Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Available online at www.sciencedirect.com

ScienceDirect

IFAC PapersOnline CONFERENCE PAPER ARCHIVE

IFAC PapersOnLine 55-20 (2022) 445–450

Time Dynamics of the Spread of Virus Mutants with Increased Infectiousness in Austria

Martin Bicher *,** **Claire Rippinger** ** **Niki Popper** *,**,***

* *Institute of Information Systems Engineering, TU Wien, Favoritenstraße 11, 1050 Vienna, Austria (e-mail: martin.bicher@tuwien.ac.at)*

** *dwh GmbH, Neustiftgasse 57-59, 1070 Vienna, Austria*

*** *DEXHELPP, Association for Decision Support for Health Policy and Planning, Neustiftgasse 57, A-1070 Vienna, Austria*

Abstract: In spring 2021, it became eminent that the emergence of higher infectious virus mutants of SARS-CoV-2 is an unpredictable and omnipresent threat for fighting the pandemic and has wide-ranging implications on containment policies and herd immunity goals. To quantify the risk related to a more infectious virus variant, extensive surveillance and proper data analysis are required. Key observable of the analysis is the excess infectiousness defined as the quotient between the effective reproduction rate of the new and the previous variants. A proper estimate of this parameter allows forecasts for the epidemic situation after the new variant has taken over and enables estimates by how much the new variant will increase the herd immunity threshold. Here, we present and analyse methods to estimate this crucial parameter based on surveillance data. We specifically focus on the time dynamics of the ratio of mutant infections among the new confirmed cases and discuss, how the excess infectiousness can be estimated based on surveillance data for this ratio. We apply a modified susceptible-infectious-recovered approach and derive formulas which can be used to estimate this parameter. We will provide adaptations of the formulas which are able to cope with imported cases and different generation-times of mutant and previous variants and furthermore fit the formulas to surveillance data from Austria. We conclude that the derived methods are well capable of estimating the excess infectiousness, even in early phases of the replacement process. Yet, a high ratio of imported cases from regions with higher variant prevalence may cause a major overestimation of the excess infectiousness, if not considered. Consequently, the analysis of Austrian data allowed a proper estimate for the Alpha variant, but results for the Delta variant are inconclusive.

Keywords: SARS-CoV-2; COVID-19; Epidemiology; Mutants; Differential Equation Modelling; SIR Model; Parameter Identification

1. INTRODUCTION

Even though Millions of people are already fully vaccinated against SARS-CoV-2 by Summer 2021, the disease still poses a vital threat to national health care systems in Europe. One reason for this problem is the evolution of dangerous virus mutants, by mid 2021 in specific variants Alpha (lineage B.1.1.7) and Delta (B.1.617.2). These two variants were evolutionary superior to the previous ones due to their increased infectiousness and therefore became dominant – Alpha replaced the original SARS-CoV-2 variants in Europe (mainly lineage B.1) and Delta replaced Alpha. Moreover, due to the increased infectiousness, the virus strains raised the overall base reproduction rate and in direct consequence also the fraction of the population required for herd immunity.

In the course of the displacement process by a more infectious mutant, the following three important questions arise:

(1) How is the displacement process going to continue? When will $x\%$ of the daily new confirmed cases be caused by the mutant?
(2) How much more infectious is the mutant compared to the prior variants?
(3) How is the effective reproduction rate of the disease going to change due to the mutant?

In specific, questions two and three decide about whether additional containment measures will become necessary to cope with the new situation. Consequently, finding answers to them as early as possible after the new variant has been detected is highly relevant.

Most countries in Europe defined the ratio $r(t)$ of new confirmed cases that are attributed to the new variant $d_m(t)$ of all reported new cases $d(t)$ as their variable of interest when monitoring the displacement process. Here, $d(t) = d_m(t) + d_w(t)$, whereas the prior stands for the number of new cases attributed to the new variant, henceforth short the *mutant*, whereas the latter stands for

10.1016/j.ifacol.2022.09.135

the cases attributed to the previous variant(s), henceforth called *wildtype*. This notation will be used throughout the paper: index m refers to quantities related to the mutant, w corresponds to the wildtype.

$$r(t) := \frac{d_m(t)}{d_m(t) + d_w(t)} = \frac{1}{1 + \frac{d_w(t)}{d_m(t)}}. \tag{1}$$

In case the mutant turns out to be more infectious, r is increasing and converges towards one. The choice of this variable turned out to be functional: The ratio is a well understandable quantity by the common public and, in contrast to the daily new confirmed cases, the ratio seems to be less volatile.

The most direct way to estimate the excess infectiousness of a new mutant would be to estimate the quotient of the individual effective reproduction rates. This can be done via standard tools (e.g. Epiestim in R or Reff in Python, see Cori et al. (2013)) from the timeseries of the daily new confirmed cases. Since the latter are typically quite fuzzy, the estimates for R_{eff} and, consequently, also the estimate for the excess infectiousness are highly uncertain, in particular when the number of new mutant cases is quite small at the beginning. Hence, this strategy is not optimal and a different concept based on the more stable ratio $r(t)$ would be preferred. Alternative strategies (e.g. see Dagpunar (2021)) have weaknesses as well, since they do not regard different imported cases or different generation-times, i.e. different average times between the infection of a primary case and one of its secondary cases.

In this work, we aim to answer questions 1-3 based on the time dynamics of the ratio $r(t)$ and knowledge about the overall effective reproduction rate. Therefore, we will derive and analyse a differential equation model to obtain a formula for the excess infectiousness. We will extend the model to deal with imported cases and different generation-times as well. Finally, we will use the formula to determine the excess infectiousness of the Alpha and Delta variant based on surveillance data from Austria and we will test the early phase applicability of the formula.

2. METHODS

We will apply a classic susceptible-infectious-recovered (SIR) approach with a second infectious compartment – we will call this approach *SIIR model*. We will apply this model to derive formulas for $r(t)$ that can be used to fit the excess infectivity of the mutant and to forecast the dynamics of the replacement process.

2.1 SIIR model

Motivated by the classic SIR model (see Kermack and McKendrick (1927)), we define the following differential equation model, henceforth denoted as SIIR model:

$$\dot{S}(t) = -\frac{S(t)}{N}\left(\beta_w(t) I_w(t) + \beta_m(t) I_m(t)\right) \tag{2}$$

$$\dot{I_w}(t) = I_w(t)\left(\frac{S(t)}{N}\beta_w(t) - \gamma_w\right) \tag{3}$$

$$\dot{I_m}(t) = I_m(t)\left(\frac{S(t)}{N}\beta_m(t) - \gamma_m\right) \tag{4}$$

$$\dot{R}(t) = \gamma_w I_w(t) + \gamma_m I_m(t). \tag{5}$$

Here, N stands for the population size, $S(t)$ denotes the total number of susceptible persons at time t, $R(t)$ stands for the recovered ones, and I_w and I_m denote the active infectious cases for wildtype and mutant, respectively. Parameter γ_m and γ_w define the recovery rate, and $\beta_m(t)$ and $\beta_w(t)$ denote the infection rate of the corresponding virus type at time t.

We identify $d_w(t) = I_w(t)\frac{S(t)}{N}\beta_w(t)$ as new infections per time unit and find the formula for the effective reproduction rate $R_{eff,w}(t) = \frac{S(t)\beta_w(t)}{N\gamma_w}$, since

$$\frac{S(t)\beta_w(t)}{N\gamma_w} < 1 \Leftrightarrow \frac{\dot{I}_w(t)}{I_w(t)} < 0.$$

Analogous formulas can be derived for d_m and $R_{eff,m}$. Moreover, we define the excess infectiousness

$$\Delta R := \frac{R_{eff,m}(t)}{R_{eff,w}(t)} = \frac{\beta_m(t)\gamma_w}{\beta_w(t)\gamma_m}, \tag{6}$$

which we assume to be time independent. We justify this assumption by the idea that both variants face the same exogenous factors such as seasonality or containment policies.

Since $I := I_m + I_w$ and

$$\frac{\dot{I}}{I} := \frac{\dot{I_m} + \dot{I_w}}{I} < 0 \Leftrightarrow \frac{\frac{I_w S}{N}\beta_w + \frac{I_m S}{N}\beta_m}{\gamma_m + \gamma_w} < 1,$$

we find the overall effective reproduction rate

$$R_{eff}(t) := \frac{\gamma_w I_w(t) R_{eff,w}(t) + \gamma_m I_m(t) R_{eff,m}(t)}{(\gamma_m + \gamma_w) I(t)} \tag{7}$$

as the weighted mean of the individual reproduction rates of the two strains. Using the definitions for d_m, d_w, $r(t)$ and ΔR and defining

$$\Delta\gamma := \frac{\gamma_m}{\gamma_w}, \tag{8}$$

we may rephrase this formula to

$$R_{eff}(t) = R_{eff,w}(t)\frac{\Delta R(r(t) + \Delta\gamma(1 - r(t)))}{\Delta R\Delta\gamma(1 - r(t)) + r(t)}. \tag{9}$$

2.2 Model for the Ratio $r(t)$

We furthermore split the regarded time-frame $[0, t_{end})$ into M intervals of fixed length $\bigcup_{i=1,M}[t_i, t_{i-1}) = [0, t_{end})$. Typically, the intervals are chosen to be weeks or days. For each of these intervals, we assume $\beta_m(t) \approx \beta_m(t_i)$, $\beta_w(t) \approx \beta_w(t_i)$ and $S(t) \approx S(t_i), \forall t \in [t_i, t_{i+1})$. With these assumptions

$$\dot{d}_m(t) = d_m(t)\left(\frac{S(t)}{N}\beta_m(t) - \gamma_m + \frac{\dot{S}(t)}{S(t)} + \frac{\dot{\beta_m}(t)}{\beta_m(t)}\right)$$

$$= d_m(t)\left(\frac{S(t_i)}{N}\beta_m(t_i) - \gamma_m\right) = d_m(t)\gamma_m\left(R_{eff,m}(t_i) - 1\right),$$

for all $t \in [t_i, t_{i+1})$, which can be solved analytically to

$$d_m(t) = d_m(t_i)\exp\left((t - t_i)\gamma_m\left(R_{eff,m}(t_i) - 1\right)\right) \tag{10}$$

The analogous formula holds for d_w. Finally, a model for the ratio $r(t)$ can be derived:

$$r(t_{i+1}) = \frac{1}{1+\frac{d_w(t_{i+1})}{d_m(t_{i+1})}} = \frac{1}{1+\frac{d_w(t_i)}{d_m(t_i)}\frac{\exp((t_{i+1}-t_i)\gamma_w(R_{eff,w}(t_i)-1))}{\exp((t_{i+1}-t_i)\gamma_m(R_{eff,m}(t_i)-1))}} = \frac{1}{1+(\frac{1}{r(t_i)}-1)\exp(-(t_{i+1}-t_i)\Psi(t_i))}, \quad (11)$$

with

$$\Psi(t_i) = \gamma_w\left(R_{eff,w}(t_i)\left(\Delta R\Delta\gamma - 1\right) - (\Delta\gamma - 1)\right). \quad (12)$$

We derived an iterative model for the ratio $r(t)$ with key parameter ΔR. Note, that $R_{eff,w}(t_i)$ can be expressed in terms of $R_{eff}(t_i)$, ΔR, and $r(t_i)$ via (9).

2.3 Model with Imports

Considering that the Delta variant replaced the prior variant in Summer, imported cases, for example due to tourism, cannot be neglected. We will assume that $\xi(t)d(t)$ with $\xi(t) \geq 0$ cases are additionally imported at time t and that $r_{imp}(t)$ of these imported cases carry the specific mutant. Adding these cases to the autochthonously generated cases at every t_i we get

$$\overline{d}_m(t_i) = d_m(t_i) + r_{imp}(t_i)\xi(t)(d_m(t_i) + d_w(t_i)),$$
$$\overline{d}_w(t_i) = d_w(t_i) + (1 - r_{imp}(t_i))\xi(t)(d_m(t_i) + d_w(t_i))$$

and

$$\overline{r}(t_i) = \frac{1}{1+\xi(t_i)}r(t_i) + \frac{\xi(t_i)}{1+\xi(t_i)}r_{imp}(t_i) \quad (13)$$

Furthermore, replacing $r(t_i)$ by $\overline{r}(t_i)$ in formulas (11) and (9) gives an extended model using imported cases.

2.4 Austrian Surveillance Data

By January 2021, the first concerning reports of the excess infectiousness of the Alpha (B.1.1.7) variant (see Donelly (2021)) have raised awareness among Austrian health policy makers. A rigorous surveillance system using specialised PCR tests and sequencing has been established to track the spread of the mutant. While sequencing surely provides the most accurate information about the genome, it is a time- and resource-consuming process. Consequently, the results gained from the Real Time Quantitative PCR tests for the N501Y mutation (characteristic mutation on the spike protein and likely cause for increased infectiousness, see Santos and Passos (2021)) turned out to be the most valuable for modellers, since the screening of the samples was fast and could be done in large quantities. By week 3 in 2021, already more than 15% of all SARS-CoV-2 positive tests were checked for mutations, by week 5 the percentage increased to more than 60% and never dropped below this level until September 2021. Data and data-analysis have been regularly published online by the AGES (Agentur für Gesundheit und Ernährungssicherheit, see AGES (2021b)).

After the first occurrence of the Delta variant in Austria, the Real Time Quantitative PCR screening program for mutation N501Y turned out to be even more valuable: Besides other negligible mutants, only the variants Alpha, Beta and Gamma share this specific mutation. Delta, on the other hand, does not. In the present study, we will apply data that display the reported results of this PCR pretest instead of official sequencing data, since the share of positive COVID tests screened with this method is larger than the one with full sequencing. This data is also provided by AGES and is publicly available via the weekly reports of the Austrian Corona Commission (see Österreichische Corona Kommission (2021)).

The data shows that those variants with the N501Y mutation slowly replaced the previous lineages in Austria in the first months of 2021. This replacement process can almost solely be attributed to the variant Alpha, since the other two variants turned out to be evolutionary inferior. By mid April 2021, almost all tested cases in Austria showed a N501Y mutation. Starting mid May 2021, the cases with the mutation started to decline again due to the introduction of the Delta variant. This new variant, again, turned out to be more infectious than the dominant Alpha variant and fully replaced the old virus by the end of August.

Besides data about the ratio of mutants, AGES also publishes an estimate of the overall effective reproduction rate $R_{eff}(t)$ (see AGES (2021a)), which we also use as input to the formula.

2.5 Fitting Austrian Surveillance Data

In order to determine the excess infectiousness of the variants Alpha and Delta in Austria, we will fit Formula (11) to the given data. We will assume that the ratio of cases with the N501Y mutation matches the ratio of Alpha cases between 2021-01-01 and 2021-05-01 and assume that cases without N501Y can be attributed to variant Delta between 2021-05-20 and 2021-08-01.

For determining the parameters for the takeover of the Alpha variant, we use the mentioned data for $R_{eff}(t)$ and assume $\gamma_m = \gamma_w = 1/5.2$, according to one of the estimates for the mean generation-time, published in Ganyani et al. (2020) (i.e. $\Delta\gamma = 1$). We furthermore fit the curve $r(t)$ to the ratio using the two free parameters ΔR and $r(t_0)$ for all available weekly estimates with more than 15% tested cases which excludes the first two reported weeks in January. Moreover, we will assume that the weekly ratio is representative for the corresponding Wednesday at 00:00 of the week.

The fit is performed using a Broyden-Fletcher-Goldberg-Shannon quasi Newton method implemented in Python's Scipy package (see Virtanen et al. (2020)). The variance and confidence levels for the fitted parameters are estimated via the fitting error.

The Delta variant replaced the Alpha variant over the Summer months. During this period, Austria has been visited by fairly many tourists, many of whom came from countries with a higher ratio of Delta cases. Therefore, imports cannot be neglected completely. We assume, that the average tourist comes from a region where the Delta variant spread is already one week ahead of Austria. That means, we define $r_{imp}(t - 7[days])$ to match the reported ratio of N501Y negative cases in Austria at time t. Furthermore, we fix $\xi(t) = \xi_0$ and vary this value. The fit is done using Formula (13).

According to information about shorter generation-times for the Delta variant, also fits with $\gamma_w = 1/5.2$ and different $\Delta\gamma$ ratios were tested.

3. RESULTS

3.1 Fitted Data for Alpha and Delta

The defined fitting strategy from Section 2.5 leads to $\Delta R = 1.36$ with 90% CI $[1.33-1.39]$ for the Alpha variant compared to the prior variant and, assuming $\Delta\gamma = 1$, $\Delta R = 2.11$ with 90% CI $[2.00-2.21]$ for the Delta variant compared to Alpha. The data for the ratios and R_{eff}, the fitted curve $r(t)$ and the modelled estimates for variant-specific reproduction rates are displayed in Figures 1 and 3. Figure 2 displays the forecasting capabilities of the equation fitting model. Using more and more data points for the fit, we increase the quality of the ΔR estimate. Even with only two points, we got a fairly reliable estimate for the excess infectiousness.

3.2 Time between 5% to 95%

According to (11) and (12), any $\Delta R > 1$ will eventually lead to takeover of the wildtype strain by the new mutant. The speed of this overtaking process depends on the parameters: a larger ΔR, $R_{eff,w}$, γ_w (i.e. smaller generation-times) will speed up the replacement process. In Figure 4 we display the number of days between $r(t) = 0.05$ and $r(t) = 0.95$ as a function of ΔR and $R_{eff,w}$ for feasible value ranges and $\Delta\gamma = 1$. Easily seen, the impact of the prior parameter on the outcome is larger.

The fitted values for the Alpha and Delta variant fit well into the plot. While the Alpha variant took about 90 days to take over from the wildtype, the Delta variant replaced the Alpha variant in less than 50 days.

3.3 Fitting Delta with Imports and $\Delta\gamma \neq 1$

Varying the level ξ_0 of imported cases from 0.00 to 0.11 and fitting Formula (13), we obtain different fitted values for ΔR. These values can be found in Table 1.

With respect to different generation-times, we varied $\Delta\gamma$ in the range between 2/5 and 7/5, meaning that the generation-time ranges from 2.5 times shorter to 1.4 times longer than the one of the prior variant. The results are displayed in Table 2.

Table 1. Fitted values for ΔR for the Delta variant with different importing ratios ξ_0.

ξ_0	0%	1%	2%	3%	4%	5%
ΔR	2.11	2.01	1.96	1.88	1.81	1.72
90% CI	± 0.11	±0.10	± 0.10	±0.10	±0.09	±0.08

ξ_0	6%	7%	8%	9%	10%	11%
ΔR	1.63	1.55	1.48	1.41	1.35	1.29
90% CI	±0.09	±0.09	±0.09	±0.10	±0.10	±0.11

4. DISCUSSION

In the present work, we established a SIR type model capable of depicting two separate virus strains and used the

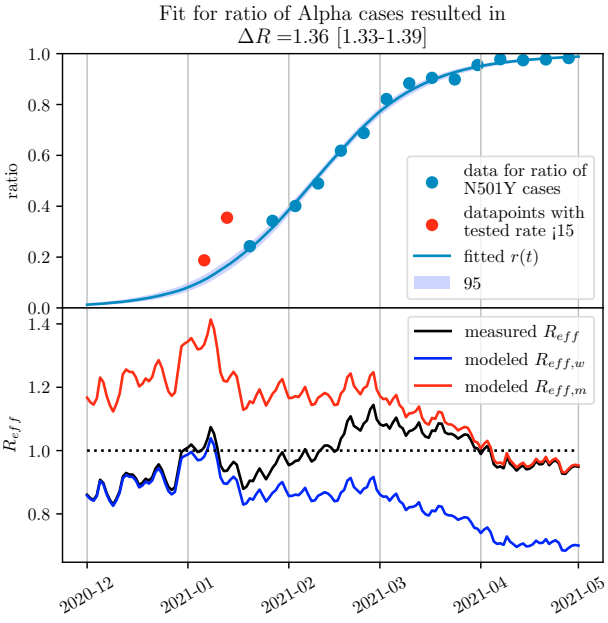

Fig. 1. Model fit for the Alpha variant. Data and fitted ratio curve $r(t)$ in upper plot. The lower plot displays the measured values for $R_{eff}(t)$ and the modelled estimates for variant specific reproduction rates.

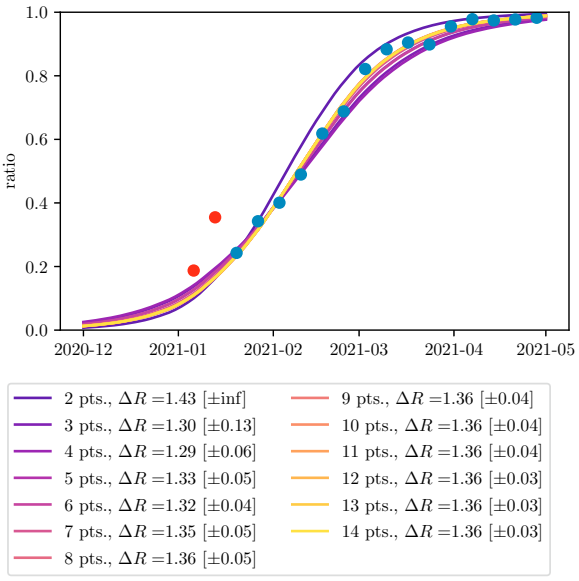

Fig. 2. Model fit for the Alpha variant using the first n measured points and using the last measured value for R_{eff} for the forecast. Even with only two given data points, the excess infectiousness and the ratio dynamics are quite properly estimated.

model to derive formulas for the ratio of mutant infections $r(t)$ and the separate effective reproduction rates $R_{eff,w}(t)$ and $R_{eff,m}(t)$ for the prior variant(s) ('wildtype') and the new variant ('mutant'). We furthermore adapted the formulas to be capable of depicting imported cases with a potentially different mutant ratio. In a case study for Austria, we applied both formulas to Austrian surveillance

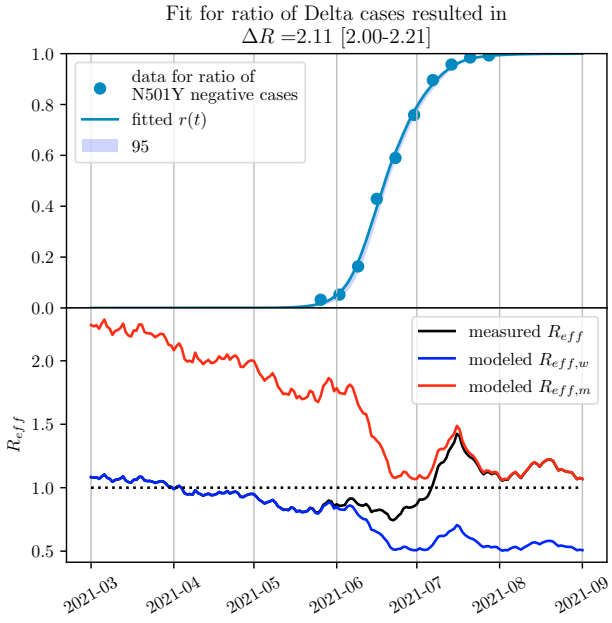

Fig. 3. Model fit for the Delta variant. Data and fitted ratio curve $r(t)$ in upper plot. The lower plot displays the measured for $R_{eff}(t)$ and the modelled estimates for variant specific reproduction rates.

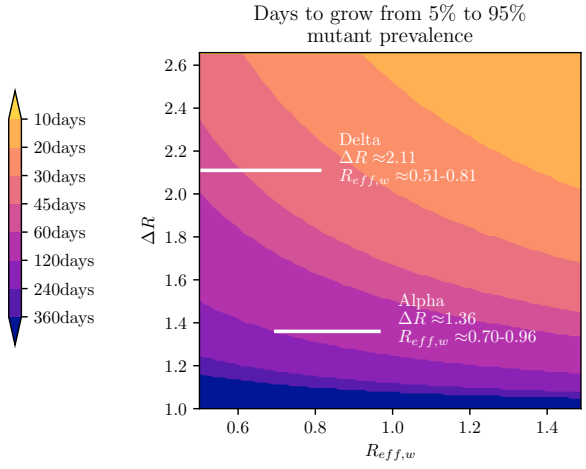

Fig. 4. Replacement speed of a mutant displayed as a function of its excess infectiousness ΔR and constant $R_{eff,w}$. Values for ΔR and $R_{eff,w}$ values for the two mutants was taken from the fitting process (see Figures 1 and 3).

data and fitted the free key parameter ΔR, the excess infectiousness, for the Alpha and the Delta variant.

In the case of the Alpha variant, the formula suggested an evolutionary advantage of $\Delta R \approx 1.36$ for the Alpha variant compared to the prior ones. This value is on the line with international estimates (see Piantham et al. (2021); Davies et al. (2021); Campbell et al. (2021)). The formula for $R_{eff,w}(t)$ indicates, that the epidemic wave seen in Austria in March 2021 was primarily caused by the new variant. Without introduction of the new virus mutant, R_{eff} would have remained far below one, which would potentially have lead to near extinction of the virus by Summer 2021 in Austria.

Table 2. Fitted values for ΔR for the Delta variant with different generation-time ratios.

γ_m/γ_w	7/5	6/5	1	4/5	3/5	2/5
ΔR	1.94	2.01	2.11	2.25	2.47	2.87
90% CI	± 0.08	±0.10	± 0.11	±0.14	±0.20	±0.22
β_m/β_w	2.71	2.41	2.11	1.80	1.48	1.15

The results for the Delta variant are less conclusive. Fitting the data with the standard Formula (11) leads to $\Delta R = 2.11$ (+110%), which would be one of the highest assumptions for the evolutionary benefit of Delta compared to the literature. Published values range from +40% in Tegally et al. (2021), +73% in Sonabend et al. (2021) up to estimates over +100% in Preprint Dagpunar (2021).

One reason for the unusually high result might be that, in contrast to Alpha, the Delta variant was introduced in a time with low case numbers and comparably many tourists visiting Austria. Our estimate, which includes 5% imported cases with higher variant prevalence, produced the best fitting curve (smallest variance) and led to the far lower estimate of $\Delta R = 1.72$, which is much closer to published numbers. Yet, considering the high sensitivity of the import parameter – as seen in Table 1, the difference between 0 and 10% imported cases almost quarters the evolutionary advantage of the variant from +111% to +29% – neither of the estimates can give a reliable answer to the actual excess infectiousness of the Delta variant. A deeper analysis of the number and origin of the actual imported cases to Austria during this period would be necessary.

Anyway, the prior observation might be one of the reasons, why estimates for Delta found in the literature are so diverse. We may generalise: In case a new variant takes over in (1) a time with a comparably high ratio of imported cases, e.g over the Summer months and (2) the variant is already highly present in typical origin countries of tourists, the fitted excess infectiousness solely based on ratio data will overestimate the actual evolutionary advantage by a large margin.

Also, varying the generation-time of the new variant leads to interesting dynamics. In case the generation-time for the new variant is shorter, the fitted estimate for the excess infectiousness $R_{eff,m}/R_{eff,w}$ grows, while the ratio of growth parameters β_m/β_w decreases. This observation implies that one needs to be meticulous when defining "excess infectiousness" for two virus strains with different generation-times, since this difference leaves a lot of space for misunderstandings. While β_m/β_w is relevant to quantify the individual contact transmission risk, we need to consider $R_{eff,m}/R_{eff,w}$ to quantify the herd-immunity threshold which increases from $100(1-\frac{1}{R_{0,w}})\%$ to $100(1-\frac{1}{R_{0,w}\Delta R})\%$ immunised persons [1].

[1] For the official reporting system, the situation becomes even more difficult, since ex-post measuring, based on case numbers, requires to estimate the effective reproduction rate for both variants with different generation-times.

Apart from interesting findings when fitting the data, direct analysis of the formula gave insights into the role of R_{eff} and ΔR with respect to duration of the variant replacement: both R_{eff} and ΔR speed up the process. With respect to typical value ranges for the two parameters, the influence of the latter can be considered more important. Nevertheless, the results indicate that the comparably low level of R_{eff} by the time of the introduction of the Alpha and Delta variants in Austria caused a comparably slow replacement process (about 90 and 45 days, respectively). In case, for example, the Delta variant would have arrived in Austria in a period with $R_{eff} \approx 1.5$, the ratio would have increased from 5% to 95% in less than 20 days (modelled without imports).

The results of this study have the typical limitations of macroscopic SIR compartment models. The used model also depicts individuals in the S-compartment equally susceptible to both virus strains, meaning that different protection levels from vaccinations or from recoveries with other strains are not taken into account. For example, recent studies confirmed, that a single CoV vaccination dose provides a lower level of protection against the Delta variant than against the Alpha variant (see Bernal et al. (2021)). Apart from model specific limitations, also data specific problems may arise. Although Figure 2 displays, that the model is well capable of good forecasts, the study is conducted using cleaned retrospective data, which might not be available by the time of the forecast. Moreover, the requirement of more than 15% of the positive tests being screened for the specific mutation is quite demanding.

In this work, we presented and applied an SIR-model-based method to estimate the excess infectiousness of a new mutant strain, which is to replace a previous less infectious variant. We have developed a logistically shaped formula, which displays the time dynamics of the ratio of mutant cases and can be fitted to observational data, if needed, to estimate (1) the excess infectiousness and (2) the future time dynamics of the ratio, and the future time dynamics of the effective reproduction rate. By fitting the model to data, we showed that the third Austrian epidemic wave in Spring 2021 was mainly caused by the Alpha variant, and that the Delta variant might have caused similar effects in autumn 2021. By adapting the model to cope with imported cases, though, we showed that fitting the curve causes overestimation if imports from regions with higher mutant prevalence are not considered.

REFERENCES

AGES (2021a). Epidemiologische parameter des covid19 ausbruchs. https://www.ages.at/wissen-aktuell/publikationen/epidemiologische-parameter-des-covid19-ausbruchs-oesterreich-20202021/. Accessed: 2021-09-10.

AGES (2021b). Sars-cov-2 varianten in österreich. https://www.ages.at/themen/krankheitserreger/coronavirus/sars-cov-2-varianten-in-oesterreich/. Accessed: 2021-09-10.

Österreichische Corona Kommission (2021). Empfehlungen der corona-kommission. https://corona-ampel.gv.at/corona-kommission/empfehlungen-der-corona-kommission/. Accessed: 2021-09-10.

Bernal, J.L., Andrews, N., Gower, C., Gallagher, E., Simmons, R., Thelwall, S., Stowe, J., Tessier, E., Groves, N., Dabrera, G., et al. (2021). Effectiveness of covid-19 vaccines against the b. 1.617. 2 (delta) variant. *New England Journal of Medicine*.

Campbell, F., Archer, B., Laurenson-Schafer, H., Jinnai, Y., Konings, F., Batra, N., Pavlin, B., Vandemaele, K., Van Kerkhove, M.D., Jombart, T., et al. (2021). Increased transmissibility and global spread of sars-cov-2 variants of concern as at june 2021. *Eurosurveillance*, 26(24), 2100509.

Cori, A., Ferguson, N.M., Fraser, C., and Cauchemez, S. (2013). A new framework and software to estimate time-varying reproduction numbers during epidemics. *American journal of epidemiology*, 178(9), 1505–1512.

Dagpunar, J. (2021). 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. *medRxiv*. doi:10.1101/2021.06.03.21258293.

Davies, N.G., Abbott, S., Barnard, R.C., Jarvis, C.I., Kucharski, A.J., Munday, J.D., Pearson, C.A., Russell, T.W., Tully, D.C., Washburne, A.D., et al. (2021). Estimated transmissibility and impact of sars-cov-2 lineage b. 1.1. 7 in england. *Science*, 372(6538).

Donelly, L. (2021). Uk to help sequence mutations of covid around world to find dangerous new variants. *The Telegraph*.

Ganyani, T., Kremer, C., Chen, D., Torneri, A., Faes, C., Wallinga, J., and Hens, N. (2020). Estimating the generation interval for coronavirus disease (covid-19) based on symptom onset data, march 2020. *Eurosurveillance*, 25(17), 2000257.

Kermack, W.O. and McKendrick, A.G. (1927). A Contribution to the Mathematical Theory of Epidemics. *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences*, 115(772), 700–721. doi:10.1098/rspa.1927.0118.

Piantham, C., Linton, N.M., Nishiura, H., and Ito, K. (2021). Estimating the elevated transmissibility of the b. 1.1. 7 strain over previously circulating strains in england using gisaid sequence frequencies. *medRxiv*.

Santos, J.C. and Passos, G.A. (2021). The high infectivity of sars-cov-2 b. 1.1. 7 is associated with increased interaction force between spike-ace2 caused by the viral n501y mutation. *BioRxiv*, 2020–12.

Sonabend, R., Whittles, L.K., Imai, N., Perez-Guzman, P.N., Knock, E.S., Rawson, T., Gaythorpe, K.A., Djaafara, B.A., Hinsley, W., FitzJohn, R.G., et al. (2021). Non-pharmaceutical interventions, vaccination and the delta variant: epidemiological insights from modelling england's covid-19 roadmap out of lockdown. *medRxiv*.

Tegally, H., Wilkinson, E., Althaus, C.L., Giovanetti, M., San, J.E., Giandhari, J., Pillay, S., Naidoo, Y., Ramphal, U., Msomi, N., et al. (2021). Rapid replacement of the beta variant by the delta variant in south africa. *medRxiv*.

Virtanen, P., Gommers, R., Oliphant, T.E., Haberland, M., Reddy, T., Cournapeau, D., Burovski, E., Peterson, P., Weckesser, W., Bright, J., et al. (2020). Scipy 1.0: fundamental algorithms for scientific computing in python. *Nature methods*, 17(3), 261–272.