COVID-19

COVID-19 MODELING EXERCISE

TECHNICAL GUIDE

Methodology and Parameters

4 May 2020

PAHO Pan American Health Organization World Health Organization Regional Office for the Americas

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CONTENT

Purpose of the modeling exercise

This modeling exercise aims to:

1. Understand the behavior of the epicurve for COVID-19 cases in countries.
2. Identify whether the current public health and social measures (PHSM) implemented in the country are having an effect on lowering the effective reproductive number (R_t).
3. Identify the effect on the epicurve and the R_t of lifting the PHSM at any given date.

This modeling, in combination with other epidemiological, healthcare, and surveillance indicators (capacity in case finding and contacting tracing), may be used to inform country decision-makers on the most appropriate timing and mechanism for lifting PHSM. This modeling need to be updated periodically and interpretation of the results and implications closely discussed with the national authorities of the country. This can be used in countries or territories where cases are reported on a daily basis.

Methodology

In order to reach the abovementioned objectives, a two-step methodology is proposed.

1. First, **estimating the effective reproductive number** (R_t) in an area or cluster of interest (nationwide or at subnational level).
   ⇨ **This is performed with EpiEstim**

2. Second, **run the projections** based on the estimated R_t, the estimated number of infectious cases, and other parameter including the implementation or lifting of certain public health measures at any given time.
   ⇨ **This is performed with CovidSIM**

The following sections specify the models as well as the parameters used at each stage.

1. Estimation of the effective reproductive number with EpiEstim

Monitoring and quantifying transmissibility over the course of the COVID-19 epidemic in countries is essential to understand the evolution of the epidemic, to forecast the impact, and to evaluate and adjust public health responses.

An important indicator for measuring transmissibility is the effective reproductive number (R_t), i.e. the average number of secondary cases caused by an infected individual in a population composed of both susceptible and non-susceptible individuals (e.g. those already immune, isolated). The R_t is an essential input for any COVID-19 related projections.

The R_t is calculated using the R-project package EpiEstim, through the command estimate_R (Cori et al., 2013), based on the daily cases reported by the country and the expected serial interval.
The parameters are defined as follows:

- The study of the epidemic curve starts from the date where there are cases occurring on a daily basis. i.e. The first day from a sequence of 3 consecutive days with a reported case.
- The incidence is computed as daily cases.
- When the cases are reported according to the confirmation date, a time gap adjustment should be applied to account for the date when the contagion took place – i.e. when the actual transmission took place. An important component of this time gap is the delay between the date of the onset of the symptoms and the date of the reporting, which is estimated to be a mean of 7 days based on the line-list data.
- The R_t was estimated on sliding weekly windows, with a parametric **serial interval mean of 4.8 days and a standard deviation of 2.3** (Liu, Funk, & Flasche, 2020; Nishiura, Linton, & Akhmetzhanov, 2020; Peak et al., 2020).

2. Projections with CovidSIM.eu

Once the R_t has been calculated, the projections are done with CovidSIM. These projections will allow a better understanding of the evolution of the epicurve. They will also help in identifying the impact of implementing or lifting interventions according to certain assumptions defined as parameters.

The proposed tool for the projections is CovidSIM (http://www.covidsim.eu/ or http://www.covidsim.de). This modeling is based on a standard deterministic SEIR model – "compartmental model" - for: susceptible [S], exposed [E], infectious [I], and recovered/removed [R]. This tool was developed specifically for COVID-19 by a modelers' group at the Eberhard-Karls-University of Tübingen at the Institute of Clinical Epidemiology and Applied Biometrics (IKEAB), Germany.

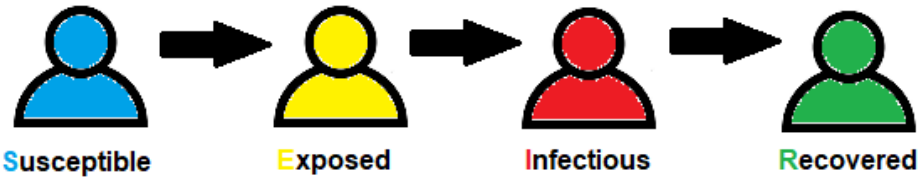


Figure 1. *Illustration of the stages in a SEIR transmission model*

The model is available free online with a dashboard display to facilitate user interaction and can be found at http://www.covidsim.eu/ or http://www.covidsim.de . Further information about CovidSIM can be found online at https://gitlab.com/exploratory-systems/covidsim/ and in publications providing examples of how this tool has been applied in some countries (N. Wilson & Baker, 2020; P. N. Wilson et al., 2020).

For additional verification, CovidSIM was compared to other SIR and SEIR models and stochastics mathematical projections to validate the results obtained, particularly with EpiEstim (Cori et al., 2019); R_0-Package (Obadia et al., 2012), review of literature for SEIR and SIR (Barraza & Pena, 2020; Ferguson et al., 2020; Kucharski et al., 2020; Leung et al., 2020; Peak et al., 2020; PinedoTaquia & Perez Nunez, 2020;

Wu et al., 2020; Zhang et al., 2020) and PAHO internal analysis. The results, when using same or similar parameters and considering differences in model structure, are comparable. The advantage of CovidSIM.eu is the embedded visualization interface provided to the user and the flexibility of the tool to accommodate different parameters.

2.1. Parameters used for modeling in CovidSIM

2.1.1. Population

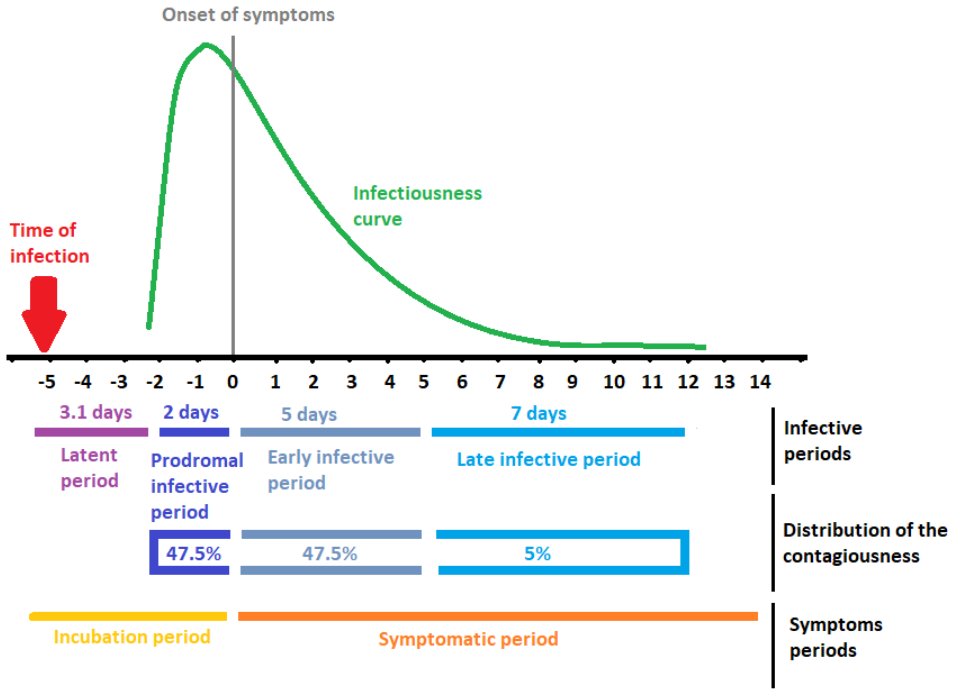
Population size: The population of the cluster/area to model, e.g. country sub-administrative divisions.
Initial infections: Cumulative number of new infections over the 7 days prior the date we want to start modelling from – i.e. those known individuals currently considered infectious. A greater number might also be considered to account for unknow asymptomatic cases.

Infections from outside of the population: Should be 0 if all transmission is assumed local.

2.1.2. Periods

Most of the parameters presented in this section and the next are based on the most up to date literature identified. The parameters are intended to reflect the Covid-19 transmission patterns (phases and periods) presented in Figure 1 below.

Figure 1. *Illustration of the transmission period of COVID-19 according to the literature (adapted by PAHO/PHE).*



The parameters used for different periods are the following:

Latency period: 3.1 days, obtained by subtracting 2 days of prodromal period to the 5.1 incubation period (He et al., 2020; Lauer et al., 2020; Li et al., 2020; Linton et al., 2020).

Prodromal period: 2 days (He et al., 2020).

Early infective period: 5 days (He et al., 2020).

Late infective period: 7 days (He et al., 2020).

Hospitalization: 14 days (suggested but can be changed by the country).

ICU admission 21 days (suggested but can be changed by the country).

Number of Erlang stages: 16 default (kept by default as suggested by the CovidSIM developers).

Modeling duration: It is recommended to perform short to medium term projections. For example, set 60 days and update the projections regularly, particularly when there are changes in the epidemiological scenario (e.g. evolution of the R_t, implementation or lifting of public health measures).

2.1.3. Contagiousness

The contagiousness parameters used are the following:

Annual average of the basic reproduction number R_o: 3.7

Amplitude of the seasonal fluctuation of R_o: 0 (Not modelled)

Day when the seasonal R_o reaches its maximum: 0 (Not modelled)

Relative contagiousness in the prodromal period: 100% (Ferretti et al., 2020; Ganyani et al., 2020; Liu, Funk, & Flasche, 2020, ; Xia et al., 2020)

Relative contagiousness in the late infective period: 2.5% (He et al., 2020; Wölfel et al., 2020)

2.1.4. Severity

The severity parameters used are the following:

Infections which will lead to sickness: 67% (P. N. Wilson et al., 2020)

Sick patients seek medical help: 50% (This parameter varies substantialy across the literature and should be modified to reflect country reality.)

Sick patients are hospitalized: 20% (European Center for Disease Prevention and Control, 2020. It can be modified to reflect country reality.)

Hospitalized cases need intensive care (ICU): 42% (European Center for Disease Prevention and Control, 2020. It can be modified to reflect country reality.)

Sick patients die from the disease: 0.7 (European Center for Disease Prevention and Control, 2020; Oke & Heneghan, 2020. This parameter varies substantially across the literature and should be modified to reflect country reality.)

2.1.5. Interventions based on case isolation

Should there be detailed information available for the country studied, these parameters should be modified accordingly.

Probability that a sick patient is isolated: 50%

Maximum capacity of isolation wards: large capacity (e.g. 1000)

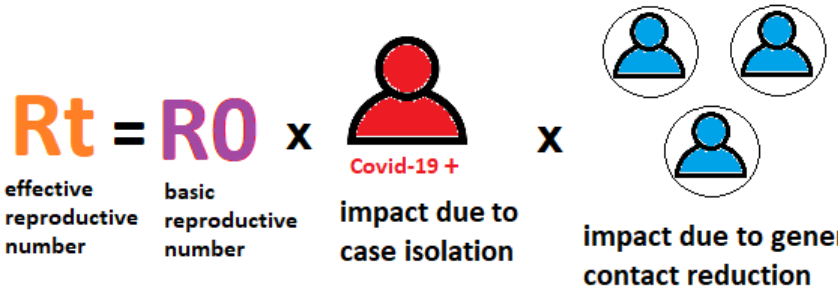
Contact reduction for cases in home isolation: 75%

Start of case isolation measures: day 1

Duration of case isolation measures: The entire duration of the modeling period. In this modelling it is easier to assume that the case isolation intervention is maintained for the entire period of the modeling, as a proportion of the cases will always be isolated.

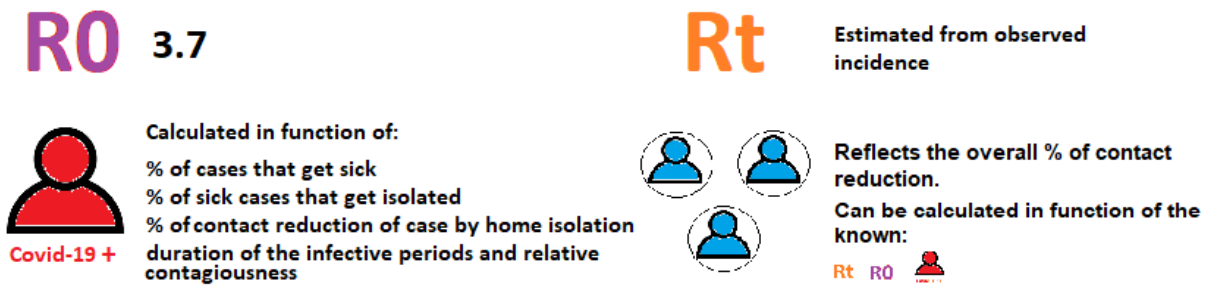
2.2. Interaction of the R_0, R_t and the interventions

The R_0, the basic reproductive number, reflects the potential behavior of COVID-19 transmission without any intervention. This R_0 is reduced by the interventions implemented in the country. It is impossible to precisely quantify the actual impact of the interventions in real life but with CovidSIM it can be modelled based on the parameters and assumptions. CovidSIM allows the user to model two interventions: the reduction of transmission by isolating the cases, and the general contact reduction (e.g. social distancing measures). The CovidSIM modelings reflect the impact of these two interventions on reducing the R_0, and on R_t as a result of the interaction, as presented in the following equation (1).

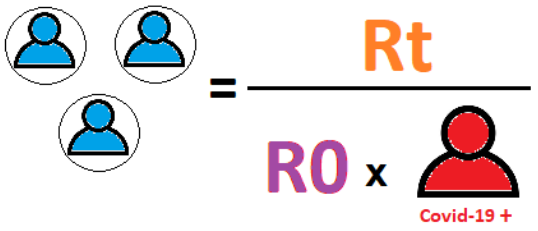


(1)

The true R_0 is unknown and, while there is a wide range of figures reported for COVID-19, for our CovidSIM modeling is assumed to be 3.7. The R_t, as explained in section 1, is based on the daily cases reported by the country and the expected serial interval, the daily incidence in the country. The R_t is a known parameter. The impact due to case isolation can be calculated based on the parameters utilized in CovidSIM, as is explored in section 2.2.5. The impact due to general contact reduction is modelled in CovidSIM only based on one parameter: the expected % reduction of contact.



Therefore, in the equation (1), we know three out of four parameters: R_t estimated based on observed incidence data, the assumed R_0 and the **calculated impact due to case isolation**. Hence, the impact due to general contact reduction will be defined by the value of the other three parameters as illustrated in the equation (2).

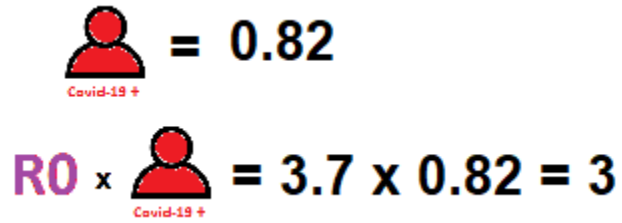


(2)

2.3. *Example for* Interaction of the R_0, R_t and the interventions

2.3.1. Adjustment of the R_0 due to case "case isolation"

With the parameters described in section 2.2. we can quantify the impact from the intervention "case isolation." For example, assuming that 67% of the cases get sick, 50% of sick patients are isolated, there is a 75% contact reduction for cases in home isolation and the different infective periods, the R_0 would be 0.82.



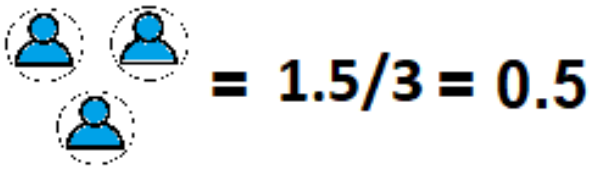
Thus, the initial R_0=3.7 considered is corrected according to the public health and social measures on contact reduction, resulting in a R_t of 3.

2.3.2. Adjustment of the R_0 due to "contact reduction"

A further intervention to reduce the R_0 is to adjust the R_t obtained above (in section 2.3.1) by applying "contact reduction." This will allow us to achieve the observed R_t, which for this example is assumed to be 1.5.

The initial R_t (adjusted by case isolation) of 3 will decrease due to the impact of contact reduction to achieve the observed R_t of 1.5. This means a further reduction of the R_t by 0.5 was achieved through the parameter "contact reduction."

(2)



Likewise, if we have a R_t of 3 (adjusted by case isolation) but want to model an observed R_t of 2, we would need a contact reduction parameter of 0.33, which is calculated as follows: [1-(2/3)] = 0.33. Lastly, to obtain an observed R_t of 1, we would need a contact reduction parameter of 0.66, which is calculated as follows: [1-(1/3)] = 0.66.

2.3.3. The "lifting of measures" scenarios

To simulate the scenarios in which measures are lifted and to visualize the projections or behavior of the epicurve after the lifting of the measures, we need to state the "contact reduction duration" (in days) up to the date at which we want to simulate the lifting of measures.

2.3.4. Examples of "contact reduction" and "lifting of measures"

Following are examples of interventions based on general contact reduction.

Scenario 1. To predict the progression of the epicurve based on an observed R_t of 1.5, with the intervention "contact reduction" in place.

Parameters:
General contact reduction: 50%
Contact reduction begins: day 1
Contact reduction duration: The whole period

Scenario 2. To predict the progression of the epicurve based on an observed R_t of 1.5, with the intervention "contact reduction" in place **to be lifted in 2 weeks**.

Parameters:
General contact reduction: 50%
Contact reduction begins: day 1
Contact reduction duration: 14 days

Scenario 3. To predict the progression of the epicurve based on an observed R_t of 2, with the intervention "contact reduction" in place.

Parameters:
General contact reduction: 33%
Contact reduction begins: day 1
Contact reduction duration: The whole period

3. Limitations

There are a number of limitations to this methodology that should be acknowledged:

- The estimated R_t is based on observed reported cases; it does not take into account asymptomatic/unreported cases.
- The parameters used to model the COVID-19 transmission and severity are based on review of current literature but may not reflect the actual behavior of the virus in the country.
- The parameters chosen to model the intervention, based on case isolation, were selected on the assumption of being the most likely to be implemented. However, it is recommended to use country specific parameters where they are known.

- As described in this document, the model projections are based on the assumed R_t. This R_t cannot be changed, so model projections vary only when interventions are added or lifted.
- The current version of CovidSIM (1.1.) does not account for country demographics in modelling. Country demographics will be available in subsequent versions.

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PAHO/IMS/PHE/COVID-19/20-0031

COVID-19

COVID-19 MODELING EXERCISE

A "HOW TO" GUIDE for CovidSIM

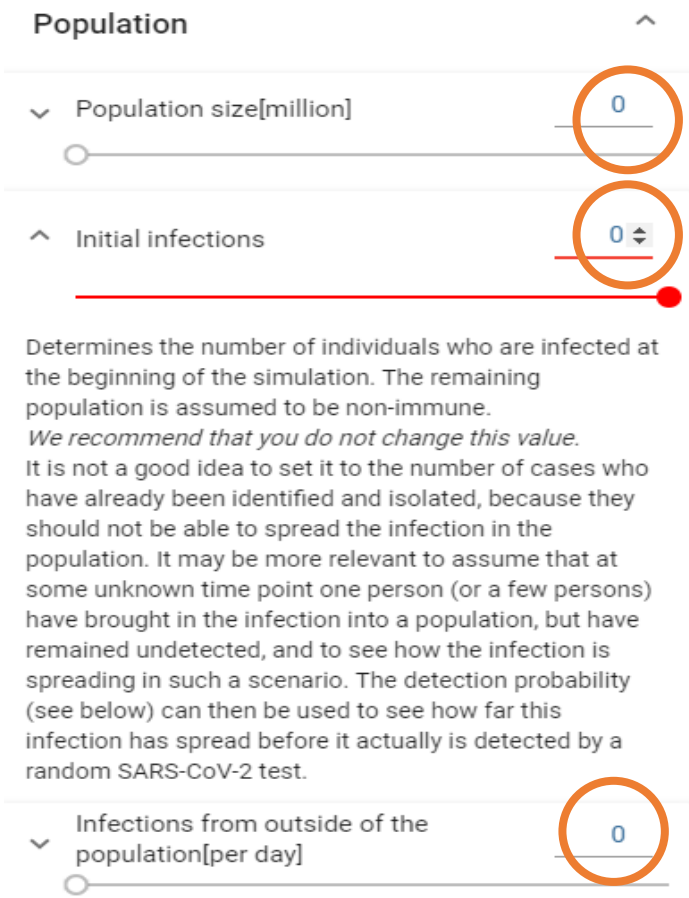
ANNEX 1

Projections with ***covidSIM.eu***

➔ Go to http://www.covidsim.eu/ or http://www.covidsim.de

Step 1:

Enter population parameters



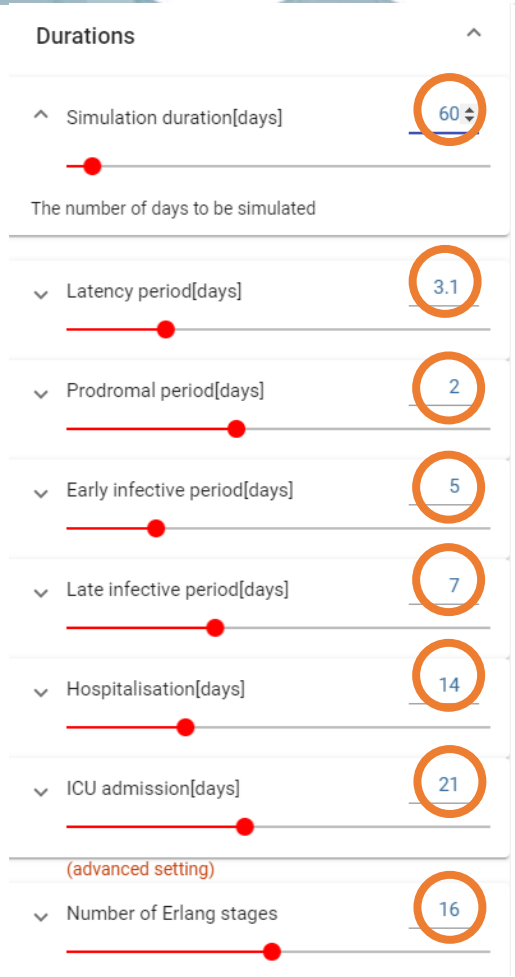
Size of population you want to model

Cumulative number of new infections over the 7 days prior the date we want to start modelling from

Should be 0 if it is assumed that all transmission is local

Step 2:

Enter Time Periods



It is recommended to perform short-median term projections e.g. 60 days

3.1 (do not change)

2 (do not change)

5 (do not change)

7 (do not change)

14 (suggested)

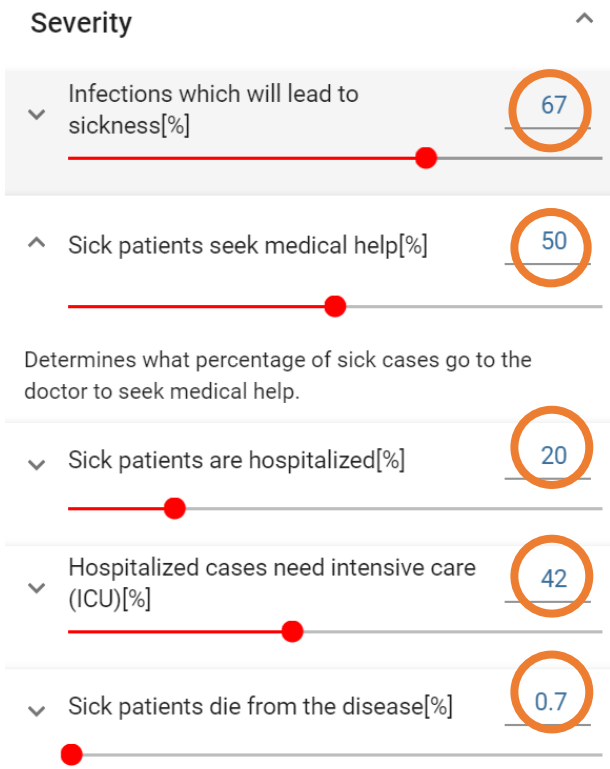
21 (suggested)

16 (default)

COVID-19

Step 3:

Enter Severity



67% (P. N. Wilson et al., 2020)

50% (by default but can be changed to reflect country reality)

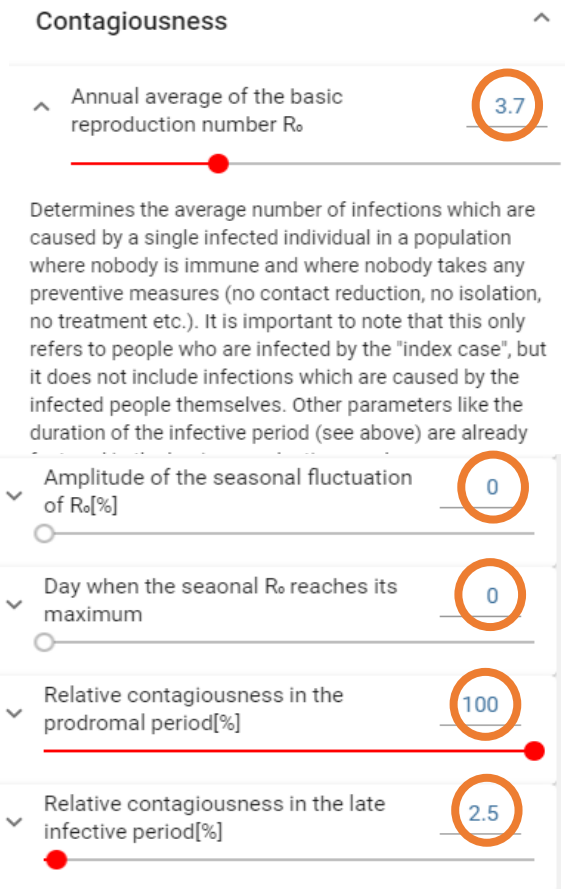
20 (European Center for Disease Prevention and Control, 2020. It can be modified to reflect country reality.)

42 (European Center for Disease Prevention and Control, 2020. It can be modified to reflect country reality.)

0.7 (European Center for Disease Prevention and Control, 2020; Oke & Heneghan, 2020. This parameter varies substantially across the literature and should be modified to reflect country reality.)

Step 4:

Enter Contagiousness



3.7 (do not change)

0 (not modeled)

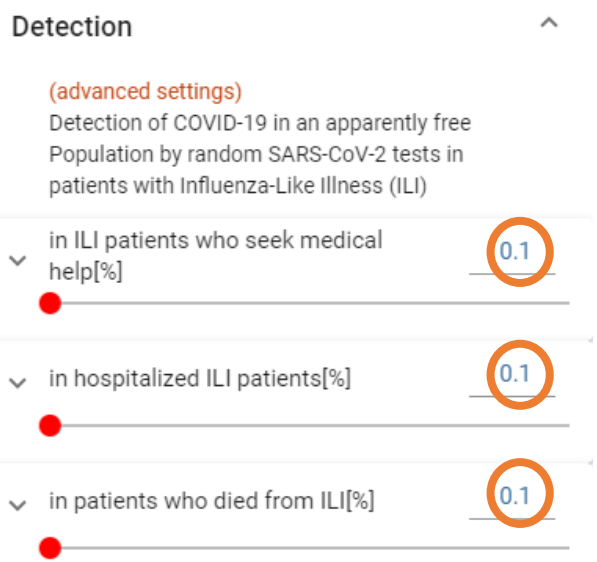
0 (not modeled)

100% (do not change)

2.5% (do not change)

Step 5:

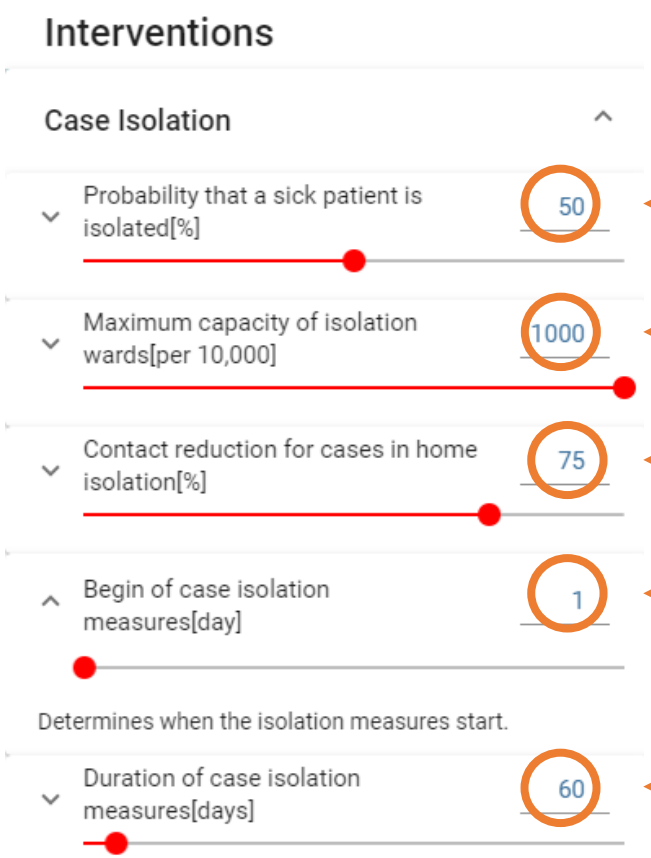
Enter Detection



Leave all parameters as set by default in the model (at 0.1).

Step 6:

Enter Interventions – Case Isolation



50% (suggested but can be changed based on country information)

Assume large capacity (e.g. 1000)

75% (suggested but can be changed based on country information)

1 day

The entire duration of the modeling period entered in Step 1 (e.g. 60 days)

With the parameters suggested here we can quantify the impact from the intervention "case isolation."

For example, assuming that 67% of the cases get sick, 50% of sick patients are isolated, and there is a 75% contact reduction for cases in home isolation, the resulting R_0 would be 0.82.

Thus, the initial R_0=3.7 considered is corrected according to the public health and social measures on contact reduction, resulting in a R_t of 3.

Step 7:

1

Lifting measures scenario: state the "contact reduction duration" (in days) up to the date at in which you want to simulate the lifting of measures.

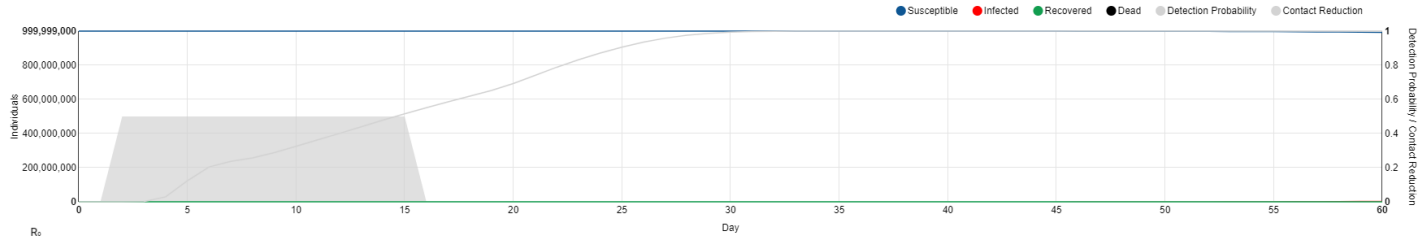
Enter General Contact Reduction

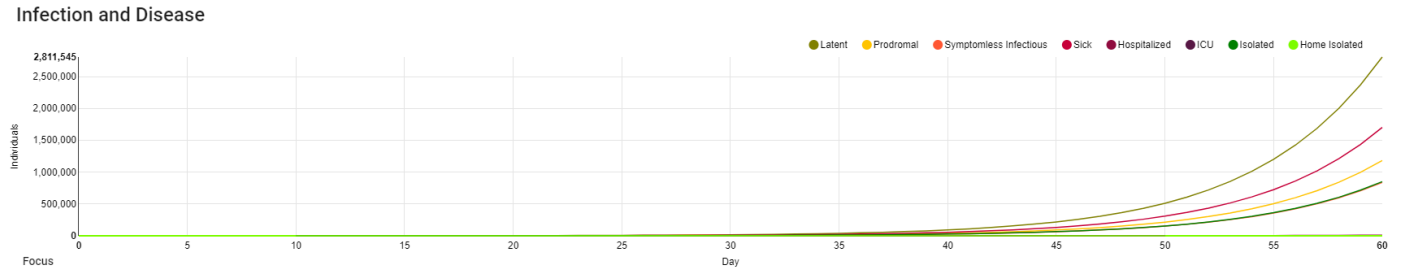
A further intervention to reduce the R_0 is to adjust the R_t obtained in Step 6 for contact reduction. This will allow us to achieve the observed R_t (the one obtained on EpiEstim in Phase 1).

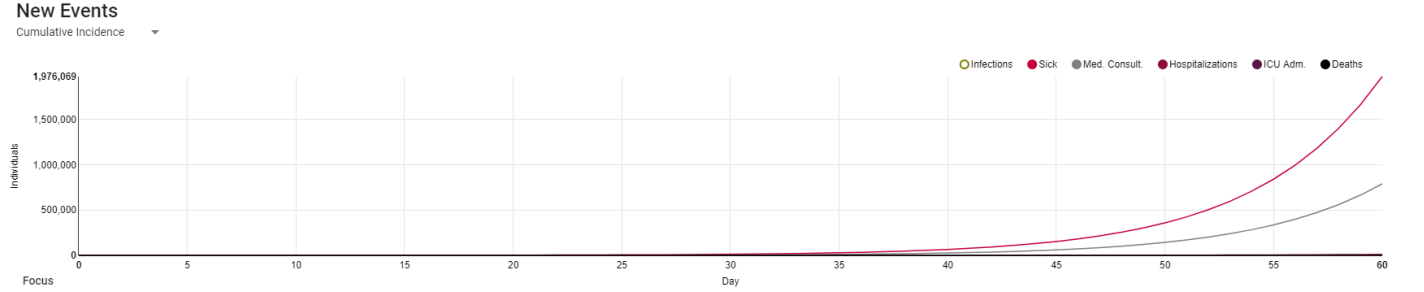
Examples :

- Hence, if we have a R_t of 3 and we want a further reduction to a R_t of 2. To obtain that we assume a further reduction of the in the Rt by 33%, through the parameter "contact reduction".
- Likewise, if we have a R_t of 3 but want to model a R_t of 1.5, we would a contact reduction parameter of 50%.
- Finally, to obtain a R_t of 1, we would need a contact reduction parameter of 66%.

COVID-19







Thank you

COVID-19 MODELING EXERCISE

A "HOW TO" calculate Rt GUIDE with EpiEstim

ANNEX 2

Calculation of Rt with ***EpiEstim***

➔ Go to https://harvardanalytics.shinyapps.io/covid19/

	A	B
1	dates	I
2	28/02/2020	2
3	29/02/2020	0
4	01/03/2020	0
5	02/03/2020	3
6	03/03/2020	0
7	04/03/2020	0
8	05/03/2020	0
9	06/03/2020	0
10	07/03/2020	0
11	08/03/2020	2
12	09/03/2020	0
13	10/03/2020	0
14	11/03/2020	0
15	12/03/2020	4
16	13/03/2020	1
17	14/03/2020	14
18	15/03/2020	15
19	16/03/2020	12
20	17/03/2020	29
21	18/03/2020	11
22	19/03/2020	25
23	20/03/2020	46
24	21/03/2020	0
25	22/03/2020	0
26	23/03/2020	87
27	24/03/2020	119
28	25/03/2020	0
29	26/03/2020	108
30	27/03/2020	0
31	28/03/2020	111
32	29/03/2020	128
33	30/03/2020	131
34	31/03/2020	145
35	01/04/2020	101

Step 1:

1. Prepare the data of incidence per day for the region/area/country of study in 2 columns: “dates” and “I”;

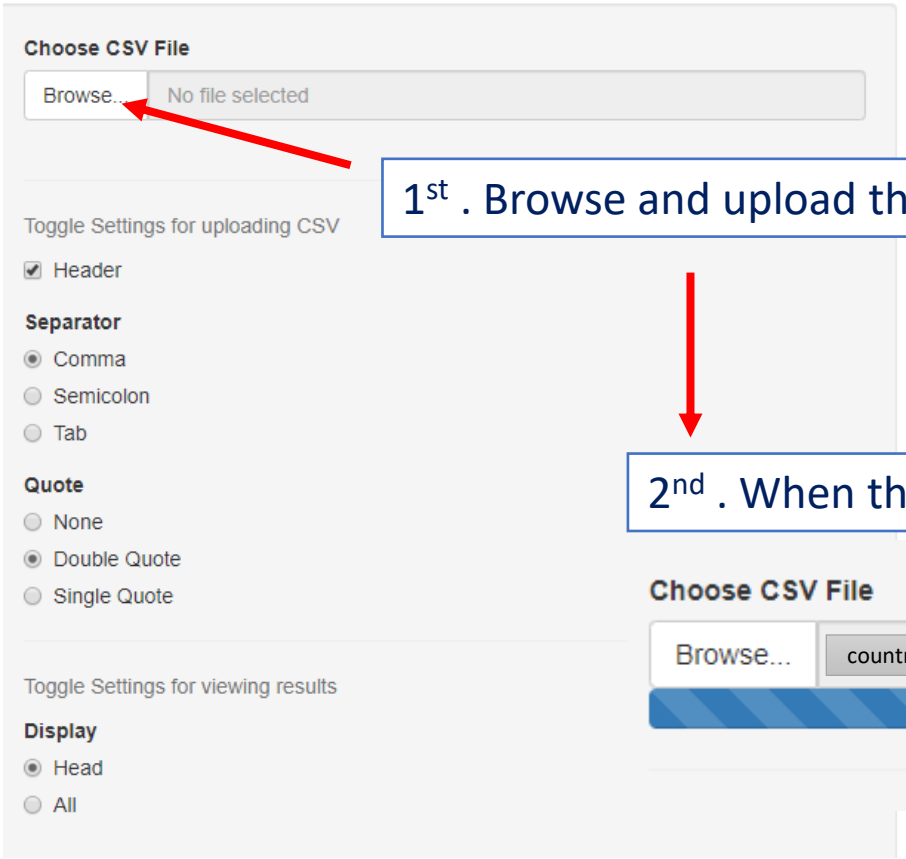
2. Save the file under a .csv format.

Prepare the region/area/country daily incidence in a .csv file

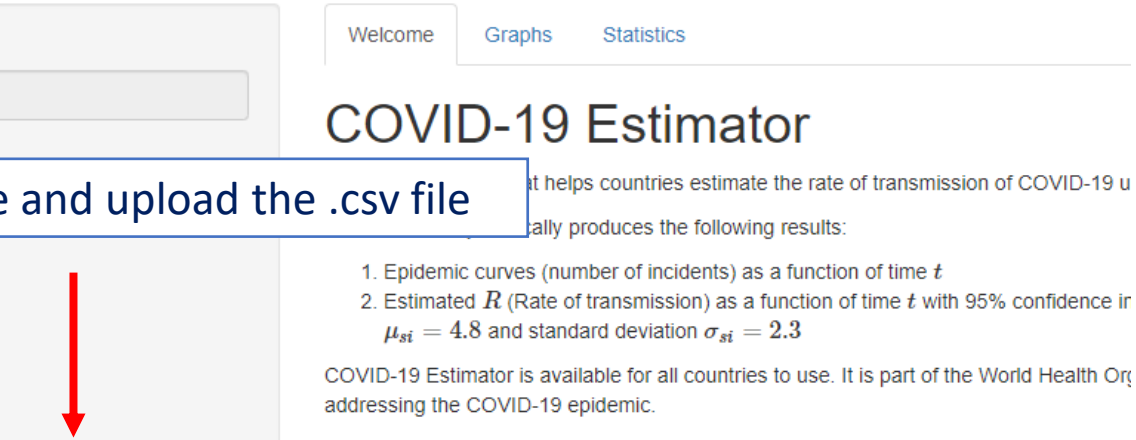
COVID-19

Step 2:

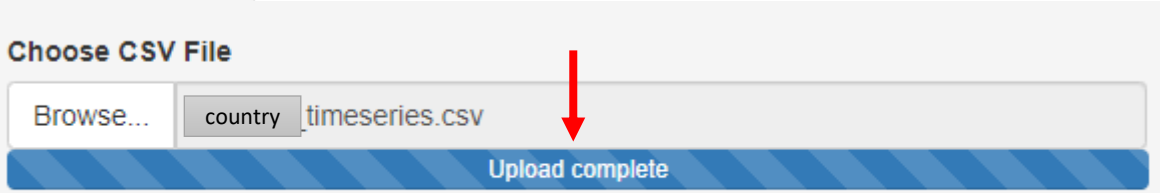
Upload csv file



1st . Browse and upload the .csv file

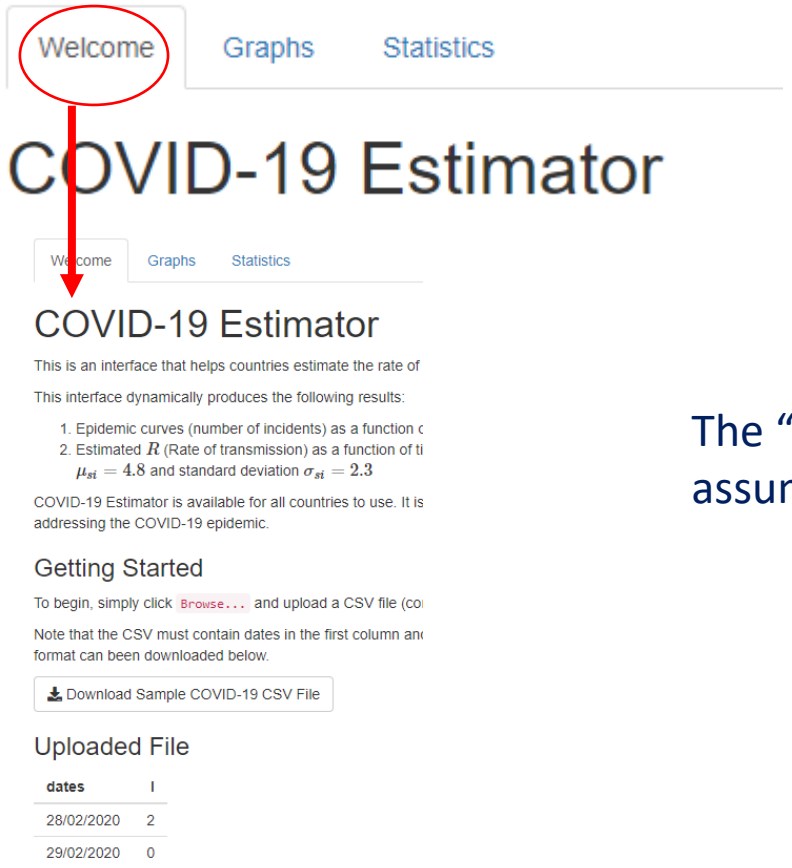


2nd . When the upload is complete, the following bar will be displayed:

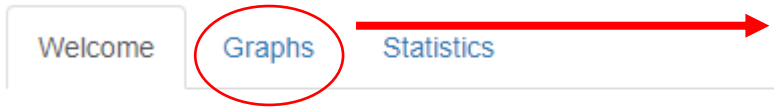


Step 3:

Check "welcome" tabs

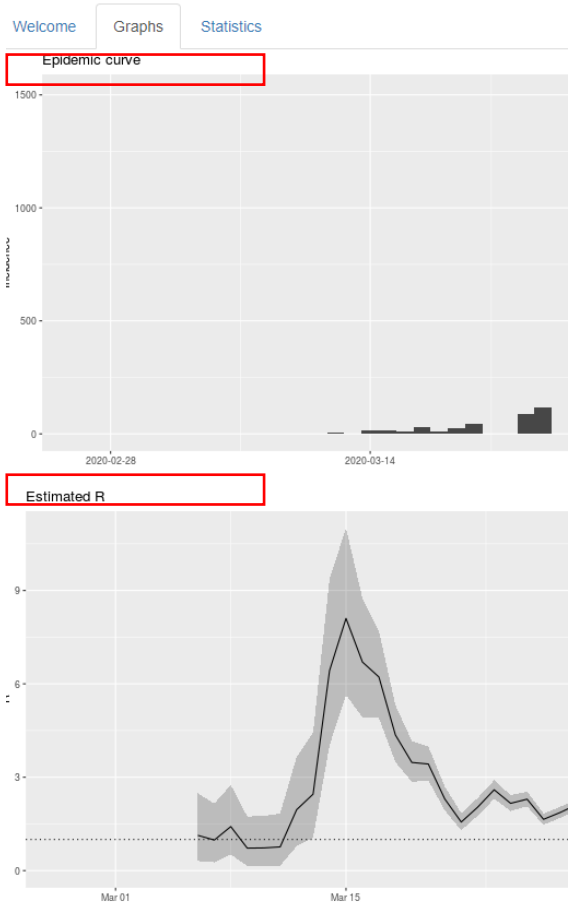


The "welcome" tab will display the assumptions and the sample uploaded



COVID-19 Estimator

In the “graphs” tab the Epicurve and the plot of the Rt fluctuation will be displayed

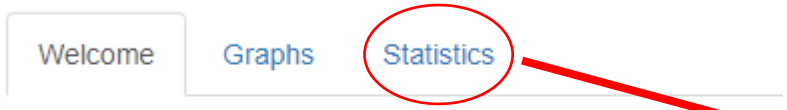


Step 4:

Check “graphs” tabs

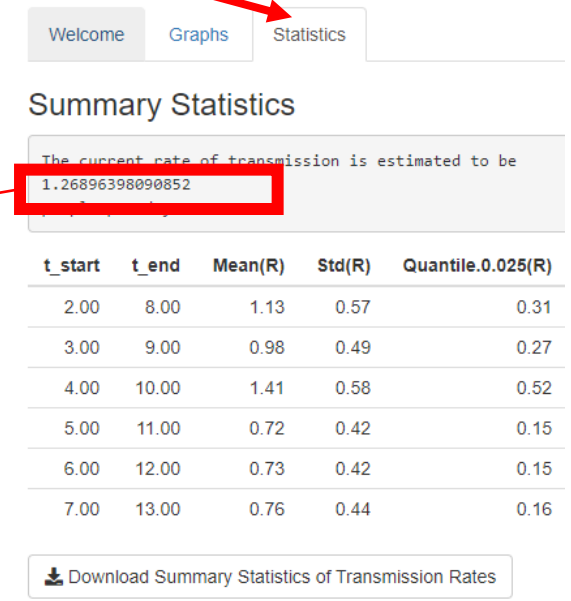
Step 5:

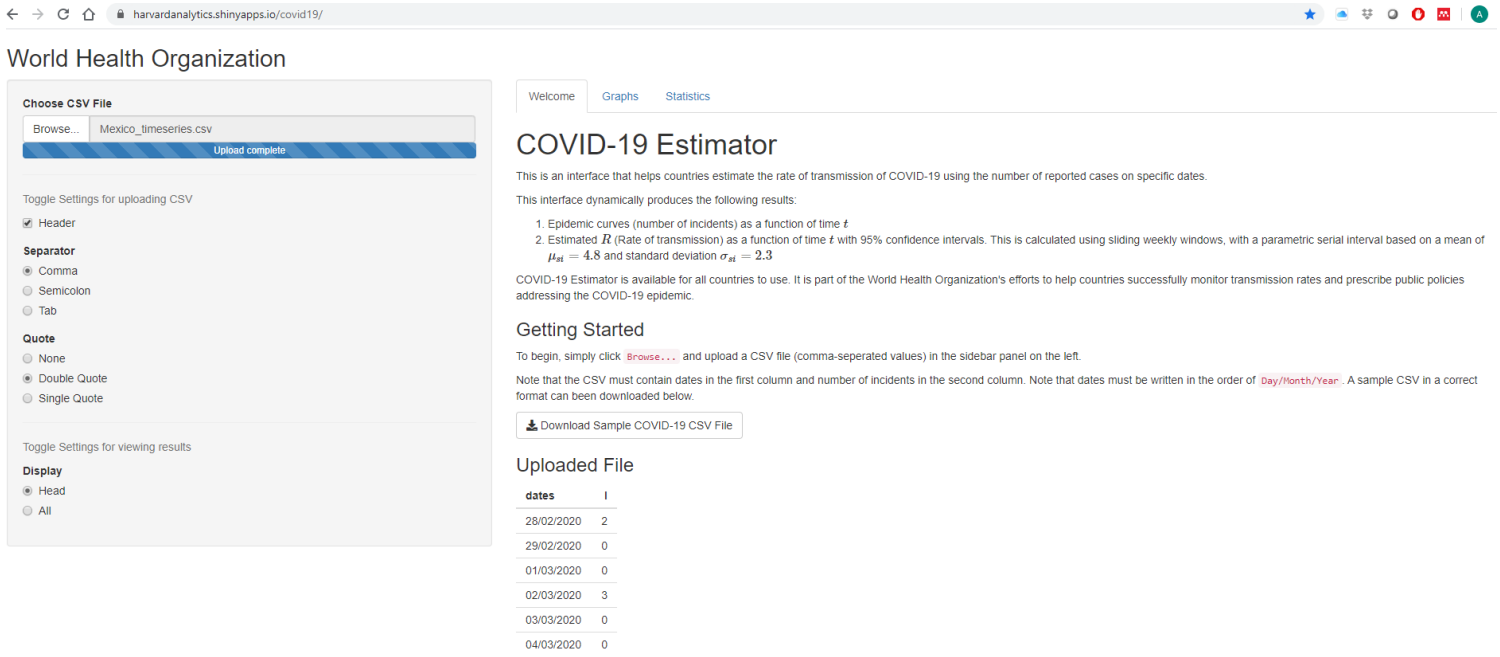
Check "statistics" tabs



COVID-19 Estimator

- In the "statistics" tab the Rt will be displayed.
- This is the number you need to use of the CovidSIM projections





Thank you

PAHO/IMS/PHE/COVID-19/20-0031