

Pre-clinical and randomized clinical trial with bromhexine and N-acetylcysteine for COVID-19

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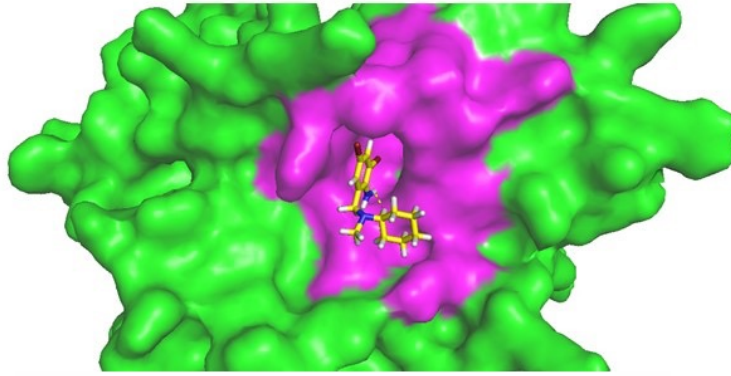
Abstract

Treatment options for mild to moderate COVID-19 is limited. N-acetylcysteine and bromhexine have antiviral activity and show potential as treatment options against SARS-CoV-2 infections. This study evaluates the *in vitro* antiviral effect of bromhexine (BMX) for SARS-CoV-2 and determines the efficacy of treatment with BMX in combination with N-acetylcysteine (NAC) to reduce clinical scores in patients with mild to moderate COVID-19. Upon evidence from pre-clinical studies, a single center randomized trial of BMX + NAC (ClinicalTrials.gov Identifier: NCT04928495) with 420 participants in total took place in Fortaleza, CE, Brazil. Out of the 420 participants 140 received placebo, 140 received NAC alone, and 140 received NAC + BMX. Patients were monitored for 10-14 days, where physicians recorded all signs and symptoms reported. Nasopharyngeal swabs and blood samples were collected for SARS-CoV-2 RNA testing during the first visit, as well as 3 and 10 days after. Blood samples were collected at first visit and 10 days after for immuno-inflammatory biomarkers measurements. Treatment with NAC+BMX reduced clinical scores and symptoms when compared to placebo group (2/26; 8% vs 7/18; 39%; $p < 0.05$). Fever ($[?]37.8^{\circ}\text{C}$) was reduced by NAC + BMX treatment when compared to treatment with NAC alone and placebo. This study was limited by a largely vaccinated population. Our analysis showed that BMX reduces SARS-CoV-2 infection *in vitro*. Clinical trial results suggested that combinatory treatment with NAC + BMX is beneficial in mild to moderate COVID-19.

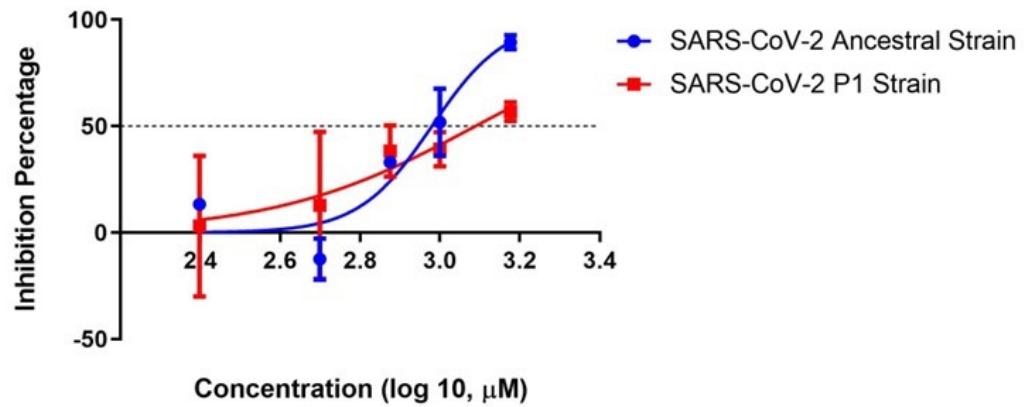
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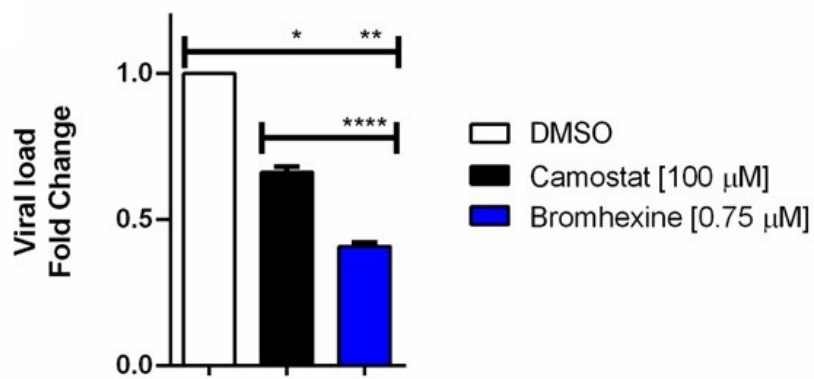
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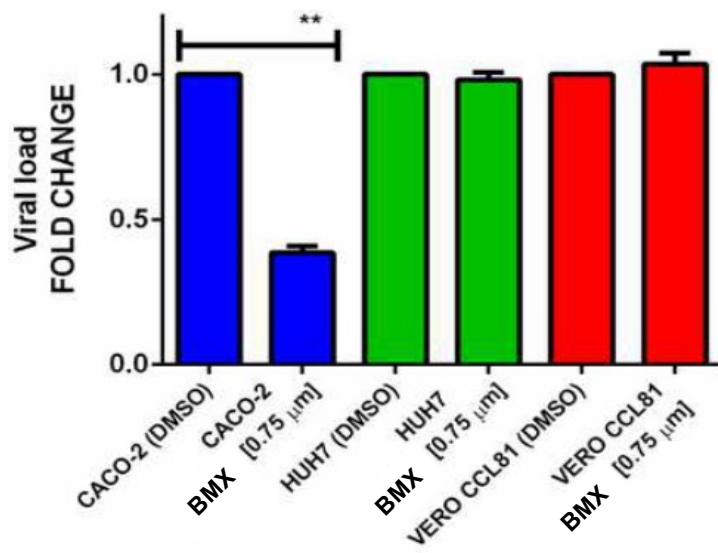
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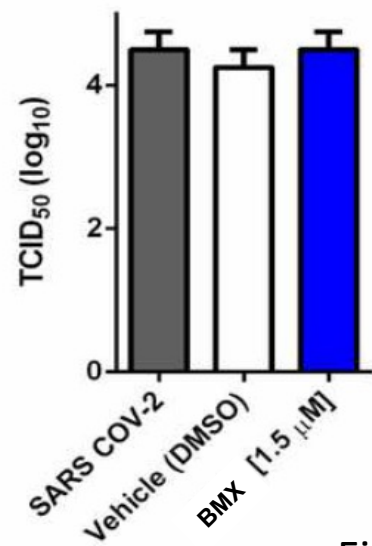


Figure 1

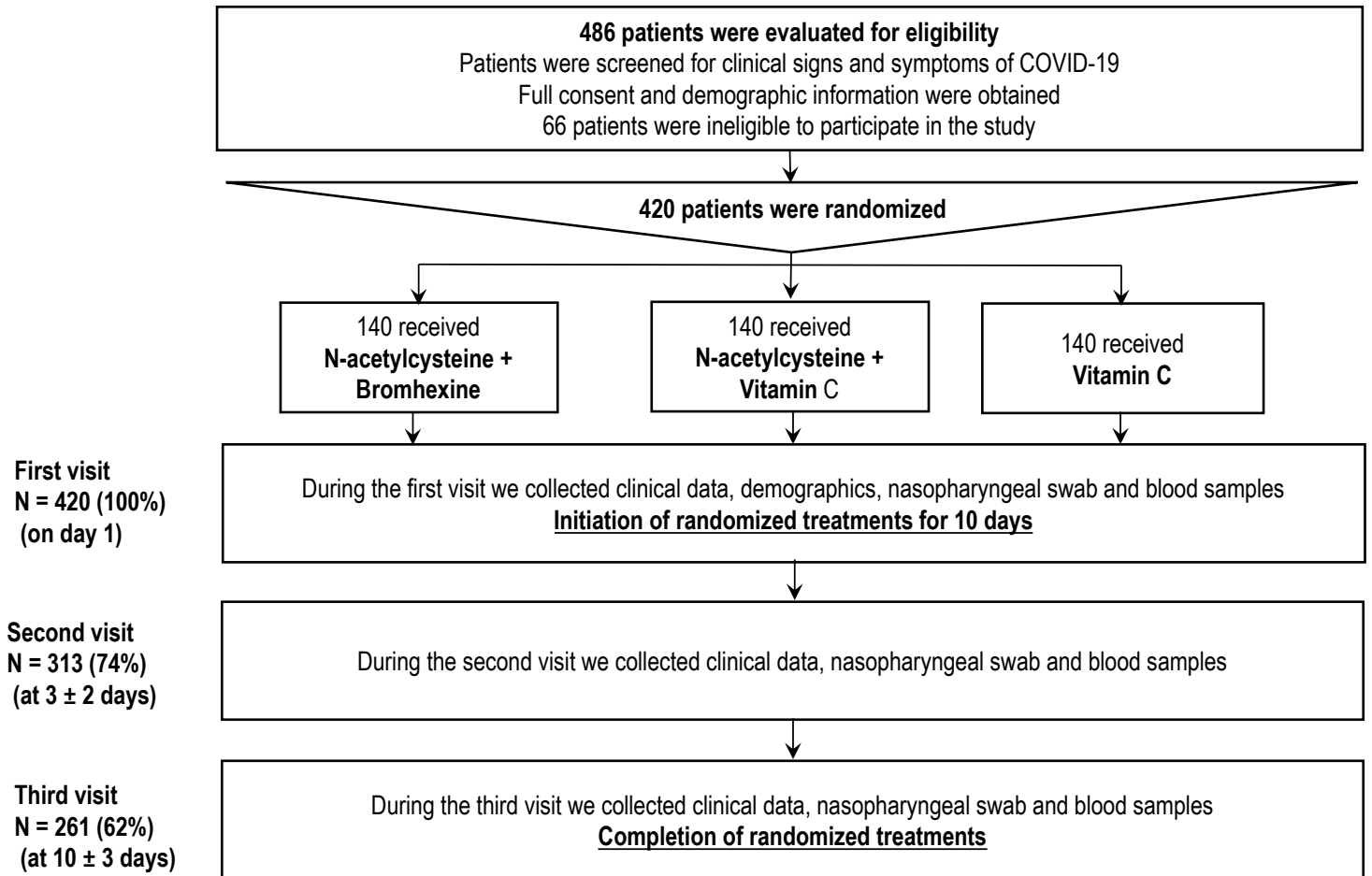


Figure 2

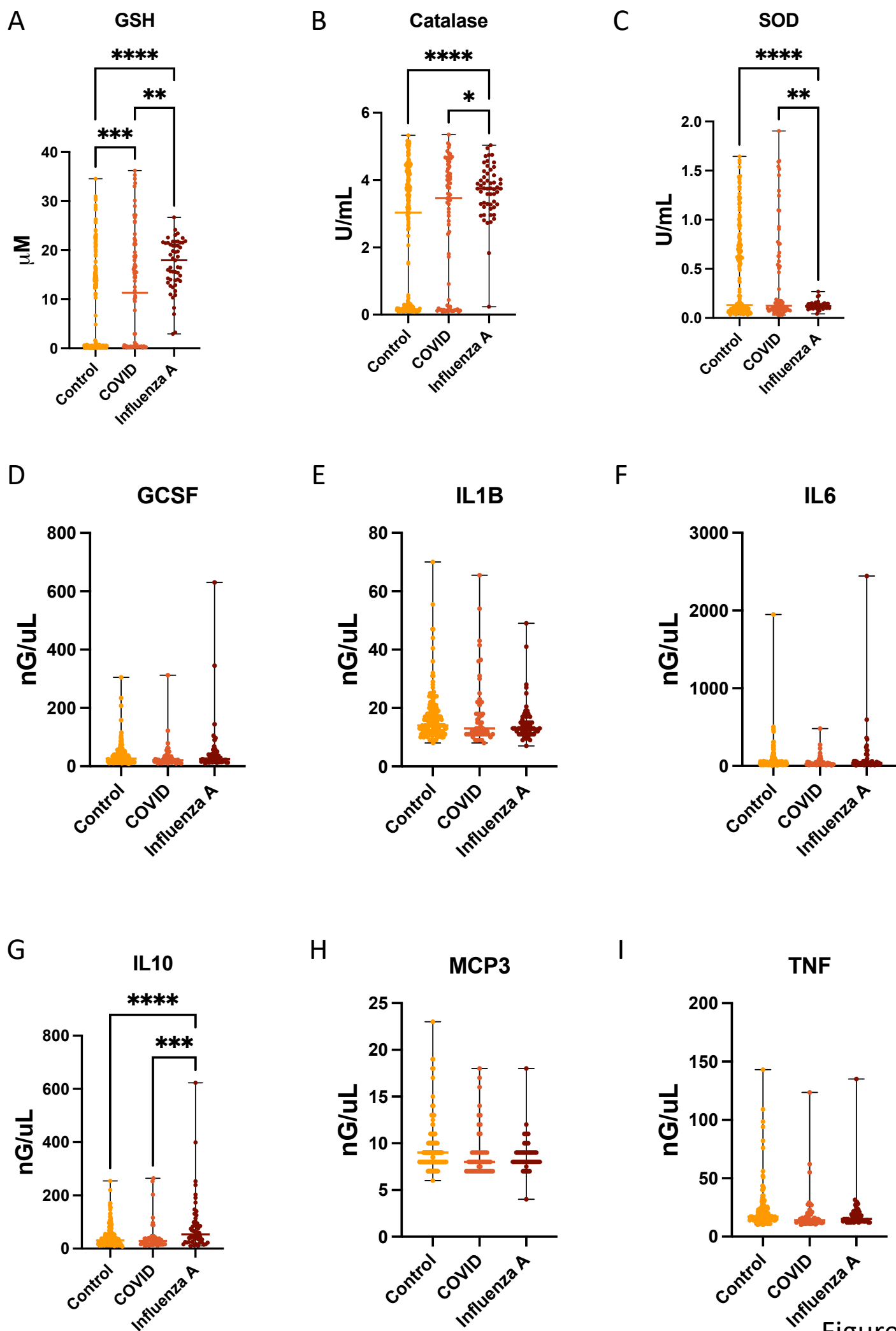
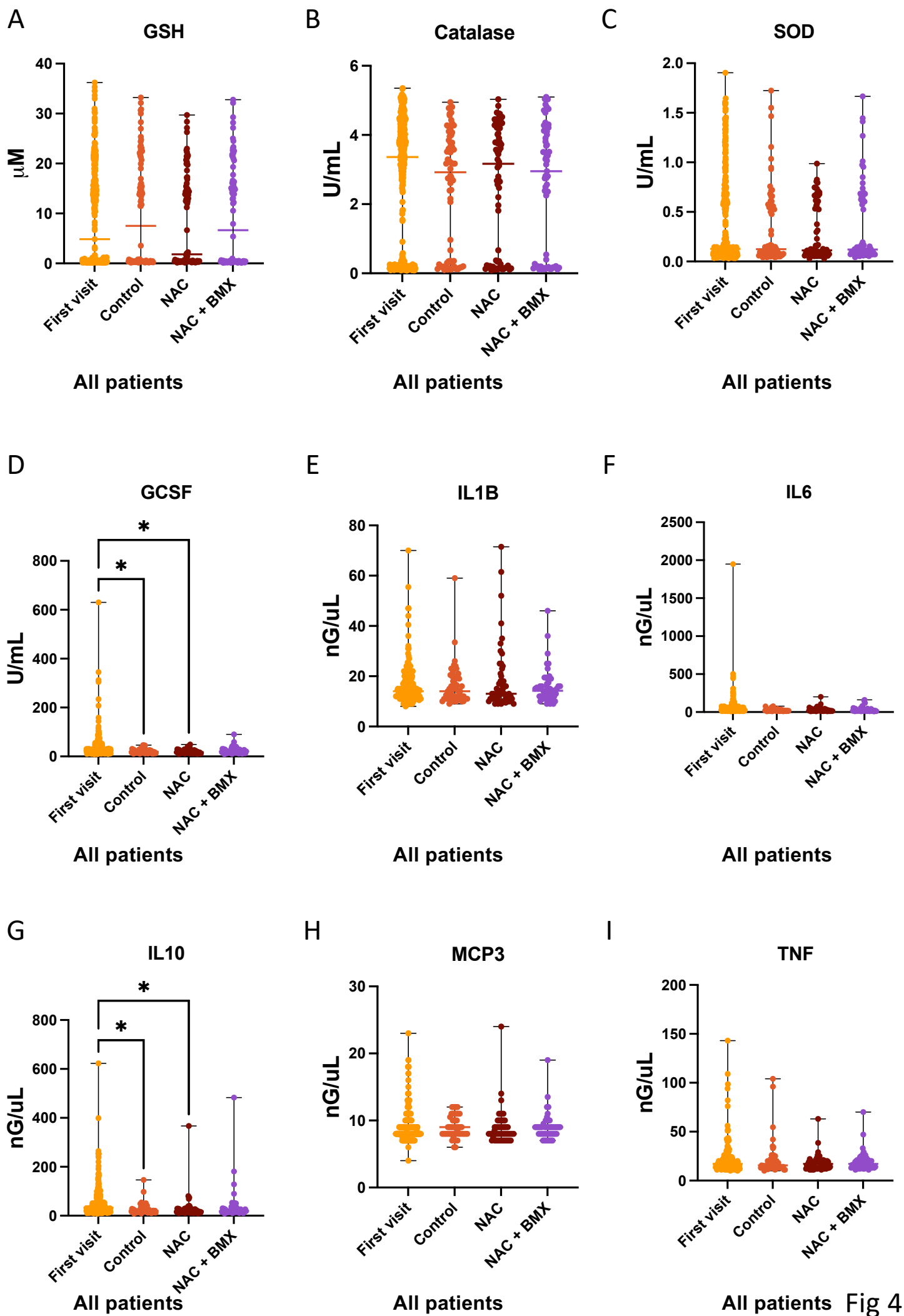
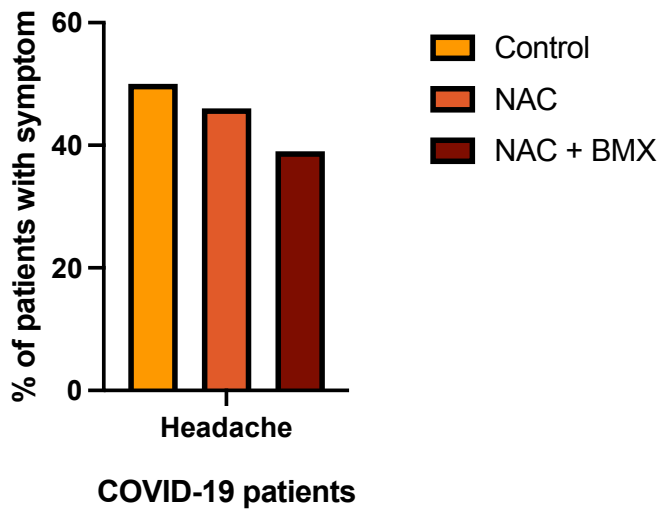


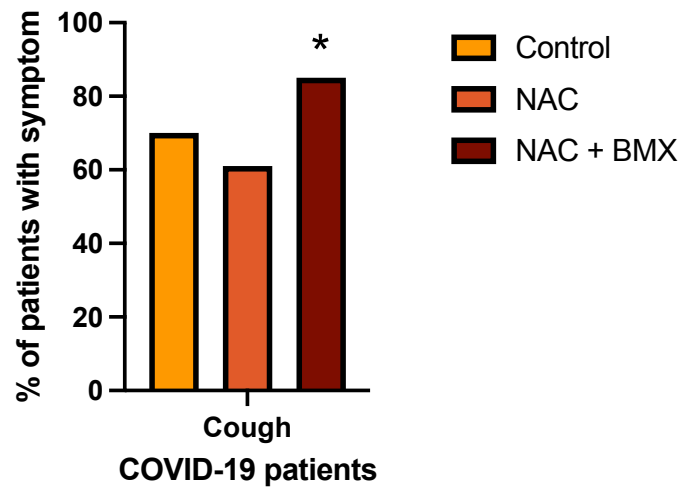
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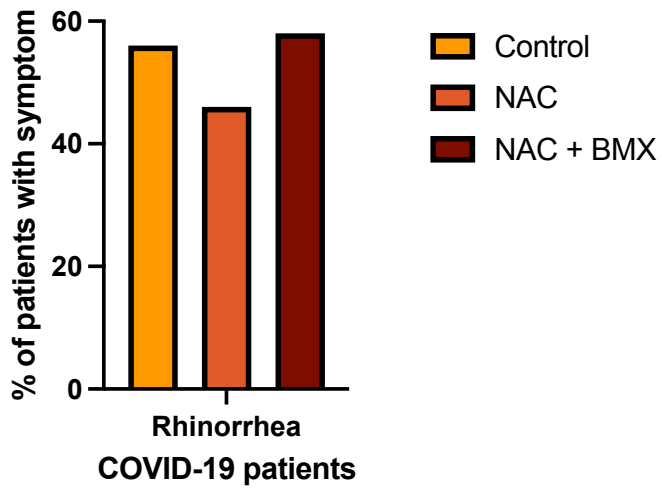
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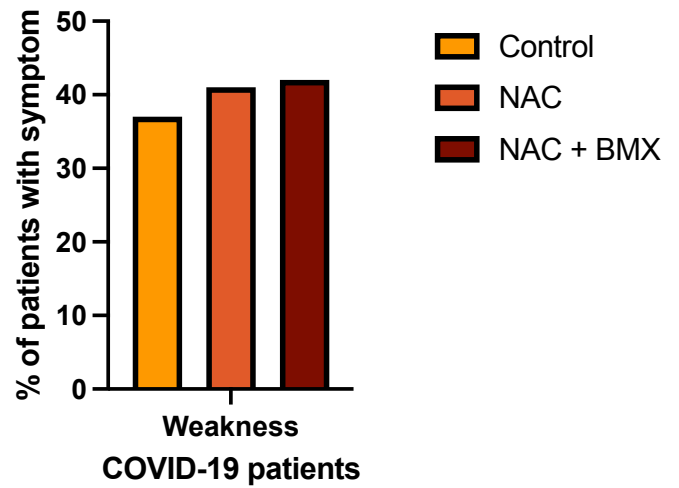
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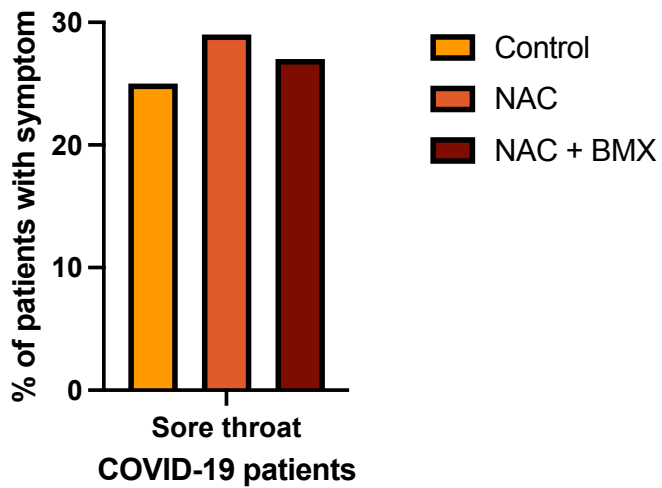
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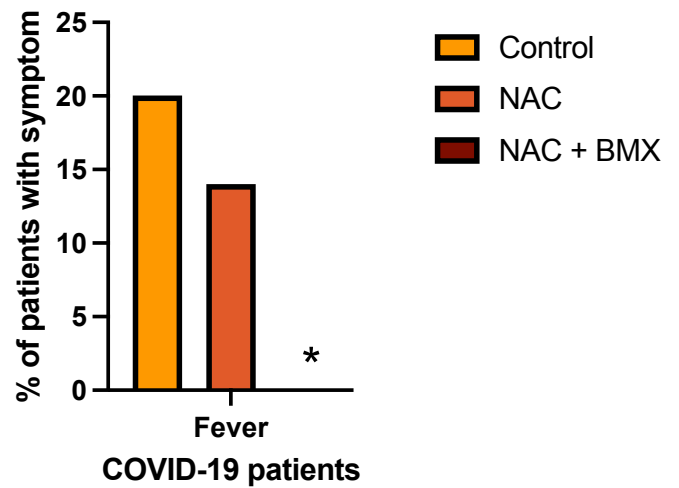
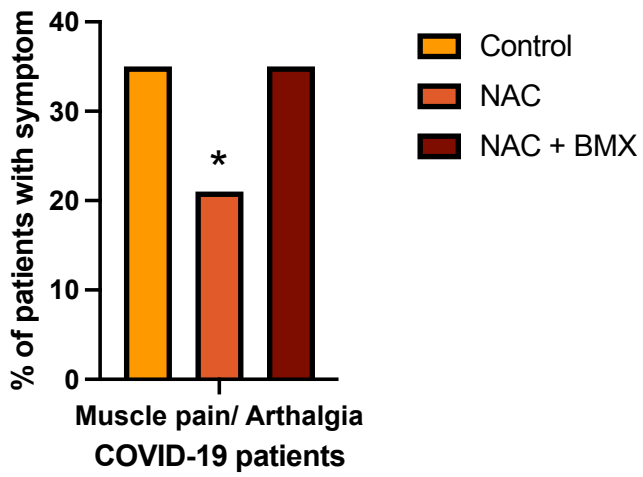
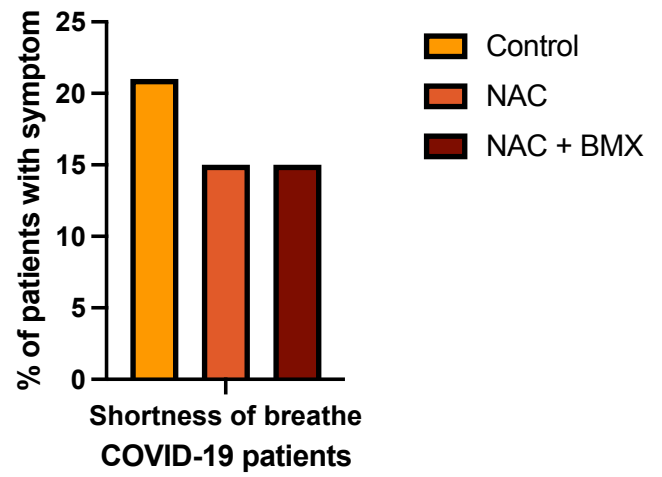


Figure 5

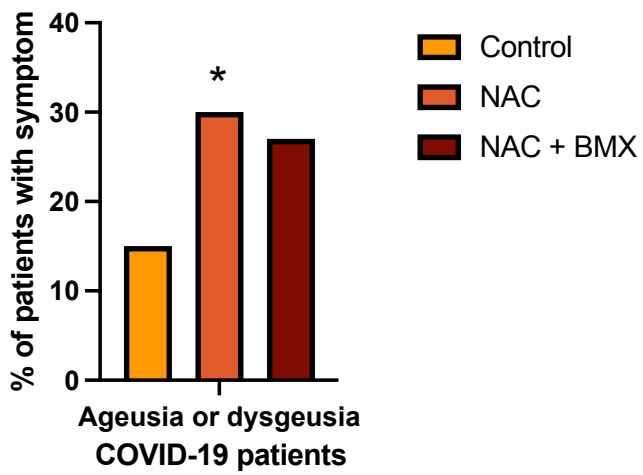
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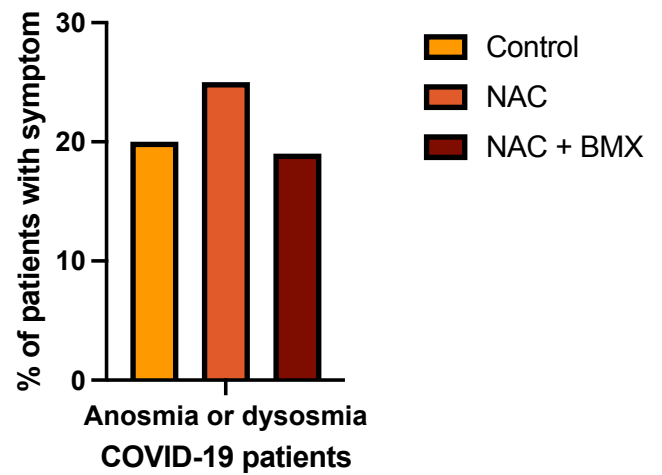
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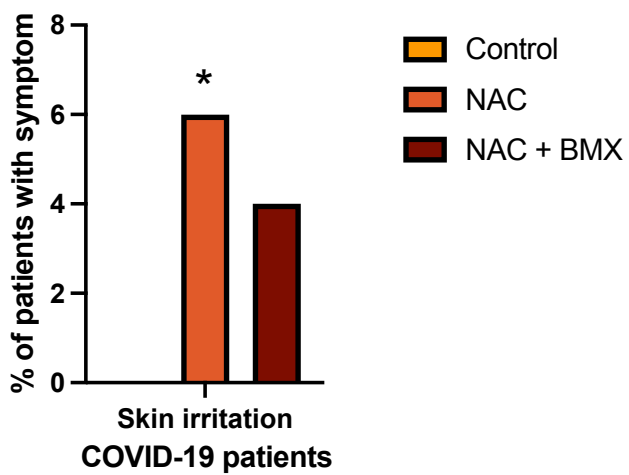


Figure 6