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1 . In the excellent paper by Parag, Thompson, and Donnelly, $\widehat{R_t} = \frac{1}{M_W(-\widehat{r_t})}$ gives the instantaneous reproduction number in terms of the instantaneous growth rate. Wallinga and Lipsitch (2007) derive $R_t = \frac{1}{M_W(-r)}$ where $M_W(.)$ is the moment generating function of the generation interval W and r is a constant growth rate. But if r is time dependent, then the renewal equation for (smoothed) incidence I(t) is

$$I(t) = R(t) \int_0^\infty I(t-u) g_W(u) du.$$

and an assumed exponential growth of

$$I(t) = I(t - u)e^{\int_{t - u}^{t} r_{\chi} dx}$$

leads to

$$R_t = \frac{1}{\int_0^\infty e^{-\int_{t-u}^t r_x dx} g_W(u) du}$$

which is slightly different from the $\widehat{R_t} = \frac{1}{M_W(-\widehat{r_t})}$. I wonder whether this difference does matter, as the growth rate can change over a generation interval, for example through increasing vaccination roll out and changing non-pharmaceutical interventions. If that is the case, I think the answer is to use the renewal equation itself, which implicitly captures changing growth rates.

- 2. Most studies seem to assume that the distribution of the generation interval doesn't change with time. But changes in quarantining, isolation, and effectiveness of contact tracing might lead to shortened generation intervals. So, is it not the case, that an assumed stationary distribution of generation interval, can easily lead to biased estimates of reproduction number? If so, that is an argument in favour of growth rate rather than reproduction number.
- 3 . It is not easy to get good estimates of the distribution of the generation interval and therefore of reproduction number and that can lead to uncertainty. For example, for a gamma distributed generation interval, with mean μ and shape parameter α , just suppose the growth rates r_{1t}, r_{2t} of two competing variants (Alpha and Delta) were reasonably constant over a generation interval. Then we could use

$$R_{t1} = \left(1 + \frac{\mu r_{1t}}{\alpha}\right)^{\alpha}$$

$$R_{t2} = \left(1 + \frac{\mu r_{2t}}{\alpha}\right)^{\alpha}.$$

The increased transmissibility of Delta over Alpha is then

$$\left[\left(\frac{1 + \frac{\mu r_{2t}}{\alpha}}{1 + \frac{\mu r_{1t}}{\alpha}} \right)^{\alpha} - 1 \right] 100\%.$$

In Dagpunar (2021), I show how sensitive the increased transmissibility and reproduction numbers are to the chosen distribution of generation interval. In this case the renewal equation method rather than the moment generating function method was used to ensure that changes in growth rate are captured.

Reproduction numbers and increased transmissibility as of 15 May 2021, (day 49).

(Mean,	$R_1(49)$	$R_2(49)$	R(49)	Increased
standard	(Alpha variant)	(Delta variant)	(Weighted Sum)	transmissibility
deviation) of				
generation				
interval in days,				
Ganyani et al.				
(2020)				
(5.2,1.72)	0.750	1.37	1.12	83%
(3.78,0.91)	0.789	1.23	1.05	56%
(6.78,3.93)	0.703	1.51	1.19	115%
(3.95,1.51)	0.788	1.25	1.06	59%
(3.01,0.74)	0.820	1.17	1.03	43%
(4.91,2.97)	0.761	1.34	1.10	76%

References:

Wallinga, J. and Lipsitch, M. (2007). How generation intervals shape the relationship between growth rates and reproductive numbers, *Proc. R. Soc. B.***274**, 599–604. https://royalsocietypublishing.org/doi/10.1098/rspb.2006.3754

<u>Dagpunar, J. S. (2021).</u> Interim estimates of increased transmissibility, growth rate, and reproduction number of the Covid-19 B.1.617.2 variant of concern in the United Kingdom. https://www.medrxiv.org/content/10.1101/2021.06.03.21258293v1

Ganyani, T., Kremer, C., Chen, D., Torneri, A., Faes, C., Wallinga, J., Hens, N. (2020). Estimating the generation interval for coronavirus (COVID-19) based on symptom onset data, March 2020. https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.17.2000257