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Markov model of hospitalized patients with COVID-19

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Motivation and Aim: The work is aimed on developing a mathematical method to evaluate the effectiveness of treatment regimens for hospitalized patients with COVID-19. One of the most dangerous complications for patients with COVID-19 is the respiratory distress syndrome, which requires respiratory support. The respiratory support includes the invasive and noninvasive mechanical lung ventilation. Because the respiratory distress syndrome is often associated with high interleukin-6 levels [1], COVID-19 is recommended to be treated with interleukin-6 inhibition, yet its effectiveness is under question [2]. Our idea is to use a Markov multistate model to describe the changes in patients' respiratory and resulting statuses via cohort analysis and then compare the dynamics for two groups: those who got interleukin-6 inhibitors, and those who didn't. Thus, we can study the effectiveness of interleukin-6 inhibition for patients with COVID-19.

Methods and Algorithms: We built the Markov chain model, that included five stages: no respiratory support, invasive (IV) and noninvasive (NIV) types of ventilation, recover with discharge from hospital, and death (Fig. 1). Patients were divided in two groups: those who were treated with inhibitors and those without. The transition probabilities of the model were estimated for two groups separately using the multinomial logistic regression. The 95 % confidence intervals were found using bootstrap method.

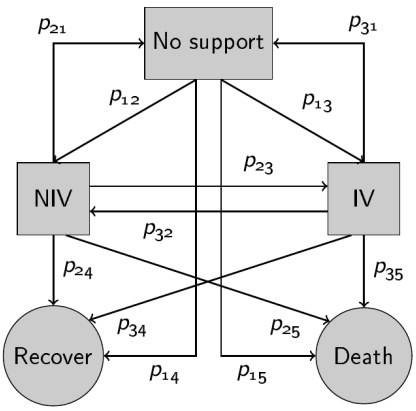

Fig. 1. Transition diagram of the Markov model of hospitalized patients with COVID-19. Arrows represent transitions between states, circles represent absorbing states. NIV = noninvasive ventilation, IV = invasive ventilation. p_{ij} are the probabilities of transitions from state i to state j

Results: The results show that using inhibitors reduces the probability of transition to death state from no support or NIV states by 4.5 times on the first five days of patient treatment. After that time the death case probabilities have no significant differences. The patients with no support who got inhibitors have 3 times lower transition rates to IV state and 1.6 times higher transition rates to NIV state. The dynamics of patients already on mechanical ventilation does not differ whether inhibitors were used or not.
Conclusion: The Markov model based on respiratory support types showed that inhibitors can prevent patients, who were not under mechanical ventilation, from receiving invasive type of ventilation. There is a reduction of death risk for those patients, but it is short termed. This indicates that the Markov modelling can be used to clarify the impact of different treatment methods on COVID-19 dynamics. The multistate approach also affords a further elaboration to model improvement, as well as estimation of cost effectiveness and the amount of required resources.
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