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Updates in Hospital Medicine

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UPDATE 1: TREATMENT OF OPIOID USE DISORDER DECREASES MORTALITY

Opioid use disorder (OUD) is an independent risk factor for suicide, a leading cause of mortality in the U.S.[1] Medication-assisted treatment (MAT) for opioid use disorder such as buprenorphine, naltrexone, methadone, etc. has been shown to improve outcomes in OUD. Researchers conducted a retrospective evaluation of approximately 62,000 U.S. Veterans Affairs patients with OUD, examining the effect of medications for opioid use disorder (MOUD) on the risk of mortality during a 14-year period from 2003–2017.[2]

The exposure of interest was MOUD starting periods (first 14 days on treatment), stopping periods (first 14 days off treatment), stable time on treatment, and stable time off treatment. The main outcomes were suicide mortality, external cause mortality, and all-cause mortality. The cohort was predominately white, male, and less than 65 years old, with co-occurring psychiatric diagnoses often requiring healthcare contact or inpatient treatment. Approximately half of the patients received buprenorphine (n=30,950), and the other half methadone (n=15,446) or naltrexone (n=15,237). The cohort was followed for a mean of 3.5 years. The adjusted hazard ratio (aHR) during stable MOUD was 0.45 (95% CI=0.32, 0.63) for suicide mortality, 0.35 (95% CI=0.31, 0.40) for external cause mortality, and 0.34 (95% CI=0.31, 0.37) for all-cause mortality. Starting periods were associated with a reduced risk of suicide mortality, but to a lesser degree than stable periods. Stopping periods were associated with an elevated mortality risk across all three outcomes compared with stable off periods.[2]

Buprenorphine was associated with a decreased risk of suicide mortality in both crude (HR=0.37, 95% CI=0.24, 0.56) and adjusted models (HR=0.34, 95% CI=0.23, 0.52). Methadone use in the crude model *suggested* a decreased risk of suicide mortality; however, after adjusting for co-existing psychiatric conditions and healthcare contact, this association was no longer found. Methadone use was associated with a significant reduction in external and all-cause mortality when adjusted. Naltrexone use was associated with a decreased risk of all-cause mortality (less so than buprenorphine and methadone) but not suicide mortality.

Overall, starting periods of MOUD were associated with an almost immediate reduction in risk for suicide-related mortality, with that risk reduction sustaining at three years of follow-up. Among the medications studied, buprenorphine was favored to "lessen the immediate and longer-term risk for suicide mortality, which perhaps reflects the medication's rapid onset and tolerability."[3] Its use was associated with reducing suicide, external cause, and all-cause mortality in all models and subgroups.

Take-away: In middle-aged, white Veterans with opiate use order, MOUD rapidly reduces mortality risk from suicide. This risk reduction is sustained while on treatment, with the preferred medication being buprenorphine. Additional research is needed across broader patient samples and multiple health care settings.

UPDATE 2: INHALED CORTICOSTEROIDS IN ADDITION TO ALBUTEROL FOR ASTHMA RESCUE

Historically, patients with asthma have been instructed to use albuterol alone as rescue medication. However, a recent multinational, randomized controlled trial challenges that practice.[4] More than 3100 predominately white adolescents and adults with uncontrolled moderate-to-severe asthma were randomized 1:1:1 to either high or low-dose albuterol/budesonide (180/160 µg or 180/80 µg) or albuterol alone (180 µg) as a rescue inhaler while continuing their current inhaled corticosteroid (ICS) or ICS/Long-acting beta agonist (LABA) therapy. Patients with COPD, glucocorticoid therapy within the prior three months, and those on biologic therapies were excluded. The primary endpoint was the first event of severe asthma exacerbation (needing systemic glucocorticoid treatment, emergency department or urgent care visit for asthma, or inpatient hospitalization for asthma) in a time-to-event analysis, which was performed in the intention-to-treat population.

The risk of severe asthma exacerbation in the intention-to-treat analysis at 24 weeks was 26% lower in the higher-dose combination group than in the albuterol-alone group (HR, 0.74; 95% CI, 0.62 to 0.89; P=0.001). The hazard ratio in the lower-dose combination group, as compared with the albuterol-alone group, was 0.84 (95% CI, 0.71 to 1.00; P=0.052). The annualized rate of severe asthma exacerbations is shown in Table 1.

The mean annualized total dose of systemic glucocorticoid (in prednisone equivalents) was approximately 84±248 mg in the higher-dose combination group and 95±318 mg in the lower-dose combination, and 130±630 mg in the albuterol alone group. A similar randomized trial in Black and Latinx adults with asthma found that rescue inhaled beclomethasone 80 µg and rescue albuterol, in addition to

Table 1. Outcomes of patients treated with inhaled corticosteroids for asthma rescue

	High dose combination group (180/160 µg)	Albuterol alone (180 µg)	Low dose combination group (180/80 µg)	Albuterol alone (180 µg)
Total patients (no.)	1013	1014	1054	1056
Severe Exacerbations (no.)	345	427	372	441
Annualized rate (95% CI)	0.43 (95% CI, 0.33 to 0.58)	0.58 (95% CI, 0.44 to 0.77)	0.48 (95% CI, 0.37 to 0.63)	0.48 (95% CI, 0.37 to 0.63)

usual care, reduced severe asthma exacerbations by 15% compared to albuterol plus placebo.[5]

Take-away: In patients with uncontrolled, moderate-to-severe asthma on maintenance therapies, high-dose 180 µg of albuterol and 160 µg of budesonide (in two actuations of 90 µg and 80 µg), administered on a PRN basis, reduces the risk of a severe asthma exacerbation compared to PRN albuterol alone.

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DISCLOSURES/CONFLICT OF INTEREST

The author declares they have no conflicts of interest

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