INTRODUCTION
Corona Virus Disease-2019 (COVID-19) is an infectious disease caused by a newly discovered coronavirus [1]. Based on guidelines from China’s National Health Commission, a combination of lopinavir and ritonavir is recommended as antiviral therapy for COVID-19 [2]. Lopinavir and ritonavir can inhibit the action of the 3CLpro enzyme, thus interfering with the replication and release of viruses from host cells [3]. However, coronavirus proteases (including 3CLpro) do not contain a symmetrical bag of C2, which is the target of HIV protease inhibitors [3]. This literature review is needed to determine the clinical outcome of using lopinavir and ritonavir in COVID-19 patients in order to find a conclusion that can be used as a basis for intervening drug administration.

METHODS
This study used a narrative review method which was carried out by searching on Pubmed and Science direct. The inclusion criteria in this study were original research articles in which they conducted research on the combination of lopinavir and ritonavir for COVID-19 therapy using established clinical outcome parameters, published in 2019 or 2020, using English, and in full text. The Article was searched using the keywords “Lopinavir and Ritonavir and COVID-19”, “Lopinavir and Ritonavir and SARS-CoV-2”, Lopinavir and Ritonavir and Coronavirus disease-19 ”, and“ Lopinavir and Ritonavir and Novel Coronavirus ”. These articles were analyzed using predetermined clinical outcome parameters, namely duration of hospital stay, composite event, clinical symptom score, time to achieve negative RT-PCR, duration of mechanical ventilation, and all-cause mortality.

RESULT
After doing abstract screening and title based on the inclusion criteria, 13 articles were left to be analyzed. For mild to moderate COVID-19, nine articles were analyzed. The main data analyzed were clinical outcome, i.e. duration of hospital stay, composite event, clinical symptom score, and time to achieve negative RT-PCR. On severe to critical COVID-19, five articles were analyzed. The main data analyzed were clinical outcome, i.e. composite event, duration of hospital stay, duration of mechanical ventilation, time to achieve negative RT-PCR and all-cause mortality. Based on all reviewed articles, the majority of clinical outcome parameters showed an outcome that was no better than standard care or other drugs.

DISCUSSION
According to Jin et al. (2020), the main clinical outcome parameters for assessing the outcome of using a combination of lopinavir and ritonavir in patients with mild to moderate and severe to critical COVID-19 were duration of hospital stay, composite event, clinical symptom score, time to achieve RT-PCR. Negative, PaO2 / FiO2, duration of mechanical ventilation, and all-cause mortality. In this study, the PaO2 / FiO2 parameter was not analyzed because no article used it.

In mild to moderate COVID-19, the duration of hospital stay and composite event parameters in all articles suggest that combined use of lopinavir and ritonavir did not result in better clinical outcomes than standard care or other drugs. Meanwhile, in the clinical symptom score and time to achieve RT-PCR negative parameters, there are differences in the results in the two articles. Based on the results of the five clinical outcome parameters, four of them showed the same results, so it can be concluded that the use of a combination of lopinavir and ritonavir did not result in better clinical outcomes than standard care or other drugs in patients with severe to critical COVID-19.

CONCLUSION
From this review, it can be concluded that the combination of lopinavir and ritonavir did not produce better clinical outcomes than standard care or other drugs in COVID-19 patients.

REFERENCES
1. World Health Organization. Coronavirus. Cited 2020. Available at: https://www.who.int/health-topics/coronavirus#tab=tab_1