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Longitudinal Association of a Medication Risk Score With Mortality Among Ambulatory Patients Acquired Through Electronic Health Record Data

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The use of electronic health records allows for the application of a novel medication risk score for the rapid identification of ambulatory patients at risk of adverse drug events. We sought to examine the longitudinal association of medication risk score with mortality. This retrospective cohort study included patients whose data were available through electronic health records from multiple health care organizations in the United States that provided data as part of a Patient Safety Organization. Patients were included if they had ≥1 visit and ≥1 medication in their record between January 1, 2011, to June 30, 2017. Cox proportional hazards regression was used to examine the association between continuous and categorized medication risk score with all-cause mortality. Among 427,103 patients, the median age was 50 years (interquartile range, 29–64 years); 61% were female; 50% were White, 11% were Black, and 38% were Hispanic; and 6873 had a death date recorded. Patients 30 to 49 years old had the highest hazard ratios (HRs), followed by the 50- to 64-year-olds and lastly those 65 years or older. Controlling for all covariates, 30- to 49-year-olds with a score of 20 to 30 (versus <10) had a 604% increase in the hazard of death (HR, 7.04; 95% confidence interval [CI], 3.86–12.85), 50- to 64-year-olds had a 254% increase (HR, 3.54; 95% CI, 2.71–4.63), and ≥65-year-olds had an 87% increase (HR, 1.87; 95% CI, 1.67–2.09). The medication risk score was independently associated with death, adjusting for multimorbidities and other conditions. Risk was found to vary by age group and score. Results suggest that pharmaceutical interventions among those with elevated scores could improve medication safety for patients taking multiple medications.

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Tabula Rasa HealthCare has funded the research included in this article, of which V.M., J.T., and R.B. are all employees and shareholders. The rest of the authors disclose no conflict of interest.

Author Contributions: W.D.P. was principal investigator on the study and led the design, analysis, and manuscript writing. A.R.R. was co-principal investigator on the study and assisted in leading the design, analysis, and manuscript writing. J.T., V.M., and H.D.A. contributed to the study design, interpretation of results, and manuscript writing. R.B. had access to a fully deidentified and aggregated data set to calculate medication risk scores, and he contributed to the interpretation of results and manuscript writing. G.P. and G.G.V. had access to standardized electronic health record data, conducted the data analysis, and contributed to interpretation of results and manuscript writing. A.R.R. also had access to standardized electronic health record data.

Supplemental digital contents are available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.journalpatientsafety.com).

Key Words: medication, risk score, polypharmacy, mortality

(*J Patient Saf* 2021;17: 249–255)

The act of prescribing a medication is the most common health care intervention in the United States, with approximately 19% of Americans aged 45 to 64 years and almost 40% of adults 65 years and older taking 5 or more prescription drugs in 2015 to 2016.[1–4] Moreover, prescribing, dispensing, and ingestion of a medication by a patient have long been recognized as the riskiest ambulatory activity in terms of absolute number of people harmed.[5,6] This results both from the high number of medications prescribed[3] and the complex processes involved between clinical decision making, communication to the pharmacy, dispensing, and actual use.[1,2] The widespread adoption of electronic health records (EHRs) has been considered the primary driver to more adequately address medication risk.[7–9] Electronic health records have improved legibility issues and perhaps dosing and disease-drug and drug interactions[10–13]; however, medication safety, and the prevention of medication errors and subsequent adverse drug events (ADEs) continues to be a significant global public health challenge.[14–17] In the United States, it is estimated that ADEs account for approximately 3.5 million physician office visits, 1 million emergency department (ED) visits, and 125,000 hospital admissions annually.[18,19] Prevention of ADEs is a key patient safety priority of many national health care-regulating agencies,[20–22] and practical, evidence-based tools for the early identification of patients at risk of ADEs are needed to significantly improve medication safety.[23] The increase in the average number of medications used by a single individual has highlighted the need to develop new methods of addressing medication risk.[3,24] As process errors in the order, dispensing, and use chain improve, more complex drug and disease interactions can be prioritized to reduce harm from therapeutic medication use.[25–27]

Multimorbidity is associated with higher complexity of medication regimens and a greater chance that complex interactions between medications and an individual's conditions may lead to harm.[28,29] In an attempt to manage medication safety, many larger health care systems have implemented Medication Therapy Management (MTM) programs, and the U.S. Centers for Medicare & Medicaid Services requires that MTM programs be included as part of the provision of Part D benefits.[30–32] These programs typically identify individuals based on the number of drugs they are using, particular disease states (e.g., diabetes mellitus or hypertension) and/or an event (e.g., hospitalization).[33–35] A clinical pharmacist is then needed to review the medication regimens and to talk with the patients to determine if adjustments are warranted. This process relies heavily on the pharmacists' clinical knowledge of the various conditions encountered in each patient. More advanced techniques are needed as knowledge increases regarding medication metabolism, side effects, and interactions with developed

and fixed (i.e., genetic) patient characteristics. In 2017, the U.S. Centers for Medicare & Medicaid Services introduced a Part D Enhanced MTM 5-year pilot program where advanced clinical decision support systems and pharmacist-directed interventions are used.[36] Computer-based risk algorithms hold the potential to efficiently and effectively support medication safety programs.[23,37]

Tabula Rasa HealthCare has developed a proprietary advanced clinical decision support system and medication risk score (MRS), which incorporates a series of algorithms that calculate an overall score, as well as subcomponent scores on sedation burden,[38–40] anticholinergic cognitive burden,[41] a competitive CYP450 drug interaction burden,[24] drug regimen relative odds ratio for ADE using the Food and Drug Administration adverse event reporting system,[42] and a drug-induced risk of creating or worsening a prolonged QT cardiac repolarization interval.[37,42,43] An observational study using claims data among participants of the Program of All-Inclusive Care for the Elderly found the total MRS to be positively correlated with increased ADEs, health care utilization, hospitalization, ED visits, and hospital length of stay.[44] However, this study did not assess an independent risk of death and did not include other clinical variables that may have a strong impact on the overall score.

The current observational study was conducted as part of the safety work of the DARTNet Institute subcomponent Patient Safety Organization (PSO).[45] We hypothesized that the MRS was an independent predictor of death among a cohort of ambulatory patients obtained through EHR data. In comparison to claims data, EHRs include clinical variables (e.g., estimated glomerular filtration rate [eGFR], blood pressure [BP] values, and laboratory measured electrolyte levels), allowing EHR-based algorithms to have the potential for greater dissemination and more rapid response to medication changes, which may improve health outcomes and reduce health care costs.

METHODS

Study Population and Eligibility

This retrospective cohort study uses EHR data from multiple U.S. health care organizations that provide data in partnership with DARTNet's PSO. This study includes community-living, ambulatory patients 5 years and older who had data present between January 1, 2011, and June 30, 2017, and who had at least one medication present (i.e., prescribed or added during medication reconciliation) within the study period.

Data Measures

The dependent variable of interest is death from any cause as determined by the presence of a date of death within the patient's EHR record. The main independent variable of interest is MRS, which ranges from 0 to 53, with a higher score indicating a higher risk of ADEs due to a particular medication regime, including anticholinergic burden, sedating effects, risk of QT-interval prolongation, and the competitive inhibition on certain cytochrome P450 isoforms.[42,46] Medication risk score was also categorized for analysis (<10, 11–14, 15–19, 20–30, >30). Details regarding the calculation of the MRS and its components have been published elsewhere.[37,42,46] The calculation of the MRS considers all prescribed medications and patients' characteristics during a given period of time. Data were extracted from EHR records and compiled into eras (i.e., time frames) to account for the dynamic nature of the MRS. An era is defined by current medication exposures (including strength); laboratory results categorized as low, normal, or high (calcium (<8.5, 8.5–10.5, and >10.5 mg/dL), potassium (<3.5, 3.5–5, and >5 mg/dL), magnesium (<1.5, 1.5–2.5, and >2.5 mg/dL); and selected conditions (i.e., end-stage renal disease, atrial fibrillation, end-stage liver disease, atherosclerotic cardiovascular disease, heart failure, cardiomyopathy, prolonged QT interval, sick sinus syndrome). A change in any of these factors closes the current era and commences a new era, as long as there continues to be at least one medication exposure.

Each patient-era includes covariates measured during that era including the following: sociodemographic factors (i.e., age, sex, and race/ethnicity as identified in the EHR, categorized as White, non-Hispanic or unknown ethnicity; Black, non-Hispanic or unknown ethnicity; Hispanic/Latino; other/mixed non-Hispanic; and unknown/missing both race and ethnicity), health-related factors (body mass index [BMI], BP, kidney function based on eGFR, chronic kidney disease, and liver disease), and total days in the era and total medications listed in the EHR during that particular era. Age was divided into quartiles (ages <30, 30–49, 50–64, and ≥65 years); systolic and diastolic BP values were limited to clinically plausible ranges of 50 to 250 and 0 to 200 mm Hg, respectively, and were categorized as normal (systolic BP <120 mm Hg or diastolic BP <80 mm Hg) or elevated (systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg); BMI values were limited to 12 to 70 kg/m^2 and were categorized for adults into underweight (<18.5 kg/m^2), normal (18.5–24 kg/m^2), overweight (25–30 kg/m^2), or obese (>30 kg/m^2); eGFR (in mL min^{-1} 1.73 m^{-2}) was categorized into stages of chronic kidney disease (stages 1–2, ≥60; stage 3a, 45–59; stage 3b, 30–44; stages 4–5, <30); and liver disease was categorized as no liver disease, chronic liver disease, or end-stage liver disease based on *International Classification of Diseases, Tenth Revision* diagnoses. All outlier values were set to missing for analyses. Finally, the Charlson-Deyo Score, calculated from the sum of scores for each comorbid condition listed in the Charlson Comorbidity Score Mapping Table, was used to account for multimorbidity.[47,48]

Statistical Analysis

Descriptive statistics were calculated using mean and SD, or median and interquartile range (IQR) for continuous measures; and frequency and percentage for categorical measures. Differences by mortality status were examined using χ^2 tests for categorical measures and *t* tests for continuous measures.

Cox proportional hazards regression modeling with time-varying covariates was used to examine the unadjusted and multivariable association of MRS with all-cause mortality and to account for within-person changes over time and eras that may occur among all variables. Proportional hazards assumptions were verified by examining Schoenfeld residuals and were determined to have been met.[49] The primary outcome was number of days from the start date of an era to the date of death if it occurred during a particular era. Patients were censored at the end of each era if they did not have a date of death ending that era. Covariates were adjusted for using a stepwise approach to determine their effect on the association of MRS with death, where variables were considered to be a confounder of this association if they changed the point estimate of the main association >10% when included into the multivariable model. Hazard ratios (HRs) with 95% confidence intervals (CIs) are reported to show strength and direction of these associations. Data were analyzed using SAS 9.4 (Cary, North Carolina), and a level of $P < 0.05$ was used to determine statistical significance.

RESULTS

A total of 427,103 patients with at least one visit to a qualifying medical practice and at least one medication record during the study period were eligible for MRS calculation. A total of 6873 patients (1.6%) died by the end of the study period. The median

age at baseline was 50 years (IQR, 29–64 years), and 25% were younger than 30 years (with 14.7% being 5–18 years old), 24% were 30 to 49 years old, 26% were 50 to 64 years old, and 24.5% were 65 years and older (Table 1). More than half were female (61%); almost 50% were White, 11% were Black, and almost 38% were Hispanic. Over the entire study period, there were a total of 2,491,399 eras present for analysis, with a median number of eras per patient of 12 (IQR, 5–25; range, 1–236) and a median number of days per era of 62 (IQR, 14–189; range, 1–2372).

Compared with patients who did not have a date of death present within their EHR, those who did were significantly more likely to be older at baseline (74 versus 49 years; $P < 0.01$), male (52.3% versus 38.7%; $P < 0.01$), and White (57.2% versus 49.4%; $P < 0.01$) (Table 1). Over the entire study period, they had a significantly higher median MRS (9 versus 5; $P < 0.01$), higher median number of medications (7 versus 4; $P < 0.01$), lower average BMI (28.7 versus 29.4 kg/m^2; $P < 0.01$), lower average eGFR (58.2 versus 78.1 mL min^{-1} 1.73 m^{-2}; $P < 0.01$), and higher average Charlson-Deyo score (4 versus 2; $P < 0.01$), and were more likely to have an elevated BP (26.8% versus 20.3%; $P < 0.01$). Furthermore, those who died had a significantly greater median number of total eras (22 versus 12; $P < 0.01$), with lower median days per era (36 versus 63; $P < 0.01$) and significantly greater average number of days in the study period (1654 versus 1530; $P < 0.01$).

Table 2 displays the results of age-stratified unadjusted Cox proportional hazards regression models examining the association

TABLE 1. Bivariate Analysis of Patient Characteristics by Overall Mortality Status Among Ambulatory Patients in the United States, 2011 to 2017

Characteristics, Baseline	Total (n = 427,103)*	Alive (n = 420,230)	Deceased (n = 6873)	$P^\dagger$
Age, y				
Median (IQR)	50 (29–64)	49 (29–64)	74 (65–82)	<0.0001
n (%)				
<30	108,074 (25.3)	107,991 (25.7)	83 (1.2)	<0.0001
30–49	102,997 (24.1)	102,688 (24.4)	309 (4.5)	
50–64	111,439 (26.1)	110,215 (26.2)	1224 (17.8)	
≥65	104,593 (24.5)	99,336 (23.6)	5257 (76.5)	
Sex, n (%)				
Male	166,299 (38.9)	162,702 (38.7)	3597 (52.3)	<0.0001
Female	260,804 (61.1)	257,528 (61.3)	3276 (47.7)	
Race/ethnicity, n (%)				
White, non-Hispanic or unknown ethnicity	211,331 (49.5)	207,401 (49.4)	3390 (57.2)	<0.0001
Black, non-Hispanic or unknown ethnicity	47,055 (11.0)	46,482 (11.1)	573 (8.3)	
Hispanic/Latino	160,610 (37.6)	158,405 (37.7)	2205 (32.1)	
Other/mixed	2499 (0.6)	2467 (0.6)	32 (0.5)	
Unknown/missing both race and ethnicity	5608 (1.3)	5475 (1.3)	133 (1.9)	
Characteristics, All Eras	**Total (n = 2,491,399)**	**Alive (n = 2,413,450)**	**Deceased (n = 77,949)**	***P***
MRS				
Median (IQR)	5 (2–10)	5 (2–10)	9 (4–15)	<0.0001
n (%)				
<10	1,795,027 (72.1)	1,754,167 (72.7)	40,860 (52.4)	<0.0001
11–14	384,085 (15.4)	367,159 (15.2)	16,926 (21.7)	
15–19	190,017 (7.6)	179,370 (7.4)	10,647 (13.7)	
20–30	112,352 (4.5)	103,739 (4.3)	8613 (11.1)	
>30	9918 (0.4)	9015 (0.37)	903 (1.2)	
Total medications, median (IQR)	4 (2–8)	4 (2–8)	7 (4–11)	<0.0001
BMI‡ (n = 318,175), mean (SD), kg/m^2	29.4 (7.4)	29.4 (7.4)	28.7 (7.2)	<0.0001
BP‡ (n = 368,907), n (%)				
Normal	293,753 (79.6)	289,251 (79.7)	4502 (73.2)	<0.0001
Elevated	75,154 (20.4)	73,502 (20.3)	1652 (26.8)	
eGFR (n = 348, 131), mean (SD), mL min^{-1} 1.73 m^{-2}	77.3 (25.7)	78.1 (25.5)	58.2 (23.5)	<0.0001
Charlson-Deyo Score, mean (SD)	2.0 (1.9)	2.0 (1.9)	4.0 (2.2)	<0.0001
Total eras per person, median (IQR)	12 (5–25)	12 (5–25)	22 (11–37)	<0.0001
Days per era, median (IQR)	62 (14–189)	63 (15–191)	36 (11–107)	<0.0001
Days in study per person, mean (SD)	1639 (964–2,221)	1530 (693.3)	1654 (625.1)	<0.0001

*Total patients available for analysis unless otherwise indicated.

†*P* values based on *t* test or χ^2 tests, and represent overall significance of differences between mortality status by each characteristic.

‡Limited to those 18 years or older.

TABLE 2. Results of Age-Stratified Cox Proportional Hazards Regression Models Examining the Unadjusted Association of MRS With Mortality Among Ambulatory Patients in the United States, 2011 to 2017

MRS	All Patients, HR (95% CI)	Ages <30 y*, HR (95% CI)	Ages 30–49 y, HR (95% CI)	Ages 50–64 y, HR (95% CI)	Ages ≥65 y, HR (95% CI)
MRS (1 unit)	1.05 (1.04–1.05)	1.09 (1.05–1.14)	1.12 (1.10–1.14)	1.08 (1.08–1.09)	1.05 (1.05–1.06)
MRS					
<10	1.00	1.00	1.00	1.00	1.00
10–14	3.00 (2.83–3.19)	2.94 (1.46–5.92)	2.66 (1.90–3.73)	2.14 (1.83–2.51)	1.65 (1.55–1.77)
15–19	4.08 (3.81–4.38)	4.87 (1.77–13.42)	4.99 (3.39–7.35)	2.92 (2.42–3.52)	1.96 (1.81–2.11)
20–30	5.70 (5.28–6.15)	—	8.95 (5.90–13.58)	4.57 (3.74–5.57)	2.49 (2.29–2.71)
>30	7.65 (6.32–9.26)	—	11.72 (2.90–47.39)	4.86 (2.73–8.63)	3.20 (2.61–3.92)

*Outcome of death was rare in the <30-year age group for MRS categories 20–30 (n = 9) and >30 (n = 0), and therefore, the point estimate could not be calculated.

of the continuous MRS, as well as MRS categorized into 5 groups, with all-cause mortality. Stratifying for age revealed that the hazard of death at any time point during the study varied by age group, with the highest HRs seen in the 30- to 49-year-old group. A 1-unit increase in MRS was associated with an 11% increase in the hazard of death among patients aged 30 to 49 years (HR, 1.12; 95% CI, 1.10–1.14). Examining the association of the categorized MRS with death, the highest HRs were seen among the 30- to 49-year-old age group, followed by the 50- to 64-year-old age group and lastly those 65 years or older. Those aged 30 to 49 years with an MRS of 20–30 had a 795% increase in the hazard of death compared than those with an MRS <10 (HR, 8.95; 95% CI, 5.90–13.58), whereas 50- to 64-year-olds had a 357% increase (HR, 4.57; 95% CI, 3.74–5.57) and ≥65 year-olds had an 149% increase (HR, 2.29; 95% CI, 2.29–2.71).

Table 3 displays the results of the multivariable Cox proportional hazards regression model controlling for Charlson-Deyo Score, sex, race/ethnicity, BMI, and eGFR showing the significance of the other covariates. Although Charlson-Deyo, sex, race/ethnicity BMI, and eGFR are all associated with death, none were found to have an HR higher than MRS. Moreover, the addition of eGFR to the model further increased the strength of the HR for some categories of MRS and age groups. Total medications, BP, total eras per person, days per era, and total days in the study were not found to change the measure of association more than 10% in multivariate modeling and were therefore not included in the final model. Among patients aged 30 to 49 years with an MRS of 20–30, the HR went from 6.27 (95% CI, 3.81–10.33; Online Supplemental Table, http://links.lww.com/JPS/A385) to 7.04 (95% CI, 3.86–12.85); and among those aged 50 to 64 years with an MRS >30, the HR

TABLE 3. Results of Age-Stratified Cox Proportional Hazards Regression Models Examining the Multivariable Associations of MRS With Mortality While Controlling for Covariates Among Ambulatory Patients in the United States, 2011 to 2017

	All Patients, HR (95% CI)	Ages <30 y, HR (95% CI)	Ages 30–49 y, HR (95% CI)	Ages 50–64 y, HR (95% CI)	Ages ≥ 65 y, HR (95% CI)
MRS*					
<10	1.00	1.00	1.00	1.00	1.00
10–14	1.65 (1.52–1.79)	2.83 (0.92–8.71)	2.09 (1.27–3.44)	1.76 (1.41–2.20)	1.50 (1.37–1.64)
15–19	1.81 (1.65–2.00)	8.57 (2.74–26.81)	3.35 (1.86–6.06)	2.28 (1.77–2.95)	1.57 (1.41–1.74)
20–30	2.25 (2.03–2.49)	—	7.04 (3.86–12.85)	3.54 (2.71–4.63)	1.87 (1.67–2.09)
>30	2.58 (2.06–3.25)	—	7.83 (1.07–57.21)	4.95 (2.60–9.41)	2.42 (1.89–3.09)
Charlson-Deyo Score (1 unit)	1.38 (1.37–1.39)	1.45 (1.19–1.78)	1.41 (1.29–1.55)	1.42 (1.37–1.46)	1.34 (1.33–1.36)
Sex					
Female	1.00	1.00	1.00	1.00	1.00
Male	1.32 (1.24–1.41)	1.33 (0.57–3.12)	3.03 (2.04–4.49)	1.58 (1.33–1.88)	1.27 (1.19–1.37)
Race/ethnicity, n (%)					
White, non-Hispanic or unknown ethnicity	1.00	1.00	1.00	1.00	1.00
Black, non-Hispanic or unknown ethnicity	0.91 (0.79–1.05)	—	1.32 (0.69–2.52)	0.88 (0.63–1.23)	0.95 (0.80–1.12)
Hispanic/Latino	0.90 (0.73–1.10)	—	1.29 (0.47–3.59)	1.52 (1.02–2.26)	0.79 (0.62–1.01)
Other/mixed	1.64 (1.37–1.98)	3.31 (0.71–15.32)	3.22 (1.67–6.20)	1.15 (0.66–2.00)	1.66 (1.35–2.05)
Unknown/missing both race and ethnicity	1.26 (1.17–1.35)	0.84 (0.34–2.06)	0.91 (0.57–1.44)	1.05 (0.86–1.29)	1.34 (1.24–1.45)
BMI	0.96 (0.95–0.96)	0.96 (0.91–1.02)	1.00 (0.98–1.03)	0.97 (0.96–0.98)	0.95 (0.95–0.96)
eGFR	0.99 (0.98–0.99)	1.01 (1.00–1.02)	0.99 (0.99–1.00)	0.99 (0.99–0.99)	0.99 (0.98–0.99)

*Outcome of death was rare in the <30-years age group for MRS categories 20–30 (n = 9) and >30 (n = 0), and therefore, the point estimate could not be calculated.

went from 4.09 (95% CI, 2.24–7.48; Online Supplemental Table, http://links.lww.com/JPS/A385) to 4.95 (95% CI, 2.60–9.41).

DISCUSSION

In this large cohort of ambulatory patients in the United States, the MRS was demonstrated to be independently associated with death after adjustments for common multimorbidities and other conditions that increase the risk of death. Furthermore, it was found that risk varies by age group and by MRS category where the highest risk was seen among patients in the 30- to 49-year-old age group who had an MRS of ≥20. Our results suggest that pharmacist-directed interventions targeted to those who have an elevated MRS could improve medication safety for ambulatory patients taking multiple medications.

The MRS encompasses a series of algorithms that consider the pharmacological characteristics of each drug's active ingredients and estimates whether the combination of drugs exhibits properties that, when taken together, put a patient at risk of ADEs. Hence, in patients with multiple chronic diseases, drugs used for each of these diseases may seem appropriate, yet their combination may predispose them to ADEs. Advanced clinical decision support systems could inform clinicians on the appropriateness of a drug regimen, indicate what elements could be improved, and offer alternatives.[46]

Results from this study expand the evidence that the MRS is correlated with increased rates of ADEs and health care utilization in an elderly population[44] by demonstrating that MRS is also significantly associated with death among a general population using EHR data. Although the use of EHR data includes clinical variables, it may also overestimate the actual medication use at the individual patient level because it includes medications prescribed rather than medications filled[50]; however, the number of medications was not found to have an effect on the association between MRS and death in this population.

Men and patients categorized as White race were at higher risk of death than women and other races/ethnicities. The reason for this is not intuitively obvious given the range of variables controlled for in this analysis. Men overall have higher cardiovascular death rates, of which arrhythmias are a contributing factor,[51] which could partially explain the higher male versus female risk; however, lower minority rates, where males also have high cardiovascular death rates,[51] are not explained by this mechanism. Furthermore, the risk varied by age group where the highest hazards were seen among those aged 30 to 49 years and the lowest among those 65 years or older, indicating that medication risk is playing a larger part in all-cause mortality among younger age groups than older age groups. Nonetheless, even the ≥65-year older age range had significantly elevated HRs. Thus, at the population level, potential medication-related deaths may be higher among older patients than among 30- to 49-year-olds given the larger number of people with high MRSs. The low number of patients 30 years and younger with high MRSs and the decreased number of deaths in this age group prohibited the estimation of HRs. Larger data sets of younger patients will be required to understand the correlation of high MRS with death in this age group.

Risk of death increased with higher MRS. Confidence intervals widened considerably at the highest risk scores, as the number of patients and therefore the number of deaths were small in these cohorts. Larger data sets with even greater multimorbidity and thus complex medication regimens would be needed to narrow the CIs in these cohorts. Nonetheless, the lower bounds of the risk of death do not approach one for any age group that had sufficient data for analysis.

Despite several strengths of this study, some limitations should be considered when interpreting these results. First, EHR data were used, which relies on data hand-entered by clinicians and documented through laboratory interfaces and medication reconciliation processes. It is unknown if the patients were actually filling and consuming the medications they were prescribed, and it is clear from other research that EHR data do not provide accurate medication use data as opposed to claims data.[50] Furthermore, EHR data provides information on clinician intent (prescribing a medication) and not patient actions (such as filling a medication). Nonetheless, our results suggest that EHR data seem adequate to predict poorer outcomes based on MRS. Electronic health record data are readily available at the clinical organization level, which may allow for more rapid recognition and intervention based on high-risk medication regimens.

It would be expected that the combination of EHR and claims data would further enhance the predictive ability of the MRS, but the finding that EHR data alone provides a reasonable estimate of possible risk allows for easier use of the risk scores and facilitates future research. Death was determined using the presence of a date of death within the EHR relying on the provider's office to enter this date, which could have led to missing death data. It was not possible to reach out to state death records to enhance death data, as many organizations strip out identifying information before submitting data to the PSO. Likewise, as far as the authors are aware, none of the organizations in the DARTNet PSO routinely collect data from their state death registries. Nonetheless, there is no reason to suspect that deaths would be differentially recorded in relationship to an MRS that was not known to the sites and was not calculated until after the deaths were recorded.

This study provides further evidence that the studied MRS is correlated with poor health outcomes across a wide range of ages. Further research is warranted to demonstrate that lowering risk scores in individuals, through changes in timing of medication use or changes in prescribed medications, results in reductions in ADEs and death. If this is demonstrated, then the application of combined, computer-generated risk scores to identify and adjust medication regimens could significantly improve health care outcomes among ambulatory patients taking medications.

ACKNOWLEDGMENTS

We gratefully thank Dr Elizabeth Juarez-Colunga for her contribution of statistical knowledge and interpretation of these results.

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