Stochastic age-structured transmission model for Switzerland

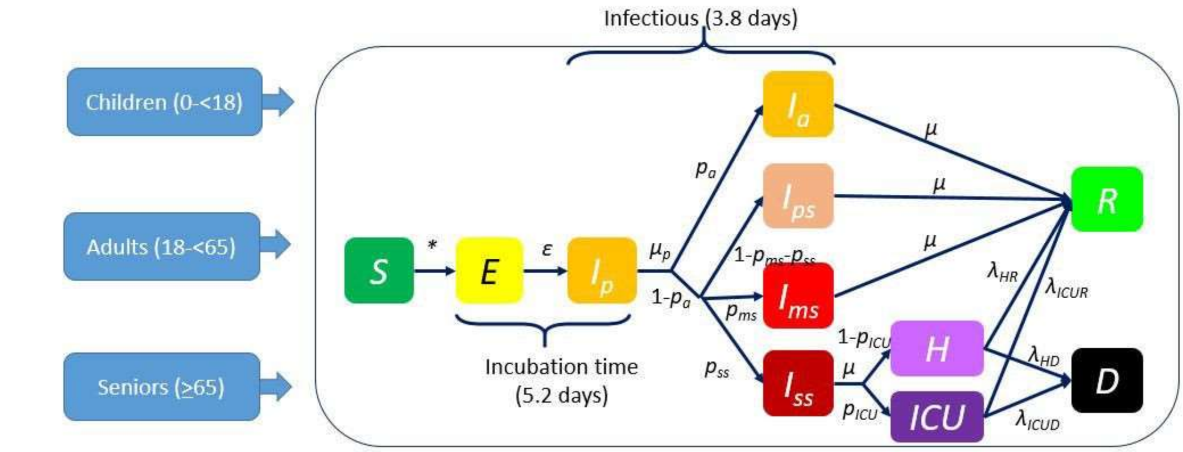
The model structure and most parameters are adapted from the model of Di Domenico et al. 2020 (1).

Transmission model methodology

We have adapted a stochastic discrete-time age-structured compartmental model for SARS-CoV-2 transmission with parameters based on Swiss transmission data and have integrated data on age profile and social contacts in order to:

i. Assess the current epidemic situation in Switzerland
ii. Evaluate the impact of the implemented lockdown
iii. Estimate the effect of possible lockdown exit strategies, with a focus on age specific interventions

The transmission dynamics follows a compartmental scheme specific for COVID-19 where individuals are divided into the following categories: susceptible, exposed, infectious, hospitalized, in intensive care (ICU), recovered, and deceased (Figure X1):



*Depends on a fitted overall infectiousness parameter *β*, contact matrix *M* between age groups, proportions of infectious individuals in each age group and severity stage, and factor *rb* reducing the infectiousness of individual in compartments I_p, I_a and I_{ps}

Figure X1: Compartmental model of SARS-CoV-2 transmission *(structure adapted from Di Domenico, L., Pullano, G., Sabbatini, C. E., Boëlle, P. Y., & Colizza, V. (2020). Expected impact of lockdown in Île-de-France and possible exit strategies.* https://www.medrxiv.org/content/10.1101/2020.04.13.20063933v1.full.pdf)

The infectious phase is divided into two steps: a prodromic phase (I_p) occurring before the end of the incubation period, followed by a phase where individuals may remain asymptomatic (I_a) or develop symptoms. In the latter case, we distinguish between different degrees of severity of symptoms, ranging from paucisymptomatic (I_{ps}), infectious individuals with mild (I_{ms}) or severe (I_{ss}) symptoms. The probability of being asymptomatic assumed to be 50%. However, there is no essential difference in the model between asymptomatic and paucisymptomatic individuals. For example, we currently assume that 50% of adults are asymptomatic and 10% (=0.50*0.20) paucisymptomatic, but the results would be exactly equivalent with the situation that there proportions of asymptomatic and paucisymptomatic adults would be 0% and 60%, respectively. Children are considered to be equally susceptible to infection as adults, and they remain either asymptomatic or paucisymptomatic. Individuals in the prodromic, asymptomatic and paucisymptomatic compartments have a lower transmission rate than symptomatic individuals. Persons with severe symptoms are always hospitalized and those who need intensive care any time during hospitalization move directly to the ICU compartment.

Social mixing is taken into account via social contact matrices, representing the average contacts per day per capita between different age groups. Three age groups are considered: 0-<18 years, 18-<65 years and 65+ years, which we refer to as children (C), adults (A) and seniors (S), respectively.

Mixing between individuals in the baseline scenario, i.e. without intervention, is derived from social contact data available from various sources and countries on the website www.socialcontactdata.org. We used the baseline contact matrix shown in Figure X2. The values were averaged from four countries for which data were available and which were assumed to be similar to the situation in Switzerland: Belgium (Willem et al., in prep), France (2), Germany (3) and Italy (3).

	Children	Adults	Seniors
Children	2.0 (1.80-3.35)	0.5 (0.48-0.67)	0.2 (0.18-0.24)
Adults	0.5 (0.48-0.67)	1.0 (Ref)	0.4 (0.38-0.46)
Seniors	0.2 (0.18-0.24)	0.4 (0.38-0.46)	1.0 (0.66-1.02)

Figure X2: Baseline (without intervention) contact matrix for Switzerland, expressed as relative number of contacts per day per capita compared to the adults-adults contacts. The ranges represent the estimates from Belgium, France, Germany and Italy.

We implemented social distancing interventions by translating them into changes in the contact matrix, accounting for the relevant reduction of social contacts in specific regions and age groups. We considered the measures implemented since early March 2020, and explored the potential effect of future lifting scenarios announced by the Federal Council on April 16th 2020 and updated later (4). Those measures are listed in Table X1. The reductions were estimated by comparing prior knowledge (e.g. school closure mainly affecting contacts between children; reduced workplace contacts affecting contacts between adults) and then fitting the corresponding reduction parameters to the observed hospitalizations.

From May 11th 2020 onwards (when the great majority of the lockdown measures were lifted), we assumed a new intervention to take place, which would cover all newly implemented measures. These include, for example, contact tracing (both the mandatory manual contact tracing, and the smartphone app which is currently in test phase), the use of masks (strongly recommended in situations like public transport where the minimum 2 m distance cannot be kept), and general awareness. We represented these scenarios by reducing the contacts between different age groups using different coefficients.

Of note, the interventions implemented in the model do not aim to represent the exact policies announced by the Federal Council, but rather the change in relative contact frequencies. Though the model cannot be used to compare explicit interventions, it can be used to compare the impact of interventions that focus on different age groups. For example, with this model the impact of closing restaurants cannot be compared to the impact of closing shops, instead we can see the impact of reducing all contacts compared to reducing contacts of seniors only.

Table X1: Social distancing policy changes in Switzerland since the beginning of the COVID-19 epidemics.

Date of policy change	Type of measure taken
March 5th 2020	Promotion of social distancing (first level), cancellation of massive gathering events (e.g. festivals, concerts etc…)
March 16th 2020	Closing schools, restaurants, non-essential shops and services
March 20th 2020	Hardening of social distancing (second level), reduction of workplace contacts (home-office)
April 27th 2020	Re-opening of some non-essential shops and services
May 11th 2020	Re-opening of obligatory schools, all non-essential shops, museums and libraries, and restaurants
June 8th 2020	Softening of social distancing back to the pre- March 20th level

Inference of model parameters

We adapted the parameters related to the natural progression and hospitalization from the model by Di Domenica (Table X2), with the exception of mortality because the preliminary fits suggested that the rates were too low. We calibrated the model first to the cantons of Geneva, Ticino and Bern. We fitted to daily new hospitalizations and deaths, except in Ticino where only deaths were available. Deaths for all three cantons and hospitalizations for Bern were taken from the corona-data.ch platform; hospitalizations for Geneva were taken directly from the cantonal daily reports. We used approximate Bayesian computing (rejection method) to choose the best-fitting parameterizations from 10,000 randomly sampled sets of parameters (R package *abc*, tolerance 0.01). The final set of parameters was selected manually from the accepted parameterisations. Mortality rates were fitted only for Geneva and adapted for the other two cantons. Other parameters, fitted to all cantons, were the starting date of the epidemic, number of infected individuals on the first day, *beta*0 parameter (overall infectiousness per day in adult-adult contacts), and the restrictions for the following interventions: light social distancing (all age groups), strong social distancing (all age groups), school closure (children-children, children-adults), workplace contact reductions (adults-adults), shop closures (adults-adults, adults-seniors, seniors-seniors), “light” social distancing (hand hygiene, general awareness; all age groups), and “strong” social distancing (strengthened “light” social distancing plus prohibition of gatherings with more than 5 people). For social distancing, the reduction was assumed to be 20% more for contacts involving seniors; and for shop closure, the reduction for contacts involving seniors by half of that between adults. After running the model for all cantons, we selected the range of canton-level parameter estimates as priors, but manually adapted this if the fit was unsatisfactory after the first run. The final set of parameters was selected manually from the set of accepted parameterisations in the ABC analysis, and the parameterisation providing the lowest square sum of differences. Table X3 shows the details of the fitting process; Table X4 summarizes the relative contact probabilities between the age groups during each intervention.

Strengths and limitations of model

Age-structuring helps to estimate the impact of interventions targeting specific populations. The three age groups cover the main essential age-related differences in contact patterns and disease severity, helping to model the impact of interventions, most of which usually focus on one of these three age groups. The model structure allows to calibrate the model with hospitalizations (in addition to deaths, which are the main indicator used by most models). The structure is flexible and allows the model to be easily adapted to e.g. smaller geographical areas, or to other countries or settings. The model also has limitations. A compartmental model cannot take directly into account the contact networks: assuming homogeneous mixing within and between age groups ignores the impact of e.g. superspreaders. Representing the entire country in a model without geographical structure does not take into account that the epidemic is in different phases across different regions, and that different sub-epidemics may have started independently of each other.

Table X2: Parameters, values, and sources used to define the compartmental model

Variable	Description	Value	Source
μ_p^-	Duration of prodromal phase	1.5*	[6]
ε^{-1}	Latency period	3.7	
p_a	Probability of being asymptomatic	0.5 (all age groups)	[7]
p_{ps}	If symptomatic, probability of being paucisymptomatic	children: 1 adults and seniors:0.2	[8]
p_{ms}	If symptomatic, probability of develop mild symptoms	children: 0 adults: 0.7 seniors: 0.6	[8]
p_{ss}	If symptomatic, probability of develop severe symptoms	children: 0 adults: 0.03 seniors: 0.35	[8-10]
s	Serial interval	7.5 d	[11]
μ^{-1}	Infectious period for I_a, I_{ps}, I_{ms}, I_{ss}	s- $^{-1}$ (2.3)	
r_b	Relative infectiousness of I_a, I_p, I_{ps}	0.51	[12]
p_{icu}	If severe symptoms, probability to go to ICU	children: 0 adults: 0.25 seniors: 0.2	[13]
$\lambda_{H,R}$	If hospitalized, daily rate entering in R	children: 0 adults: 0.072 seniors: 0.022	[13]
$\lambda_{ICU,R}$	if in ICU, daily rate entering in R	children: 0 adults: 0.05 seniors:0.036	[13]

*computed as a fraction of pre symptomatic transmission events out of pre symptomatic plus symptomatic transmission events

Table X3: Prior and posterior parameter values for the modelled three cantons (Geneva, Bern, Ticino) and Switzerland

	Prior (cantonal models)	**GE**	**BE**	**TI**	**CH**
Mortality from H, adults (day^{-1})	0.0042-0.0126	0.0094	0.0094***	0.0094***	0.0093
Mortality from H, seniors (day^{-1})	0.0140-0.1400	0.0282	0.0282***	0.0282***	0.0297
Mortality from ICU, adults (day^{-1})	0.0074-0.0222	0.0161	0.0161***	0.0161***	0.0155
Mortality from ICU, seniors (day^{-1})	0.0290-0.4350	0.2727	0.2727***	0.2727***	0.3500
Starting date	1 Feb – 25 Feb	18 Feb	19 Feb	15 Feb	11 Feb
Initial number of exposed	5-20	15	18	20	49
beta0	0.5-1.0	0.894	0.724	0.983	0.793
Contact reductions					
School closure: C-C	90% – 98%	94.6%	95.7%	92.1%	92.2%
School closure: C-A	0% – 50%	16.9%	49.4%	20.1%	48.7%
Home office: C-A	20% – 80%	78.8%	56.8%	75.7%	76.4%
Full shop closure: A-A*	20% – 80%	60.2%	63.4%	73.4%	70.4%
Light social distancing**	0% – 50%	10.5%	12.7%	48.6%	12.1%
Strong social distancing **	20% – 50%	48.1%	31.2%	49.4%	44.4%

*During the period when all essential shops and services were closed; contacts A-S and S-S reduced by half

**Contacts involving seniors reduced 1.2 times more

***Value from GE taken directly

Table X4: Reduction in contacts compared to no intervention. Values applied in the Switzerland model.

Policy	CC	CA	CS	AA	AS	SS	Period
Social distancing (first level)	0.88	0.88	0.70	0.88	0.70	0.70	5 March – 19 March 8 June –
Closing schools	0.08	0.51	1	1	1	1	16 March – 10 May
Social distancing (second level)	0.56	0.56	0.44	0.56	0.44	0.44	20 March – 7 June
Reduced workplace contacts	1	1	1	0.24	1	1	20 March –
Closing all non-essential shops and services	1	1	1	0.30	0.30	0.30	16 March – 26 April
Closing most non-essential shops	1	1	1	0.65	0.65	0.65	16 March – 10 May
Closing restaurants	1	1	1	0.80	0.80	0.80	16 March – 10 May
School summer holiday	0.08	0.51	1	0.37	1	1	4 July – 9 August
Contact tracing, testing	*	*	*	*	*	*	11 May – ?

*Depends on scenario (see Results)
CC: between children, CA: between children and adults, CS: between children and seniors, AA: between adults, AS: between adults and seniors, SS: between seniors.

Results

The results are updated on the Gitlab repository of this project (https://gitlab.com/igh-idmm-public/covid-19/modelling_jestill)

Sensitivity analyses:

We conducted the following sensitivity analyses:

- We added a seasonal force, i.e. a coefficient of the *beta*0 parameter, following a sinus function with a maximum value 0 on 1st February, and minimum value 0.6 on 1st August. As the first wave happened essentially during the spring season, we did not reparameterise the model and used this assumption exclusively to see how a reduction in infectiousness during summer could change the epidemic.
- We added an extra compartment for "post-symptomatic" individuals, where all infected (except those with severe symptoms who become hospitalized) will follow before recovery. Post-symptomatic individuals can also transmit the infection, but they are less infectious than those symptomatic. For this sensitivity analysis, we reran the fitting process for the Canton of Geneva and Switzerland (including also the relative infectiousness of post-symptomatic individuals, and the mean duration of this phase).
- We used a shorted serial interval (4.8 days, in line with other modelling studies) and reparameterised the model for the Canton of Geneva and Switzerland. We assumed that the duration of the latency period was reduced by 2.7 days (7.5-4.8), and the duration of the infectious period remained as before. The remaining parameters were refitted.

Team members contributing to all these activities (alphabetical order):

- Alexander Temerev (text mining, contributes to network model)
- Amaury Thiabaud (hospital surveillance)
- Barbara Bertisch (general support, clinical care)
- Erol Orel (contributes to text mining, mathematical model, hospital surveillance, website)
- Isotta Triulzi (volunteer and former visiting student, general support)
- Janne Estill (mathematical model)
- Janos Nadaban (volunteer, general support)
- Liudmila Rozanova (volunteer, network model)
- Maroussia Roelens (hospital surveillance, website)

- Olivia Keiser (supervision)
- Plamenna Venkova (hospital surveillance, mathematical model, website)
- Rachel Esra (general support)

If you are interested to contribute to our activities or if you want to get in touch, then please contact olivia.keiser[at]unige.ch
Link to our group website: https://www.unige.ch/medecine/isg/en/research/988keiser/

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