KN-20 regular meeting note at July 13th 2021

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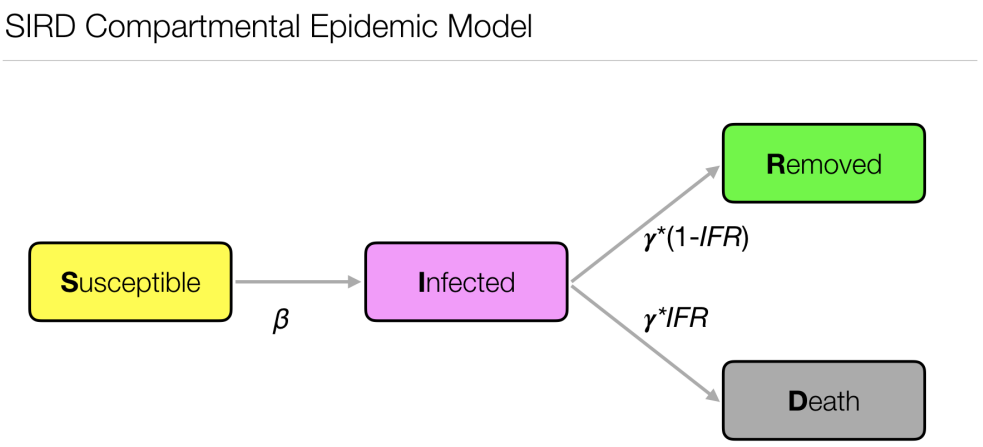
On the principally unbreakable link in between the incidence and daily bad outcomes

Abstract

Preventing bad outcomes - here modelled as deaths, but it can be also used for daily hospital admissions, etc. - is mathematically described using an efficacy measure. Usually, a vaccine efficacy is meant, but other interventions can be modelled this way, as well. Anyway, unless it was 100 %, this efficacy is not about *breaking the link*, i.e. the flow in between two compartments. Instead, it moderates the former transfer parameters. The link itself, however, stays there. This has several important implications. To see them, simple qualitative experiments are included bellow. They show the role played by the IFR (Infection Fatality Ratio) in itself, as it helps to understand what can and cannot be achieved by a simple multiplicative modification of this parameter. Please note, the aim here is for progress in understanding, not perfection.

SIRD model definition



In[496]:=
```
Clear["Global`*"]
equationS[β_, γ_, IFR_] =
 s'[t] == -β * s[t] * i[t]
equationI[β_, γ_, IFR_] =
 i'[t] == β * s[t] * i[t] - γ * i[t]
equationR[β_, γ_, IFR_] =
 r'[t] == γ * (1 - IFR) * i[t]
equationD[β_, γ_, IFR_] =
 d'[t] == γ * IFR * i[t]
```

Out[497]= $s'[t] == -\beta\, i[t] \times s[t]$

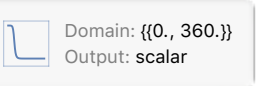
Out[498]= $i'[t] == -\gamma\, i[t] + \beta\, i[t] \times s[t]$

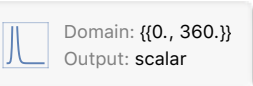
Out[499]= $r'[t] == (1 - IFR)\, \gamma\, i[t]$

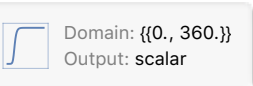
Out[500]= $d'[t] == IFR\, \gamma\, i[t]$

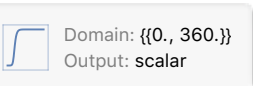
SIRD model solving for example transfer parameters

In[543]:=
```
With[{β = 27/100, γ = 1/10, IFR = 5/100, i0 = 200/10 000 000},
 solution = NDSolve[{equationS[β, γ, IFR], equationI[β, γ, IFR],
    equationR[β, γ, IFR], equationD[β, γ, IFR], s[0] == 1 - i0,
    i[0] == i0, r[0] == 0, d[0] == 0}, {s, i, r, d}, {t, 360}];
 solutionS = First[s /. solution];
 solutionI = First[i /. solution];
 solutionR = First[r /. solution];
 solutionD = First[d /. solution];
 incidence[t_] := β * solutionS[t] * solutionI[t];
 ddead[t_] := γ * IFR * solutionI[t];
 Print[{solutionS, solutionI, solutionR, solutionD}]
]
```

{InterpolatingFunction[],

InterpolatingFunction[],

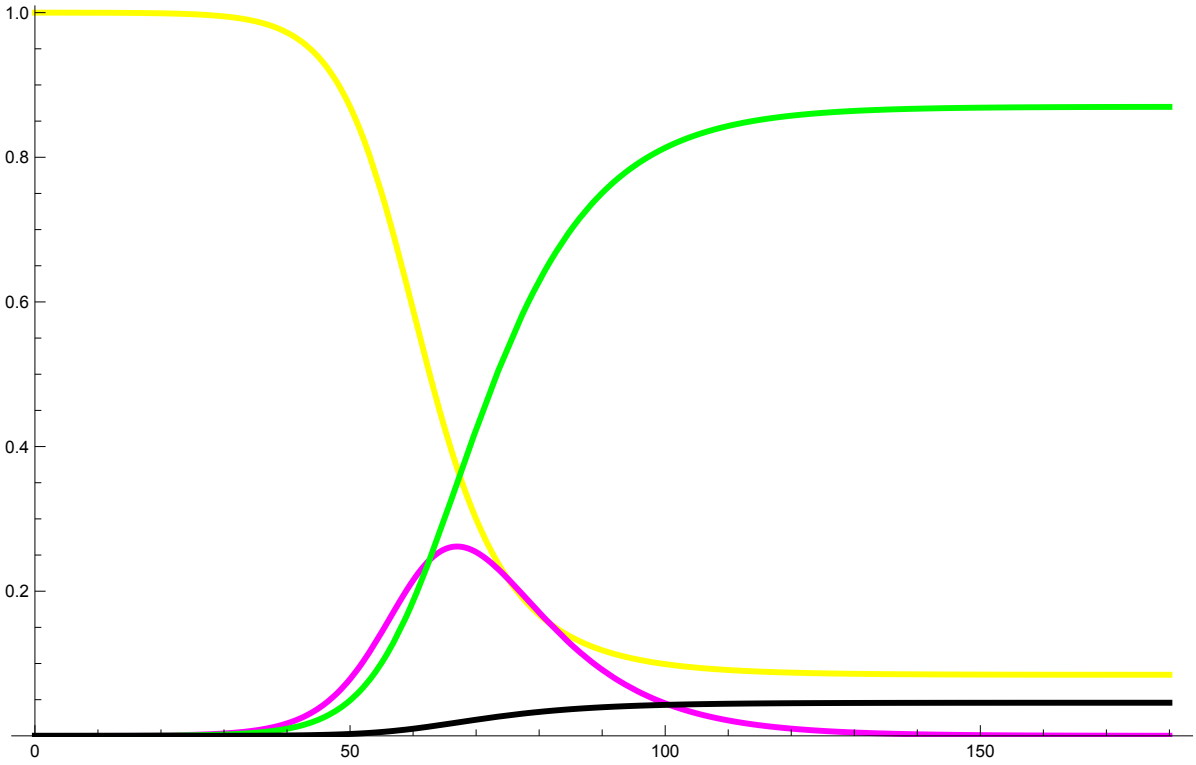
InterpolatingFunction[],

InterpolatingFunction[]}

Show the numerical solution overview

In[544]:=
```
Plot[{solutionS[t], solutionI[t], solutionR[t], solutionD[t]},
 {t, 0, 180}, PlotRange → {0, 1.01}, PlotStyle →
  {{RGBColor[255, 251, 0], Thickness[0.005]}, {Magenta, Thickness[0.005]},
   {Green, Thickness[0.005]}, {Black, Thickness[0.005]}}, ImageSize → Full]
```

Out[544]=

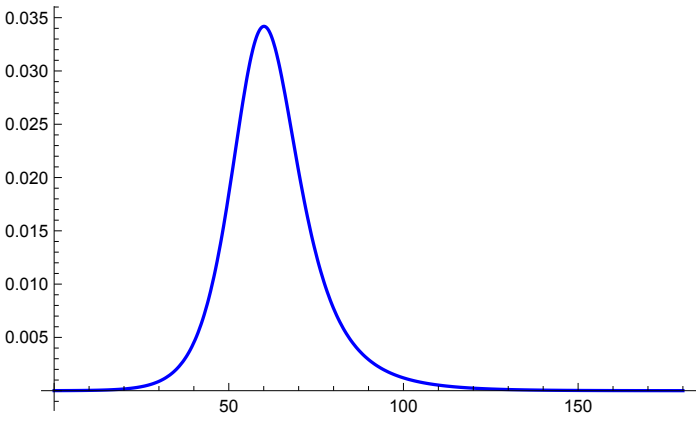


Experiment with incidence vs. daily bad outcomes

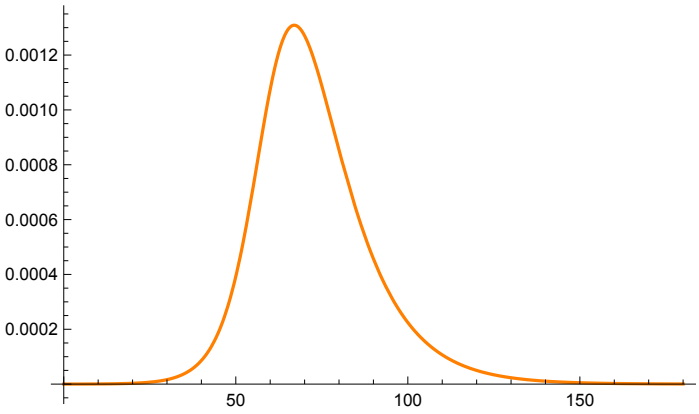
Let us see that, besides an apparent time shift and a simple affine transformation, both types of these daily rates are of a very similar shape. Their ratio stays in a narrow interval and exhibits a piecewise constant course. The connection with particular IFR, as it was set up for the experiment above, is observable clearly. The conclusion is that the patterns noticed for the incidence are then to be expected for the daily bad outcomes as well. The link is just *damped, not broken*.

In[545]:=
```
Plot[{incidence[t]}, {t, 0, 180},
 PlotStyle → {Blue, Thickness[0.005]}, ImageSize → Medium]
Plot[{ddead[t]}, {t, 0, 180}, PlotRange -> Automatic,
 PlotStyle → {Orange, Thickness[0.005]}, ImageSize → Medium]
Plot[{incidence[t], 26.12 * ddead[t + 7]}, {t, 0, 180}, PlotRange → {0, 0.037},
 PlotStyle → {{Blue, Thickness[0.005]}, {Orange, Thickness[0.005]}},
 ImageSize → Full]
Plot[{ddead[t + 7]/incidence[t], incidence[t], ddead[t + 7]}, {t, 0, 180},
 PlotRange -> Automatic, PlotStyle → {{Brown, Thickness[0.005]},
   {Blue, Thickness[0.005]}, {Orange, Thickness[0.005]}}, ImageSize → Medium]
```

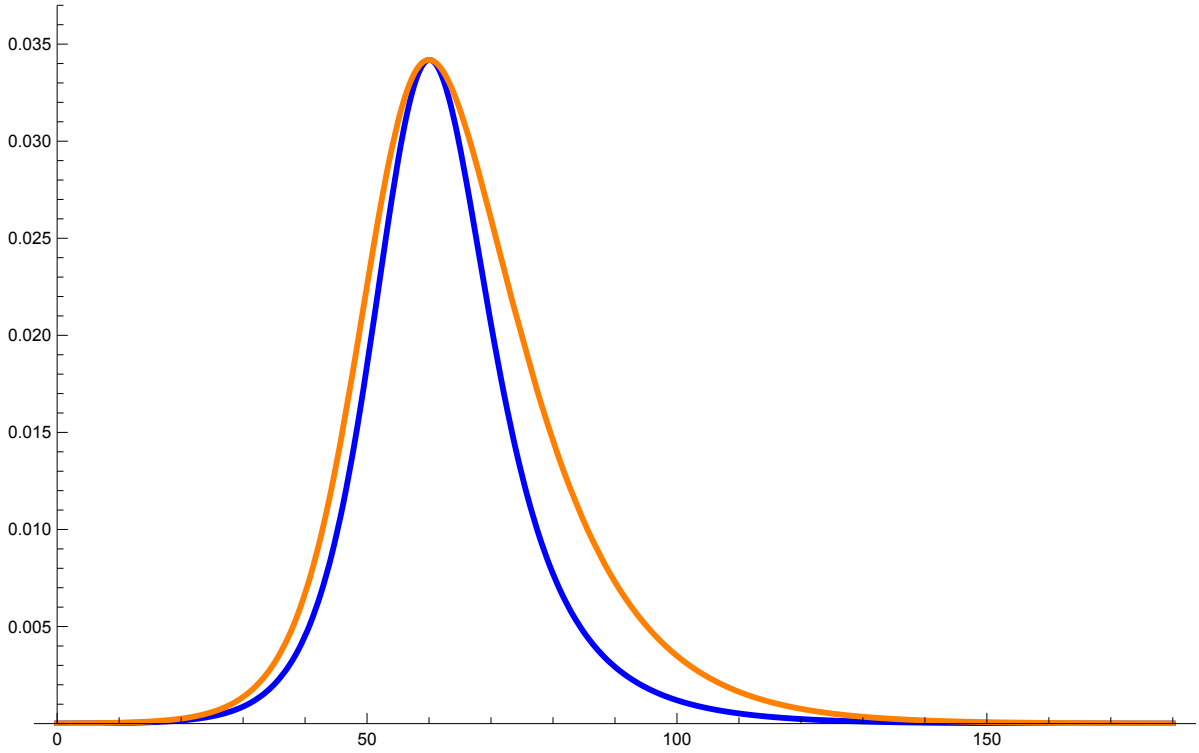
Out[545]=



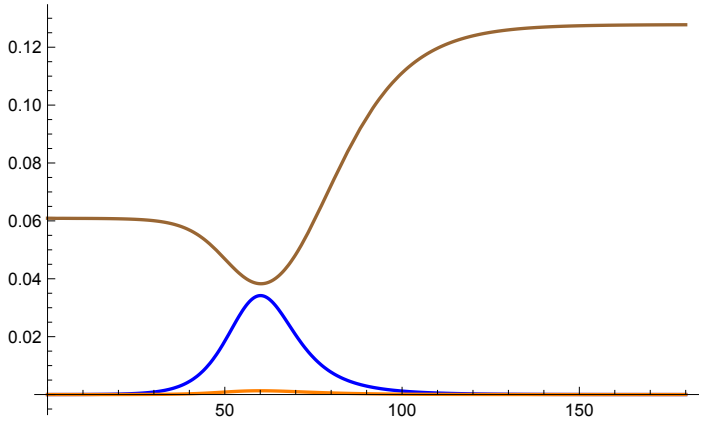
Out[546]=



Out[547]=



Out[548]=



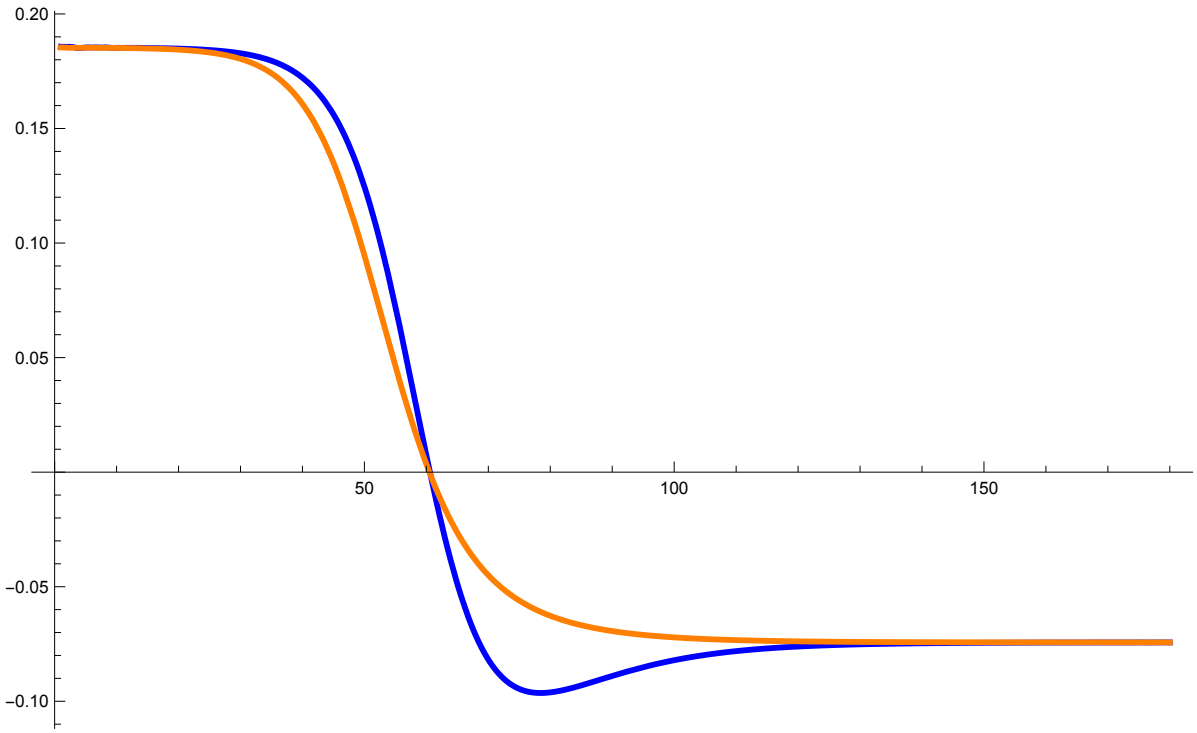
Compare the relative growths of the incidence and daily bad outcomes

Let us see the strong relationship in between the both growth rates, holding up to a simple time shift. This further corresponds with and supports the behaviour observed above. Again, this qualitatively supports the link is not totally broken, it is only damped. What we see for the incidence growth is again to be expected for the daily bad outcomes growth. This time, even *without notable rescaling*.

Also interesting is to compare the growth decrease phase with the main SIRD numeric solution plot above. In these short-term models without demography, the incidence relative growth rate actually decreases since the whole beginning, as this corresponds to the monotonically decreasing effective reproduction number. Therefore, a very first observation of the decreasing incidence relative growth rate by no means implies the particular wave pulse is over. It has rather just started.

In[553]:=
```
igrowt[t_] := incidence[t] / incidence[t - 1] - 1;
ddgrowt[t_] := ddead[t] / ddead[t - 1] - 1;
Plot[{igrowt[t], ddgrowt[t + 7]}, {t, 1, 180}, PlotRange → Automatic, PlotStyle →
  {{Blue, Thickness[0.005]}, {Orange, Thickness[0.005]}}, ImageSize → Full]
```

Out[555]=



Backup section (not expanded in final)

As a second point, the actual risk estimates by Public Health England

For the sake of completeness, note PHE is, together with the testing and tracking service, a part of the UK Health Security Agency (UKHSA), now.

First, for the Delta variant, then for the Lambda variant

8 July 2021 Risk assessment for SARS-CoV-2 variant: Delta (VOC-21APR-02, B.1.617.2) Public Health England

Indicator	RAG*	Confidence	Assessment and rationale
Transmissibility between humans		**HIGH**	**Transmissibility appears greater than wild type (first wave) virus.** All analyses support increased transmissibility for Delta compared to both wild type virus and Alpha. There is in vitro evidence suggestive of increased replication in biological systems that model human airway, and evidence of optimised furin cleavage. There is epidemiological evidence from secondary attack rates, household transmission studies, and growth rate modelling. The finding of lower CT values in routine testing data, compared to Alpha, may be relevant to the mechanism of increased transmissibility, however there may be multiple contributors.
Infection severity		**LOW**	**Increased severity (hospitalisation risk) when compared to Alpha.** Iterated analysis continues to suggest an increased risk of hospitalisation compared to contemporaneous Alpha cases. Analyses using 2 different sources of hospital data (SARIwatch sentinel surveillance and routine hospital episode data) do not yet find any evidence of increased severity once in hospital, in hospital inpatients since Delta became predominant. There is a high level of uncertainty in the estimates for the past 2 months due to data lag and these will be iterated. Data from COCIN (hospitalised patients) are broadly consistent with this, but additional analyses are being undertaken to adjust for age and vaccination status.
Immunity after natural infection		**LOW**	**Experimental evidence of functional evasion of natural immunity but insufficient epidemiological data** Pseudovirus and live virus neutralisation using convalescent sera from first wave and Alpha infections shows a reduction in neutralisation. National surveillance analyses are underway but there is currently insufficient evidence to assess whether the risk of reinfection differs between Delta and Alpha.
Vaccines		**HIGH**	**Epidemiological and laboratory evidence of reduced vaccine effectiveness** There are now analyses from England and Scotland supporting a reduction in vaccine effectiveness for Delta compared to Alpha against symptomatic infection. This is more pronounced after one dose. Iterated analysis continues to show vaccine effectiveness against Delta is high after 2 doses. Current evidence suggests that VE against hospitalisation is maintained. Although this is observational data subject to some biases, it holds true across several analytic approaches and the same effect is seen in both English and Scottish data. It is strongly supported by pseudovirus and live virus neutralisation data from multiple laboratories. There are no data on whether vaccine effectiveness to prevent transmission is affected.
Overall assessment			Delta is predominant in the UK and there is very rapid global spread. All analyses continue to support increased transmissibility and reduced vaccine effectiveness against symptomatic infection. Whilst risk of hospitalisation appears increased, early data on hospitalised patients does not show indicators of increased severity once in hospital and further analyses are required to resolve this. The priority investigations are to improve understanding of asymptomatic transmission in the vaccinated, to monitor for new mutations occurring on Delta, and continued investigation of the viral kinetics and clinical course of disease.

The therapeutics risk assessment is under review for all variants and is not included.
*refer to scale and confidence grading slide

8 July 2021 Risk assessment for SARS-CoV-2 variant: LAMBDA (VUI-21JUN-01, C.37) Public Health England

Indicator	RAG*	Confidence	Assessment and rationale
Transmissibility between humans			**Insufficient information** Lambda (C.37) appears to have transmitted successfully in South America with some wider spread. There is a single study with some evidence of enhanced ACE2 binding. There is insufficient genomic structured genomic surveillance to understand the contribution of Lambda (C.37) to the high levels of transmission that have been seen in some South American countries.
Infection severity			**Insufficient information**
Immunity after natural infection		**LOW**	**Experimental evidence of evasion of naturally acquired immunity** There is only one small study available, which finds find a reduction in neutralisation with convalescent sera when compared to virus from earlier in the pandemic. The magnitude of the reduction in this single study is moderate (less than B.1.351) but further assessments are required. There are no clinical or epidemiological data on reinfections.
Vaccines		**LOW**	**Very limited experimental evidence of evasion of vaccine derived immunity** There are only 2 pseudovirus studies available (US, Chile). Both find neutralisation by vaccinee sera to be reduced for Lambda compared to viruses from earlier in the pandemic. These are small studies and it is difficult to make any clinical extrapolation from this early data.
Overall assessment			Lambda has spread successfully in South America with evidence of some wider global transmission. There is no evidence as yet of a country where it is outcompeting Delta, though careful monitoring of the epidemiology in Chile and Peru is required. There are a small number of cases in the UK which are largely travel associated. Lambda contains a novel combination of mutations and very limited laboratory data are available. The priority studies are pseudovirus and live virus neutralisation with UK vaccinee sera, assessment of growth using *in vitro* systems and genomic surveillance of those countries where both Lambda (C.37) and Delta are present.

The therapeutics risk assessment is under review for all variants and is not included.
*refer to scale and confidence grading slide