Population-level immunity and the spread of COVID-19

ECDC Forecast Hub meeting

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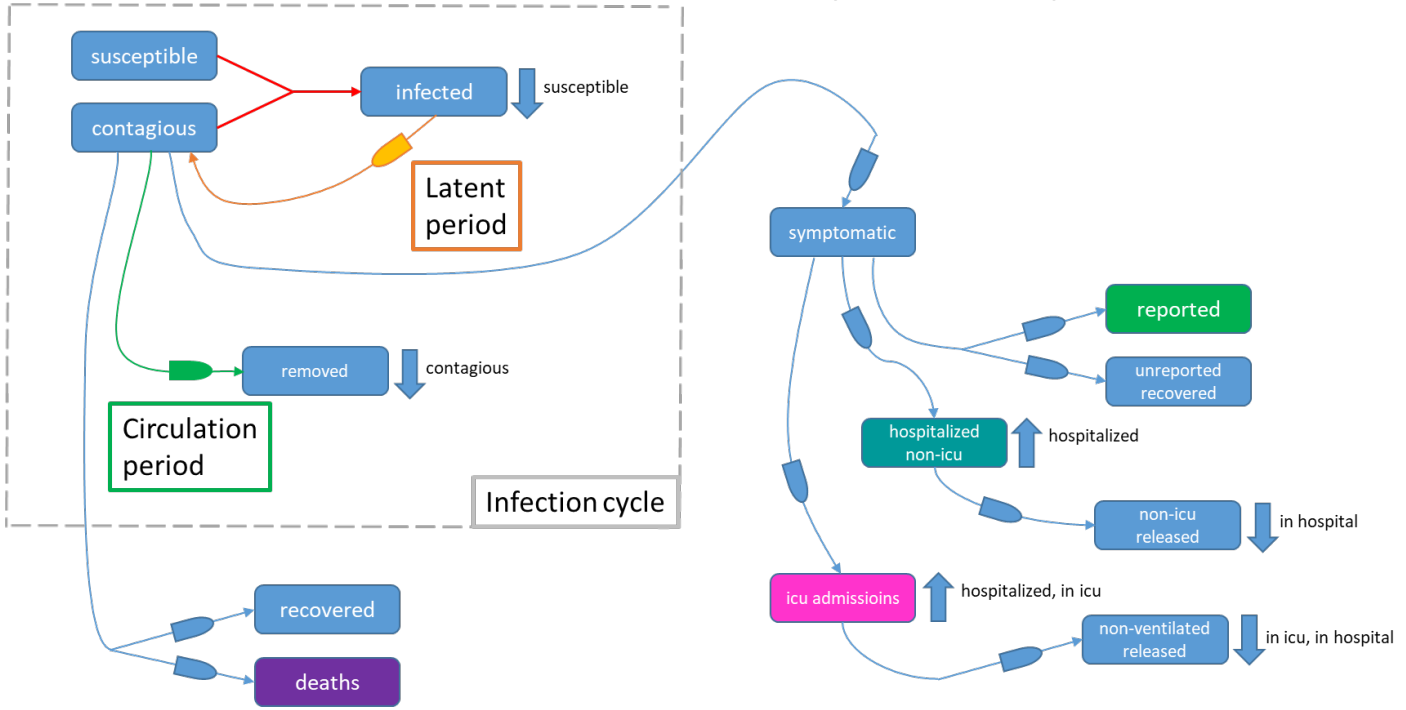
Population-level immunity

- Immunity is now a major factor determining the spread of COVID-19
  - The timing and magnitude of the peaks in recent waves were determined by immunity (not by public health measures)
  - To accurately forecast the magnitude of future waves requires a good model of immunity dynamics and data to estimate the immunity model parameters

$$E[\Delta I_{t+1}] = \alpha \frac{E[S_t]}{E[N_t]} E[C_t]$$

α: transmission rate. Initially, the average number of people that a contagious person infects per day

- Immunity (waning) reduces (increases) the susceptible population
- Immunity escape increases an independent susceptible population



Simplified model for Feb 2022 and beyond

- Homogeneous
  - The model represents a homogeneous population that produces a similar time history of hospital admissions as the jurisdiction under study
- Transmission rates are constant
  - Social behaviours and NPI assumed to be unchanged
- Immunity only reduces susceptible population
  - The probability for an infected person to be hospitalized or to transmit to a susceptible person is assumed to be constant within a jurisdiction in 2022
- The model is calibrated with hospital admission data
  - Infections are detected only in those admitted to hospital (some who are admitted due to COVID-19, others incidentally have COVID-19).
    - Measuring immunity parameters with these data imposes some unknown weighting of factors related to the reduction in infection, transmission, and hospitalization

Immunity parameters

- Two critical parameters for early 2022:
  - Initial susceptible fraction of population
  - Rate that susceptible population declines
    - Assumed to be proportional to the rate of hospital admissions: the proportionality constant is the second critical parameter

- Later (with BA.4/5 escape and waning of early 2022 immunity):
  - Reduction of BA.4/5 immunity effectiveness due to escape (1 parameter)
  - Waning of immunity, specified by three parameters:
    - Fraction of immunity that wanes
    - Mean waning period
    - Standard deviation of waning period

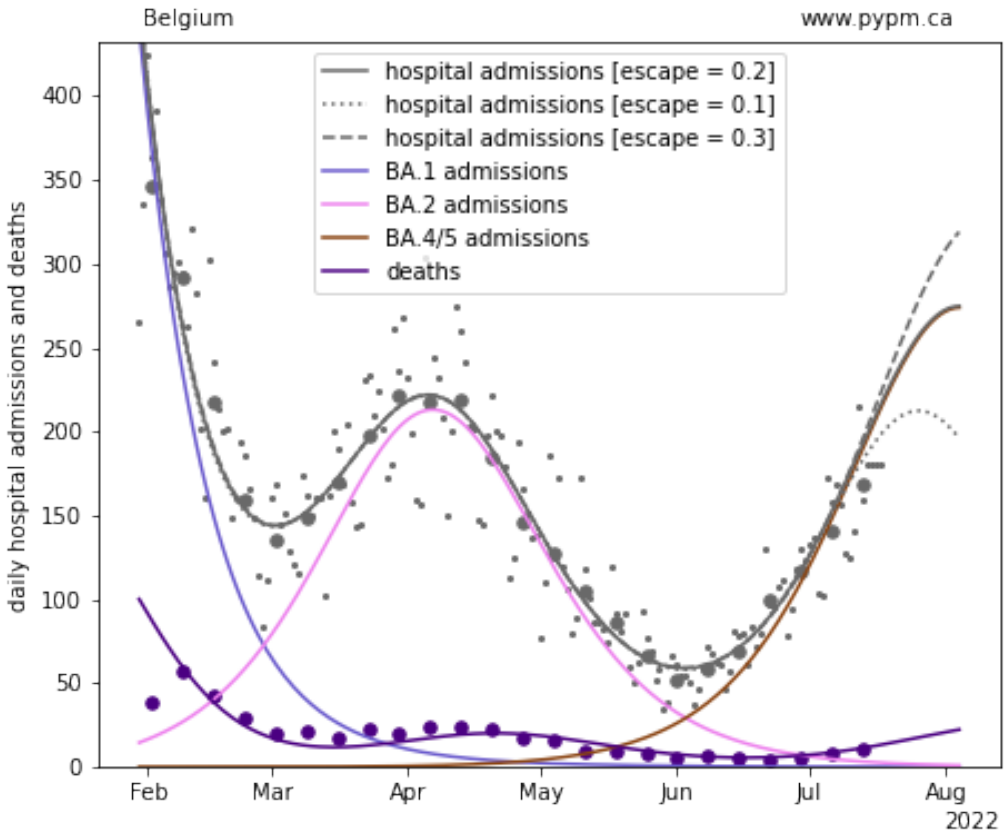
How to calibrate immunity parameters

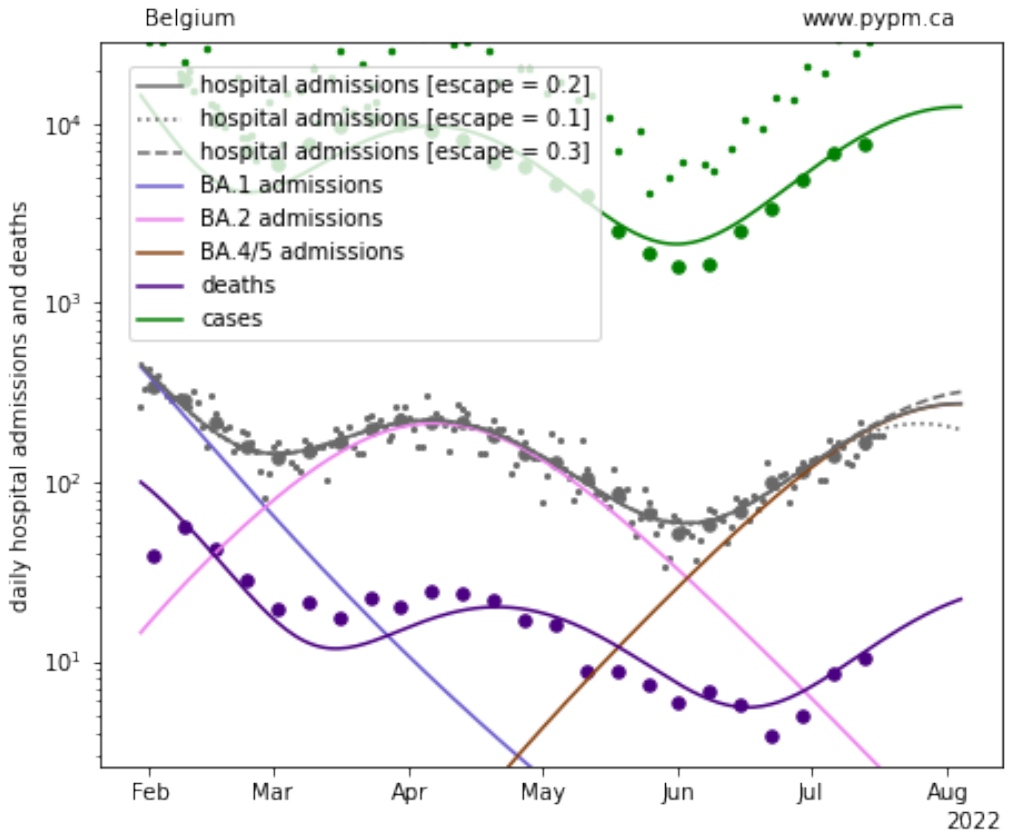
- Model parameters are adjusted to match the shape of the BA.2 wave, thereby fixing the two critical immunity parameters
  - The corresponding model parameters that capture these are:
    - magnitude and timing of a hypothetical BA.1 wave that produces the immunity present in the population in February 2022
      - Note: vaccination immunity is not treated separately. It is included as part of the natural immunity coming from the hypothetical BA.1 wave. This is a reasonable approximation: vaccine effectiveness against Omicron was low and recent vaccination rates much lower than infection rates
    - fraction of immunity generating infections that lead to hospitalization
      - This fraction is determined only from the shape of the BA.2 wave

- The following shows this approach applied to 6 nations in Europe
  - All have a distinct 2nd omicron wave (BA.2) to calibrate immunity parameters
  - The 3rd omicron wave has additional parameter: escape fraction (no waning)
  - Predictions are shown for each week (not post-dictions!)

Belgium

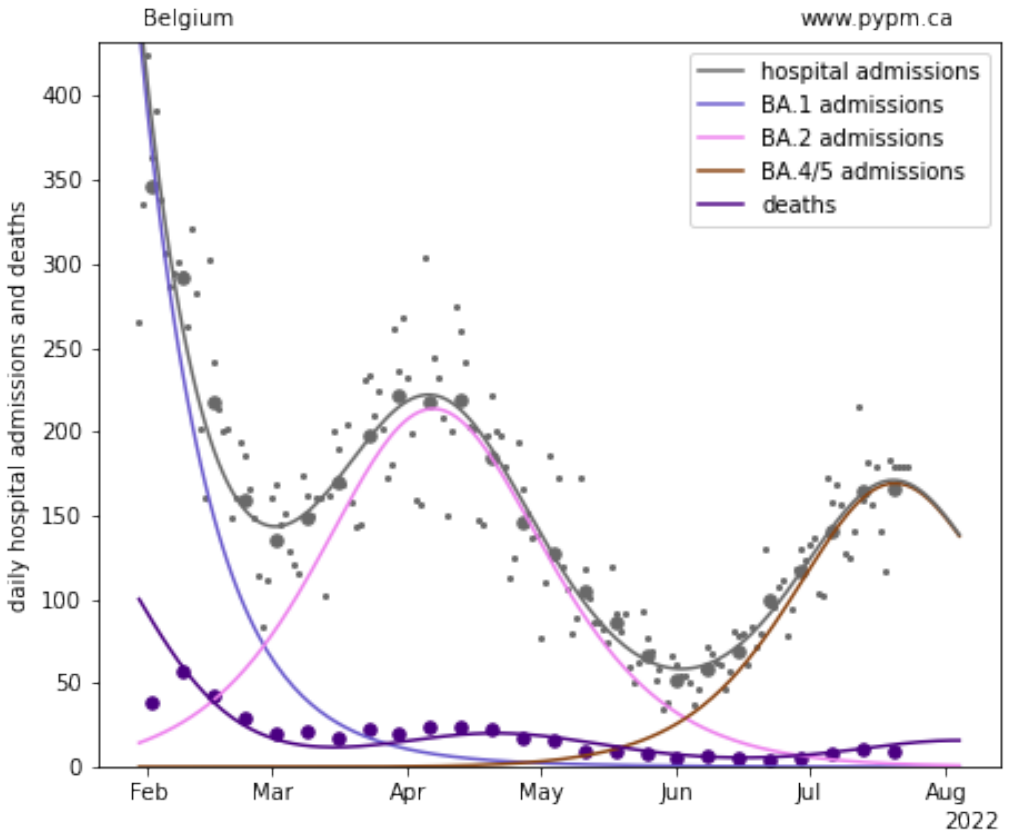
Belgium – July 17 data

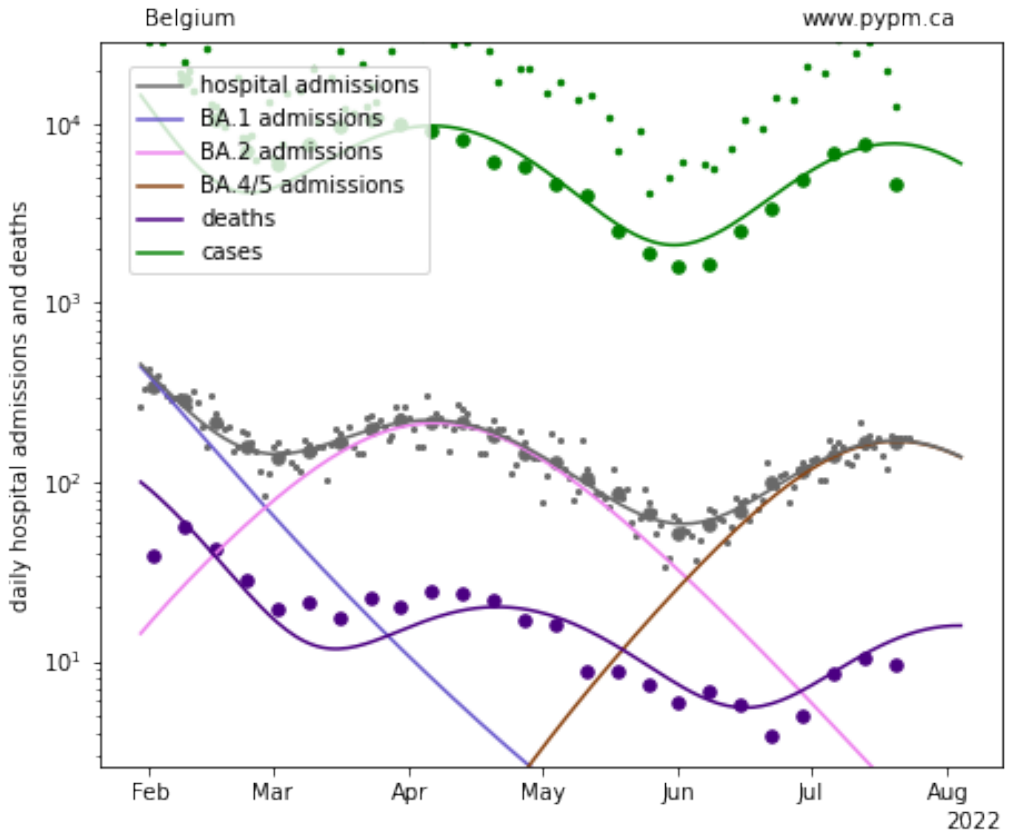




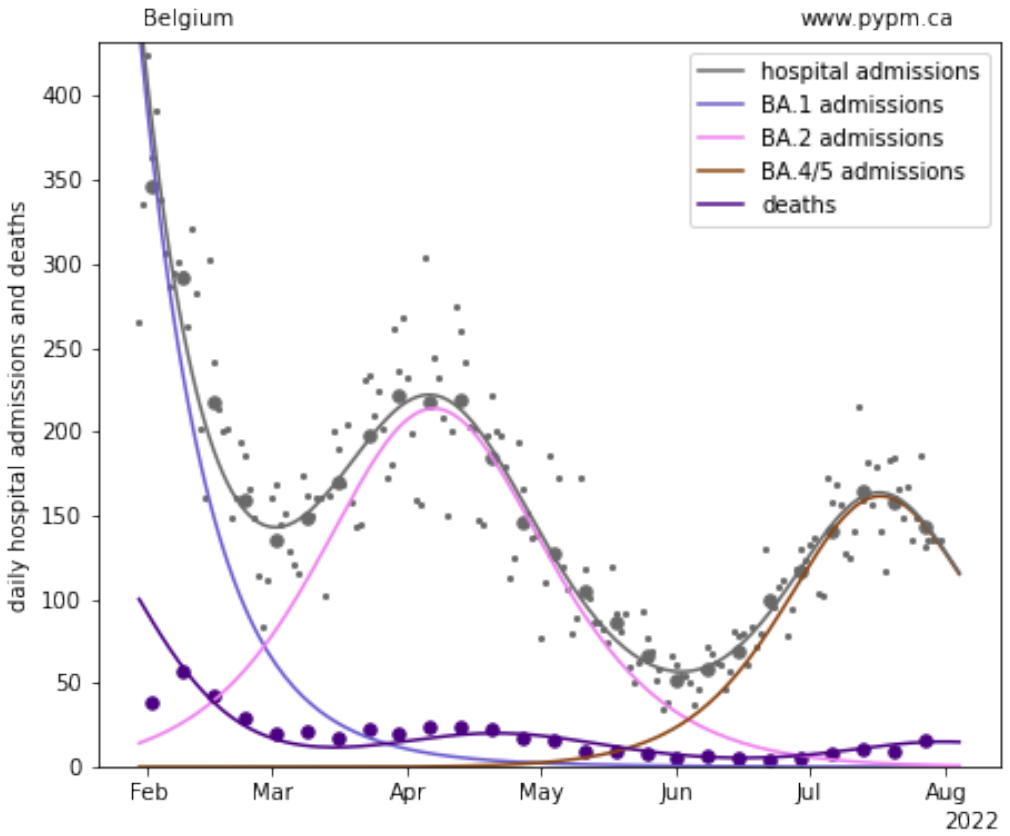
7 parameters fit: (2) for initial strain (timing and magnitude) (2) for BA.2 strain (2) for BA.4/5 strain
(1) hospitalization fraction

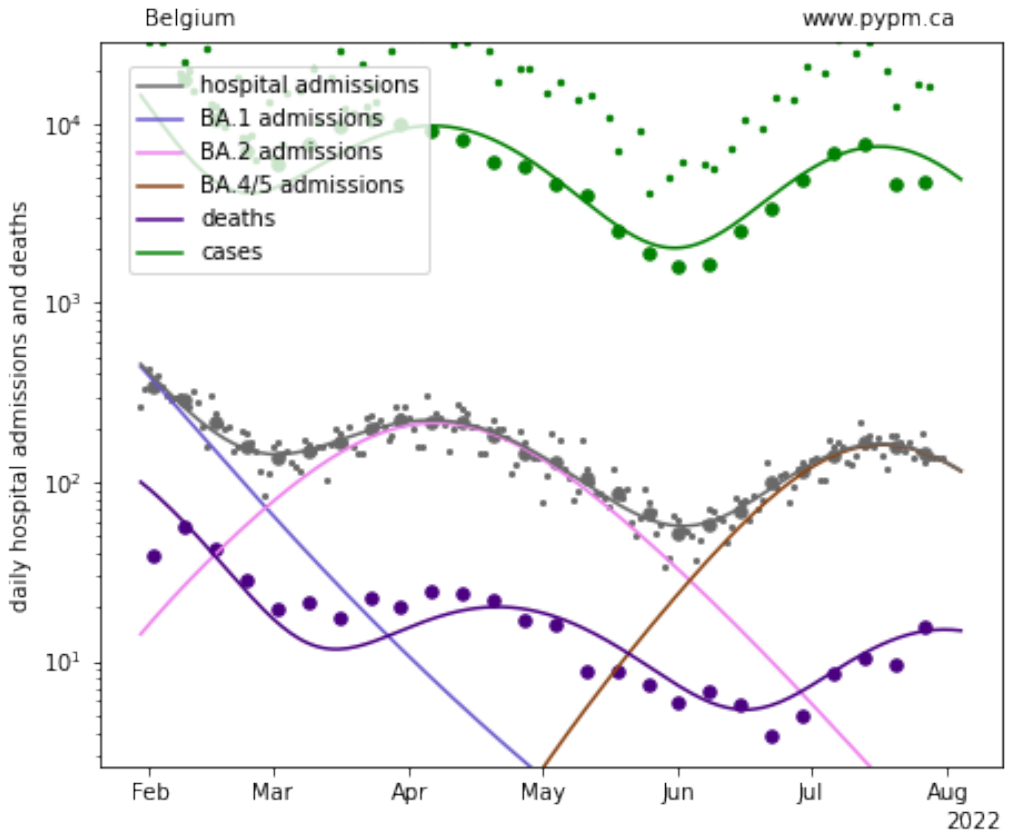
Belgium – July 24 data



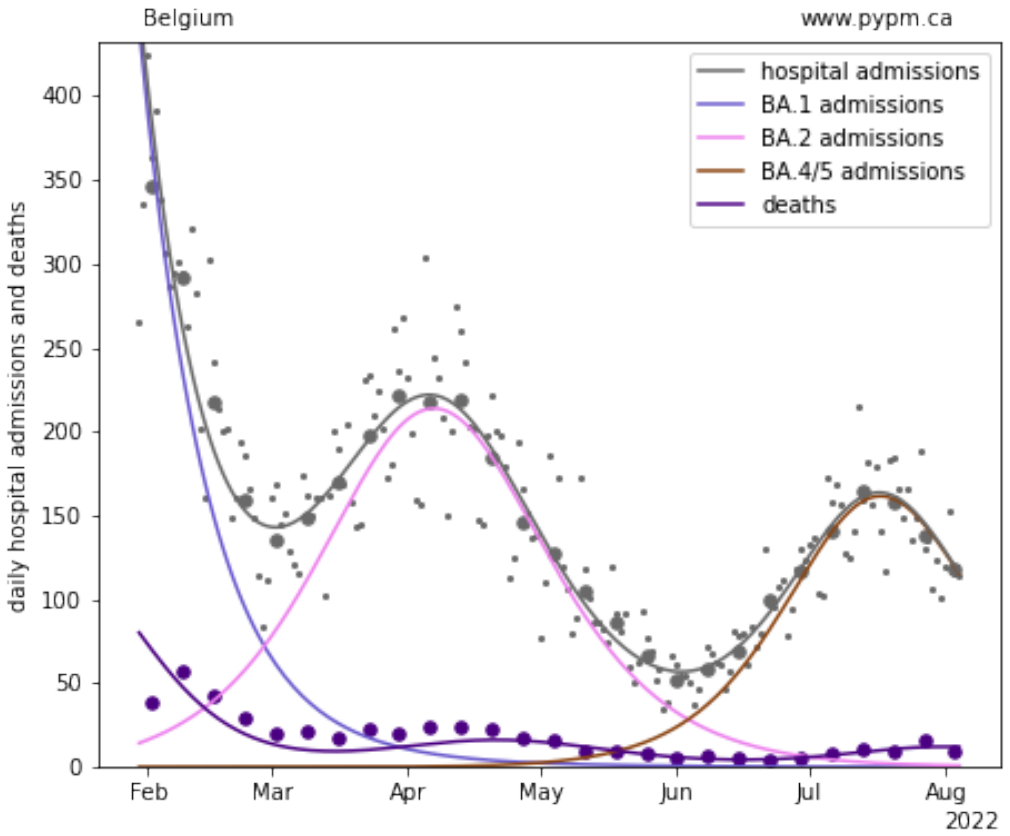


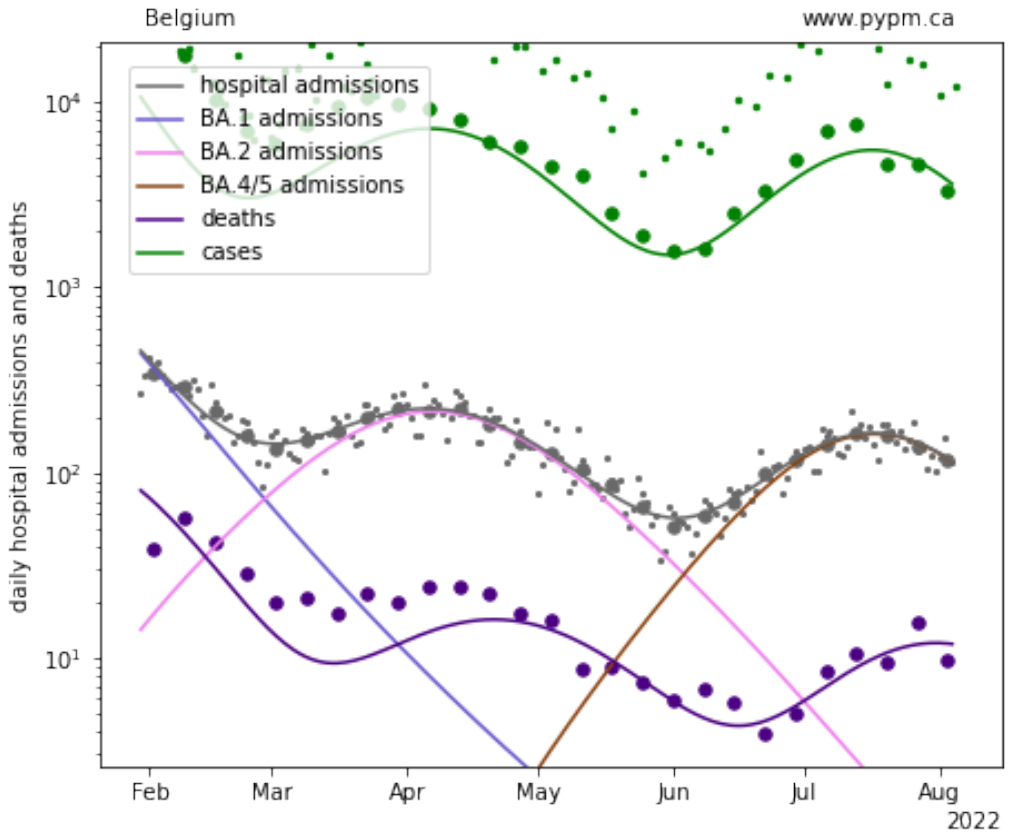
Belgium – July 31 data





Belgium – August 7 data





Switzerland

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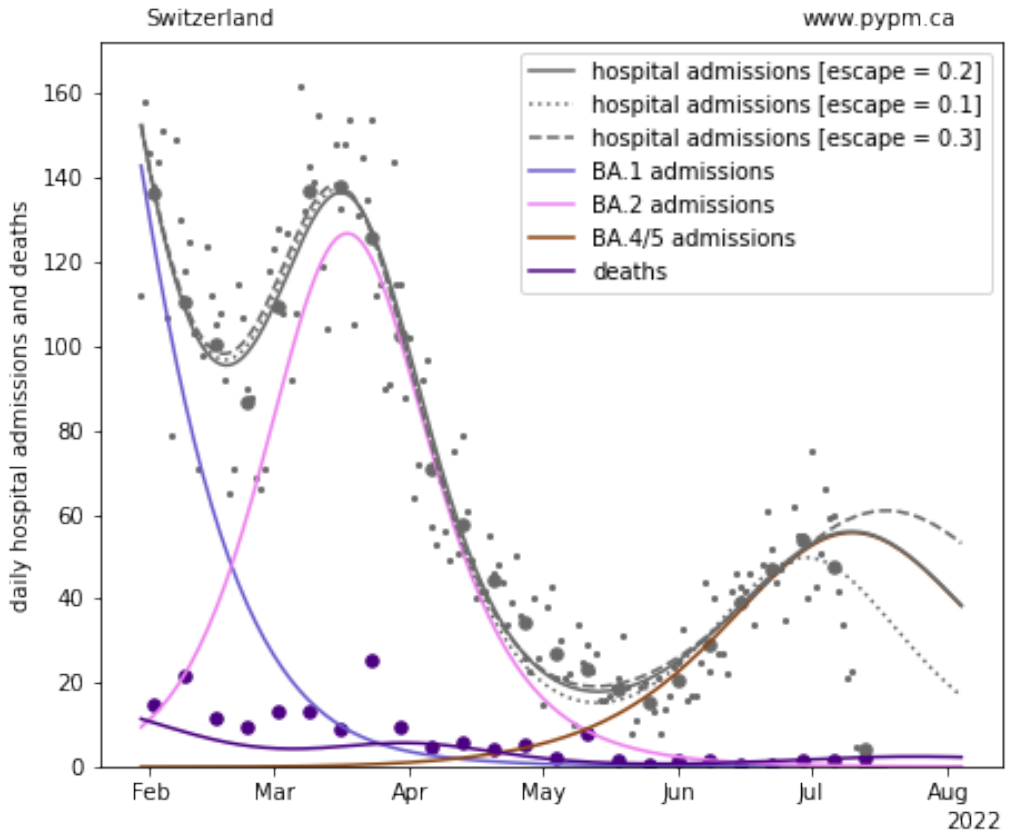

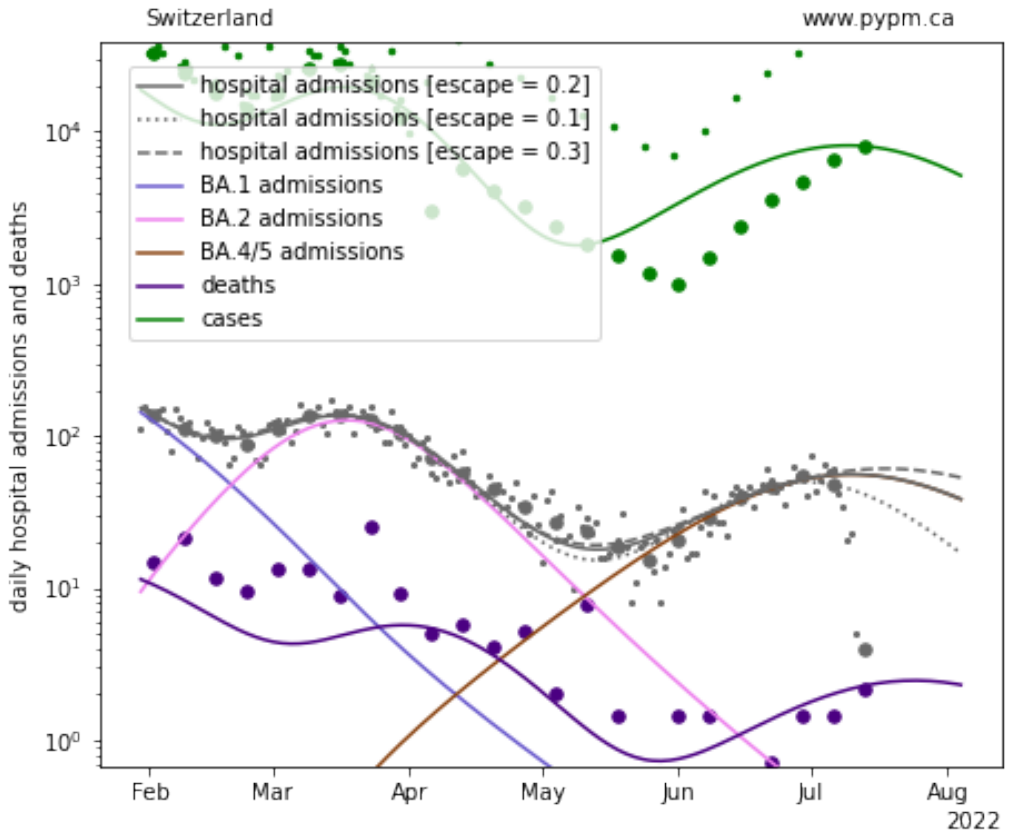

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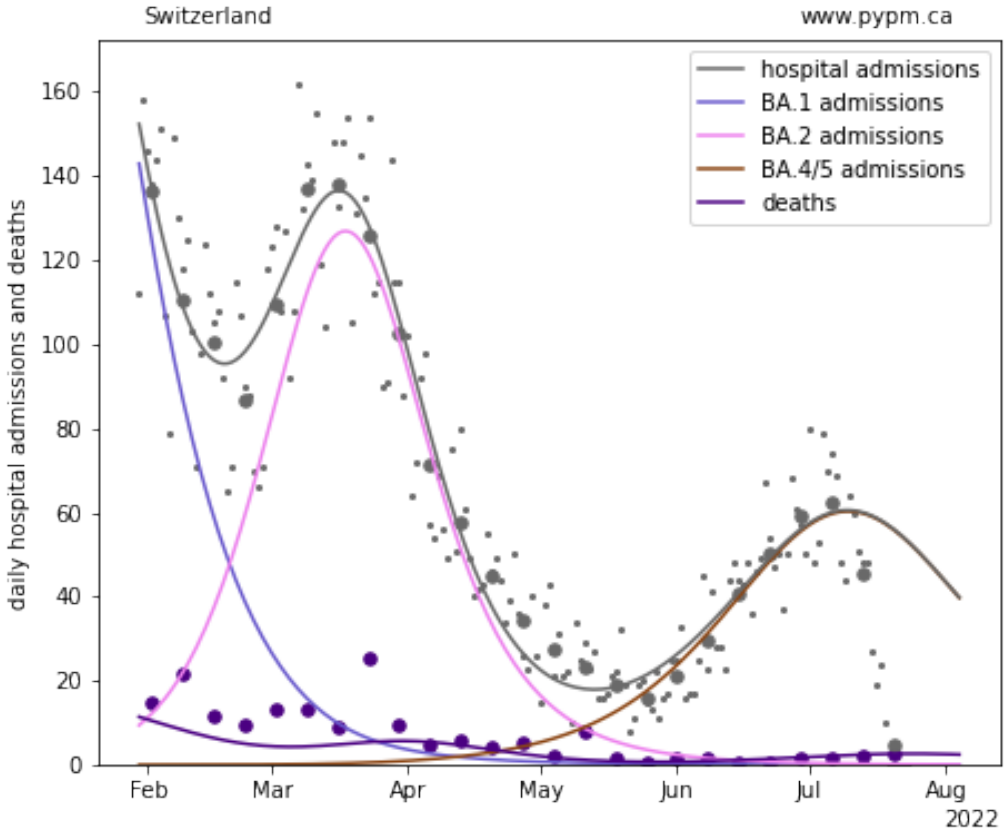

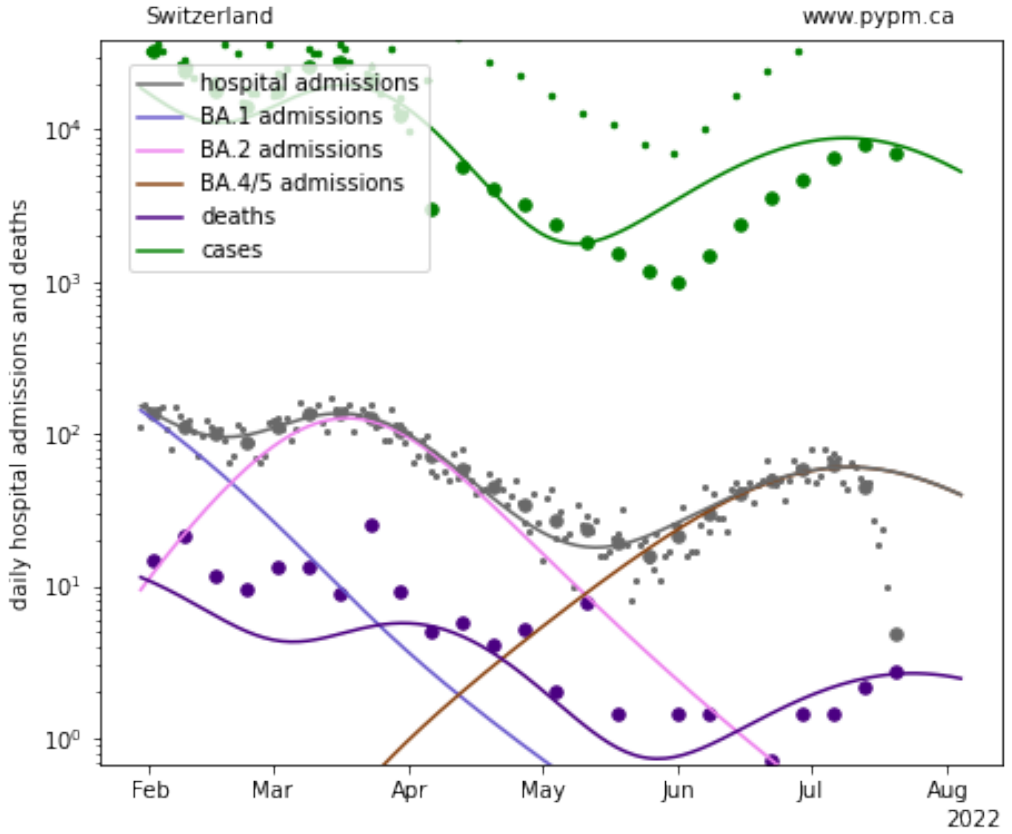

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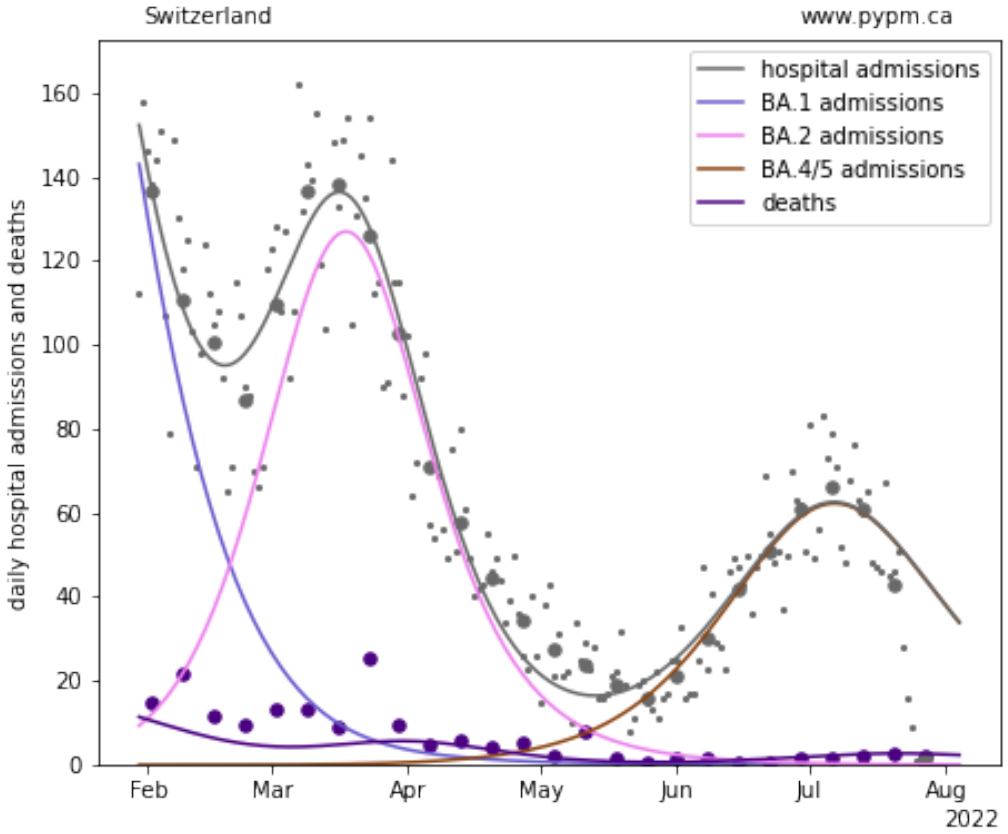

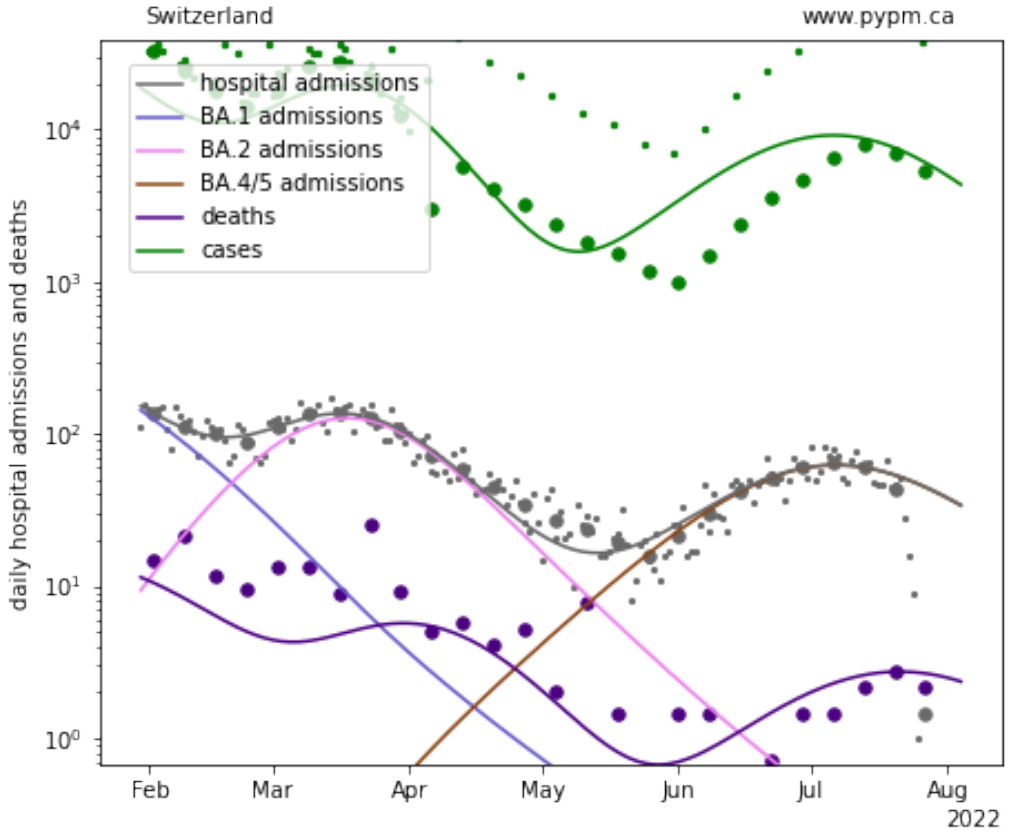

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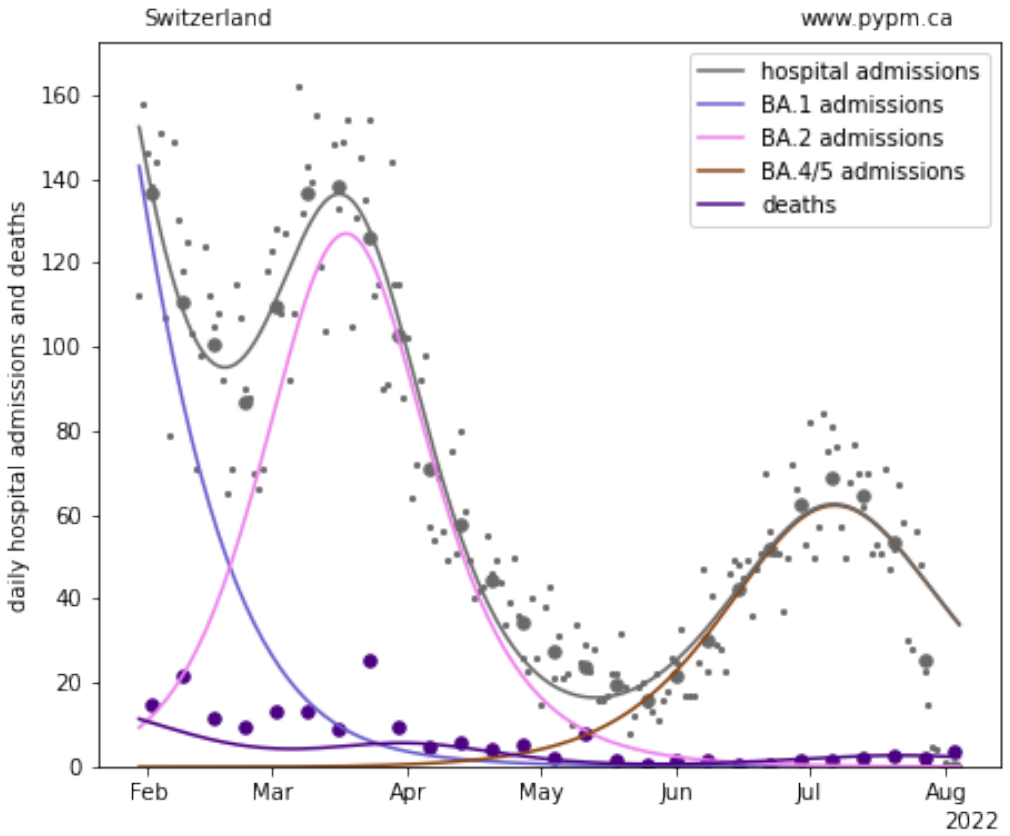

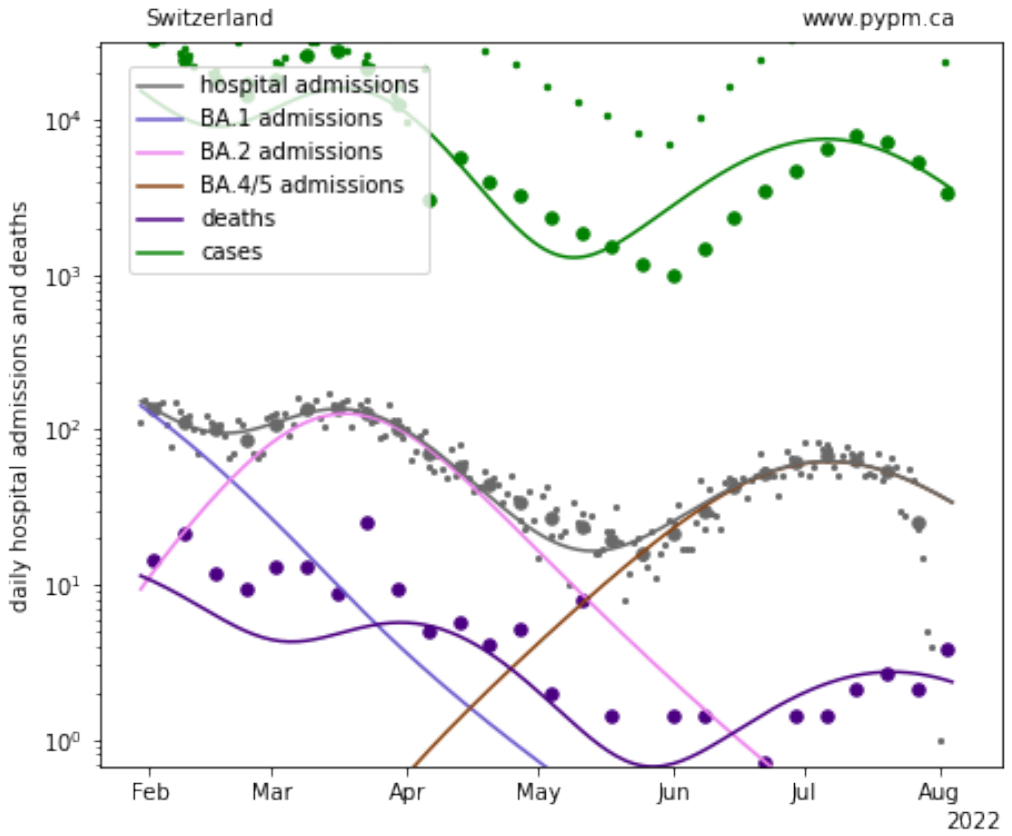

France

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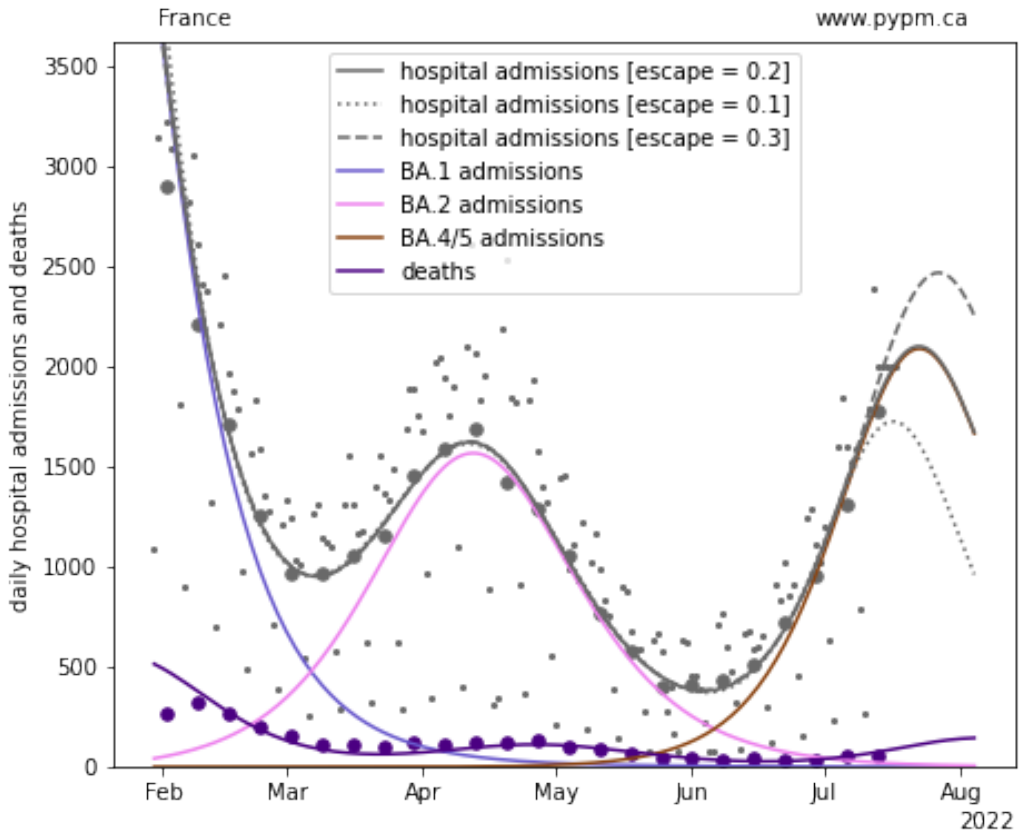

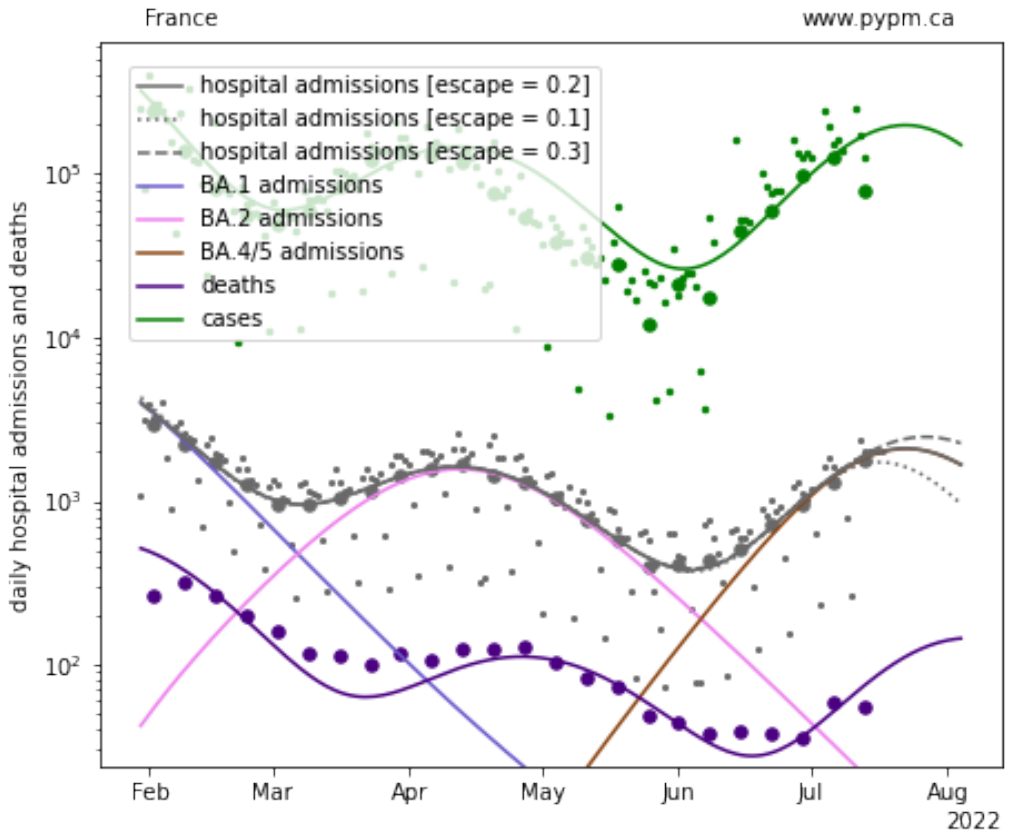

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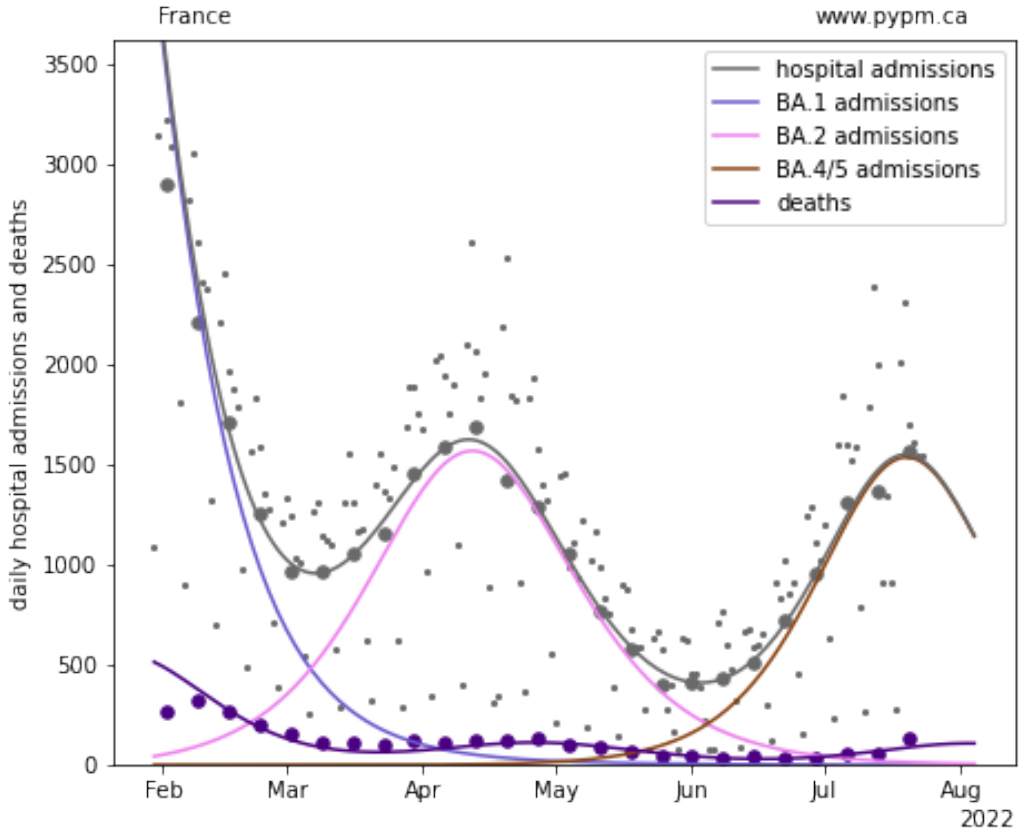

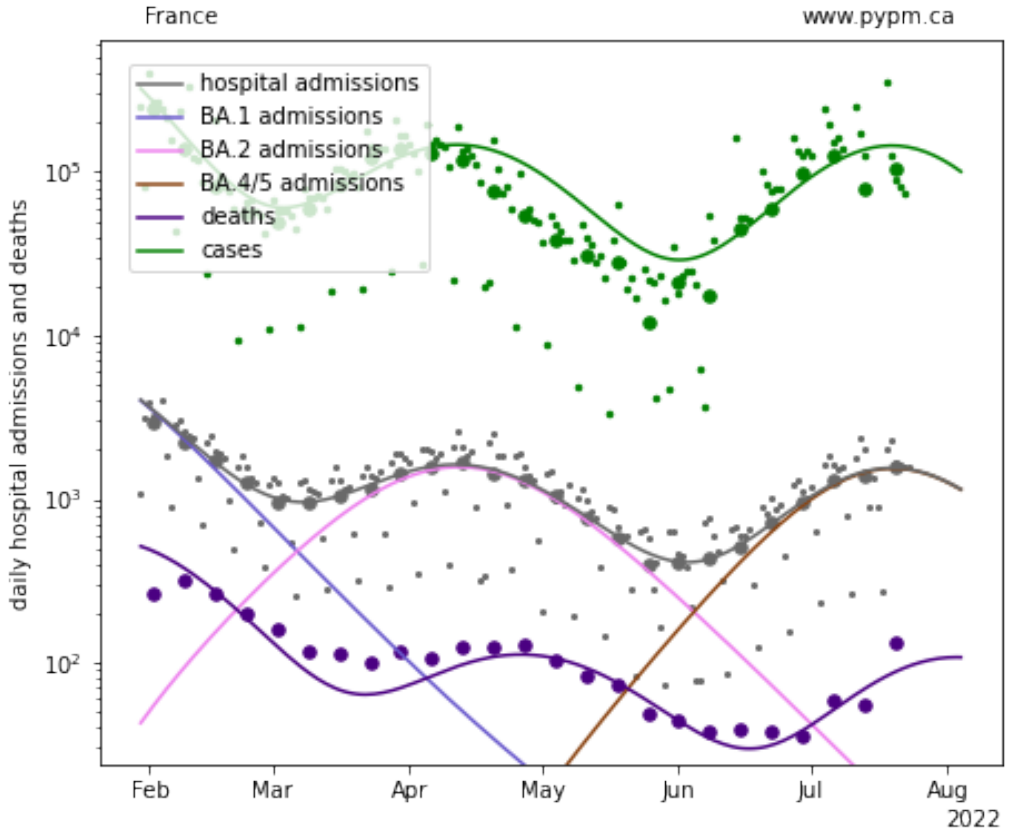

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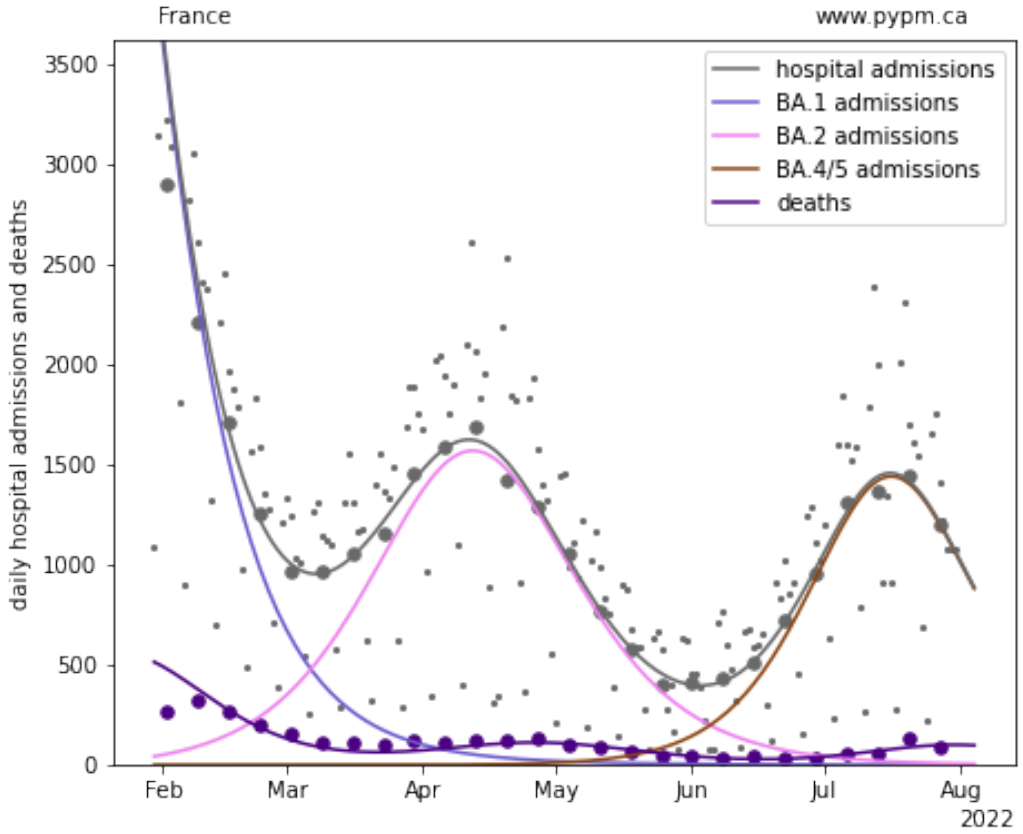

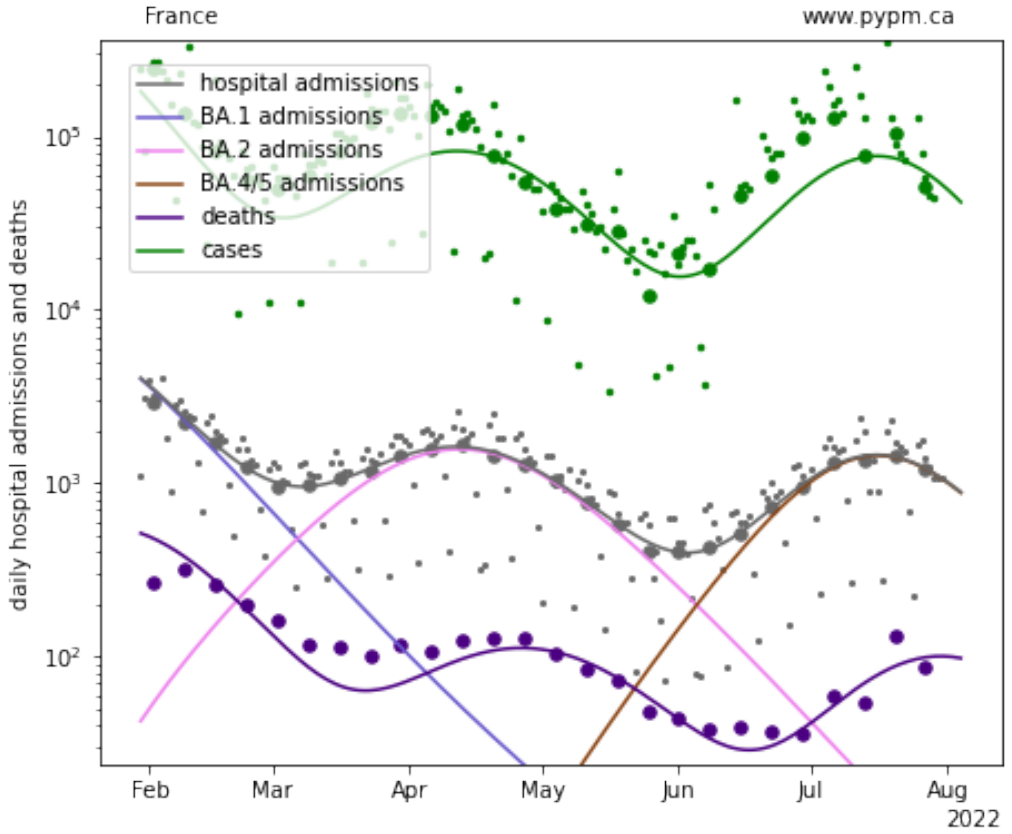

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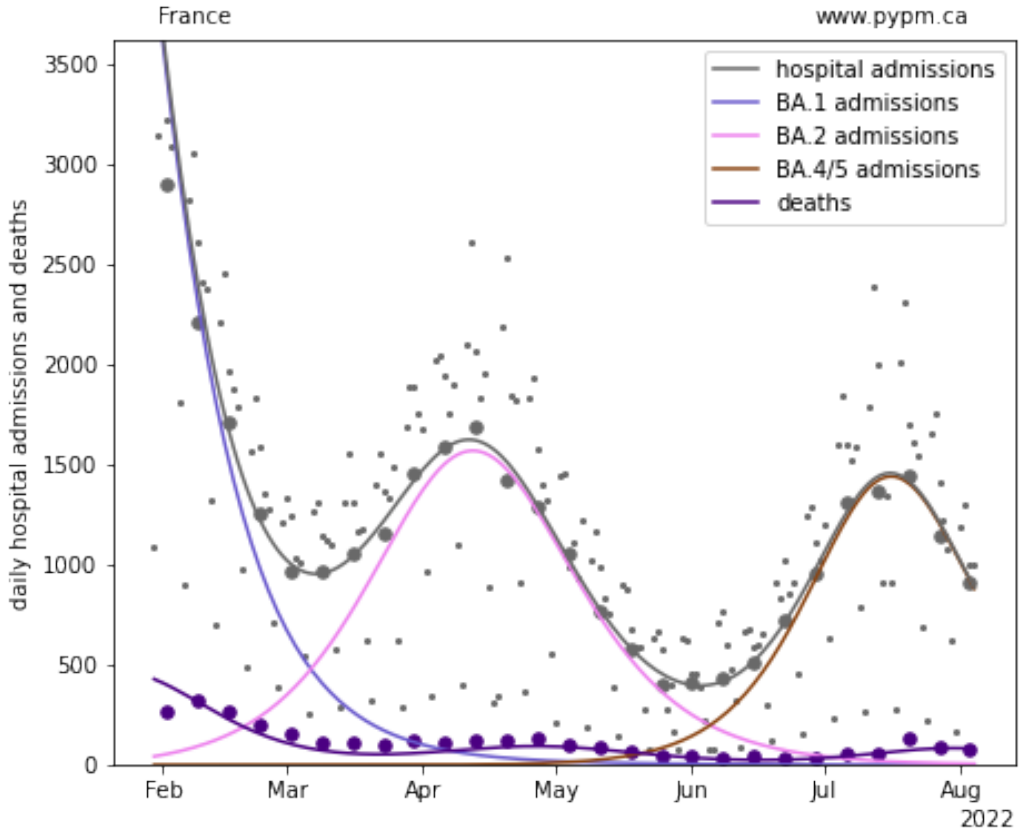

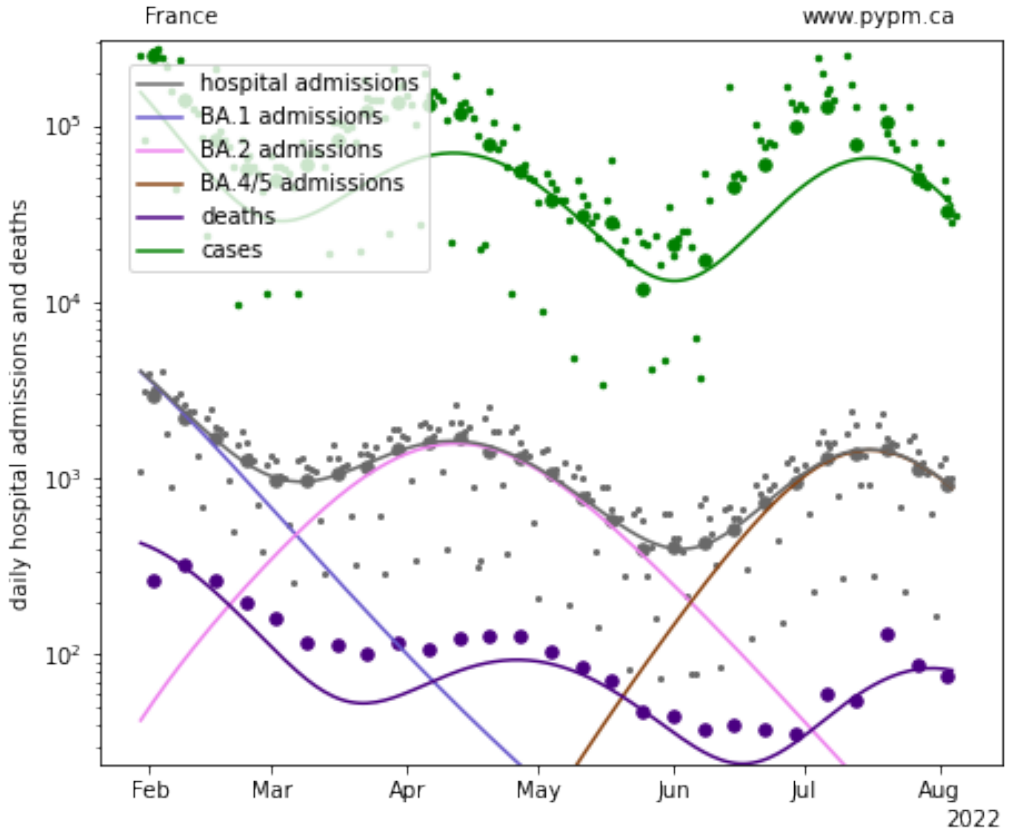

UK

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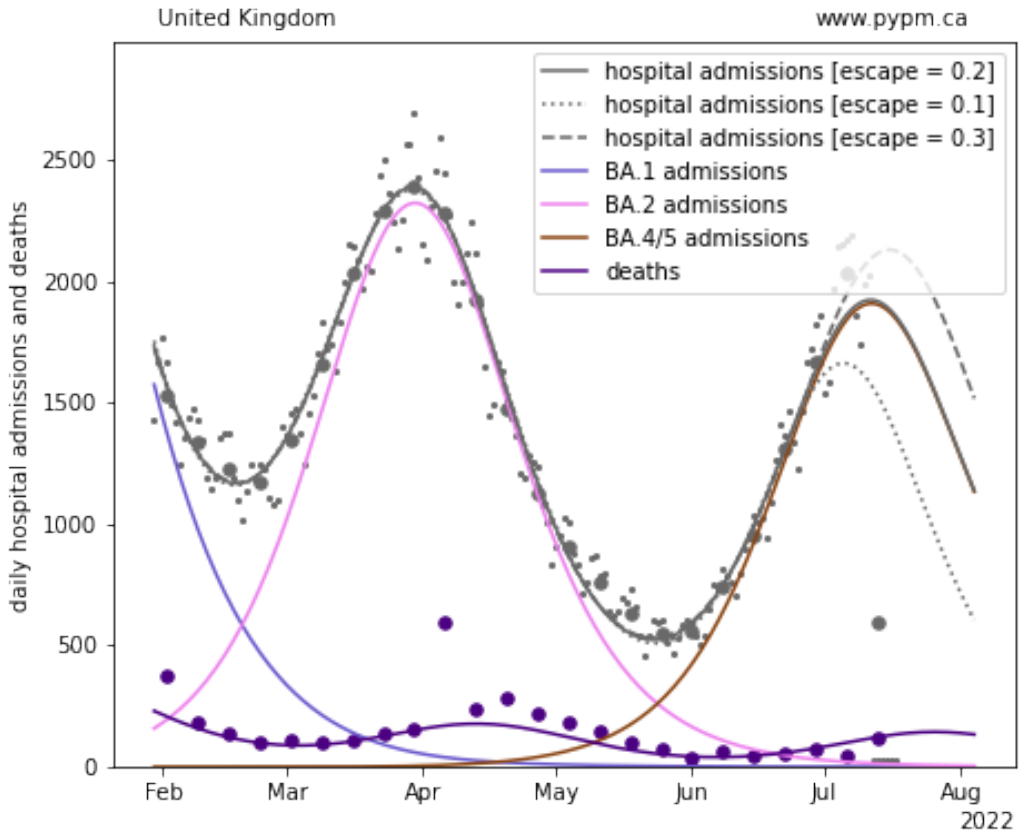
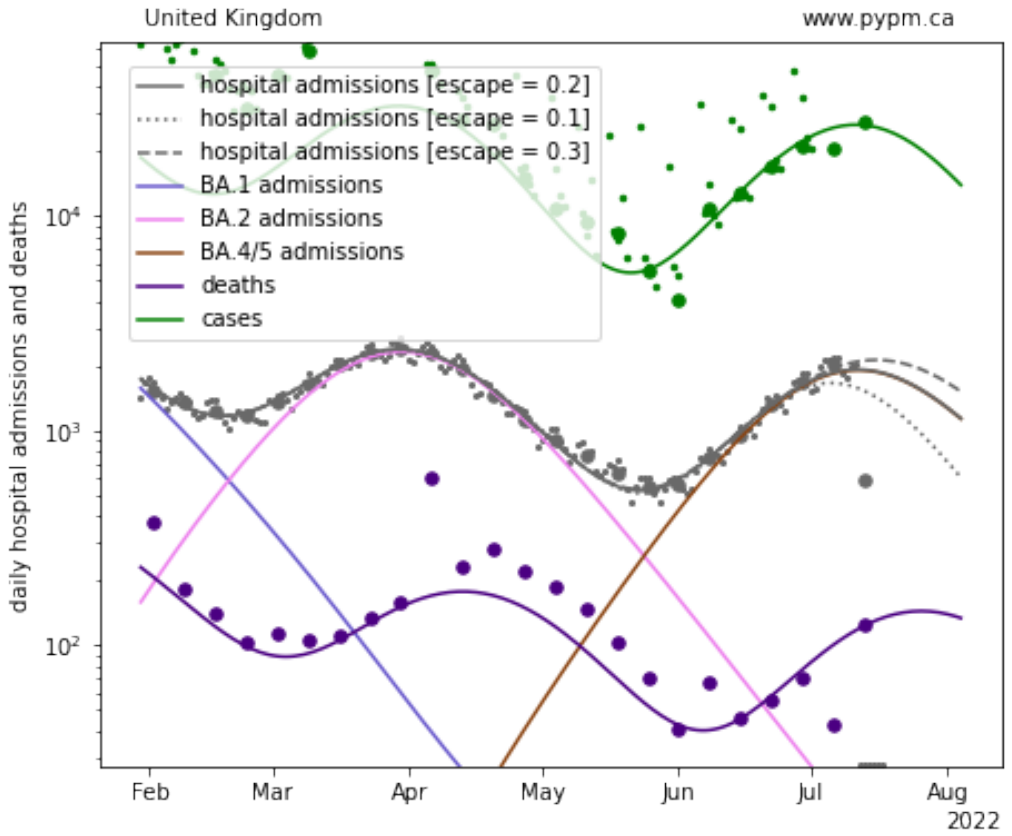
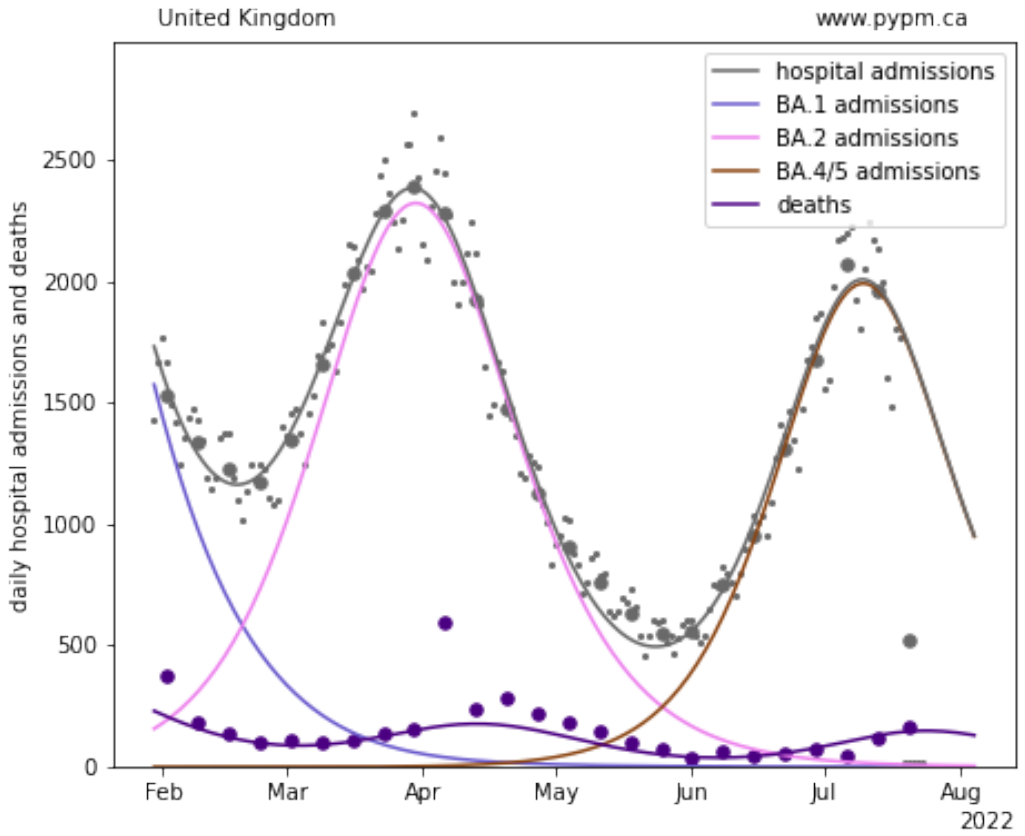
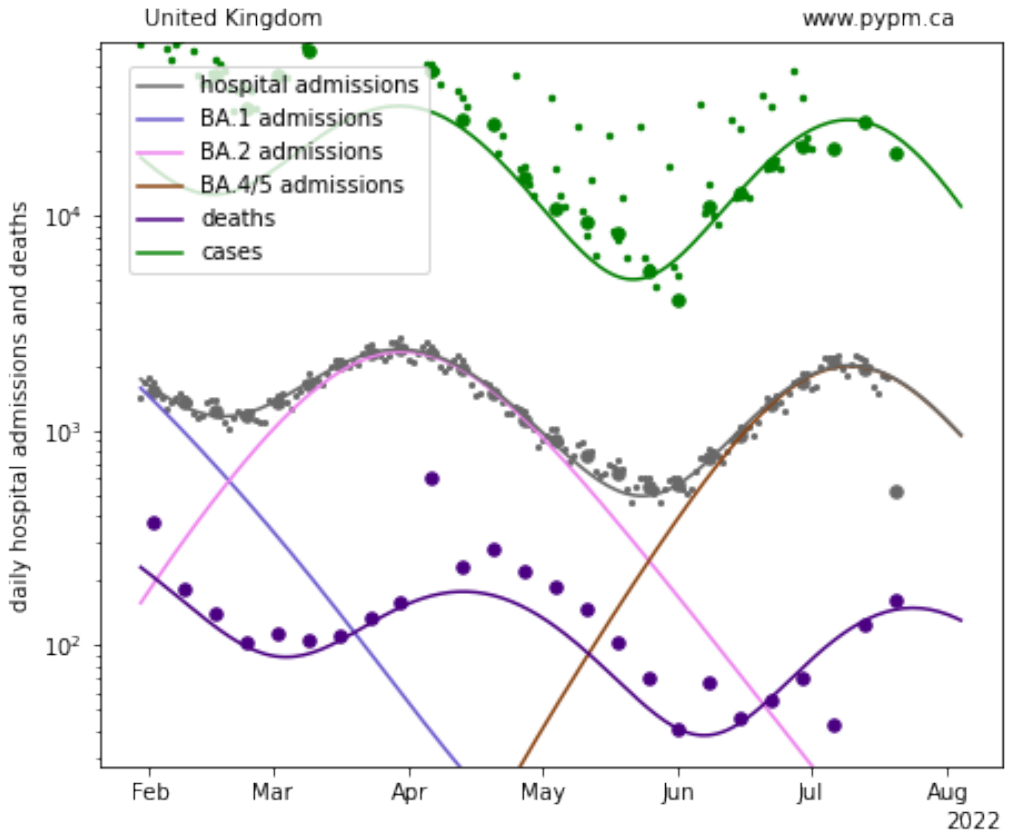




UK – July 24 data





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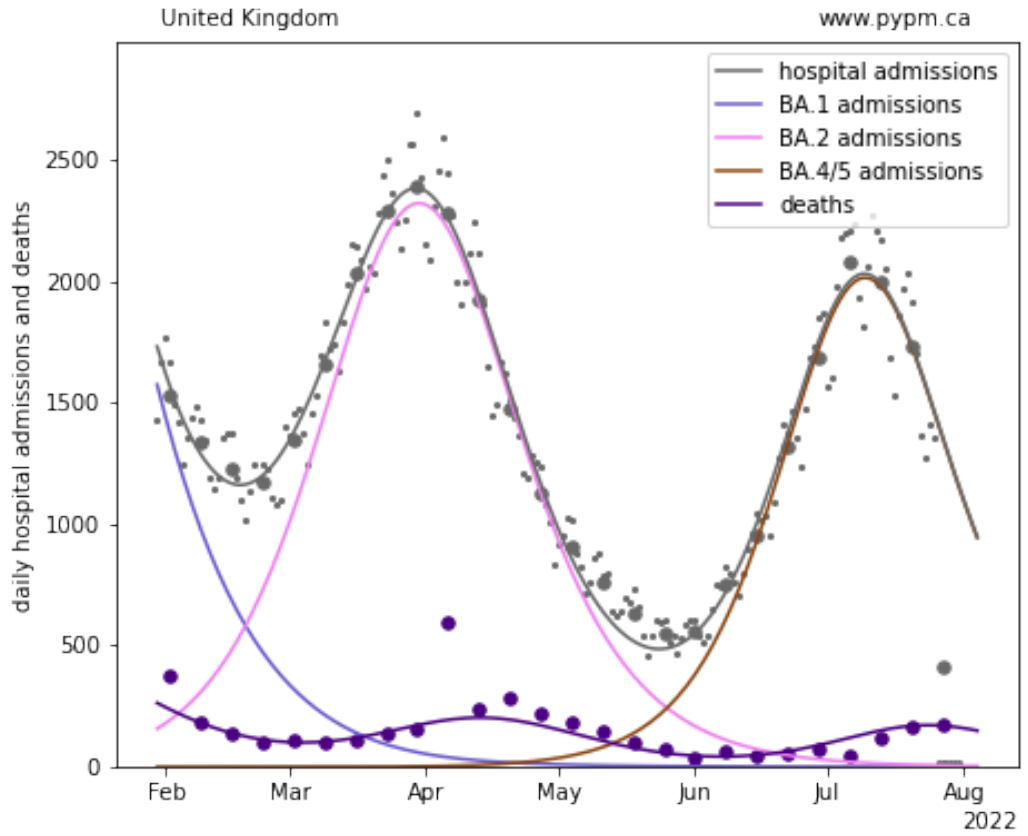

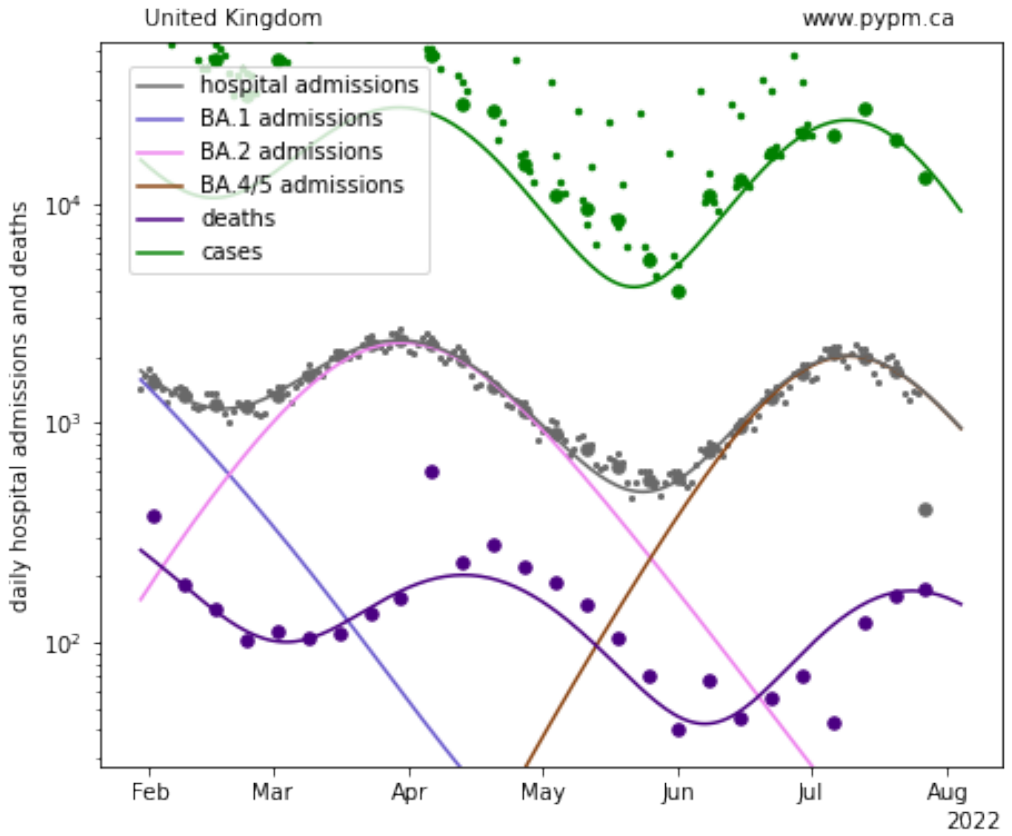

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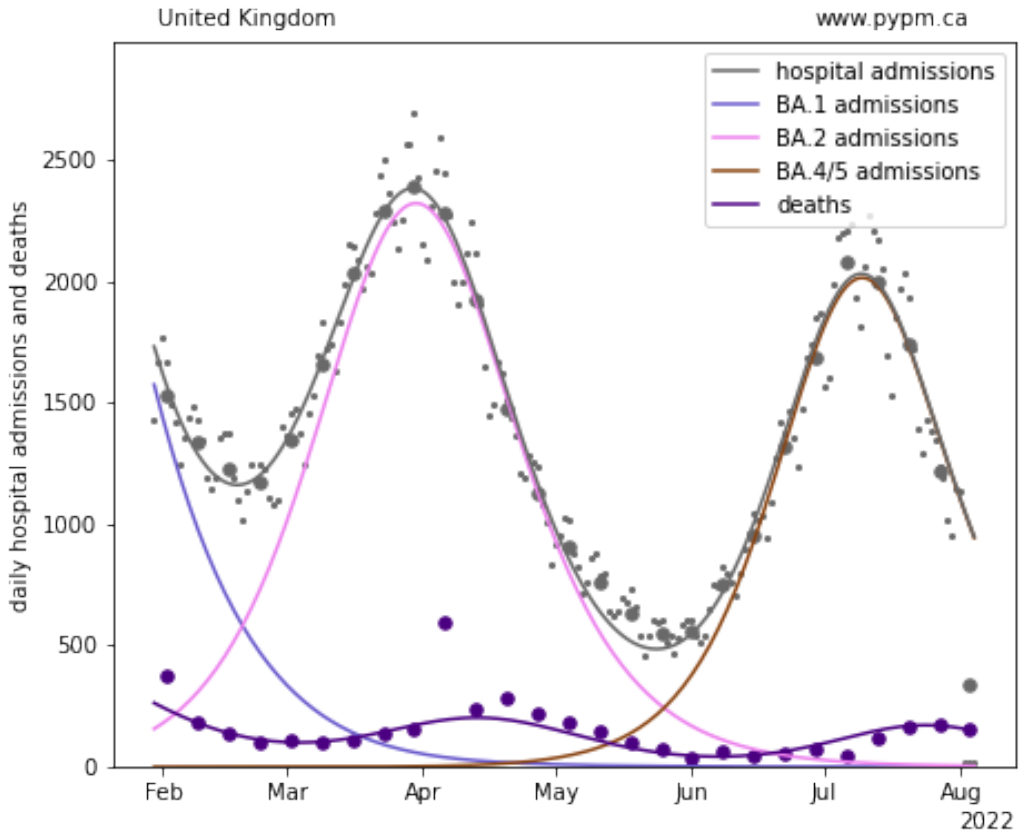

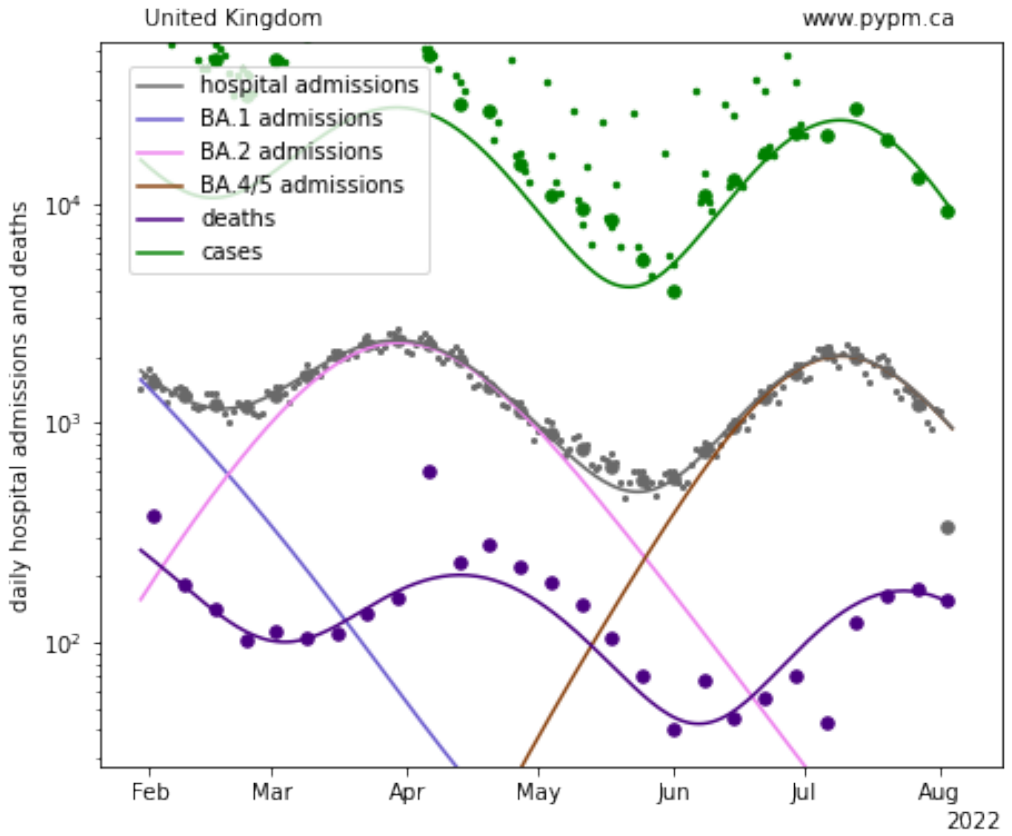

Ireland

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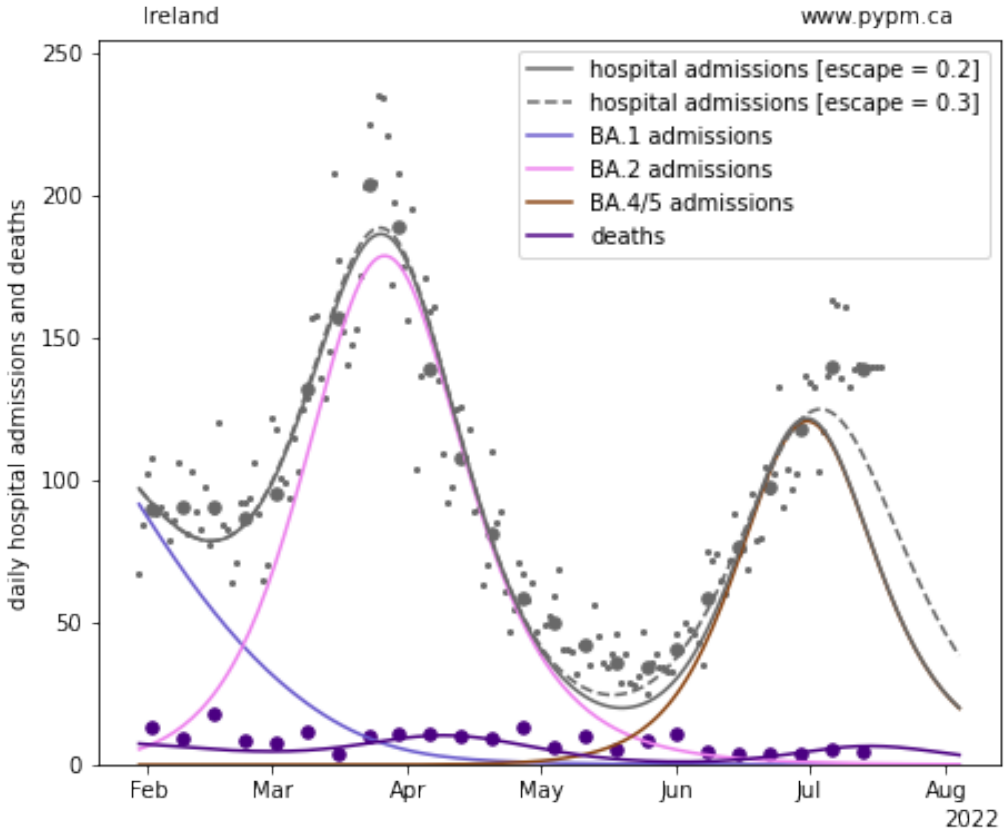

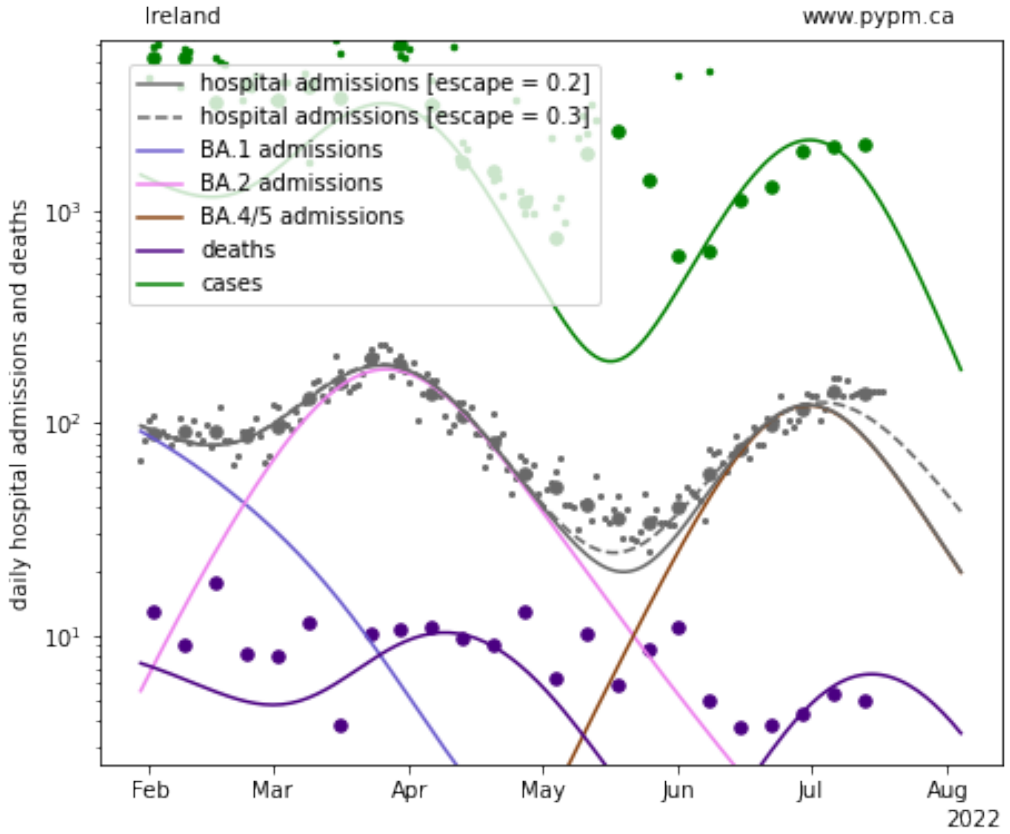

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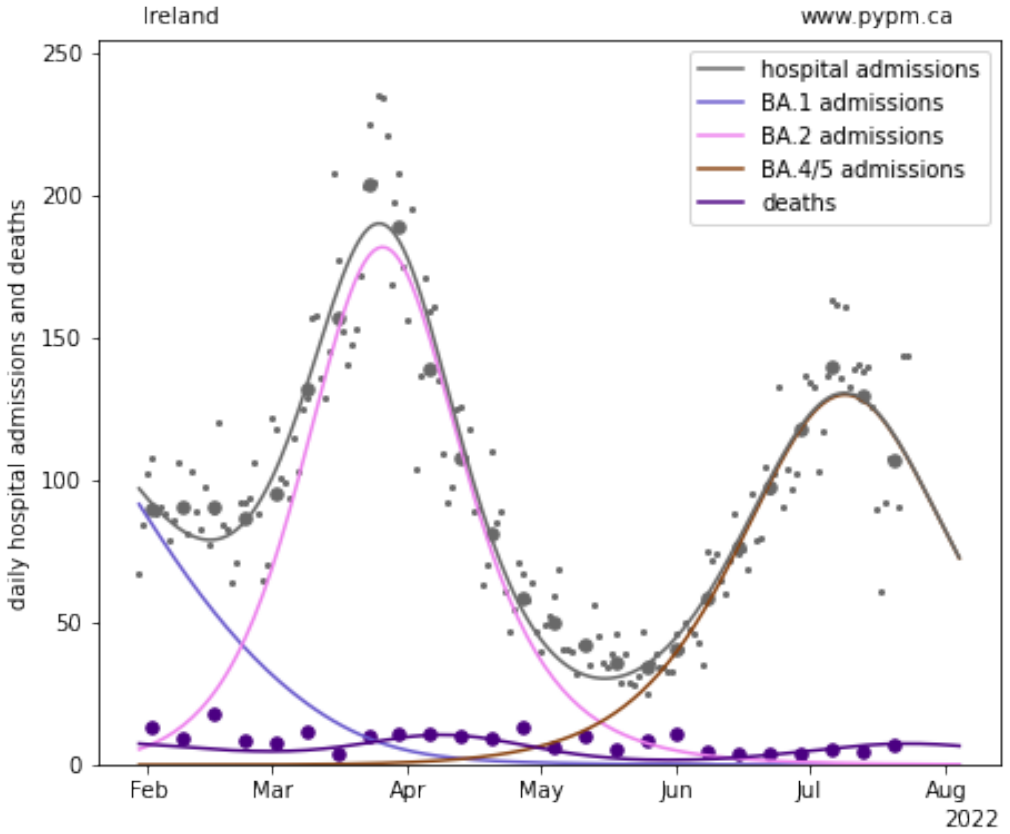

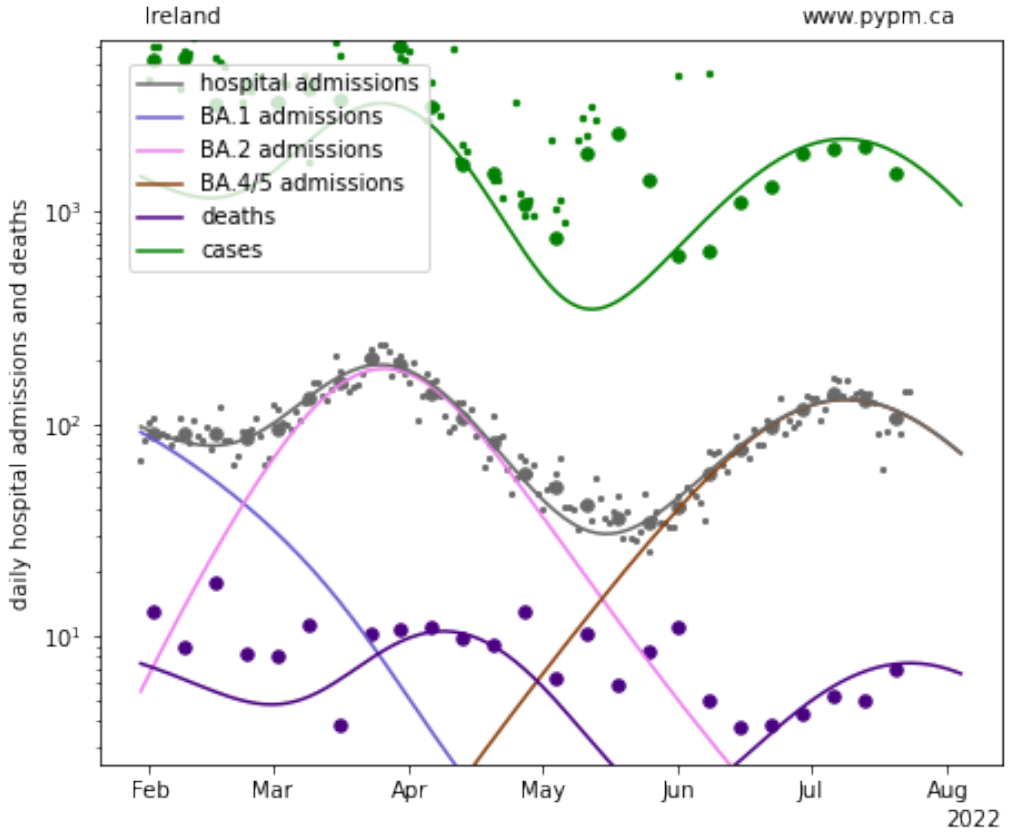

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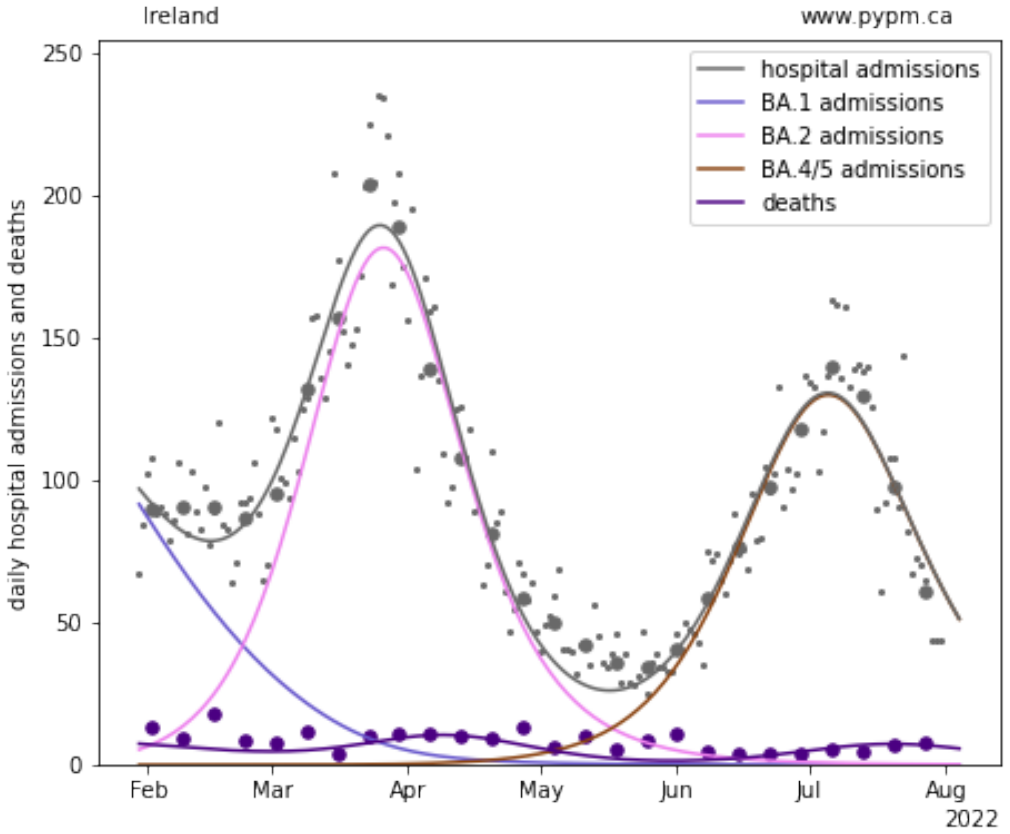

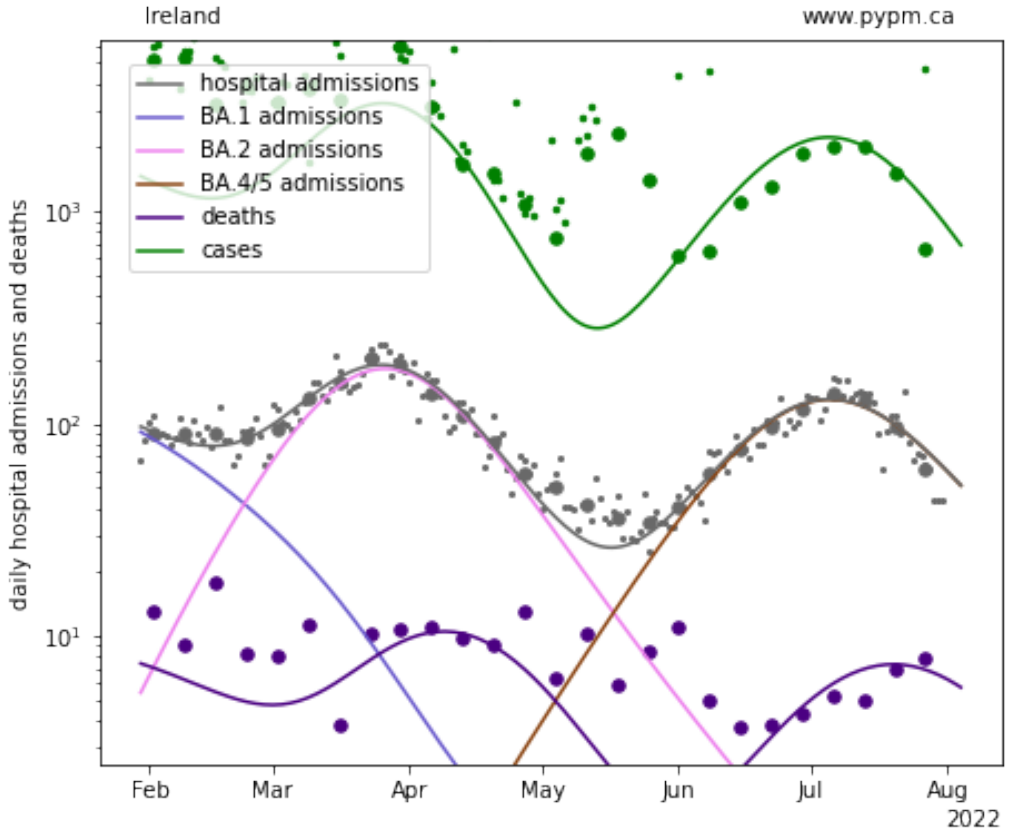

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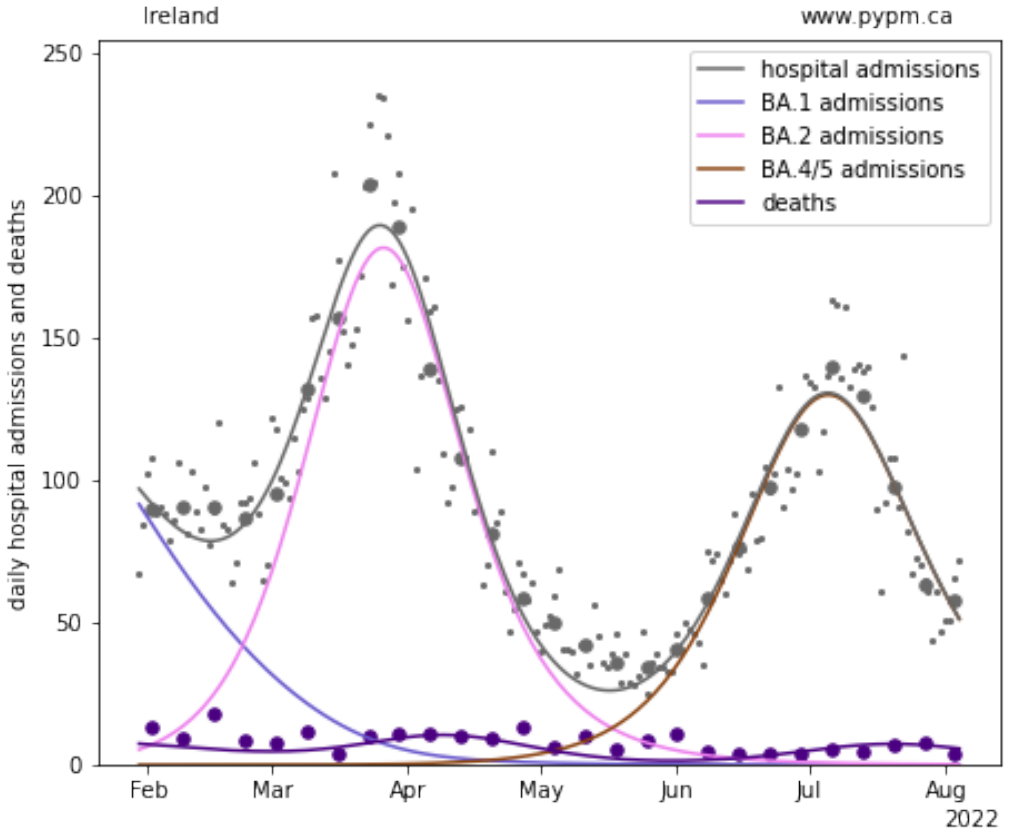

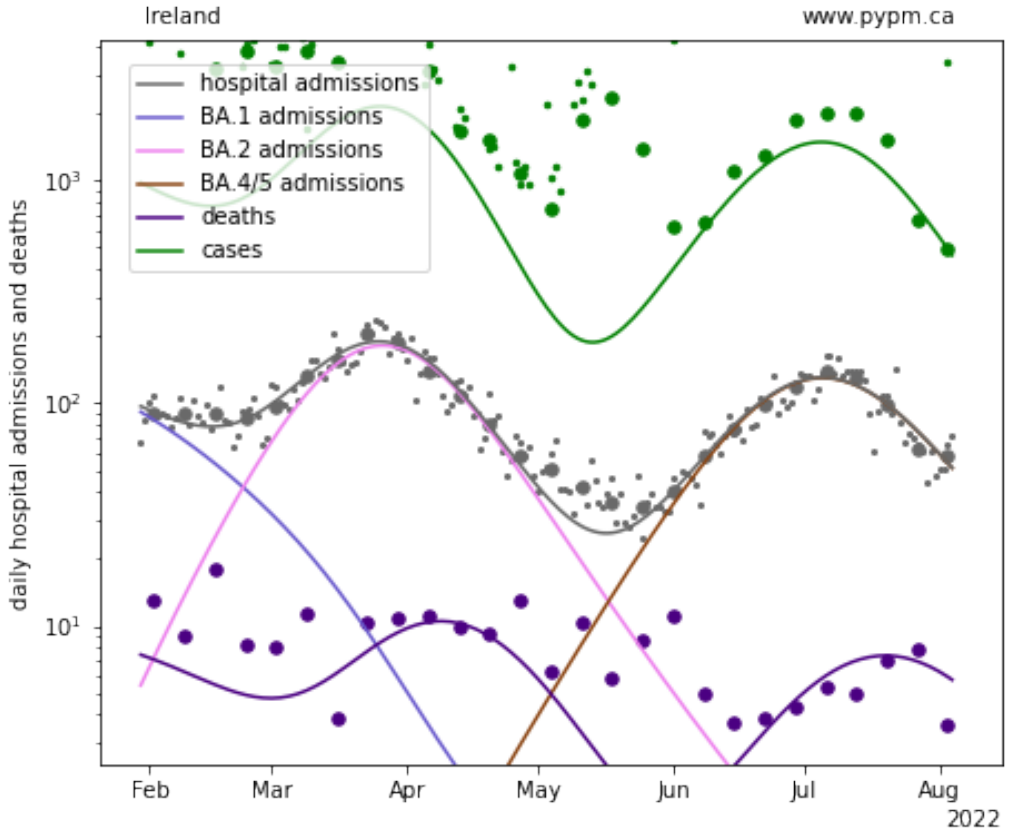

Norway

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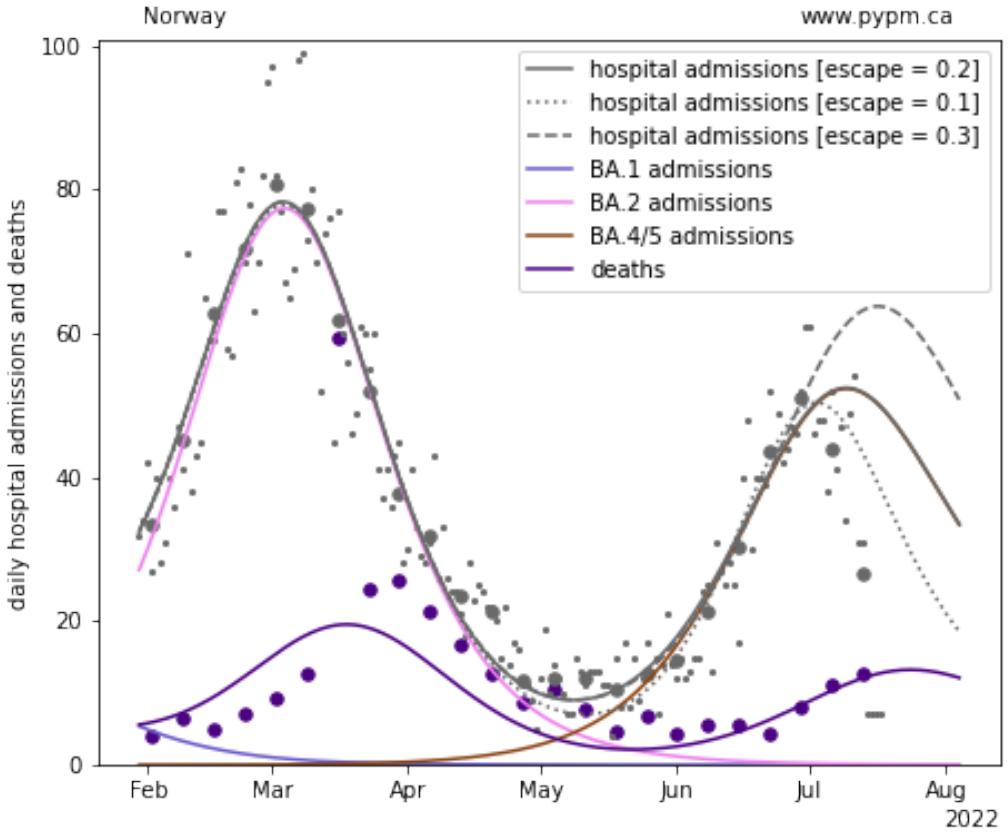
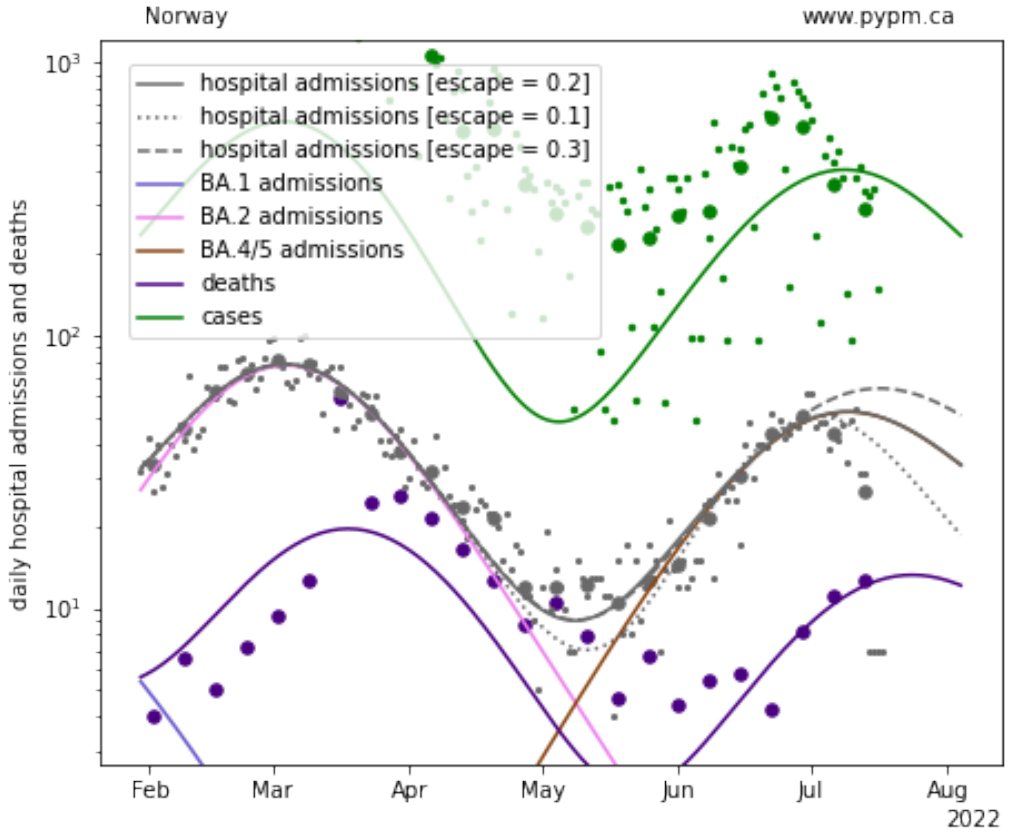
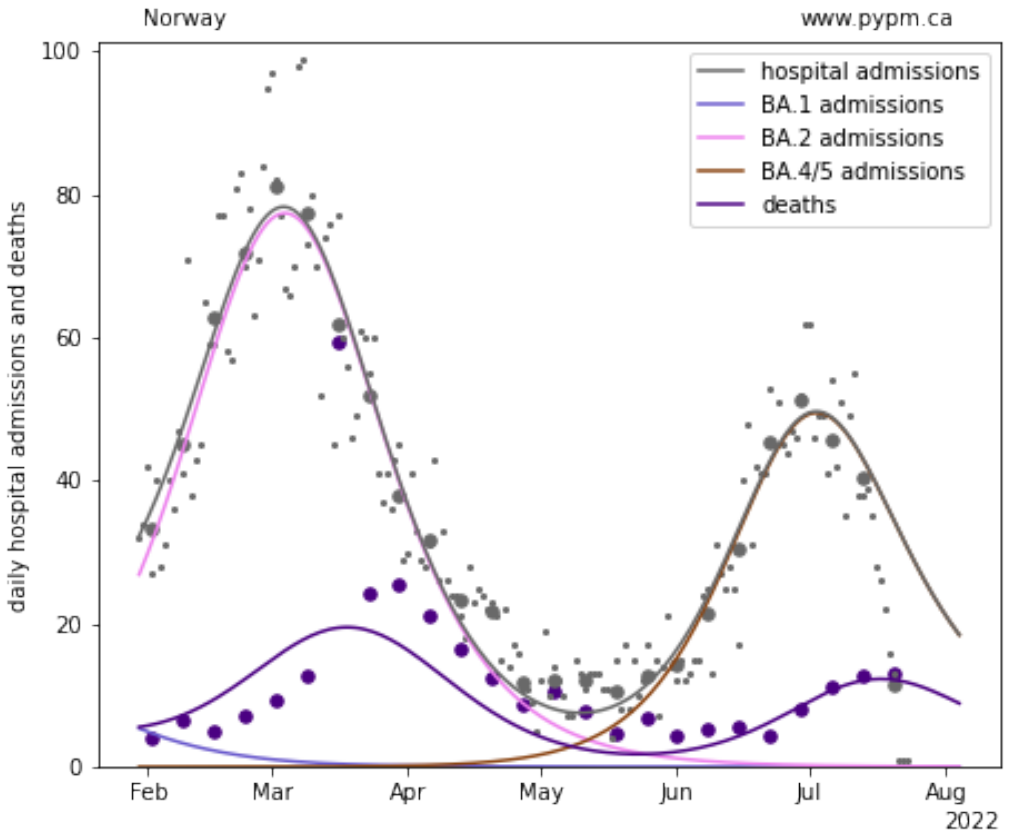
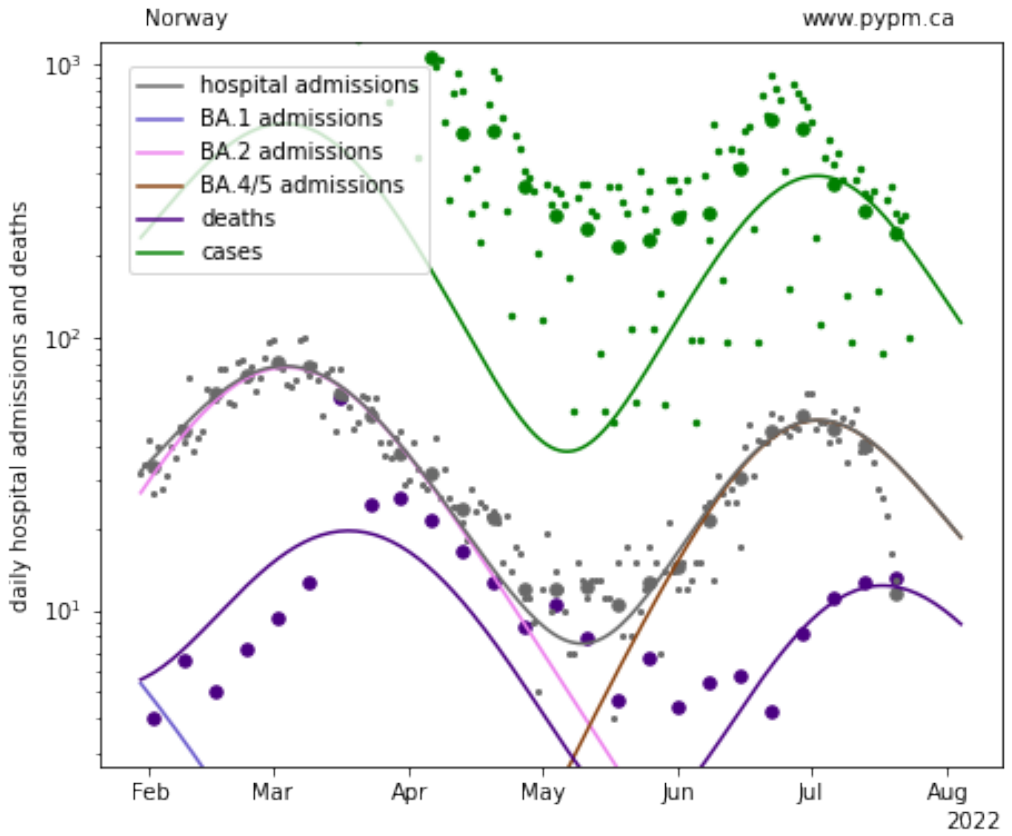




Norway – July 24 data





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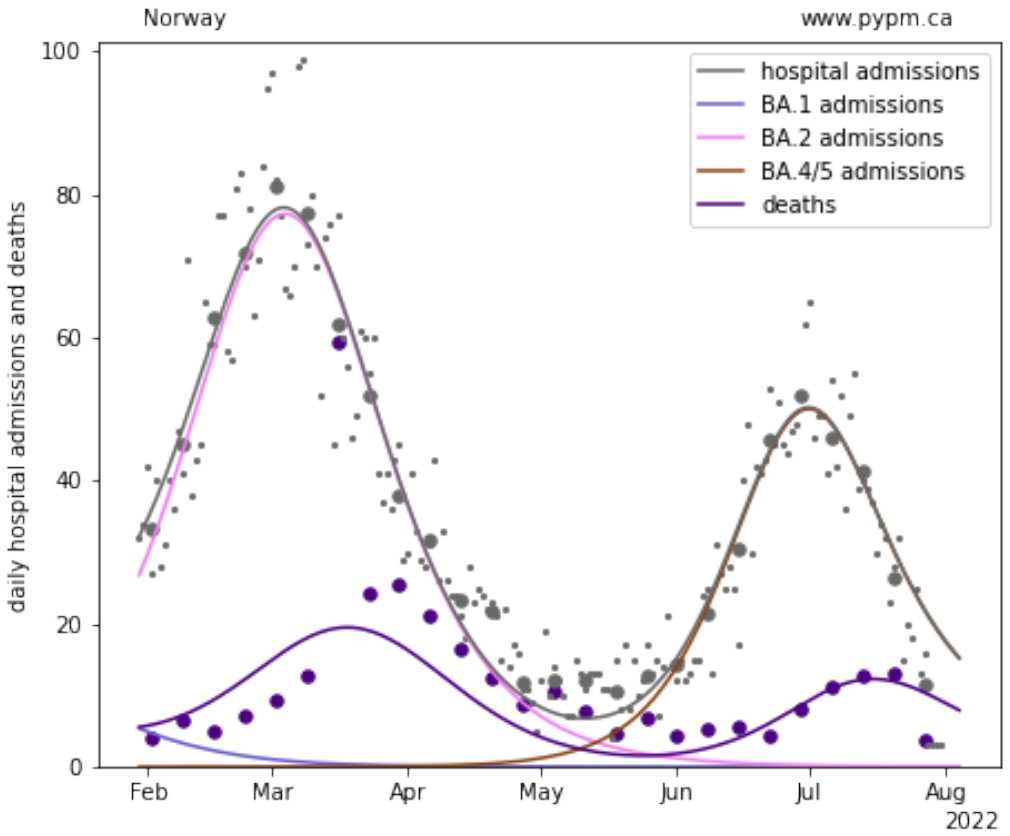

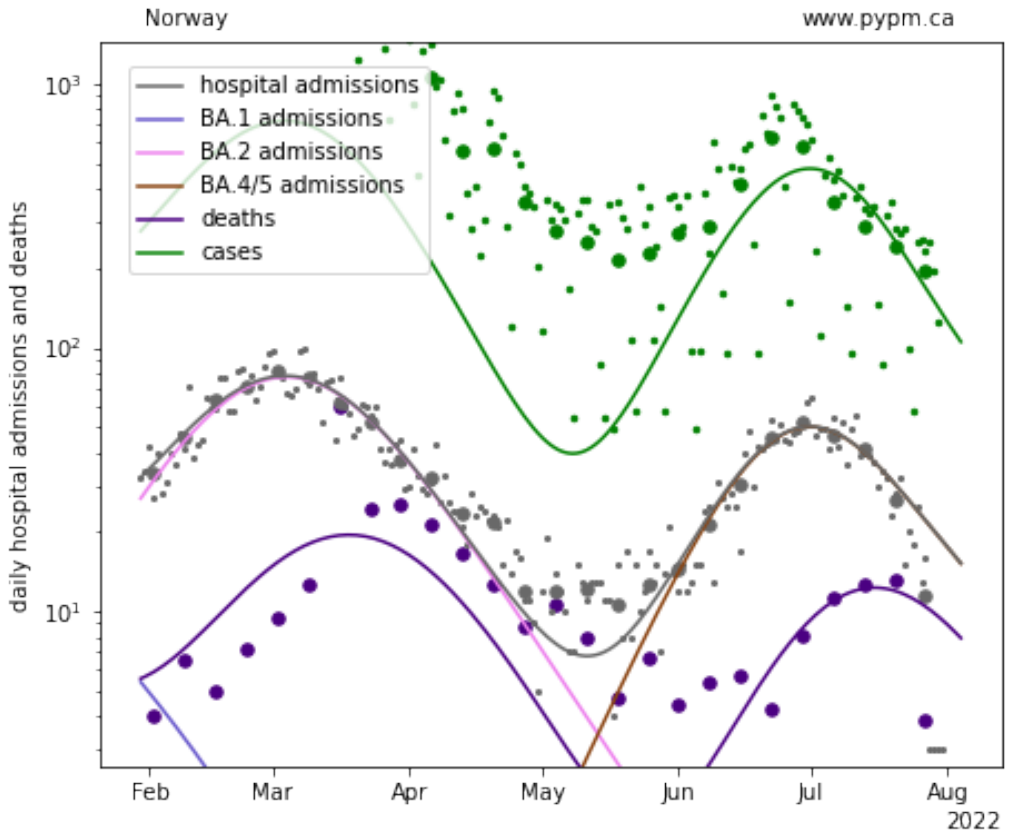

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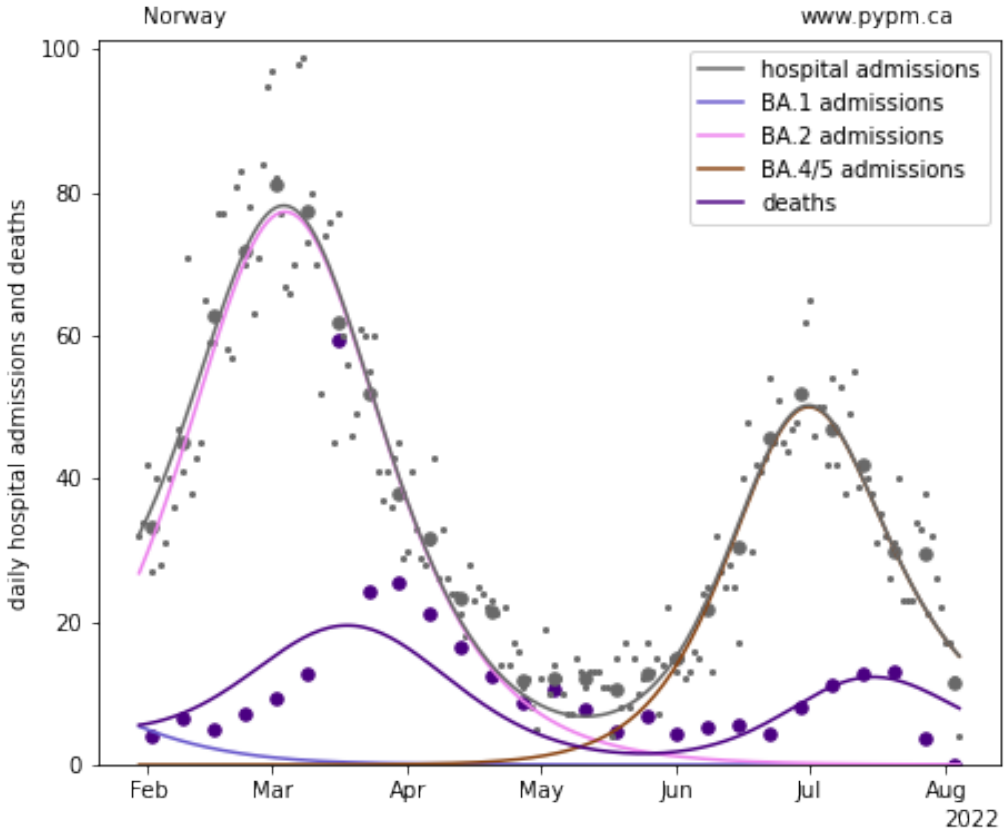
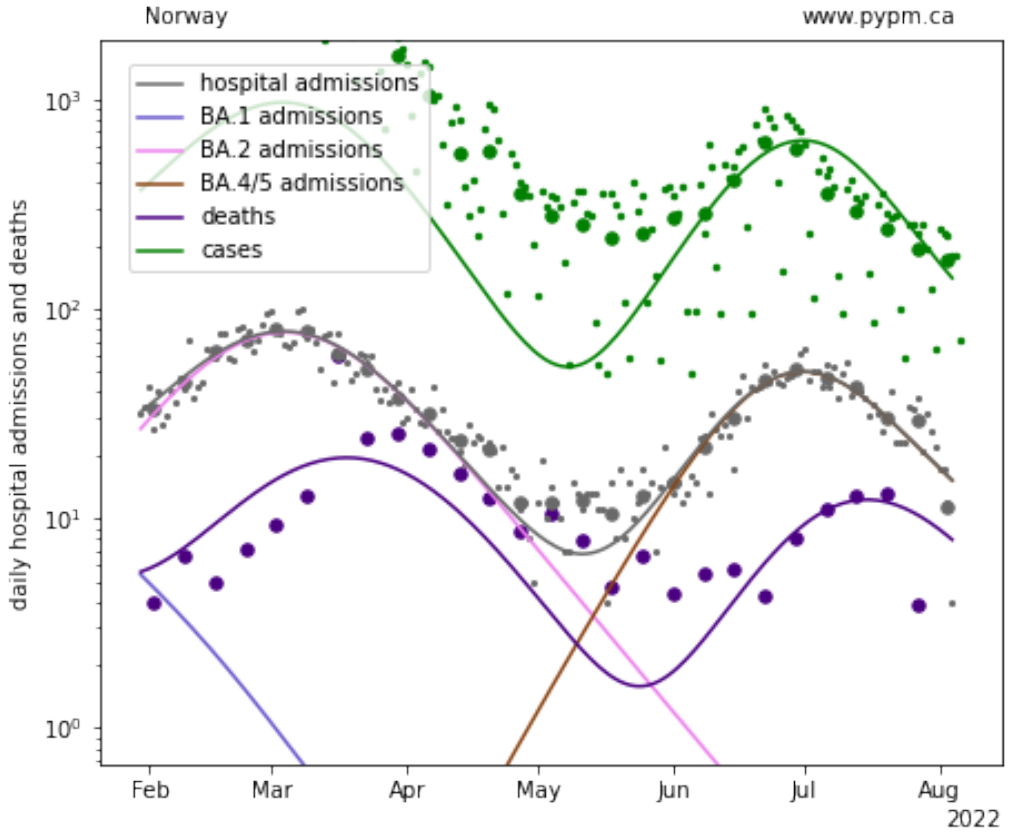
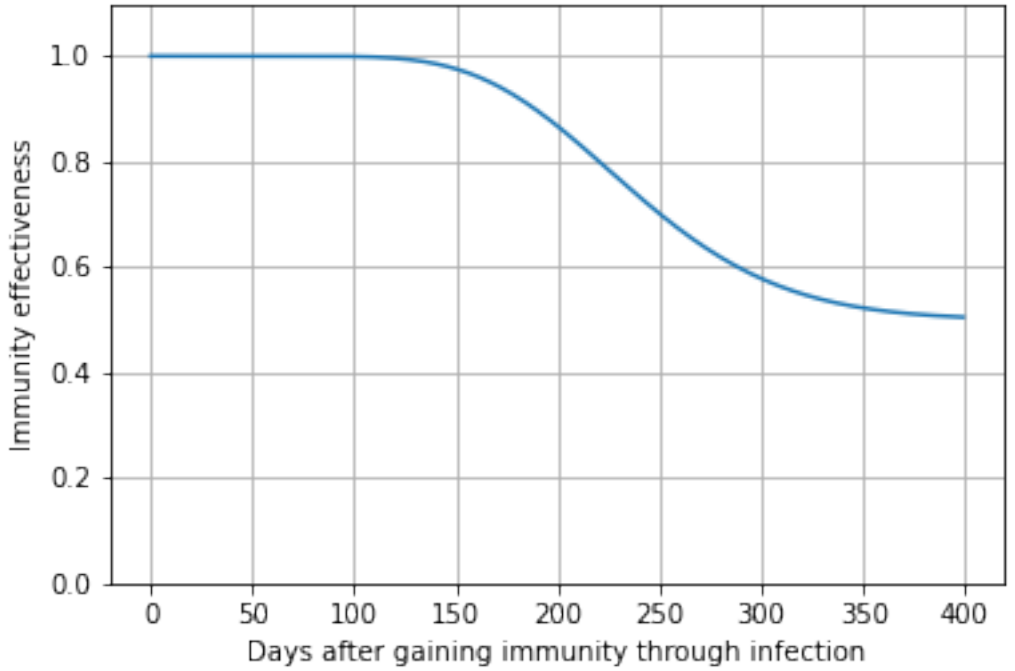




Signs of waning?

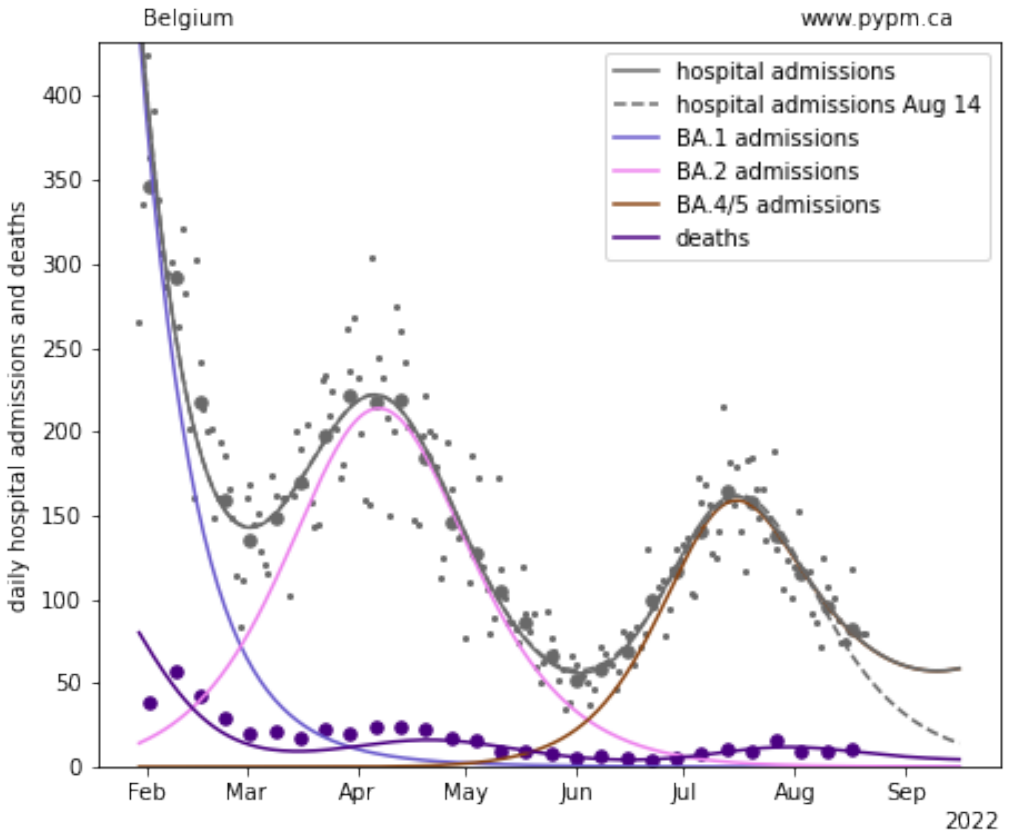
Waning activated in models starting August 21

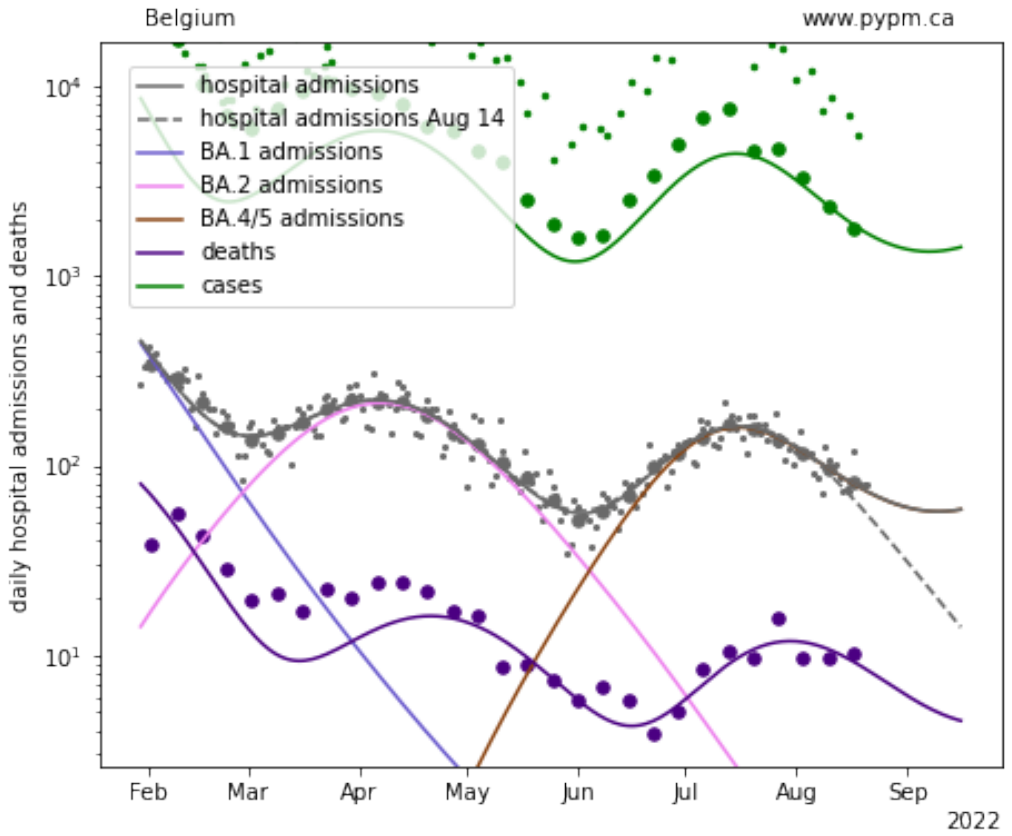
- Starting with August 21, models (with waning turned off) began to fit data poorly.
- Waning of immunity was activated to fit data:
  - Fraction of immunity that wanes: free parameter (figure shows 0.5)
  - Mean waning time (set to 8 months)
    - later changed to be a free parameter
  - Standard deviation of waning time (2 months)



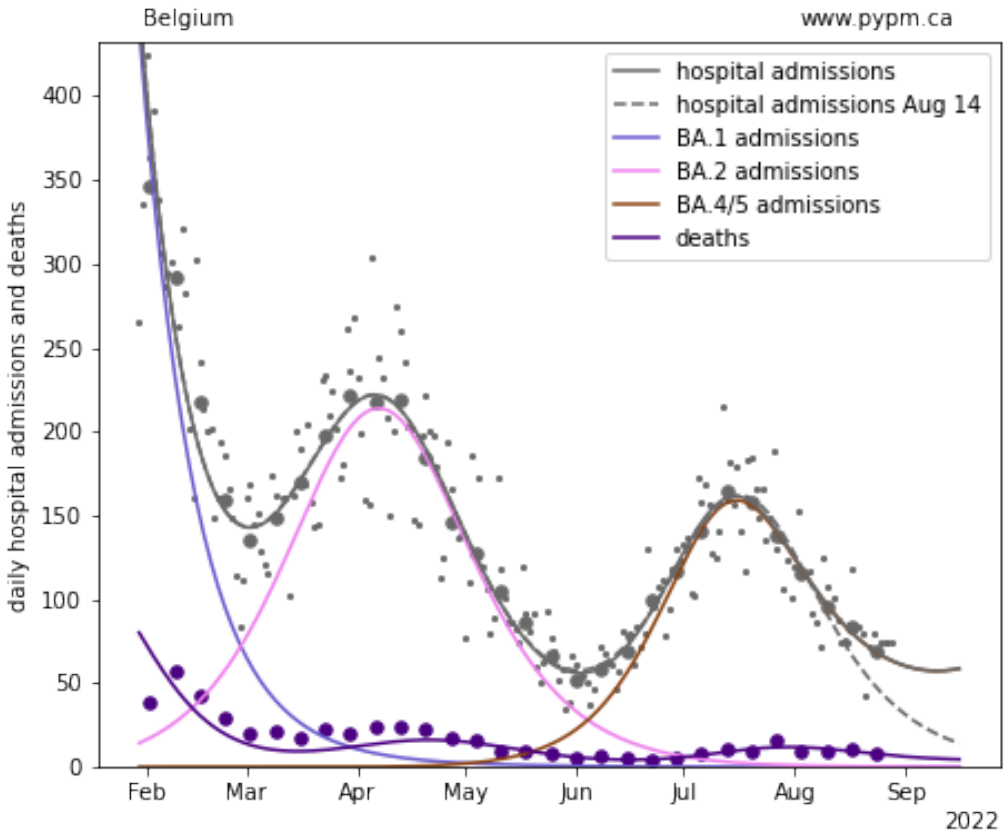
Belgium

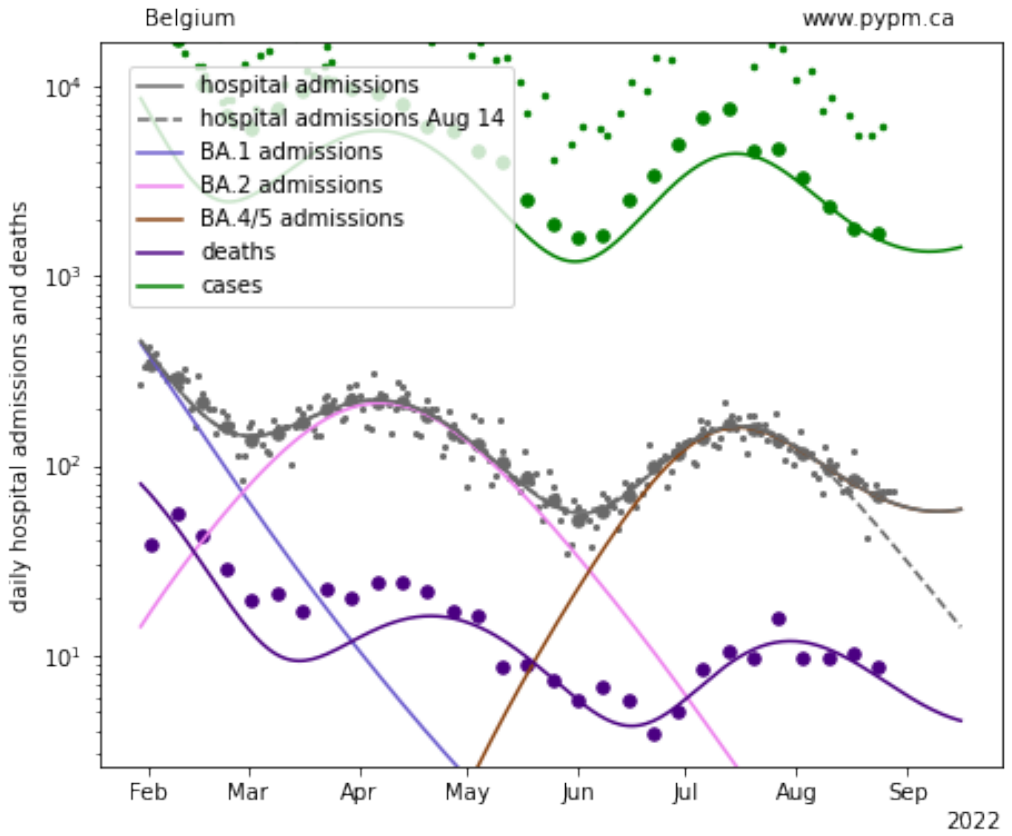
Belgium – August 21



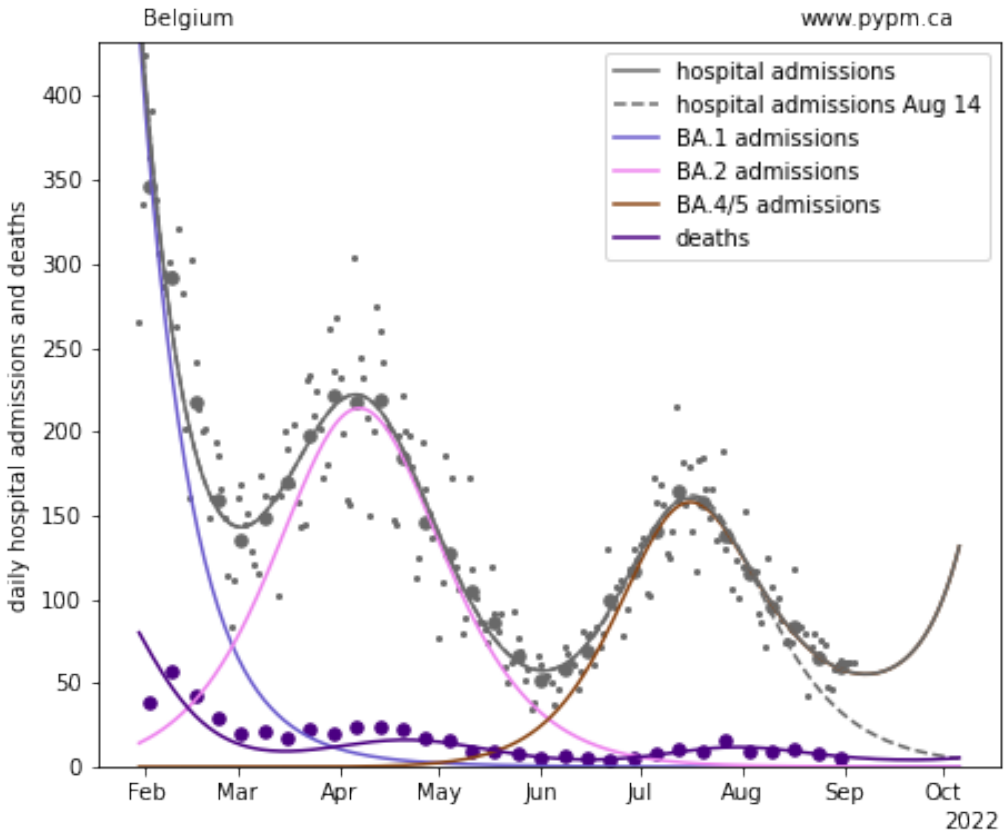


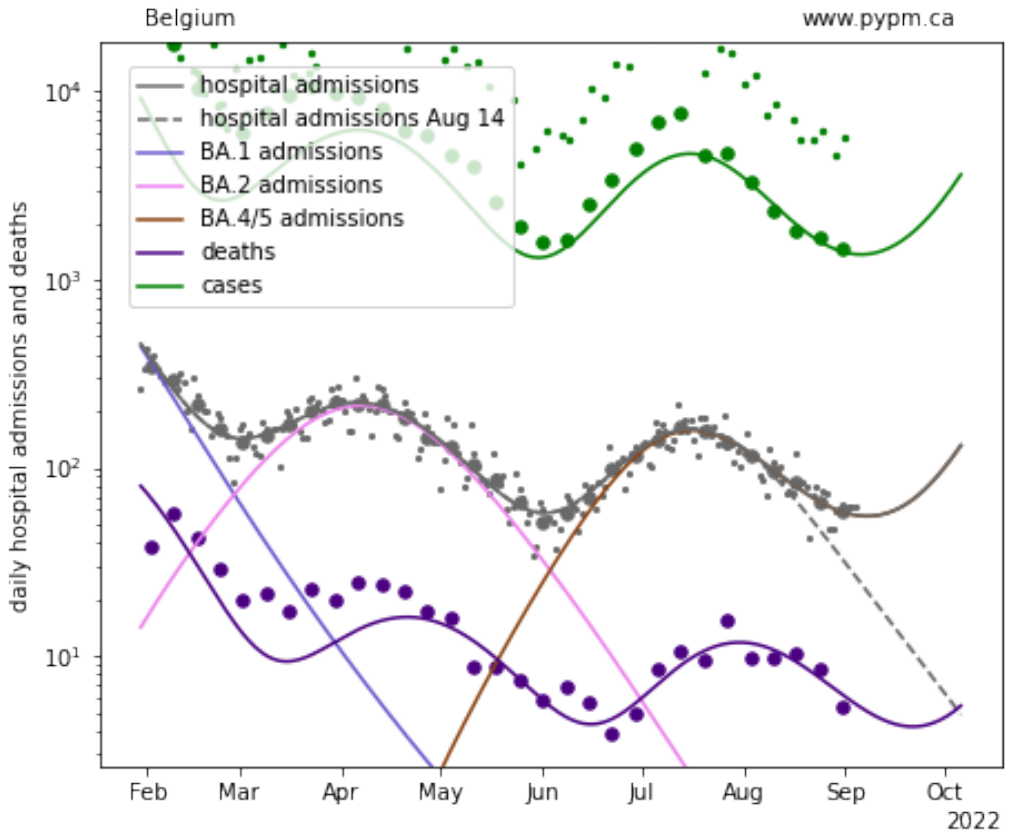
Belgium – August 28



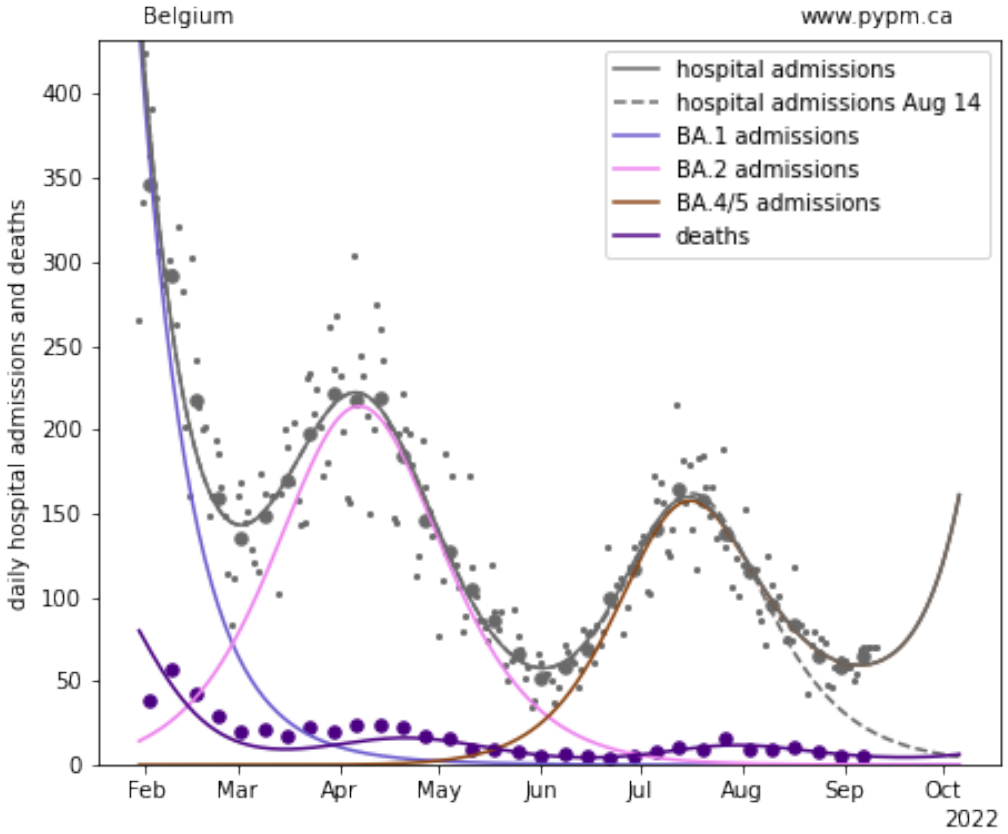


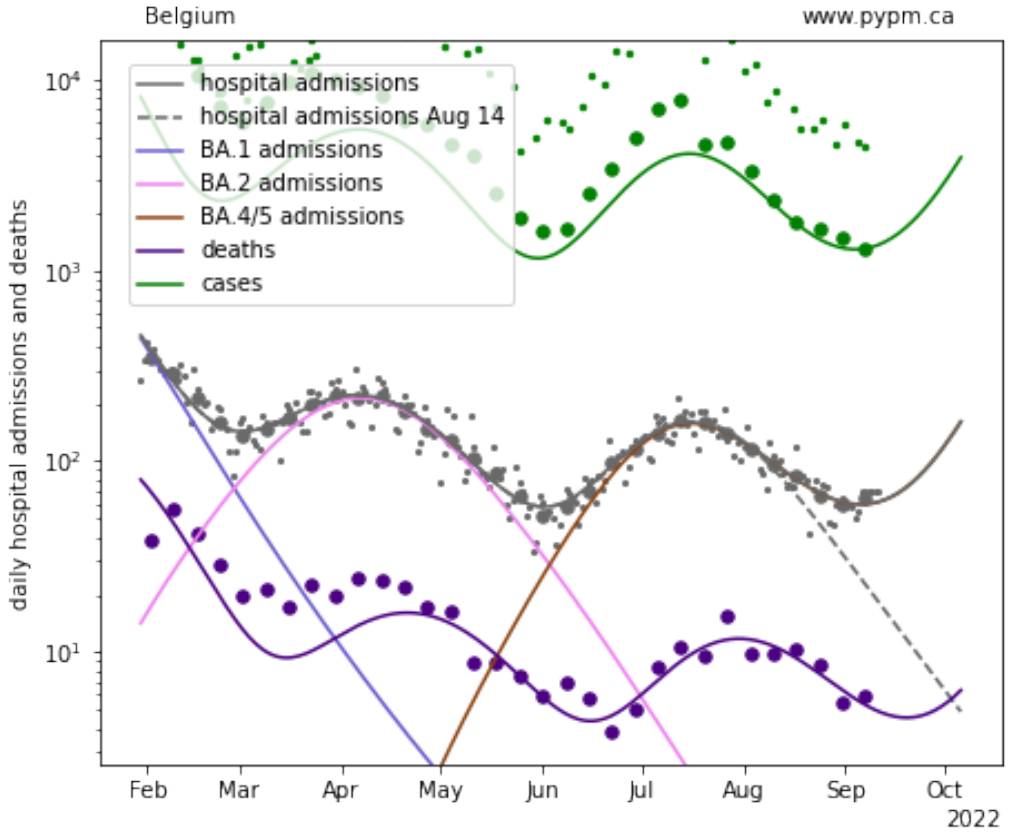
Belgium – September 4



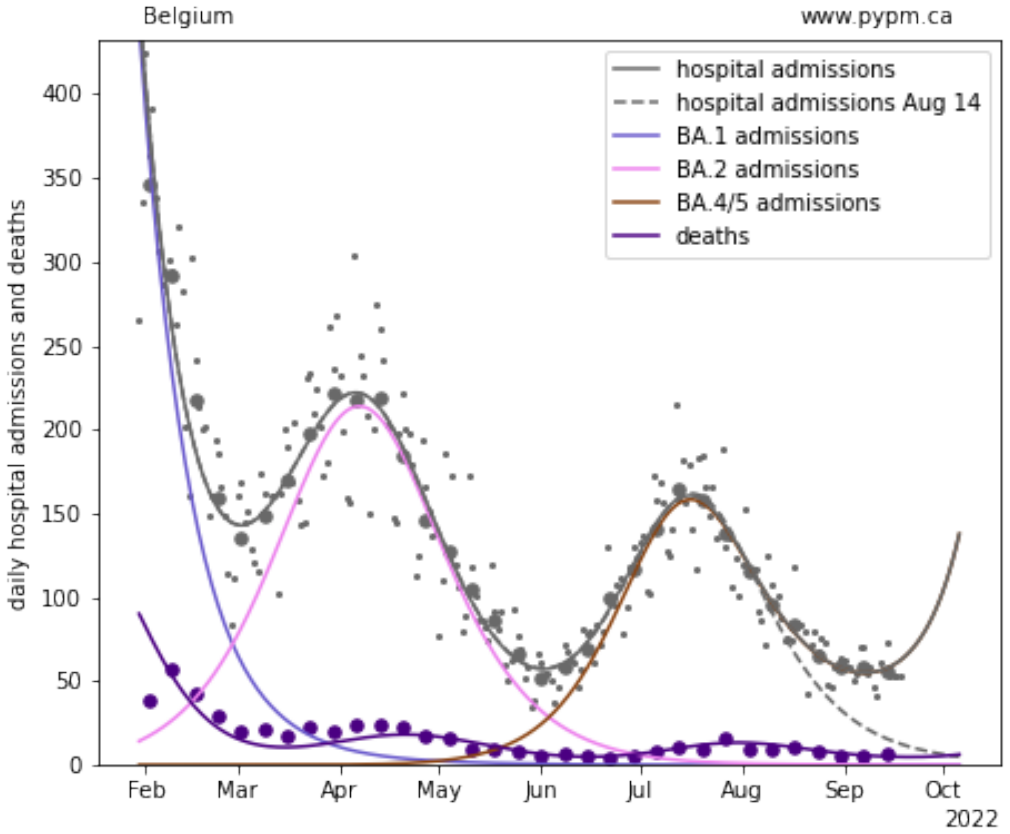


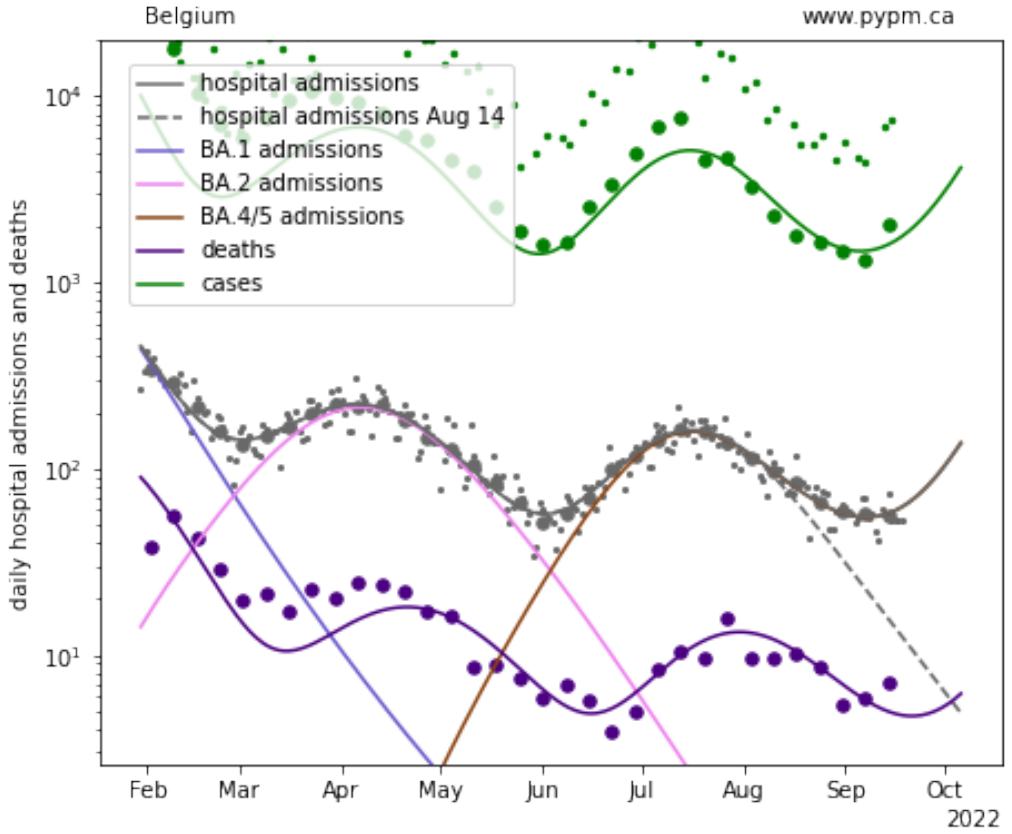
Belgium – September 11





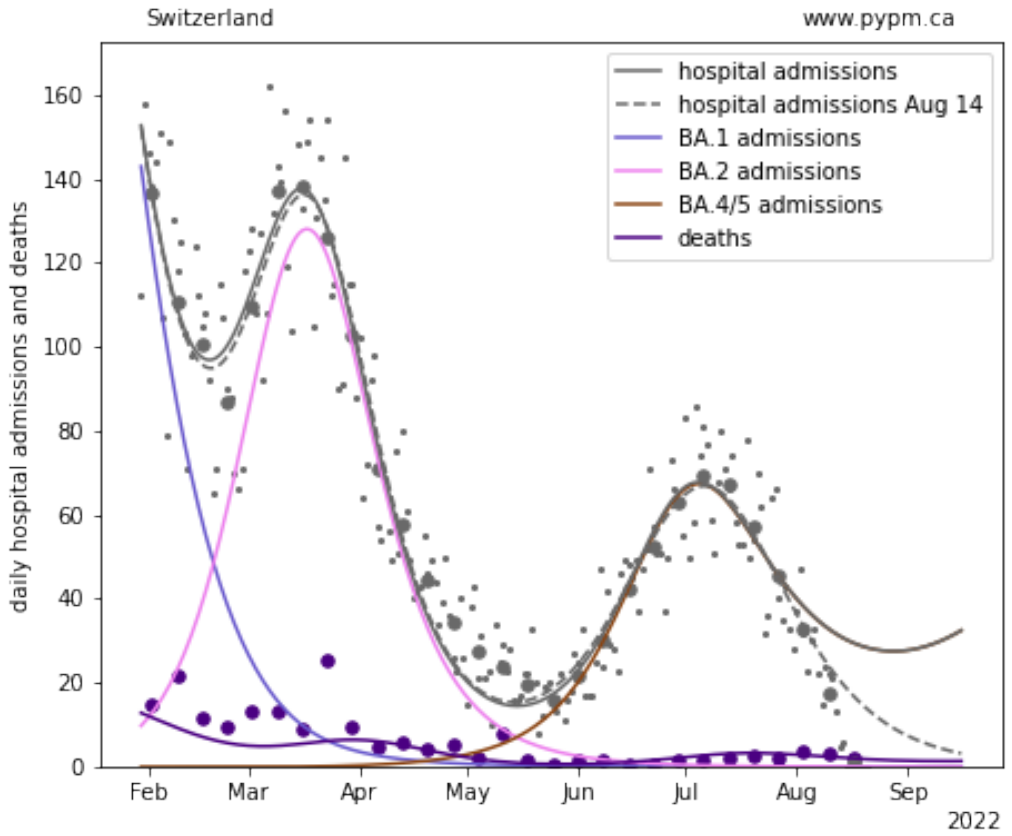
Belgium – September 18

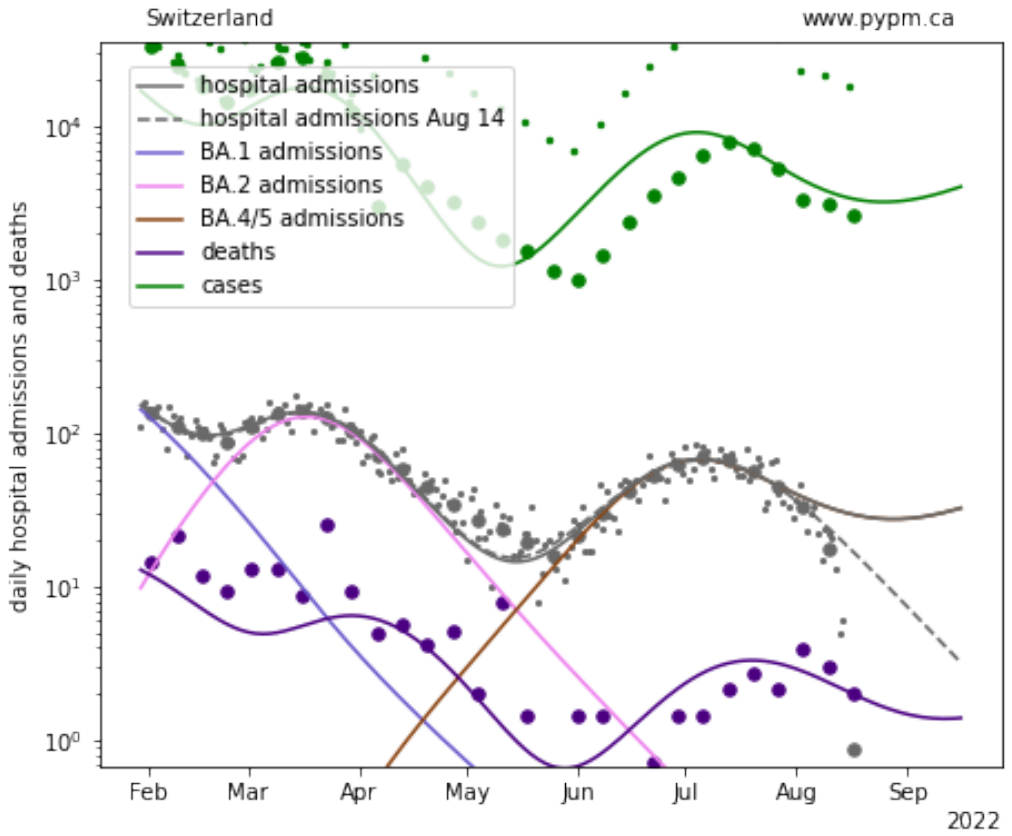




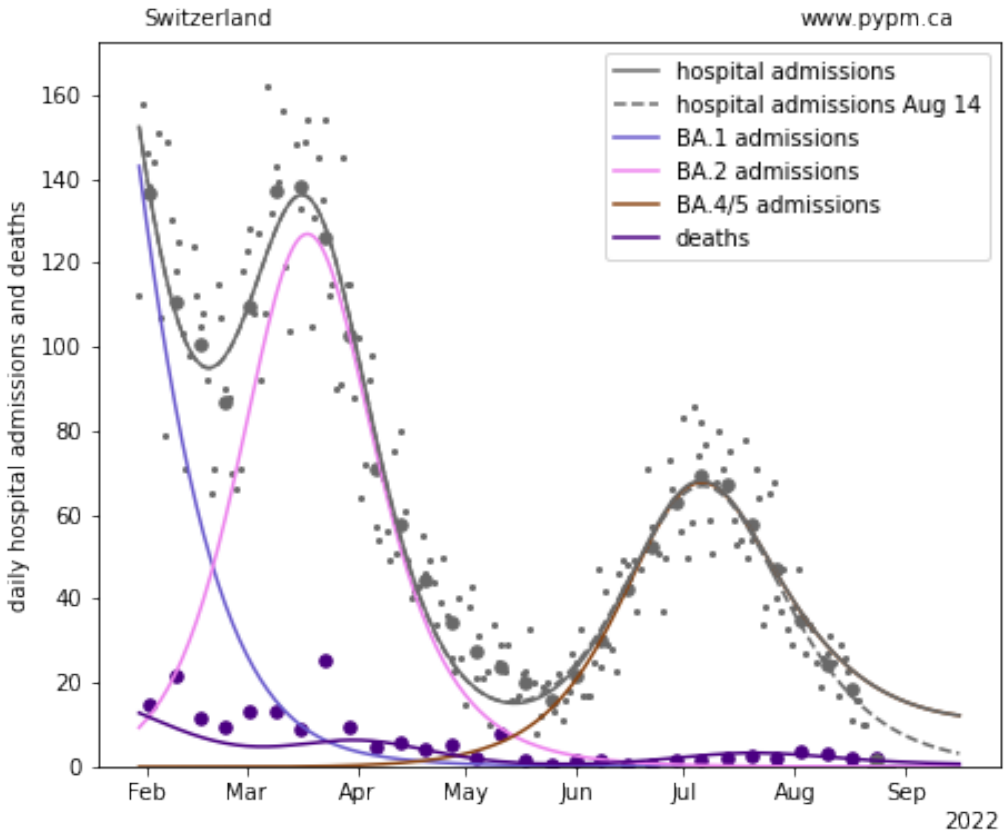
Switzerland

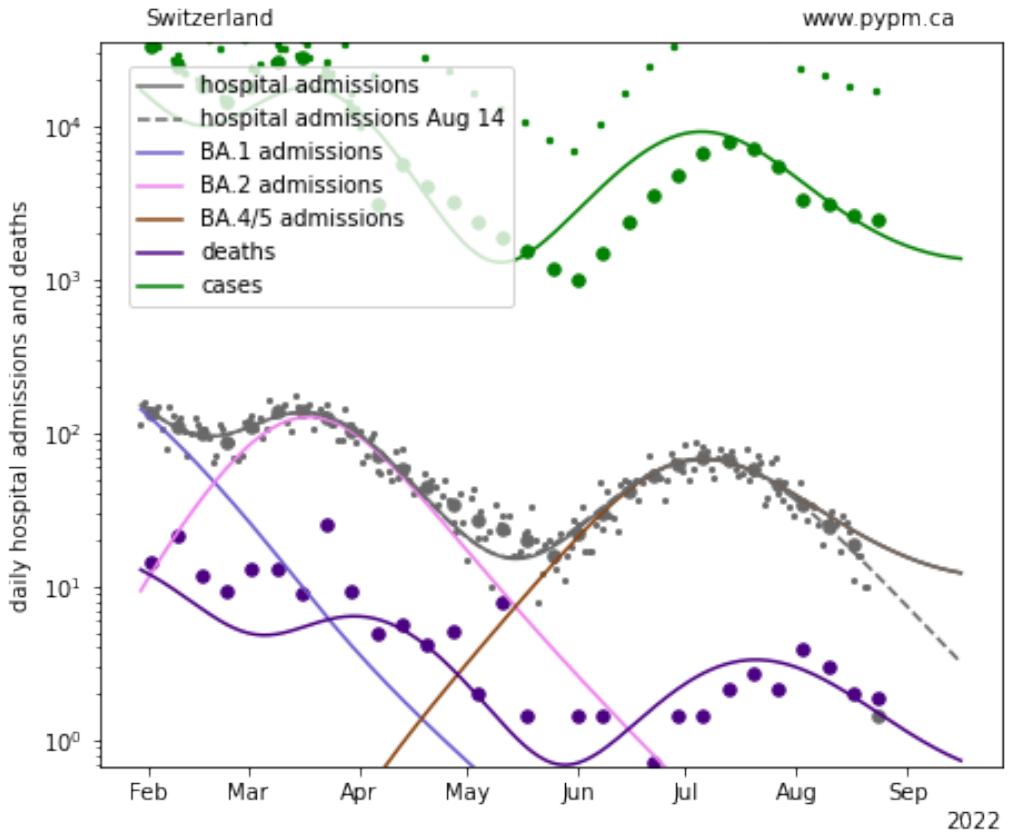
Switzerland – August 21



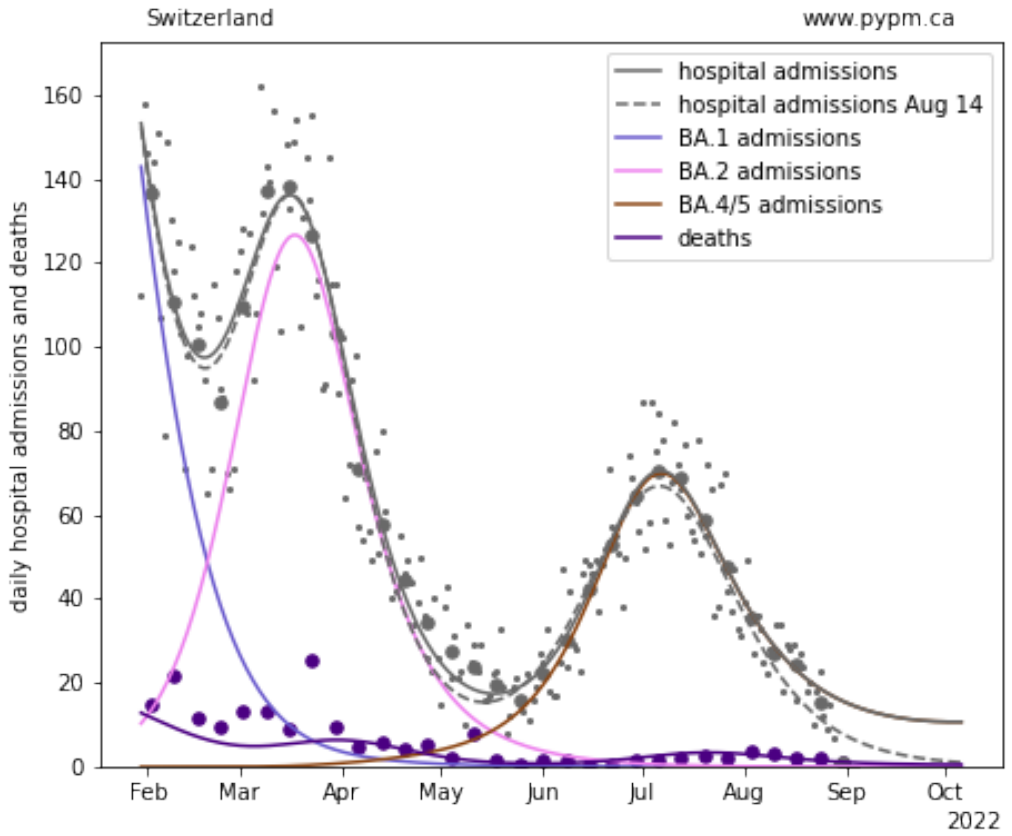


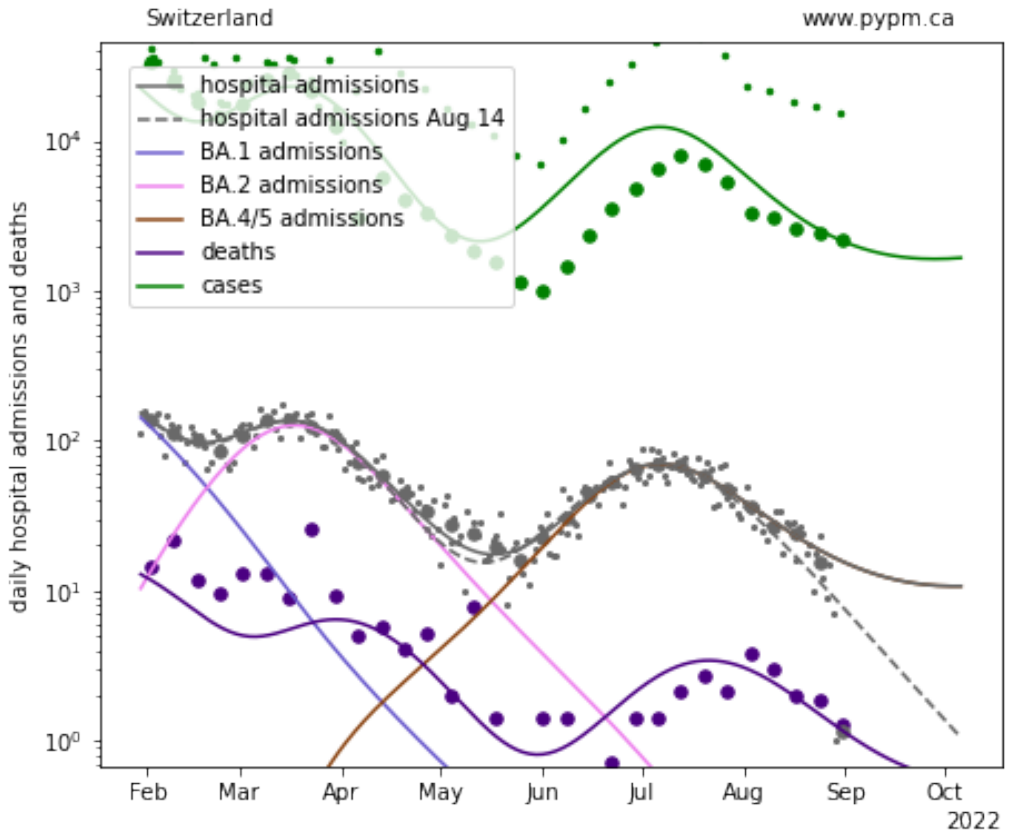
Switzerland – August 28



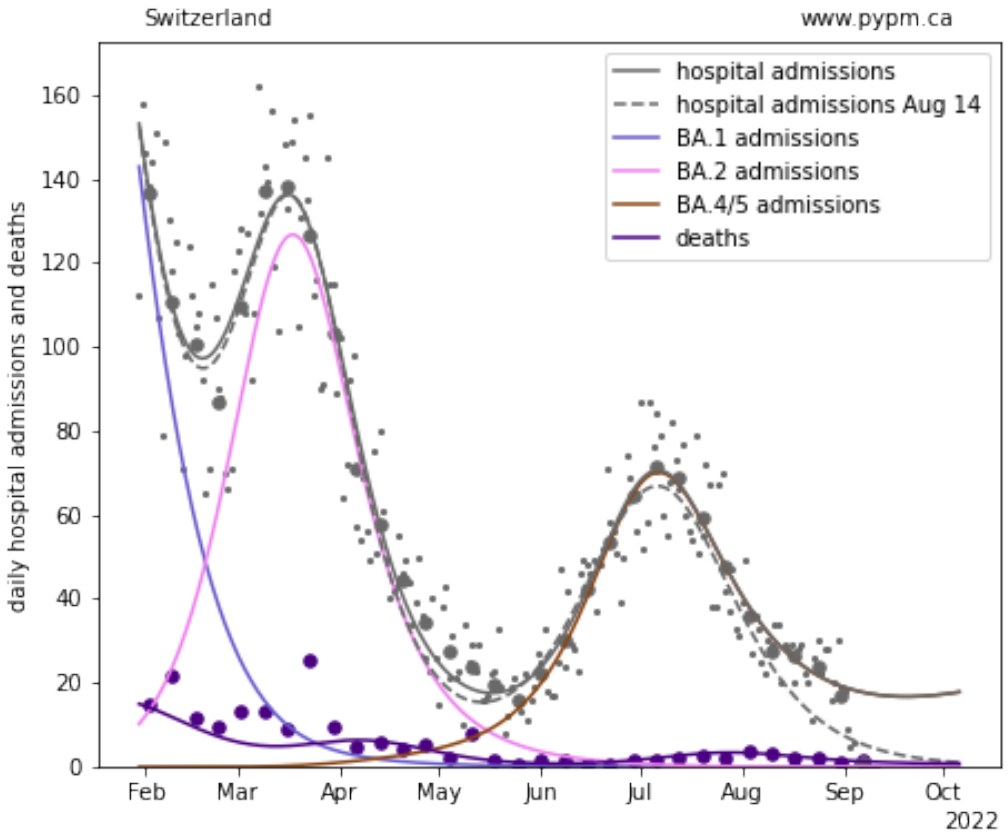


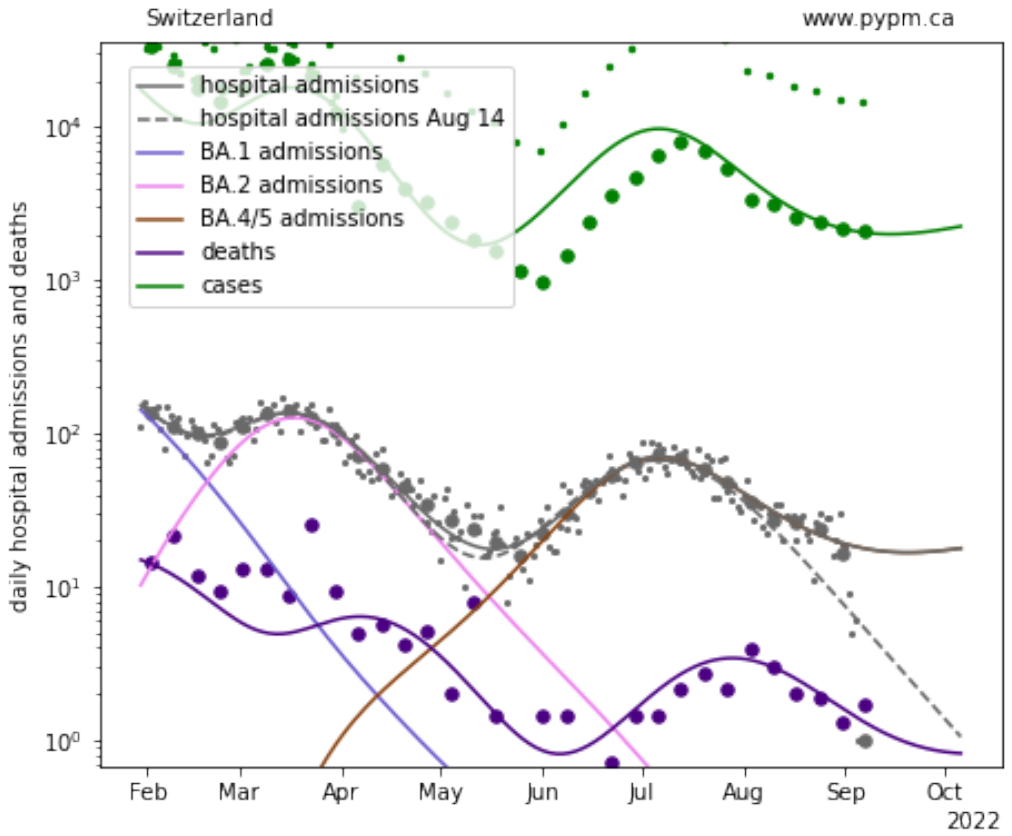
Switzerland – September 4



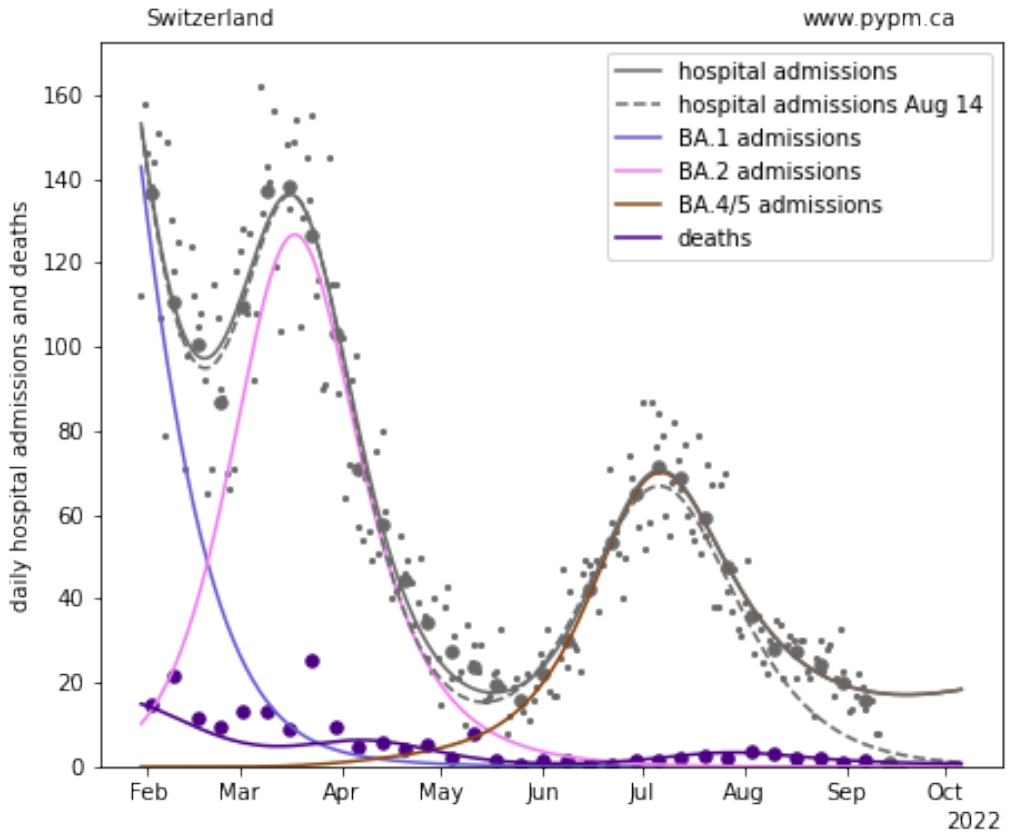


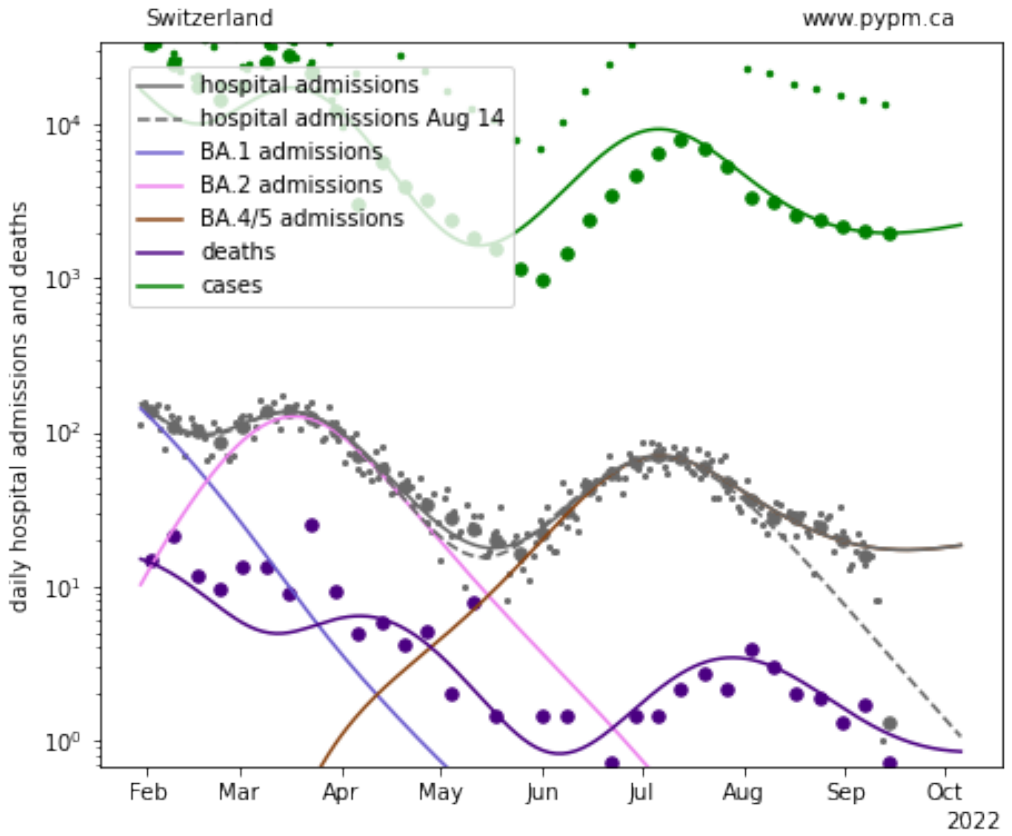
Switzerland – September 11





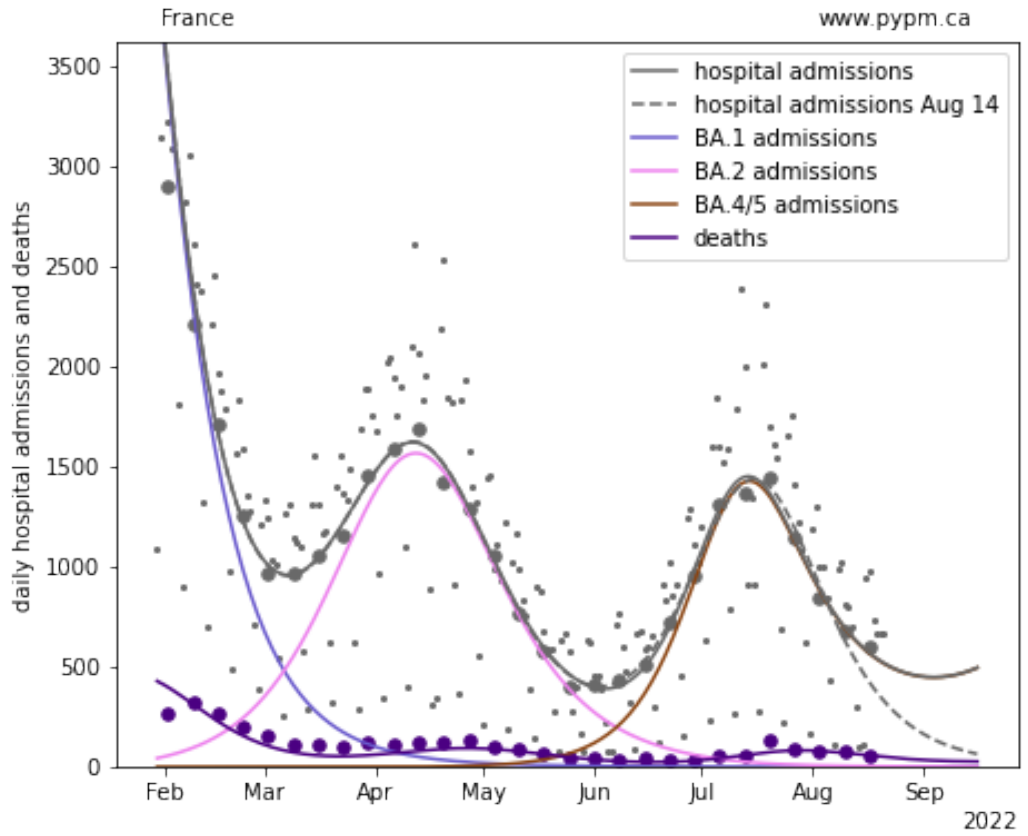
Switzerland – September 18

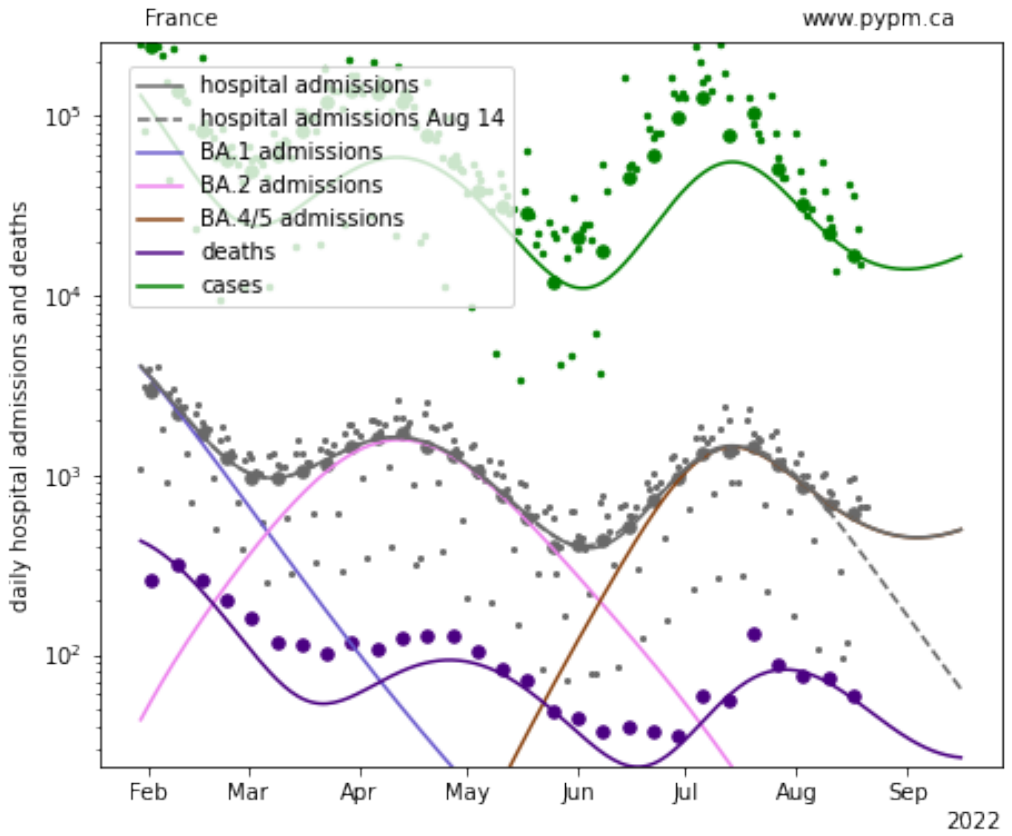




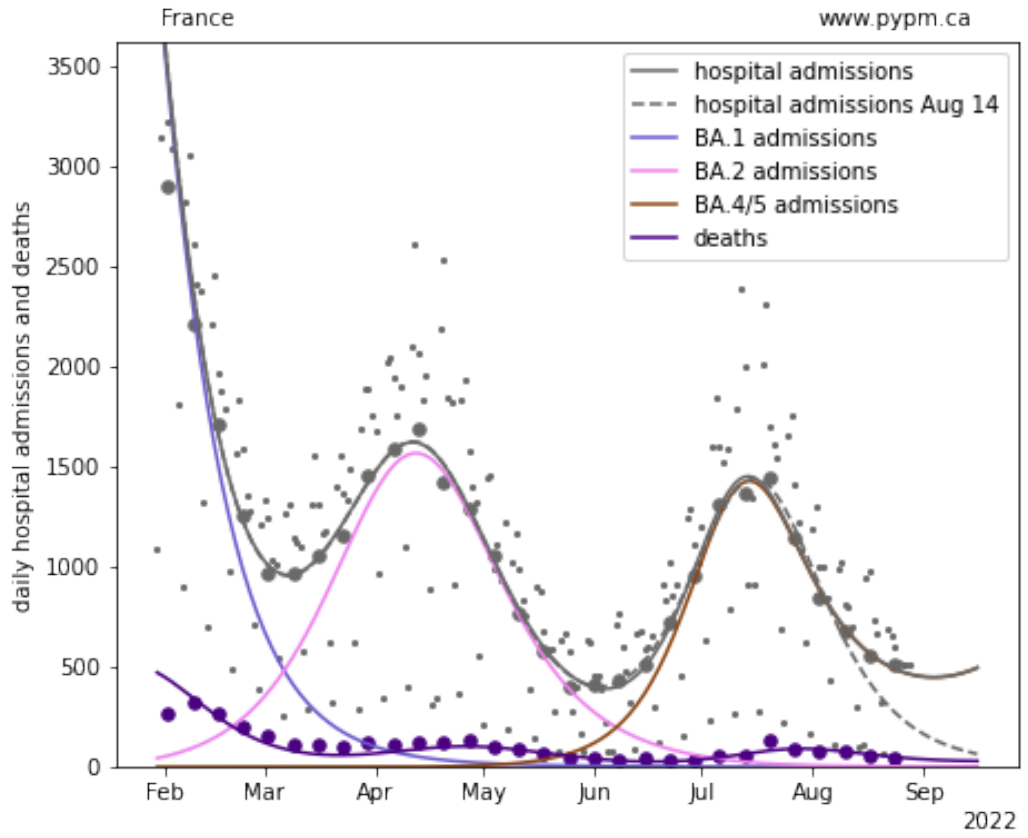
France

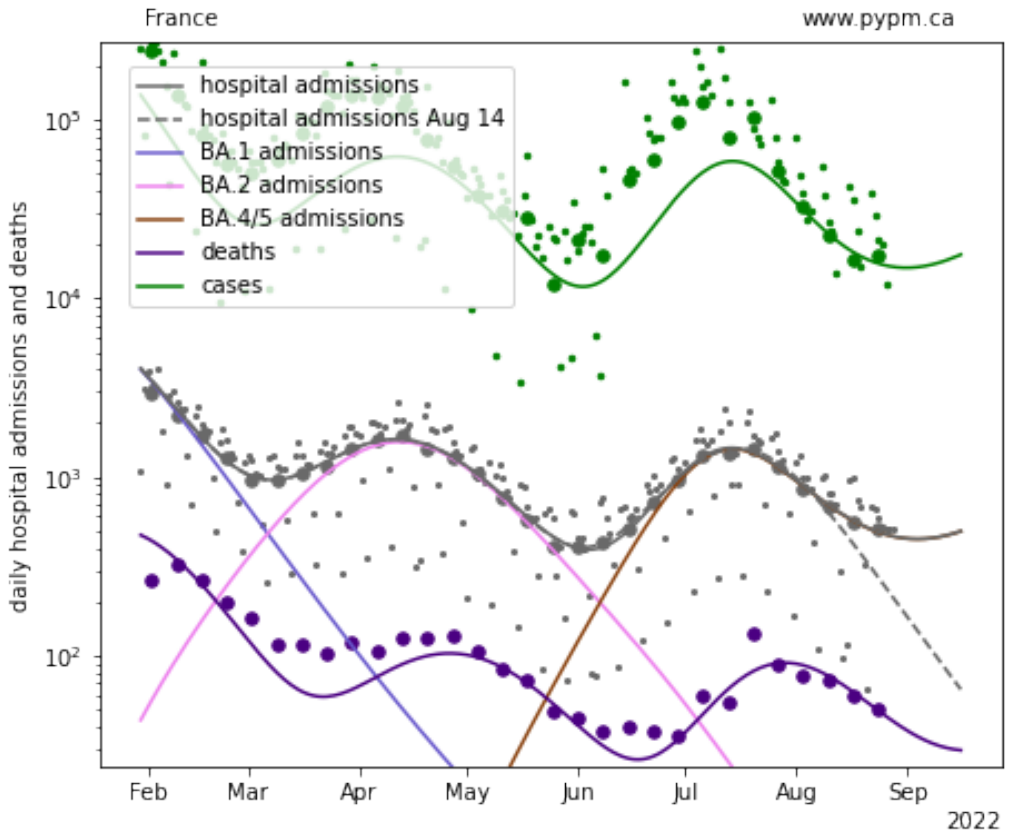
France – August 21



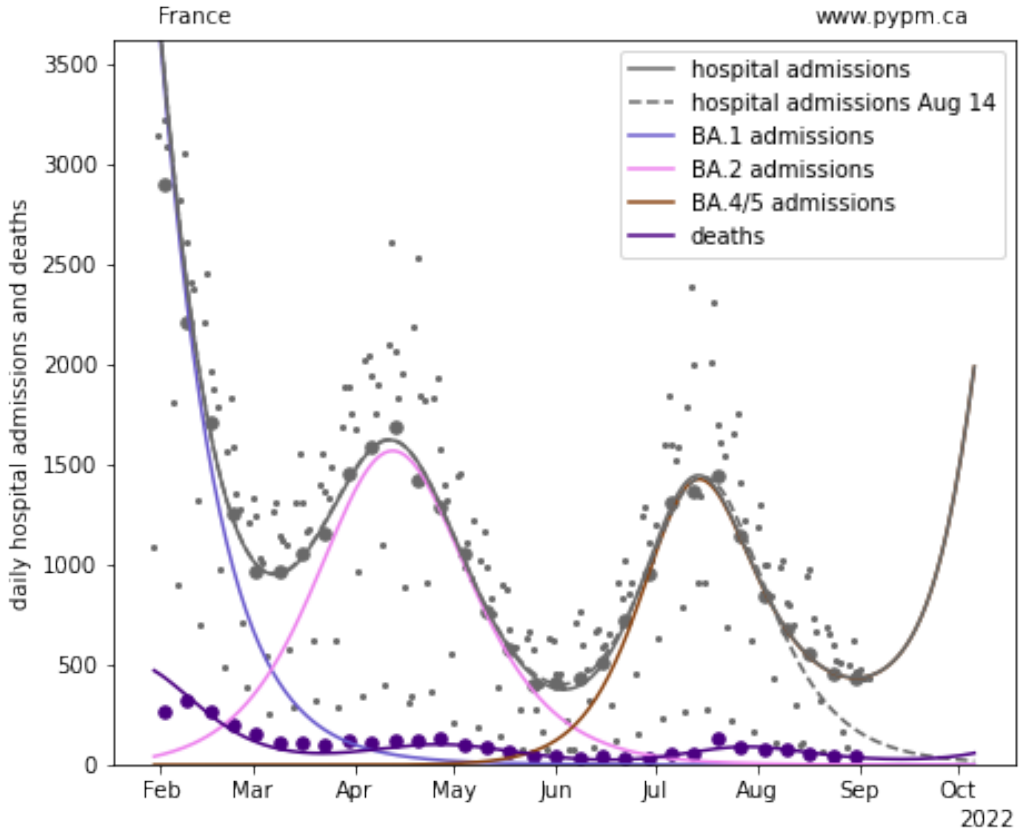


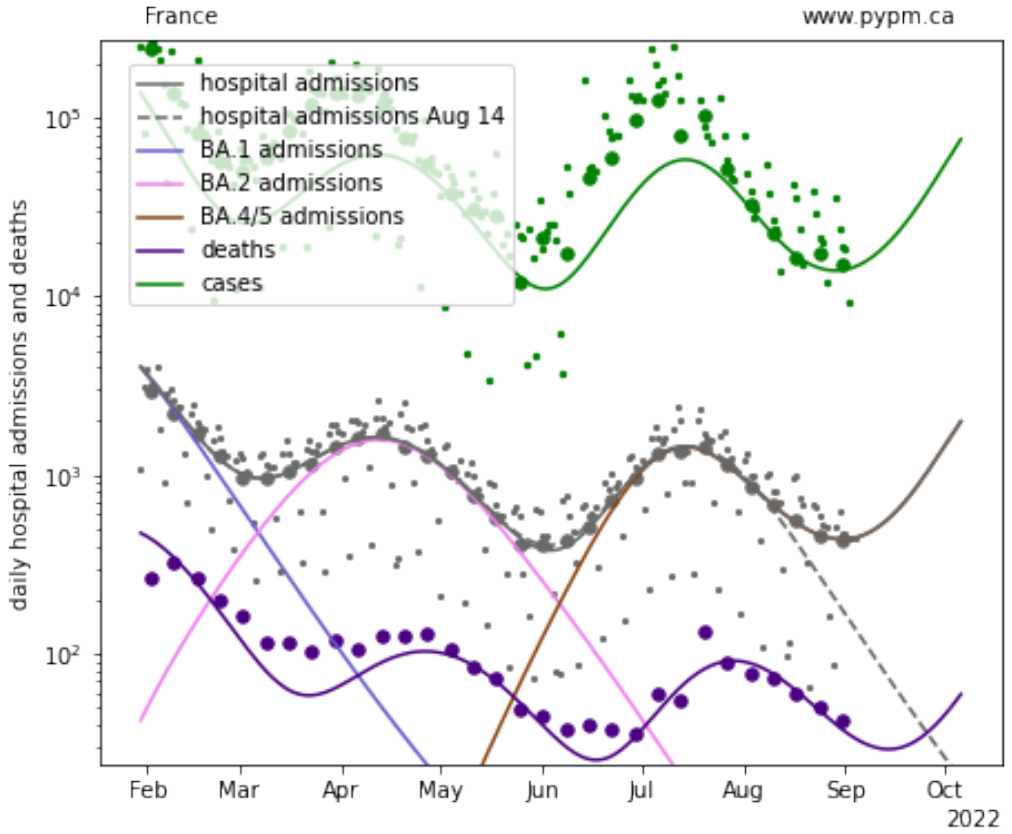
France – August 28



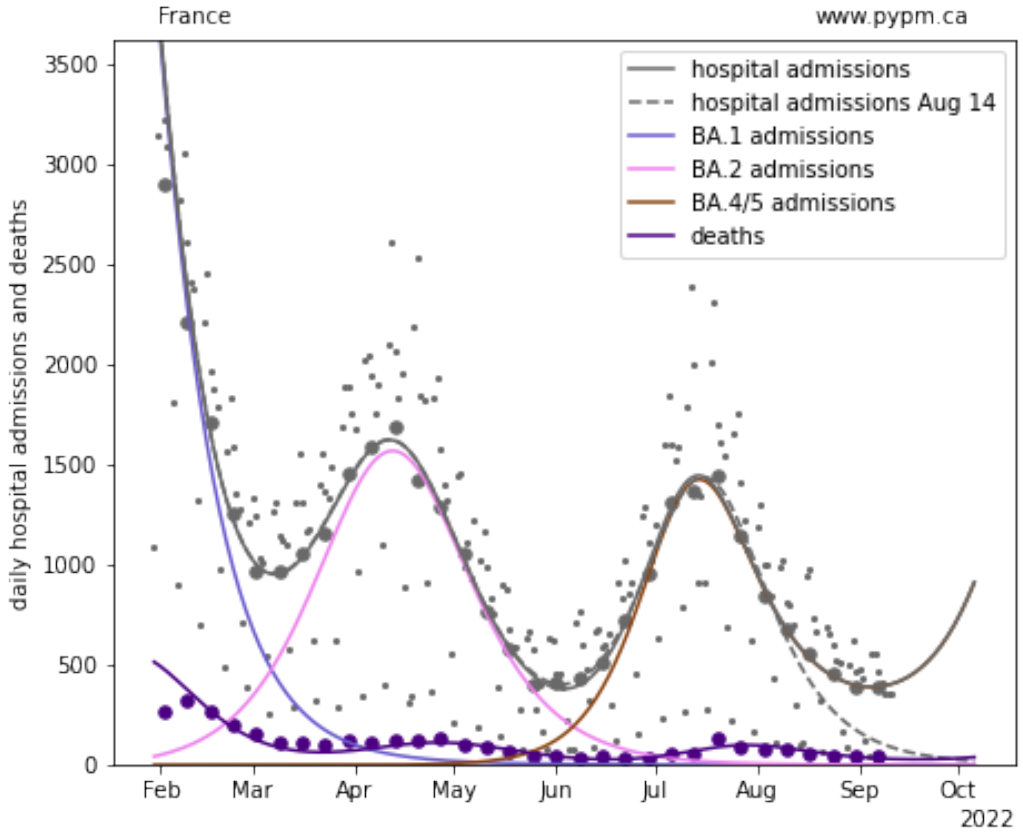


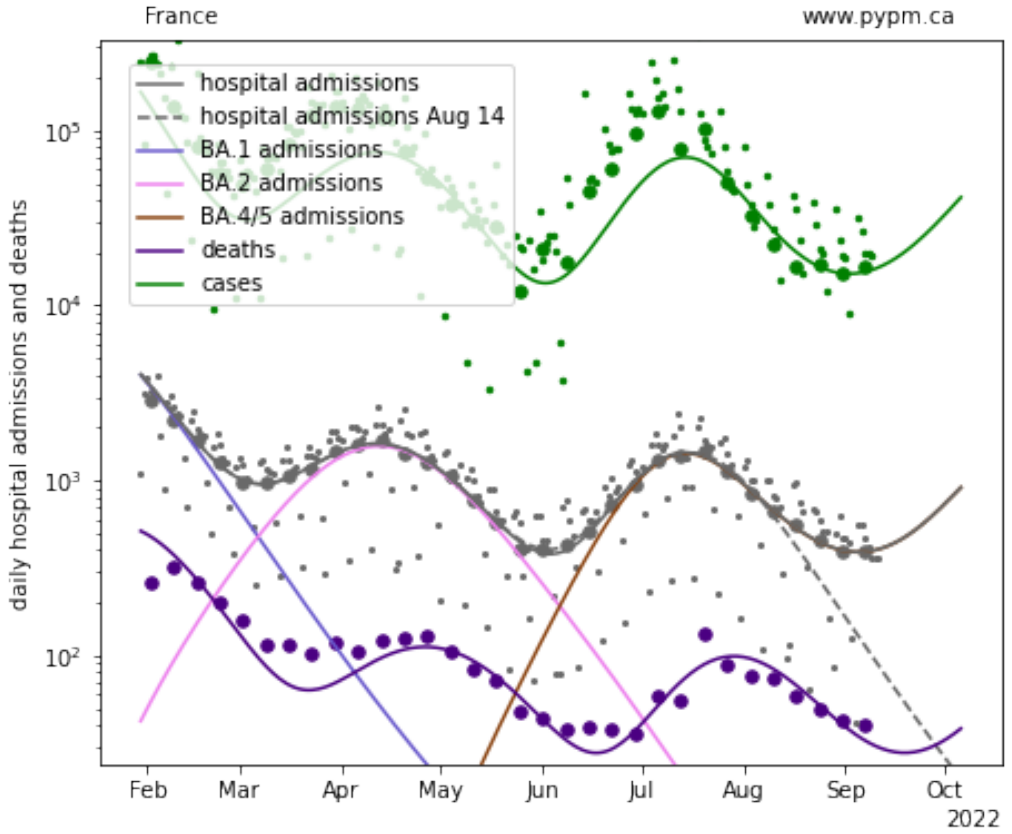
France – September 4



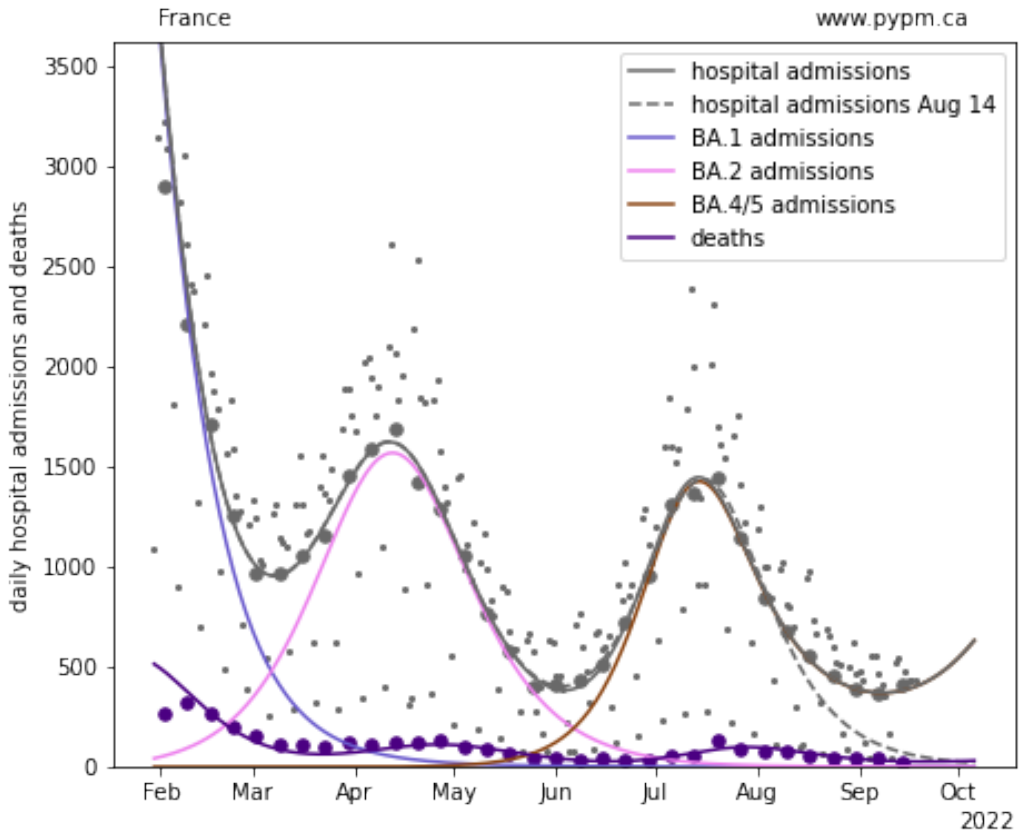


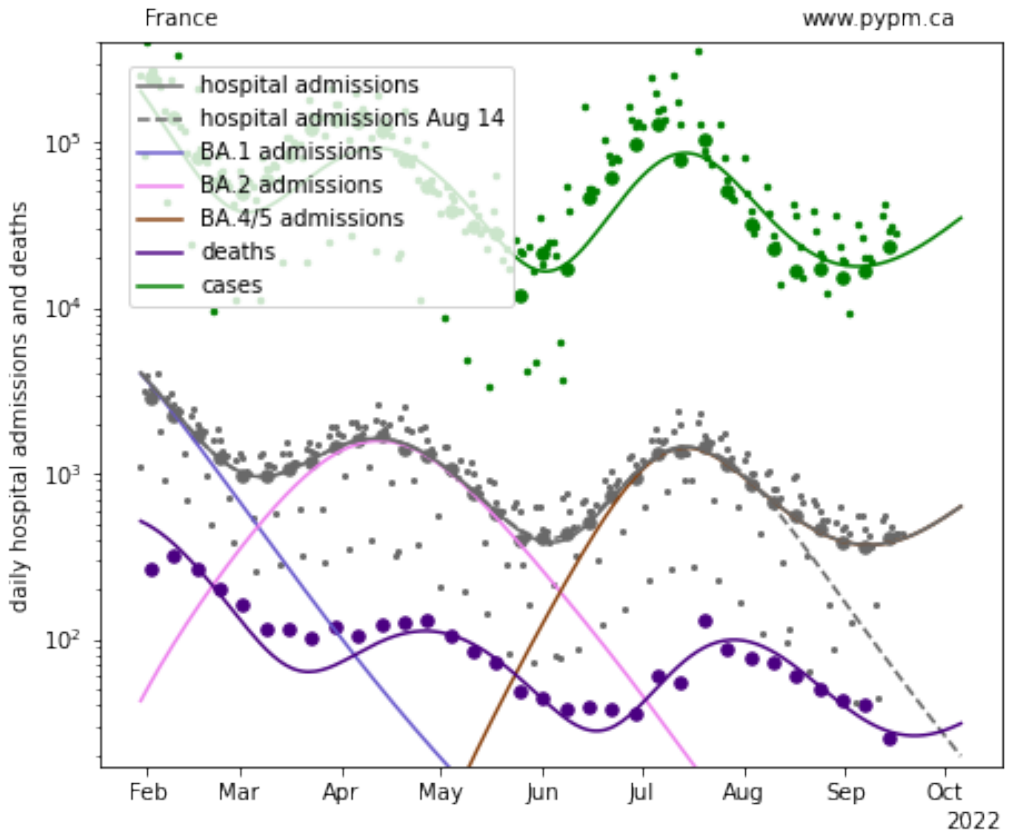
France – September 11





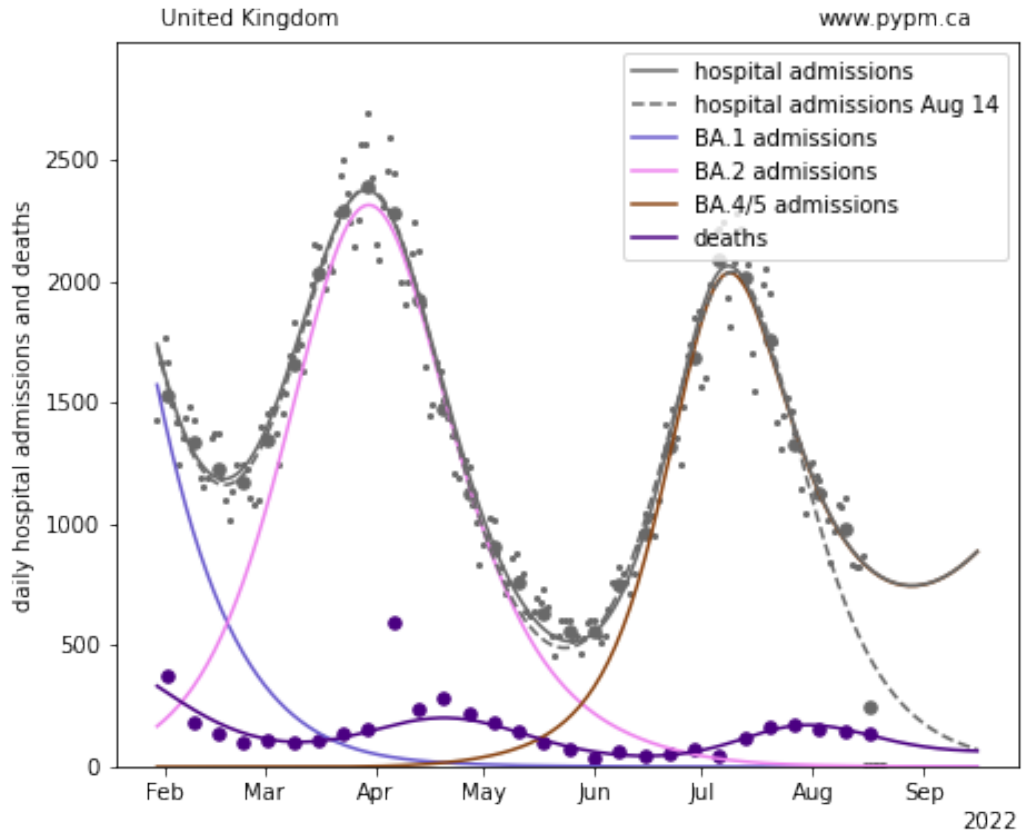
France – September 18

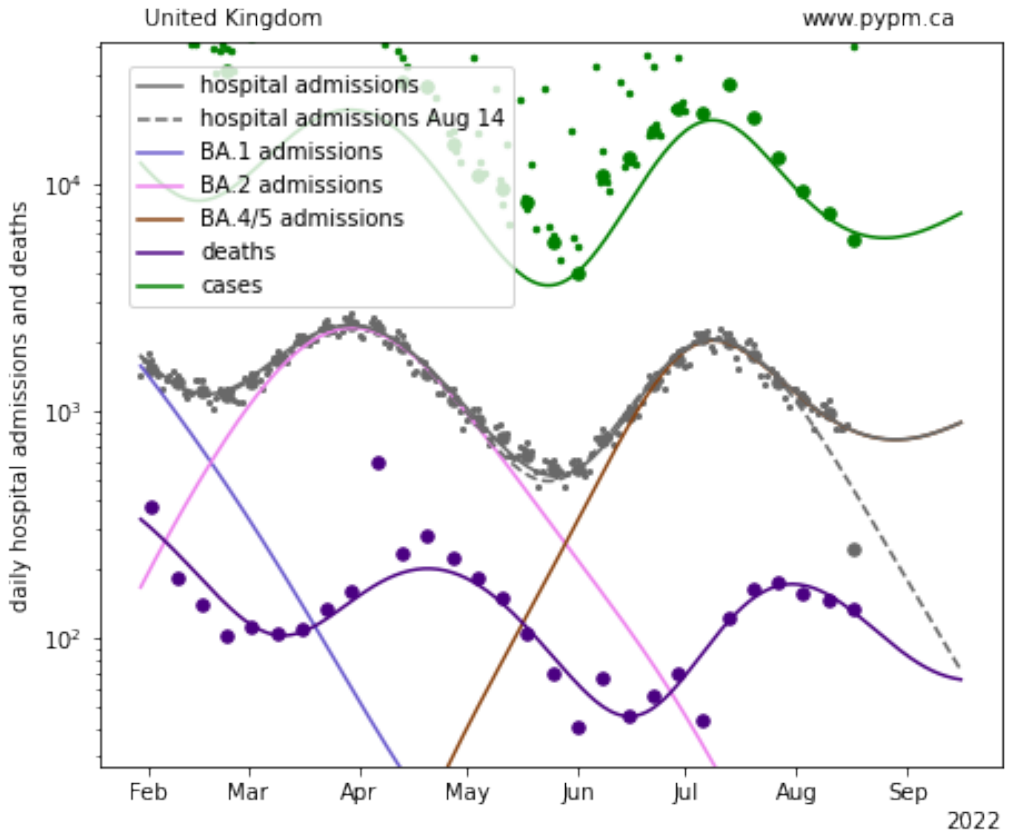




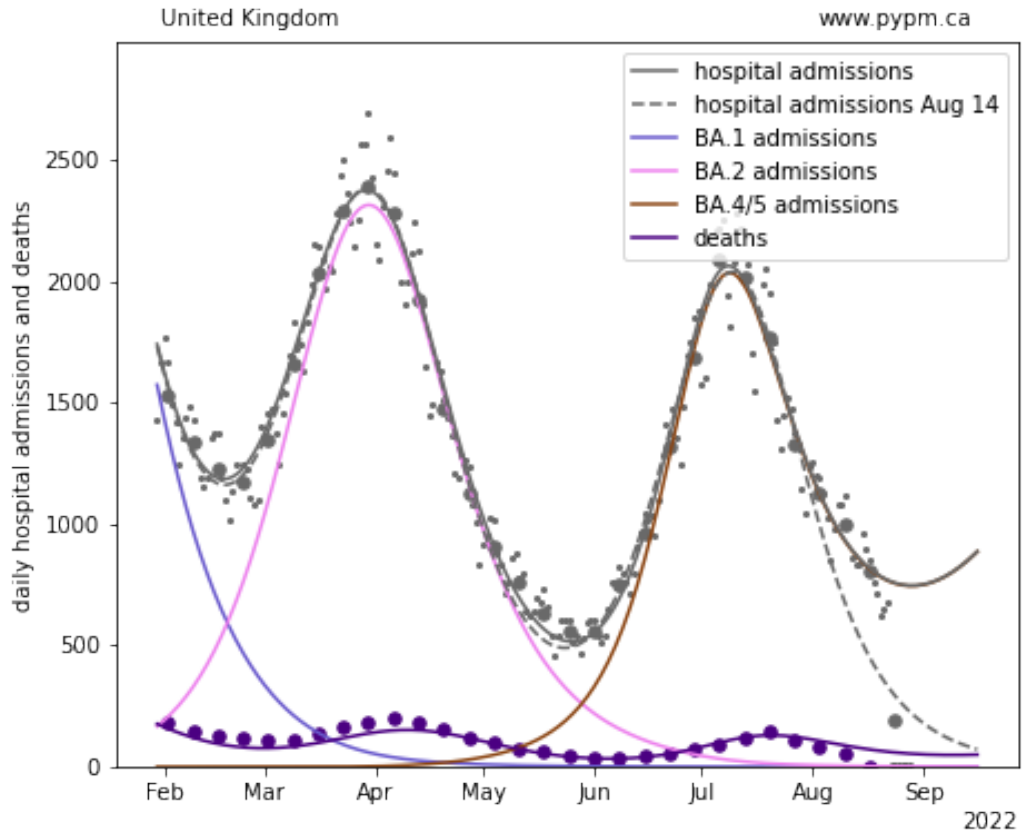
UK

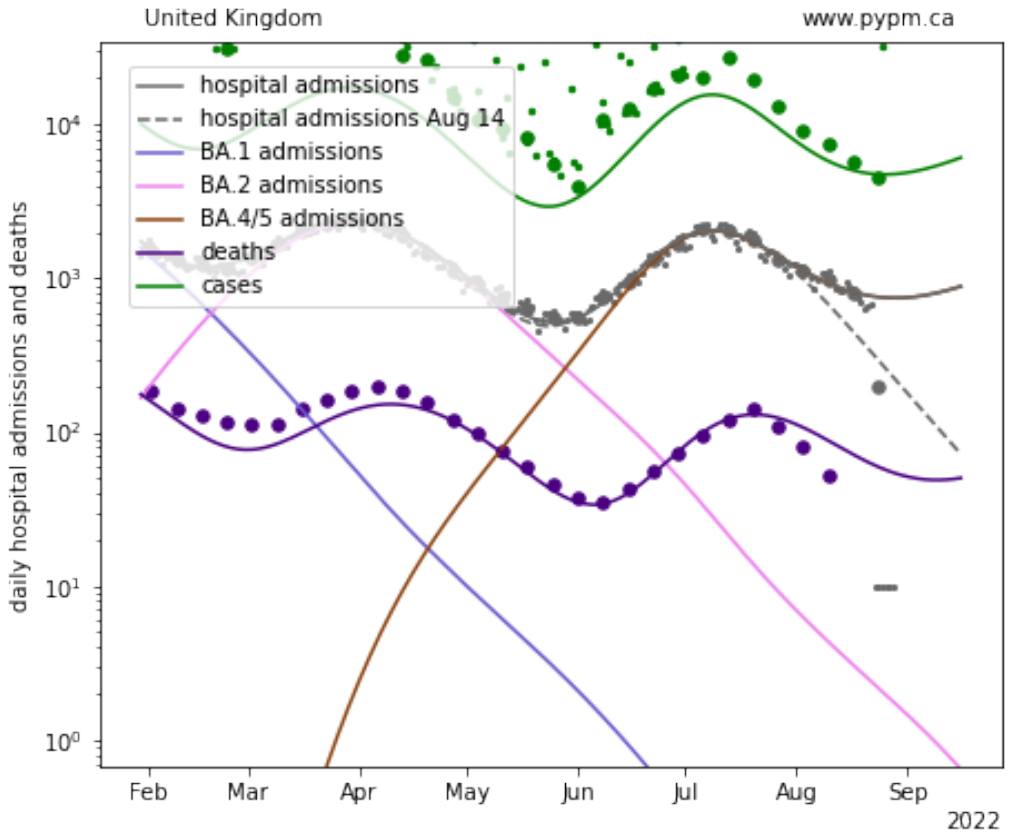
UK – August 21


United Kingdom
www.pypm.ca
hospital admissions
hospital admissions Aug 14
BA.1 admissions
BA.2 admissions
BA.4/5 admissions
deaths
daily hospital admissions and deaths
0
500
1000
1500
2000
2500
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
2022


United Kingdom
www.pypm.ca
hospital admissions
hospital admissions Aug 14
BA.1 admissions
BA.2 admissions
BA.4/5 admissions
deaths
cases
daily hospital admissions and deaths
10^4
10^3
10^2
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
2022

UK – August 28


United Kingdom
www.pypm.ca
hospital admissions
hospital admissions Aug 14
BA.1 admissions
BA.2 admissions
BA.4/5 admissions
deaths
daily hospital admissions and deaths
0
500
1000
1500
2000
2500
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
2022


United Kingdom
www.pypm.ca
hospital admissions
hospital admissions Aug 14
BA.1 admissions
BA.2 admissions
BA.4/5 admissions
deaths
cases
daily hospital admissions and deaths
10^0
10^1
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10^3
10^4
Feb
Mar
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Jul
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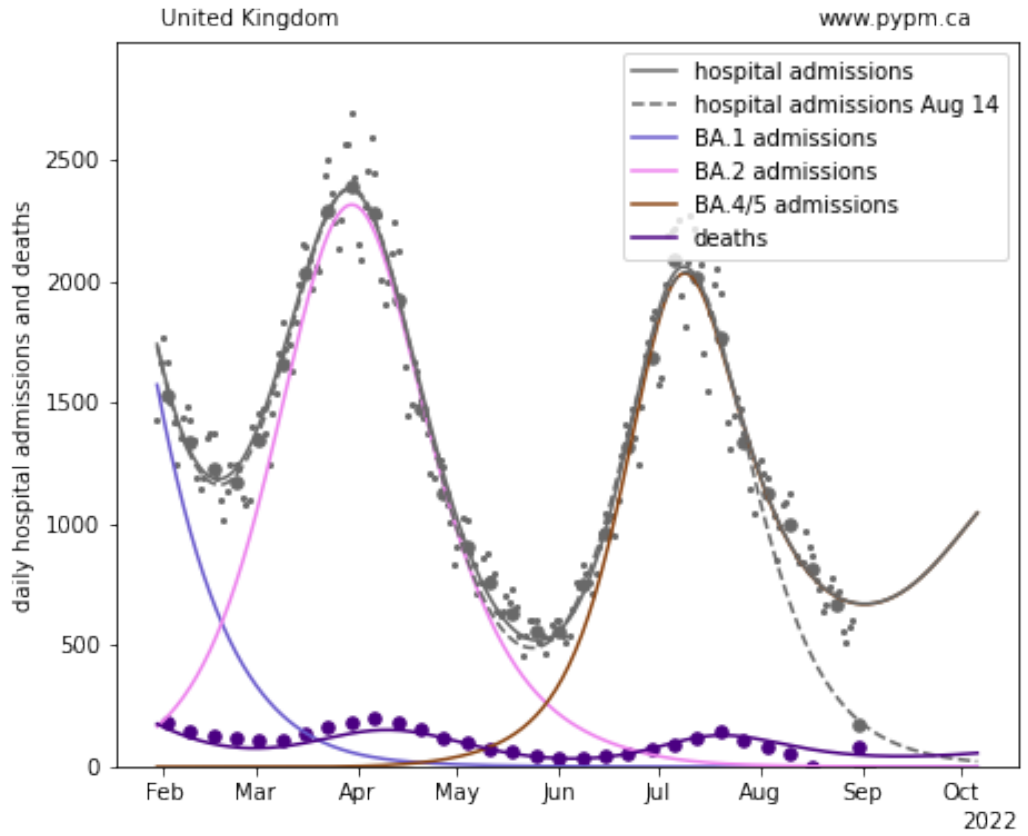
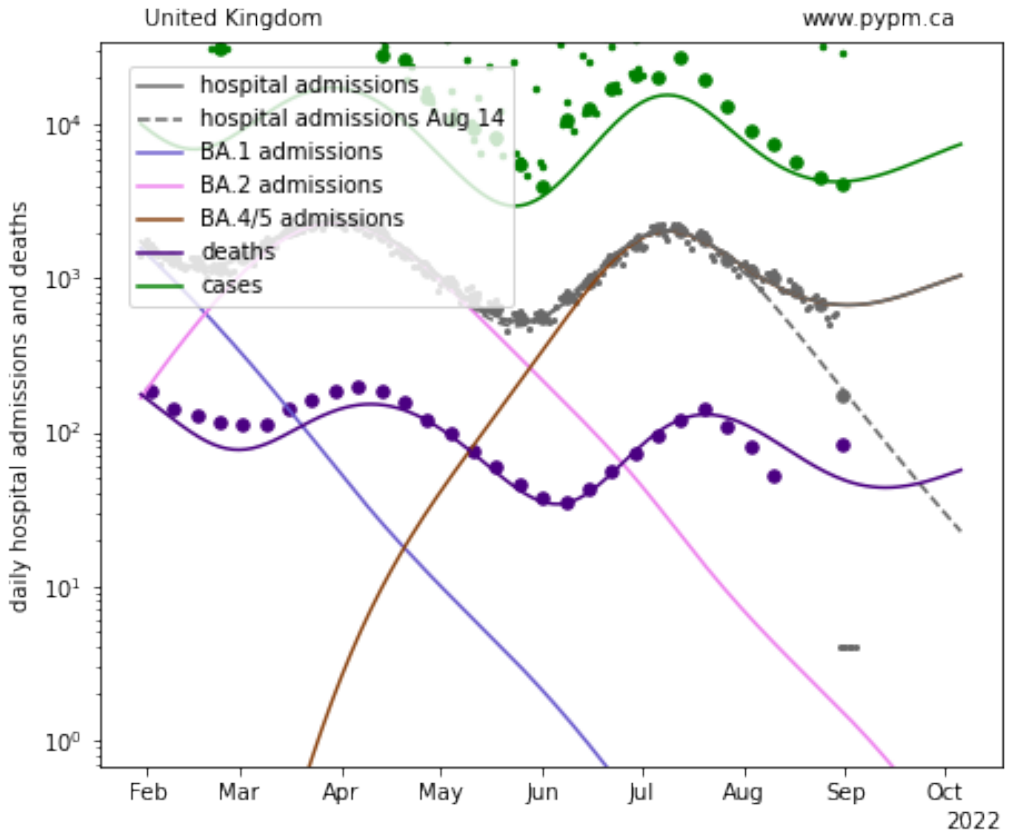
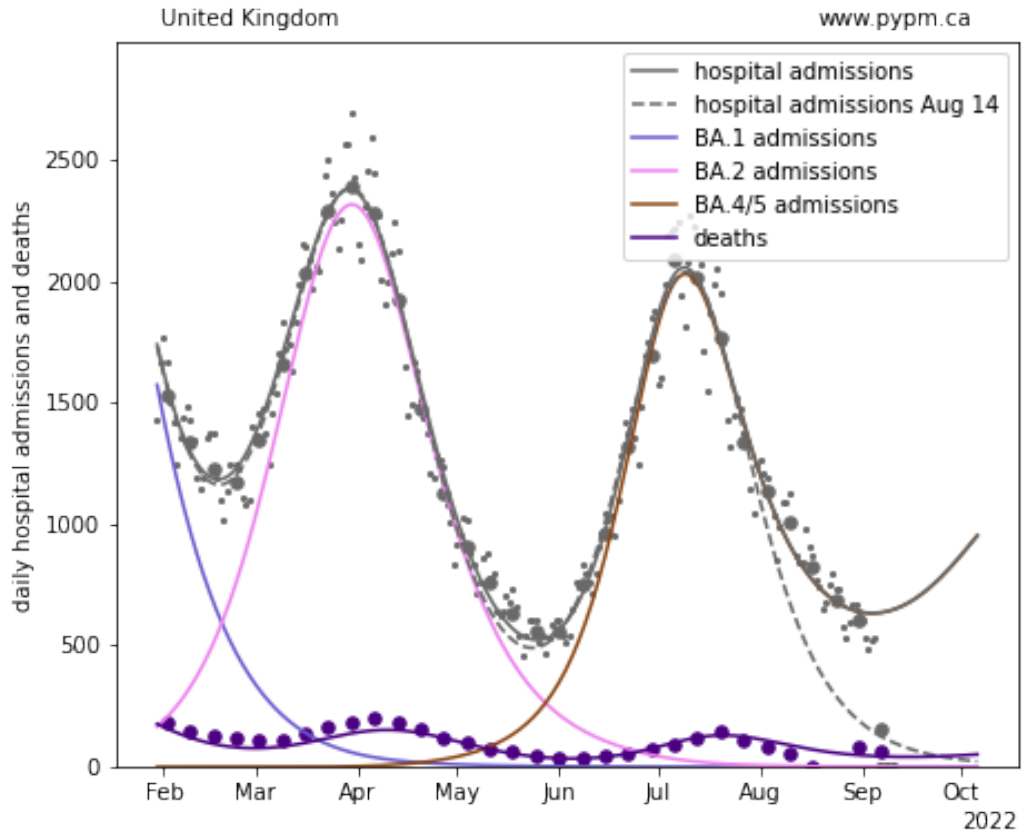
Sep
2022

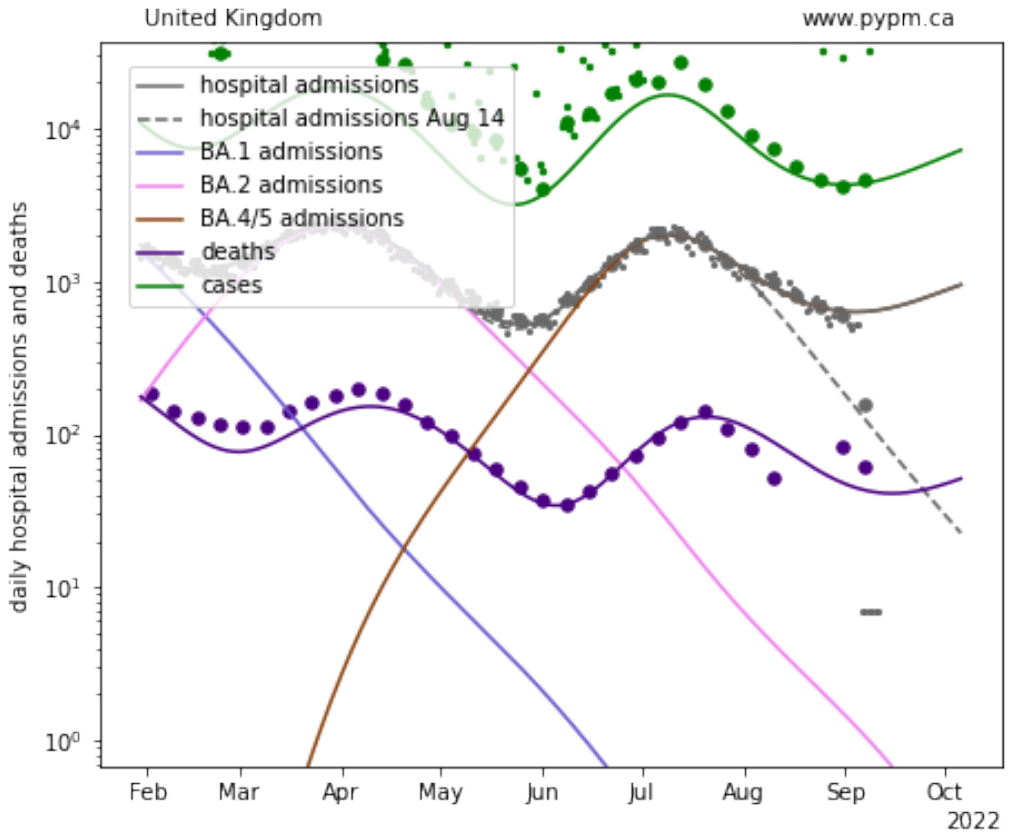
UK – September 4



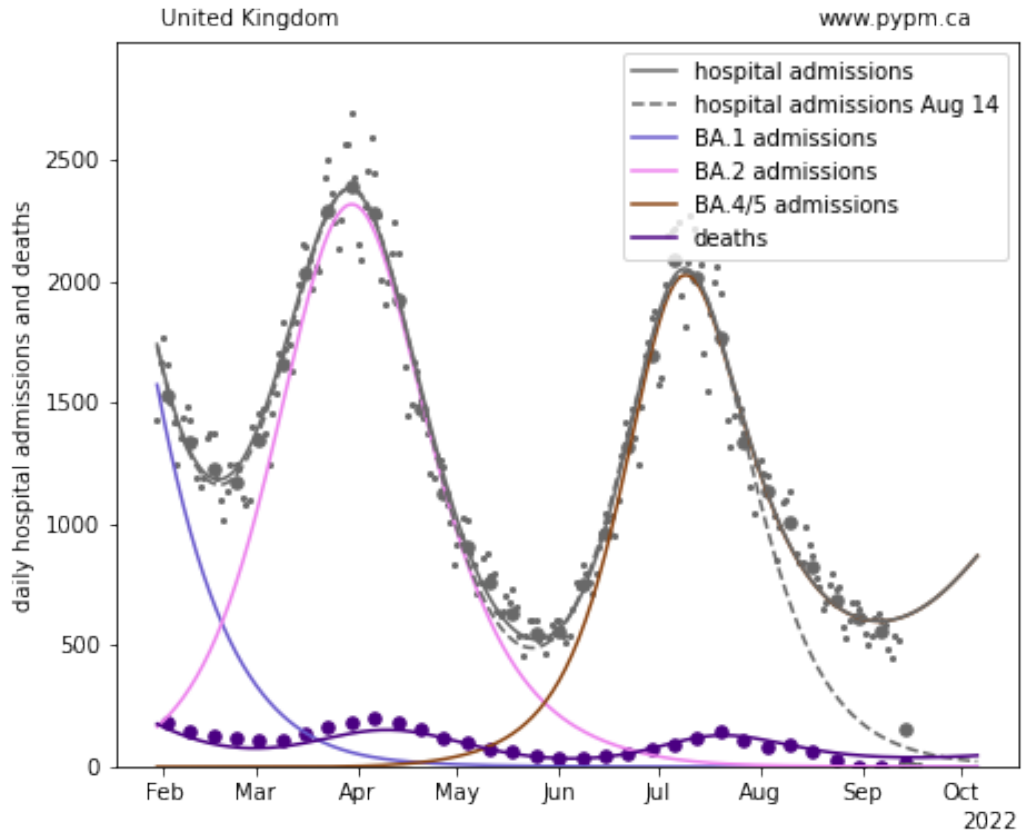


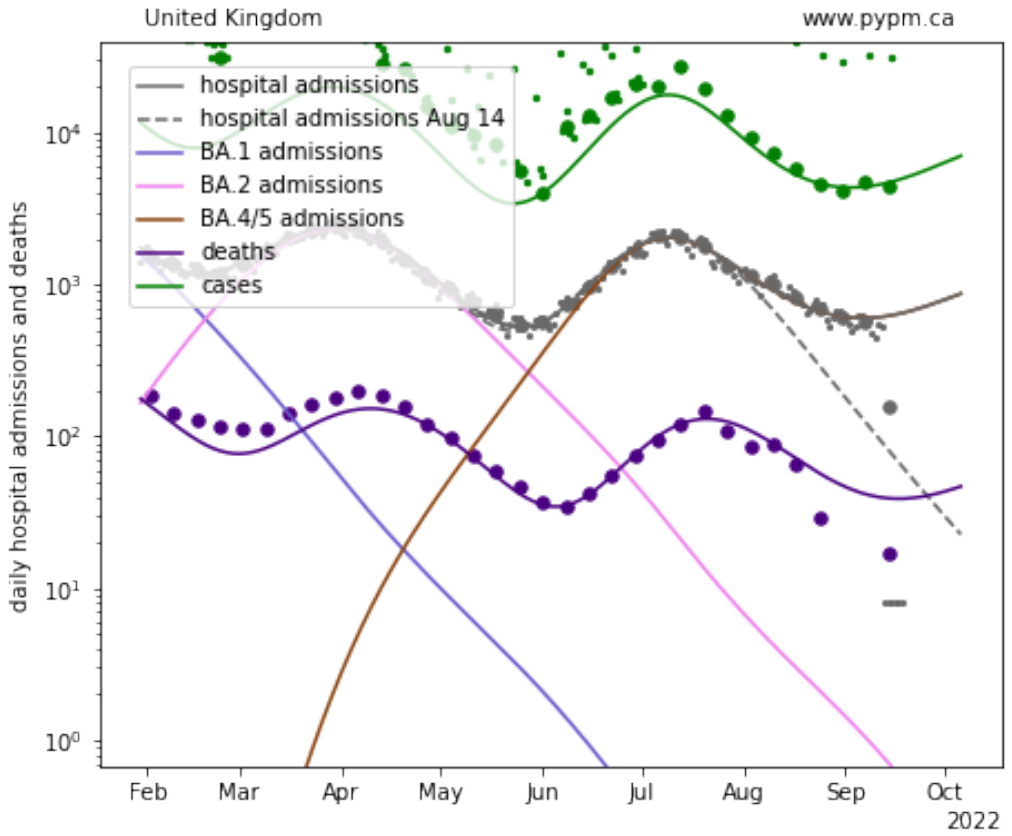
UK – September 11





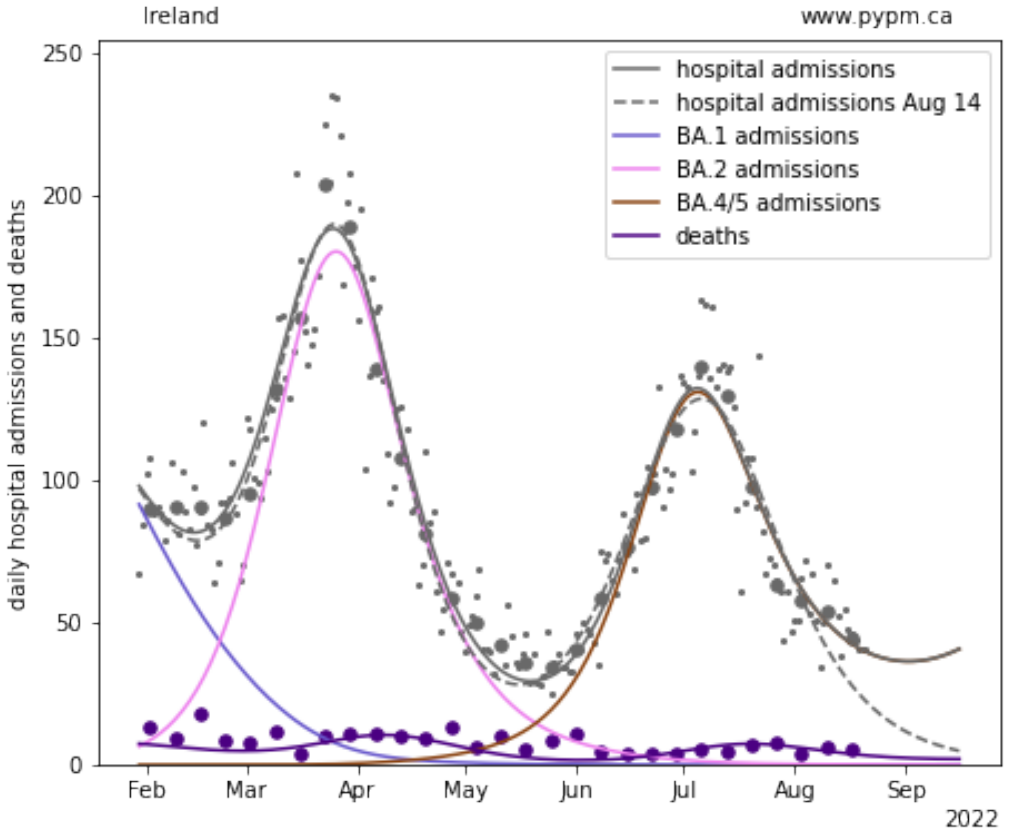
UK – September 18

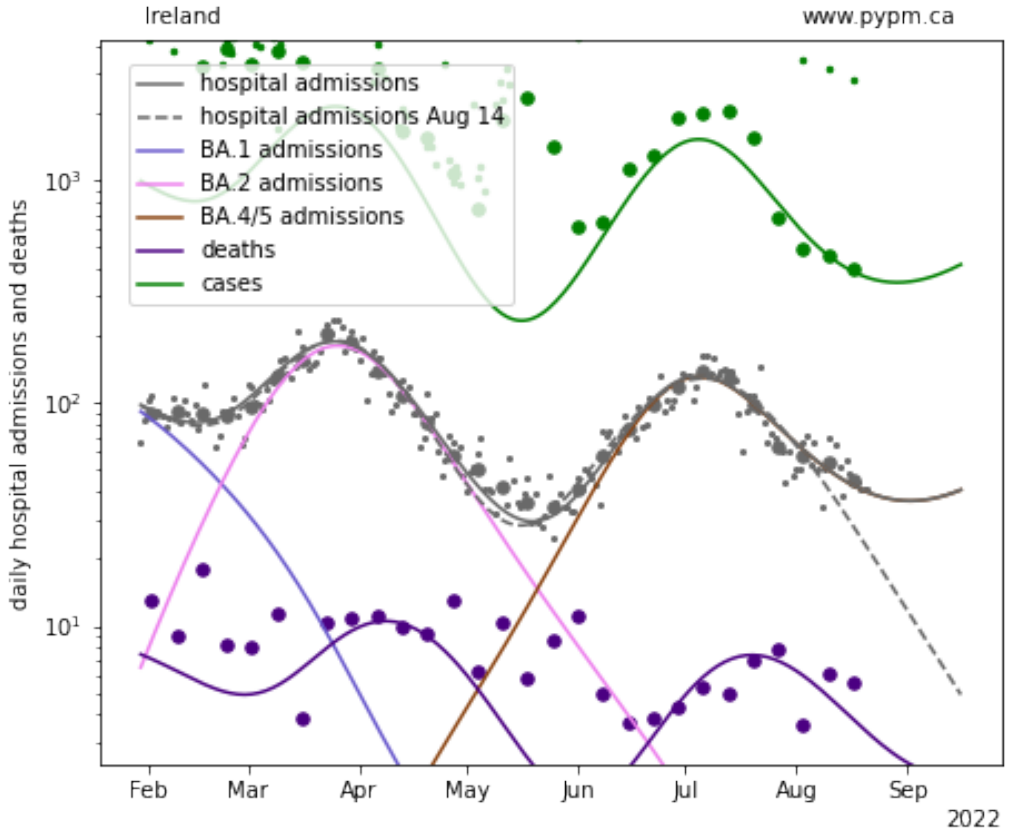




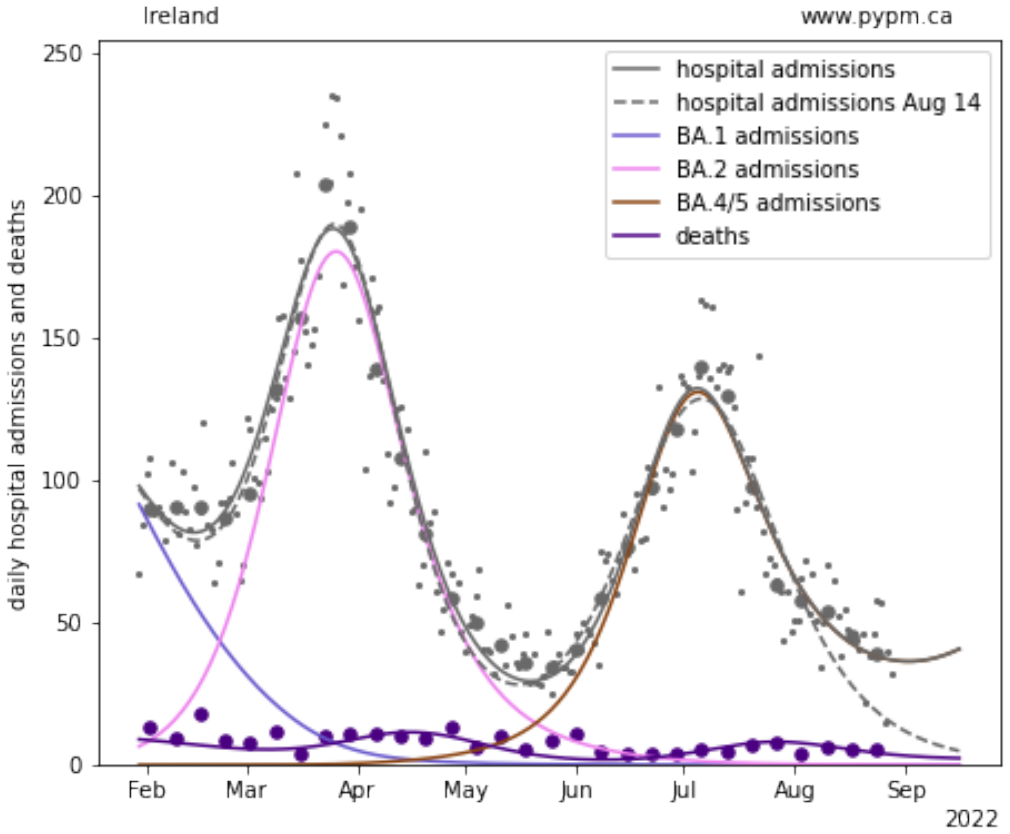
Ireland

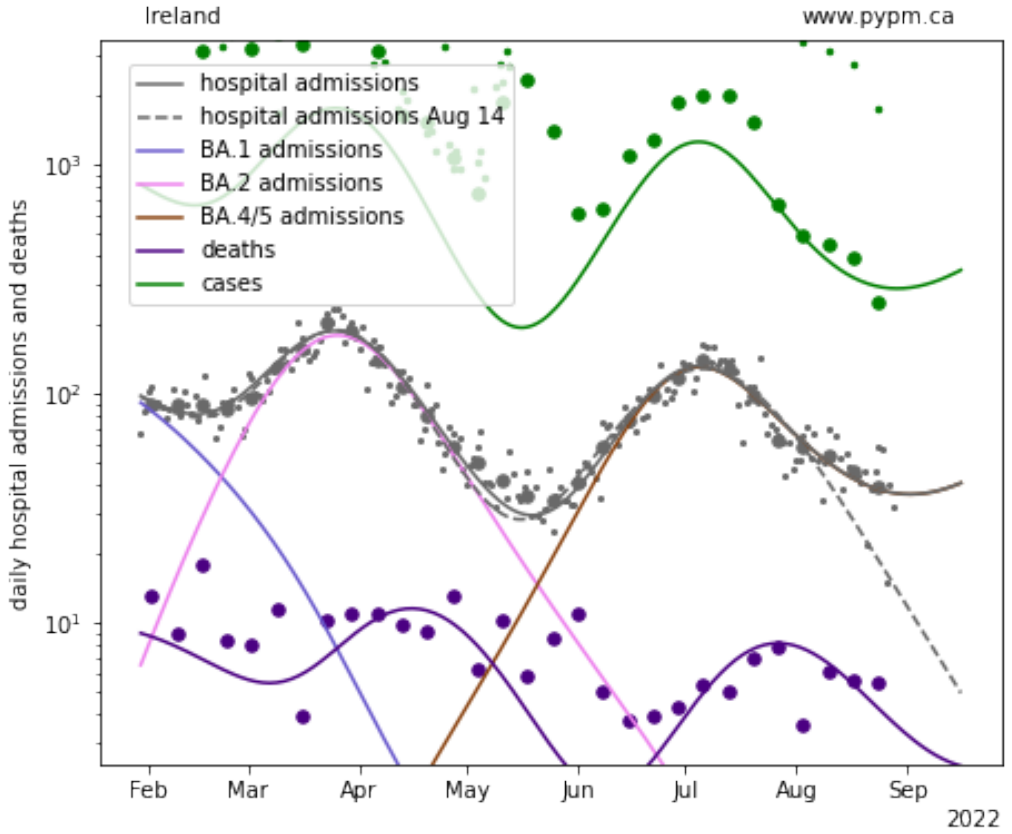
Ireland – August 21



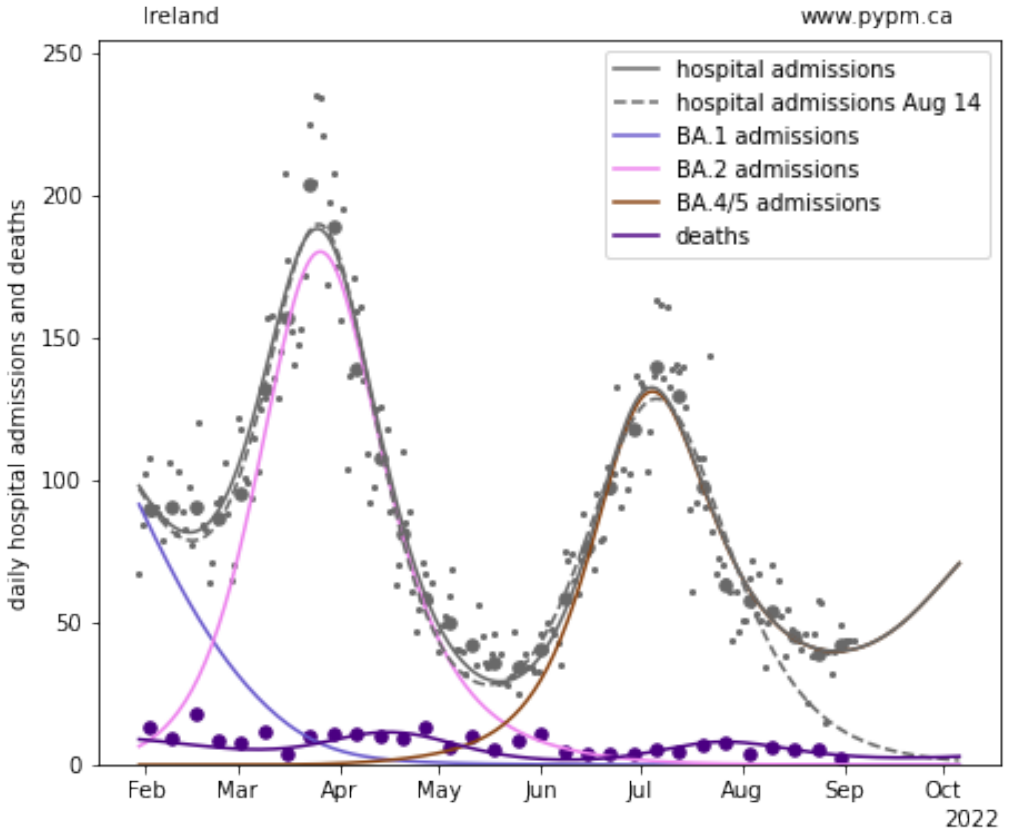


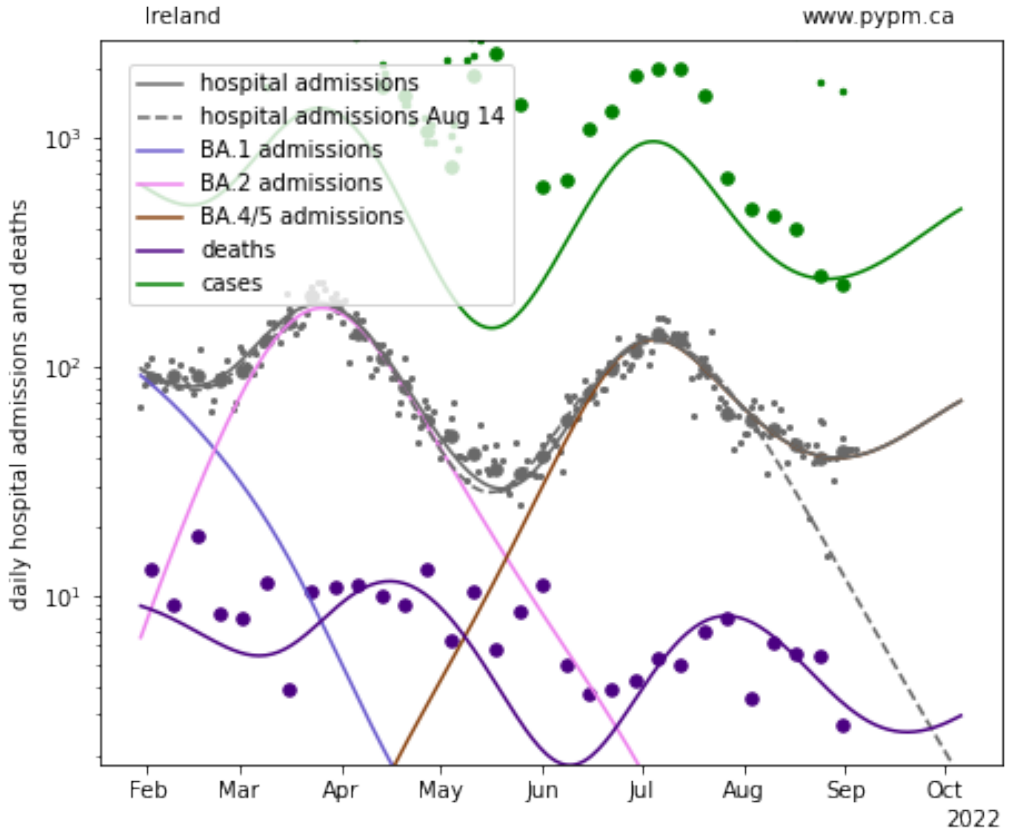
Ireland – August 28



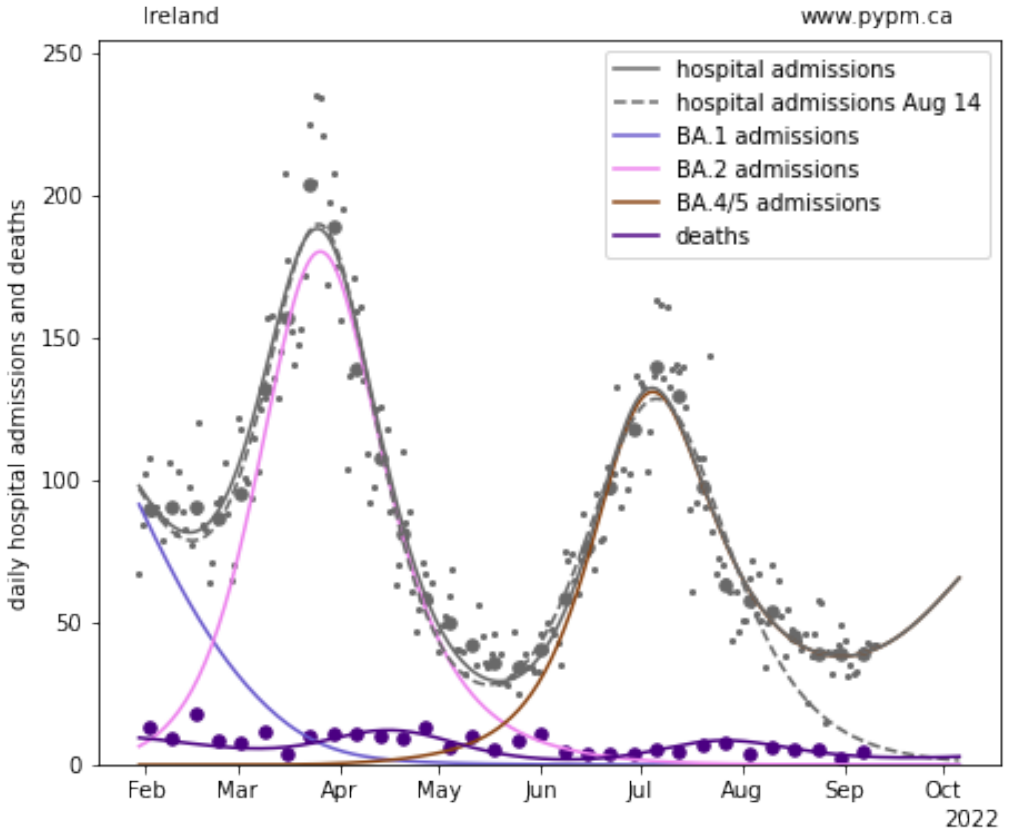


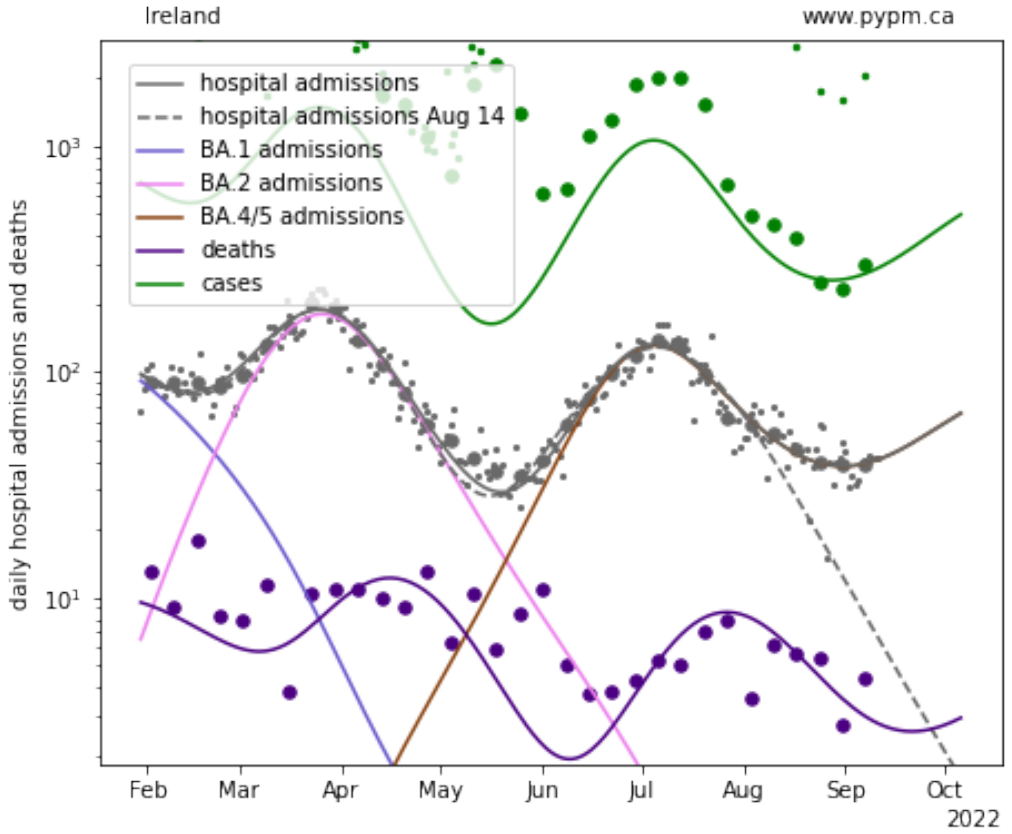
Ireland – September 4



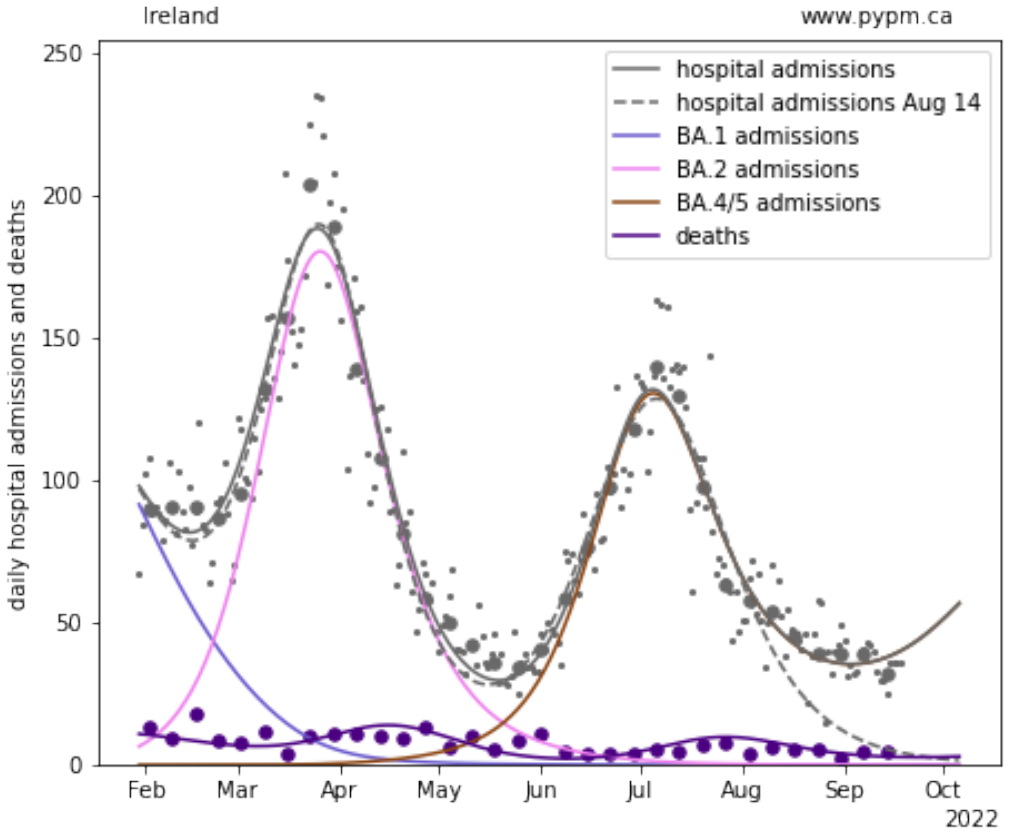


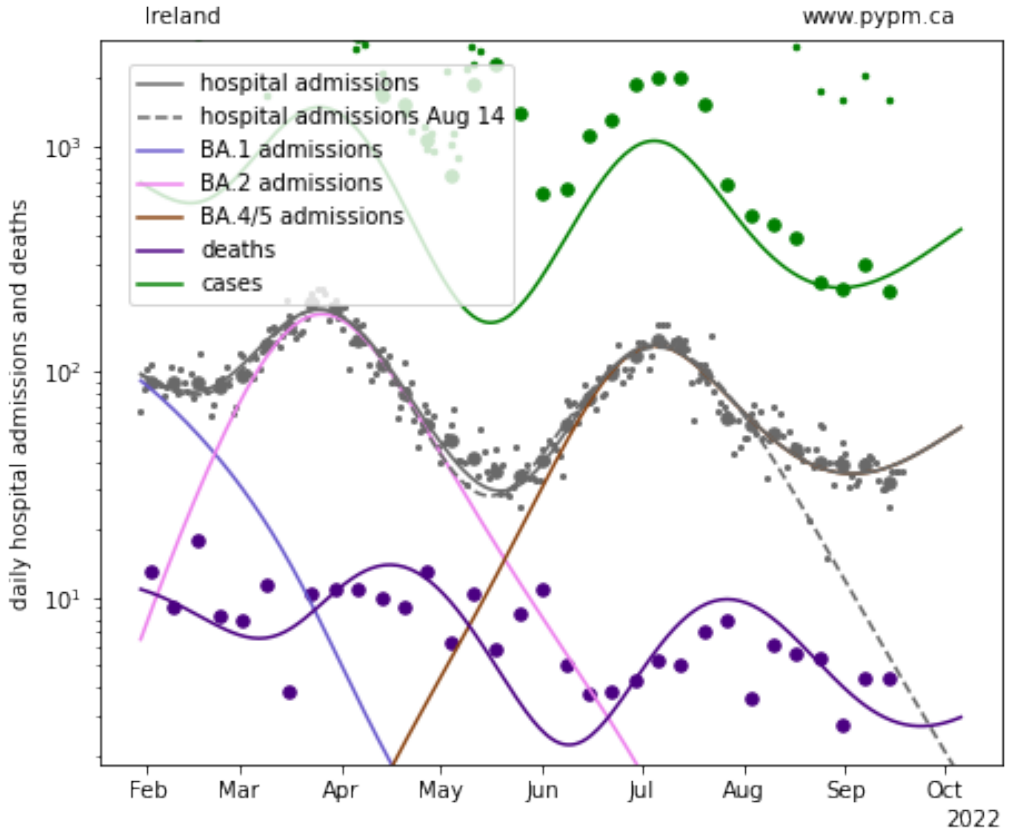
Ireland – September 11





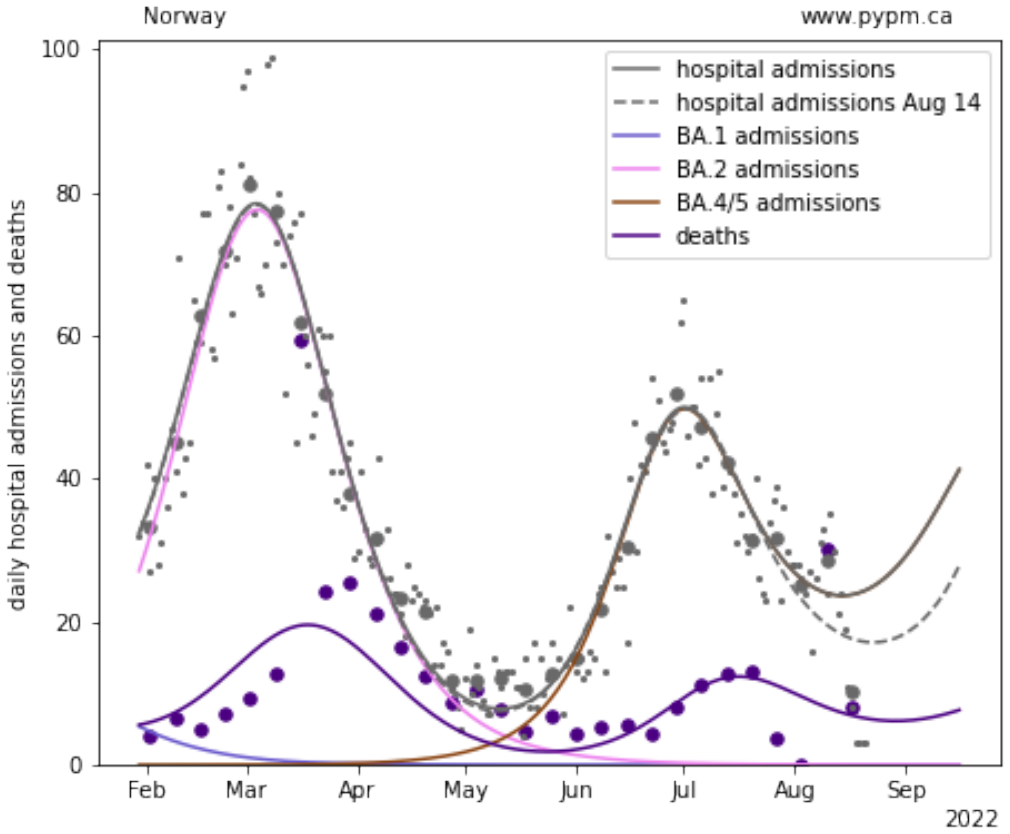
Ireland – September 18

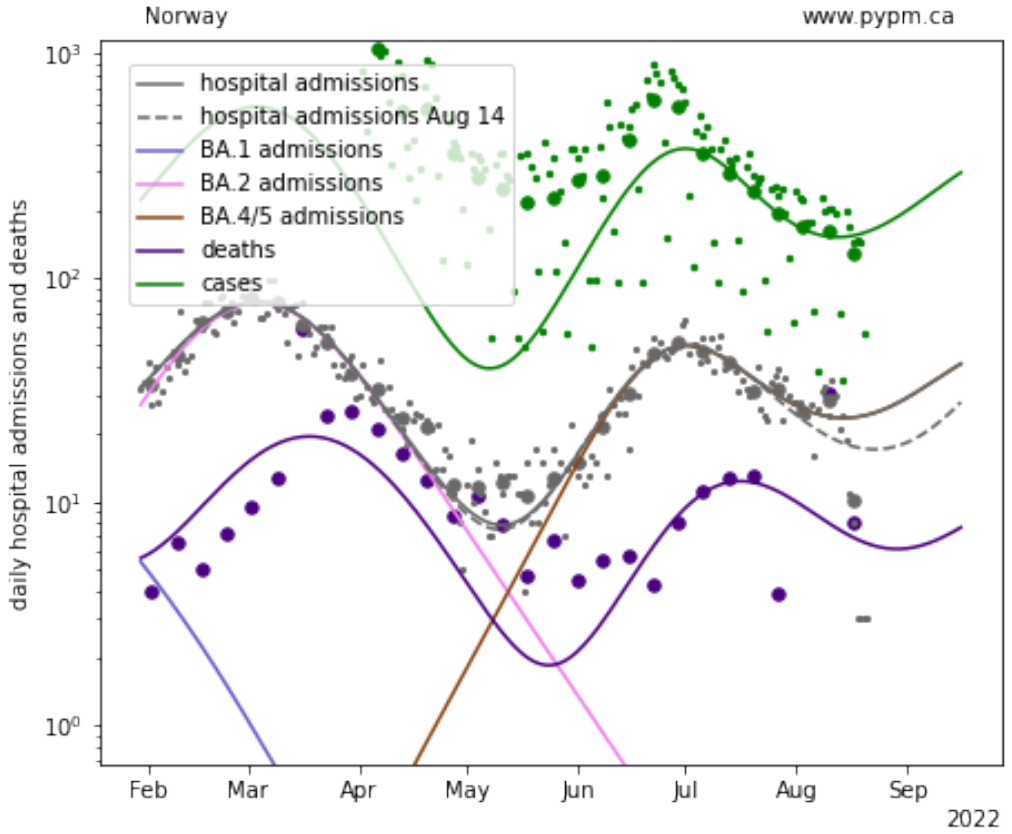




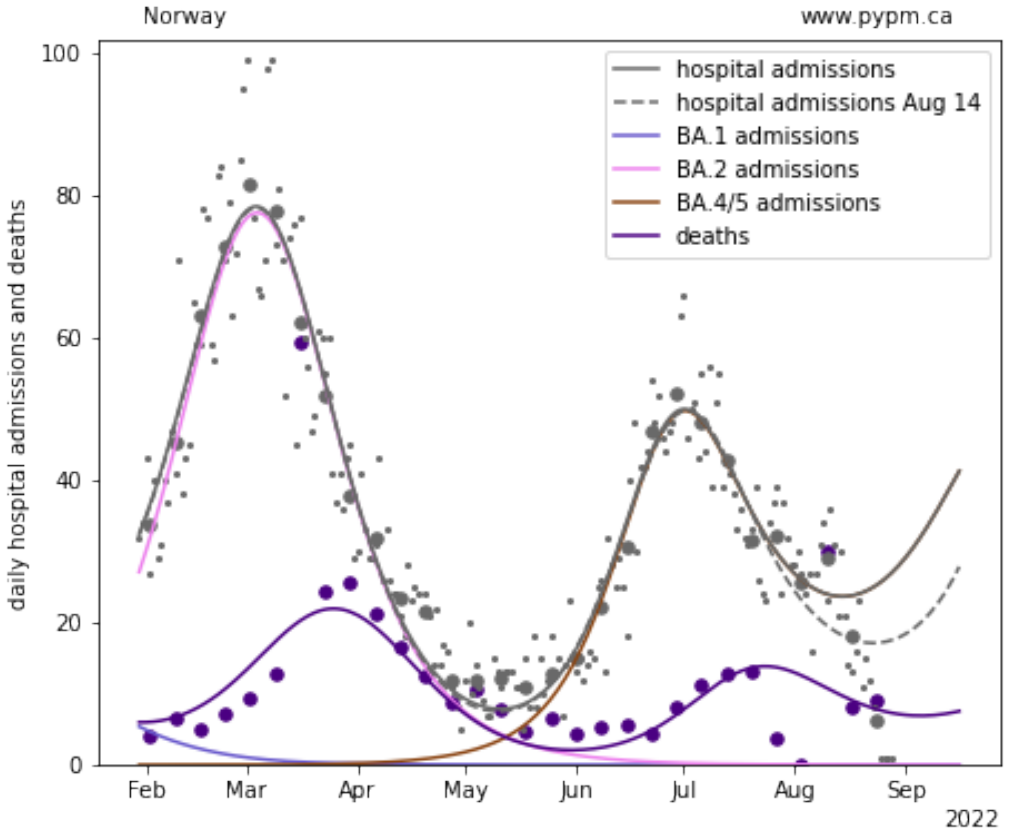
Norway

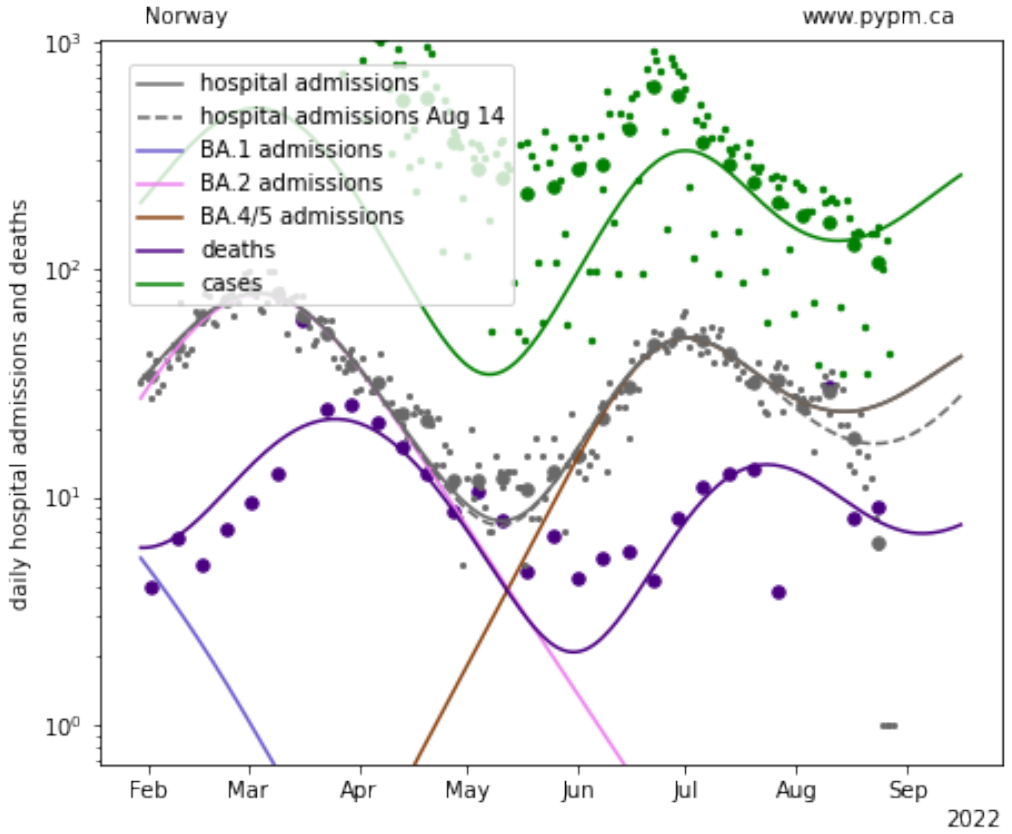
Norway – August 21



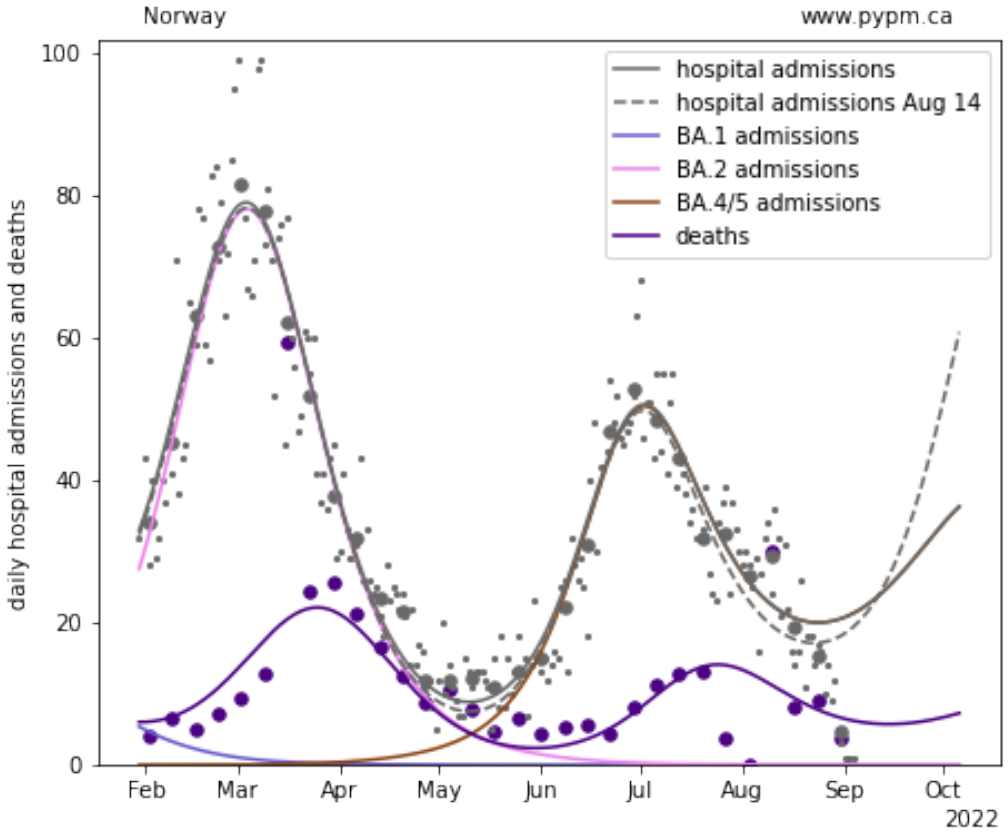


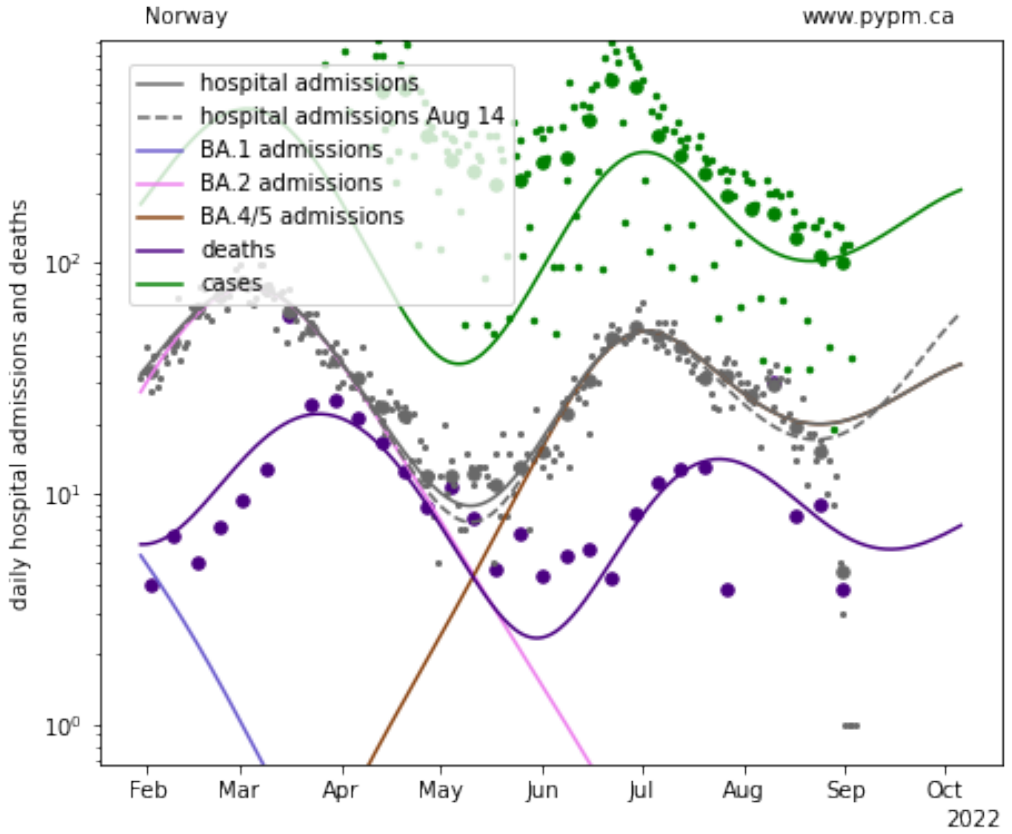
Norway – August 28



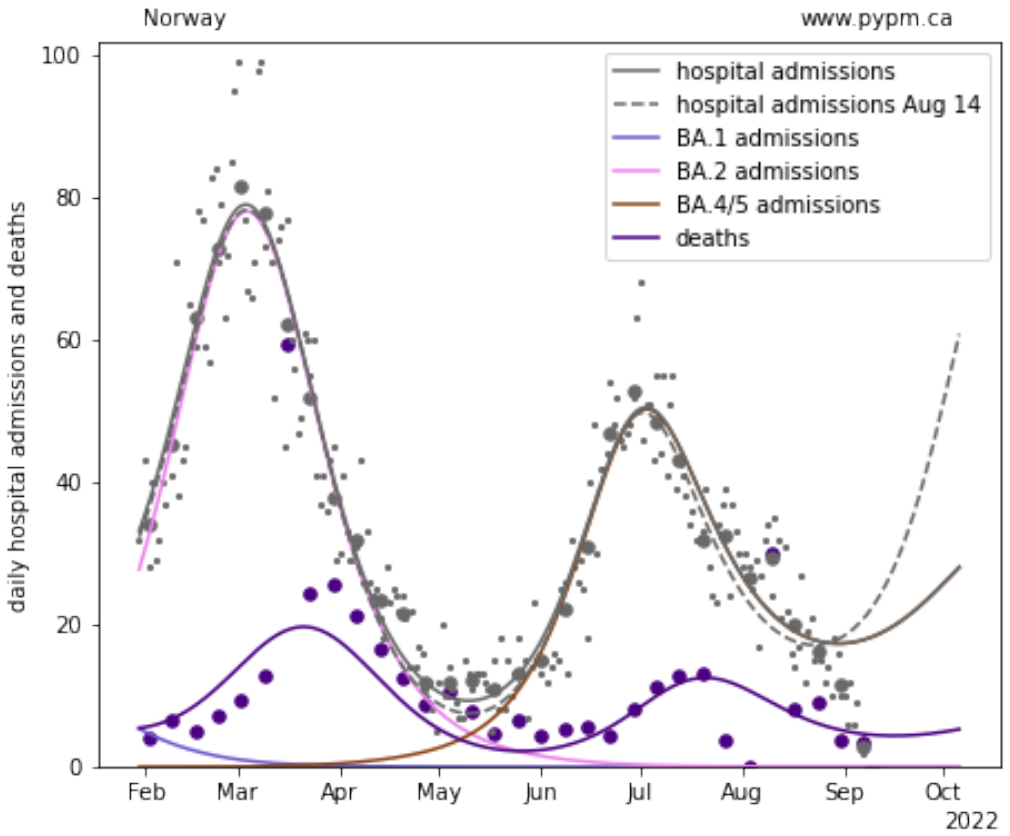


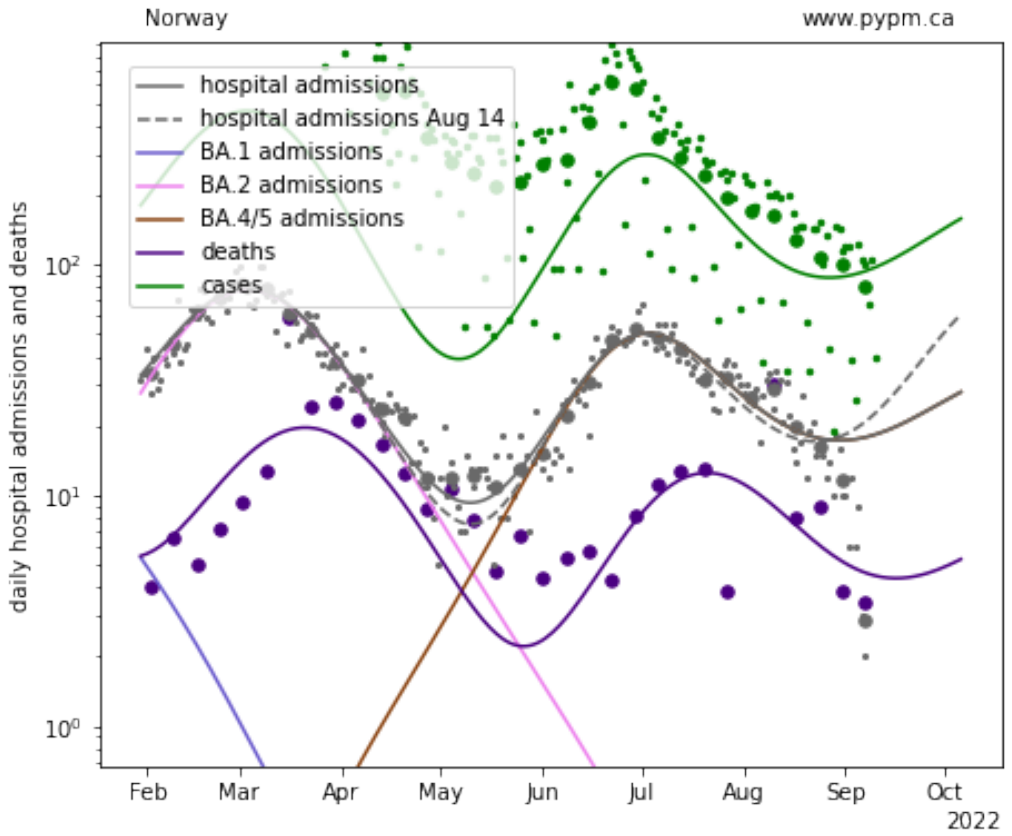
Norway – September 4



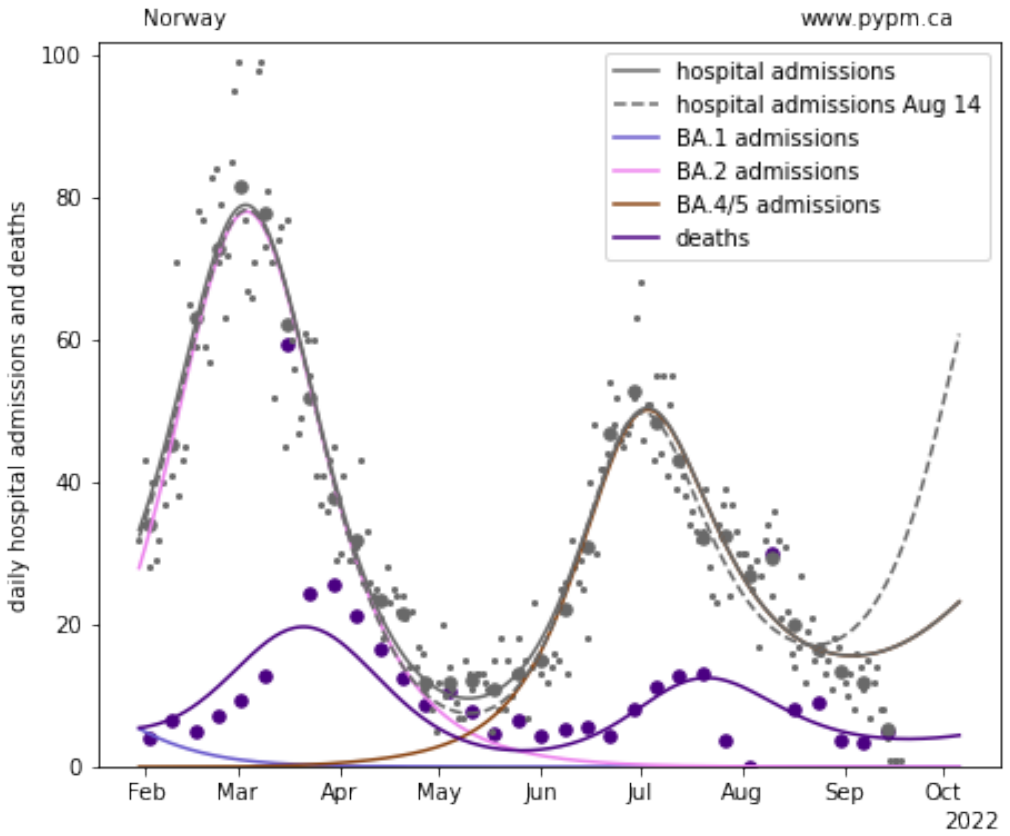


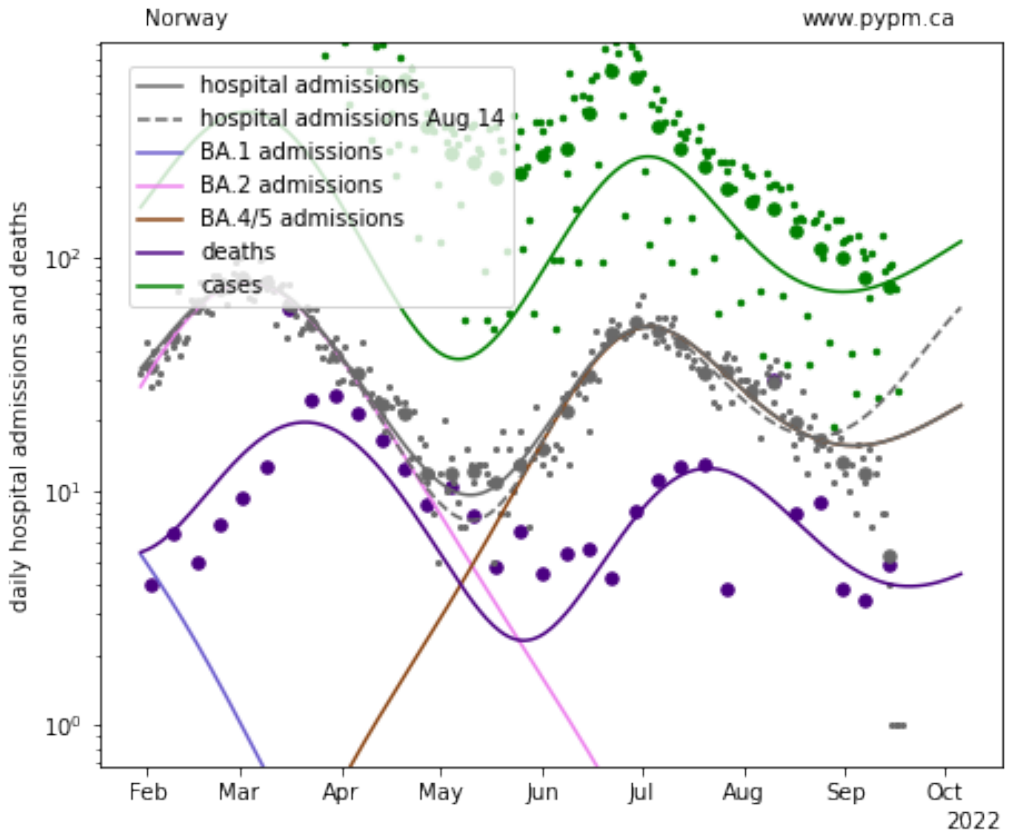
Norway – September 11

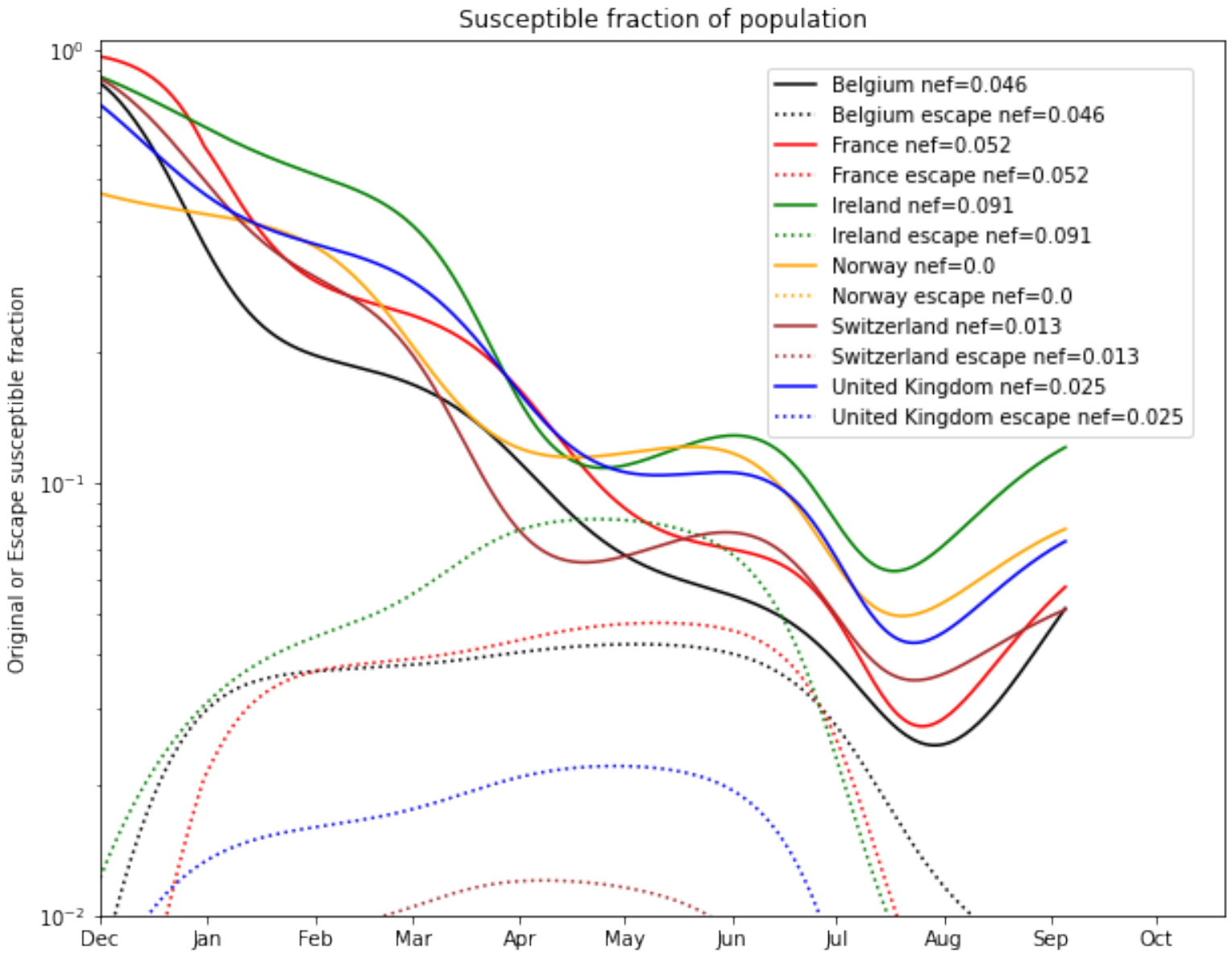




Norway – September 18






Susceptible fraction of population
Original or Escape susceptible fraction
10^{0}
10^{-1}
10^{-2}
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Belgium nef=0.046
Belgium escape nef=0.046
France nef=0.052
France escape nef=0.052
Ireland nef=0.091
Ireland escape nef=0.091
Norway nef=0.0
Norway escape nef=0.0
Switzerland nef=0.013
Switzerland escape nef=0.013
United Kingdom nef=0.025
United Kingdom escape nef=0.025

Waning fit parameters

Country	a_5	escape frac	wane frac	wane delay
Belgium	3.0	0.046	0.7	342.0
France	2.9	0.052	0.306	260.0
Ireland	1.4	0.091	0.602	200.5
Norway	2.2	0.0	0.5	290.9
Switzerland	3.0	0.013	0.24	197.4
United Kingdom	2.3	0.025	0.417	240.9

- a_5: transmission rate for BA.5 variant
- escape frac: fraction of BA.1 and BA.2 infections that BA.4/5 infections escape
- wane frac: fraction of immunity that wanes with time after infection
- wane delay: time required for half of the immunity waning to take place (std dev is fixed at 2 months)

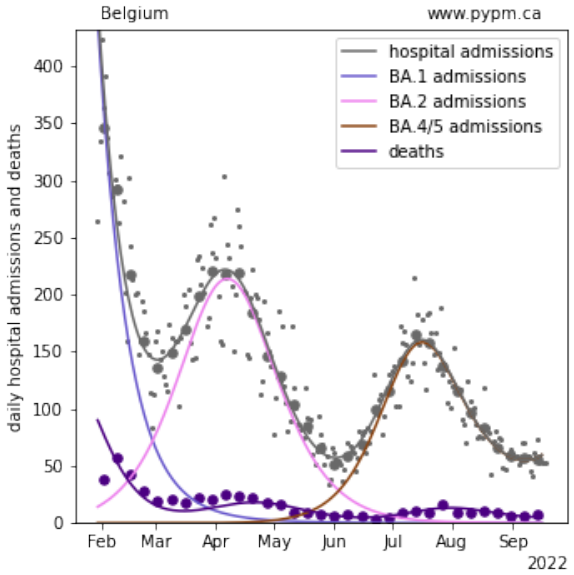
Be thankful that BA.2 emerged when it did!

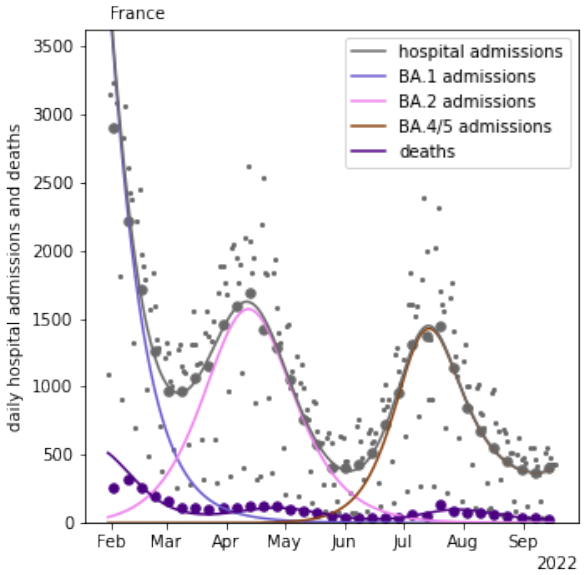
- This study uses the BA.2 wave to calibrate the immunity model:
  - Initial population-level immunity
  - rate at which the immunity grew in the population

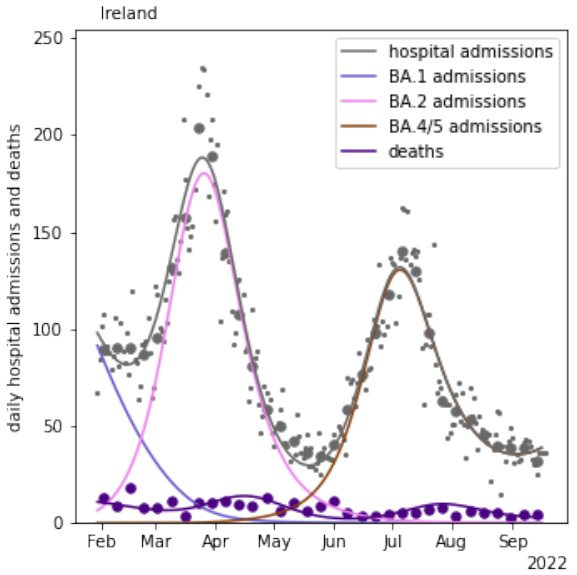
- Using this model, we can consider the situation without BA.2
  - Turn off the BA.2 outbreak in the model
  - In other words, suppose the mutation that produced the original BA.2 did not happen, but the mutation that produced BA.5 did happen

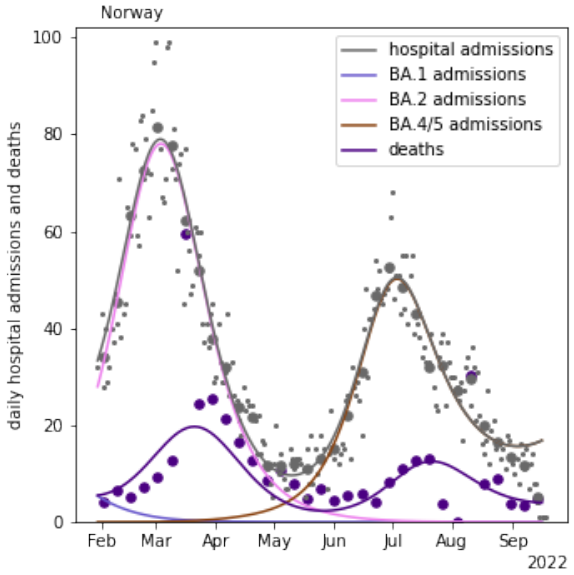
- Having an intermediate-strength variant between BA.1 and BA.5 helped significantly reduce peak hospital demand…

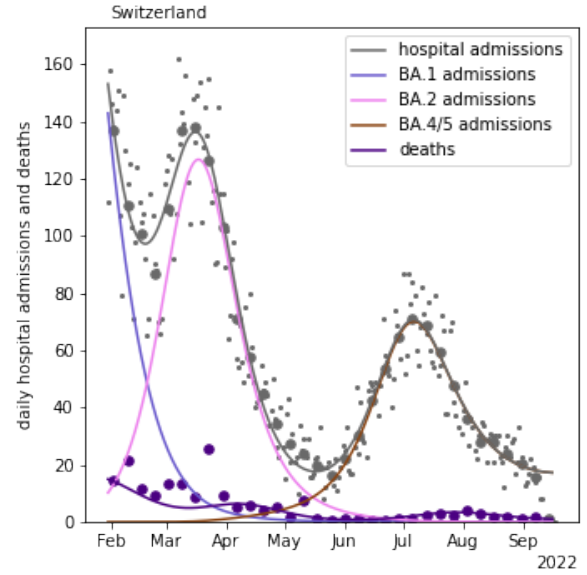
Models with BA.2

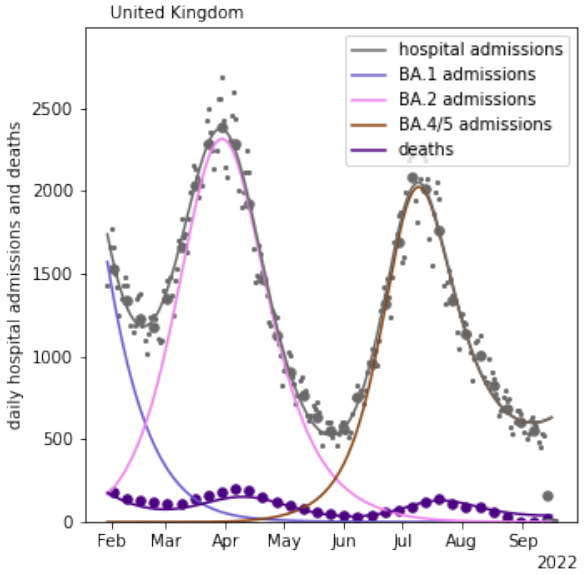




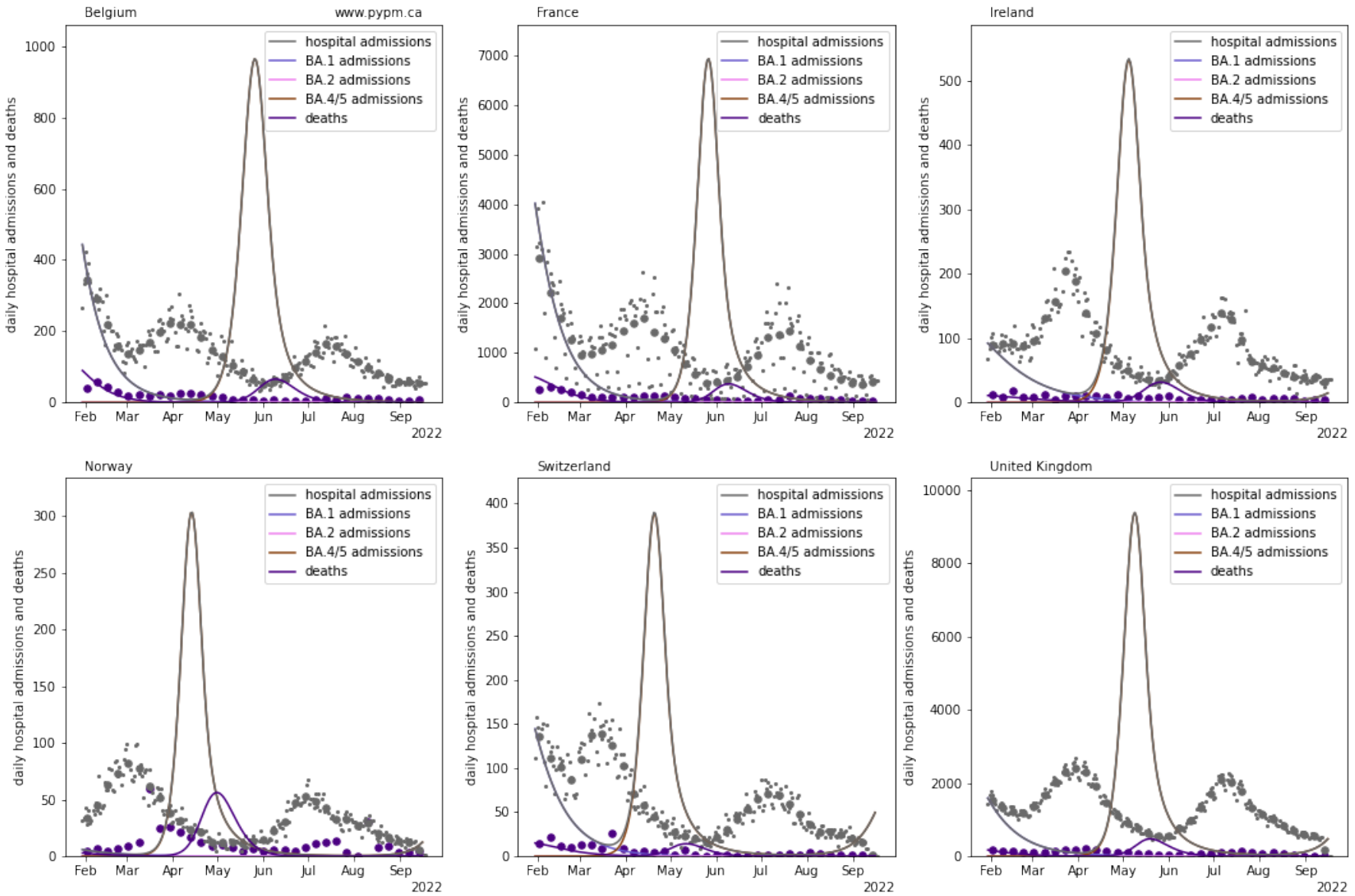








Models without BA.2



Timing of peaks very sensitive to details of BA.5 emergence

Summary

- A homogeneous model can reproduce the 2022 hospital admission time series with relatively few parameters
  - The model waves result from new variants and dynamic immunity
- Critical immunity parameters can be estimated by the shape of a wave (BA.2 used in this analysis)
- Models only fit BA.4/5 wave if they include immunity escape/waning
- The plateauing of hospital admissions is consistent with predictions from models that incorporate waning
  - Evidence is building for immunity waning in these data
  - Estimating the magnitude of the next waves (due to waning) is highly uncertain at this point. Several more weeks of data are needed.