McMasterPandemic: getting started

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Abstract

McMasterPandemic is an R package that provides tools for simulating and forecasting infectious disease outbreaks, using compartmental epidemic models. The primary mechanistic framework is a susceptible-exposed-infectious-removed (SEIR) model, with additional compartments for individuals in acute and intensive care units in hospitals.

Contents

1 Installation

Use `remotes::install_github("bbolker/McMasterPandemic")` to install the latest version of the package.

```
library(McMasterPandemic)
```

In this vignette we'll also use some other packages:

```
library(ggplot2); theme_set(theme_bw())
library(cowplot)
```

2 Data requirements

Parameters To run simulations, a few parameter values must be specified. Set these by editing the example params file, which is converted to a `params_pansim` object by `read_params()`. In the example, the time unit is assumed to be days.

The term "in acute care" means "in hospital but not in the intensive care unit (ICU)".

```
params1 <- read_params("ICU1.csv")
```

(by default `read_params` looks first in the working directory for CSV files, then in the `params` directory installed with the package (`system.file("params", package="McMasterPandemic")`). All the built-in parameter files can be found as follows:

```
folder <- system.file("params", package="McMasterPandemic")
list.files(folder)

#>  [1] "CI_base.csv"             "CI_updApr1.csv"
#>  [3] "ICU_diffs.csv"           "ICU1.csv"
#>  [5] "midas_estimates_ali.csv" "midas_estimates.csv"
#>  [7] "mistry-cmats"            "PHAC_testify.csv"
#>  [9] "PHAC.csv"                "stanford_estimates.csv"
```

If you want to edit one of these files, you need to copy it to your working directory first. To find the full path to `ICU1.csv`, for example, use:

```
system.file("params/ICU1.csv", package="McMasterPandemic")

#> [1] "/Users/runner/work/_temp/Library/McMasterPandemic/params/ICU1.csv"
```

If `p` is a parameter set (e.g., the result of `read_params`), then `print(p, describe=TRUE)` or, equivalently, `describe_params(p)` will return a data frame with a column giving the meaning of each parameter.

```
knitr::kable(describe_params(params1))
```

symbol	value	meaning
beta0	1	Baseline (non-intervention) transmission across categories
Ca	0.667	relative asymptomatic transmission (or contact)
Cp	1	relative presymptomatic transmission (or contact)
Cm	1	relative mildly symptomatic transmission (or contact)
Cs	1	relative severely symptomatic transmission (or contact)
alpha	0.333	Fraction of cases asymptomatic
sigma	0.192	1/time in exposed class
gamma_a	0.143	1/time for asymptomatic recovery
gamma_m	0.143	1/time for mildly symptomatic recovery
gamma_s	0.175	1/time for severely symptomatic transition to hospital/death
gamma_p	2	1/time in pre-symptomatic class
rho	0.1	1/time in hospital (acute care)
delta	0	Fraction of acute-care cases that are fatal
mu	0.956	Fraction of symptomatic cases that are mild (or moderate)
N	1e+06	Population size
E0	5	Initial number exposed
nonhosp_mort	0	probability of mortality without hospitalization
iso_m	0	Relative self-isolation/distancing of mild cases
iso_s	0	Relative self-isolation/distancing of severe cases
phi1	0.76	Fraction of hospital cases to ICU
phi2	0.5	Fraction of ICU cases dying
psi1	0.05	Rate of ICU back to acute care
psi2	0.125	Rate of ICU to death
psi3	0.2	Rate of post-ICU to discharge
c_prop	0.1	fraction of incidence reported as positive tests
c_delay_mean	11	average delay between incidence and test report
c_delay_cv	0.25	coefficient of variation of testing delay
proc_disp	0	dispersion parameter for process error (0=demog stoch only)
zeta	0	phenomenological heterogeneity parameter

The `summary` method for `params_pansim` objects returns the initial exponential growth rate (r_0), the doubling time ($\log 2/r_0$), the mean generation interval ($\overline{G}$), and the basic reproduction number

$$\mathcal{R}_0 = \beta_0 \left\{ \alpha \frac{C_\mathrm{a}}{\gamma_\mathrm{a}} + (1-\alpha)\left[\frac{C_\mathrm{p}}{\gamma_\mathrm{p}} + \mu(1-\mathtt{iso}_\mathrm{m})\frac{C_\mathrm{m}}{\gamma_\mathrm{m}} + (1-\mu)(1-\mathtt{iso}_\mathrm{s})\frac{C_\mathrm{s}}{\gamma_\mathrm{s}} \right] \right\} .$$

```
knitr::kable(round(t(summary(params1)),2))
```

r0	R0	Gbar	CFR_gen	dbl_time
0.23	6.52	12.19	0.04	3.04

The components of $\mathcal{R}_0$ (the reproduction number associated with each infectious compartment) can also be extracted.

```
knitr::kable(round(t(get_R0(params1, components=TRUE)),2))
```

asymptomatic	pre-symptomatic	mild	severe
1.56	0.33	4.46	0.17

It is also possible to change parameter settings without editing a parameter file, via the `fix_pars()` function. For example:

```
params2 <- fix_pars(params1, target = c(R0 = 5, Gbar = 5.2))
knitr::kable(round(t(summary(params2)),2))
```

r0	R0	Gbar	CFR_gen	dbl_time
0.39	5	5.2	0.04	1.79

Initial conditions The initial state must also be set, but it is sufficient to specify the parameter set (a `params_pansim` object), in which case the population size and initially exposed population will be taken from the parameters (in this case all non-exposed individuals are assumed to be susceptible).

```
state1 <- make_state(params=params1)
```

Start and end dates Dates on which the simulation starts and ends must be stated. If there are no observations that you are aiming to match, then these dates are arbitrary and only the length of time matters.

```
sdate <- "2020-02-10"
edate <- "2020-06-01"
```

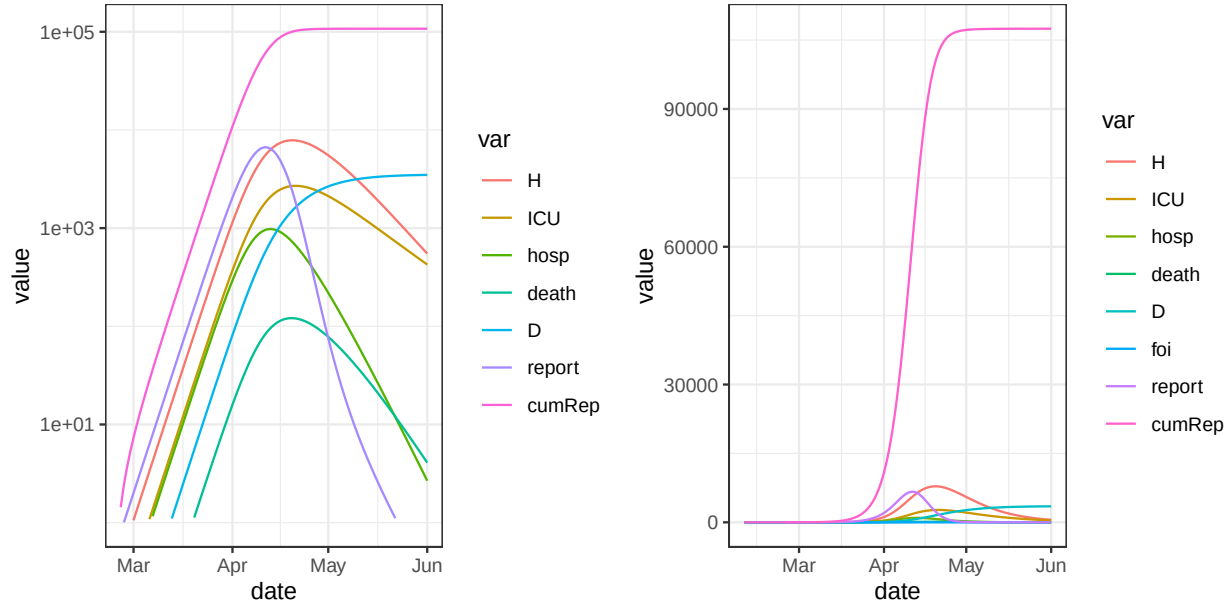
3 Running a simulation

A simple deterministic simulation is run as follows, and returns a `pansim` object. The `summary` method computes the times and magnitudes of peak demands on acute care (H) and intenstive care (ICU), and the basic reproduction number $\mathcal{R}_0$.

```
res1 <- run_sim(params=params1, state=state1, start_date=sdate, end_date=edate)
summary(res1)

#>   peak_ICU_date peak_ICU_val peak_H_date peak_H_val       R0
#> 1    2020-04-21         2695  2020-04-20       7846 6.518009
```

The `plot` method for `pansim` objects returns a `ggplot` object, optionally on a log scale.

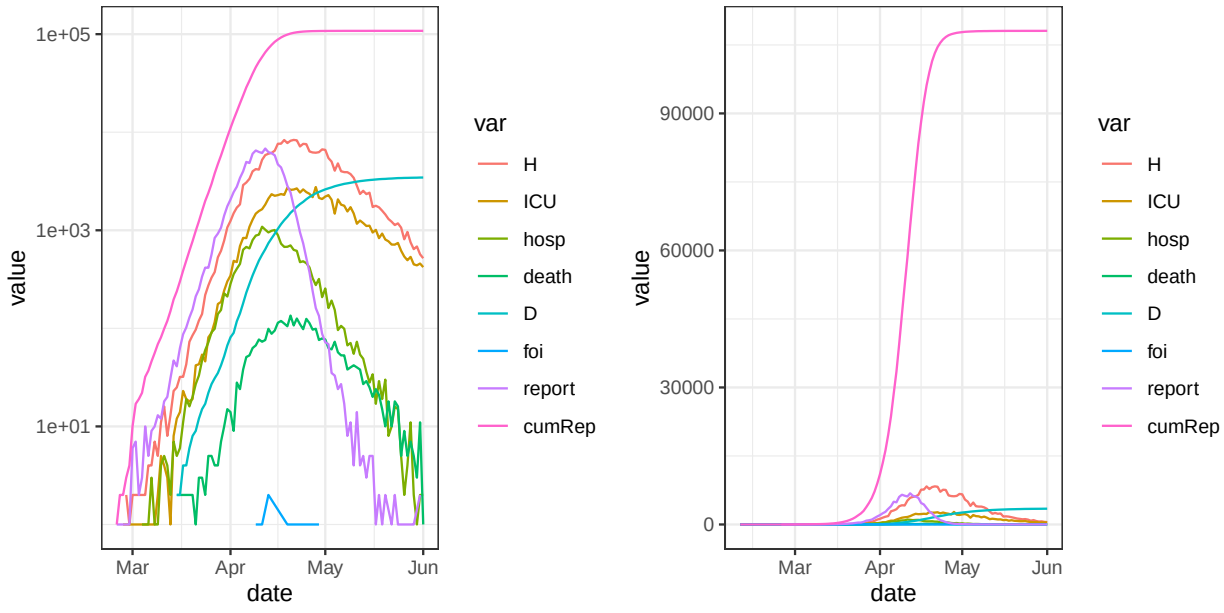
```
plot_grid(plot(res1, log=TRUE),  ## logarithmic
          plot(res1))  ## linear
```



3.1 Stochasticity

The effects of observation error are easy to explore with the `stoch` argument to `run_sim`. The `obs_disp` parameter is the dispersion parameter for a negative binomial (if the mean and variance are μ and σ^2, respectively, then $\sigma^2 = \mu + \frac{\mu^2}{\texttt{obs\_disp}}$).

```
set.seed(101)
params1obs <- update(params1, obs_disp=200)
res1obs <- run_sim(params1obs, state1, start_date=sdate, end_date=edate,
                   stoch=c(obs=TRUE, proc=FALSE))
summary(res1obs)

#>   peak_ICU_date peak_ICU_val peak_H_date peak_H_val       R0
#> 1    2020-04-28         2760  2020-04-21       8345 6.518009

plot_grid(plot(res1obs, log=TRUE),
          plot(res1obs))
```

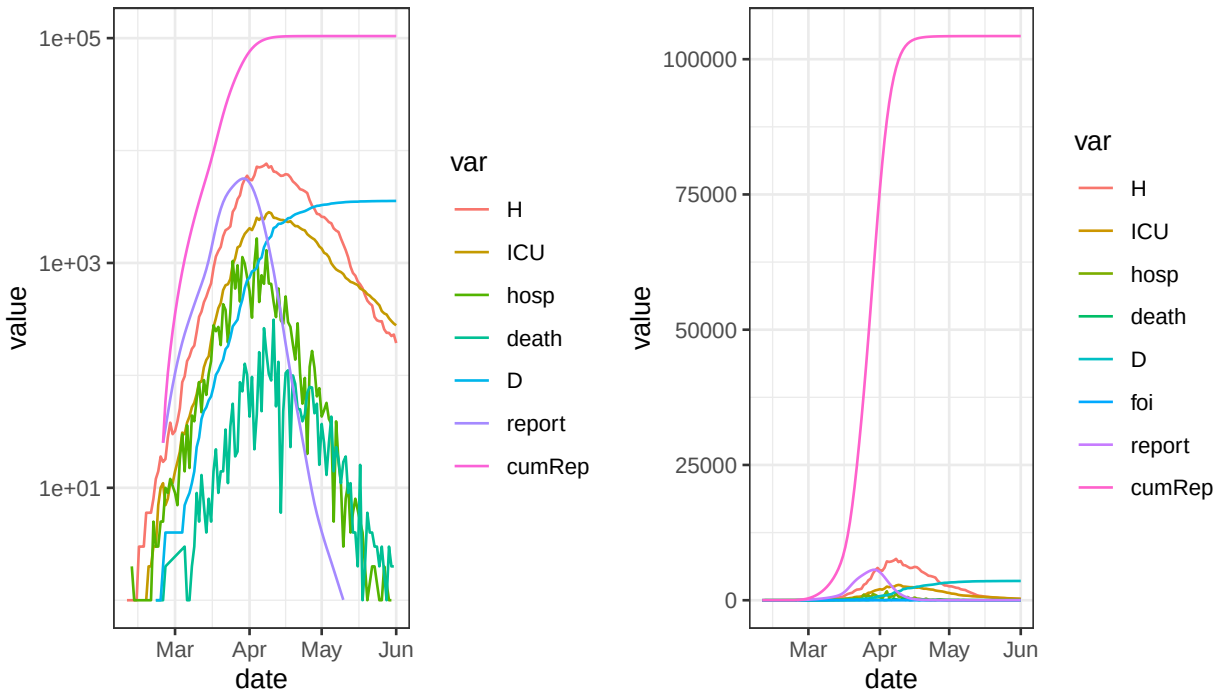


To simulate with process error, use `stoch=c(..., proc=TRUE)`. By default, this simulates only demographic stochasticity, which has little effect in a large epidemic.

```
params1proc <- update(params1,E0=200,proc_disp=0)  ## demog stoch only
res1proc <- run_sim(params1proc, start_date=sdate, end_date=edate,
                    stoch=c(obs=FALSE, proc=TRUE))
```

Making `proc_disp` positive simulates with additional process noise:

```
params1proc2 <- update(params1,E0=200, proc_disp=0.5, obs_disp=5)
res1proc2 <- run_sim(params1proc2, start_date=sdate, end_date=edate,
                    stoch=c(obs=FALSE, proc=TRUE))
plot_grid(plot(res1proc2, log=TRUE), plot(res1proc2))
```



Technical note. Demographic noise is included by calculating probabilities from the rates and then drawing a multinomial sample to determine how many individuals move from one compartment to each of the others. With pure demographic noise, the CV is very small with only ~ 1000 individuals moving among compartments. Process dispersion (`proc_disp`; "overdispersed demographic stochasticity") is implemented using `pomp::reulermultinom`, which adds gamma white noise to the event rates. For some discussion of this, see p. 274 and Appendix A of the "plug-and-play" paper by He *et al.* (2010, *J. R. Soc. Interface* **7**, 271–283, doi:10.1098/rsif.2009.0151. [**DE:** *The intensity of the gamma white noise process (`proc_disp`) has units (*cf. σ_{SE} *in He* et al.*); it would be easier to think about the cofficient of variation (CV) rather than standard deviation (sd).*]

[**DE:** *Notes scribbled from discussion with BB: To get CIs on a forecast, we could hack by adjusting `proc_disp` until getting CIs that are plausibly wide; estimating this number is a can of worms. A slighty more principaled way to decide on that number: fit params, then run sims with different combinations of obs and proc noise that yield noise like in the data: then infer how observed noise is divided btw proc and measurement error.*]

[**DE:** *DC commented on 19 Apr 2020 ('MP updates' thread): "5/ I have had the same question for a while regarding noise amplitude… I usually look at the variance of the data as a guidance, but never did anything formal. 6/ I often find myself starting with MCMC, just to give it up for ABC or something else a few days/weeks down the road because I end up spending way too much time in trying to fix more or less technical issues regarding convergence (I use Stan nearly all the time, maybe that's why…)."*]

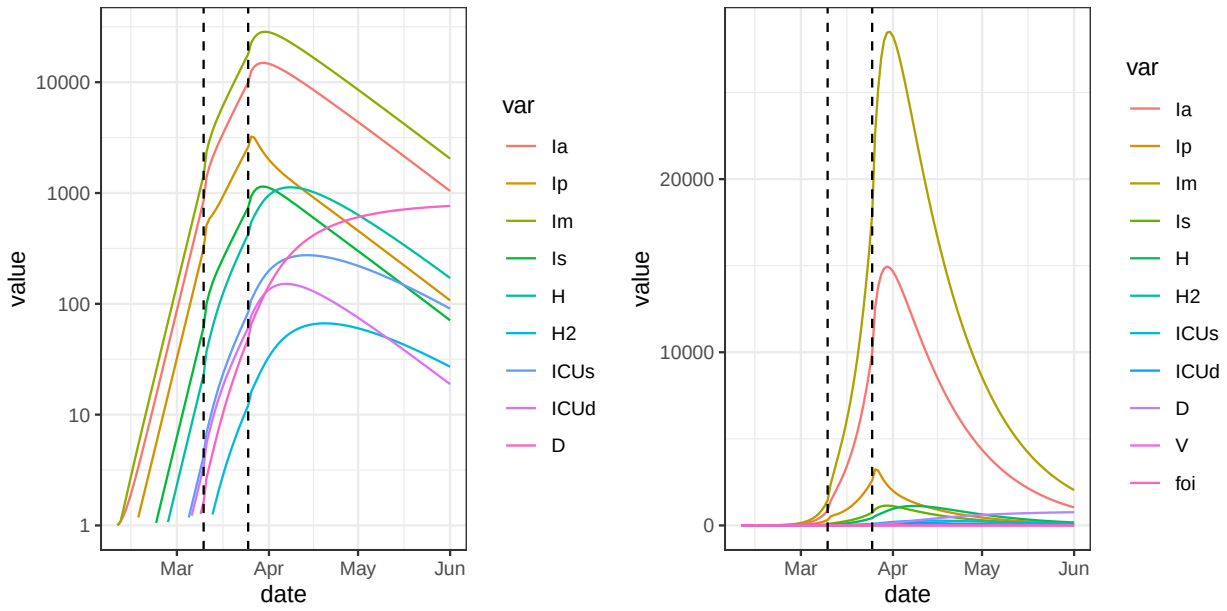
3.2 Time-dependent transmission rate

Implementing known changes in transmission rate (e.g., resulting from social distancing measures) is straighforward via the `time_pars` argument. The following reduces β_0 (and hence $\mathcal{R}_0$) to 50% of its original value on 10 March 2020, and to 10% of its original value on 25 March 2020.

Setting `ndt=20` forces 20 intermediate time steps to occur between each saved step. (Try it with `ndt=1` to see why this is a good idea.)

Setting `condense=FALSE` retains all variables in the output, rather than collapsing into a single I class *etc.*

```
time_pars <- data.frame(Date=c("2020-03-10","2020-03-25"),
                        Symbol=c("beta0","beta0"),
                        Relative_value=c(0.5,0.1))
restimedep <- run_sim(params1,state1,start_date=sdate,end_date=edate,
                        params_timevar=time_pars,ndt=20, condense=FALSE)
summary(restimedep)

#>   peak_ICU_date peak_ICU_val peak_H_date peak_H_val       R0
#> 1    2020-04-11          417  2020-04-09       1181 6.518009

plot_grid(plot(restimedep, log=TRUE, condense=FALSE),
          plot(restimedep, condense=FALSE))
```



4 Changing parameters

Some parameters you might wish to change are not directly available in the parameter file. Instead, you can adjust them using `fix_pars()`. For example, if you would like to change the default value of $\mathcal{R}_0$ implied in the parameter list `params1` you can do the following.

```
print(summary(params1))

#>         r0         R0       Gbar    CFR_gen   dbl_time
#>  0.2278149  6.5180089 12.1897402  0.0352000  3.0425898

## Change R0 to 2
newparams1 <- fix_pars(params1, target=c(R0=2))
print(summary(newparams1))

#>          r0          R0        Gbar     CFR_gen    dbl_time
#>  0.06649208  2.00002038 12.18974018  0.03520000 10.42450796
```

[**DE:** *See* ***refactor.Rmd*** *for functions not yet described here.*]

5 Calibration

In a typical epidemic forecasting application, we have imperfect information about the parameters and a time series of reported events (e.g., cases, hospitalizations, deaths, *etc.*). Our goal is to predict the future course of the outbreak, and to determine how it will differ under various intervention scenarios.

The natural approach is to find a set of parameters that lies within the estimated constraints and best fits the observed part of the epidemic. This is referred to as "calibrating" the model to the data.

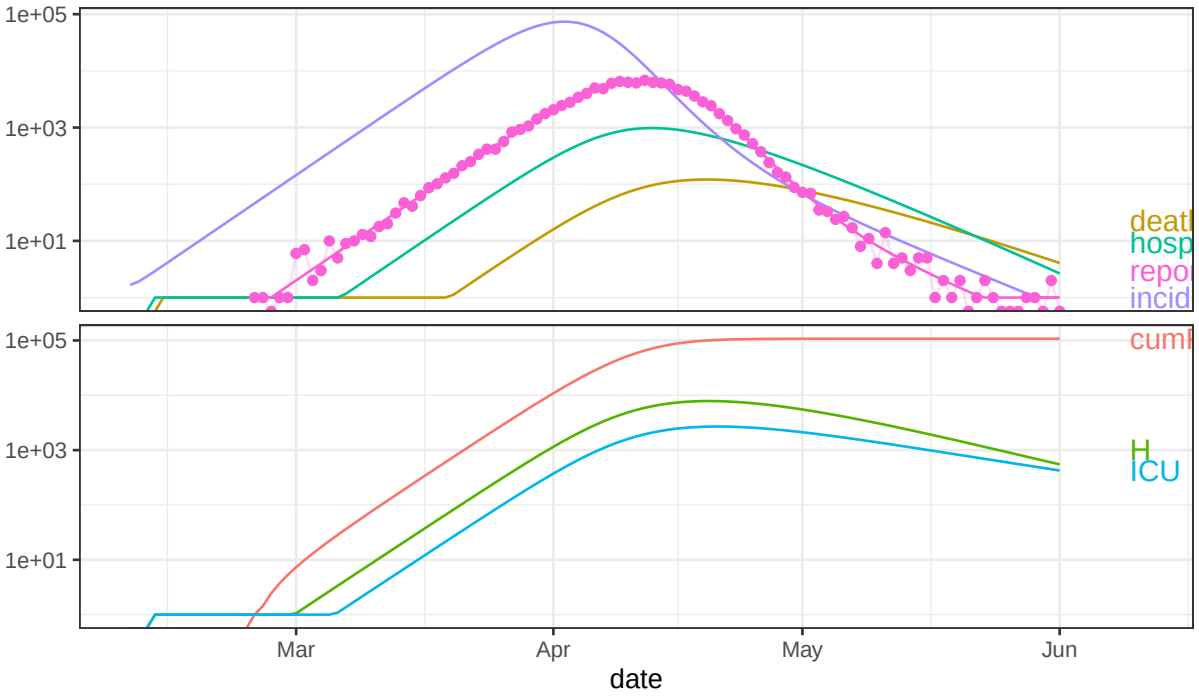
Unsurprisingly, there is a function `calibrate()` for doing just this.

Imagine that the simulated data saved in `res1obs` were the observed data to which want to fit the model. We can calibrate to these data as follows.

Note that `calibrate()` requires the data come in "long form", which means that for each date on which we have data, there are separate rows for each type of data (report, death, hospitalization, *etc*). This is in contrast to "wide form", for which there is one row for each date, and separate columns for each observed variable.

```
library(dplyr)
```

```r
## pull out only the reported cases and convert to long form:
report_data <- (res1obs
    %>% mutate(value=round(report), var="report")
    %>% select(date, value, var)
    %>% na.omit()
)
head(report_data)

#>          date value    var
#> 16 2020-02-25     1 report
#> 17 2020-02-26     1 report
#> 18 2020-02-27     0 report
#> 19 2020-02-28     1 report
#> 20 2020-02-29     1 report
#> 21 2020-03-01     6 report

## beta0 is the only parameter we're going to optimize:
opt_pars <- list(params = c(beta0=0.1))
## fit beta0 based on the report data:
fitted.mod <- calibrate(
    data = report_data
  , start_date = sdate
    ## skip breaks that are present by default:
  , time_args = list(break_dates = NULL)
  , base_params = params1obs
  , opt_pars = opt_pars
  ##, debug_plot = TRUE # instructive plotting during optimization
)
## plot the resulting fit
plot(fitted.mod, data=report_data)
```




```
## spit out fitted parameters (in this case, just beta0)
coef(fitted.mod, "fitted")

#> $params
#>    beta0
#> 1.000625
```

That worked well, given that the value of `beta0` used for the simulation was 1. You might want to try running the above interactive without commenting out "`debug_plot = TRUE`". This will allow you to see the process of fitting the model to the data. Note, however, that this instructive visualization of the optimization process will slow down the optimization by an order of magnitude.

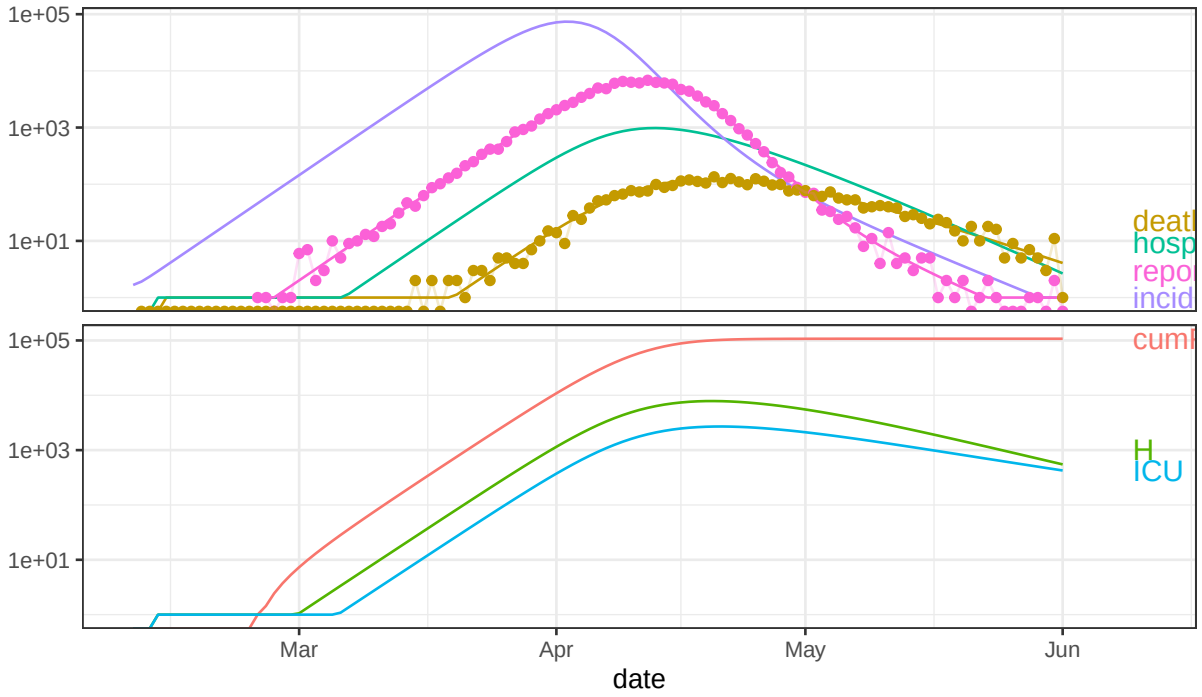
Let's now now try to fit the model to both reports and deaths. It is easiest to create the required long-form data frame using the `pivot_longer` function in the `tidyr` package.

```
library(tidyr)
```

```
report_death_data <- (res1obs
    %>% select(date, report, death)
    %>% pivot_longer(names_to = "var", -date)
    %>% mutate(value=round(value))
    %>% na.omit()
)
head(report_death_data, n=12)

#> # A tibble: 12 x 3
#>    date       var   value
#>    <date>     <chr> <dbl>
#>  1 2020-02-11 death     0
#>  2 2020-02-12 death     0
#>  3 2020-02-13 death     0
#>  4 2020-02-14 death     0
#>  5 2020-02-15 death     0
#>  6 2020-02-16 death     0
#>  7 2020-02-17 death     0
#>  8 2020-02-18 death     0
#>  9 2020-02-19 death     0
#> 10 2020-02-20 death     0
#> 11 2020-02-21 death     0
#> 12 2020-02-22 death     0
```

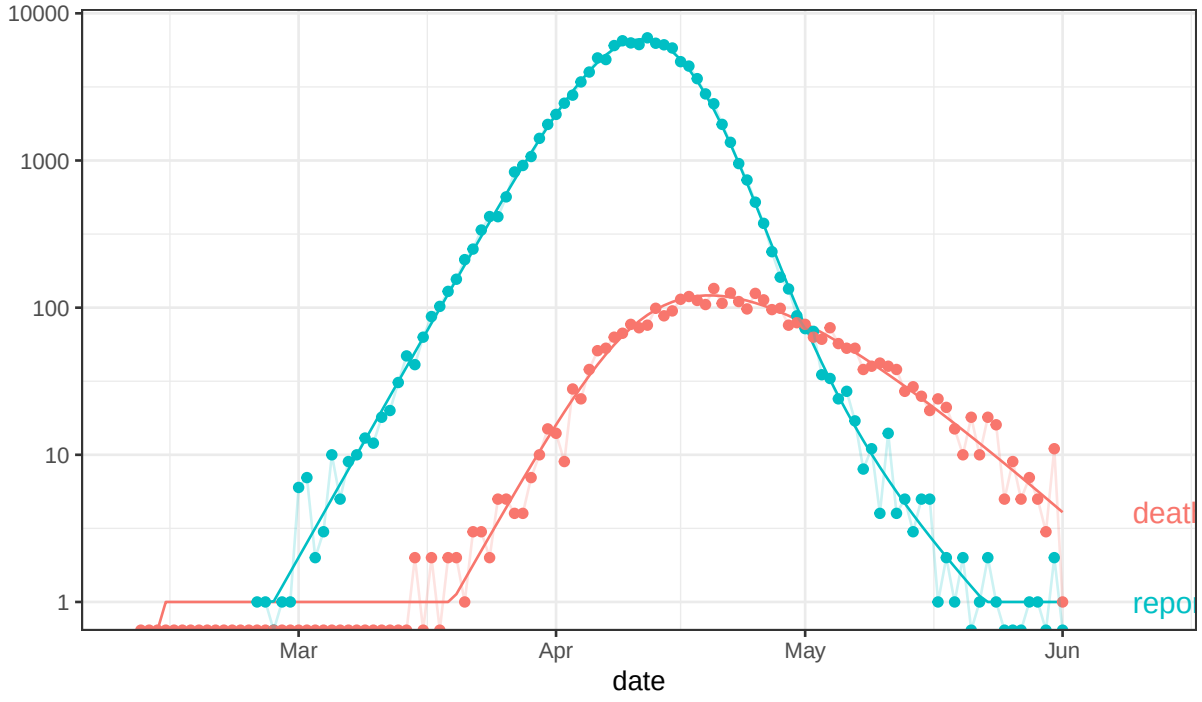
Now let's fit to both reports and deaths.

```
## beta0 is the only parameter we're going to optimize:
opt_pars <- list(params = c(beta0=0.1))
fitted.mod <- calibrate(
    data = report_death_data
  , start_date = sdate
    ## skip breaks that are present by default:
  , time_args = list(break_dates = NULL)
  , base_params = params1obs
  , opt_pars = opt_pars
  ##, debug_plot = TRUE # instructive plotting during optimization
)
plot(fitted.mod, data=report_death_data)
```



If you wish, you can plot just the data being fitted, and the fitted model, via:

```
plot(fitted.mod, data=report_death_data,
     predict_args=list(keep_vars=c("report","death")))
```



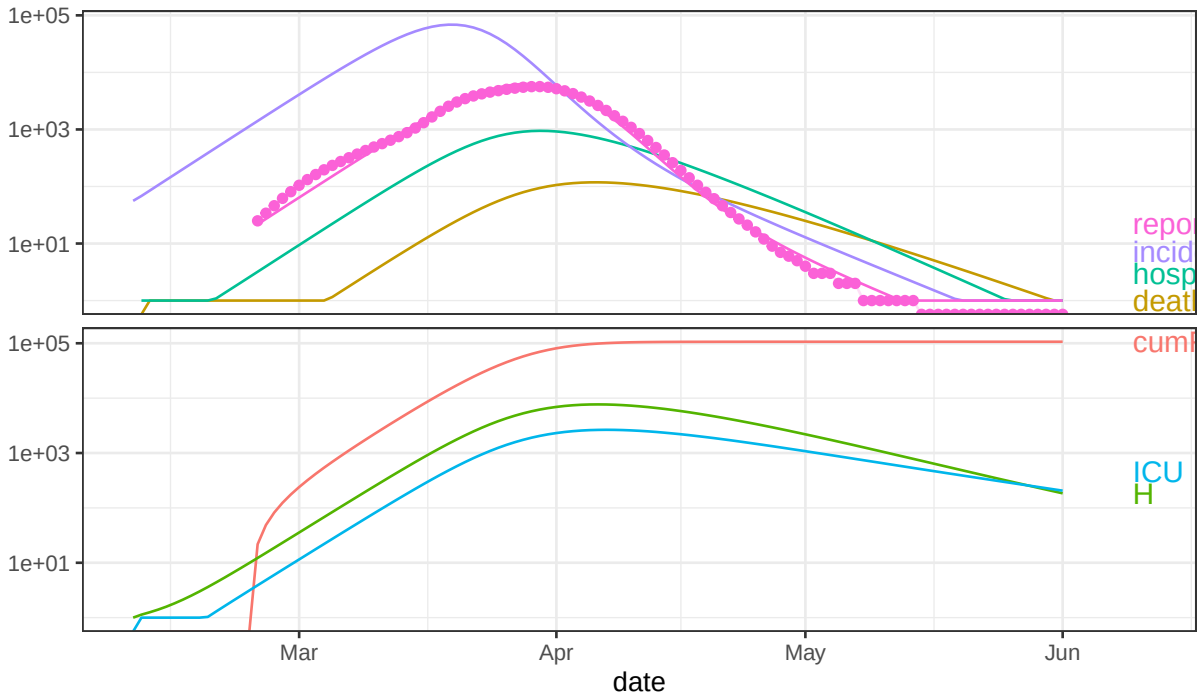
That fit looks remarkably good. Let's see how good:

```
coef(fitted.mod, "fitted") # spit out fitted parameters

#> $params
#>    beta0
#> 1.000625

summary(coef(fitted.mod))

#>         r0         R0       Gbar    CFR_gen   dbl_time
#>  0.2279195  6.5220826 12.1897402  0.0352000  3.0411926
```

Amazing: our fitted `beta0` is exactly the value used in the simulation that generated the data. Note that in the summary at the end, `r0` refers to the initial exponential growth rate from the fitted model. This provides an alternative to the `epigrowthfit` package for fitting epidemic growth rates.

Finally, consider the case where we have both observation and process noise. Fitting to these data won't do as well, because `calibrate()` does not have a way of fitting to process noise. Consequently, the quality of our fit can be expected to be worse. Of course, real data always contain process noise...

```
report_data <- (res1proc2
    %>% mutate(value=round(report), var="report")
    %>% select(date, value, var)
    %>% na.omit()
)
## beta0 is the only parameter we're going to optimize:
opt_pars <- list(params = c(beta0=0.1))
fitted.mod <- calibrate(
    data = report_data
  , start_date = sdate
    ## skip breaks that are present by default:
  , time_args = list(break_dates = NULL)
  , base_params = params1proc2
  , opt_pars = opt_pars
  ##, debug_plot = TRUE # instructive plotting during optimization
)
plot(fitted.mod, data=report_data)
```

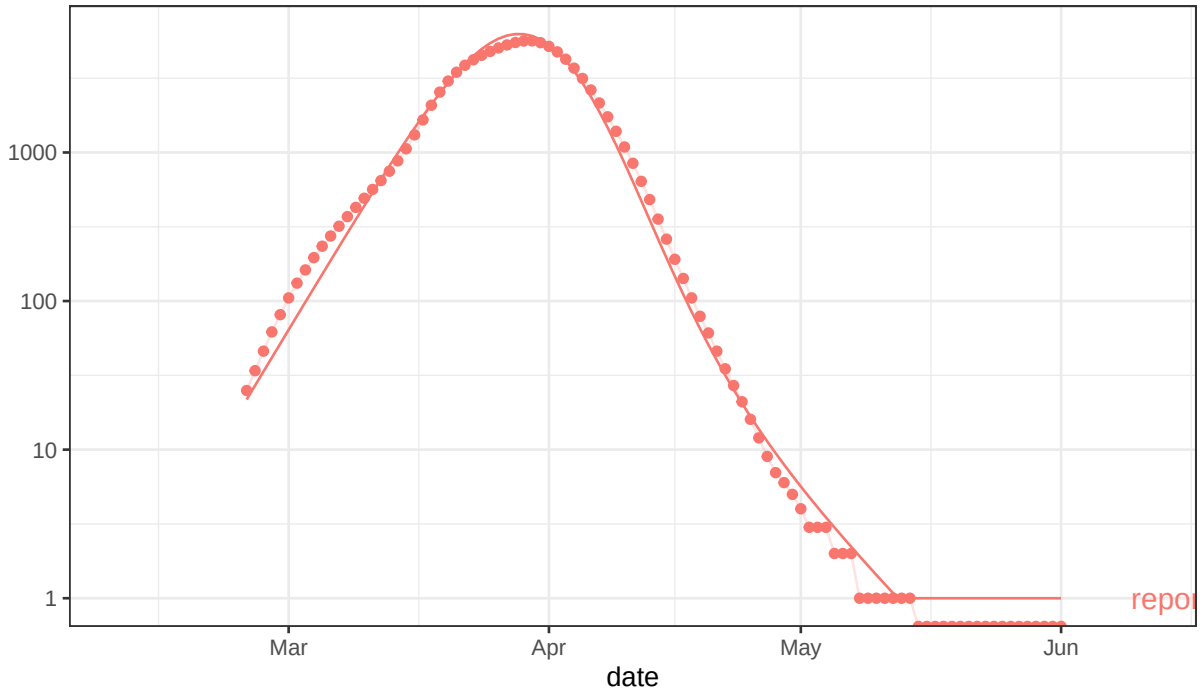


145

```
coef(fitted.mod, "fitted") # spit out fitted parameters

#> $params
#>   beta0
#> 0.92375

summary(coef(fitted.mod,"all"))

#>          r0          R0        Gbar     CFR_gen    dbl_time
#>  0.2147032  6.0210107 12.1897402  0.0352000  3.2283965
```

146 As above, you can plot just the data being fitted, and the fitted model, via:

```
plot(fitted.mod, data=report_data, predict_args=list(keep_vars="report"))
```



5.1 Troubleshooting calibrations

If you find that the fitted model trajectory is peculiarly jagged, the likely culprit is the time step. In this case, increase the number of internal time steps per time step (`ndt`), via adding `sim_args` to your `calibrate()` call, e.g. `sim_args = list(ndt=2)`.
You may need to experiment with `ndt` to get a smooth result.

6 Scenario exploration

Typically, after calibrating to observed data, you are likely to be interested in forecasting what might happen in the future, under various scenarios of possible changes in control measures/policies. Here, we give an example involving changing the transmission rate (β) in the future.

First we load some data manipulation packages for convenience.

```
library(zoo)
library(tidyverse)
```

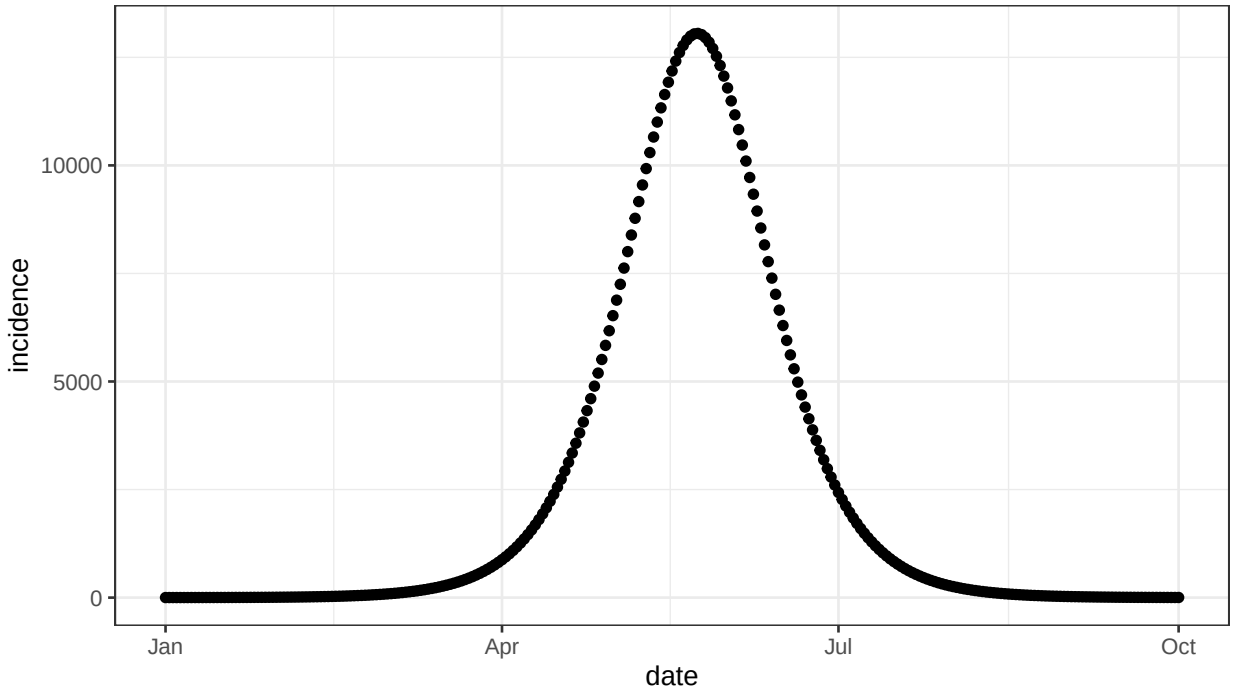
Now we modify the `run_sim` example (Section 3). We first check that setting `Relative_value=1` and using non-`timevar` `run_sim` yield the same results.

```
params <- read_params("ICU1.csv")
```

```
pp <- fix_pars(params, target = c(R0 = 1.3, Gbar=6))
state <- make_state(params=pp)
startdate <- as.Date("2020-01-01")
enddate <- as.Date("2020-10-01")
```

This is checking if we can get the same thing if we don't add stoch:

```
sim0 <- run_sim(pp,state,start_date=startdate,end_date=enddate)
gg0 <- (ggplot(sim0,aes(x=date))
        + geom_point(aes(y=incidence))
)
print(gg0)
```

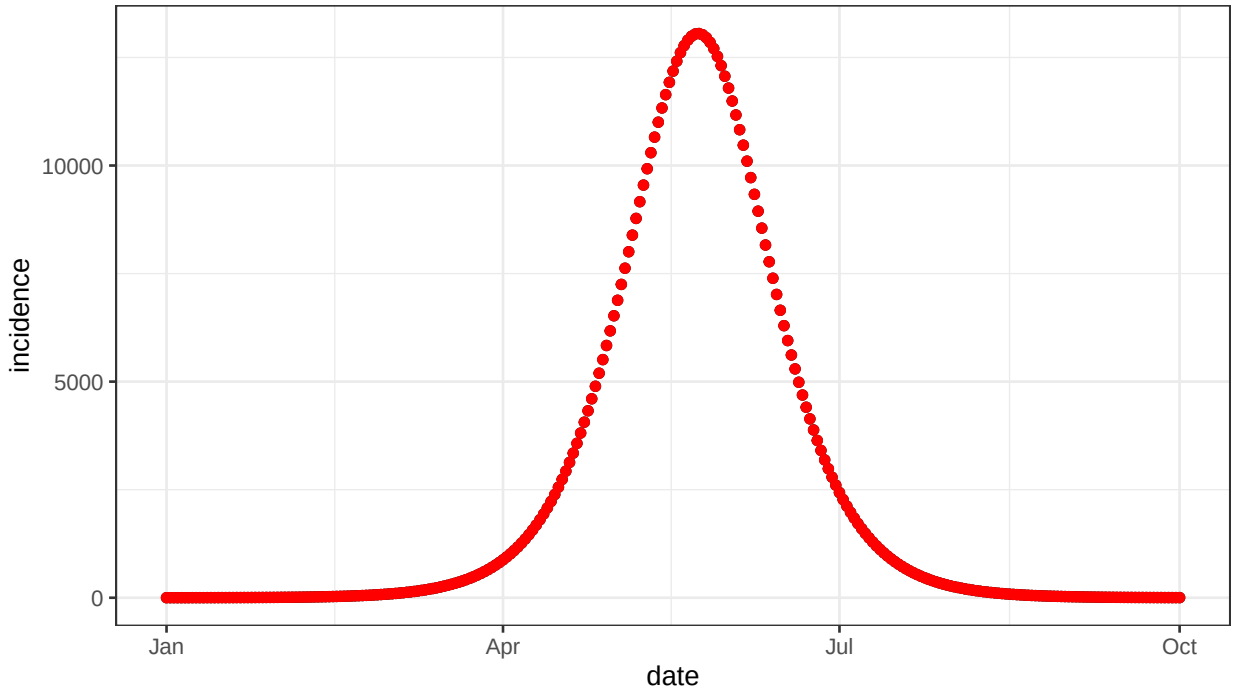


We want a dataframe that includes the time varying relative β at each saved time point. If relative β is constant though time, it should give back the same trajectory.

```
time_pars <- data.frame(Date=as.Date(startdate:enddate)
        , Symbol="beta0"
        , Relative_value=1
)
        # , stringsAsFactors=FALSE)
```

This fits a `timevar` dataframe where `beta0=1`:

```
sim0_t <- update(sim0, params_timevar=time_pars)
print(gg0
        + geom_point(data=sim0_t, aes(x=date,y=incidence), color="red")
)
```



Now, as an example, we set relative β to drop by a factor of 2 (linearly) between 1 July 2020 and 1 Oct 2020.

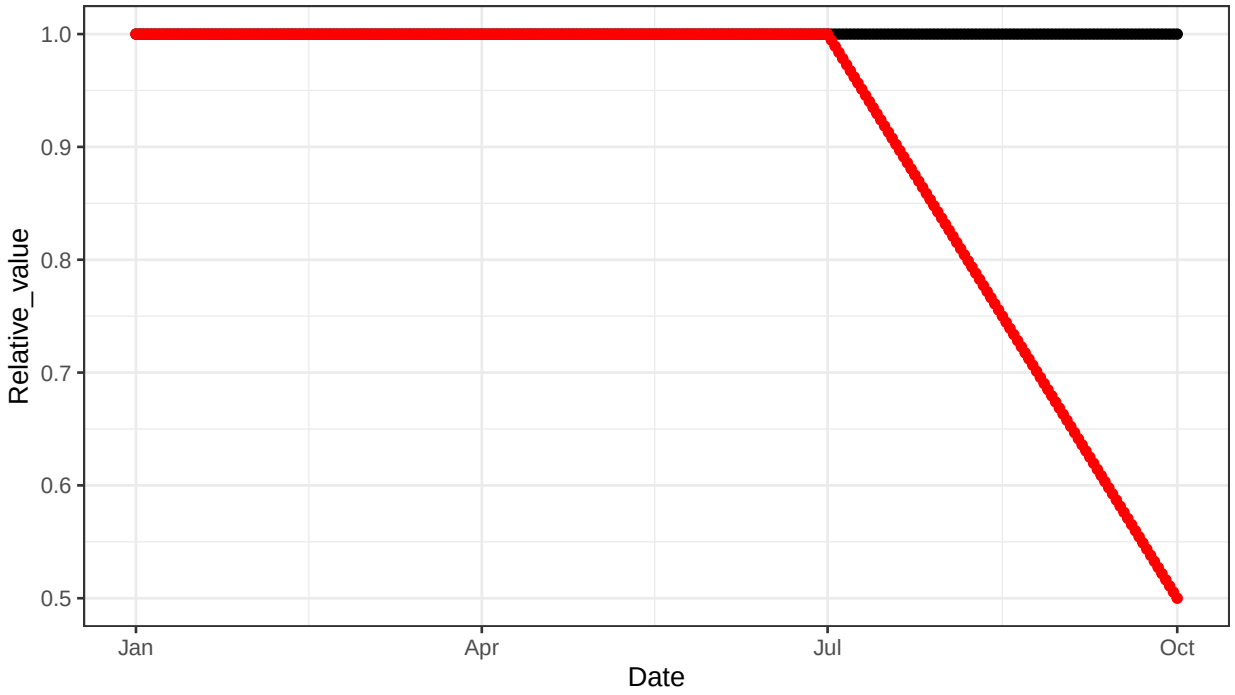
```
lockdown <- as.Date("2020-07-01")
```

```
time_pars2 <-
    data.frame(Date=as.Date(startdate:enddate)
               , Symbol="beta0"
               , Relative_value =
                     c(rep(1, length(startdate:lockdown)-1)
                     , seq(1,0.5,length.out = length(lockdown:enddate))
                       )
                 )
##print(time_pars2)
head(time_pars2)

#>         Date Symbol Relative_value
#> 1 2020-01-01  beta0              1
#> 2 2020-01-02  beta0              1
#> 3 2020-01-03  beta0              1
#> 4 2020-01-04  beta0              1
#> 5 2020-01-05  beta0              1
#> 6 2020-01-06  beta0              1
```

```
sim0_t_reduce <- update(sim0, params_timevar=time_pars2)
gg_rel_beta <- (ggplot(time_pars, aes(x=Date))
        + geom_point(aes(y=Relative_value))
        + geom_point(data=time_pars2, aes(x=Date, y=Relative_value), color="red")
)
```

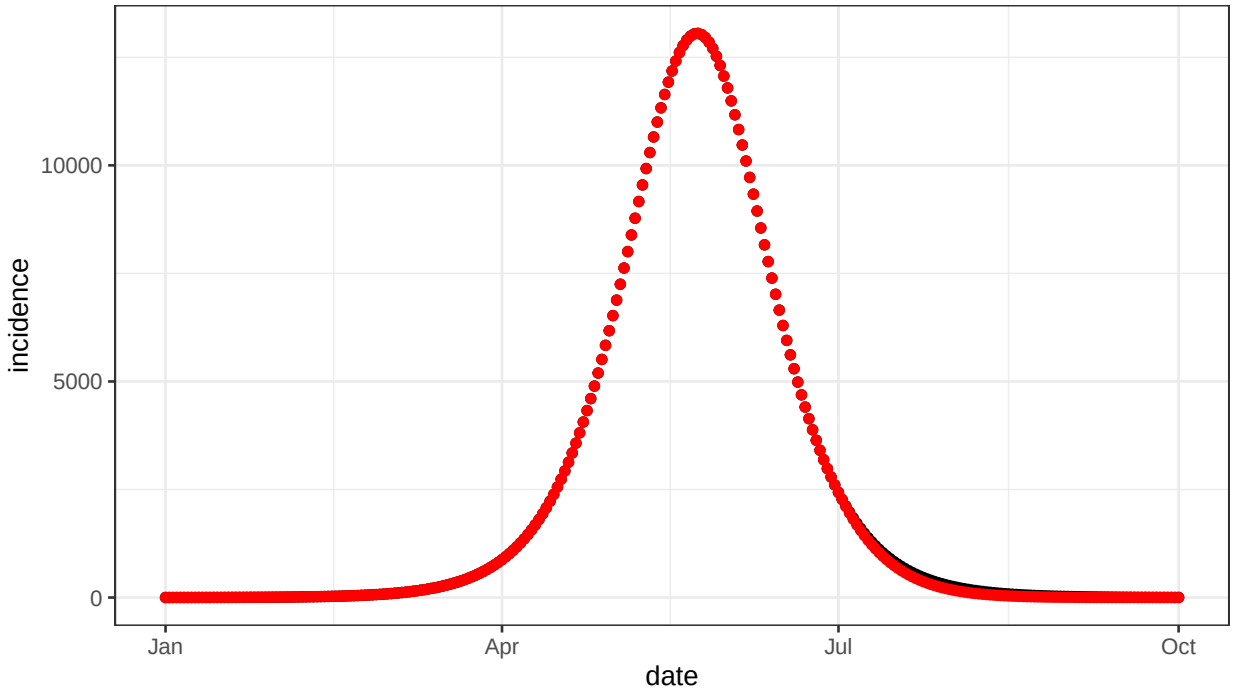
We can now look at the relative value of β in each scenario, and the corresponding forecasted epidemic curves.

```
print(gg_rel_beta)
```



172

```
print(gg0
        + geom_point(data=sim0_t_reduce, aes(x=date,y=incidence), color="red")
)
```



173

174