**Supplemental Digital Content – Table 1. MRC-ICU Score**

|  |  |
| --- | --- |
| **Parameter** | **Value** |
| **High Priority Medications** |
| Aminoglycosides (amikacin, gentamicin, tobramycin) | 3x |
| Amphotericin B and liposomal amphotericin B | 1 |
| Antiarrhythmics (amiodarone, dofetilide, sotalol) | 1x |
| Anticoagulants (direct acting oral anticoagulants, fondaparinux) | 1x |
| Anticonvulsants (carbamazepine, phenobarbital, phenytoin, valproic acid) | 3x |
| Argatroban | 2 |
| Azole antifungals (posaconazole, voriconazole) | 2x |
| Blood Products (Factor products, Antithrombin III) | 2x |
| Chemotherapy (active inpatient) | 3x |
| Clozapine | 3 |
| Digoxin | 3 |
| Ganciclovir/valganciclovir | 1x |
| Hyperosmolar fluids (hypertonic saline (1.5%, 3%, 23.4%), mannitol) | 1x |
| Immunosuppressants (cyclosporine, sirolimus, tacrolimus) | 3x |
| Lidocaine (continuous infusion) | 2 |
| Lithium | 3 |
| Prostacyclins (epoprostenol, iloprost, treprostinil) | 2x |
| Theophylline | 3 |
| Therapeutic heparins (enoxaparin, heparin infusion) | 2x |
| Vancomycin (intravenous) | 3 |
| Warfarin | 3 |
| Neuromuscular Blockade | 2 |
| Continuous infusions (exclude those listed elsewhere) | 1x |
| **Parenteral Nutrition** |
| Managed by non-pharmacist service | 1 |
| Managed by clinical specialist pharmacist | 3 |
| **Prophylaxis and FAST HUGS BID** |
| Thromboembolic prophylaxis  | 1 |
| Stress ulcer prophylaxis (exclude pantoprazole infusion) | 1 |
| Glycemic control (subcutaneous insulin; exclude intravenous insulin) | 1 |
| Bowel regimen | 1 |
| Chlorhexidine | 1 |
| **Analgesia and Sedation** |
| Opioids and sedatives (scheduled and PRN) | 1x |
| Continuous infusion opioids and sedatives  | 2x |
| **Antimicrobial Agents** |
| Antimicrobials (include HIV medications, exclude those listed elsewhere) | 1x |
| Restricted antimicrobials | 2x |
| **Devices** |
| Continuous renal replacement therapy | 2 |
| Extracorporeal membrane oxygenation (ECMO) | 2 |
| Intra-aortic balloon pump (IABP) / Left ventricular assist device (LVAD) | 1 |
| Mechanical ventilation | 2 |
| **Total Score** | Sum |

**Supplemental Digital Content – Table 2. Development and evaluation of the MRC-ICU**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Study Design**  | **Population** | **Outcomes** | **Summary** |
| **1 – 20191** | Retrospective, cohort (n = 130) | Single-center, Medical ICU | Discriminant validity, convergent validity, inter-rater & test-retest validity, correlation to mortality ICU LOS, APACHE II | MRC-ICU demonstrated appropriate validity and significant correlation was observed between the score and patient acuity and patient outcomes, indicating appropriate initial internal validity  |
| **2 – 20192** | Retrospective, cohort (n = 130) | Single-center, Medical ICU | Correlation of modified MRC-ICU to original score, evaluation of how MRC-ICU changes from 24 hours to 48 hours and discharge | Modified MRC-ICU demonstrated significant correlation to the MRC-ICU; scores changes significantly from 24 hours to 48 hours and discharge, indicating dynamic nature of the score |
| **3 – 20203** | Prospective, observational cohort (n = 153) | Two-center,Medical ICU | Correlation of MRC-ICU to pharmacist interventions and DDIs | Significant correlation between MRC-ICU and pharmacist interventions and DDIs was observed, indicating a relationship to pharmacist workload |
| **4 – 20204** | Retrospective, cohort (n = 230) | Two-center,Medical ICU,Surgical ICU | Correlation of MRC-ICU from external site to validation measures (e.g., convergent, validity, etc.) | Appropriate correlation of an MRC-ICU from an external site was observed, indicating appropriate, initial external validity  |
| **5 – 20205** | Retrospective, cohort (n = 130) | Single center, Medical ICU  | Positive predictive value (PPV) of machine learning (ML) models for mortality | Inclusion of MRC-ICU with APACHE III using artificial intelligence resulted in higher PPV compared to APACHE III and other variables alone, indicating potential for future ML based investigation |
| **6 – 20216** | Retrospective, cohort (n = 125) | Two-center, Medical ICU | Correlation of MRC-ICU to incidence of fluid overload  | Association with fluid overload and weak correlation to balance was observed, indicating potential for relationship to ICU adverse events  |
| **7 – 20217**  | Post hoc analysis, retrospective cohort (n = 100) | Single-center, mixed medical-surgical ICU | Correlation of MRC-ICU vs. APACHE II to interventions and DDIs | MRC-ICU showed superior association to APACHE II for interventions; APACHE II did not correlate with DDIs, indicating potential need for medication specific predictive metrics |
| **8 – 20228**  | Descriptive report of implementation into EHR | Single-center, 4 ICUs (medical, neurosurgical, trauma/surgical, cardiovascular/cardiac surgical) | Description of scores calculated and implementation process | Over 3-months, MRC-ICU was calculated for 1,205 ICU patients over 5,083 patient-days; easy retrieval from EHR observed 6,500 individual MRC-ICU calculations and differences among medical vs. other ICUs in scores, all indicating feasibility of MRC-ICU EHR-incorporation  |
| **9 – 2022\*** | Retrospective, cohort (n = 149) | Single-center,Medical ICU | Mortality association of MRC-ICU in COVID-19 to mortality, mechanical ventilation, and WHO severity category  | MRC-ICU showed acceptable mortality prediction for mortality as well as a novel relationship to both mechanical ventilation and WHO severity categories, indicating relationship to ICU events |
| **10 –2022\*** | Retrospective, cohort (n = 1,205) | Single-center, 4 ICUs (medical, neurosurgical, trauma/surgical, cardiovascular/cardiac surgical) | Correlation of EHR calculated MRC-ICU to orders verified and i-Vent documentation | Significant correlation to orders verified by clinical pharmacists and i-Vents placed was observed, indicating further relationship to pharmacist workload |
| **11 – 2023\*** | Retrospective, cohort (n = 150) | Single-center,Medical ICU | Correlation of MRC-ICU to medication errors | Higher versus lower scores of MRC-ICU had numerically higher major interventions to prevent errors and higher potential harm scores  |
| *APACHE = Acute Physiologic Assessment and Chronic Health Evaluation, EHR = electronic health record, DDI = drug-drug interactions, ICU = intensive care unit, LOS = length of stay, WHO = World Health Organization, MRC-ICU = medication regimen complexity-intensive care unit**\*indicates preliminary data from manuscripts under review and/or abstract presentation of results only; results included to demonstrate ongoing and future analyses*  |

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**Supplemental Digital Content – Table 3. Low, medium, and high intensity intervention categories**

|  |
| --- |
| **Low Intensity Intervention** |
| * Medication reconciliation with no adverse drug event prevention
* Medication route (intravenous to oral conversion)
* Medication route for hypertension management
* Medication route for hypotension management
* Discontinuation of clinically unwarranted medications
* Initiation of venous thromboembolism prophylaxis
* Utilization of most appropriate venous thromboembolism prophylaxis
* Initiation of stress ulcer prophylaxis
* Initiation of ventilator associated pneumonia prophylaxis
* Antivenom stewardship
* Patient own medication evaluation
* Therapeutic interchange
* Rejection of a restricted medication
 |
| **Medium Intensity Intervention** |
| * Minor adverse drug event Prevention
* Medication reconciliation with minor adverse drug event prevention
* Preventing unnecessary labs and/or tests
* Prevention of inappropriate screening for heparin-induced thrombocytopenia
* Dosage adjusted by pharmacist
* Antimicrobial therapy initiation and streamlining
* Anticoagulant therapy management
* Antimicrobial pharmacokinetic evaluation
* Parenteral nutrition management
* Emergency Code Blue participation
* Rapid Response team participation
* Emergency Code Sepsis participation
* Medication teaching or discharge education
* Prevention of unnecessary high-cost medications
 |
| **High Intensity Intervention** |
| * Major adverse drug event prevention
* Medication reconciliation with major adverse drug event prevention
* Recommend laboratory monitoring
* Initiation or recommendation to initiate a non-antimicrobial therapy
* Bedside monitoring
* Emergency Code Stroke participation
* Blood factor stewardship and emergency anticoagulation reversal
* Emergency procedural sedation and rapid sequence intubation participation
* Drug information consultation
* Drug information consultation – toxicology specific
* Pharmacist-provided drug protocol management pursuant to a collaborative practice agreement
 |
| Major ADE prevention was defined as an action that could prevent temporary or permanent patient harm such as the following: drug-disease state contraindication, inappropriate dosage, duplicate therapy of a high-risk drug (e.g., anticoagulant, sedative, etc.), significant allergy to a drug prescribed, major drug-drug or drug-food interaction (i.e., risk of harm likely outweighs potential for benefit and most frequently classified as category D or X interaction), and drug prescribed for the incorrect patient.” Minor ADE prevention was defined as an “action similar to major ADE prevention except the expected patient harm and subsequent resource utilization is lower. |

**Supplemental Digital Content – Table 4. Univariate and multivariable regression of factors associated with intervention quantity**

|  |  |  |
| --- | --- | --- |
|  | **Univariate Analysis** | **Multivariable Analysis** |
| **Factor** | Δ **Interventions** | **95% CI** | **p-value** | Δ **Interventions** | **95% CI** | **p-value** |
| MRC-ICU  | 0.07 | 0.04 – 0.09 | <0.01 | 0.08 | 0.05 – 0.11 | < 0.01 |
| Patient:Pharmacist Ratio | -0.03 | -0.03 – -0.02 | <0.01 | -0.03 | -0.04 – -0.02 | < 0.01 |
| **Institution type** |  |  | 0.04 |  |  | 0.30 |
| Academic | Ref | --- | --- | Ref | --- | --- |
| Community teaching | 0.09 | -0.3 – 0.49 | 0.64 | 0.13 | -0.33 – 0.58 | 0.58 |
| Community non-teaching | 1.01 | -0.04 – 2.05 | 0.06 | -0.26 | -1.35 – 0.82 | 0.64 |
| **Region** |  |  | < 0.01 |  |  | < 0.01 |
| Midwest | Ref. | --- | --- | Ref. | --- | --- |
| Northeast | 0.26 | -0.26 – 0.79 | 0.33 | -0.51 | -1.11 – 0.1 | 0.10 |
| South | 1.19 | 0.88 – 1.15 | < 0.01 | 0.65 | 0.25 – 1.06 | < 0.01 |
| West | -1.11 | -1.64 – -0.59 | 0 | -1.99 | -2.61 – -1.37 | < 0.01 |
| **ICU Type** |  |  | < 0.01 |  |  | 0.11 |
| Medical | Ref. | --- | --- | Ref. | --- | --- |
| Burn | -0.92 | -2.18 – 0.33 | 0.15 | -0.45 | -1.6 – 0.7 | 0.44 |
| Cardiac  | -0.2 | -0.9 – 0.5 | 0.57 | -0.74 | -1.35 – -0.13 | 0.02 |
| Cardiovascular surgery | 0.72 | 0.02 – 1.42 | 0.05 | 1.14 | 0.45 – 1.82 | < 0.01 |
| Decentralized/Mixed | -2.72 | -3.13 – -2.3 | 0 | 1.25 | 0.61 – 1.89 | < 0.01 |
| Neurosciences | 0.1 | -0.43 – 0.63 | 0.71 | 0.03 | -0.46 – 0.53 | 0.90 |
| Surgery | 0.89 | 0.33 – 1.45 | 0 | -0.24 | -0.84 – 0.35 | 0.42 |
| Trauma | 0.52 | -0.35 – 1.39 | 0.25 | 1.33 | 0.47 – 2.18 | < 0.01 |
| **Patient Outcomes** |  |  |  |  |  |  |
|  ICU LOS | 0.03 | 0.01 – 0.05 | < 0.01 | -0.03 | -0.05 – -0.01 | < 0.01 |
|  ICU mortality  | 0.46 | 0.01 – 0.90 | 0.05 | 0.21 | -0.21 – 0.63 | 0.33 |
| \**β-coefficients represent change in number of interventions. Quantity of interventions includes the entire study period.*  |
| *ICU: intensive care unit, OR: odds ratio, CI: confidence interval, LOS: length of stay* |

**Supplemental Digital Content – Table 5. Univariate and multivariable regression of factors related to intervention intensity**

|  |  |  |
| --- | --- | --- |
|  | **Univariate Analysis** | **Multivariable Analysis** |
| **Factor** | Δ **composite score** | **95% CI** | **p-value** | Δ **composite score** | **95% CI** | **p-value** |
| MRC-ICU | 0.19 | 0.11 – 0.28 | < 0.01 | 0.2 | 0.08 – 0.31 | < 0.01 |
| Patient:Pharmacist Ratio | -0.03 | -0.06 | 0.02 | -0.05 | -0.09 – -0.01 | 0.01 |
| **Institution type** | --- | --- | 0.04 | --- | --- | 0.78 |
| Academic | Ref. | --- | --- | Ref. | --- | --- |
| Community teaching | 0.09 | -0.3 – 0.49 | 0.64 | -3.56 | -5.37 – -1.75 | < 0.01 |
| Community non-teaching | 1.01 | -0.04 – 2.05 | 0.06 | -4.58 | -8.92 – -0.25 | 0.04 |
| **Region** | --- | --- | < 0.01 | --- | --- | --- |
| Midwest | Ref. | --- |  | Ref. | --- | < 0.01 |
| Northeast | 3.28 | 1.21 – 5.35 | < 0.01 | 1.56 | -0.85 – 3.97 | 0.21 |
| Southeast | 3.98 | 2.75 – 5.22 | < 0.01 | 3.22 | 1.6 – 4.83 | < 0.01 |
| West | -2.83 | -4.9 – -0.76 | 0.01 | -4.23 | -6.69 – -1.78 | < 0.01 |
| **ICU Type** | --- | --- | < 0.01 | --- | --- | 0.26 |
| Medical | Ref. | --- | --- | Ref. | --- | --- |
| Burn | -2.2 | -6.2 – 1.8 | 0.28 | -2.09 | -6.68 – 2.51 | 0.37 |
| Cardiac  | -0.7 | -2.93 – 1.53 | 0.54 | -1.72 | -4.15 – 0.7 | 0.16 |
| Cardiovascular surgery | -1.15 | -3.39 – 1.09 | 0.32 | -1.4 | -4.13 – 1.34 | 0.32 |
| Decentralized/ Mixed | -5.19 | -6.51 – -3.88 | < 0.01 | 4.6 | 2.05 – 7.16 | < 0.01 |
| Neurosciences | 3.03 | 1.36 – 4.71 | < 0.01 | 2.53 | 0.56 – 4.51 | 0.01 |
| Surgery | 2.18 | 0.39 – 3.97 | 0.02 | -2.22 | -4.58 – 0.15 | 0.07 |
| Trauma | 0.67 | -2.11 – 3.45 | 0.64 | 1 | -2.42 – 4.42 | 0.57 |
| **Patient Outcomes** |  |  |  |  |  |  |
|  ICU LOS | 0.14 | 0.08 – 0.21 | < 0.01 | 0.02 | -0.06 – 0.1 | 0.63 |
|  ICU mortality  | 1.34 | 2.69 | -0.06 | 0.41 | -1.27 – 2.09 | 0.63 |
| \**β-coefficients represent change in number of interventions. Quantity of interventions includes the entire study period.*  |
| *ICU: intensive care unit, OR: odds ratio, CI: confidence interval, LOS: length of stay* |

**Supplemental Digital Content – Table 6. MRC-ICU Score Characteristics**

|  |  |
| --- | --- |
| **MRC-ICU Score by Characteristic** | **ICU Patients (N=3,908)** |
|  **Institution Type, mean** ± SD (n) |  |
|  Academic | 10.6 (6.6) (991) |
|  Community Teaching | 9.7 (4.4) (105) |
|  Community Non-Teaching | 13.3 (4.5) (26) |
|  **ICU Type, mean** ± SD (n) |  |
|  Medical | 9.5 (6.0) (1786) |
|  Burn  | 8.2 (4.5) (60) |
|  Cardiac  | 6.1 (5.1) (209) |
|  Cardiovascular surgery  | 12.7 (7.0) (206) |
|  Decentralized/Mixed | 9.4 (5.5) (765) |
|  Neurosciences  | 7.3 (4.8) (406) |
|  Surgical | 10.9 (6.1) (347) |
|  Trauma | 11.6 (5.6) (129) |
| *Data are presented as n (%) unless otherwise stated.**ICU: intensive care unit; SD: standard deviation* |