SEIR Age Cohort model for COVID-19

IEMAG Epi Modelling Group

V0.1, 19th April 2020

The SEIR Age cohort model builds on the SEIR Model for COVOD-19 (April 8th) in the following ways:

- Given the requirement to add additional compartments, the structure has been simplified to now cater for three main infectious compartments: pre-symptomatic, symptomatic and asymptomatic. Reported cases are treated as a parallel stream (7) and (8), and the immediate isolation compartment has been removed.

- Informed by the recent model[1] by Inserm (Paris), three age cohorts are proposed for the model exploration. These are: Children (0-18), Adults (18-64) , and Seniors (65+).

The high-level equations are shown below, and these are based on the calibrated SEIR model informing projections. Given that the age cohort model will increased the compartments by a factor of 3, the original model has been adjusted to simplify the number of infectious classes. This should have minimal effect on the results, given that in calibrations the numbers flowing into these compartments in the original model was low, for example the value for the quarantine parameter q was between 1-2%. An initial calibration of the updated model is also presented, which calculates an initial growth rate of 26% and an R_0 of 4.31.

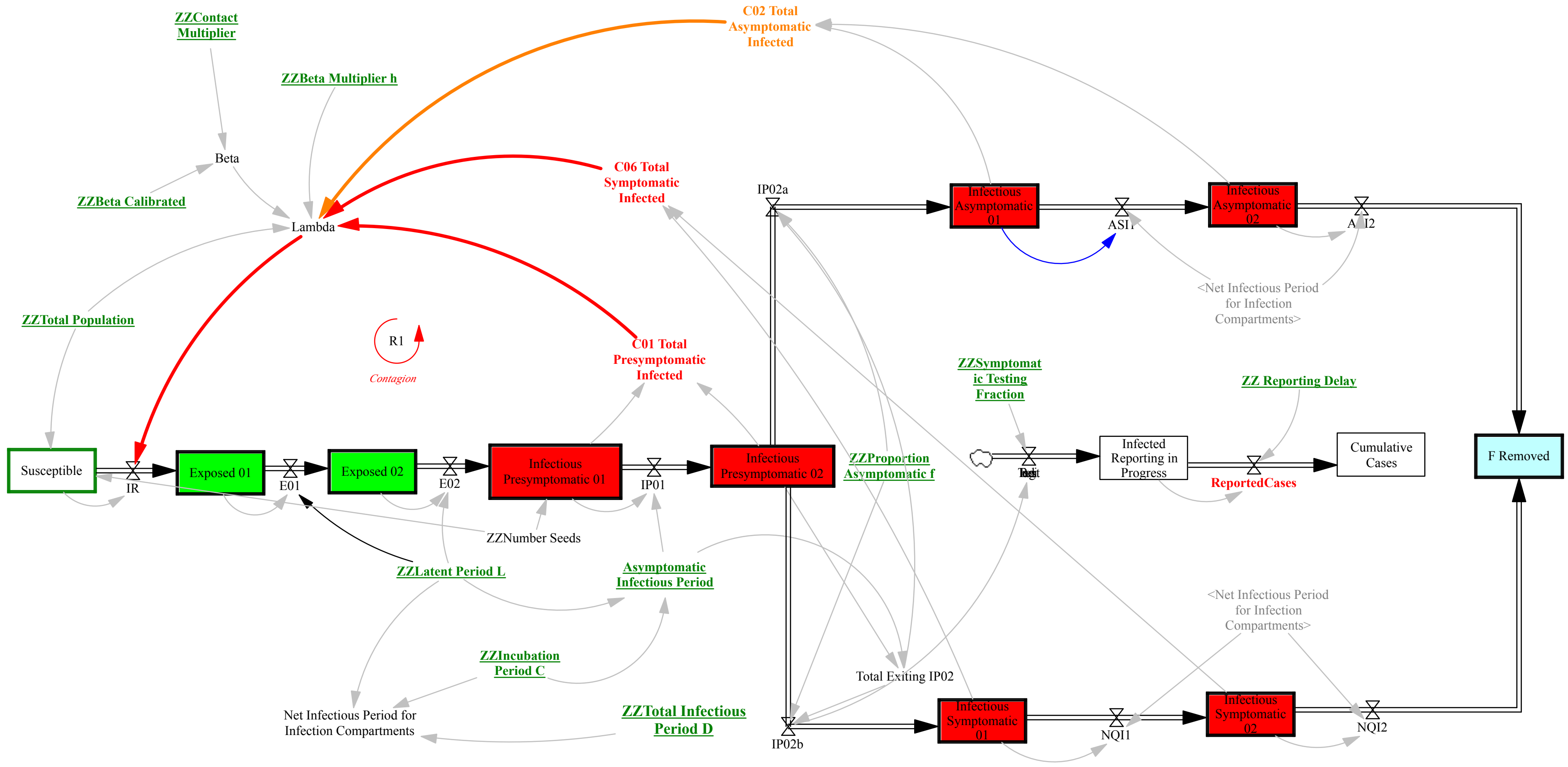
$\frac{dS}{dt} = -\frac{\beta S(IP + h.IA + IS)}{N}$	(1)
$\frac{dE}{dt} = \frac{\beta S(IP + h.IA + IS)}{N} - \frac{1}{L}E$	(2)
$\frac{dIP}{dt} = \frac{1}{L}E - \frac{1}{C-L}IP$	(3)
$\frac{dIA}{dt} = \frac{f}{C-L}IP - \frac{1}{D-C+L}IA$	(4)
$\frac{dIS}{dt} = \frac{1-f}{C-L}IP - \frac{1}{D-C+L}IS$	(5)
$\frac{dR}{dt} = \frac{1}{D-C+L}IA + \frac{1}{D-C+L}IS$	(6)
$\frac{dRC1}{dt} = g\,\frac{1-f}{C-L}IP - \frac{1}{T}RC1$	(7)
$\frac{dRC2}{dt} = \frac{1}{T}RC1$	(8)

The parameter g is introduced, which is the fraction of symptomatic that are tested positive. A visualiation of the modified compartment model is shown on the next page.

[1] https://www.epicx-lab.com/uploads/9/6/9/4/9694133/inserm-covid-19_report_lockdown_idf-20200412.pdf

Compartmental SEIR Model of Equations (1-8), with 2nd Order Delays (Erlang) for E and I compartments, See Appendix 2 for equations.

Parameters are shown in green text (underlined). Parameters used for calibration are Beta Calibrated, Beta Multiplier h, Proportion Asymptomatic f, Symptomatic Testing Fraction, Reporting Delay, Incubation Period C, Latent Period L, Total Infectious Period D.



Model Calibration

The model was calibrated (using Vensim DSS - Powell method) against the initial Irish data set of cumulative reported cases (up until day 14). The ranges and results are:

Parameter ranges:	**Sample Maximum payoff found at:**
0.5<=Beta Multiplier h<=1	Beta Multiplier h = 1
0.2<=Proportion Asymptomatic f<=1	Proportion Asymptomatic f = 0.382801
0.1<=Symptomatic Testing Fraction<=1.0	Symptomatic Testing Fraction = 1
1<= Reporting Delay<=3	Reporting Delay = 1.02499
5.0<=Incubation Period C<=6.4	Incubation Period C = 6.4
3.4<=Latent Period L<=3.7	Latent Period L = 3.4
4<=Total Infectious Period D<=6	Total Infectious Period D = 6
0.5<=Beta Calibrated<=3	Beta Calibrated = 0.803863

Analysis of the growth rate (spectral radius of the Jacobian matrix) and a calculation for R_0 (eigenvalues of FV^{-1}) provided the following initial results (see appendix).

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Initial exponential growth rate =  0.2645673
R0 Estimated Value =  4.309928
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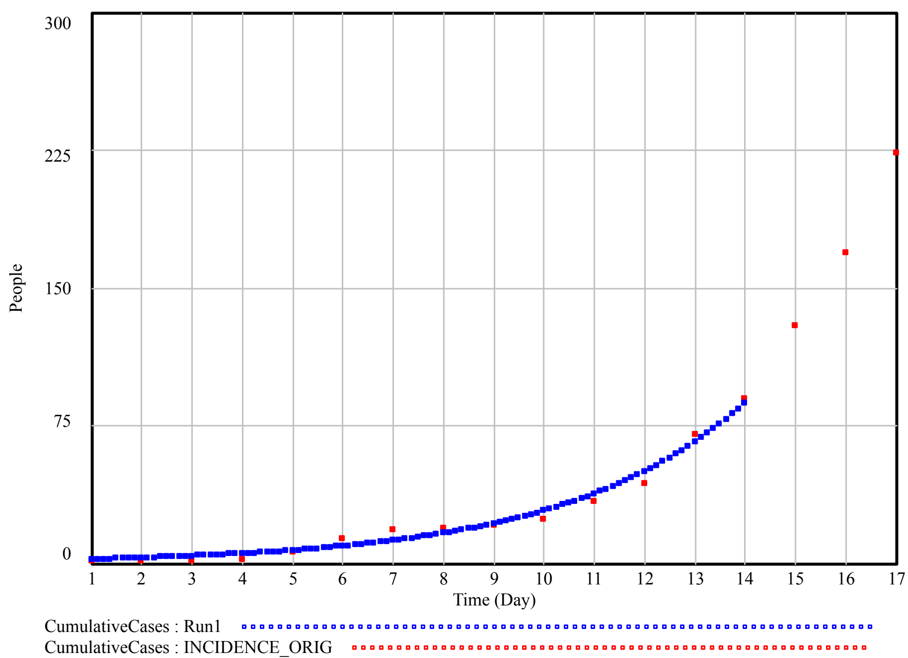
Plots for the model fit for cumulative cases and reported cases are shown below (model offset of -8).



Equations (1-8) are now disaggregated into three age cohorts, with subscripts c, a and s for children, adults and seniors. The transmission parameter beta is divided into 9 to represent effective social contacts between the three cohorts.

Age Cohort Model Equations

Susceptible Equations

$$\frac{dS_c}{dt} = -\frac{\beta_{cc}S(IP_c + h.IA_c + IS_c)}{N_c} - \frac{\beta_{ca}S(IP_a + h.IA_a + IS_a)}{N_c} - \frac{\beta_{cs}S(IP_s + h.IA_s + IS_s)}{N_c} \quad (1a)$$

$$\frac{dS_a}{dt} = -\frac{\beta_{ac}S(IP_c + h.IA_c + IS_c)}{N_a} - \frac{\beta_{aa}S(IP_a + h.IA_a + IS_a)}{N_a} - \frac{\beta_{as}S(IP_s + h.IA_s + IS_s)}{N_a} \quad (1b)$$

$$\frac{dS_s}{dt} = -\frac{\beta_{sc}S(IP_c + h.IA_c + IS_c)}{N_s} - \frac{\beta_{sa}S(IP_a + h.IA_a + IS_a)}{N_s} - \frac{\beta_{ss}S(IP_s + h.IA_s + IS_s)}{N_s} \quad (1c)$$

Exposed Equations

$$\frac{dE_c}{dt} = \frac{\beta_{cc}S(IP_c + h.IA_c + IS_c)}{N_c} + \frac{\beta_{ca}S(IP_a + h.IA_a + IS_a)}{N_c} + \frac{\beta_{cs}S(IP_s + h.IA_s + IS_s)}{N_c} - \frac{1}{L}E_C \quad (2a)$$

$$\frac{dE_a}{dt} = \frac{\beta_{ac}S(IP_c + h.IA_c + IS_c)}{N_a} + \frac{\beta_{aa}S(IP_a + h.IA_a + IS_a)}{N_a} + \frac{\beta_{as}S(IP_s + h.IA_s + IS_s)}{N_a} - \frac{1}{L}E_a \quad (2b)$$

$$\frac{dE_s}{dt} = \frac{\beta_{sc}S(IP_c + h.IA_c + IS_c)}{N_s} + \frac{\beta_{sa}S(IP_a + h.IA_a + IS_a)}{N_s} + \frac{\beta_{ss}S(IP_s + h.IA_s + IS_s)}{N_s} - \frac{1}{L}E_s \quad (2c)$$

Infectious (Presymptomatic) Equations

$$\frac{dIP_c}{dt} = \frac{1}{L}E_C - \frac{1}{C-L}IP_c \tag{3a}$$

$$\frac{dIP_a}{dt} = \frac{1}{L}E_a - \frac{1}{C-L}IP_a \tag{3b}$$

$$\frac{dIP_s}{dt} = \frac{1}{L}E_s - \frac{1}{C-L}IP_s \tag{3c}$$

Infectious (Asymptomatic) Equations

$$\frac{dIA_c}{dt} = \frac{f}{C-L}IP_c - \frac{1}{D-C+L}IA_c \tag{4a}$$

$$\frac{dIA_a}{dt} = \frac{f}{C-L}IP_a - \frac{1}{D-C+L}IA_a \tag{4b}$$

$$\frac{dIA_s}{dt} = \frac{f}{C-L}IP_s - \frac{1}{D-C+L}IA_s \tag{4c}$$

Infectious (Symptomatic) Equations

$$\frac{dIS_c}{dt} = \frac{1-f}{C-L}IP_c - \frac{1}{D-C+L}IS_c \tag{5a}$$

$$\frac{dIS_a}{dt} = \frac{1-f}{C-L}IP_a - \frac{1}{D-C+L}IS_a \tag{5b}$$

$$\frac{dIS_s}{dt} = \frac{1-f}{C-L}IP_s - \frac{1}{D-C+L}IS_s \tag{5c}$$

Removed Equations

$$\frac{dR_c}{dt} = \frac{1}{D-C+L} IA_c + \frac{1}{D-C+L} IS_c \tag{6a}$$

$$\frac{dR_a}{dt} = \frac{1}{D-C+L} IA_a + \frac{1}{D-C+L} IS_a \tag{6b}$$

$$\frac{dR_s}{dt} = \frac{1}{D-C+L} IA_s + \frac{1}{D-C+L} IS_s \tag{6c}$$

Reported Cases Equations (Used for calibration)

$$\frac{dRC1_c}{dt} = g\,\frac{1-f}{C-L} IP_c - \frac{1}{T} RC1_c \tag{7a}$$

$$\frac{dRC1_a}{dt} = g\,\frac{1-f}{C-L} IP_a - \frac{1}{T} RC1_a \tag{7b}$$

$$\frac{dRC1_s}{dt} = g\,\frac{1-f}{C-L} IP_s - \frac{1}{T} RC1_s \tag{7c}$$

$$\frac{dRC2_c}{dt} = \frac{1}{T} RC1_c \tag{8a}$$

$$\frac{dRC2_a}{dt} = \frac{1}{T} RC1_a \tag{8b}$$

$$\frac{dRC2_s}{dt} = \frac{1}{T} RC1_s \tag{8c}$$

Age Cohort Calibration Process

The beta parameters will be estimated based on whom acquires infection from whom (WAIFW) matrices, with the following possible structure[2] (derived from Vynnycky and White p197).

<table>
<tr><th>Matrix</th><th>Structure</th><th>Assumptions</th></tr>
<tr><td>A</td><td><table>
<tr><th></th><th>c</th><th>a</th><th>s</th></tr>
<tr><td>c</td><td>β_1</td><td>β_4</td><td>β_5</td></tr>
<tr><td>a</td><td>β_4</td><td>β_2</td><td>β_5</td></tr>
<tr><td>s</td><td>β_5</td><td>β_5</td><td>β_3</td></tr>
</table></td><td>The rate at which individuals of the same group come into effective contact is assumed to differ for each of the age cohorts
Interactions are symmetric.
Interaction rates are different between children and adults, and children and seniors.</td></tr>
<tr><td>B</td><td><table>
<tr><th></th><th>c</th><th>a</th><th>s</th></tr>
<tr><td>c</td><td></td><td></td><td></td></tr>
<tr><td>a</td><td></td><td></td><td></td></tr>
<tr><td>s</td><td></td><td></td><td></td></tr>
</table></td><td>TBD</td></tr>
<tr><td></td><td></td><td></td></tr>
</table>

The age-cohort model will be calibrated to these values, initially with all the biological parameters fixed. Cumulative time series for Irish cases for each of the age cohorts will be used to fit the model. Once calibrated, the POLYMOD study can be used to experiment with the impact of physical distancing measures. These are the

<table>
<tr><th>Matrix</th><th>Structure</th></tr>
<tr><td>Symmetric</td><td><pre>$Symmetric$matrix
         contact.age.group
             [0,19) [19,65)   65+
  [0,19)   7.8571429 5.248999 0.5020621
  [19,65) 2.3098289 7.952632 0.9785811
  65+   0.9012281 3.991818 1.7142857</pre></td></tr>
<tr><td>Population Demographics</td><td><pre>$Symmetric$demography
   lower.age.limit population upper.age.limit
1:               0   1305630   19
2:              19   2966995   65
3:              65   727349   80</pre></td></tr>
</table>

[2] Vynnycky, Emilia, and Richard White. An introduction to infectious disease modelling. OUP Oxford, 2010.

Appendix 1

Calculating the exponential growth rate and R_0 (see page 6 of SEIR Model for COVID-19, 8th April 2020). The compartments for calculating V are {E, IP, IA and IS}.

$$V = \begin{pmatrix} \frac{1}{L} & 0 & 0 & 0 \\ -\frac{1}{L} & \frac{1}{C-L} & 0 & 0 \\ 0 & -\frac{f}{C-L} & \frac{1}{D-C+L} & 0 \\ 0 & -\frac{(1-f)}{C-L} & 0 & \frac{1}{D-C+L} \end{pmatrix}$$

$$F = \begin{pmatrix} 0 & \beta & \beta h & \beta \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

Appendix 2: Vensim Model Equations – Aggregate Model

Note: variables that have a prefix ZZ are constants. The use of this prefix is necessary to facilitate translating the model into R (seirR package). The model units are dimensionally consistent, which has been verified in Vensim.

(01) ASI1 = Infectious Asymptomatic 01 / (Net Infectious Period for Infection Compartments / 2)
Units: People/Day

(02) ASI2 = Infectious Asymptomatic 02 / (Net Infectious Period for Infection Compartments / 2)
Units: People/Day

(03) Asymptomatic Infectious Period = ZZIncubation Period C - ZZLatent Period L
Units: Day

(04) Being Tested = ZZSymptomatic Testing Fraction * IP02b
Units: People/Day
Number of people being tested per day

(05) Beta = ZZContact Multiplier * ZZBeta Calibrated
Units: 1/Day
Transmission parameter = R0/Total Infectious Period

(06) C01 Total Presymptomatic Infected = Infectious Presymptomatic 01 + Infectious Presymptomatic 02
Units: People
Total Presymptomatic Infected (Subclinical infectious)

(07) C02 Total Asymptomatic Infected = Infectious Asymptomatic 01 + Infectious Asymptomatic 02
Units: People

(08) C06 Total Symptomatic Infected = Infectious Symptomatic 01 + Infectious Symptomatic 02
Units: People

(09) CumulativeCases = INTEG(ReportedCases , 0)
Units: People
Cumulative number of reported infections

(10) E01 = Exposed 01 / (ZZLatent Period L / 2)
Units: People/Day
Exit rate from Exposed 01

(11) E02 = Exposed 02 / (ZZLatent Period L / 2)
Units: People/Day
Exit rate from Exposed 02

(12) Exposed 01 = INTEG(IR - E01 , 0)
Units: People
Number Exposed (compartment 1)

(13) Exposed 02 = INTEG(E01 - E02 , 0)
Units: People
Number Exposed (compartment 2)

(14) F Removed = INTEG(ASI2 + NQI2 , 0)
Units: People
Total removed

(16) Infected Reporting in Progress = INTEG(Being Tested - ReportedCases ,
0)
Units: People
Number of people awaiting test results

(17) Infectious Asymptomatic 01 = INTEG(IP02a - ASI1 , 0)
Units: People
Number asymptomatic infectious (compartment 1)

(18) Infectious Asymptomatic 02 = INTEG(ASI1 - ASI2 , 0)
Units: People
Number asymptomatic infectious (compartment 2)

(19) Infectious Presymptomatic 01 = INTEG(E02 - IP01 , ZZNumber Seeds)
Units: People
Number presymptomatic infectious (compartment 1)

(20) Infectious Presymptomatic 02 = INTEG(IP01 - IP02a - IP02b , 0)
Units: People
Number presymptomatic infectious (compartment 2)

(21) Infectious Symptomatic 01 = INTEG(IP02b - NQI1 , 0)
Units: People
Number symptomatic infectious (compartment 1)

(22) Infectious Symptomatic 02 = INTEG(NQI1 - NQI2 , 0)
Units: People
Number symptomatic infectious (compartment 2)

(24) IP01 = Infectious Presymptomatic 01 / (Asymptomatic Infectious Period
/ 2)
Units: People/Day
Exit rate from Infected Presymptomatic 01

(25) IP02a = Total Exiting IP02 * ZZProportion Asymptomatic f
Units: People/Day

(26) IP02b = Total Exiting IP02 * (1 - ZZProportion Asymptomatic f)
Units: People/Day

(27) IR = Lambda * Susceptible
Units: People/Day
Infection rate (indicence) in the population

(28) Lambda = ((Beta * C01 Total Presymptomatic Infected) + (Beta * ZZBeta Multiplier h
* C02 Total Asymptomatic Infected) + (Beta * C06 Total Symptomatic Infected
)) / ZZTotal Population
Units: 1/Day
Force of infection, with contributions from all of the infected compartments.

(29) Net Infectious Period for Infection Compartments = ZZTotal Infectious Period D + ZZLatent Period L - ZZIncubation Period C
Units: Day
Infectious period to be applied to infectious compartments

(30) NQI1 = Infectious Symptomatic 01 / (Net Infectious Period for Infection Compartments / 2)
Units: People/Day

(31) NQI2 = Infectious Symptomatic 02 / (Net Infectious Period for Infection Compartments / 2)
Units: People/Day

(32) ReportedCases = Infected Reporting in Progress / ZZ Reporting Delay
Units: People/Day
Reported Cases

(34) Susceptible = INTEG(- IR , ZZTotal Population - ZZNumber Seeds)
Units: People
Model Equation (1)

(36) Total Exiting IP02 = Infectious Presymptomatic 02 / (Asymptomatic Infectious Period / 2)
Units: People/Day
Total exit rate from Infected Presymptomatic 02

(37) ZZ Reporting Delay = 1
Units: Day
Reporting delay in obtaining results.

(38) ZZBeta Calibrated = 0.157925
Units: 1/Day
Infectiousness of a contact between an infected and susceptible.
To be initially estimated using calibration methods

(39) ZZBeta Multiplier h = 0.516055
Units: Dmnl
Multiplicative factor for reduction in infectiousness of
asymptomatic infected compartment

(40) ZZContact Multiplier = 1
Units: Dmnl
A multiplier to model physical distancing. 1 = normal contacts

(41) ZZIncubation Period C = 5
Units: Day
Duration of time at incubation stage

(42) ZZLatent Period L = 3.7
Units: Day
Duration of time in incubation stage

(43) ZZNumber Seeds = 1
Units: People
Number of seeds initially importing the virus

(44) ZZProportion Asymptomatic f = 0.23354
Units: Dmnl
Proportion of infected who show symptoms

(45) ZZSymptomatic Testing Fraction = 0.735
Units: Dmnl
Fraction of symptomatic people tested

(46) ZZTotal Infectious Period D = 4
Units: Day
Duration of infectiousness

(47) ZZTotal Population = 4.99997e+06
Units: People
Total Population at outset of epidemic