive care. For example, black and white patients may have differential preferences for end-of-life care, including intensity of care during the period immediately preceding death.[30]

This study had several limitations. First, it focused on black and white patients with stage IV breast cancer who received fee-for-service Medicare and Medicare Part D coverage. It is unclear whether the results extend to other populations of patients with cancer. Second, the measurement of receipt of supportive cancer care by using claims data can be challenging because some important aspects of supportive care (eg, counseling, decision support) may be undercoded. We attempted to measure supportive care by using a binary indicator of supportive medication use, but this may have been insufficient because pharmacologic symptom management is just one aspect of supportive care. Third, similar studies that focus on decedents (versus patients who are dying) may be subject to bias, which results from subject selection and time period.[55] Finally, we were unable to account for patient preferences for supportive medication use and end-of-life care, which, as in previous research, may differ between black and white patients. Thus, the present analyses may be subject to unmeasured confounding. These limitations notwithstanding, we present novel observational data on the use of supportive care services among patients with stage IV breast cancer that may point to important gaps in receipt of these services.

In conclusion, we found evidence of racial disparities in the use of some supportive medications and in patterns of end-of-life care. Although the results do not suggest that supportive medications attenuate disparities in end-of-life care, disparities in supportive medication use may be of concern regardless of their effect on end-of-life outcomes, if they point to disparities in adequacy of symptom management, given the potential implications for QOL. To determine whether disparities in medication use indicate disparities in care quality, future research should include data on patients' supportive care needs and preferences around medication use.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

AUTHOR CONTRIBUTIONS

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Table A1. Generic Names of Medications Included in Analysis

Supportive Medication Category	Generic Drug Name
Opioid pain medications	Buprenorphine
	Fentanyl
	Hydrocodone
	Hydromorphone
	Levorphanol
	Meperidine
	Methadone
	Morphine
	Nalbuphine
	Oxycodone
	Oxymorphone
	Propoxyphene
	Tapentadol
	Tramadol
Nonopioid psychotropic medications	
Antidepressants	Amitriptyline
	Amoxapine
	Bupropion
	Citalopram
	Clomipramine
	Desipramine
	Desvenlafaxine
	Doxepin
	Duloxetine
	Escitalopram
	Fluoxetine
	Fluvoxamine
	Imipramine
	Isocarboxazid
	Maprotiline
	Milnacipran
	Mirtazapine
	Nefazodone
	Nortriptyline
	Paroxetine
	Phenelzine
	Protriptyline
	Sertraline
	Tranylcypromine
	Trazodone
	Trimipramine
	Venlafaxine
	Vilazodone
Nonbenzodiazepine sleep aid	Buspirone
	Eszopiclone
	Hydroxyzine
	Pregabalin
	Zaleplon
	Zolpidem