Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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The primary endpoint was change from baseline in PEC total at 2h. The secondary endpoint was earliest time of a statistically significant separation from placebo. Severity of agitation at baseline was assessed by the CGI-S score at Screening and immediately prior to dosing. The CGI-S was focused on the severity of agitation rather than the severity of the overall illness.

Results: 760 patients enrolled in the 2 trials. All doses of dexmedetomidine SF met the primary endpoint of statistically significant change from baseline in PEC total at 2h vs placebo (P<.001). Mean (SD) reductions in PEC total at 2h were -10.4 (4.4), -8.7 (5.0), and -4.8 (4.7) for 180 mcg, 120 mcg, and placebo, respectively. Statistically significant separation from placebo occurred as early as 10 minutes at 180 mcg (P<.0004) and 20 minutes at 120 mcg (P=.015).

The PEC total score and PEC change from baseline were stratified by baseline CGI-S score, mild (2-3), moderate (4), and severe (5-6). Mean (SD) 2-hour PEC total scores for 180 mcg were 5.5 (3.1), 7.5 (3.4), and 8.2 (4.8); for 120 mcg were 7.6 (3.9), 8.8 (4.2), 10.2 (5.7), and for placebo groups were 8.4 (3.6), 12.7 (4.6), and 16.2 (5.4) for those with baseline mild, moderate, and severe CGI-S scores, respectively. Least squares mean change difference from placebo for 180 mcg were -3.1 (0.8), -5.0 (0.4), and -8.2 (1.1) (all P<.001) and for 120 mcg were -0.7 (0.9; P=.45), -3.9 (0.4; P<.001), -6.2 (1.1; P<.001) for those with mild, moderate, and severe CGI-S scores, respectively.

There were no drug-related serious or severe AEs in either trial. No participant was unarousable either by AE reporting or by the Agitation and Calmness Evaluation Scale (ACES). The most common treatment emergent adverse events (TEAEs) were somnolence (21.5%), dry mouth (5.9%), hypotension (5.3%), dizziness (4.9%), orthostatic hypotension (4%), oral hypotension (3.8%), and headache (3.6%). Of 110 somnolence reports, 86% were mild and 14% moderate.

Conclusions: Dexmedetomidine sublingual film treated acute agitation associated with SCZ or BPD, with an onset of action as early as 10 minutes at 180 mcg and was well tolerated with somnolence the most common AE. Dexmedetomidine provides a novel mechanism of action, making it a potential addition to noninvasive treatments for acute agitation.

Yes, authors have interests to disclose
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Clinical Confirmation of Improved Likelihood of Survival Associated With the Use of the Head-Up CPR
Bundle for Non-Shockable Cardiac Arrest Presentations
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Study Objectives: The modified physiologic approach to CPR that uses gradual automated head-up/oro/oro positioning (AHUP) with concurrent application of other CPR adjuncts designed to augment circulation and lower intracranial pressure has consistently facilitated normalized cerebral perfusion pressures and neuro-intact survival pre-clinically (eg. Resuscitation 2021;158:220) and is also associated with markedly improved odds of survival for out-of-hospital cardiac arrest (OHCA) patients in early clinical evaluations (eg, Crit Care Med 2022;50[suppl]:1). Similar to automated defibrillators (AEDs) in shockable cases, the sooner AHUP is applied, the better the outcome. Accordingly, given that >80% of OHCA cases are those with non-shockable presentations (NS-OHCA) that predict an extremely poor outcome with unlikely chances of successful survival to hospital discharge (SURV), the specific aims here were to: 1) confirm if the overall association of improved SURV seen with AHUP CPR (compared to conventional CPR [C-CPR]) also carries into the subcategory of NS-OHCA cases; and 2) confirm if time elapsed from 9-1-1 call receipt to AHUP initiation (T911-AHUP CPR) is also associated with higher SURV in NS-OHCA cases.

Methods: Prospectively-collected data were obtained from a national AHUP registry in which 5 early-adopting EMS agencies routinely tracked OHCA SURV, T911-AHUP CPR, and used basic 1st responders for faster AHUP initiation. In all cases, AHUP was combined with manual (or automated) active compression-decompression and impedance threshold devices (all FDA-cleared). AHUP devices steadily elevate the head/torso during CPR over several minutes (ociput reaching 22 cm). For the most rigorous comparison, C-CPR controls were purposely derived from 2 large-scale published NIH-funded trials involving >10,000 OHCA patients studied in high-performance EMS systems including those that closely monitored, recorded and reported quality of CPR for study inclusion. Overall comparisons of SURV between AHUP and control groups were calculated using Fisher’s exact tests. In additional analyses, AHUP and C-CPR cases were also matched for T911-AHUP CPR (time from 9-1-1 call receipt to start of 1st responder CPR) when assessing the relationship between start of AHUP CPR and SURV. P-values <0.05 were considered statistically significant.

Results: Most patients did have asystole presentations (61.2% [248/405 AHUP] and 61.3% [1,159/1,892 controls]; p=1.0). Overall, AHUP CPR for NS-OHCA patients was associated with a 2.4-fold increase in SURV compared with C-CPR counterparts from the high-performance / highly-monitored systems (7.9% [32/405] vs 3.3% [63/1,892]; p=0.0001). When matched for T911-AHUP CPR and then assessed according to T911-AHUP CPR, associated SURV advantages with AHUP CPR (vs C-CPR) became progressively higher with shorter T911-AHUP CPR. When T911-AHUP CPR was <12 mins, SURV was 10.8% (23/213) vs 3.2% (54/1709) for C-CPR (p<0.0001) and if <10 mins, SURV was 12.2% (15/123) vs 3.5% (42/1199); p=0.0001. Relevant to these findings, median T911-AHUP CPR for both AHUP and C-CPR control groups was 8 mins and the median T911-AHUP was 11 mins.

Conclusions: For the great majority of OHCA patients who have non-shockable presentations, AHUP CPR was associated with markedly improved odds of survival vs C-CPR. Moreover, shorter times to AHUP CPR initiation augmented survival chances and did so within very achievable response intervals.

Yes, authors have interests to disclose
Disclosure: Advanced CPR Solutions Board Member/Officer/Trustee Advanced CPR Solutions

Background and Objective: Vulnerable patients whose primary access to care occurs in emergency departments (EDs) have suffered high morbidity and mortality during the COVID-19 pandemic; yet, they are disproportionately hesitant to receive COVID-19 vaccines. We sought to determine whether provision of COVID-19 vaccine messaging platforms, which were developed via in-depth interviews and qualitative analysis of vaccine hesitant ED patients, results in greater COVID-19 vaccine acceptance and uptake in unvaccinated ED patients. Herein, we present the findings of our first formal analysis of our trial.

Methods: This prospective, cluster randomized controlled trial (unit of randomization = one week) includes alert, non-critically ill, adult (> 17 years) patients who have not received a COVID-19 vaccine at seven hospital EDs in four US cities. The intervention is delivery of three COVID-19 vaccine messaging platforms (an English or Spanish 4-minute video, a 1-page informational flyer and a brief, scripted message delivered by an ED physician or nurse) during ED waiting times. Our primary outcomes are survey responses to “Would you accept the COVID vaccine in the emergency department today if your doctor asked you” and receipt of a COVID-19 vaccine within 32 days ascertainment in a blinded manner by electronic health record review and telephone follow-up.

Results: Of 630 eligible patients screened from 12/6/21 to 4/7/22, 333 (52.9%) agreed to participate (156 during intervention weeks, 177 during control weeks). Intervention and Control groups were similar in terms of their baseline characteristics - See Table. More intervention group patients stated they would accept a COVID-19 vaccine if offered (43 [28%] vs 20 [11%]: difference in proportions ¼ 17%, 95% CI 10 to 25%; number needed to treat [NNT] ¼ 6).

Conclusions: With a low NNT of 6). More intervention group patients received a COVID-19 vaccine at 32 days after their ED visit (35 [22%] vs 9 [5%]; difference in proportions ¼ 17%, 95% CI 10 to 25%; NNT ¼ 6).

Conclusion: Implementation of COVID-19 vaccine messaging platforms in EDs leads to greater COVID-19 vaccine acceptance and uptake in unvaccinated ED populations. This ongoing trial may pave the way for the broad
delivery of COVID-19 (and other vaccine) messaging to improve vaccine acceptance and uptake in vulnerable ED populations nationally.

Table: Participant Characteristics

|                          | All (333) | Intervention (156) | Control (177) |
|--------------------------|-----------|--------------------|---------------|
| Median age in years, (IQR) | 39 (30, 53) | 38 (31, 52) | 39 (28, 54) |
| Female gender            | 140 (42%) | 62 (40%) | 78 (44%) |
| African American         | 133 (40%) | 58 (37%) | 75 (42%) |
| Latino                   | 60 (18%)  | 30 (19%) | 30 (17%) |
| White, non-Latino        | 121 (36%) | 56 (36%) | 65 (37%) |
| No primary care          | 148 (44%) | 73 (47%) | 75 (42%) |

Yes, authors have interests to disclose

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Frequency of Tick-borne Infections in Children With Suspected Lyme Disease

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Introduction: In endemic regions, Ixodes species ticks can transmit Borrelia species as well as other tick-borne pathogens. The frequency of tick-borne infections and co-infections in children with suspected Lyme disease is poorly characterized due to shortcomings of current microscopy and serologic diagnostic methods. Importantly, this creates clinical uncertainty about the optimal approach to diagnosis and management of suspected tick-borne infections in children.

Methods: We performed a prospective eight-center study of children 1 to 21 years of age presenting to a Pedi Lyme Net emergency department for evaluation for Lyme disease between June 2015 and December 2021. We defined a case of confirmed Lyme disease based on presence of erythema migrans (EM) lesion or positive two-tier serology in the appropriate clinical context. For this study, we selected Lyme cases with either a single EM lesion or neurologic Lyme disease (facial palsy and/or meningitis) matched by age, sex and clinical center to clinical mimics (ie children with facial palsy or meningitis but negative two-tier Lyme disease serology). We also included children with a recent tick bite without symptoms of tick-borne infection. Using bio-banked whole blood research samples, we performed a research multiplex high definition polymerase chain reaction (HDPCR) panel (ChromaCode, Carlsbad, CA) to test for 8 bacterial and 1 protozoan tick-borne pathogens. We report the frequency of tick-borne co-infections in children with Lyme disease and matched clinical mimics.

Results: Of the 617 study patients, 306 (49.6%) had a single EM lesion or neurologic Lyme disease, 302 (48.9%) clinical mimics and 9 (1.5%) had a recent tick bite without evidence of infection. The median patient age was 10 years (interquartile range 6-14 years) and 370 (59.9%) were male. To date, we have run 183 multiplex PCR panels of which 4 (2.2%) failed sample quality checks. Of the 179 completed multiplex PCR panels to date, 6 children with early neurologic Lyme disease had a previously unknown tick-borne pathogen identified using the HDPCR panel (2 Anaplasma phagocytophilum and 4 Babesia microti) and 1 had B. burgordferi/B. mayonii detected. Tick-borne coinfections were identified more frequently in children with confirmed Lyme disease (7.1% Lyme disease vs. 0% clinical mimics; p=0.07). Clinically, all 4 with Babesia spp. and 1 with A. phagocytophilum were treated with antibiotics ineffective for this coinfection.

Conclusion: A significant minority of children with suspected Lyme disease also had other tick-borne infections identified by multiplex HDPCR panel. Reliance on traditional diagnostic methods and clinical presentation may underdiagnose or misdiagnose these infections leading to ineffective antibiotic therapy. Further study is needed to identify children at highest risk of tick borne co-infections to guide clinical decision-making.

No, authors do not have interests to disclose

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Extended-release Naltrexone and Case Management for Treatment of Alcohol Use Disorder in the Emergency Department

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Objectives: Assess the feasibility of initiating treatment for alcohol use disorder with extended-release Naltrexone (XR-Naltrexone) and case management services in the emergency department (ED), and estimate the intervention’s impact on daily alcohol consumption (DAC) and quality of life (QOL).

Design: This is a twelve week, prospective open-label single-arm study of a multimodal treatment for AUD consisting of monthly XR-naltrexone injections and case management services initiated at a single urban academic ED. Participants were actively drinking adult ED patients with known or suspected AUD and AUDIT-C score > 4. The main feasibility outcomes were the proportions of participants enrolled/ approached, completed/enrolled, and continuing naltrexone after the trial/enrolled. Efficacy outcomes were the change in DAC (drinks/day, 14g ethanol/drink) measured by 14-day timeline follow back, and the change in QOL measured with single-item Kemp QOL scale.

Results: 179 patients were approached and 32 enrolled (18%). 25/32 (78%) completed all visits, 22/32 (69%) continued naltrexone after the trial. Baseline DAC was 7.6 drinks/day (IQR 4.5, 13.4) and mean QOL 3.6 (SD 1.7) on a 7-point scale. After 12 weeks of treatment, median DAC change was -7.5 drinks/day (Hodges-Lehman 95% CI -8.6, -5.9). Mean QOL change was 1.2 points (95% CI 0.5, 1.9; P < 0.01).

Conclusions: We found initiation of treatment of AUD with XR-naltrexone and case management is feasible in an ED setting and observed significant reductions in drinking with improved quality of life in the short term. Multi-center RCTs are needed to further validate these findings.

Trial Registration: clinicaltrials.gov NCT04904584

Figure 2

- median daily drinks per person
- Interquartile range

Extended-release Naltrexone injections given wks 0, 6, 12
One drink contains 14 grams of ethyl alcohol

No, authors do not have interests to disclose