# Neuroimaging overuse is more common in Medicare compared with the VA

James F. Burke, MD, MS Eve A. Kerr, MD, MPH Ryan J. McCammon, MA Rob Holleman, MPH Kenneth M. Langa, MD, PhD Brian C. Callaghan, MD, MS

Correspondence to Dr. Burke: jamesbur@med.umich.edu

## ABSTRACT

**Objective:** To inform initiatives to reduce overuse, we compared neuroimaging appropriateness in a large Medicare cohort with a Department of Veterans Affairs (VA) cohort.

**Methods:** Separate retrospective cohorts were established in Medicare and in VA for headache and neuropathy from 2004 to 2011. The Medicare cohorts included all patients enrolled in the Health and Retirement Study (HRS) with linked Medicare claims (HRS-Medicare; n = 1,244 for headache and 998 for neuropathy). The VA cohorts included all patients receiving services in the VA (n = 93,755 for headache and 183,642 for neuropathy). Inclusion criteria were age over 65 years and an outpatient visit for incident neuropathy or a primary headache. Neuroimaging use was measured with Current Procedural Terminology codes and potential overuse was defined using published criteria for use with administrative data. Increasingly specific appropriateness criteria excluded nontarget conditions for which neuroimaging may be appropriate.

**Results:** For both peripheral neuropathy and headache, potentially inappropriate imaging was more common in HRS-Medicare compared with the VA. Forty-nine percentage of all headache patients received neuroimaging in HRS-Medicare compared with 22.1% in the VA (p < 0.001) and differences persist when analyzing more specific definitions of overuse. A total of 23.7% of all HRS-Medicare incident neuropathy patients received neuroimaging compared with 9.0% in the VA (p < 0.001), and the difference persisted after excluding nontarget conditions.

**Conclusions:** Overuse of neuroimaging is likely less common in the VA than in a Medicare population. Better understanding the reasons for the more selective use of neuroimaging in the VA could help inform future initiatives to reduce overuse of diagnostic testing. *Neurology*® 2016;87:792-798

### GLOSSARY

**HRS** = Health and Retirement Study; **ICD-9** = International Classification of Diseases-9; **NCS** = nerve conduction studies; **SPEP** = serum protein electrophoresis; **VA** = Veterans Affairs.

Neuroimaging is common and costly,<sup>1</sup> and it is likely that both overuse and underuse exist. Recently, Choosing Wisely guidelines have focused on overuse by questioning the use of diagnostic neuroimaging in 2 highly prevalent neurologic conditions: headache and peripheral neuropathy.<sup>2,3</sup> Guideline discordant neuroimaging overuse appears to be common for head-ache<sup>4,5</sup> and peripheral neuropathy.<sup>6–8</sup> At the same time, underuse of neuroimaging in some high-risk headache patients<sup>9</sup> and diagnostic laboratory testing<sup>10</sup> in neuropathy patients likely exists.<sup>6</sup>

The Veterans Affairs (VA) health system is a single-payer health system that is largely separate from the private sector health care system. Prior comparisons between VA and non-VA systems have suggested that quality of care in the VA is no worse, and often better, than comparable non-VA systems with lower costs.<sup>11-14</sup> However, most comparisons have focused exclusively on underuse of medical services.<sup>15</sup> The VA system offers a variety of structural and organizational contrasts with the private sector health care system.<sup>11,14</sup> Therefore, any differences in inappropriate services between the VA and other health care systems may be partially due to these organizational differences. Consequently, we sought to explore whether rates of inappropriate neuroimaging for headache and neuropathy differs between the VA and a fee-for-service

From the Department of Neurology (J.F.B., B.C.C.), Department of Internal Medicine (E.A.K., R.J.M., K.M.L.), Institute for Healthcare Policy and Innovation (J.F.B., E.A.K., K.M.L., B.C.C.), and Institute for Social Research (K.M.L.), University of Michigan, Ann Arbor; and Neurology Section (J.F.B., B.C.C.) and Center for Clinical Management and Research (E.A.K., R.H., K.M.L.), VA Ann Arbor Healthcare System, MI. Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article. Medicare population. We also examined difference in appropriately performed laboratory studies for the workup of neuropathy. We hypothesized that less overuse and underuse would exist in the VA and that differences in overuse would be more pronounced as more specific definitions of overuse were applied.

**METHODS** We performed a retrospective, cross-sectional comparison of the use of diagnostic testing for 2 neurologic conditions (headache and peripheral neuropathy) in the VA and the fee-for-service Medicare population (Health and Retirement Study [HRS]–Medicare) enrolled in the HRS. Our primary goal was to compare the frequency and appropriateness of diagnostic testing between systems.

**Standard protocol approvals, registrations, and patient consents.** The Ann Arbor VA Human Studies Committee approved this study with a waiver of informed consent.

**Data.** The VA National Corporate Data Warehouse, which contains information on all outpatient encounters and ICD-9 diagnoses in all VA hospitals in the United States, was used to identify outpatient visits for neuropathy and headache in the VA. Data from Medicare Standard Analytic Files (MedPAR, carrier, outpatient) that were linked to the HRS were used to identify the same diagnoses, comorbidities, and care setting. Datasets were limited to individuals age 66 and above for headache (to allow time for Medicare enrollment) and 67 and above for neuropathy (to verify a 2-year neuropathy-free period), and to 2004–2011.

**Definition of target conditions.** We identified headache visits in both datasets using the Healthcare Cost and Utilization Program Clinical Classification System<sup>16</sup> definition of headache identified at an outpatient visit as the primary diagnosis, ICD-9-CM codes 339.xx, 784.0x, 346.xx, and 307.81. We selected visits with a primary headache diagnosis to maximize specificity of the headache diagnosis and did not exclude patients who had prior headache visits because headache neuroimaging is not necessarily obtained at the initial headache visit. Headache visits identified in either the inpatient or emergency department settings were excluded.

Neuropathy visits were identified with ICD-9-CM codes (354.5, 356.0–9, and 357.0–9) in any diagnosis position in individuals with no neuropathy diagnosis within the prior 24 months.<sup>6</sup> We selected visits for patients who had no prior diagnosis of neuropathy (incident) in the previous 24 months because appropriate testing should occur around the time that a new diagnosis is made. We included both primary and all secondary diagnoses because testing should occur when a new diagnosis of neuropathy is made regardless of whether this is the main reason for the visit. Population characteristics including demographics and comorbidities were abstracted from claims to ensure comparability between populations. This approach is known to relatively undercount comorbidities in patients who obtain care in both systems, but particularly in the VA, because there is a lack of financial incentive for complete comorbidity coding.<sup>17</sup>

**Identification of neuroimaging.** Separate episodes of care were defined around the time of the index visit for both headache (6 months after) and neuropathy (6 months before or after). For headache, neuroimaging was identified with Current Procedural Terminology codes for head CT (70450, 70460, 70470) and

MRI brain (70551, 70552, 70553). Imaging that was performed in the inpatient or emergency department setting was excluded. For neuropathy, we included 6 months before and after the diagnosis, because testing commonly occurs before a formal diagnosis is made. The definition of neuroimaging for neuropathy was extended to include MRI of the cervical (72141, 72142, 72156), thoracic (72146, 72147, 72157), and lumbar (72148, 72149, 72158) spine. In addition, neurophysiologic (EMG and nerve conduction studies [NCS]) and laboratory testing (fasting glucose, hemoglobin A1C, glucose tolerance test, B<sub>12</sub>, serum protein electrophoresis [SPEP]) were identified using previously published methods.<sup>6</sup>

Definitions of appropriateness/potential overuse. The appropriateness of headache neuroimaging depends on a variety of relatively uncommon clinical factors-red flags in the history and abnormal findings on neurologic examination.18 As these factors are not reliably included in existing datasets, comparisons of appropriateness across health care systems are necessarily limited. To explore the magnitude of potential overuse of neuroimaging without access to these factors, we used a series of increasingly specific definitions for potential overuse. The magnitude of misclassification using these measures should decrease with more specific definitions of overuse. For example, the yield of significant intracranial findings in unselected headache patients is about 2% but decreases by an order of magnitude in patients with migraine; thus a migraine-focused definition of potential overuse should identify fewer false-positives than a definition based on unselected headache.19

To identify potential overuse of headache neuroimaging, we used 3 definitions of increasing specificity. For the least specific definition, we relied on the prior published definition of Schwartz et al.20 and then used 2 additional definitions with increasingly stringent criteria: definition 1, nontraumatic headache (maximally sensitive, nonspecific): any headache diagnosis excluding posttraumatic ICD-9 codes (339.20-339.22, 339.43); definition 2, excluding nontarget conditions: based on the more specific Schwartz et al.20 definition of potential overuse, which excludes a variety of conditions (either in the year prior or in the 6 months after incident diagnosis) where neuroimaging may be appropriate: (cancer [14xx-208.xx, 230xx-239xx], hemiplegic migraine [346.3.x, 346.6x], giant cell arteritis [446.5], epilepsy [345.xx, 780.3x], cerebrovascular disease including TIA [43xx], head or neck trauma [800xx-804xx, 850xx-854xx, 870xx-873xx, 9590x, 910xx, 920xx-921xx], altered mental status [78097 781xx 7845x], and personal history of stroke/TIA or cancer [V1254 V10xx]).20 We added 2 additional nontarget exclusions to the Schwartz et al. criteria to maximize specificity-multiple sclerosis (340.xx) and dementia (290.0, 290.1x, 290.2x, 290.3, 290.4x, 291.2, 294.1x, 046.1, 331.0, 331.1x, 331.2, 331.82); definition 3: migraine excluding nontarget conditions (maximally specific, insensitive)-all nontarget exclusions from definition 2 with narrowing of the included population to only include migraine headaches (346.xx), as guidelines recommend against routine neuroimaging in this population.<sup>21,22</sup>

For neuropathy, given that neuroimaging should not be obtained as part of the typical evaluation, our least specific definition of potential overuse (definition 1) included all neuroimaging use in patients with neuropathy. To clarify the overall appropriateness of the diagnostic evaluation, we also measured the use of appropriate laboratory testing (B<sub>12</sub>, SPEP, and glycemic testing) as well electrophysiologic (EMG, NCS) testing, which is of uncertain appropriateness in an unselected neuropathy population.<sup>23</sup> We also applied a more specific definition of potential overuse (definition 2): any neuroimaging in patients with neuropathy after

793

Neurology 87 August 23, 2016

excluding nontarget conditions potentially meriting imaging including dementia (as above), MS/myelopathy/central patterns of weakness (336.x, 340.x, 341.x, 342.x, 344.x), epilepsy (345.x), cervical radiculopathy (723.4), lumbar radiculopathy (724.3, 724.4), and stroke (as above).

Statistical analysis. Descriptive statistics were used to describe neuroimaging utilization for each condition, measure, and population. Comparisons between the VA and non-VA populations were made using 2-sample, 2-tailed tests of proportions across each condition and measure of potential overuse. Neuropathy measures were separately estimated in the overall population and in the population with and without diabetes. Given the substantial differences in the sex of VA and non-VA populations, we also explored whether differences in neuroimaging exist by sex.

**RESULTS Patient populations.** The VA headache population was slightly younger (mean age 75 vs 77 years), generally had fewer coded comorbidities, and, most strikingly, was overwhelmingly composed of men (96% vs 37%) compared with the HRS-

Medicare population. Similar patterns were seen in the neuropathy population. Other details of the study populations are summarized in table 1.

Potential overuse of headache neuroimaging. Of the 93,461 VA patients with a primary nontraumatic headache diagnosis (definition 1), 22.1% received neuroimaging, compared with 49.0% of the 1,224 patients in HRS-Medicare (p < 0.001) (table 2). Rates of headache neuroimaging decreased in both systems when looking at more specific definitions of potential overuse. Despite small numbers, a significant difference in imaging rates (8.5% VA vs 18.8% HRS-Medicare, p = 0.04) was observed using the most specific definition of potential overuse. Headache neuroimaging was obtained, on average, 47.1 (SD 47.6) days after the index visit at the VA and 14.2 days (SD 35.3) in HRS-Medicare (p < 0.001). As increasingly specific definitions of potentially inappropriate imaging were

Table 1	Baseline characteristics of Veterans Affairs (VA) and Health and Retirement Study (HRS)-Medicare
	patients with headache and neuropathy including demographics and all individual Charlson comorbidities

	Headache, n (%)		Neuropathy, n (%)			
	VA	HRS-Medicare	VA	HRS-Medicare		
Total	72,966	1,007	183,642	998		
Age, y, mean (SD)	74.9 (6.7)	76.6 (7.1)	76.9 (6.2)	77.5 (6.8)		
Male	70,085 (96.1)	320 (31.8)	180,719 (98.4)	437 (43.8)		
Race/ethnicity						
Hispanic	3,058 (4.2)	86 (8.5)	5,909 (3.2)	83 (8.3)		
Non-Hispanic white	52,136 (71.5)	792 (78.6)	133,576 (72.7)	775 (77.7)		
Non-Hispanic black	8,168 (11.2)	106 (10.5)	13,596 (7.4)	122 (12.2)		
Non-Hispanic other	2,376 (3.3)	22 (2.2)	4,504 (2.5)	18 (1.8)		
Missing	7,228 (9.9)	1 (0.1)	26,057 (14.2)	0 (0.0)		
Cancer	10,791 (14.8)	140 (13.9)	22,562 (12.3)	178 (17.8)		
Cerebrovascular disease	10,667 (14.6)	262 (26.0)	19,253 (10.5)	254 (25.5)		
Congestive heart failure	6,760 (9.3)	179 (17.8)	18,704 (10.2)	210 (21.0)		
Chronic obstructive pulmonary disease	16,975 (23.3)	280 (27.8)	32,766 (17.8)	276 (27.7)		
Connective tissue disease	2,034 (2.8)	70 (7.0)	3,506 (1.9)	67 (6.7)		
Dementia	1,930 (2.6)	69 (6.9)	3,265 (1.8)	43 (4.3)		
Diabetes with complications	5,836 (8.0)	80 (7.9)	30,082 (16.4)	186 (18.6)		
Diabetes without complications	20,320 (27.8)	288 (28.6)	91,173 (49.6)	438 (43.9)		
HIV	103 (0.1)	1 (0.1)	247 (0.1)	0 (0.0)		
Metastatic carcinoma	723 (1.0)	15 (1.5)	1,451 (0.8)	24 (2.4)		
Myocardial infarction	2,801 (3.8)	74 (7.3)	5,807 (3.2)	60 (6.0)		
Mild liver disease	1,353 (1.9)	56 (5.6)	2,419 (1.3)	63 (6.3)		
Moderate to severe liver disease	119 (0.2)	2 (0.2)	305 (0.2)	4 (0.4)		
Paraplegia or hemiplegia	759 (1.0)	23 (1.3)	1,779 (1.0)	20 (2.0)		
Peptic ulcer disease	1,642 (2.3)	45 (2.6)	2,738 (1.5)	25 (2.5)		
Peripheral vascular disease	8,517 (11.7)	417 (23.9)	25,902 (14.1)	281 (28.2)		
Renal disease	6,350 (8.7)	185 (10.6)	18,781 (10.2)	125 (12.5)		

Neurology 87 August 23, 2016

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Table 2

2 Number and proportion of Veterans Affairs (VA) and Health and Retirement Study (HRS)-Medicare patients receiving neuroimaging representing potential overuse

	VA		HRS-Medicare		
Potential overuse definition	Population size	% Receiving neuroimaging	Population size	% Receiving neuroimaging	p Value
1: Nontraumatic headache	93,461	22.1	1,244	49	< 0.001
2: Nontraumatic headache excluding nontarget conditions	41,957	15.3	329	27.1	<0.001
3: Migraine excluding nontarget conditions	7,883	7.1	45	15.6	0.027

Each row represents an increasingly specific definition of overuse.

applied, the relative rates of neuroimaging in VA and HRS-Medicare remained stable (table 2). There were no differences in neuroimaging by sex in the VA on definition 1 (22.0% in men vs 22.2% in women) or in HRS-Medicare (50.5% in men vs 48.4% in women).

Potential overuse of neuroimaging in neuropathy. A total 183,117 VA patients and 998 HRS-Medicare patients received a neuropathy diagnosis. On the least specific definition of potential overuse (definition 1, all neuropathy patients), neuroimaging of any component of the neuroaxis was obtained in 9.0% of VA patients vs 23.7% of HRS-Medicare patients (p < 0.001). Appropriate use of laboratory testing varied by setting, with less nonglycemic testing in the VA (SPEP in 6.7% vs 12.7%, p < 0.001, and B<sub>12</sub> in 2.9% vs 39.4%, p <0.001), but more glycemic testing (fasting glucose in 28.0% vs 13.9%, p < 0.001, and hemoglobin A1c in 65.7% vs 45.7%, p < 0.001). Glucose tolerance tests were ordered rarely in both populations (1.2% in both). Lower utilization of neurophysiologic testing, which is of uncertain appropriateness in an unselected population, was also seen at the VA (14.5% vs 32.3% received EMG or NCS, p < 0.001). Similar trends were observed in patients with and without diabetes, although neuroimaging was less common and glycemic testing more common in patients with diabetes (table 3). On the more specific definition of potential overuse, after excluding nontarget conditions (definition 2), imaging rates decreased in both VA and HRS-Medicare, but use of neuroimaging in VA remained significantly lower than in HRS-Medicare (6.1% vs 15.0%, p < 0.001).

**DISCUSSION** For patients with common neurologic diagnoses, we found that potential overuse of neuroimaging was much less common for patients treated in the VA compared with those receiving care through Medicare coverage. While a number of explanations exist, this result suggests that differences in these health care environments may mediate differential use of neuroimaging. Importantly, neuroimaging overuse appears to be high in both the VA and HRS-Medicare populations, indicating that substantial room for improvement exists in both systems.

To meaningfully measure and promote highquality care, it is important not to reward solely underuse or overuse.24,25 While prior performance measures may have incentivized overuse,26 unnecessary care reduction initiatives, such as Choosing Wisely,27 do the opposite. Without detailed clinical data, it is difficult to know whether the VA's lower headache neuroimaging utilization reflects a global reduction of imaging regardless of indication or a specific reduction in inappropriate utilization. We hypothesized that the difference in neuroimaging utilization between the VA and HRS-Medicare would increase with more specific definitions of potential overuse, but this was not the case. One possible explanation is that VA headache patients had incomplete listings of comorbid diagnostic codes, thereby overstating the degree of inappropriate imaging in the VA. Another possibility is that the number of migraine cases in the HRS-Medicare sample was so small that our analysis may have failed to detect a true difference. Finally, VA headache patients may receive fewer inappropriate imaging tests, but also may have fewer appropriate imaging tests. Further studies with detailed clinical information are needed to definitely determine if the VA promotes less overuse or less testing in general in headache patients.

For neuropathy, we were able to measure not only potential imaging overuse, but also appropriate use of other elements of the neuropathy evaluation. Similar to headache neuroimaging, neuropathy neuroimaging was lower in the VA compared with HRS-Medicare. However, while the VA had higher rates of screening for diabetes, B<sub>12</sub> and SPEPs were obtained less commonly in the VA. Screening for diabetes among obese patients is encouraged by VA guidelines,<sup>28</sup> so VA's diabetes screening rate may partially reflect diabetes testing not related to neuropathy. So, if one defines quality as limiting both underuse and overuse, neither system performed optimally for neuropathy workup. In addition, even after excluding diagnoses that may

795

Neurology 87 August 23, 2016

Table 3 Definition 1 (entire neuropathy population) and definition 2 (neuropathy), excluding nontarget conditions

	Definition 1: Entire neuropathy population								
	All		Diabetes			No diabetes			
	VA % (n = 183,117)	HRS % (n = 998)	p Value	VA % (n = 121,052)	HRS % (n = 662)	p Value	VA % (n = 62,065)	HRS % (n = 336)	p Value
Likely Inappropriate neuroimaging									
Brain MRI	4.3	11.4	<0.001	3.7	11.3	<0.001	5.4	11.6	<0.001
C-spine MRI	2.6	6.0	<0.001	2.0	4.5	<0.001	3.7	8.9	<0.001
T-spine MRI	0.7	1.9	<0.001	0.5	1.7	<0.001	1.0	2.4	0.01
L-spine MRI	4.1	13.3	<0.001	3.2	12.7	< 0.001	5.7	14.6	<0.001
Any MRI of neuroaxis	9.0	23.7	<0.001	7.4	22.8	<0.001	12.0	25.6	<0.001
Appropriate laboratory testing									
SPEP	6.7	12.7	<0.001	5.1	10.3	<0.001	10.0	17.6	<0.001
Glucose tolerance test	1.2	1.2	1	1.0	1.1	0.80	1.5	1.5	1
Vitamin B <sub>12</sub>	32.9	39.4	<0.001	29.5	34.7	<0.001	39.6	48.5	0.001
Fasting glucose	28.0	13.9	<0.001	30.2	16.8	< 0.001	23.5	8.3	<0.001
A1C	65.7	45.7	<0.001	82.0	63.0	<0.001	34.0	11.6	<0.001
Electrophysiologic testing of uncertain appropriateness									
EMG	9.5	22.4	<0.001	7.4	19.0	<0.001	13.8	29.2	<0.001
NCS	14.3	32.2	<0.001	11.1	30.7	<0.001	20.4	35.1	<0.001
EMG or NCS	14.5	32.3	<0.001	11.3	30.7	<0.001	20.7	35.4	<0.001
	Definition 2: Neuropathy, excluding nontarget conditions								

	All			Diabetes			No diabetes		
	VA % (n = 152,052)	HRS % (n = 592)	p Value	VA % (n = 101,589)	HRS % (n = 399)	p Value	VA % (n = 50,463)	HRS % (n = 193)	p Value
Likely inappropriate neuroimaging									
Brain MRI	3.0	8.4	< 0.001	2.5	9.8	< 0.001	3.9	5.7	0.2
C-spine MRI	1.6	2.2	0.25	1.2	2.3	0.01	2.4	2.1	0.79
T-spine MRI	0.4	0.7	0.25	0.3	0.8	0.03	0.6	0.5	0.86
L-spine MRI	2.6	6.9	< 0.001	2.0	6.5	< 0.001	3.6	7.8	0.002
Any MRI of neuroaxis	6.1	15.0	<0.001	5.0	15.5	<0.001	8.3	14.0	0.004

Abbreviations: NCS = nerve conduction studies; SPEP = serum protein electrophoresis.

justify neuroimaging, potential overuse of neuroimaging was relatively common even in the VA, where 6.1% of patients received a neuroimaging study. These results indicate that the VA system does not necessarily promote less testing across the board, but that neither health care system provides optimal care.

Understanding the factors that mediate the appropriateness of testing between these 2 large health care systems has the potential to inform future efficiency initiatives. Many differences between the VA and Medicare exist and are potential contributory factors: the fixed resource VA environment, the centrality of primary care in the VA,<sup>4</sup> use of electronic medical records in the VA,<sup>29</sup> provider practice patterns,<sup>30</sup> and provider financial incentives.<sup>31</sup> Understanding

which, if any, of these hypotheses account for the differences in appropriateness may inform future quality improvement initiatives.

While VA patients appear to have less inappropriate imaging than Medicare patients, significant overuse occurs in both systems. Despite extensive literature and guidelines recommending against unnecessary imaging, a significant proportion of headache and neuropathy patients are still receiving these tests. Interventions to curb overutilization are needed in both VA and Medicare. As more and more Veterans receive care in the community due to the Choice Act, it will become even more important to ensure that promoting access to necessary care does not also result in an increase of inappropriate testing.

This study has a number of potential limitations. First, in the absence of detailed clinical data, conclusions about the appropriateness of care can only be tentatively advanced. Second, the VA patient population differs from the HRS-Medicare population in readily measured (i.e., sex) and likely in unmeasured ways. Sex differences are unlikely to explain the lower neuroimaging rates in the VA because neuroimaging rates by sex were similar in both settings. It is plausible that clinically unmeasured factors meriting neuroimaging (red flags) may differ between settings. However, if such differences exist, it is unlikely that they would account for the neuroimaging differences between settings as red flags are not strong predictors of receiving neuroimaging.4 Second, the diagnostic reliability of our ICD-9 algorithms may differ between the VA and HRS-Medicare settings.<sup>32,33</sup> Reassuringly, the primary limitation of these definitions is imperfect sensitivity as opposed to limited specificity.33 As VA coding practices also tend toward lower sensitivity,<sup>17</sup> this means it is possible that we have understated the difference in neuroimaging utilization between VA and Medicare settings. Third, some VA patients may also be receiving care outside of the VA, and to the extent that VA providers knew the results, they may have refrained from repeating tests. Finally, our Medicare population is limited to patients with fee-for-service Medicare and excludes Medicare Advantage patients. While the financial incentive in capitated Medicare Advantage should lead to less use of imaging, imaging utilization has comparably slowed both in private plans with radiology benefit management strategies<sup>34,35</sup> and in Medicare fee-for-service36 in recent years, suggesting this is unlikely to be a major effect.

Our results suggest that the use of inappropriate neuroimaging for headache and neuropathy is relatively common, but less so in the VA than among HRS-Medicare patients. Appropriate laboratory testing for neuropathy is more common in the VA for diabetes testing and more common in HRS-Medicare for other tests. While both constraints in availability of imaging and lack of financial incentives for test ordering may promote less overuse of neuroimaging in the VA, the reasons for underuse of certain laboratory tests are unknown. Future initiatives to reduce overuse of diagnostic testing should learn from what is working in the VA to limit inappropriate imaging but not lose sight of the imperative to enhance the overall quality of care by also motivating appropriate use of needed services.

### AUTHOR CONTRIBUTIONS

J.F.B. helped design the study, interpreted data, drafted the manuscript, and performed part of the statistical analysis. E.A.K. conceived of the study, aided in data acquisition, critically revised the manuscript, obtained funding, and provided administrative support and supervision. R.J.M. helped design the study, acquired and analyzed data, critically revised the manuscript, and performed statistical analyses. R.H. helped design the study, acquired and analyzed data, critically revised the manuscript, and performed statistical analyses. K.M.L. helped design the study, interpreted data, critically revised the manuscript, and obtained funding and provided administrative support. B.C.C. helped design the study, interpreted data, critically revised the manuscript, and provided technical support.

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797

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