ily due to retrospective patient selection. Studies that contained combination measurements had at least one domain rated as high risk of bias. Septal deviation had a sensitivity of 0.31 (95% CI 0.25-0.38; $I^2 = 51.6\%$), and the highest specificity at 0.98 (95% CI 0.90-1.00; $I^2 = 46.9\%$) for predicting RV dysfunction compared to echocardiography. It also had the highest positive likelihood ratio (+LR) at 13.6 (95% CI 3.1-60.4) suggesting it can be used to rule in RV dysfunction when present. It had a negative likelihood ratio (-LR) of 0.7 (95% CI 0.64-0.77). It had an IVC reflux had a sensitivity of 0.75 (95% CI 0.40-0.93; I2 = 95.9%) and specificity 0.75 (95% CI 0.47-0.91; I2 = 91.1%) for detecting RV dysfunction. It had a +LR of 3.0 (95% CI 1.5-6.1) and a -LR of 0.33 (95% CI 0.12-0.86). Increased RV/LV ratio had the highest sensitivity of all measures at 0.82 (95% CI 0.78-0.86; $I^2 = 81.8$), with a specificity of 0.75 (95% CI 0.66-0.82, $I^2 = 94.2$). It had a +LR of 3.3 (95% CI 2.4-4.6). Increased RV/LV ratio also had the lowest -LR for ruling out RV dysfunction at 0.23 (95% CI 0.18-0.29). Subgroup analyses showed that the studies at high or unclear risk of bias also had a significantly lower sensitivity for RV/LV ratio.

A few studies evaluated criteria in combination. Two studies noted that increased RV/LV ratio or septal deviation had a sensitivity of 78% and 92% respectively and a specificity of 100% in both studies. One study reported that both septal deviation and RV/LV ratio >1.0 had sensitivity of 67% and specificity of 100%. Another study reported the combination of any septal deviation, IVC contrast reflux, or RV/LV >1.0 had a sensitivity of 95% and specificity of 88%.

Overall the authors concluded that CT imaging can detect RV dysfunction in acute PE but the diagnostic accuracy of specific findings varies compared to echocardiography. Absence of increased RV/LV ratio was found to be the best measure for ruling out RV dysfunction while septal deviation was best for ruling in RV dysfunction. These conclusions are limited by many of the studies being high risk for bias, and by the significant difference in prevalence of RV dysfunction between studies. This difference was likely related to differences in proportions of patients with hemodynamic instability and may have affected the sensitivities, specificities, positive and negative predictive values, thus skewing the pooled analysis data. The authors note several limitations to this review, one of which is that the studies they included used echocardiography as the reference standard rather than the "gold standard" pulmonary capillary wedge pressure for measuring RV dysfunction.

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Comments: This review provides low-moderate quality evidence that CT imaging can be used to rule in RV dysfunction when septal deviation is seen (+LR 13.6) or with a combination of other findings. The other findings used in isolation only shifted probability of RV dysfunction marginally though when seen on echocardiography. Of note, both the high heterogeneity of the variables included in the pooled estimates and the amount of high risk bias associated with the studies presented raise concerns about the quality of evidence in this review. We must therefore be cautious about how we interpret these data and apply it to the role of CT imaging in PE patients. We suggest that for the emergency department, the combination of CT and point-of-care echocardiography evidence for RV dysfunction (rather than CT alone) should be incorporated into the standard of care for deciding treatment plans in acute PE patients, as this study helps to show that CT does not always provide a definitive answer as to RV dysfunction in PE.

□ INHALED BUDESONIDE FOR COVID-19 IN PEOPLE AT HIGH RISK OF COMPLICATIONS IN THE COMMUNITY IN THE UK (PRINCIPLE): A RANDOMISED, CONTROLLED, OPEN-LABEL, ADAPTIVE PLATFORM TRIAL

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COVID-19 infections placed a heavy burden in the community. Multiple studies looked for potential treatments to decrease hospitalization and death. Speculation that inhaled corticosteroids could be protective during the beginning of the pandemic due to low prevalence of admitted patients with asthma and chronic obstructive pulmonary disease. Early studies had mixed results, and none of the studies were large prospective trials. This study sought to understand the effectiveness of inhaled budesonide in reducing the recovery time and rates of COVID-19 related admissions and death of high-risk patients.

The PRINCIPLE trial is an open-label, multi-arm, prospective, randomized controlled trial involving patients with COVID-19. PRINCIPLE studied interventions with hydroxychloroquine, azithromycin, doxycycline, colchicine, favipiravir, and inhaled budesonide. This was a multi-center study, and participants across the UK could enroll online or by telephone. Patients were eligible at 65 years old or 50 years old with comorbidities and had ongoing symptoms of COVID-19. The comorbidities included were heart disease, hypertension, asthma or lung disease, diabetes, hepatic impairment, stroke or neurological problems, weakened immune system, and obesity. Patients were allocated 1:1 to open groups of budesonide and usual care and were stratified by their age and presence of comorbidity. The intervention group received inhaled budesonide 800 μg twice daily in addition to usual care. Participants were followed up using an online symptom diary for 28 days after randomization. The primary outcome was hospital admission or death within 28 days, but illness duration was included later due to lower rates of hospital admission in the UK.

Patients in PRINCIPLE were enrolled into the budesonide group between April 2, 2020, and March 31, 2021. Of the 38,520 patients screened for eligibility, 2,530 (95%) of 2,655 SARS-CoV-2 positive participants were randomly assigned to inhaled budesonide (n=787), usual care alone (n=1,069), and other treatments (n=674). The observed median time to recovery was 11 days in the budesonide group compared to 15 days in the usual care group. There was evidence of benefit of time-to-first-recovery in the intervention group versus the usual care group, with a hazard ratio of 1.21 (95% Bayesian credible interval [BCI] 1.08-1.36), an estimated 11.8 days (95% BCI 10.0-14.1)

versus 14.7 days (12.3-18.0), and an estimated median benefit of 2.94 days (1.19-5.11). Of the budesonide group, 72 (9%) of 787 patients were admitted or died (71 hospital admissions with 5 deaths and one death without admission) compared to 116 (11%) of 1,069 patients in the usual care group (114 hospital admissions with 9 deaths and two deaths without admission). The odds ratio was 0.75 (95% BCI 0.55 to 1.03) with an estimated rate of 6.8% (95% BCI 4.1-10.2) versus 8.8% (5.5-12.7) and an estimated absolute percentage difference of 2.0% (-0.2-4.5).

From these data, the authors concluded that high risk patients with COVID-19 treated with inhaled budesonide recovered approximately 3 days sooner, felt better while recovering, and often had sustained recovery. The study reported that the budesonide group initially did not meet the prespecified superior threshold rate for hospital admissions or death due to a decreased in hospital admissions and deaths in the UK, presumably from vaccinations and lockdown measures. Main limitations discussed were the open-label design and the change in primary outcome after initiation of the trial due to low rates of admissions and deaths.

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Comment: With recent COVID-19 surges and vaccine hesitancy, hospitals have been overwhelmed. While open-label and not showing a statistical improvement in hospitalizations or deaths, this study provides moderate to high quality evidence for ED providers that inhaled budesonide is an inexpensive and safe treatment to reduce time to recovery for patients who are older and have comorbidities. More studies are needed, particularly evidence for vaccinated individuals, as the proportion of those vaccinated in this study was low.