True pandemic state and a lack of capacity of hospitals and mechanical ventilations in Slovakia during the SARS-COV-2 pandemic wave in August 2020 -May 2021

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Abstract. During the second SARS-COV-2 pandemic wave in Slovakia (August 2020 - June 2021) reported data did not capture real health care demand and the capacity of hospitals and mechanical ventilations for COVID-19 patients was exceeded. Real time quantitative polymerase chain reaction (RT-qPCR) and lateral flow antigen (LFAg) test incidences were strongly biased due to a variation of the total volume of tests administered and sample selection. Also, confirmation of COVID-19 related deaths was often significantly delayed. Available data thus failed to characterize the true extent of the pandemics. To fill this gap we perform a retrospective analysis of the time series of epidemic indicators and estimate dynamics of the true pandemic state in Slovakia during the pandemic wave. We estimate that on average approximately 20.0% more hospital beds and 19.2% more mechanical ventilators were needed in hospitals than reported bed occupancy in Slovakia during the period November 2020 -March 2021. Our estimates rely on a linear relationship between total adjusted incidence in a form of weighted linear combination of RT-qPCR and LFAg incidences and hospitalizations data lagged by 8 days. The linear relationship systematically emerges before and after the epidemic peak and the real epidemic state is estimated by a projection of the observed data on the corresponding linear manifold. The methodology is applicable to epidemic data worldwide.

Summary of Results

- The demand exceeded the capacity of the hospital beds for COVID patients in the Slovak Republic by approximately 20.0% during the peak of the pandemic wave in December 2020 March 2021.
- The demand exceeded the capacity of the hospital beds with mechanical lung ventilation for COVID patients in the Slovak Republic by approximately 19.2% during the pandemic wave in November 2020 February 2021.
- The average clinical sensitivity of the lateral flow antigen tests compared to RT-qPCR tests was approximately 37% during the pandemic wave in October 2020 - June 2021 in the Slovak Republic.

1 Introduction

1.1 Uncertainty in epidemic data

Reliable data are critical for monitoring of epidemic dynamics and for decision making on public health policies. Despite a vast amount of data on SARS-CoV-2 pandemics there is a large degree of uncertainty in all types of epidemic data including infection incidence, number of hospitalized patients with COVID-19 and number of COVID-19 related deaths.

The sources of uncertainty in the data are diverse: observed incidence measured by testing programs is limited by sample size, sample bias, and test parameters, hospitalization data are subject to limited bed, equipment, and personnel capacities, particularly during epidemic peaks, and data on COVID-19 related deaths are limited by methodological issues including sample bias and staff shortage during the epidemic peaks [1-4]. All data are furthermore subject to (often significant) delays in reporting [5]. See also [6] for a survey of biases in seroprevalence data. These limitations need to be taken into account in an estimation of dynamics of the real extent of the pandemics, particularly during periods of a severe epidemic state.

The uncertainty in data has consequences. Public health policies depend on observed epidemiological data and under- or over- reporting may lead to wrong decisions. It also creates a significant hurdle in epidemic modelling as limitations in observed data impede model calibration. This in turn makes the decision process on health policies and other epidemic mitigation measures even more difficult and partially blind.

1.2 Our work

We combine multiple publicly available data sources to identify a robust linear relationship in data that emerges outside of the periods of severe epidemics. During these periods we assume that the true pandemic state is also governed by the same linear relationship, however, the limitations in the observed data violate it and the data points do not lie on the identified linear pandemic manifold. We estimate the true pandemic state by a projection of the observed data onto the linear manifold. The particular form of the projection (orthogonal projection in normalized data sets) reflects an equal distribution of

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uncertainty between various sources of the data. The estimate of true pandemic state allows us to measure the extent of a lack of capacity of hospitals and mechanical ventilations during the peak of the pandemic wave.

We apply the methodology developed in this work to the epidemic data from the Slovak Republic during its second SARS-CoV-2 pandemic wave (August 2020 - June 2021). For a period of more than a month during this wave Slovakia ranked within the top 3 countries with the largest number of reported COVID-19 related deaths per capita in the world [7]. Our particular choice to study data from the Slovak Republic introduces an additional interesting and important feature that stems from complexity in infection incidence data. Slovakia conducted massive rapid antigen testing by lateral flow antigen (LFAg) tests complementary to regular real time quantitative polymerase chain reaction (RT-qPCR) tests [8]. On average 0.53 RT-qPCR and 7.84 LFAg tests per capita were performed in Slovakia before July 1st, 2021 [9,10]. Due to significant differences in these two diagnostic technologies and a disproportion between the number of tests administered using them, the observed infection incidence needs to be viewed as a twodimensional vector with individual components - the volume of the positive RT-qPCR and LFAg tests. Similarly the total number of tests is a vector. Our approach identifies a linear combination of the two incidences into total adjusted incidence that robustly agrees with the lagged hospital bed occupancy outside of the epidemic peaks.

2 Data

While most countries report their RT-qPCR incidence as a diagnostic characteristic of their epidemic situation, during the studied period Slovakia used two types of tests for monitoring. Individuals could choose between an RT-qPCR and an LFAg test. While the scope of RT-qPCR test program was limited, the LFAg testing was conducted on a massive scale with mass antigen testing in October-November 2020 [8] and the mass antigen screening program in January-April 2021.



Fig. 1. Time series of 7-day moving averages of hospitalizations and mechanical ventilations and

RT-qPCR and LFAg 7-day incidences in Slovakia. Hospitalizations are lagged by 8 days behind the incidence , MLV are lagged for additional 14 days (see Section 3.2 for details) and scaled to fit hospitalizations (see Section 3.3

for details) in March-June 2021.

Throughout this work we use the following public data sets [11] from the Slovak Republic shown in Fig. 1:

• **RT-qPCR** daily incidence

The RT-qPCR test detects viral genetic material through the reverse transcription quantitative polymerase chain reaction. The sample is collected using two nasopharyngeal and one throat swab. Various unidentified types of RT-qPCR tests were used during the second pandemic wave in Slovakia (August 2020 – June 2021). The tests were available to the public for free in case the individuals were indicated by the Regional Public Health Authority or self-indicated due to a presence of COVID-19 symptoms or a close contact with an infected individual. RT-qPCR tests were also offered on a commercial basis to the general public. The incidence is reported daily by the National Health Information Center [12] and updated retrospectively by the Ministry of Health of the Slovak Republic [11].

• LFAg daily incidence

The LFAg test detects specific SARS-CoV-2 antigens in nasopharynx through a rapid lateral flow chromatographic immunoassay. Slovakia used almost 43 million rapid lateral flow antigen tests during the studied time period. The majority of the tests used were STANDARD Q COVID-19 Ag (SD Biosensor) complemented by Panbio COVID-19 Ag (Abbott). Biocredit COVID-19 Ag (RapiGen) was used to a limited extent. The tests were available for free to the general public on a mass scale. The LFAg incidence data have limitations as they were significantly updated a few months back in time repeatedly during the second pandemic wave in Slovakia and they contained errors on a daily basis. None of the three types of the LFAg tests were validated on a large sample in Slovakia by RTqPCR tests. The incidence is reported daily by the Ministry of Investments, Regional Development and Informatization of the Slovak Republic [9] and updated retrospectively by the Ministry of Health of the Slovak Republic [11]. We use solely the updated data set in our analysis. We do not include the data from the mass LFAg testing in October-November 2020 in our data set as they create significant deviations from the long term testing trend. Inclusion of the data disturbs the linear relationship between incidence and hospitalizations to a much larger extent than the underestimation of the incidence by omission of the data used here.

Both types of tests had their advantages and disadvantages: different accessibility of testing for the public, duration of test evaluation, number of sample swabs

collected from a tested individual, and reliability of the test result. Individuals were often selecting their diagnostic test type based on their current situation, time constraints, presence of disease symptoms, or contacts with positively tested individuals. While RT-qPCR tests were typically used in hospitals in all suspected cases (from January 2021), in the general public many tested individuals opted for a simpler, quicker and easily accessible LFAg test instead, even if they were symptomatic. Negative test results within the last 7 days (or 14 or 21 days) of any of these two types of tests were required in certain regions or in the whole country for a relief from a mandatory home isolation for the most of the duration of the second pandemic wave in Slovakia. Fig. 2 shows the total volume of the tests administered.



Fig. 2. Total volume of administered RT-qPCR (red) and LFAg (black) tests. The mass antigen testing in October – November 2020 is not included in the data and it is also not added to the corresponding incidence.

Although in some countries each admitted SARS-COV-2 positive case diagnosed by an LFAg test is confirmed by a RT-qPCR test, this was not the case in Slovakia where in many cases only LFAg was performed instead of a RT-qPCR test, particularly in many hospitals during the period November - December 2020.

• Hospitalizations

The daily hospitalization data represent the reported total number of occupied beds in hospitals in the Slovak Republic by patients with confirmed positive COVID-19 tests. The capacity of the beds designated for the COVID-19 patients was adjusted when possible and needed throughout the second wave by a reprofilization (repurposing) of the other types of hospital beds. The data are reported by the regional hospitals to the Ministry of Health of the Slovak Republic and published [11].

• Mechanical lung ventilations

The MLV data represent the reported total number of occupied beds in hospitals by patients connected to MLV with positive COVID-19 tests. The capacity of the beds equipped with MLV designated for the COVID-19 patients was adjusted when possible and needed throughout the second wave by a reprofilization of the other types of hospital beds. The data are reported by the regional hospitals to the Ministry of Health of the Slovak Republic and published [11].

The numbers of occupied beds and MLV are reported daily. However, the publicly available data on hospital admissions and discharges also published by the Ministry of Health of the Slovak Republic [11] disagree with the number of occupied beds. According to the analytic unit of the Ministry, the published admissions and discharges data are subject to significant underreporting on both sides due to lack of reporting from certain hospitals [13]. Nevertheless, the data on daily hospital admissions contain additional information that we use for a check.

In addition to data from the Slovak Republic we also study the data from Spain as an example of a linear dependence of lagged hospitalizations behind incidence. We use two data sources: hospitalizations [14] and daily RT-qPCR positive tests incidence [15] which cover the studied time period Oct 12, 2020 - May 2, 2021. We selected Spain as a demonstrative example here as it shows an excellent consistent agreement with the linear trend between incidence and hospitalization data. We have surveyed all European countries for such a linear trend and identified it at least partially (in time) in all countries.

Note that to eliminate natural weekly oscillations in all sources of data we systematically use moving 7-day averages or 7-day totals. Each 7-day average and total is identified with the day in the middle to eliminate the time shift introduced by the averaging and summation.

3 Results

3.1 Total Adjusted Incidence

The RT-qPCR and LFAg incidences are typically added up to describe the total incidence. This is also the practice of the COVID automaton policy in Slovak Republic enforced by the Ministry of Health that monitors the epidemic situation weekly in 79 individual counties and nationwide [16]. However, to account for diagnostic differences in tests we model the observed total adjusted incidence as a weighted linear combination of the RT-qPCR and the LFAg incidence:

Here we set the coefficient of RT-qPCR incidence to be equal to one without loss of generality. The weight coefficient c of the LFAg incidence can be interpreted as a ratio of relative diagnostic performance of the tests, i.e. a multiplicator characterizing how many samples tested by LFAg would be positive on average per one LFAg positive test if the samples were tested by RT-qPCR tests. There are numerous studies of sensitivity of various types of LFAg tests compared to (various types) of RT-qPCR tests (see the comprehensive summary in the SI of [10]). However, caution is necessary in an interpretation of these parameters as most of these studies were conducted on symptomatic patient samples that significantly differ from the sample tested in Slovakia. Note that here we neglect the difference in clinical specificity of the two types of tests as we believe its effect on our analysis is negligible.

We select the value of the coefficient c based on the best linear fit between the total adjusted incidence and the lagged hospitalization data outside of the epidemic peaks (see the next section for details). We consider the values of c in the interval [0,5], where c = 1 and c = 2 represent, respectively, estimated 100% and 50% average sensitivity of a LFAg test compared to a RT-qPCR test. On the other hand c = 0.5 represents 50% average sensitivity of a RTqPCR test compared to a LFAg test.

3.2 Linear pandemic manifold

Existing studies and datasets identify the proportion of cases that required a hospitalization from reported positive COVID-19 cases [17,18] and the lag of reported hospitalizations behind the new case detection by a test [19]. Similar ratio estimates are for the proportion of cases that required a mechanical lung ventilation and their reporting delay [19]. The proportion varies with the age of infected individuals. However, all these studies rely on a single source of measured observed incidence - RT-qPCR tests.

A linear relationship is apparent in some countries between the observed incidence and the lagged hospitalizations, see an example of Spain in Fig. 3.



Fig. 3. Relation of the 7-day RT-qPCR incidence and the moving 7-day average of hospitalizations lagged by 8 days in Spain (October 12, 2020 – May 2, 2021). An observed linear trend is displayed in red for an illustration. The slope

of the red line is 0.66 (95% CI: 0.61-0.70). The intercept with the vertical axis is at 6759 (95% CI: 6013-7505).

For Slovakia such a good approximation by a linear relationship cannot be identified for any reasonable lags (0-14 days) if incidence is measured solely by the RT-qPCR tests or solely by the LFAg tests. Thus we search for a linear relationship of the total adjusted incidence that includes both RT-qPCR and LFAg tests and the reported hospitalization data lagged by *D* days. To keep the number of parameters of the model as small as possible, we do not introduce a parameter for the mutual lag between RT-qPCR LFAg incidence. Its inclusion influences our results only very marginally (not shown).

Hospitalizations (t+D) = a+b*Total Adjusted Incidence (t)

The linear pandemic manifold serves as a basis of an estimate of the true pandemic state. Outside of the epidemic peaks and the periods of mass testing, the data lie on the manifold. We calculate the parameters of the linear manifold by a linear regression of the total adjusted incidence and lagged hospitalizations (both with 7-day moving averages) on the data outside of the epidemic peak - 60 days at the onset of the wave (Oct 10 - Dec 9, 2020) and 60 days at the tail of the wave (Apr 16 - Jun 15, 2021). The relative diagnostic sensitivity parameter c and the lag D were optimized simultaneously by minimization of the residuals of the linear regression along with parameters a and b, see Fig.4. The cut-off dates (Dec 9 and Apr 16) were selected to obtain a robust data fit that does not significantly change when the interval is shortened or extended by a few days (eventually, these dates can be selected simultaneously as a part of the optimization process). The optimization was performed in MATLABC.



Fig. 4. Sum of squares of residuals of a linear regression of total adjusted incidence and the lagged 7-day moving average of hospitalizations over the time periods Oct 10 – Dec 9, 2020 and Apr 16 - Jun 15, 2021. The optimized parameters are the coefficient of relative test sensitivity *c* and the lag of hospitalization data *D*. The dark color corresponds to low values of the error.

The optimal parameters c = 2.68 and D = 8 days correspond to approximately 37% clinical sensitivity of LFAg tests on a large predominantly asymptomatic sample compared to the RT-qPCR tests and 8 days lag of reported hospitalization behind the reported incidence. Note that the value of c in the interval (2, 3) does not significantly alter the total error. The value of the slope parameter b = 0.48(95% CI: 0.46-0.50) of the pandemic manifold has a practical implication: the bed occupancy in hospitals is approximately a half of the 7-day total adjusted incidence 8-days ago. The vertical intercept is at a = 68.35 (95% CI: 25.85-110.86). If we take into account the large volume of the total tests (RT-qPCR+LFAg) administered, the calculated rate b is in agreement with the estimate for Spain (Fig. 3).

During the peak of the epidemic wave, we estimate the true epidemic state by a perpendicular projection of the observed data to the linear pandemic manifold. Note that perpendicular projection is not invariant to scaling of the axes. Therefore we first normalize the observed data averages (Total Adjusted Incidence and Hospitalizations) to the same mean over the studied period (Total Adjusted Incidence was scaled in this calculation by a factor F =0.36, not shown in the figure). The perpendicular projection thus distributes uncertainty in both data series equally. Fig. 5 shows the resulting linear manifold and also illustrates the projection in the rescaled variables. Fig. 6 shows a comparison of the observed data time series and the inferred estimate of the true pandemic state. The result of the projection method is not a simple linear interpolation of the underlying data: in some phases, the true pandemic state is closer to the hospitalizations, and in others to the total adjusted incidence.



Fig. 5. Total adjusted 7-day incidence vs. the 7-day moving average of hospitalizations lagged by 8 days. The linear pandemic manifold (shown in red) was calculated as a linear regression line for the subset of the data (indicated by blue and yellow, respectively, for the first and last 60 data points). A perpendicular projection is displayed for illustration (red dashed lines) at two data points. The projection was calculated for the incidence rescaled to fit the means of the two data sets.



Fig. 6. The inferred estimate of the true pandemic state compared to observed data time series. Hospital admissions are lagged and rescaled to match hospitalizations in March-June 2021.

3.3 Lack of Hospital Capacity

The obtained estimates of the dynamics of the true pandemic state allow us to additionally estimate the lack of capacity in the hospitals for both the total bed capacity for COVID-19 patients and for mechanical lung ventilations. Fig. 7 shows a comparison of the estimated real demand for hospital beds by the projection method. During the period December 2020 – March 2021 we estimate that about 20.0% of the demand exceeded the hospital's capacity. These patients would be hospitalized if they fell ill outside of the period of epidemic peak.

We see that the capacity for hospital beds was saturated at the end of November. Even the increase of the bed capacity through reprofilization of beds in the next few months could not meet the steadily increasing demand for hospitalizations. The demand exceeded the capacity the most around the end of December. After a short improvement in the first half of January a worsening trend in the second half of January followed. After a two week stagnation the excess of demand started to shrink significantly and it disappeared completely in the middle of March.

A partial check of our estimate can be performed using the hospital admission data. As discussed above, the reported hospital admission data do not agree with the reported hospital bed occupancy by patients with COVID-19 due to reporting issues with the health system. However, here we use them as an independent data set. Fig. 6 shows that our estimated true pandemic state agrees well with the hospital admissions from mid-October to mid-November (a much better fit than hospitalization and incidence data that were used in the projection method to obtain the estimate). Later the hospital admissions start to deviate from the true epidemic state similarly to hospitalization data due to the lack of hospital capacity. However, the hospital admissions data have a local peak starting after Jan 1, 2021 that is not present in the hospitalization data but it is reflected in the estimate of the true pandemic state. Finally, the hospital admissions have a peak in February followed by a systematic long-term decrease in agreement with the true pandemic state estimate.



Fig. 7. The estimate of the lack of hospital capacity (December 2020 – March 2021). The area in blue corresponds to reported hospitalizations, the area in grey corresponds to the inferred number of extra hospital beds needed over the capacity as predicted by the model. The grey region has an area 20.0% of the blue region.

A similar analysis provides an estimate of an excess of demand for the mechanical lung ventilations over the hospital capacity. Here we first need to transform the MLV data by a proper rescaling and a time lag to agree with the scale of the total adjusted incidence data. To remove any potential bias, we fit the MLV data to the hospitalization data outside of the epidemic peaks. The reciprocal value of the resulting scaling factor 1/k = 0.14 captures the proportion of hospital beds with COVID-19 patients occupied by patients on MLV. It corresponds to an average ratio of MLV and hospitalizations over a long time period. A lag D2 = 14 days represents the average lag of the MLV occupancy data behind the hospital bed occupancy. Fig. 8 shows the comparison of the estimated real demand for MLV by the projection method to the linear pandemic manifold with the reported MLV occupancy. During the period November 2020 - February 2021 we estimate that about 19.2% of the demand exceeded the mechanical ventilation bed capacity of the health system.

The dynamics of the excess demand for MLV agrees with the excess demand for the total hospital bed occupancy with a few differences: (i) our estimate captures one additional wave of excess demand for MLV in October - November 2020, (ii) hospitalizations excess demand is lagging approximately 2 weeks behind the MLV excess demand.



Fig. 8. The estimate of the lack of mechanical lung ventilations capacity (November 2020 – February 2021). The area in blue corresponds to reported bed occupation, the area in grey corresponds to the inferred number of extra

hospital beds with MLV over the capacity needed as predicted by the model. The grey region has an area 19.2% of the blue region.

4 Discussion

We have estimated the dynamics of the true pandemic state during the second pandemic wave in Slovak Republic. The true pandemic state is a characterization of the true demand for the hospital beds and the corresponding expected epidemic incidence. It does not characterize the true number of infected individuals in the population as the available data do not offer any direct characterization of this quantity. Nevertheless, the hospitalizations are typically of the main interest during peaks of epidemic outbursts and thus the estimated true pandemic state provides a useful characterization of the epidemic situation.

We also provide estimates of the lack of capacity of hospital beds and mechanical lung ventilations. These estimates may serve for an evaluation of the hospital capacity during the future waves, in a design of programs of patient reallocation and in a retrospective evaluation of the real pandemic costs.

One of the interesting features brought by the analysis is a comparison of the observed RT-qPCR and particularly LFAg incidence with the estimated true pandemic state. From mid November 2020 to March 2021 the total adjusted incidence is above (and often significantly above) the true epidemic state. We suspect that it indicates that the information provided by the observed incidence at that time was overestimating the true pandemic state, particularly, during the period mid-December 2020 to mid-January 2021. The positive case detection was thus higher during the period close to the peak of the pandemic wave. There are multiple reasons that may cause this effect: a larger proportion of tested individuals in an early stage of infection causing higher detection rate by the LFAg tests, larger public awareness of the pandemic situation and higher willingness of potentially infected individuals to get

tested, a larger proportion of cases within hospitals with better testing surveillance, a larger overall testing capacity relative to the need. Additional factors can also be involved. Note that if the detection rate were not overestimating the true pandemic state, the estimate of the excess demand for hospital beds and mechanical lung ventilations would be even higher than presented here.

Also note that we do not evaluate any effects of testing efforts to mitigate pandemics, just the information value of the observed incidence for the estimation of the true pandemic state.

We have also derived a coefficient of relative test sensitivity *c* between RT-qPCR and LFAg antigen tests. The estimated value that corresponds to a sensitivity ratio approximately 37% is well below the values in validation studies (typically 50-70% see [10] for a summary). We suspect that the low sensitivity ratio is mainly due to a different sample composition in a mass testing setting in the Slovak Republic with a majority of tested individuals with no medical or epidemiological indication for the test. Our result also offers an alternative methodology for total incidence calculation as a simple addition of RT-qPCR and LFAg tests may not provide an accurate characteristic of the situation that predicts the future hospitalizations.

The true pandemic state estimates can be compared with reported deaths and excess deaths (excess mortality) [20-22]. The reported deaths data show a very high level of temporal variation due to fluctuations in the sample selection and methodological changes and thus it is impossible to directly compare to theoretical linear trends in data even with 7-day averaging. Separately reported excess deaths data (the relative comparison of the volume of all deaths with a 5-year average over the same week or month of a year) are often used to characterize the extent of the pandemics. However, there are multiple possible interpretations of the base level of excess deaths as during the pandemics and periods of strong pandemic mitigation measures the deaths due to other reasons than COVID-19 may have non-stationary character compared to previous years. In the case of the Slovak Republic, an important issue is also a systematic delay in reporting: excess deaths in Slovakia are often adjusted more than three months back in time. A short comparison shows that the true pandemic state agrees well with the excess deaths data until mid January 2021. After that the excess deaths [22] show a systematic decline consistent with the decline of the estimated true pandemic state, however, the decline of excess deaths data starts about 5 weeks earlier.

Additional factors can improve the match of the estimated true pandemic state to the fitted data. A natural choice is an addition of lagged incidences exponentially discounted in time to total adjusted incidence to reflect the distribution of the admission of the hospitalized patients at a given time. The total quadratic residuals error of the linear pandemic manifold from the fitted data points can be decreased by adding two additional lagged incidences (by 4 and by 8 days) by approximately 20%. Although these factors change the dynamics of the estimated true pandemic state, the estimate for scope and time of the excess need for hospitalizations and MLV change only very marginally. Therefore we do not show these improved results here.

Our methodology has some limitations. The genomic data from Slovakia reveal that during the period September 2020 - June 2021 the dominant variant of the virus was changing. These different variants of SARS-COV-2 may eventually have different epidemiological parameters - relative sensitivity of detection by LFAg test compared to RT-qPCR tests and ratio of hospitalized patients to the total number of cases. Thus the constant parameters derived within our analysis are just a crude approximation of eventual time dependencies. Also, our method relies on available data with significant limitations and possible inaccuracies.

Although the analysis is limited to the second pandemic wave in the Slovak Republic and involves particular data limitations that may not be applicable elsewhere, the overall methodology of using a linear pandemic manifold for an estimation of a true pandemic state during the pandemic peaks is universal with potential application in other geographical locations.

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