An age-structured compartmental model of SARS-CoV-2 transmission in Geneva

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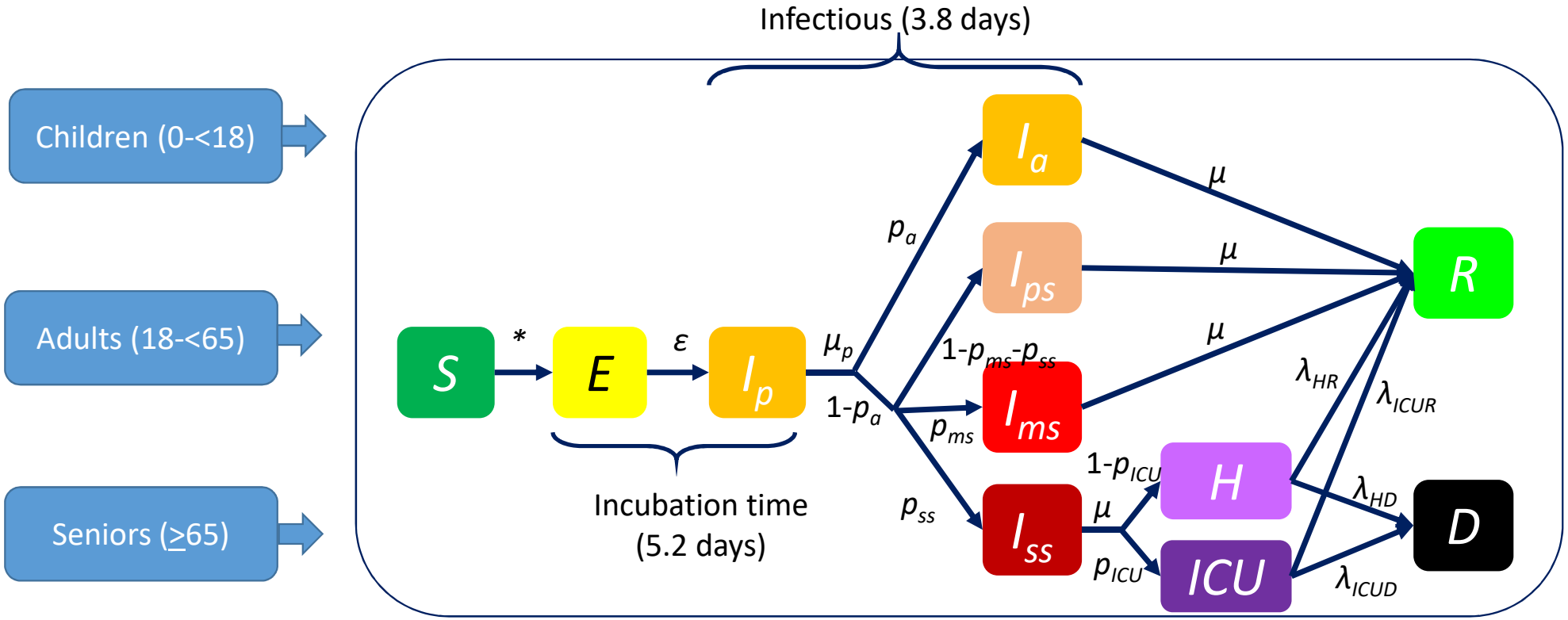
Methods

- Follows the structure of a model for Ile-de-France (Di Domenica *et al*)
- Compartmental discrete-time model (both deterministic and stochastic versions available)



*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}

Model structure and parameterisation adapted from Di Domenica *et al* https://www.medrxiv.org/content/10.1101/2020.04.13.20063933v1.full.pdf+html

- Most parameters were taken from the Di Domenica model
- Contact patterns between age groups were taken from literature (see next slide)
- Infectiousness, starting conditions of the epidemic, mortality, and contact reductions of interventions were fitted using approximate Bayesian computing

Variable	Description	Value	Source
μ_p^{-1}	Duration of prodromal phase	1.5*	[6]
ε^{-1}	Latency period	3.7	[5,6]
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], fitted
s	Serial interval	7.5 d	[11]
μ^{-1}	Infectious period for I_a, I_{ps}, I_{ms}, I_{ss}	$s-\mu_p^{-1}-\varepsilon^{-1}$ (2.3)	
r_β	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]
$\lambda_{H,D}$	if hospitalized, daily rate entering in D	children: 0 **Adults and seniors: fitted**	[13], fitted
$\lambda_{ICU,R}$	if in ICU, daily rate entering in R	children: 0 adults: 0.05 seniors:0.036	[13]
$\lambda_{ICU,D}$	if in ICU, daily rate entering in D	children:0 **Adults and seniors: fitted**	[13], fitted

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

Reference numbers: see https://gitlab.com/igh-idmm-public/covid-19/modelling_jestill/-/blob/master/covid_model_full_description.pdf for list of references
All parameters are given either as days, or rates per day

Contact matrix between age groups

- Without intervention:

	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)

Contacts per day **per capita**.

www.socialcontactdata.org

- Belgium (data from 2010; manuscript in preparation)
- France (Béraud *et al* PLoS One 2015)
- Germany (POLYMOD: Mossong *et al* PLoS Med 2008)
- Italy (POLYMOD)
- Other countries available; for this model, the values taken by reviewing the above four analyses
- The values were estimated by averaging across the four country estimates (range represents the four countries).

	Prior (range)	Best fit
λ_{HD}: adults	0.0042 – 0.0126	0.0094
λ_{HD}: seniors	0.014 – 0.140	0.0282
λ_{ICUD}: adults	0.0074 – 0.0222	0.0161
λ_{ICUD}: seniors	0.029 – 0.290	0.2727
Starting date	1st Feb – 25th Feb 2020	18th Feb 2020
Initial seed	1 – 20	15
β_0	0.5 – 1.0	0.894
schoolCC*	0.02 – 0.1	0.054
schoolCA*	0.5 – 1.0	0.931
workAA*	0.2 – 0.8	0.212
shopAA*	0.2 – 0.8	0.398
social1*	0.5 – 1.0	0.895
social2*	0.5 – 0.8	0.519

*Relative decrease in contact rates due to school closure (children-children, children-adults), home office (adults-adults), shop closures (adults-adults), light social distancing 5-15 March and strog social distancing after 16 March (al age groups, contacts involving seniors reduced by additional 20%)

Reference numbers: see https://gitlab.com/igh-idmm-public/covid-19/modelling_jestill/-/blob/master/covid_model_full_description.pdf for list of references

All parameters are given either as days, or rates per day

Variable	Description	Value	Source
μ_p^{-1}	Duration of prodromal phase	1.5	[3]
ϵ	Latency period	3.7	[5,6]
p_a	Probability of being asymptomatic	0.5 for all age groups	[4]
p_{ps}	If symptomatic, probability of being paucisymptomatic	children: 1 adults and seniors:0.2	[5]
p_{ms}	If symptomatic, probability of develop mild symptoms	children: 0 adults: 0.7 seniors: 0.6	[5]
p_{ss}	If symptomatic, probability of develop severe symptoms	children: 0 adults: 0.03 seniors: 0.035	[5-7]
s	Serial interval	7.5 d	[8]
μ^{-1}	Infectious period for $I_a, I_{ps}, I_{ms}, I_{ss}$	$s-\mu_p^{-1}-\epsilon^{-1}$ (2.3)	
r_β	Relative infectiousness of I_a, I_p, I_p	0.51	[9]
p_{icu}	If severe symptoms, probability to go to ICU	children: 0 adults: 0.36 seniors: 0.2	[10]
$\lambda_{H,R}$	If hospitalized, daily rate entering in R	children: 0 adults: 0.072 seniors: 0.022	[10]
$\lambda_{H,D}$	if hospitalized, daily rate entering in D	children: 0 **Adults and seniors: fitted**	
$\lambda_{icu,R}$	if in ICU, daily rate entering in R	children: 0 adults: 0.05 seniors: 0.036	[10]
$\lambda_{icu,D}$	if in ICU, daily rate entering in D	children: 0 **Adults and seniors: fitted**	

Interventions and other behavioural changes

	CC	CA	CS	AA	AS	SS	Period
Light social distancing	0.90	0.90	0.72	0.90	0.72	0.72	5 March – 19 March, 9 June –
Closing schools	0.05	0.93	1	1	1	1	16 March – 10 May
Strong social distancing	0.52	0.52	0.42	0.52	0.42	0.42	20 March – 7 June
Reduced workplace contacts	1	1	1	0.21	1	1	20 March – 7 June
Closing most non-essential shops	1	1	1	0.40	0.40	0.40	16 March – 26 April
Closing some shops	1	1	1	0.60	0.60	0.60	27 April – 10 May
Closing restaurants	1	1	1	0.80	0.80	0.80	16 March – 10 May
School summer holiday	0.05	0.93	1	0.76	1	1	4 July – 9 August
Contact tracing, testing, masks...	?	?	?	?	?	?	11 May –

The numbers represent the reduction in contacts (compared to no intervention; CC=between children, CA=between children and adults, etc)

The interventions do not aim to represent precisely the exact policies (so the model cannot be used to compare the efficacy of the interventions), but rather the general trend in relative contact frequency

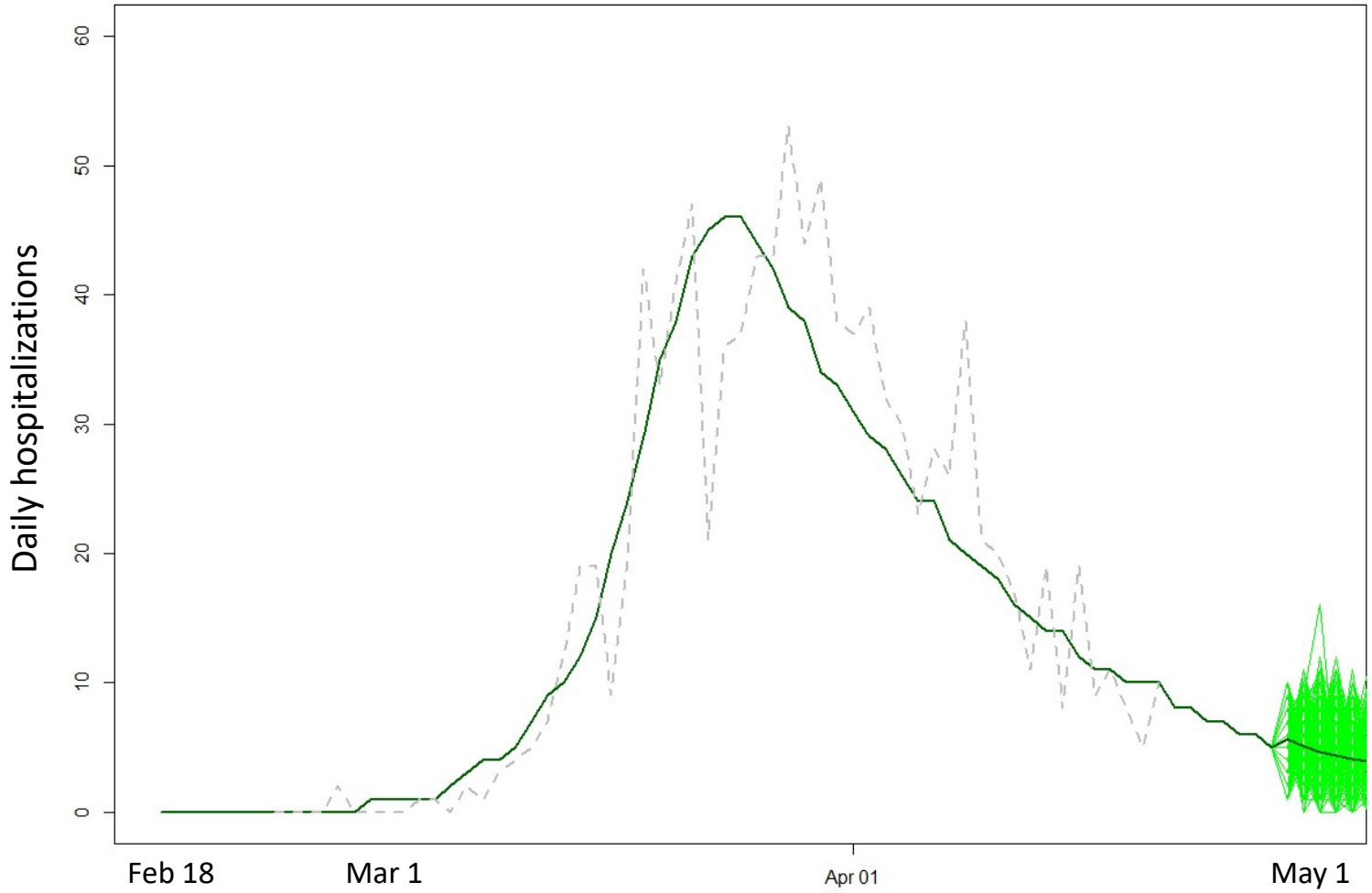
Model application for Geneva

- Population: canton of Geneva, 510,000 inhabitants (https://www.bfs.admin.ch/bfs/de/home/statistiken/bevoelkerung.gnpdetail.2020-0162.html with expected growth)
- We assumed a closed population (no new infections from other cantons or abroad)
- We selected a best-fitting set of parameters using approximate Bayesian computation (rejection method), calibrated against cantonal data on daily hospitalizations and deaths (https://www.ge.ch/document/covid-19-situation-epidemiologique-geneve/telecharger, accessed on 27 April 2020)
- Deterministic version applied until 28 April; thereafter stochastic version (results of 1000 runs presented)

Scenarios modelled

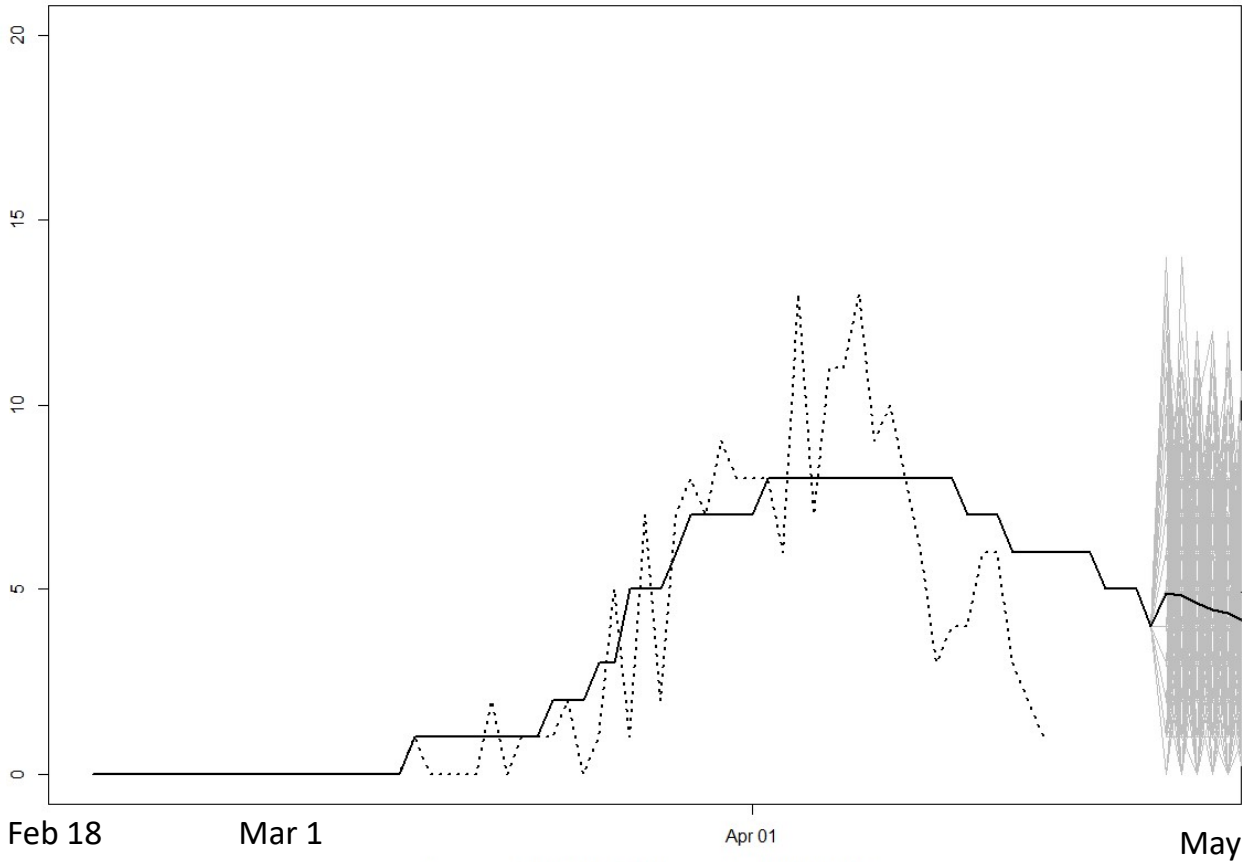
Baseline (“back to normal”)	Restrictions lifted according to plan; only light social distancing from 8 June onwards
Epidemic control	All contacts are reduced to a level that will prevent ICU overflow (assumed capacity in Geneva: 114 beds; icumonitoring.ch, accessed 28 April 2020)
Epidemic control (children excluded)	As “epidemic control”, but contacts involving children not reduced
Isolating seniors	Contacts involving seniors strongly reduced; mild contact reduction for other age groups
Contact reduction focusing on adults	As “epidemic control”, but contacts among children and seniors reduced less

New hospitalizations per day



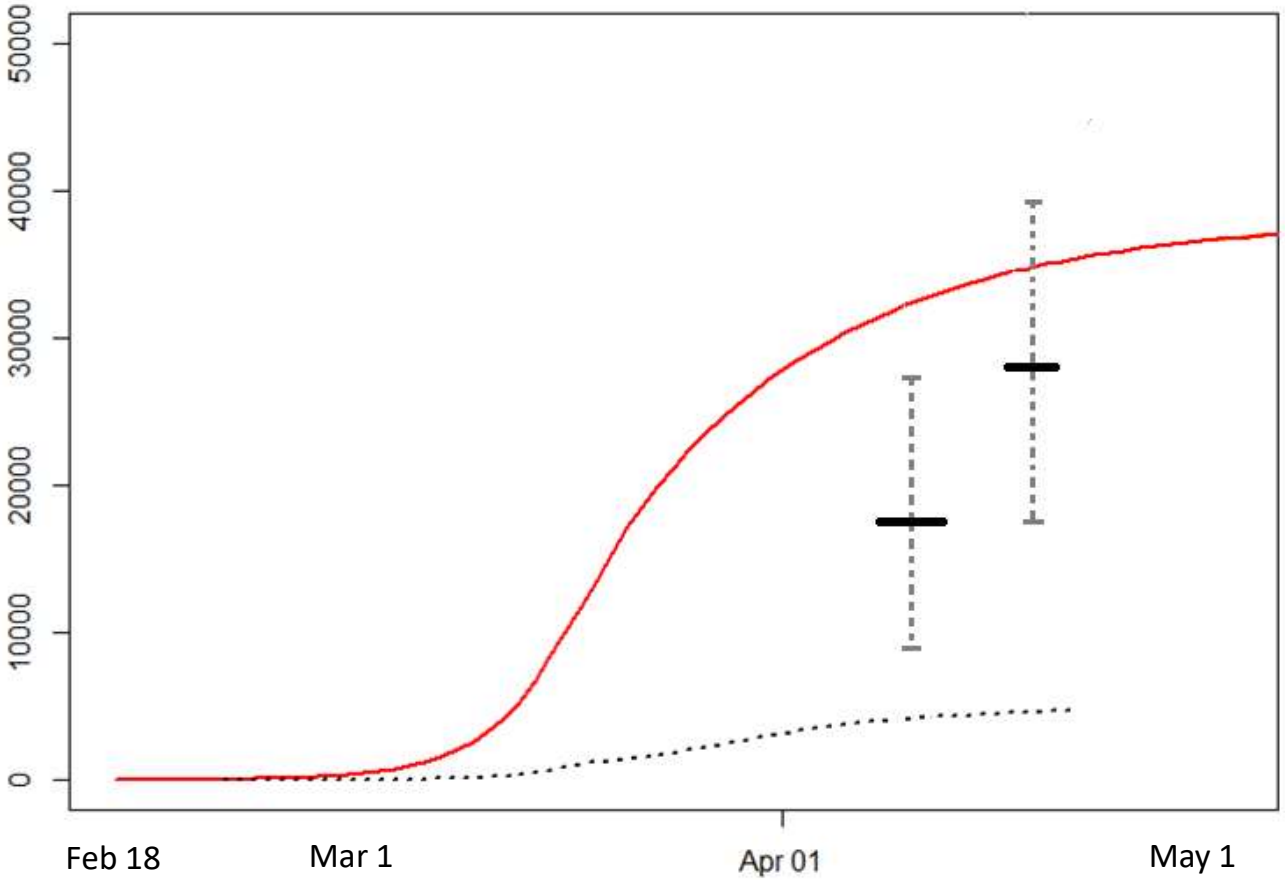
Solid curves represent model projection (dark green: mean over all simulations; light green: 1000 individual simulations). Dashed curve: data (cantonal data on hospitalizations)

Deaths due to COVID-19 per day



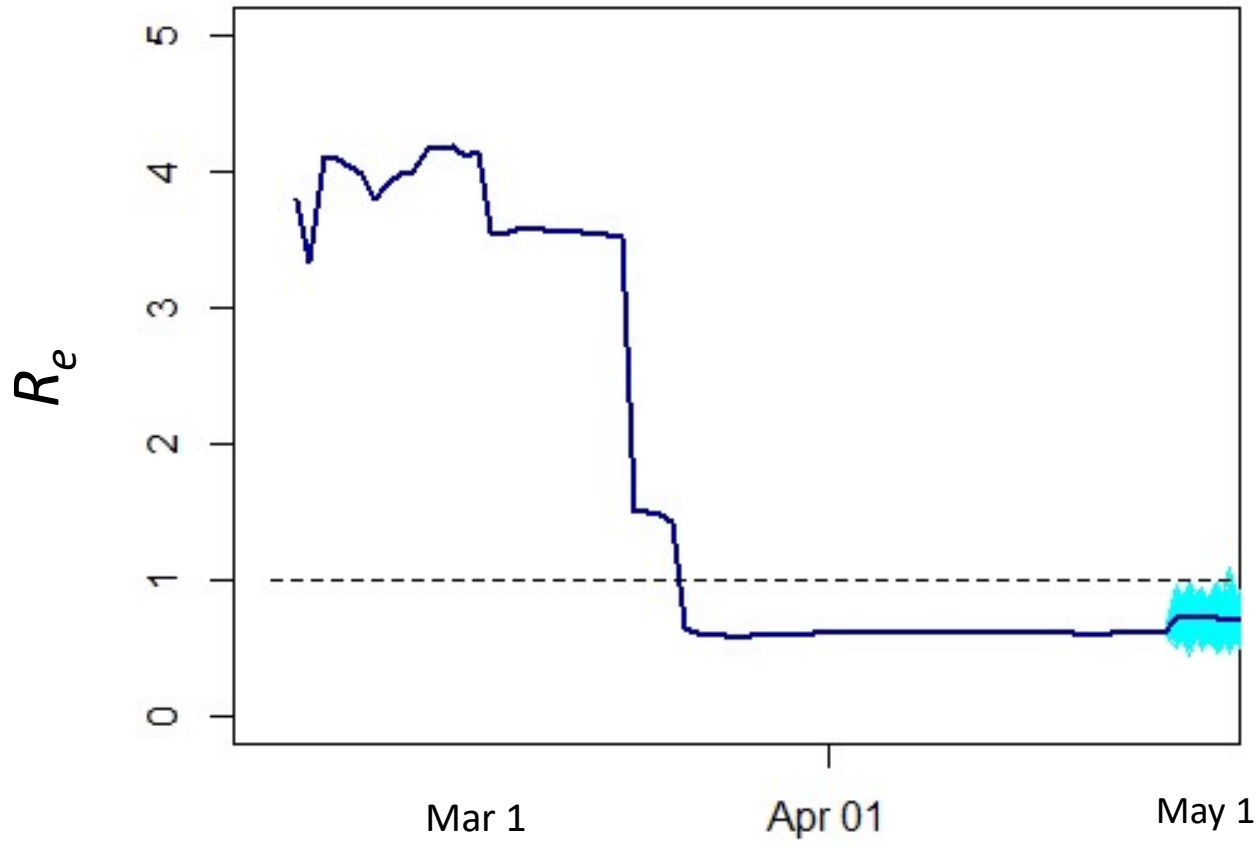
Solid curves represent model projection (black: mean over all simulations; grey: 1000 individual simulations). Dotted curve: data (cantonal data on daily deaths)

Cumulative cases



Solid red curves represent model projection (all infected); dashed curve data (confirmed cases); whisker graphs seroprevalence from the serosurvey with 95% CI (https://www.hug-ge.ch/medias/communique-presse/seroprevalence-covid-19-premiere-estimation)

Effective reproductive number

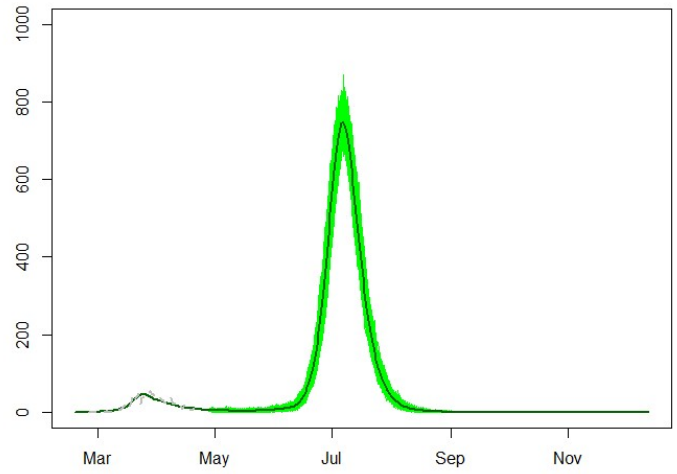


The effective reproductive number decreased from about 4 (beginning of the epidemic) to **0.6** (from 20 March onwards)

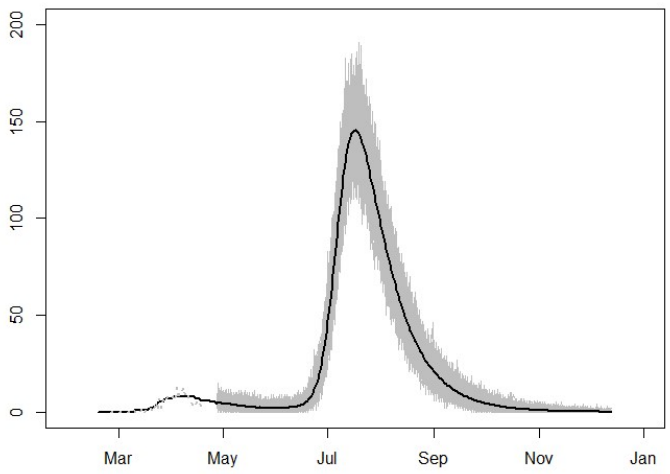
Baseline scenario: “back to normal”

- All restrictions except social distancing are lifted according to the Federal Council’s plan
- Working will return to normal (no home office) from 8 June
- Social distancing will return to first level (=equivalent to 5-15 March) on 8 June
- First level of social distancing (first set of recommendations form 5 March) will be applied throughout the year

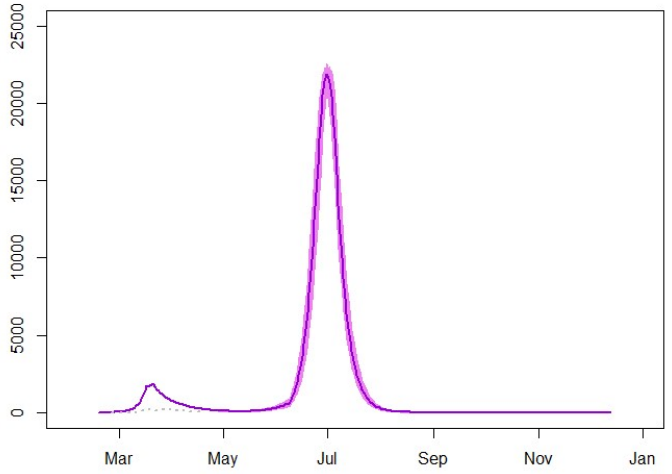
New hospitalizations per day



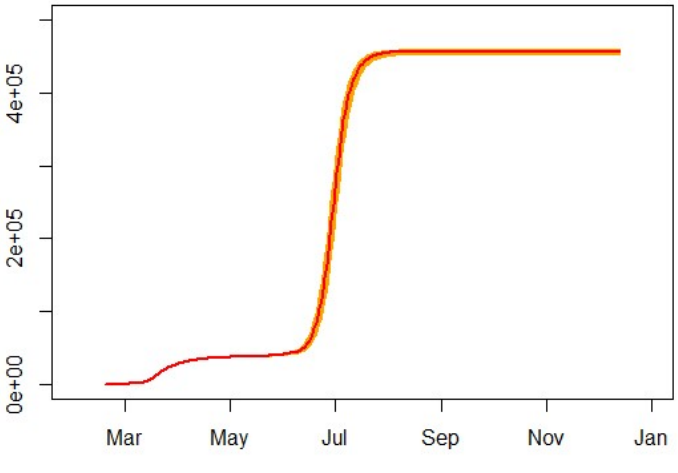
New deaths per day



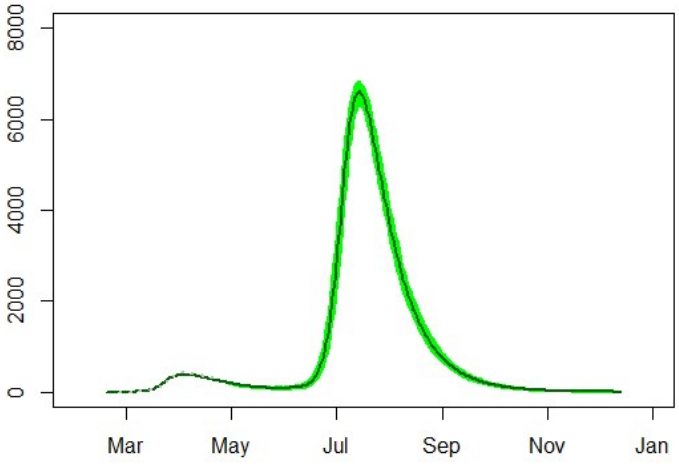
New infections per day



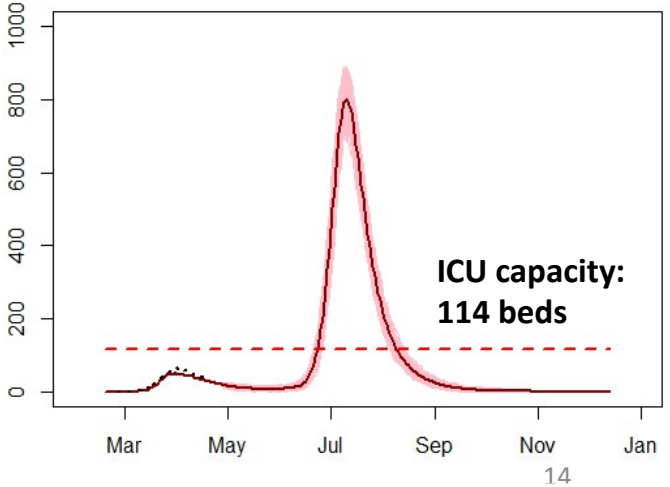
Cumulative cases



People in hospital



People in ICU



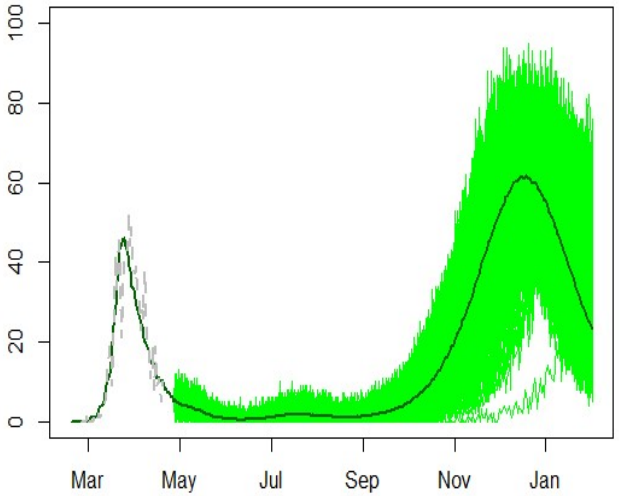
Baseline scenario: conclusions

- A second wave will be expected from late June
- The infection will go through most (~90%) of the population by the end of July
- Peak in hospitalizations expected in mid-June: up to 7000 patients in hospital, of whom 800 in ICU
  - 7 times more than available ICU beds
- 5600 to 6100 people will die during the second wave
- Unlikely to be a realistic scenario (in reality, restrictions will likely be reintroduced as soon as the incidence starts to increase) – this should be seen as a comparator («worst case» scenario, showing what happens if nothing is done)

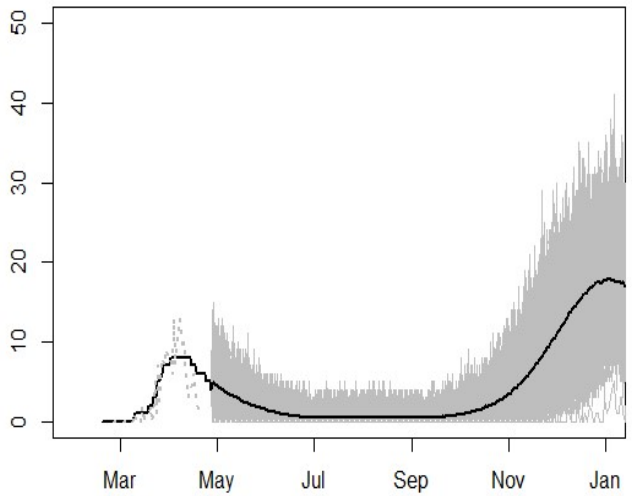
Epidemic control scenario

- An additional intervention will be applied from 11 May, reducing the contacts between all individuals (regardless of age group)
- We set the contact reduction to the minimum value that allows to keep the number of ICU patients within the capacity limits
- Practical interpretation may be a combination of various interventions:
  - Frequent use of masks or other forms of protection
  - Increased testing: people tested positive will be isolated for a part of infectious period
  - Tracing app and other contact tracing methods: Those exposed will be identified early and can be isolated through the whole infectious period

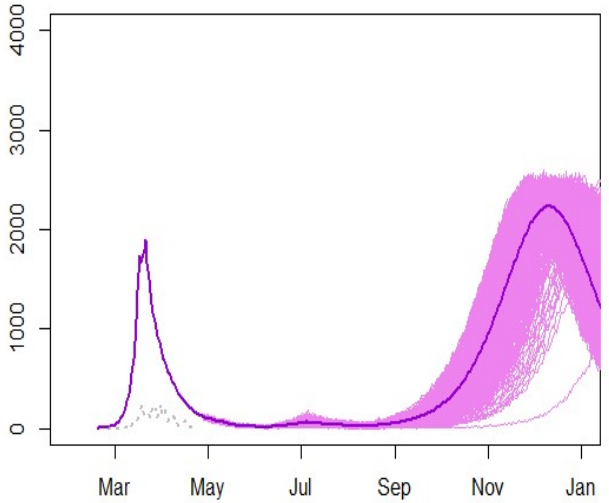
New hospitalizations per day



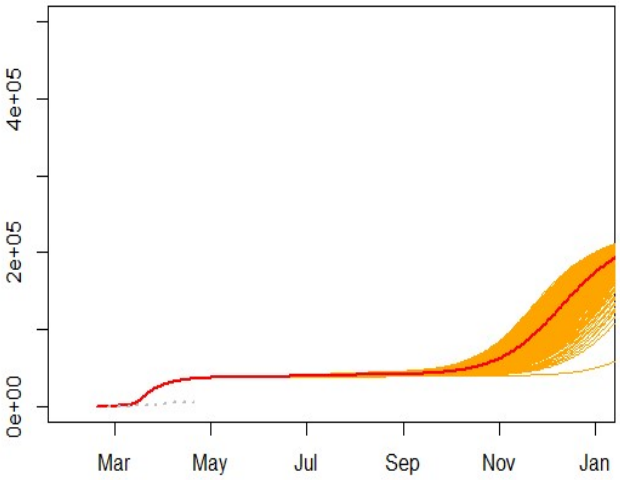
New deaths per day



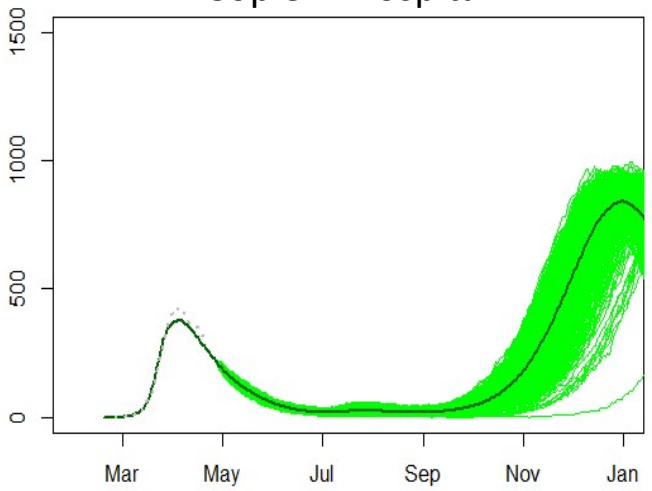
New infections per day



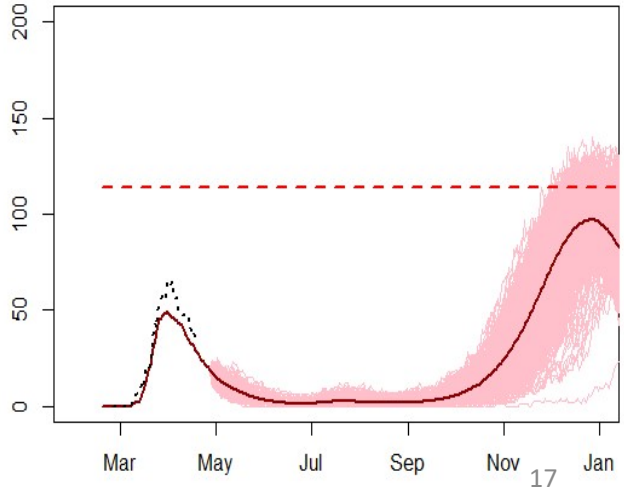
Cumulative cases



People in hospital



People in ICU



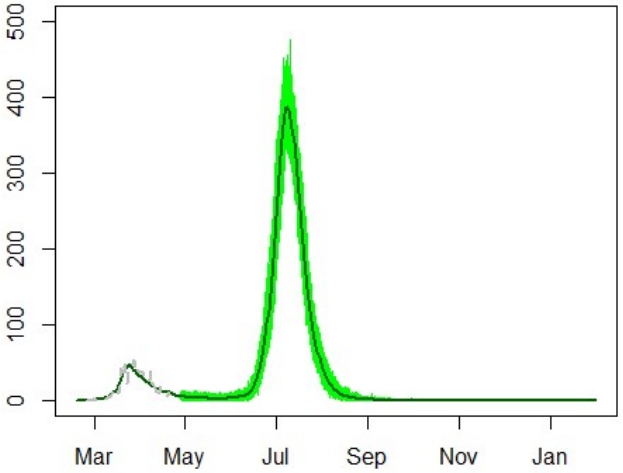
Epidemic control scenario: conclusions

- Minimum reduction in all contacts: 58% compared with “light social distancing” only
  - => Overall **62% reduction** in contacts not involving seniors, **70% reduction** in contacts involving seniors, compared with normal (pre-coronavirus) situation
- A second wave is expected to peak in December 2020 – January 2021
  - More severe than current epidemic (about 170,000 infected and 1300 deaths in Geneva)
  - However, the level of the epidemic is manageable: need of ICU places will exceed the capacity (114 beds) only with very low probability
  - Maximum number of people simultaneously in hospital will be about 1000 (at the end of the year)

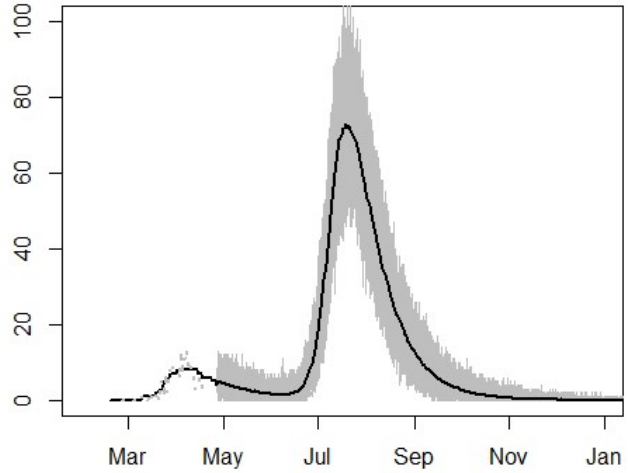
Epidemic control, excluding children

- Contact reduction among adults and seniors as in the full suppression scenario (58% reduction compared with “light social distancing”)
- Children assumed to have normal contacts among themselves, and with adults and seniors (level of “light social distancing”, accounting for school closure during summer holidays)

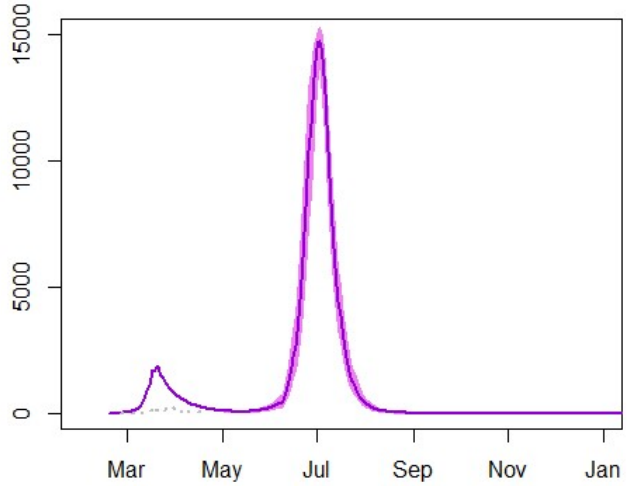
New hospitalizations per day



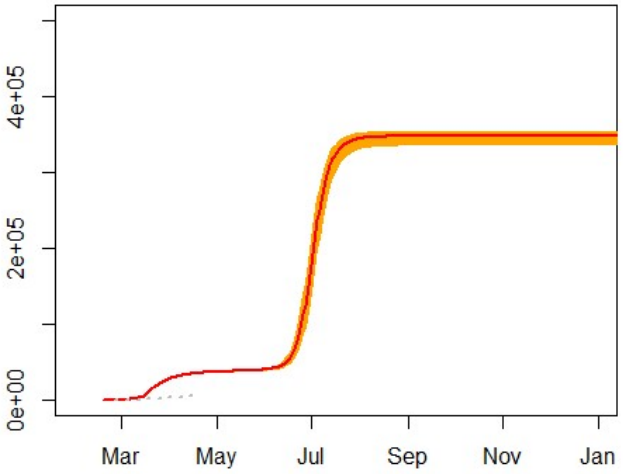
New deaths per day



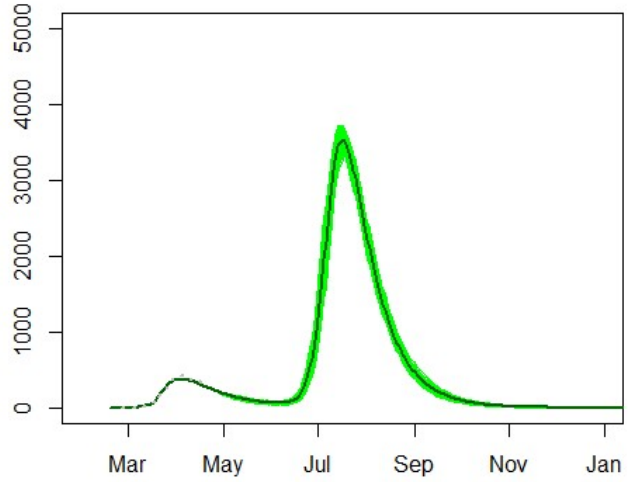
New infections per day



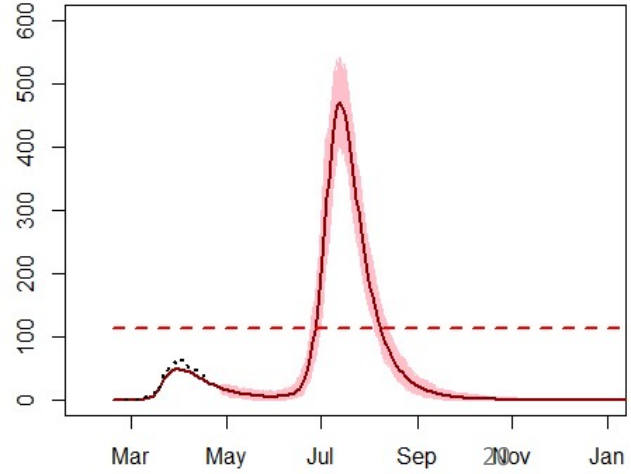
Cumulative cases



People in hospital



People in ICU



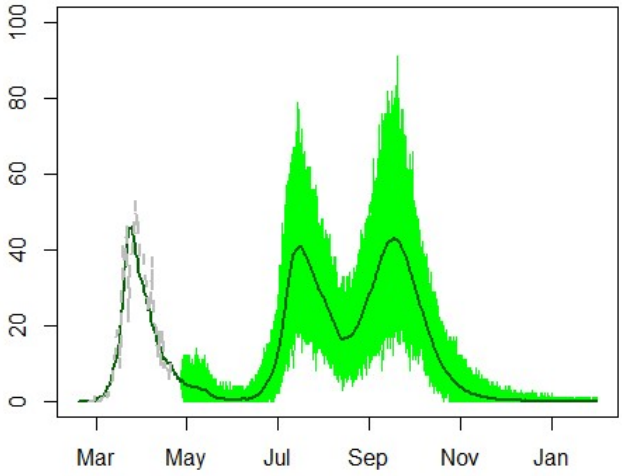
Epidemic control excluding children: conclusions

- Reducing contacts among adults and seniors only will not be sufficient to stop or delay a strong second wave (unless the contacts among adults and seniors are reduced even further)
- The second wave is expected in July (as in the “back to normal” scenario, but will be slightly milder):
  - About two thirds of the population will get infected
  - About 3000 deaths
  - Maximum 3800 patients in hospitals, of whom 500 in ICU
- Reducing also contacts between children and seniors resulted in only slightly milder peak (not shown)

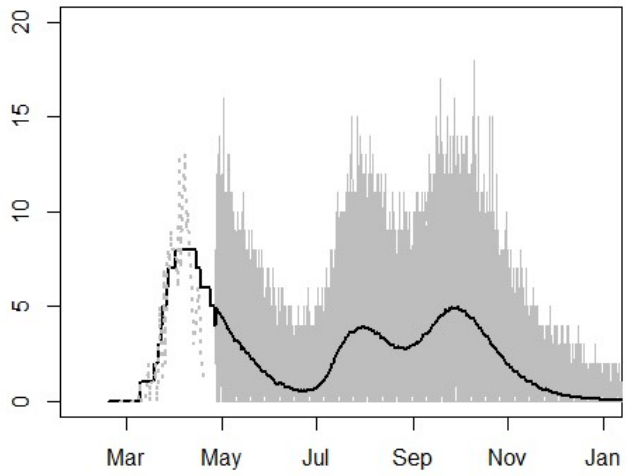
Scenario isolating seniors

- Mild contact reduction among children and adults (29%: half of the reduction in the “epidemic control” scenario)
- Contacts between seniors reduced to minimum (95% reduction)

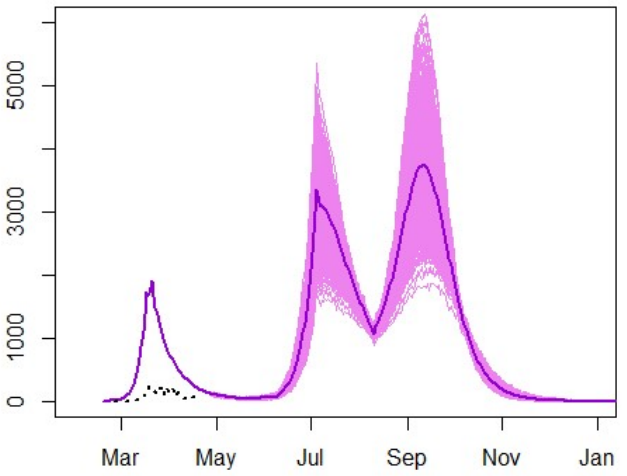
New hospitalizations per day



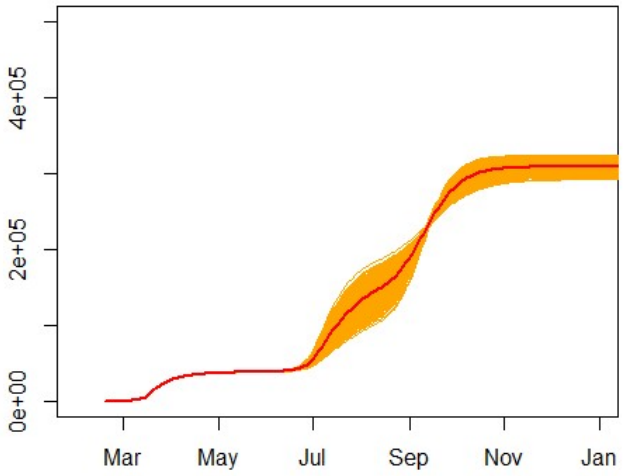
New deaths per day



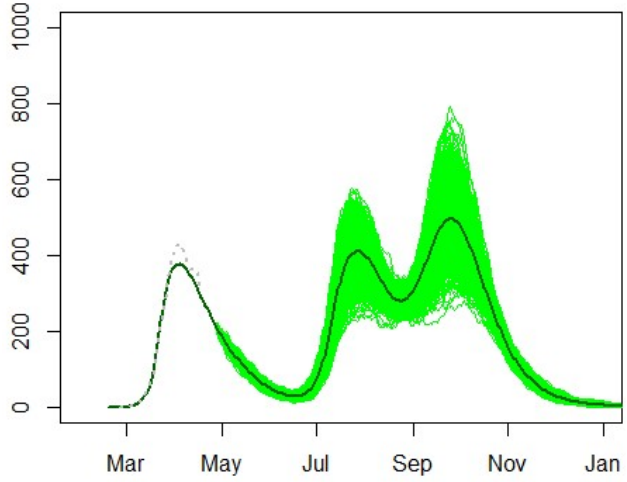
New infections per day



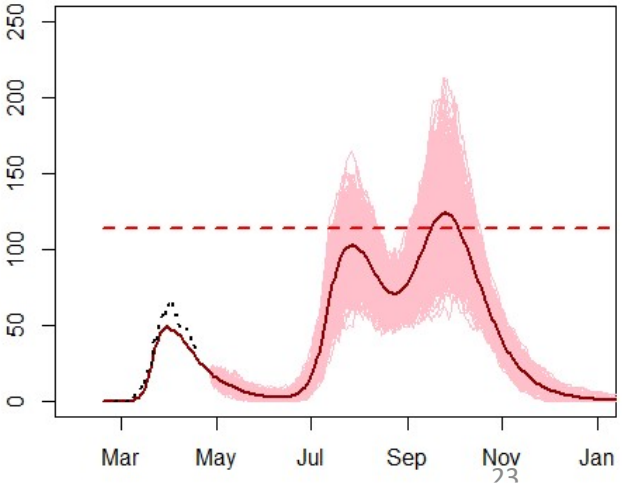
Cumulative cases



People in hospital



People in ICU

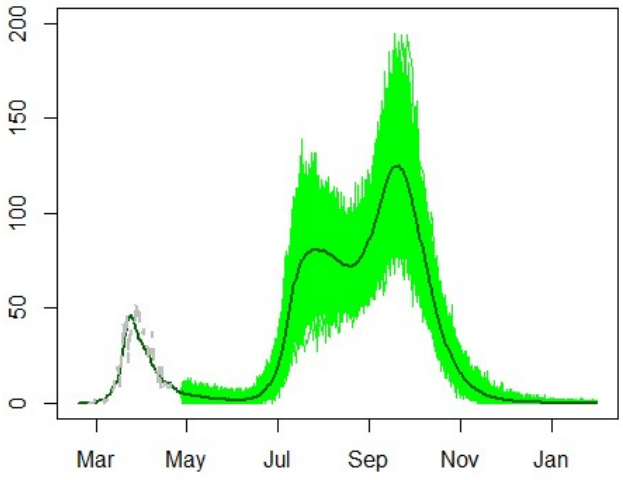


Scenario isolating seniors: conclusions

- Strong contact restrictions for seniors, combined with mild contract restrictions among the rest of the population, can keep the epidemic under control
- Two coming waves expected: second wave peaking in July (following the ending of strong restrictions), and a third wave peaking in late September (following the end of summer holiday season)
- About 250,000-280,000 infections expected during the second and third wave (from now until November)
- Peak number in hospitalizations between 400 and 800; about 50% probability that the need of ICU care will exceed the capacity during the third wave

Scenario focusing on adults

- Contacts involving adults will be reduced by 58%; contacts among children and seniors only by 29% (compared with “light social distancing” only)
- Represents e.g. a scenario mainly relying on smartphone based contact tracing (likely to be better adopted by adults than seniors or children)
- Adults form the majority of the population (62% in the model), so preventing infection in adults may protect seniors indirectly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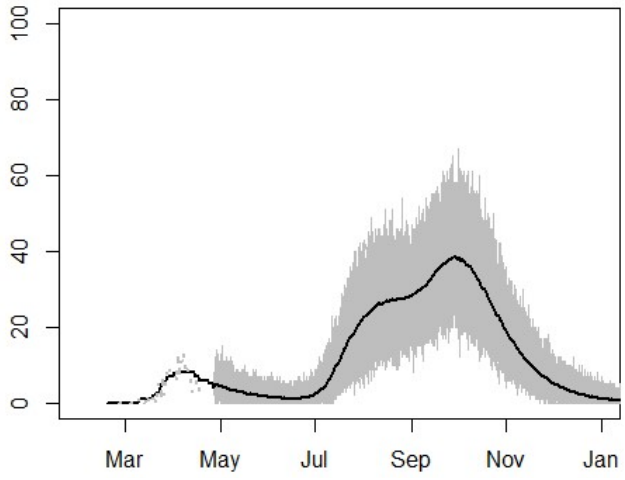
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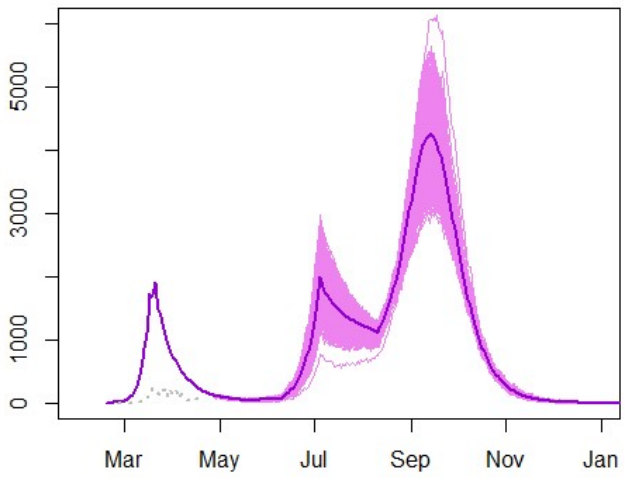
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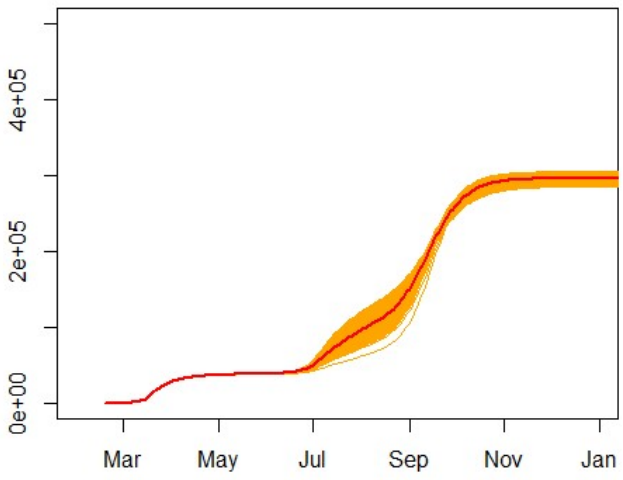
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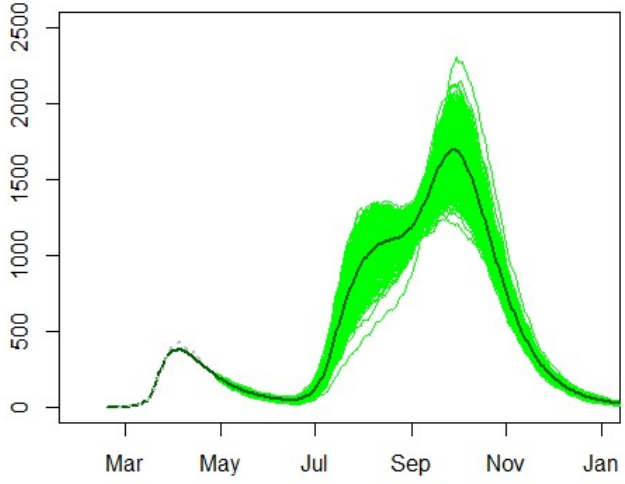
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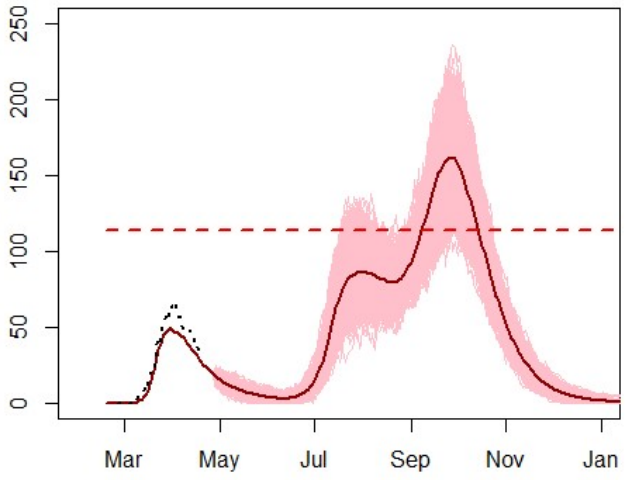
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Scenario focusing on adults: conclusions

- Two coming waves expected: second wave in July (after the restrictions lifted); and a third wave in September (after the end of the summer holiday season)
- About 250,000 infections expected during the second and third wave (from now until November)
- During second wave, the 114 ICU beds should be sufficient
- The third wave will be the most severe, peaking in about 1200-2200 people hospitalized, among whom 120-240 in ICU

Discussion and limitations

- Geneva modelled as a closed population (traffic in and out not included)
- Interventions are modelled using contact reductions as proxies – difficult to distinguish between specific interventions
- Potential effect of seasonality not taken into account
- Details on infectiousness and susceptibility of children still unknown and based on assumptions:
  - Presymptomatic, asymptomatic and paucisymptomatic individuals 49% less infectious than symptomatic individuals
  - Children per se as infectious as adults (but on average, less infectious because all children assumed asymptomatic or paucisymptomatic)
  - No difference in susceptibility

Conclusion (1)

- Keeping simple social distancing alone is not sufficient to prevent a strong second wave of the epidemic
- Contacts need to be reduced among all age groups including children (at least to some extent) – ignoring even one age group means that reductions among the rest of the population will not work
- The second wave is likely already in July
  - Note: seasonality not taken into account in the model
- If contacts continue to be reduced, we may expect two waves still this year: one in July and one in the early autumn

Conclusion (2)

- The aim should be to **reduce all contacts** (or, more likely to track the infected individuals so that the reduction in infectious contacts is equivalent) **by about 60-70%% compared with pre-coronavirus situation** – this only a mild second wave in the late autumn will be expected
- Age-specific interventions should primarily focus on the adult population (who are the largest population group and thus drive the epidemic)
- Protecting the most vulnerable population (seniors) directly is in theory also very effective, but only if contacts involving seniors are heavily (>95%) reduced during the rest of the year