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# The Medication Appropriateness Index at 20: Where it Started, Where it has been and Where it May be Going

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## Abstract

Potentially inappropriate prescribing for older adults is a major public health concern. While there are multiple measures of potentially inappropriate prescribing, the Medication Appropriateness Index (MAI) is one of the most common implicit approaches published in the scientific literature. The objective of this narrative review is to describe findings regarding the MAI's reliability, comparison of the MAI with other quality measures of potentially inappropriate prescribing, it's predictive validity with important health outcomes, and it's responsiveness to change within the framework of randomized controlled trials. A search restricted to English-language literature involving humans aged 65+ years from January 1992 to June 2013 was conducted using MEDLINE and EMBASE Databases for the search term "Medication Appropriateness Index". A manual search of the reference lists from identified articles and the authors' article files, book chapters, and recent reviews was conducted to identify additional articles. A total of 26 articles were identified for inclusion in this narrative review. The main findings were that the MAI has acceptable inter- and intra- rater reliability, more frequently detects potentially inappropriate prescribing than a commonly used set of explicit criteria, predicts adverse health outcomes and is able to demonstrate the positive impact of interventions to improve this public health problem. We conclude that the MAI may serve as a valuable tool for measuring potentially inappropriate prescribing in older adults.

## 1.0. INTRODUCTION

Prescription of medications for older adults is a complex and challenging task [1]. The health and functional status of older populations varies widely so a "one size fits all"

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approach to prescribing is inadequate to meet patient needs [2]. Therefore the types of prescribing habits that clinicians learn for general adult populations may not be appropriate, and sometimes even dangerous, for older patients. Among the population of older people, a disproportionate amount of medications are prescribed for vulnerable elders with multiple co-morbidities. These individuals have limited physiological reserve, high rates of disability, experience disease and age-related changes in pharmacokinetics and pharmacodynamics, and are at high risk for adverse drug reactions [3]. It's no wonder that choosing the right drug and dose for the right condition at the right time for older patients while reaping maximal benefit and avoiding adverse drug reactions is difficult. This complexity of prescribing is an important factor in well documented phenomenon of suboptimal prescribing in elderly patients [1,4].

Concerns regarding the quality of prescribing have been raised for over four decades [4]. Early approaches included the development of explicit criteria for specific drug classes. When these criteria are applied retrospectively to medication dispensed to groups of patients, the process is referred to as Drug Utilization Reviews (DUR) [5]. Typically DURs used pharmacy claims data and examined potential problems such as excessive dosage, drug-drug interactions and therapeutic duplication. In the early 1990's Dr. Mark Beers and others created a drugs-to-avoid list ("Beers criteria") as a measure for use in a randomized controlled trial designed to reduce the prescribing of these high risk drugs in nursing home patients [6]. Since that time there has been an explosion of explicit criteria developed internationally to measure various aspects of potentially inappropriate medications. These have recently been reviewed by other authors [7,8]. While these explicit criteria have value, they do not take into account for patient preferences, life expectancy or prescribers knowledge of the patient and they are difficult to keep up to date.

Implicit judgment is used all the time in clinical medicine. One of the early attempts to standardize and structure this approach was the development of reliable and valid adverse drug reaction causality algorithms [9]. Drawing on this approach and the previous work of other investigators, in 1992, with the help of clinicians, a psychologist, a sociologist, and a biostatistician, we developed and published a new implicit prescribing quality measure known as the Medication Appropriateness Index (MAI) [10,11]. The MAI's purpose was to serve as a sensitive measure of potential improvement in prescribing quality due to a clinical pharmacist intervention within the framework of a randomized controlled trial [12]. The MAI consists of 10 questions that allow three rating choices; "A" being appropriate, "B" being marginally appropriate and "C" being inappropriate. To provide clarity for evaluators and improve reliability, the MAI has general instructions for use, and specific definitions of each criterion, instructions on how to answer each of the 10 questions, and specific examples of "A", "B" and "C" s [10]. In addition, the MAI has numerous appendices as references to help evaluators to accurately answer questions [10]. We also surveyed a group of health care professionals to develop a weighting system for each MAI question in which a "C" rating could be given based on the respondent's judgment about the importance of each item [11]. All items were deemed to be important and all items were weighted from 1–3 with three being the worse score per item and 18 was the highest score per drug. To get a total MAI score per person, the scores for individual drugs are summated. Since the time of these original publications, we have kept the instructions and appendices for the MAI up to date (last revision 6/13) and is available upon request from the first author.

Given that over 20 years have passed since the initial MAI publications and the instrument has been employed in multiple studies, we thought it will be useful to summarize the body of literature regarding the MAI. Therefore the objective of this narrative review is to describe findings regarding the reliability of the MAI, comparison of the MAI with other quality measures of potentially inappropriate prescribing, the predictive validity of the MAI

with important health outcomes, and the responsiveness of the MAI to change within the framework of randomized controlled trials.

## 2.0. METHODS

The MEDLINE and EMBASE databases were searched for articles published for the term "Medication Appropriateness Index" from January 1992 to June 2013. A manual search of the reference lists of the identified articles and the authors' article files, book chapters, and recent reviews was conducted to retrieve additional publications. The abstracts of all articles were examined by one of the authors (JTH). Only articles written in English, focused on the aged and that examined the MAI's reliability, comparison with other quality measures, predictive validity, and responsiveness in randomized controlled trials were included. Articles not meeting these inclusions and were not written in English was excluded. The MEDLINE search identified 54 articles whereas the EMBASE search identified 84 articles. A total of 26 articles were included for this narrative review.

## 3.0 DATA SYNTHESIS

### 3.1. MAI Reliability

We identified eight manuscripts (three involving the MAI developers) where some aspect of the original 10 item MAI's reliability was evaluated (Table 1) [10,11,13–18]. The kappa statistic for inter-rater reliability of each of the MAI's 10 items were calculated in six studies [10,14–18]. In four studies, using clinical data from elderly hospital inpatients or outpatients from Belgium, Ireland and the US, the kappa statistic for each item was >0.40 indicating good reproducibility regardless of whether the pair of evaluators were both pharmacists, both physicians or a pharmacist and physician [10,14,16,18]. Two studies from Europe (Netherlands and Denmark) examining medications from older primary care and nursing home patients both found kappa statistics <0.40 for the effectiveness item whereas similar disagreement with the indication, therapeutic duplication and expense items were found in the Denmark study only [15,17]. It is important to note that the overall kappa statistic in both studies were >0.40 as was that from four other studies [10,13,14,16]. Four studies reported good inter-rater reliability overall for the summated MAI score (all intraclass correlation coefficients>0.73) [11,13,14,17]. Intra-rater reliability was reported by three studies [10,15,17]. As one might expect the agreement was higher than seen with inter-rater reliability in all three studies (Kappa>0.70).

### 3.2. MAI Compared to Other Measures

We identified three manuscripts where the MAI was compared to other measures of potentially inappropriate prescribing (Table 2) [19–21]. Among studies of the MAI in primary care clinics, two investigations compared only the Beers criteria and MAI scores or elements in Veterans Affairs (VA) patients in Iowa, USA. These studies found that the identification of problem medications was higher with the MAI compared to the Beers criteria or that MAI scores were significantly higher in meds not on the Beers list among patients who also were prescribed Beers criteria drugs [19–20]. In the only inpatient study, investigators assessed prescribing in two hospitals in Northern Ireland comparing the MAI, Beers criteria, IPET and HEDIS measures to assess changes in medication appropriateness over time during the hospital stay [21]. The MAI was best at detecting prescribing improvement over time but was the most time consuming to apply.

### 3.3. Predictive Validity with MAI

We identified seven studies that evaluated the predictive validity of the MAI in relation to various health outcomes (Table 3) [22–28]. Three studies involved VA outpatients in North

Carolina, Iowa, or 11 VA Medical Centers across the USA [22–24]. In these studies, higher MAI scores were significantly associated with unscheduled ambulatory or ED visits and inadequate blood pressure control [22], adverse drug events using a modified MAI scores [23], and adverse drug reactions by drug-disease interaction criteria [24]. Although higher MAI scores were associated with hospital admission [22], adverse drug events (standard MAI score) [23] and adverse drug reactions using dose, directions and drug-drug interaction criteria [24], they were not statistically significant. Four studies involved inpatients in Sweden and Belgium [25–28]. In these studies, higher MAI scores were significantly associated with lower quality of life as measured by EQ-5D and EQ-VAS [25], and drug-related hospital admissions [26–28].

### 3.4. Randomized Controlled Trials that Used the MAI

There have been 10 published randomized controlled trials that have utilized the MAI as an outcome measure [12, 18, 28–35]. The types of interventions include education (n=1) or multifaceted (n=1) approaches, clinical pharmacy activities (n=5) and multidisciplinary team approaches (n=3). Five studies were conducted in the hospital setting, three in ambulatory care and two in nursing homes. Table 4 summarizes each individual trial. In all trials, MAI scores were lower (better) in intervention than control groups.

## 4.0. DISCUSSION

This narrative review showed that in a small number of studies (8) that the MAI overall had acceptable inter- and intra- rater reliability. Two studies did however show lower agreement for several specific MAI items [15,17]. Some possible explanations for the lower inter-rater reliability for some items include potential difficulties in the MAI translation from English, lack of sufficient training and discussion of discordances before formal reliability training (10–20 patients recommended), low number of inappropriateness ratings (resulting in paradoxical kappa values), and comparison of pairs of evaluators to each other. It is however important to note that the MAI evaluation requires a skilled clinician, can be time consuming to apply and may be subject to reliability issues when more than one evaluator are used.

When compared to the older versions of the Beers explicit criteria, only three studies showed that the MAI was able to detect more instances of potentially inappropriate prescribing. The MAI was however used in a randomized control trial as an outcome measure where the STOPP criteria were used in an educational intervention [18]. It is important to emphasize that all these measures identify instances of potential inappropriate prescribing and that no gold standard exists. Moreover, the MAI score per drug does not help the clinician to prioritize which drugs should be changed. The MAI also does not provide guidance as to how to modify drug regimens to avoid adverse drug withdrawal events that can rarely occur in older adults.

This narrative review identified only seven studies suggesting that lower quality prescribing as measured by the MAI was associated with adverse health events including drug-related readmissions and adverse drug events/reactions. Previous studies have shown mixed results regarding the association of Beers criteria drugs with adverse drug events/reactions whereas there is emerging literature relating the STOPP criteria with adverse drug events [36–38]. It is important to note that few studies used a causality algorithm to reliably and accurately measure adverse drug reactions [9, 36]. It was also encouraging to see that the MAI was used in a number of randomized controlled trials and various types of interventions were effective in reducing overall scores. However these studies are heterogeneous, differ in intervention type and in study setting making it difficult to draw robust conclusions.

It is important to note that there are potential limitations to using the MAI as a measure of potentially inappropriate prescribing (PIP) as well as with the methods used in this narrative review. In particular, the MAI does not address other aspects of suboptimal prescribing (i.e., polypharmacy or underuse of medically necessary medications). Readers should note however that there are other implicit measures developed by our group to address these aspects of suboptimal prescribing [39, 40]. While the MAI weighting for specific items was based on their importance as determined by a survey of clinicians, clinician assessment of importance may not be in agreement with what older patients believe is most important [41, 42]. It is possible we may have missed relevant articles about the MAI despite the comprehensive approach taken. Moreover, due to heterogeneity between studies it was not possible to conduct a formal meta-analysis of MAI data.

## 5.0. CONCLUSIONS

Despite these potential limitations regarding the MAI and our methods used for this review, as it enters its third decade since its inception, the findings show that the MAI may serve as a valuable research tool for measuring potentially inappropriate prescribing in the elderly. We also believe that the MAI may have value in providing a structure and process for clinical learners to conduct a comprehensive review of complex drug regimens taken by older adults. The MAI may become a viable quality measure for identifying potentially inappropriate prescribing in older patients especially if those with higher MAI scores can be more easily identified by applying explicit criteria to readily available pharmacy claims data [20]. In regards to future research, it may be of interest to compare the most up-to date version of the MAI with the new 2012 American Geriatrics Society Beers Criteria and the forthcoming version two of the explicit measure from Europe entitled “Screening Tool of Older Persons Potentially Inappropriate Prescriptions” (STOPP) [43, 44]. As recommended by Spinewine et al. in the most up to date MAI, question 3 has been updated to specifically capture separately under dosage from over dosage [16]. It may be warranted to combine these underdosing ratings with those from the Assessment of Underutilization (AOU) and conduct additional reliability/validity studies of this new expanded implicit underuse of medications measure [40]. Finally, MAI question 9 for duration has been updated to take into account defining certain medications (i.e., antiplatelet agents, lipid lowering agents, antineoplastics, immune modulators, leukotriene receptor antagonists, sex hormones) as having too long of duration of use when their risks might outweigh their potential benefits given limited life expectancy with severe dementia [45]. Research studies applying an expanded unnecessary drug use measure (MAI questions 1,2,8, and 9 for indication, effectiveness, duplication, and duration) in these and other end-of life patients could be of value[46].

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**Table 1**

Studies of the Inter-Rater Reliability of the MAI

| Author/Year | Raters | # of Patients/ Drugs Rated | Country/Setting | Kappa or (ICC) |
|---|---|---|---|---|
| Hanlon/1992[10] | physician & pharmacist; 2 pharmacists | 10/60<br>10/105 | US/Ambulatory care | 0.83<br>0.59 |
| Samsa/1994[11] | physician & pharmacist | 10/105 | US/Ambulatory care | (0.74) |
| Fitzgerald/1997[13] | 2 pharmacists | 10/65 | US/Ambulatory care | 0.64 (0.80) |
| Kassam/2003[14] | 2 pharmacists | 32/160 | US/Ambulatory care | 0.65 (0.86) |
| Bregnhoj/2005[15] | 2 pairs (2 clinical pharmacologists vs a clinical pharmacologist & pharmacist) | 30/211 | Denmark/Ambulatory care | 0.50 |
| Spinewine/2006[16] | physician & pharmacist | 16/113 | Belgium/Hospital | 0.84 |
| Stuijt/2009[17] | 3 pharmacist pairs | 15/81 | Netherland/Nursing Home | 0.47 (0.74) |
| Gallagher/2011[18] | 2 physicians | 40/268 | Ireland/Hospital | >0.85 for all 10 criterion |

ICC= intraclass correlation coefficient; US=United States

**Table 2**

Studies of Comparing the MAI with Other Measures of Potentially Inappropriate Prescribing

| Author/Year | Patients/Setting | # of Patients | No. Drugs Rated | Design | Measures | Results |
|---|---|---|---|---|---|---|
| Steinman/2007[19] | Outpatients/VA primary care clinics/ Iowa, USA | 196 | 1582 | Cross-sectional | MAI; Beers drugs to avoid | Patients with ≥1 problem meds: Beers 37%, MAI 82% |
| Lund/2011[20] | Outpatients/Primary care clinics, Iowa, USA | 407 | N/A | Observational | MAI; Beers criteria | Non-Beers MAI scores significantly higher in patients also receiving Beers med |
| Luo/2012[21] | Inpatients/University Hospital, Northern Ireland | Admit: 176<br>Inpatient: 186<br>Discharge: 179 | Admit: 1378<br>Inpatient: 1813<br>Discharge: 1271 | Retrospective observational | MAI, Beers, IPET, HEDIS | MAI best at detecting prescribing improvement over time; Beers and IPET acceptable |

HEDIS= Healthcare Effectiveness Data and Information Set; IPET=Improving Prescribing in the Elderly Tool; MAI=Medication Appropriateness Index; USA=United States of America; VA=Veterans Affairs

**Table 3**

Studies of the Predictive Validity of the MAI

| Author/Year | Patients/Setting | # of Patients/ Mean # Drugs Rated | Outcome | Results |
|---|---|---|---|---|
| Schmader/1997[22] | Outpatients/ VA Primary Care Clinics, Durham, NC, USA | 208/7.9 | Hospital admission<br>Unscheduled ambulatory or ED visits<br>Blood Pressure control | MAI scores higher for hospital admission (18.9 vs. 16.9, p = 0.07; unscheduled ambulatory or ED visits (18.8 vs. 16.3, p = 0.05); inadequate blood pressure control (4.7 vs. 3.1, p =0.02) |
| Lund/2010[23] | Outpatients/VA Primary Care Clinics, Iowa City, IA, USA | 236/10.6 | Adverse drug event | MAI standard score (Adj. OR 1.03; 95% CI 0.99–1.06)<br>MAI modified score (Adj. OR 1.13; 95% CI 1.02–1.25) |
| Hanlon/2011[24] | Outpatients/11 VA Medical Centers, USA | 359/7.6 | Type A adverse drug reactions | Drug-drug interaction (Adj. OR=2.37; 95% CI 0.91–6.11); Drug-disease interaction (Adj. OR 1.93; 95% CI 1.00–3.72) |
| Olsson/2011[25] | Hospital discharge to home/University Hospital, Orebro, Sweden | 150/10 | EQ-5D Index; EQ VAS | Higher MAI scores associated with lower quality of life; EQ-5D index (p = 0.001 study start; p = 0.001 at 6 months; p = 0.013 at 12 months); EQ VAS (p = 0.026 at study start; p = 0.003 at 6 months; p = 0.007 at 12 months) |
| Hellstrom/2011[26] | Inpatients/University Hospital, Lund, Sweden | 210/8 | Drug-related hospital visits after Lund Integrated Medicine Management model intervention | Lower MAI scores associated with fewer drug-related hospital visits in intervention group compared to control group |
| Somers/2012[27] | Inpatients/University Hospital, Ghent, Belgium | 50/8.6 | Drug-related hospital admissions | Significantly higher MAI scores for drug-related hospitalizations (p = 0.04 geriatrician; p = 0.03 pharmacist) |
| Gillespie/2013[28] | Inpatients/University Hospital, Uppsala, Sweden | 386/8.1 | Drug-related hospital readmissions | Greater risk of risk of drug-related hospital readmission with higher MAI scores (RR 1.09; 95% CI 1.04–1.14) |

Adj=adjusted; CI=confidence interval; MAI=Medication Appropriateness Index; OR=odds ratio; RR= relative risk; USA=United States of America; VA=Veterans Affairs

**Table 4**

Randomized Controlled Trials to Improve Prescribing as Measured by MAI for Older Adults

| Author/year | Patients/Setting | Intervention | Duration | Changes in MAI |
|---|---|---|---|---|
| ***Educational Approach*** | | | | |
| Gallagher/2011[18] | 382 hospital patients 65+ from single site In Ireland | STOPP criteria applied to medication regimen by research physician who verbally and in writing with attending medical physician | Until hospital d/c | Change in MAI from baseline to d/c intervention group (mean=10 to mean=3); no change in MAI in control group 8 at both time points) |
| ***Multi-Faceted Approach*** | | | | |
| Bregnhoj/2009[29] | 212 outpatients 65+ cared by 41 GPs in Netherlands | Combined intervention of interactive educational meeting and feedback vs single interactive educational meeting | 3 months | Medication appropriateness improved intervention group (MAI mean change −5.1) but did not in the single intervention or control group (MAI mean change −0.7 and −0.8, respectively; P < 0.05) |
| ***Clinical Pharmacy Activities*** | | | | |
| Hanlon/1996[12] | 208 outpatients 65+ from single VA clinic in US | Clinical pharmacist medication history, medication review and oral/written recommendations to primary care MD | Up to 12 months | Medication appropriateness improved more in the intervention group (MAI mean change −4.9) than control group (MAI mean change −1.1; P < 0.001) |
| Crotty/2004[30] | 110 older adults assigned to 85 Ltcfs in Australia | Pharmacist coordinator from hospital to Ltcfs; medication reviews by community pharmacists, and case conferences | 8 weeks | P: At closeout, mean MAI scores were better in intervention group than control group (2.5 vs. 6.5, respectively; P = 0.007) |
| Burnett/2009[31] | 117 hospital patients 65+ in US | Medication history, monitoring and medication education by pharmacist | Until d/c | Medication appropriateness improved more in the intervention group (MAI mean change −11.79) than control group (MAI mean change −3.19; P < 0.01) |
| Bryant/2011[32] | 350 community dwelling elders 65+ from UK | Medication regimen review and meeting with GP by 17 community pharmacists | Up to 12 months | Medication appropriateness by 6 months improved more in the intervention group (MAI mean change −2.0) than control group (MAI mean change −0.3; P=0.003) |
| Gillespie/2013[28] | 386 hospital patients 80+ from Sweden | Medication regimen reconciliation/review and patient education | 12 months after admission | Between admission and discharge, MAI scores improved more in the intervention group (MAI mean change −3.5) than control group patients (MAI mean change 1.3; P<0.001) |
| ***Multidisciplinary Approaches*** | | | | |
| Crotty/2004[33] | 10 high-level aged care facilities; 154 residents from Australia | Two multidisciplinary case conferences with general practitioner, a geriatrician, a pharmacist and staff | 3 months | Greater improvement in intervention group (MAI mean change 4.1) vs. control (MAI mean change 0.4; P < 0.001); significant reduction in the MAI for BZDs in the intervention compared to control (0.73 vs. −0.38; respectively; P = 0.017) |
| Schmader/2004[34] | 400 frail inpatients 65+ from 11 VA sites in US | Geriatric Evaluation and Management team care | Until discharge | Medication appropriateness improved in the intervention group (MAI mean change −4.7) but worsened in the control group (MAI mean change +1.9; P < 0.001) |
| Spinewine/2007[35] | 203 inpatients 70+ from single site in Belgium | Pharmacist added to Geriatric Evaluation and Management team | Until discharge | Greater improvement in the intervention (MAI mean change −17.0) than control group (MAI mean change 1.9; P < 0.001) |

BZDs=benzodiazepines; GP=General Practitioner; Ltcfs= long-term care facilities; MAI=Medication Appropriateness Index; MD=physician; STOPP= Screening Tool of Older Persons Potentially Inappropriate Prescriptions; UK=United Kingdom; USA=United States of America; VA=Veterans Affairs