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Remdesivir for the treatment of Covid-19: A Meta-analysis of randomized controlled trials

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in restrictive transfusion practices and determine whether any variation in transfusion practices was associated with patient's demographic (age, gender, race) or clinical characteristics (comorbidities, length of stay (LOS)).
METHODS: Hospitalized general medicine patients with a Hb<10g/dL were eligible for study participation. Patients with sickle cell anemia were excluded. Transfusion and Hb data were collected from the hospital's administrative data mart. Multiple linear regression was used to test the association between receipt of a transfusion as the dependent variable, and patients demographic (age, gender, race, ethnicity) and clinical characteristics (Charlson Comorbidity Index (CCI), LOS) as the independent variables, controlling for patient's admission and nadir Hb levels.
RESULTS: 4,096 patients consented to participate, of which 26% received a transfusion. The average age was 60 (±17), 57% were female, 71% were African American, and 95% were non- Hispanic/Latino. The mean nadir Hb was 7.9g/dL (±1 g/dL). The rate of transfusion was 1% for patients with a nadir Hb 9-10g/dL, 21% for patients with a nadir Hb 7-8g/dL, and 83% for patients with a nadir Hb<7g/dL. In the regression model, Hispanic/Latino patients were less likely to receive transfusion compared to non-Hispanic/Latino patients (β=-0.26, p=0.05), African American patients were less likely to receive transfusion (β=-2.03, p<0.01), and patients reporting a race of "other" were more likely to receive a transfusion (β=1.73, p<0.01), compared to white patients. A longer LOS (β=0.1, p< 0.01) was also associated with a higher likelihood of receiving a transfusion. There was no association between transfusion and age, gender, or CCI.
CONCLUSIONS: Within restrictive transfusion ranges the rate of transfusion differs by race, ethnicity, and LOS. The differences in transfusion by race and ethnicity are surprising findings, and future work should examine whether these differences reflect disparities in care.
LEARNING OBJECTIVE #1: Examine variation in restrictive red blood cell transfusion practices.
LEARNING OBJECTIVE #2: Examine whether variation transfusion practices is associated with patient's demographic or clinical characteristics.

RANDOMIZED TRIAL OF THE EFFECT OF A HIPAA AUTHORIZATION FORM ON SURVEY RESPONSE FOR A RESEARCH COHORT IN A CLUSTER-RANDOMIZED ADVANCE CARE PLANNING TRIAL

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BACKGROUND: The Health Insurance Portability and Accountability Act (HIPAA) protects patients by setting limits on who can view and receive their health information. HIPAA requires adherence to institutional regulations and forms include legal language that can be confusing to patients. Although HIPAA forms would ideally be described in detail by study staff, this is not always feasible, especially for large pragmatic trials. Therefore, we evaluated the effect of including a HIPAA authorization in mailed survey packets on study enrollment.
METHODS: Enrollment packets (i.e., consent forms, +/- HIPAA and surveys) were mailed to English and Spanish-speaking seriously ill eligible patients (i.e. advanced cancer, heart failure, COPD, cirrhosis, renal failure, ALS, vulnerable elder with comorbidity) as part of a population-based advance care planning (ACP) pragmatic trial at three University of California Health Systems. Participants were excluded if clinicians reported the patient had cognitive impairment or the survey might cause psychological harm. The Community Advisory Group raised concerns that the 3-page HIPAA form required by the institution would hinder enrollment. Therefore, we randomized 1/3 of eligible patients to have the HIPAA authorization included in their mailed packet and 2/3 to not have it included. Mailed packets included a self-addressed, stamped envelope and were followed by up to three reminder phone calls. We compared enrollment rates within 3 months of outreach for the two groups.
RESULTS: We mailed enrollment packets to 4634 eligible patients; 1544 patients received an enrollment packet that included a HIPAA authorization form and 3090 patients received an enrollment packet that did not. Patients were 51% male, 63% white, 63% were $\geq$ 70 years old, and 10% were Spanish speaking; demographic characteristics were similar between the two groups. There was no difference in rates of telephone follow up between the two groups. Patients randomized to receive the enrollment packet without the HIPAA form were significantly more likely to enroll in the study (13.9% v. 9.8%, p<0.001). For subsequent enrollment (phase 2) of the study, we excluded the HIPAA authorization form from all enrollment packets and met our enrollment target. Follow-up will be needed to collect HIPAA authorization forms for enrolled patients.
CONCLUSIONS: Inclusion of HIPAA authorization in mailed enrollment packets led to lower rates of study enrollment. Although HIPAA forms are more easily described in person or by phone, this is often too resource intensive for large pragmatic trials. HIPAA authorization forms must be redesigned to meet the health literacy needs of patients and to prevent unnecessary barriers to research enrollment.
LEARNING OBJECTIVE #1: Understand the Health Insurance Portability and Accountability Act (HIPAA) and its role in protecting patient information.
LEARNING OBJECTIVE #2: Understand how HIPPA authorization form and how it can have an impact on response rates in clinical trials.

REMDESIVIR FOR THE TREATMENT OF COVID-19: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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BACKGROUND: The global pandemic of Coronavirus Disease 2019 (COVID-19) has led to over 80 million confirmed cases worldwide and has been attributed to nearly 2 million deaths. Remdesivir, an adenosine analog pro-drug, has shown effectiveness in previous in vitro and clinical studies. However, most randomized studies are preliminary or are limited by small sample sizes and conflicting findings. As a result, this meta-analysis of randomized, controlled trials (RCTs) was performed to compare intravenous remdesivir to control in patients hospitalized for COVID-19.
METHODS: A comprehensive literature search of EMBASE, PubMed, Clarivate Web of Science, and clinical trial registries such as Clinicaltrials.gov and the World Health Organization International Clinical Trials Registry Platform. The titles and abstracts of eligible studies were reviewed independently by two authors according to inclusion-exclusion criteria established a priori. A third author resolved the disputes. A second round of screening by in-depth full-text review was then performed. A total of two randomized controlled trials met criteria for inclusion into quantitative synthesis. The primary outcome was clinical improvement as indicated by a reduction in ordinal scores based on patient clinical status. Secondary outcomes included mortality rate and adverse events. Standardized mean differences (SMD) and 95% Confidence Intervals (CI) were used for continuous outcomes. Odds ratios (OR) and 95% CIs were used for dichotomous outcomes. The significance level was set at 0.05.
RESULTS: This meta-analysis analyzed data from 1,295 patients from 70 clinical sites included in 2 RCTs. Remdesivir was administered as a 200 mg loading dose on Day 1 followed by 100 mg maintenance doses on Days 2-10. Remdesivir significantly reduced ordinal scores (2.4 ± 1.7 vs 2.8 ± 1.9, SMD =

-0.21, 95% CI = -0.33 to -0.09, p < 0.001), indicating clinical improvement, and significantly reduced mortality (6.8% vs 10.2%, OR = 0.62, 95% CI = 0.41 to 0.94, p = 0.02). The use of remdesivir did not significantly increase anemia, acute kidney injury, cardiac arrest, deep vein thrombosis, pulmonary embolism, respiratory failure, or septic shock (all ps > 0.05).

CONCLUSIONS: The findings of this meta-analysis suggest that intravenous remdesivir significantly improves clinical status and reduces mortality in patients with COVID-19. Moreover, remdesivir appears to be well-tolerated among hospitalized patients. Further studies are needed to complete the side-effects profile of the drug as well as optimize dosing, timing, and mode of delivery. Clinicians should decide whether to administer remdesivir based on the highest level of evidence available in the literature.

LEARNING OBJECTIVE #1: Recognize whether intravenous remdesivir improves clinical status.

LEARNING OBJECTIVE #2: Recognize whether intravenous remdesivir affects mortality rates compared to control.

SEX DIFFERENCES IN THE SYMPTOMS AND TOLERANCE OF ANEMIA DURING HOSPITALIZATION

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BACKGROUND: The WHO defines anemia in females as a hemoglobin (Hb)<12g/dL and in men as a Hb<13g/dL. These different Hb cutoffs for defining anemia represent well established differences in normal baseline Hb concentration between females and males. There are also differences in the prevalence of anemia in females and males over the life course. Despite these known differences in baseline Hb concentration and rates of anemia, there is little data describing whether females and males may also differ in their tolerance of anemia symptoms, such as fatigue. This is important because if either males or females have higher anemia-related fatigue levels, then using the same Hb threshold to transfuse all hospitalized patients may not be the optimal management for either sex. Importantly, the RCT's that have informed restrictive transfusion practices have not reported on sex differences in baseline Hb levels or how such differences may impact transfusion thresholds with respect to patients' symptoms. The purpose of this study was to measure the fatigue levels of hospitalized patients with anemia, and to test for differences in the anemia-related fatigue levels of females and males.

METHODS: From 7/2017-2/2020, hospitalized general medicine patients with a Hb<10g/dL were approached for consent. Patient's fatigue was measured using the Patient-Reported Outcome Measurement Information System Fatigue instrument. Patients' Hb values and clinical data were abstracted from hospital administrative data. Multiple linear regression was used to test the association between fatigue as the dependent variable, patients' sex as the primary predictor variable, controlling for age, race, ethnicity, nadir Hb level, Charlson Comorbidity Index, receipt of a transfusion, and length of stay (LOS).

RESULTS: 1,931 patients consented and 58% were female. Females were older than males (58 vs. 56, p=0.01). There was a higher percentage of African American females than males (76% vs 66%), and a lower percentage of white females compared to white males (46% vs 54%) (p<0.01). Females had a shorter LOS (9 vs. 10 days, p<0.01) and higher fatigue levels at admission (27 vs 24, p<0.01) compared to males. There were no other differences in baseline characteristics between males and females with respect to ethnicity, nadir Hb (7.7g/dL), receipt of a transfusion (31%), or number of comorbidities. In the regression model, controlling for the above characteristics females had clinically significant higher fatigue levels than did males (β=3.0, p<0.01).

CONCLUSIONS: Hospitalized female patients have higher anemia-related fatigue levels than do hospitalized male patients. This difference in fatigue levels may represent different tolerances to anemia and should be further examined to work determine whether different transfusion thresholds may mitigate the effects of anemia on fatigue for females and males.

LEARNING OBJECTIVE #1: To measure fatigue leves in hospitalized patients with anemia

LEARNING OBJECTIVE #2: To compare fatigue levels between hospitalized men and women with anemia

THE ASSOCIATION OF PRESCRIBED OPIOIDS AND INCIDENT CARDIOVASCULAR DISEASE IN THE VETERANS AGING COHORT STUDY

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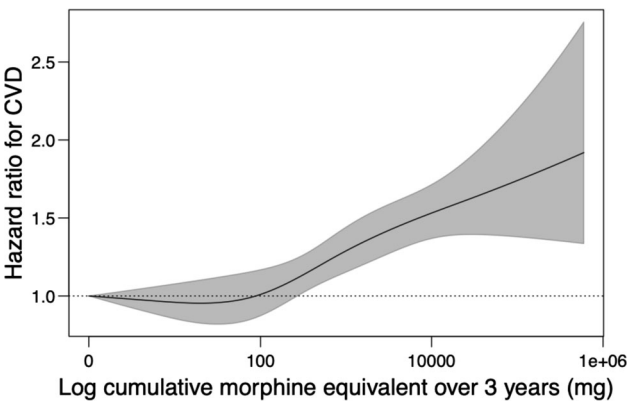
BACKGROUND: Recent data suggest that prescription opioids (PO) may increase cardiovascular disease (CVD) risk. Compared to those without HIV, people with HIV have higher risk for CVD and are more likely to have chronic pain for which they receive PO and at higher doses. We assessed the association of outpatient PO with incident CVD in the Veterans Aging Cohort Study (VACS).

METHODS: VACS, a national cohort of Veterans with and without HIV, were eligible at their first clinic visit on or/after 4/1/2003 (index date). Patients were excluded if, in the year after index date (baseline period), they had: died, an opioid use disorder diagnostic code, more than minimal PO receipt (>14 days PO or >100mg average morphine-equivalent daily dose [MEDD]), or severe illness (VACS Index >100). The primary exposures of interest, PO receipt and total MEDD,were determined in the 3 years after baseline period. Follow-up for incident CVD began at the end of the opioid exposure window among those free of CVD and cancer. We used Cox proportional hazards regression to estimate hazard ratios (HR) with inverse probability weighting to balance confounders by probability of PO receipt. Models were adjusted for covariates assessed at the index date: CVD risk factors, HIV, pain intensity rating, VACS Index, hepatitis C (HCV), alcohol/cocaine use disorder, depression, antidepressant receipt.



RESULTS: Of 38,024 participants, 40% received any PO during the three year period. Median age was 48 years. The sample was 97% male, 49% black, and 48% current smokers. HIV, HCV, and diabetes mellitus prevalence were 28%, 5%, and 12% respectively. Alcohol use disorder was greater among those