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Mathematical modeling of COVID-19 with partial comorbid subpopulations and two isolation treatments in Indonesia

Muhammad Abdurrahman Rois, Fatmawati, Cicik Alfiniyah

Department of Mathematics
Faculty of Science and Technology
Universitas Airlangga
Surabaya 60115, Indonesia

email: roizmuhammad.math@gmail.com, fatmawati@fst.unair.ac.id,
cicik-a@fst.unair.ac.id

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Abstract

In this study, we analyze a mathematical model of COVID-19 with comorbidity to understand the transmission dynamics of COVID-19 with other infectious diseases. Mathematical analyses were presented, including model validation, positivity and boundedness of solutions, equilibrium points, basic reproduction number, and stability of the equilibrium point. Moreover, this disease is endemic in Indonesia, with the obtained basic reproduction number $R_0 = 1.57$. As a result, subpopulation infections increased significantly with decreased detection rates for both individuals with or without comorbidities.

Key words and phrases: COVID-19, comorbid subpopulations, basic reproduction number, stability.
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1 Introduction

In December 2019, the COVID-19 virus was discovered in the Wuhan-Hubei Province of China and it spread quickly to many other countries [1, 2, 6, 8]. In general, the COVID-19 main symptoms are fever, dry cough, and fatigue. Other symptoms include chest pain and tenderness, nasal congestion, headache, conjunctivitis, diarrhea, loss of taste or smell [2, 7]. Additionally, human infections might first cause minor symptoms before progressing to more serious ones [5]. Individuals with previous comorbidity (such as diabetes, lung and heart disease) are more likely to develop a severe disease with stronger COVID-19 symptoms than individuals who do not have comorbidity [3]. In the case of COVID-19 comorbidity in Indonesia, 12 different diseases have been recorded which range from the most at risk to the least at risk; namely, hypertension, diabetes mellitus, heart, pregnancy, lung, kidney, immune disorders, cancer, other respiratory disorders, asthma, tuberculosis, and liver [4].

2 Model formulation

The COVID-19 infection model is divided into eight subpopulations; namely, susceptible (S), Exposed without comorbidity (E), Exposed with comorbidity (E_C), infected without comorbidity (I), infected with comorbidity (C), isolated with treatment (H), isolated without treatment (J), and recovered (R).

In this model, the susceptible subpopulation increases with recruitment or birth rate, denoted by π, and can become infected by contact with infected individuals without comorbidity and with comorbidity, denoted by β_1 and β_2 with α as the proportion. Furthermore, δ_1 and δ_2 are the progressions from exposed to infection without comorbidity and with comorbidity, respectively. Isolation from infection, denoted by h_1, h_2 and θ, δ, as the proportion without comorbidity and with comorbidity, respectively. The parameters r_1, r_2, r_3, and r_4 indicate the recovery rate of the subpopulations infected without comorbidity, infected with comorbidity, isolation with treatment, and isolation without treatment. Furthermore, deaths from each subpopulation are denoted by μ and deaths from COVID-19 in subpopulations I, C, H, and J are denoted by d_1, d_2, d_3, and d_4. The compartment diagram in Figure 1 describes the COVID-19 model.

Based on the compartmental diagram in Figure 1, we have the following

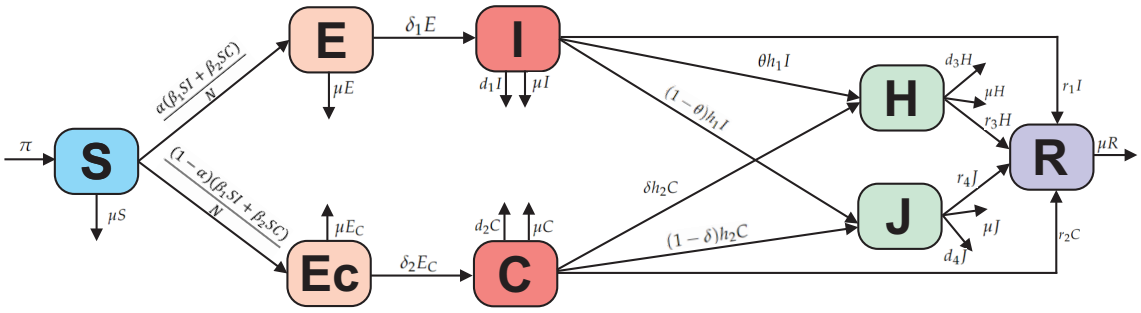

Figure 1: Compartmental diagram of the COVID-19 model with comorbidity

system of differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \pi - \frac{\beta_1 SI}{N} - \frac{\beta_2 SC}{N} - \mu S,\\
\frac{dE}{dt} &= \frac{\alpha\left(\beta_1 SI + \beta_2 SC\right)}{N} - \delta_1 E - \mu E,\\
\frac{dE_c}{dt} &= \frac{(1-\alpha)\left(\beta_1 SI + \beta_2 SC\right)}{N} - \delta_2 E_c - \mu E_c,\\
\frac{dI}{dt} &= \delta_1 E - h_1 I - r_1 I - d_1 I - \mu I,\\
\frac{dC}{dt} &= \delta_2 E_c - h_2 C - r_2 C - d_2 C - \mu C,\\
\frac{dH}{dt} &= \theta h_1 I + \delta h_2 C - r_3 H - d_3 H - \mu H,\\
\frac{dJ}{dt} &= (1-\theta)\, h_1 I + (1-\delta)\, h_2 C - r_4 J - d_4 J - \mu J,\\
\frac{dR}{dt} &= r_1 I + r_2 C + r_3 H + r_4 J - \mu R.
\end{aligned} \tag{2.1}$$

3 Results and discussion

3.1 Model validation

Parameter fitting of the system (2.1) based on cumulative data infected in Indonesia from November 1, 2020, to May 19, 2021, to validate the model in Figure 2. Parameter fitting using the command *lsqcurvefit* with the obtained value $MAPE = 0.028579$ and the new parameter values are obtained in Table 1.

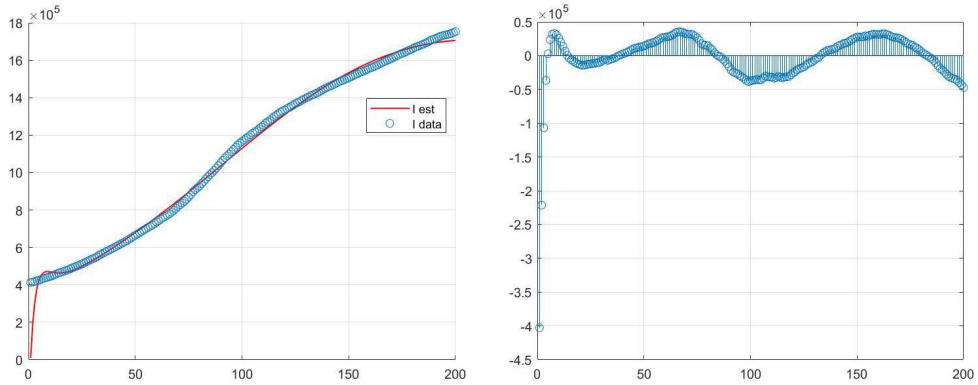

Figure 2: Parameter fitting results and their residues from the model.

Table 1: Parameter values according to fitting of COVID-19 in Indonesia.

Parameter	Value	Parameter	Value	Parameter	Value
π	3783175.865	r_1	0.087527	δ	0.2349
β_1	0.5524	r_2	3.987×10^{-5}	θ	0.25353
β_2	55348	r_3	0.54385	h_2	0.11161
α	0.49383	r_4	0.37245	d_4	0.34042
δ_1	0.028911	d_1	0.036233	μ	0.0138
δ_2	0.22241	d_2	0.18549		
h_1	0.11791	d_3	0.28641		

3.2 Positivity and boundedness of solutions

The change in total population is given by

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dE_C}{dt} + \frac{dI}{dt} + \frac{dC}{dt} + \frac{dH}{dt} + \frac{dJ}{dt} + \frac{dR}{dt} \leq \pi - \mu N,$$

whose solutions gives

$$N(t) \leq \frac{\pi}{\mu} + \left(N(0) - \frac{\pi}{\mu} \right) e^{-\mu t}.$$

Consequently, $\lim_{t\to\infty} N(t) \leq \frac{\pi}{\mu}$. We can then conclude boundedness $N(t) \leq \frac{\pi}{\mu}$.

Considering the above solutions, we have that the model has a bounded solution in a feasible region Ω, where

$$\Omega = \left\{ (S,\ E,\ E_C,\ I,\ C,\ H,\ J,\ R) \mid N(t) \leq \frac{\pi}{\mu} \right\}.$$

Next, we show the positivity of the solution of system (2.1).

Theorem 3.1. *Let* $S,\ E,\ E_C,\ I,\ C,\ H,\ J,$ and R *be the system solution* (2.1). *If* $S(0) \geq 0$, $E(0) \geq 0$, $E_C(0) \geq 0$, $I(0) \geq 0$, $C(0) \geq 0$, $H(0) \geq 0$, $J(0) \geq 0$, *and* $R(0) \geq 0$, *then all solutions are positive for every* $t \geq 0$.

1. Take the first equation of the system (2.1) as follows:

$$\frac{dS}{dt} = \pi - \frac{\beta_1 SI}{N} - \frac{\beta_2 SC}{N} - \mu S.$$

Let $\eta = \frac{\beta_1 I}{N} + \frac{\beta_2 C}{N}$.

$$\frac{d\left(e^{\mu t + \int_0^t \eta ds} S(t)\right)}{dt} = \pi e^{\mu t + \int_0^t \eta ds},$$

From homogeneous and non-homogeneous solutions, we get

$$S(t) = \int_0^t \pi e^{\mu y + \int_0^y \eta\ dx} dy \times e^{-\mu t - \int_0^t \eta\ ds} + S(0) e^{-\mu t - \int_0^t \eta\ ds}.$$

So $S(t)$ is positive for $t \geq 0$.

2. Take the fifth equation of the system (2.1) as follows:

$$\frac{dE}{dt} = \frac{\alpha(\beta_1 SI + \beta_2 SC)}{N} - \delta_1 E - \mu E \geq -\delta_1 E - \mu E, \text{ or } \frac{dE(t)}{dt} \geq -E(\delta_1 + \mu),$$

Hence

$$E(t) \geq E(0) e^{-(\delta_1 + \mu)t},$$

Thus $E(t)$ is positive for $t \geq 0$. Additionally, the same method may be demonstrated progressively starting with $E_C(t)$, $I(t)$, $C(t)$, $H(t)$, $J(t)$, $R(t)$.

3.3 Equilibrium point and basic reproduction number

The equilibrium point of the system (2.1) is obtained by setting the right-hand side to zero. Therefore, the disease-free equilibrium point is:

$$X^0 = (S_0,\ E_0,\ E_{C0},\ I_0,\ C_0,\ H_0,\ J_0,\ R_0) = \left(\frac{\pi}{\mu},\ 0,\ 0,\ 0,\ 0,\ 0,\ 0,\ 0\right).$$

Furthermore, the basic reproduction number, denoted R_0, is obtained using the next-generation matrix method FV^{-1} [5, 6]:

$$FV^{-1} = \begin{bmatrix} \frac{\alpha\beta_1\delta_1}{a_1a_3} & \frac{\alpha\beta_2\delta_2}{a_2a_4} & \frac{\alpha\beta_1}{a_3} & \frac{\alpha\beta_2}{a_4} \\ \frac{(1-\alpha)\beta_1\delta_1}{a_1a_3} & \frac{(1-\alpha)\beta_2\delta_2}{a_2a_4} & \frac{(1-\alpha)\beta_1}{a_3} & \frac{(1-\alpha)\beta_2}{a_4} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix}.$$

So $R_0 = \rho(M) = R_I + R_C$, with $R_I = \dfrac{\beta_1\delta_1\alpha}{a_1a_3}$ and $R_C = \dfrac{\beta_2\delta_2(1-\alpha)}{a_2a_4}$.

Next, we obtain the second equilibrium point; namely, the endemic equilibrium point $K^* = (S^*,\ E^*,\ E_C^*,\ I^*,\ C^*,\ H^*,\ J^*,\ R^*)$ with:

$$S^* = \frac{\pi}{\mu R_0},\ E^* = \frac{\pi\alpha}{a_1}\left(1-\frac{1}{R_0}\right),\ E_C^* = \frac{(1-\alpha)\pi}{a_2}\left(1-\frac{1}{R_0}\right),\ I^* = \frac{\pi\alpha\delta_1}{a_1a_3}\left(1-\frac{1}{R_0}\right),$$
$$C^* = \frac{(1-\alpha)\pi\delta_2}{a_2a_4}\left(1-\frac{1}{R_0}\right),\ H^* = \frac{\pi K_1}{a_5}\left(1-\frac{1}{R_0}\right),\ J^* = \frac{\pi K_2}{a_6}\left(1-\frac{1}{R_0}\right),\ \text{and}$$
$$R^* = \frac{\pi}{\mu}\left(1-\frac{1}{R_0}\right)\left(\frac{r_1\alpha\delta_1}{a_1a_3} + \frac{r_2\delta_2(1-\alpha)}{a_2a_4} + \frac{K_1r_3}{a_5} + \frac{K_2r_4}{a_6}\right).$$

with $K_1 = \frac{\theta\alpha h_1\delta_1}{a_1a_3} + \frac{\delta h_2\delta_2(1-\alpha)}{a_2a_4}$ and $K_2 = \frac{(1-\theta)\alpha h_1\delta_1}{a_1a_3} + \frac{(1-\delta)h_2\delta_2(1-\alpha)}{a_2a_4}$.

The existence of the endemic equilibrium point X^* depends on the value of R_0. Moreover, if $R_0 > 1$ then $S^*,\ E^*,\ E_C^*,\ I^*,\ C^*,\ H^*,\ J^*$, and R^* is positive and the endemic equilibrium point X^* exists.

3.4 Global stability analysis

3.4.1 Global stability of the disease-free equilibrium point

Theorem 3.2. *The disease-free equilibrium point* $X^0 = (S_0,\ E_0,\ E_{C0},\ I_0,\ C_0,\ H_0,\ J_0,\ R_0)$ *is said to be globally asymptotically stable if* $R_0 < 1$ *and unstable if* $R_0 > 1$.

Proof. Define the Lyapunov function:

$$L = \kappa_1 E + \kappa_2 E_C + \kappa_3 I + \kappa_4 C + \frac{\kappa_5 E^2}{2} + \frac{\kappa_6 E_C^2}{2} - \frac{\kappa_7 I^2}{2} - \frac{\kappa_8 C^2}{2}, \qquad (3.2)$$

where

$$\kappa_1 = \frac{a_1 a_2 a_3 a_4}{\alpha}, \kappa_2 = \frac{a_1 a_2 a_3 a_4}{1-\alpha}, \kappa_3 = \frac{\pi \beta_1 a_1 a_2 a_4}{\mu N}, \kappa_4 = \frac{\pi \beta_2 a_1 a_2 a_3}{\mu N},$$
$$\kappa_5 = \frac{\pi \beta_2 a_1^2 a_3 \delta_2 (1-\alpha)}{\alpha \mu N}, \kappa_6 = \frac{\pi \beta_1 a_2^2 a_4 \delta_1 \alpha}{\mu N (1-\alpha)}, \kappa_7 = \frac{\pi \beta_1 a_1 a_2 a_3 a_4}{\mu N}, \kappa_8 = \frac{\pi \beta_2 a_1 a_2 a_3 a_4}{\mu N}.$$

We now determine whether the Lyapunov function L is strong or weak for X^0.

$$L\left(\overrightarrow{x}^*\right) = \kappa_1 E_0 + \kappa_2 E_{C0} + \kappa_3 I_0 + \kappa_4 C_0 + \frac{\kappa_5 E_0^2}{2} + \frac{\kappa_6 E_{C0}^2}{2} - \frac{\kappa_7 I_0^2}{2} - \frac{\kappa_8 C_0^2}{2} = 0.$$

Thus $L\left(\overrightarrow{x}^*\right) = 0$. Next,

$$L\left(\overrightarrow{x}\right) = \kappa_1 E + \kappa_2 E_C + \kappa_3 I + \kappa_4 C + \frac{\kappa_5 E^2}{2} + \frac{\kappa_6 E_C^2}{2} - \frac{\kappa_7 I^2}{2} - \frac{\kappa_8 C^2}{2},$$

because $\forall (S,\ E,\ E_C, I, C, H, J, R) \neq (S_0,\ E_0,\ E_{C0},\ I_0,\ C_0,\ H_0,\ J_0,\ R_0)$, so it is proved that $L\left(\overrightarrow{x}\right) > 0$.

Thus, the equation (3.2) can be reduced to

$$\frac{\partial L}{\partial t} = \kappa_1 \frac{dE}{dt} + \kappa_2 \frac{dE_C}{dt} + \kappa_3 \frac{dI}{dt} + \kappa_4 \frac{dC}{dt} + \kappa_5 E + \kappa_6 E_C - \kappa_7 I - \kappa_8 C,$$

Let $S = \frac{\pi}{\mu}$. Then $a_1 a_2 a_3 a_4 (R_0 - 1)\left(\frac{a_1 E}{\alpha} + \frac{a_2 E_C}{1-\alpha}\right)$.

Consequently, $\frac{\partial L}{\partial t} < 0$ if $R_0 < 1$ and $\frac{\partial L}{\partial t} = 0$ if $E = 0$ and $E_c = 0$. By Lasalle's invariance principle, the disease-free equilibrium point in the spread of COVID-19 (X^0) is globally asymptotically stable if $R_0 < 1$. □

3.4.2 Global stability of the endemic equilibrium point

Theorem 3.3. *If $R_0 > 1$, then there is a global asymptotically stable and endemic equilibrium point.*

Proof. The Lyapunov function is defined as follows:

$$L = \frac{1}{2}[S_S + E_E + E_{cE_c} + I_I + C_C + H_H + J_J + R_R]^2, \qquad (3.3)$$

where $S_S = (S - S^*)$, $E_E = (E - E^*)$, $E_{cE_c} = (E_c - E_c^*)$, $I_I = (I - I^*)$, $C_C = (C - C^*)$, $H_H = (H - H^*)$, $J_J = (J - J^*)$, and $R_R = (R - R^*)$. We now determine whether the Lyapunov function is strong or weak for X^*.

$$L\left(\overrightarrow{x}^*\right) = \frac{1}{2}\left[S_S^* + E_E^* + E_{cE_c}^* + I_I^* + C_C^* + H_H^* + J_J^* + R_R^*\right]^2,$$

where $S_S^* = (S^* - S^*)$, $E_E^* = (E^* - E^*)$, $E_{cE_c}^* = (E_c^* - E_c^*)$, $I_I^* = (I^* - I^*)$, $C_C^* = (C^* - C^*)$, $H_H^* = (H^* - H^*)$, $J_J^* = (J^* - J^*)$, $R_R^* = (R^* - R^*)$ Thus $L\left(\overrightarrow{x}^*\right) = 0$. Next,

$$L\left(\overrightarrow{x}\right) = \frac{1}{2}[S_S + E_E + E_{cE_c} + I_I + C_C + H_H + J_J + R_R]^2.$$

Since $\forall\,(S,\ E,\ E_C, I, C, H, J, R) \neq (S^*,\ E^*,\ {E_c}^*,\ I^*,\ C^*,\ H^*,\ J^*,\ R^*)$, we have $L\left(\overrightarrow{x}\right) > 0$. Next, we reduce equation (3.3) to:

$$\frac{\partial L}{\partial t} = [S_S + E_E + E_{cE_c} + I_I + C_C + H_H + J_J + R_R]\,\frac{d}{dt}\,[S + E + E_C + I + C + H + J + R]\,.$$

Let $\pi = \mu\left(S^* + E^* + E_C^* + I^* + C^* + H^* + J^* + R^*\right)$. Then π is the product of

$$-\left[S_S + E_E + E_{CE_C} + I_I + C_C + Q_Q + H_H + J_J + R_R\right]$$

and

$$[\mu(S_S + E_E + I_I + C_C + Q_Q + H_H + J_J + R_R) + d_1 I_I + d_2 C_C + d_3 H_H + d_4 J_J]\,.$$

Consequently, $\frac{\partial L}{\partial t} < 0$ if $R_0 > 1$ and $\frac{\partial L}{\partial t} = 0$ if $S = S^*,\ E = E^*,\ E_C = E_C^*,\ I = I^*,\ C = C^*,\ H = H^*,\ J = J^*,\ R = R^*$. By Lasalle's invariance principle, the endemic equilibrium point in the spread of COVID-19 (X^*) is globally asymptotically stable if $R_0 > 1$. □

3.5 Simulation

In this simulation, the graph of the stability of the disease-free equilibrium point is shown in Figure 3 with the parameter values given in Table 1 except for the parameter $h_1 = h_2 = 0.4$, the value is $R_0 = 0.784 < 1$. Furthermore, the graph of point stability endemic is shown in Figure 4 given in Table 1, the value is $R_0 = 1.57 > 1$. Some initial values can show behavior toward the equilibrium point. Thus, the disease-free and endemic equilibrium points is globally asymptotically stable. Based on the given parameter values obtained $R_0 > 1$, there is an outbreak of disease due to COVID-19. Therefore, it is necessary to take control measures to reduce this outbreak.

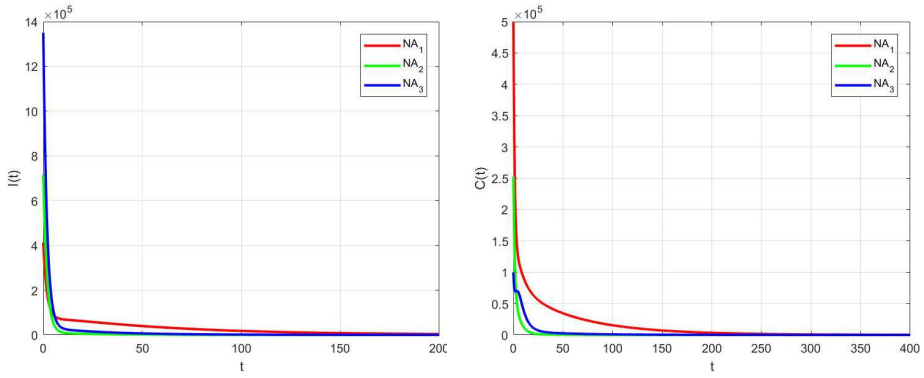

Figure 3: Graph of model ($R_0 < 1$).

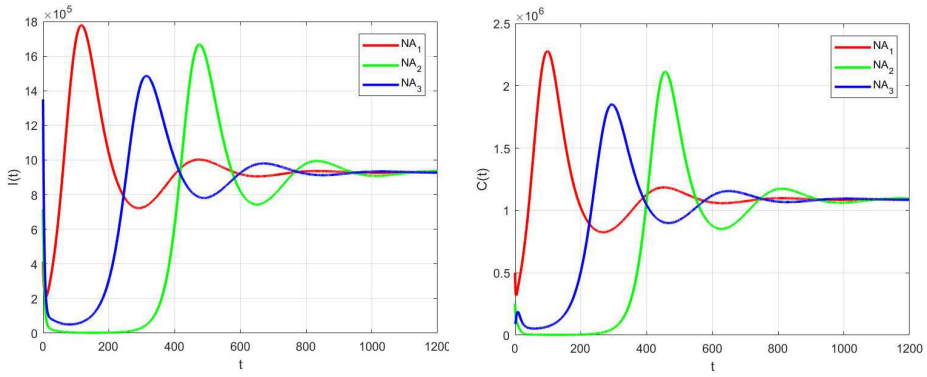

Figure 4: Graph of model ($R_0 > 1$).

4 Conclusions

In this article, we proposed and investigated a mathematical model for the dynamics of COVID-19 disease that considers comorbidity when predicting COVID-19 consequences. The suggested model has been calibrated using the total confirmed infection cases in Indonesia. Using the next-generation matrix approach, the basic reproduction number was obtained. The model has an asymptotically stable disease-free equilibrium provided that the basic reproduction number is less than one. Furthermore, the model has an asymptotically stable endemic equilibrium provided that the basic reproduction number is more than one. Individuals with comorbidity have a greater

risk of infection and so there is a need for more supervision and preventive measures such as wearing masks, maintaining distance, proper sanitation, etc.

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