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Beers Criteria as a Proxy for Inappropriate Prescribing of Other Medications Among Older Adults

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Abstract

BACKGROUND—The Beers criteria are a compilation of medications deemed potentially inappropriate for older adults, and widely used a prescribing quality indicator.

OBJECTIVE—To determine whether Beers criteria serve as a proxy measure for other forms of inappropriate prescribing, as measured by comprehensive implicit review.

METHODS—Data for patients 65 years and older were obtained from the VA Enhanced Pharmacy Outpatient Clinic (EPOC) and the Iowa Medicaid Pharmaceutical Case Management (PCM) studies. Comprehensive measurement of prescribing quality was conducted using expert clinician review of medical records according to the Medication Appropriateness Index (MAI). MAI scores attributable to non-Beers medications (non-Beers MAI) were contrasted between patients who did and did not receive a Beers criteria medication.

RESULTS—Beers criteria medications accounted for 12.9% and 14.0% of total MAI scores in the two studies. Importantly, non-Beers MAI scores were significantly higher in patients receiving a Beers criteria medication in both studies (EPOC: 15.1 vs. 12.4, $p = 0.02$; PCM: 11.1 vs. 8.7, $p = 0.04$), after adjusting for important confounding factors.

CONCLUSIONS—Beers criteria utility extended beyond direct measurement of a limited set of inappropriate prescribing practices by serving as a clinically meaningful proxy for other inappropriate practices. Using prescribing quality indicators to guide interventions should thus identify patients for comprehensive medication review, rather than identifying specific targets for discontinuation. Future research should explore both the quality measurement and the intervention targeting applications of the Beers criteria, particularly when integrated with other indicators.

Keywords

Beers criteria; inappropriate drug use; older adult; quality indicators; health care

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Introduction

Pharmacotherapy is a crucial component of medical care and the consequences of inappropriate prescribing are significant, with roughly 1.5 million preventable adverse drug events in the U.S. annually at a cost in excess of \$4 billion.¹ Efforts to improve prescribing quality rely on valid measures for initial assessment and ongoing monitoring. Prescribing quality measures are often classified as *explicit* (criterion based) versus *implicit* (judgment based).^{2–3} *Explicit* measures rely on fixed criteria that apply uniformly to all patients and can therefore be computerized and easily determined for large patient samples. In contrast, *implicit* measures rely on clinical judgment to allow for the needs of individual patients, but are simultaneously criticized for lacking structure and reliability. Moreover, implicit measures require access to detailed clinical data and highly trained clinician assessors. For these reasons, explicit measures are usually selected over implicit approaches in real-world applications.

One of the most widely used prescribing quality indicators is an explicit compilation of medications determined by expert consensus to be inappropriate for use in older adults, commonly known as the Beers criteria.^{4–6} One major criticism is that these criteria represent only a small fraction of all possible inappropriate prescribing practices and associated adverse outcomes.^{7–9} In one study, Beers criteria medications accounted for only 13.6% of drugs deemed inappropriate by implicit review and 14.6% of drugs targeted for intervention by a physician-pharmacist team.^{7–8} Similarly, a mere 3.6% of adverse event related emergency department visits were due to Beers criteria medications, compared to 17.3% and 13.0% due to warfarin and insulin, respectively.⁹ While these findings have been used to highlight the limitations of the Beers criteria, it is important to recognize that predicting adverse drug events is a very different application than measuring prescribing quality. While warfarin and insulin exposure may be important when predicting adverse drug events, their use in older adults is not considered potentially inappropriate, and therefore not suitable as prescribing quality measures. In contrast, Beers criteria are comprised of medications where risk generally outweighs benefit when used in older adults.⁶ It is reasonable to require a process measure of prescribing quality, such as Beers criteria, to be a risk factor for adverse drug events in order to establish validity. However, it is unreasonable to expect them to perform as well as other measures specifically designed for this purpose, and does not diminish their value in measuring prescribing quality.

While an infrequent cause at the individual drug level, Beers criteria medications have been frequently associated with adverse event risk when examined at the patient level.^{10–17} For example, one study found only 6.0% of adverse drug events attributable to Beers criteria medications, yet patients who received these drugs were significantly more likely to have an adverse drug event (35.0% vs. 20.9%).¹⁴ Although Beers criteria medications did not account for many adverse events at the individual drug level, their utility may be higher at the patient level. In addition, the magnitude of association between Beers criteria medication exposure and adverse events is often diminished by adjusting for potential confounders.^{12, 15} These observations suggest that Beers criteria may serve as a proxy measure for other forms of inappropriate prescribing. That is, patients receiving a Beers criteria medication may be exposed to other inappropriate prescribing practices at higher rates, which collectively contribute to adverse event risk. While this may be seen as unwanted confounding from a causality perspective, this is an acceptable or even desirable property for a quality indicator. Strong correlations have been observed between quality indicators in related clinical areas, such as myocardial infarction and congestive heart failure.¹⁸ However, these relationships remain unclear for broadly defined prescribing indicators, which are not limited to specific disease states.

Therefore, the objective of this study was to determine whether Beers criteria are a proxy measure for other forms of inappropriate prescribing. We conducted replicate analyses using two independently collected patient samples, where inappropriate prescribing was measured by comprehensive implicit review according to the Medication Appropriateness Index (MAI). Total MAI scores attributable to non-Beers medications were compared between patients receiving versus not receiving a Beers criteria medication.

Methods

The VA EPOC study

The Enhanced Pharmacy Outpatient Clinic (EPOC) study enrolled veterans 65 years and older seen in primary care clinics at the Iowa City Veterans Affairs Medical Center (VAMC) and receiving at least 5 prescription medications. Patients were randomized to receive either a pharmacist-physician collaborative intervention or usual care.¹⁹ The goal of the intervention was to improve prescribing quality and medication safety. This sample has been used in several prior studies examining the interrelationships between various measures of inappropriate prescribing, including the Medication Appropriateness Index (MAI), an implicit measure, and the explicit Beers criteria.^{7-8, 20-21} Of 532 patients enrolled in EPOC, a convenience subset of 240 received a baseline MAI evaluation and forms the sample for this analysis. These individuals did not differ significantly from patients without MAI ratings on key characteristics including age, sex, race, education, medical comorbidity, or Beers medication frequency.²¹

The Iowa Medicaid PCM study

The Iowa Medicaid Pharmaceutical Case Management study (PCM) examined the effectiveness of reimbursing community pharmacists to provide outpatient pharmaceutical case management services.²² Patients were non-institutionalized Medicaid eligible individuals taking at least four chronic medications. Out of 2,211 individuals eligible to receive the intervention, 524 patients actually received PCM services. Of these, 507 (97%) had sufficient baseline clinical records to allow an evaluation of prescribing appropriateness with the MAI. After restricting to individuals aged 65 years and older for whom the Beers criteria are applicable, 167 patients were available for this analysis.

Inappropriate Prescribing Measures

Inappropriate prescribing was assessed at enrollment in both studies using the Medication Appropriateness Index (MAI).²³ The MAI includes 10 items assessing multiple domains and is generally considered among the best available tools for implicit measurement of inappropriate prescribing. Examples of MAI items include the presence of drug-disease interactions, incorrect dosing, and therapeutic duplication. Each of the 10 items were determined to be appropriate or inappropriate by expert clinical judgment based on detailed review of all available clinical records. MAI ratings for both studies in this analysis were completed by a research pharmacist. After applying standard scoring weights, MAI scores range from 0 to 18 for each medication and patient level scores are generated by summing medication scores across the regimen. High MAI scores reflect increasing levels of inappropriate prescribing. MAI score differences of approximately 2 points are generally considered clinically meaningful.^{22, 24} The MAI has been shown to have excellent interrater ($\kappa = 0.88$) and intrarater ($\kappa = 0.92$) reliability.²³ In addition to total scores, we calculated patient-level sub-scores for Beers criteria medications (Beers MAI score) and separately for all other, non-Beers medications in the regimen (non-Beers MAI score).

Inappropriate prescribing was also assessed in both studies according to Beers criteria.⁵⁻⁶ The Beers criteria represent a compilation of medications determined by expert panel to

have an unfavorable risk-benefit ratio when used in older adults. These criteria include medications considered inappropriate independent of other considerations (e.g. propoxyphene), inappropriate above certain dosage limits (e.g. lorazepam > 3mg), and inappropriate given specific concurrent medical conditions (e.g. tricyclic antidepressants in patients with syncope or falls). Applying Beers criteria does not account for patient-specific decision-making and assumes these medications are always inappropriate for use in elderly individuals. Therefore, the term *potentially* inappropriate prescribing is often used when referring to the Beers criteria and other similar explicit measures. The Beers criteria were originally published in 1991, with subsequent updates in 1997 and 2003.⁴⁻⁶ Different versions of the Beers criteria were selected by the original investigators of the two studies examined in this analysis; EPOC investigators used the 2003 revision and PCM investigators used the 1997 revision. This provided an opportunity to determine whether the findings of the current analysis were consistent for different versions of the Beers criteria. Updates made from the 1997 criteria are specified in the 2003 revision, and included the addition of 44 new criteria, elimination of 11 criteria, and modification of 4 criteria.⁶ Since the preponderance of updates involved the addition of criteria, the 1997 criteria can broadly be considered a subset of the 2003 criteria.

Statistical Analysis

MAI scores were compared between patients exposed versus unexposed to Beers criteria medications using a general linear model approach. SAS procedure GLM (version 9.2) was used to generate the test statistic comparing these groups (F-test), adjusting for age and sex. Further adjustment for medical comorbidity was conducted in a sensitivity analysis using EPOC study data.²⁵ However, medical comorbidity did not affect the models and was not available for the PCM study, so was not included in the final analysis. A t-test was used to compare the number of drugs between groups. An exploratory subanalysis was conducted comparing non-Beers MAI scores for each of the 10 individual MAI items between patients exposed versus unexposed to Beers criteria medications. The purpose of the subanalysis was to examine whether patients receiving Beers criteria medication were at risk for specific aspects of inappropriate prescribing. Neither the EPOC nor PCM studies were powered for this purpose and the subanalysis should be considered exploratory. Because item-level MAI scores are not normally distributed, the nonparametric Wilcoxon rank sum test was used to make comparisons between Beers exposed and unexposed groups. In addition to individual items, the subanalysis included an alternative algorithm for scoring the MAI that was created specifically to assess risk for adverse drug events.²¹

All analyses were conducted using SAS procedure GLM (version 9.2). Data from the two independently conducted studies (EPOC and PCM) were examined separately using identical methods. As the purpose of including data from these two studies was purely for replication, no statistical comparisons were made between studies. This study was approved by the Institutional Review Board of the University of Iowa and Research and Development Committee at the Iowa City VA Healthcare System.

Results

Patients

Patient characteristics for the two analysis samples are descriptively contrasted in Table 1. EPOC study patients were predominantly men (98.3%), with a mean age of 74.6 (S.D.=5.4) years. PCM study patients were of similar age 76.4 (S.D.=7.5), but with proportionately fewer men (13.8%). The number of medications and total MAI scores were higher among EPOC study patients.

Beers Criteria as Direct Measurement of Inappropriate Prescribing

Beers criteria medications accounted for a disproportionate amount of inappropriate prescribing. In the EPOC study, only 6.0% of all medications were Beers criteria medications, yet these drugs accounted for 12.9% of total MAI scores. In examining MAI scores for individual drugs, Beers criteria medications received a mean MAI score of 3.2, compared to only 1.4 for non-Beers medications. PCM study findings were similar, where 4.6% of medications met Beers criteria yet accounted for 14.0% of total MAI scores. Mean drug-level MAI scores in the PCM study for a Beers medication were 4.0, versus 1.2 for a non-Beers medication.

Beers Criteria as a Proxy for Other Inappropriate Prescribing

Comparisons of MAI scores between patients exposed versus unexposed to Beers criteria medications are presented in Table 2. Significant elevations were observed among patients exposed to a Beers criteria medication, where total MAI scores were over 50% higher in the EPOC study and nearly doubled in the PCM study. A substantial portion of this elevation was directly attributable to Beers criteria medications. As shown in Table 2, mean MAI scores due to Beers medications in the exposed group were 4.6 in the EPOC study and 4.9 in the PCM study. The contribution of these drugs to total MAI scores was removed to generate patient-level MAI scores for non-Beers medications. Non-Beers MAI scores were significantly higher in patients exposed to Beers criteria medication in both studies, a difference of 2.7 in the EPOC study and 2.4 in the PCM study (Table 2). Thus, patients exposed to a Beers criteria medication were at increased risk for inappropriate prescribing of other medications. The number of non-Beers medications was not significantly different between Beers exposed versus unexposed patients in either study (Table 2).

An exploratory subanalysis of the 10 individual MAI items was conducted, again comparing patients exposed versus unexposed to Beers criteria medications (Table 3). Each MAI item was scored at the patient level across all non-Beers medications, using the standard weights presented in Table 3. In the EPOC study, all 10 items were numerically higher among patients taking Beers criteria medication, indicating a higher level of inappropriate prescribing. The two items that reached the threshold for statistical significance were duration of use and correct directions for use. Similar results were seen in the PCM study, where nearly all items demonstrated higher levels of inappropriateness among patients receiving Beers criteria medication. The drug-drug interaction and dosage items reached statistical significance and the cost and practical directions for use items approached significance, in this exploratory analysis. The modified MAI scoring algorithm also approached statistical significance, with consistent findings between studies.

Discussion

Beers criteria medications directly accounted for 12.9–14.0% of total inappropriate prescribing in older adults, as comprehensively measured by the MAI, with consistent findings drawn from two independently collected patient samples. In keeping with prior criticism, using Beers criteria as a measurement tool thus failed to capture more than 85% of inappropriate prescribing in older adults.^{7–9} However, this critique is limited to a drug-level perspective and does not consider the potential for Beers criteria to serve as a proxy for other inappropriate prescribing practices when applied at higher aggregate levels, such as the level of patient or facility. Therefore, the focus of this analysis was to determine whether patients exposed to Beers medications were at increased risk for other forms of inappropriate prescribing. Our novel finding was supported by two independent samples, where inappropriate prescribing scores attributable to non-Beers medications were significantly higher in patients exposed to Beers criteria medications. The magnitude of this difference

was 2.4 – 2.7 points on the MAI, and is above the threshold generally considered clinically significant.

Examination of individual MAI items was generally consistent with the overall findings. It should be noted that these studies were not designed and powered for this level of analysis, and the findings should be considered exploratory. With this caveat in mind, the general trend was toward increases in inappropriate prescribing practices among patients receiving a Beers criteria medication. Some individual items did reach or approach statistical significance, but were not consistent between studies. We also examined an alternative MAI scoring algorithm developed specifically to predict adverse drug events, a clinically meaningful outcome.²¹ While not statistically significant in this exploratory analysis, the findings were consistent between studies and suggested that patients receiving Beers criteria medications may be at increased risk for adverse drug events. Taken together, we interpret these findings as Beers criteria medication exposure being broadly associated with other inappropriate prescribing practices, and not linked to any one specific practice.

The observation of a clinically meaningful association between a measured quality indicator and typically unmeasured aspects of quality has important implications for health care quality measurement and intervention. Such associations are beneficial from a measurement perspective since aspects of quality that are impractical to adequately measure may be indirectly accounted for when making comparisons across providers or facilities. Ideally, a useful quality indicator should provide a suitable intervention target to enable providers, facilities, and health care systems to demonstrate improvement. From this intervention perspective, our findings highlight the limitations of using quality indicators as isolated targets. Interventions focused exclusively on reducing Beers criteria medication use would miss an opportunity to improve other aspects of inappropriate prescribing that are disproportionately common among these individuals. Instead, using Beers criteria to identify patients for a comprehensive medication review would likely generate a more meaningful improvement in quality.

A particular strength of this analysis is the replication of key findings across two independently collected patient samples. Both samples included older adults with complex medication regimens and multiple medical comorbidities. However, these groups differed in several important ways. The EPOC study was conducted in a single outpatient VA primary care clinic and involved principally men. In contrast, the PCM study was conducted in the community pharmacy setting, involved multiple practice sites, and enrolled Medicaid eligible adults, which were mostly women. Despite these differences, the results were consistent across both studies.

There are a number of limitations that need to be considered. First, it is unclear whether these findings can be generalized to other patients groups, particularly those with less complicated medication regimens. Second, geographic variation in Beers criteria frequency has been documented and it is possible that the results from these studies, both conducted in a single state, may not apply to other regions.²⁶ Third, different versions of the Beers criteria were used in the two cohorts, thus preventing direct comparison between the groups. However, the consistent findings between studies support the general premise of Beers criteria serving as a general marker of prescribing quality, regardless of which version is used.

An additional consideration is how to address the impact of number of medications on these findings. While the number of non-Beers medications was not significantly different between patients who received and did not receive a Beers medication, these groups differed numerically by approximately one medication in both studies. We did not adjust for number

of medications in our statistical models for two important reasons. First, we were not attempting to establish a causal pathway for Beers criteria medication exposure leading to other forms of inappropriate prescribing. This stands in contrast to validation studies attempting to causally link Beers medication exposure and risk for adverse drug events, for example, where adjustment for number of medications may be more appropriate.² Rather, in examining Beers criteria as a proxy for other forms of inappropriate prescribing it is expected that some of the association may be non-causal, but that does not impair its function as a proxy measure. The second reason for not adjusting for number of medications is that some forms of inappropriate prescribing directly produce additional medications. For example, two items included on the MAI are therapeutic duplication and drug use without indication. If one of two hypothetically identical patients is exposed to these inappropriate prescribing practices, the result will be an additional medication in the patient's regimen that would not be present in the other individual. In such cases, including number of medications would over-adjust the model, thereby eliminating the precise effect that the analysis was attempting to measure.

Safe and effective medication use is an important aspect of health care and efforts to improve prescribing quality require valid and useful measures. Our findings demonstrate that the utility of Beers criteria extends beyond the direct measurement of a limited set of inappropriate prescribing practices by serving as a clinically meaningful proxy for other forms of inappropriate prescribing. Thus when used to guide interventions, prescribing quality indicators may be more optimally used to identify individuals for comprehensive medication review, rather than merely as specific targets for discontinuation. Applied at a higher level, such indicators could be used to create clinic or facility level benchmarks to identify locations of care that might benefit most from intervention. Future research should explore both the quality measurement and the intervention targeting applications of the Beers criteria, particularly when integrated with other indicators. Quality-oriented research should emphasize how multiple indicators may be combined to provide more comprehensive measurement of prescribing quality. Intervention-oriented research should explore how quality indicators may be integrated with risk-based indicators (e.g. number of drugs, drug requiring therapeutic drug monitoring) to target patients most likely to benefit from interventions of varying types and intensity.

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Table 1

Characteristics of the Two Study Samples.

Characteristic	EPOC Study (N = 240)	PCM Study (N = 167)
Age, mean (SD), y	74.6 (5.4)	76.4 (7.5)
Men, No. (%)	236 (98.3)	23 (13.8)
Total Medications, mean (SD)	10.5 (4.0)	8.2 (3.7)
Beers Criteria Medication Present, No. (%) ^a	106 (44.2)	52 (31.1)
Total MAI Score, mean (SD)	15.6 (10.1)	10.9 (8.1)

EPOC = Veterans Affairs Enhanced Pharmacy Outpatient Clinic study; PCM = Iowa Medicaid Pharmaceutical Case Management study

^aBeers criteria medication frequencies are not directly comparable since EPOC used the 2003 revision⁶ and PCM used the 1997 revision⁵. The 2003 revision contains more criteria and thus generates higher frequencies.

Table 2

MAI Scores Among Patients Exposed and Unexposed to Beers Criteria Medication

MAI Scores, mean (SD)	EPOC Study (N=240)				PCM Study (N=167)			
	Beers Medication Exposure		Beers Medication Exposure		Beers Medication Exposure		Beers Medication Exposure	
	Yes (N=106)	No (N=134)	Statistics	Yes (N=52)	No (N=115)	Statistics	Yes (N=52)	No (N=115)
MAI Total	19.7 (11.3)	12.4 (7.7)	F=35.4; p<0.001 ^a	16.0 (8.5)	8.7 (6.9)	F=34.7; p<0.001 ^a		
MAI, Beers Drugs	4.6 (4.0)	0.0	--	4.9 (3.3)	0.0	--		
MAI, Non-Beers Drugs	15.1 (9.6)	12.4 (7.7)	F=5.9; p=0.016 ^a	11.1 (7.3)	8.7 (6.9)	F=4.3; p=0.039 ^a		
Non-Beers Drugs, No. (SD)	10.4 (3.9)	9.5 (3.6)	t=1.7, p=0.08	8.5 (3.8)	7.5 (3.5)	t=1.8, p=0.07		

MAI = Medication Appropriateness Index; EPOC = Veterans Affairs Enhanced Pharmacy Outpatient Clinic study; PCM = Iowa Medicaid Pharmaceutical Case Management study

^aWithin study comparison of MAI scores between patients exposed and unexposed to Beers criteria medication (adjusted for age and sex).

Table 3
Comparison of Item Level MAI Scores Among Patients Exposed and Unexposed to Beers Criteria Medication

MAI Item	ADE Weight ^a	Standard Weight ^b	EPOC Study (N=240)			PCM Study (N=167)		
			Beers Medication Exposure		p-value ^c	Beers Medication Exposure		p-value ^c
			Yes (N=106)	No (N=134)		Yes (N=52)	No (N=115)	
Drug-drug interactions	2	2	0.30	0.16	0.289	1.4	0.71	0.048
Drug-disease interactions	2	2	0.53	0.36	0.422	1.0	0.82	0.264
Indication	1	3	1.4	1.0	0.321	0.58	0.68	0.905
Effectiveness	1	3	0.82	0.69	0.906	1.2	1.2	0.632
Duplication	1	1	0.31	0.22	0.228	0.65	0.56	0.259
Duration	1	1	0.81	0.55	0.029	0.62	0.54	0.190
Dosage	0	2	2.6	2.5	0.960	2.2	1.3	0.026
Directions correct	0	2	6.3	5.1	0.007	1.7	1.4	0.233
Directions practical	0	1	0.75	0.68	0.738	0.58	0.43	0.096
Cost	0	1	1.2	1.1	0.940	1.3	1.0	0.104
Modified ADE risk score ^a			2.7	1.9	0.063	4.3	3.2	0.058

MAI = Medication Appropriateness Index; EPOC = Veterans Affairs Enhanced Pharmacy Outpatient Clinic study; PCM = Iowa Medicaid Pharmaceutical Case Management study; ADE = adverse drug event

^a Modified MAI scoring algorithm for assessing ADE risk, using the specified item weights as an alternative to standard scoring weights²¹

^b Standard MAI scoring weights²³

^c Wilcoxon rank sum test