

European and US lockdowns and second waves during the COVID-19 pandemic

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Abstract

This paper investigates the lockdowns to contain the spread of the SARS-CoV-2 coronavirus in France, Germany, Italy, Spain, the UK and the US and also recent developments since these lockdowns have been relaxed. The analysis employs a two-stage SEIR model with different reproductive numbers pre- and post-lockdown. These parameters are estimated from data on the daily number of confirmed cases in a process that automatically detects the time at which the lockdown became effective. The model is evaluated by considering its predictive accuracy on current data and is then extended to a three-stage version to explore relaxations. The results show the extent to which each country was successful in reducing the reproductive number and demonstrate how the approach is able to model recent increases in the number of cases in all six countries, including the second peak in the US. The results also indicate that the current levels of relaxation in all five European countries could lead to significant second waves that last longer than the corresponding first waves. While there is uncertainty about the implications of these findings at this stage, they do suggest that a lot of vigilance is needed.

1 Introduction

Many countries throughout the world introduced lockdowns to prevent the rapid spread of the SARS-CoV-2 virus. How effective have these measures been and to what extent should they be relaxed? As many countries have subsequently relaxed their lockdowns to greater or lesser extents, these questions have become an urgent matter. Furthermore, there is also concern about the possibility of a second wave¹ in a lot of countries. This paper explores these issues in the context of five European countries – France, Germany, Italy, Spain and the United Kingdom – and the United States. The approach is to investigate the spread of the virus within these countries both before and after their respective lockdowns took effect and this is achieved by fitting a variant of the SEIR model to data on COVID-19 in each country. As variations of the Kermack-McKendrick model [1], SEIR models have been widely used in

¹The expression 'second wave' is used here in the general sense of a second peak in the number of cases that is comparable to the first peak in a given country.

the modelling of the COVID-19 pandemic [2–11]. They have been developed in various ways including one that incorporates interactions between different cities in a network [5] and another that divides the population into different subgroups by age to include differing levels of interaction in society [2, 8].

Here the focus is on simpler two- and three-stage SEIR models that can nevertheless model lockdowns and relaxations of them effectively. The first stage in these models applies to the period before the lockdown and the second afterwards, while the third stage is introduced to model a subsequent relaxation of the lockdown. By learning the parameters of the model from the data on the number of cases, this approach is able to determine the impact of the lockdowns. The two-stage component is similar to another SEIR model used to study COVID-19 containment in Mexico, where transmission rates were reduced linearly to a lower level as a result of interventions [12]. In terms of the assumption that the reproductive number changes immediately at the time of lockdowns and in its application to European countries, the work is similar to another study of the impact of interventions in Europe which assumed the reproductive number only changed with each intervention, though the approaches differ in other respects [13]. Also, in that study the focus was on the number of deaths rather than the number of confirmed cases which are the primary focus here. However, the results here are compared with corresponding results based on the number of deaths as well as the number of hospital patients in the case of the UK. The model for each country is then evaluated by investigating how well it is able to predict the number of cases of COVID-19 recorded on a given day based on parameters learned from previous days. The models are then used to compare the effectiveness of the lockdowns in the different countries, make projections for the number of cases in the future and explore the effect of relaxing the restrictions in each country.

2 Methodology

Since the goal of the lockdowns is to reduce the transmission rate, β , the two-stage SEIR model proposed here involves different values for β before and after the lockdown came into effect, but keeps the other parameters fixed. The dynamics of various subgroups of the population before and after a lockdown occurring at $t_{lockdown}$ are given by the following ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta(t)\frac{SI^c}{N} - \alpha\beta(t)\frac{SI^u}{N} \\
\frac{dE}{dt} &= \beta(t)\frac{SI^c}{N} + \alpha\beta(t)\frac{SI^u}{N} - \sigma E \\
\frac{dI^c}{dt} &= \rho\sigma E - \gamma I^c \\
\frac{dI^u}{dt} &= (1 - \rho)\sigma E - \gamma I^u \\
\frac{dR}{dt} &= \gamma(I^c + I^u)
\end{aligned} \tag{1}$$

where $\beta(t)$ is the transmission rate that has the following values before and after the lockdown

$$\beta(t) = \begin{cases} \beta^{Pre} & : t < t_{lockdown} \\ \beta^{Post} & : t \geq t_{lockdown} \end{cases} \tag{2}$$

and N is the total population of the country, which is assumed to be constant, S , E , I^c , I^u and R are the susceptible, exposed, infected (confirmed), infected (unconfirmed) and removed (or recovered)

groups respectively, σ the rate at which those in the exposed group transition to become infectious, γ the rate at which those in the infectious groups transition to removed, while ρ represents the proportion of confirmed cases out of the total number of cases. In dividing the infected group into two subgroups, the approach is similar to other work that allows one subgroup described as undocumented [5] or sub-clinical / asymptomatic [8] to have a transmission rate reduced by a factor α .

The basic reproduction number R_0 is given by $\rho\beta/\gamma + (1 - \rho)\alpha\beta/\gamma$. This expression is obtained from finding the dominant eigenvalue of the next generation matrix [14]. Just as for the transmission rate, we can say that different values of R_0 are used before and after the lockdown. Let us denote these as R_0^{Pre} , the value before the lockdown, and R_0^{Post} , the value afterwards, corresponding to β^{Pre} and β^{Post} respectively. The approach is then to learn the values of R_0^{Pre} and R_0^{Post} from the daily data on the number of new cases of COVID-19 using the two-stage SEIR model. Parameter learning is achieved by integrating the differential equations using the fourth order Runge-Kutta method and finding parameters that fit the data best in the sense of minimising the sum of the squared residuals.

While some parameters are learned from the data, others need to be specified (see table 1 for a summary of the key parameters in the model). The parameter $\sigma = 1/t_l$, where t_l represents the mean latent period, is related to the incubation period and pre-symptomatic infection. There have been many studies of the incubation period for COVID-19 (see for example [15–17]). A meta-analysis of relevant literature gives a mean incubation period of 5.8 days [18]. There is also evidence of pre-symptomatic transmission of COVID-19 (see for example [19, 20]) with a pre-symptomatic period of infection of about 2 days [21]. Hence, the selected value for σ is based on the difference between these two estimates to give a latent period, t_l , of 3.8 days, which is similar to that used by Li *et al* [5].

The rate of transition from infectious to removed groups is $\gamma = 1/t_i$, where t_i represents the mean infectious period and this presents a challenge since a wide range of values have been estimated in the literature (for discussion see [21]). Here, t_i is set to 3.4 days based on estimates of the infectious period in China before and after travel restrictions were introduced [5]. This is at the low end of the estimates found in the literature, but it seems justified in the current context for two reasons. First, it is not the infectious period of the disease *per se* that is relevant for SEIR models, but the period during which the infection could contribute to transmission. As Brauer *et al* note, ‘ $R(t)$ denotes the number of individuals who have been infected and then removed from the possibility of being infected again or of spreading infection’ [22, p. 23]. They note that this can happen in various ways including via isolation, which is relevant here since isolation measures were in place in the countries considered and so would have limited the scope for transmission. This would apply to those who are symptomatic irrespective of whether they are in the confirmed or unconfirmed groups, but not to those who are asymptomatic. Nevertheless, this point provides some justification for a low value of t_i . Second, there is evidence that transmissibility is highest around the onset of symptoms. In a secondary analysis of published data, Casey *et al* [23] suggest that transmission is most likely in the day before symptom onset and estimate that 56.1% of transmission occurs during the pre-symptomatic period based on a pooling of published results (see also [24, 25]). Assuming asymptomatic transmissibility is also highest at an early stage of infection, the same value of γ is used for both the confirmed and unconfirmed groups. It is worth noting that the selected

values for both the latent and infectious periods are in line with estimates of the generation time and serial interval [26]. Other values of several parameters are considered in supplementary material to see how they affect results.

In order to fit the model to the number of newly confirmed cases, it is necessary to estimate the proportion (ρ) of confirmed cases out of the total number of cases (confirmed and unconfirmed) for a given country. For the results presented in the main paper, ρ is obtained as follows. The cumulative number of confirmed cases up to the date being used in a given calculation for a particular country is divided by an estimate of the total number of cases, which is obtained by dividing the cumulative number of deaths up to the same date by a mortality rate of $m = 0.66\%$ [27]. Since there is a lot of uncertainty about the mortality rate, other values are considered in supplementary material. Furthermore, there is a limitation to this approach since ρ would be expected to increase over time given increased levels of testing during the pandemic. This point is explored in section S9 of supplementary material by increasing ρ linearly over time to see how it affects the results. It turns out that this has little affect for fitting the model to the data, but results in significant changes for the height of second peaks.

Table 1: Summary of key parameters. Results for several other values of t_l , t_i and m are explored in supplementary material.

Parameter	Value
mean latent period, t_l	3.8 days
mean infectious period, t_i	3.4 days
mortality rate, m	0.66%
proportion of confirmed cases, ρ	based on m and % deaths in given country
pre-lockdown reproductive number, R_0^{Pre}	estimated from fitting model to data
pre-lockdown reproductive number, R_0^{Post}	estimated from fitting model to data
initial number of exposed cases, E_0	estimated from fitting model to data
initial number of infections, I_0^c and I_0^u	sum equal to E_0 and proportions based on ρ
effective date of lockdown, $t_{lockdown}$	estimated from fitting model to data

Recall that α allows for a reduction in the transmission rate for the unconfirmed cases or alternatively for asymptomatic or sub-clinical cases if the infectious group is divided up differently. While a reduction, and hence a value of α of less than one, would make sense for an asymptomatic group, it is more difficult to assign an appropriate value of α for the unconfirmed group because a) this would depend on what proportion of the unconfirmed group is asymptomatic and b) this would be different for each country since the level of testing carried out varies from one country to another. Hence, different α values would be needed for different countries, but these values would be difficult to justify. Furthermore, there is a lot of uncertainty at present about the proportion of asymptomatic cases in general as well as their level of transmission, which further exacerbates the difficulties. However, for the results in the main paper, where the proportion of confirmed cases, ρ , for a given country is kept fixed, α does not play a crucial

role in the calculations. It turns out that changing the value of α amounts to a rescaling of β^{Pre} (and β^{Post}) that nevertheless results in the same value of R_0^{Pre} (and R_0^{Post}) and hence has no effect on the dynamics. For this reason, α is set to one for the results in the main paper and hence no distinction is made between confirmed and unconfirmed cases in terms of transmission rates. When linearly increasing values of ρ are explored in section S9 of supplementary material, two different values of α are considered to investigate the effect of α on the results.

In terms of fitting the two-stage SEIR model to data, data are used from the first day on which there were 100 or more reported new cases confirmed in the country. This date is taken to be day zero and the calculations proceed from there. A value of 100 was selected because there can be uncertainty about the numbers of cases at the early stages of an outbreak due to very low numbers and the influence of imported cases rather than local transmission. Also, the goal here is to model the situation for several weeks prior to the lockdown rather than at the earliest stages of the outbreak. However, in most cases, starting with a lower value of 10 cases made almost no difference to the results. A related issue concerns how the initial number of exposed (E_0) and infected (I_0^c and I_0^u) cases should be specified. The approach adopted here is to treat E_0 as a further parameter to be fitted to the data and then to set $I_0^c = \rho E_0$ and $I_0^u = (1 - \rho)E_0$. For further details on this point and other issues relating to fitting the model to the data, see section S2 in supplementary material.

When the model is fitted to the newly confirmed cases this means that $t_{lockdown}$ represents the number of days after day zero that the lockdown is reflected in the number of confirmed cases. Intuitively, it might seem easy to model the lockdown in a given country. Since the date of day zero is known from the available data and the date of the lockdown is also known, it might be thought that the number of days between day zero and the lockdown could be used to incorporate it in the model. However, there is a time delay between infection and subsequent confirmation. Lin *et al* report a 14 day delay between two datasets with largely the same group of patients [6]. This delay can depend on the availability of testing and on when people seek medical advice, for example, and so can differ from one country to another. Hence, rather than specifying this time delay *a priori*, it is learnt from the data by determining the value of $t_{lockdown}$ in equation (2) that gives the best fit (see section S2 in supplementary material for details). $t_{lockdown}$ can be thought of as the effective date of the lockdown in terms of the data. Throughout the paper, data are presented by date of confirmation, but it needs to be borne in mind that the respective time delays have been taken into account when fitting the model to the data. In the context of identifying $t_{lockdown}$, it is also worth noting that other restrictions were introduced in all the countries before the lockdowns, so the results are not intended to isolate the effects of the lockdowns compared to these other measures. As reported in another study, the close spacing of the interventions meant that their individual effects were not identifiable [13].

The predictive accuracy of the models is evaluated using time series cross-validation [28]. This lets us see how well the two-stage model generalises to unseen data. The metrics used for this evaluation are the root mean squared error (RMSE):

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n_t} (y_i - \hat{y}_i)^2}{n_t}} \quad (3)$$

and mean absolute error (MAE):

$$MAE = \frac{\sum_{i=1}^{n_t} |y_i - \hat{y}_i|}{n_t}. \quad (4)$$

where y represents the actual number of cases, \hat{y} the predicted values and n_t the number of days being treated as test cases.

The results on predictive accuracy are relevant for the final part of the paper which explores the consequences of relaxing the lockdowns. In effect, this amounts to extending the two-stage model to a three-stage version. The two-stage component is used first to learn the pre- and post-lockdown parameters (R_0^{Pre} and R_0^{Post}) and the value of $t_{lockdown}$ automatically from the data. After that, the simulation runs until the specified time of the relaxation where R_0^{Post} is the pre-relaxation value of R_0 and a new post-relaxation value R_0^{Relax} is introduced. The three-stage model can be expressed as a simple extension of the model that replaces equation (2) with

$$\beta(t) = \begin{cases} \beta^{Pre} : & t < t_{lockdown} \\ \beta^{Post} : & t_{lockdown} \leq t < t_{relax} \\ \beta^{Relax} : & t_{relax} \leq t. \end{cases} \quad (5)$$

Values of t_{relax} and R_0^{Relax} can be introduced arbitrarily to model a relaxation to a certain degree at a specified time or, alternatively, their values can be estimated from the data in the same way as $t_{lockdown}$, R_0^{Pre} and R_0^{Post} . The approach employed is first to use the two-stage model to determine $t_{lockdown}$ and then use this value in the three-stage model to learn t_{relax} , R_0^{Pre} , R_0^{Post} and R_0^{Relax} . In fact, this process can be extended further as will be discussed when modelling the US data.

The calculations were carried out using MATLAB and a non-linear curve-fitting function (lsqcurvefit) has been used to find the best fitting parameters E_0 , R_0^{Pre} and R_0^{Post} (and in some cases R_0^{Relax}) simultaneously.

3 Results

This section presents results for each of the six countries. In particular, it includes results for fitting the two-stage model to the number of confirmed cases, predictive accuracy, and relaxations of the lockdowns using the three-stage version of the model. Details on the data used in the study as well as further results on identifying the lockdowns and time delays, sensitivity of the results to changes in parameters, the effect of increasing levels of testing, and estimates of the same parameters based on the number of deaths (and also numbers of hospital patients in the UK) for comparative purposes are presented in supplementary material. Information about day zero, the date the lockdowns were introduced and the proportion of deaths in each country is presented in table 2. Results in sections 3.1 and 3.2 are based on data up to 1st June 2020, while details of the relevant dates are specified for particular results in section 3.3. Note that the US is rather different from the other countries in that lockdowns were introduced at different times in different states whereas in each European country the time of the lockdown can be identified reasonably accurately. This might suggest that the two-stage approach is inappropriate for the US, but as we shall see it still models the US data quite well.

Table 2: Dates for day zero (the first day on which at least 100 confirmed new cases were reported), the lockdowns (see [29–34] and note that dates correspond to their introduction even if they were announced the previous day), and the number of deaths as a percentage of the total number of confirmed cases (based on data up to 22/08/20).

	Day zero	Lockdown	% deaths
France	05/03/20	17/03/20	12.8
Germany	05/03/20	23/03/20	4.0
Italy	27/02/20	10/03/20	13.7
Spain	05/03/20	15/03/20	7.5
UK	10/03/20	24/03/20	12.8
US	06/03/20	Various	3.1

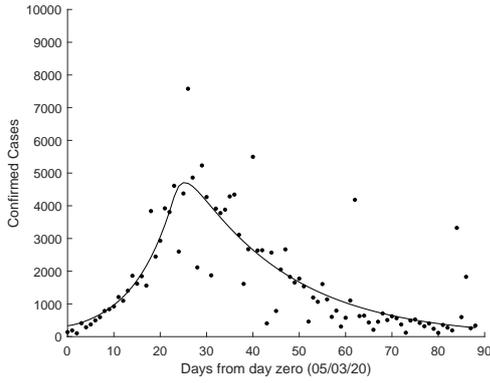
3.1 Fitting the two-stage SEIR model to the data

Figure 1 presents the two-stage SEIR model that gives the best fit to the daily number of confirmed cases following day zero for each country based on data up to 1st June 2020. In all cases, the model fits the data reasonably well and this is quantified by the R^2 values which highlight that the model fits the Italian data best, whereas the fit is poorest for France. For each country, the impact of lockdown is evident and the two-stage model captures the resulting effect on the number of confirmed cases. Despite the fact that all of these countries have eased their respective lockdowns since early May 2020, there is no evidence in the results from the number of cases up to 1st June of an increase in the level of transmission. However, the situation changes with more recent data as we shall see in section 3.3.

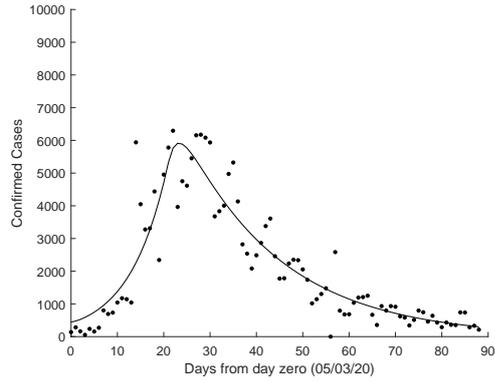
Table 3: Estimates for the pre- and post-lockdown reproduction numbers with 95% confidence intervals.

	R_0^{Pre}	R_0^{Post}	R^2	RMSE	MAE
France	2.02 (1.69-2.35)	0.73 (0.67-0.79)	0.68	891	500
Germany	2.09 (1.83-2.34)	0.70 (0.66-0.74)	0.84	749	508
Italy	2.16 (2.01-2.31)	0.84 (0.82-0.85)	0.94	439	355
Spain	2.42 (2.19-2.66)	0.71 (0.68-0.74)	0.92	707	482
UK	2.03 (1.81-2.25)	0.94 (0.92-0.96)	0.83	637	502
US	2.22 (1.94-2.49)	0.98 (0.96-0.99)	0.88	3774	2635

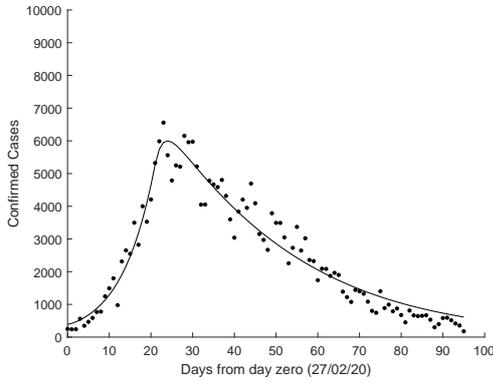
The pre- and post-lockdown reproductive numbers as given by R_0^{Pre} and R_0^{Post} are presented in table 3, together with R^2 values (and RMSE and MAE which are relevant to results on predictive accuracy in section 3.2). It should be noted that it is not the goal of this work to estimate R_0 at the earliest stages of the outbreak of the pandemic in each of the countries. Rather, the pre-lockdown R_0 values, R_0^{Pre} , represent the situation for about two weeks prior to the lockdown in each country. The pre-lockdown values in table 3 are consistent with other results found in the literature [4, 5, 10, 16]. The results are



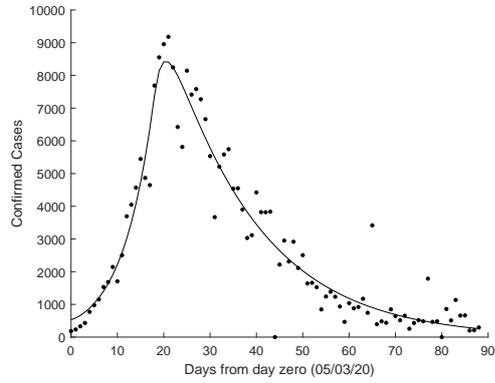
a) France, $R^2 = 0.68$



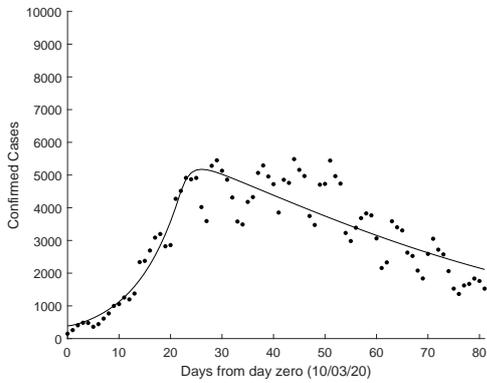
b) Germany, $R^2 = 0.84$



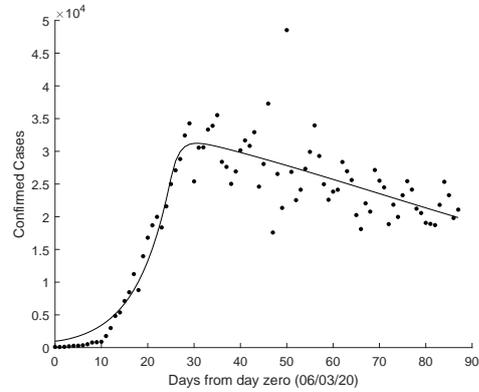
c) Italy, $R^2 = 0.94$



d) Spain, $R^2 = 0.92$



e) UK, $R^2 = 0.83$



d) US, $R^2 = 0.88$

Figure 1: Results obtained by applying the two-stage SEIR model to the daily confirmed cases for each of the six countries. Note that the results for the US are on a different scale.

somewhat lower than those found in the study of European countries by Flaxman *et al* [13], though their results were for initial values whereas the current results relate to the period just before the lockdown as noted above. It also needs to be noted that the results for the R_0^{Pre} and R_0^{Post} values depend to some extent on the choice of parameters used. This issue is explored in section S5 of supplementary material. In terms of post-lockdown values, notice that all the post-lockdown values are below one. This is in agreement with the findings in [13] for European countries and in general the results are similar. For

example, Flaxman *et al* quote results for France of 0.68 and Germany of 0.71, while the results here are 0.73 and 0.70 respectively. The average here over the five European countries is 0.78 whereas Flaxman *et al* report an average of 0.66 for 11 countries. It should also be noted that the results here are based on data on the number of new cases up to 1st June whereas the results in [13] were based on data on the number of deaths up to 4th May. In section S4 of supplementary material, corresponding results are also presented for R_0^{Pre} and R_0^{Post} values obtained by fitting the two-stage model to the number of recorded deaths. While there are some differences between those results and the results in table 3, particularly where the R^2 value is low, the results in table 3 are similar to those based on the number of deaths, especially for R_0^{Post} . This confirms the general picture that all the post-lockdown values are not only lower, but less than one. Hence, in that sense all the lockdowns have been successful, though at 0.94 and 0.98 the estimates for the UK and US values of R_0^{Post} respectively are higher than would have been hoped. According to the results in table 3, Spain’s lockdown was the most successful in terms of reducing the reproductive number by the greatest amount, though overall the number of deaths as a proportion of the number of cases has been lower in Germany and the US than in other countries (see table 2), and Germany has succeeded in keeping the number of deaths much lower than other countries (see figure S1 in supplementary material).

Related to the higher R_0^{Post} value for the UK and US, note that the peak in figure 1 for these countries is less pronounced than it is for the other countries. Also, fitting the model to the number of deaths gives lower values of $R_0^{Post} = 0.84$ (95% CI: 0.80-0.88) for the UK and 0.86 (95% CI: 0.81-0.90) for the US. A possible explanation for the differences between these results and those in table 3 is that the higher values based on the numbers of cases are due to increased testing, which could mask the impact of the lockdown to some extent. The situation in the UK is explored further with an application of the model to UK hospital data in section S10 of supplementary material.

3.2 Predictive accuracy

Assessing predictive accuracy is relevant here since the model is used in section 3.3 to explore the consequences of relaxing the lockdowns and potential second waves. As noted earlier, the approach adopted is that of time series cross-validation. In each case the last 10 data points (i.e. the number of confirmed cases for the 10 days up to 1st June 2020) are used for testing and k -step ahead prediction is used. That is, the model is learned from data up to k days before the day that is to be predicted. The two-stage model is evaluated using the metrics RMSE and MAE.

Table 4 presents results for k -step prediction with values of $k = 5$ and 10. Results for $k = 1$ and $k = 20$ as well as corresponding results for a SIR model are presented in section S6 of supplementary material. It is instructive to compare the values of these metrics for the two-stage model in table 4 with those for all the data for a given country (see table 3). If the results are much poorer on the former than on the latter, that could highlight a potential concern with overfitting and hence for using the model for prediction. Note that the RMSE and MAE values for prediction in table 4 are lower than those in table 3 for France, Germany, Italy, Spain and the US, which is encouraging.

While the prediction results for the UK are higher compared to those in table 3, they are not too

Table 4: Results for k -step ahead prediction for the number of confirmed cases on the 10 days up to 1st June 2020. [†]These results exclude two outliers.

	k -step	SEIR	
	prediction	RMSE	MAE
France [†]	5	157	118
	10	151	112
Germany	5	182	117
	10	184	118
Italy	5	321	298
	10	344	322
Spain	5	365	281
	10	368	282
UK	5	962	934
	10	1149	1118
US	5	2301	1795
	10	2438	1880

dissimilar and the higher values can be explained. In the case of the UK, day zero occurred later than in other countries (see table 2) and it takes longer after the lockdown for the trend in the results to become clear than is the case for the other countries (see figure 1). For both of these reasons, more post-lockdown data are needed for good predictions, but going to higher values of k restricts the number of data points for training and so affects the predictions. Hence, when more post-lockdown data available are used, as they are when it comes to investigating the relaxation of the lockdowns, the predictions should be more reliable. However, the application of the model to UK hospital data is also explored in section S10 of supplementary material to provide further validation.

The main focus here is not simply on maximising predictive accuracy since it may well be possible to do that by ignoring the pre-lockdown phase altogether and just fitting models to the post-lockdown data. Instead, the goal is to evaluate the two-stage SEIR model, which can then provide a basis for extending it to the three-stage version to explore the consequences of relaxing the lockdowns. The results presented so far provide confidence that it captures the lockdown transition and can be used to make reasonable predictions.

3.3 Effect of relaxing the lockdowns

Having fitted the two-stage SEIR model to the data and evaluated its predictive accuracy, it is now extended to explore the potential effects of partially relaxing the lockdowns in the different countries. Just as the lockdowns were represented as a change in the reproductive number at a single point in time, the same assumption is made for relaxing the lockdowns. The idea is to model relaxations by increasing

the reproductive number by a percentage of the difference between the pre- and post-lockdown values, which translates into a corresponding change in the average number of interactions in society compared to the situation during the period before lockdown (see section 4 for further discussion). Three scenarios are considered to start with:

- i) no relaxation - keep the lockdown intact so that R_0^{Relax} remains unchanged at R_0^{Post} ,
- ii) 25% relaxation - $R_0^{Relax} = 0.75 \times R_0^{Post} + 0.25 \times R_0^{Pre}$, and
- iii) 50% relaxation - $R_0^{Relax} = 0.5 \times R_0^{Post} + 0.5 \times R_0^{Pre}$.

Hence, a given percentage relaxation corresponds to increasing R_0^{Post} by that percentage of the difference between R_0^{Pre} and R_0^{Post} . The particular percentages selected are used for illustrative purposes since, as we shall see, there is a significant difference between the results for the two values, with 50% leading to a significant second wave in all cases, while at 25% the numbers flatten out in most cases. Also, these values turn out to be close to the actual data for some countries. Later, we shall see how R_0^{Relax} can be estimated from data.

In an earlier version of this paper, results were presented for relaxations that were assumed to take effect in terms of numbers of cases at the end of May / beginning of June (here it is assumed to be 1st June) [35]. Based on the results for the time delay between infection and confirmation (see supplementary material), this corresponds to the introduction of partial relaxation of the lockdowns from about 20th May. These calculations have been re-run, based on data available up to 12th May, but the results here take account of any subsequent changes that were made retrospectively to the data. Also, results are now included for the UK and US.²

Results are presented in figure 2 for numbers of daily confirmed cases and include estimates up to the end of July. The difference between a 25% and 50% relaxation is dramatic in most cases with the latter leading to a significant increase in the number of cases in all six countries by the end of July. In Italy, the UK and the US such a relaxation was estimated to result in numbers as high or higher than the earlier peak by the end of July. A 25% relaxation was estimated to lead to a significant increase in numbers in the US and to bring a halt to the decline in numbers in other countries.

In the earlier version, there was no evidence to suggest that relaxations introduced up to that point had increased the transmission rate, but in figure 2 subsequent data points until the end of July have been included and it is clear that the situation had changed by that stage. In the case of France, Germany, Spain and the US, these data points are close to the predictions based on the model up to the point at which the different relaxations were introduced. It is equally clear that after that point, the data points for these four countries do not continue to fall in line with the no relaxation scenario. In Germany, the number of cases increased slightly after the time of the relaxation, but otherwise the data up to the end of July remain fairly level and are in line with a 25% relaxation. In France, there was an increase in

²In the earlier version, results for the UK were for hospital data, which are now included in supplementary material. In the results in figure 2, data up to 1st June have been used for the UK since the post-lockdown trend is not clear if only data up to 12th May are used. There are some other changes compared to the earlier version such as a different formulation of the transition rates, σ and γ , but the results are very similar.

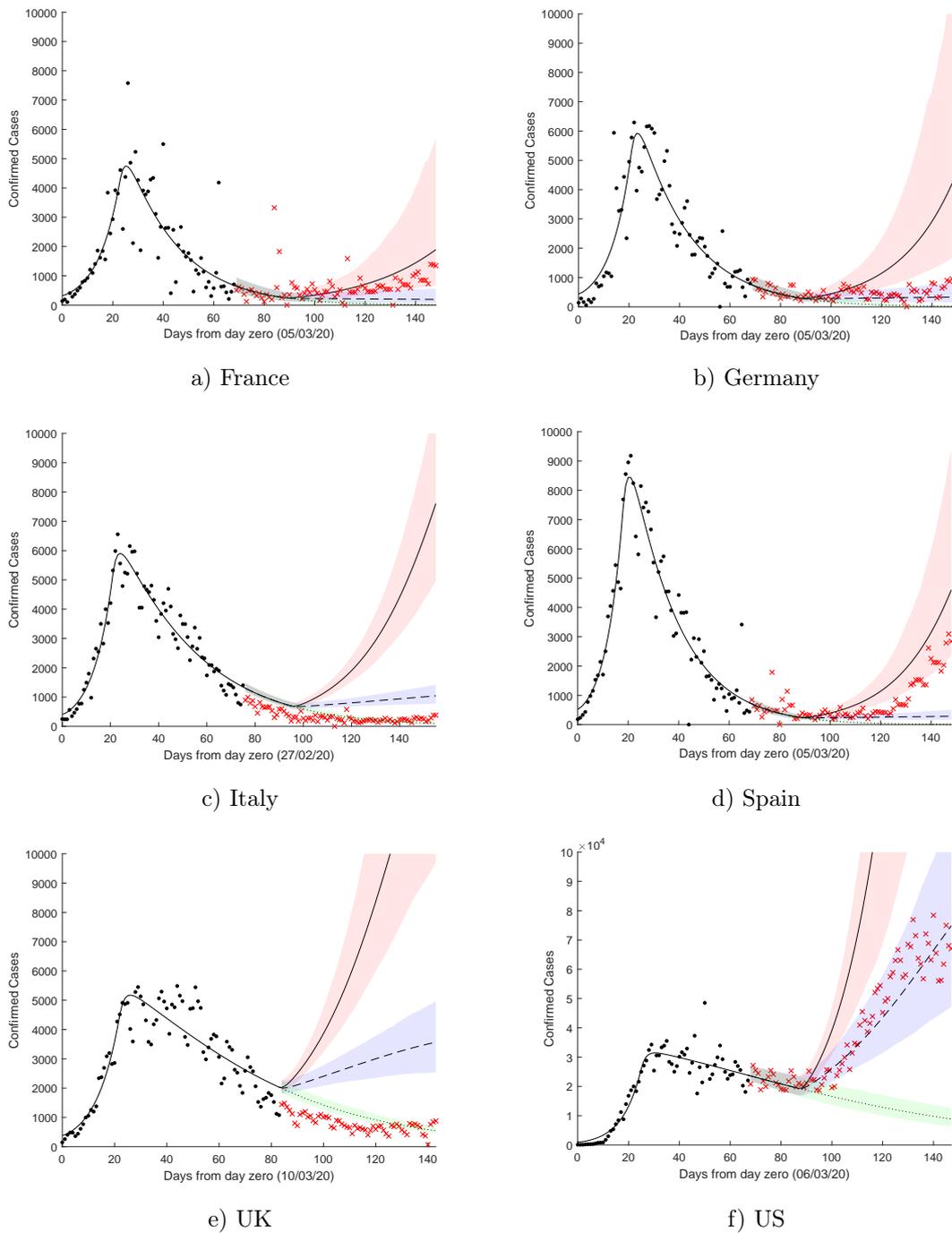


Figure 2: The effect on the daily number of confirmed cases of keeping the lockdown fully in place (\cdots), relaxing it by 25% ($---$) and relaxing it by 50% ($—$). Shaded regions represent 95% confidence intervals. Data points include those from day zero to 12/05/20 (1/06/20 for the UK) used to learn the model (\bullet) and subsequent numbers of cases up to 31/07/20 (\times). In each case the relaxation is assumed to take effect by 01/06/20, which corresponds to the implementation of the relaxation around 20/05/20. Note that the results for the US are on a different scale.

the number of cases slightly below the 50% relaxation level, while in Spain, there was also an increase in numbers, this time more in line with a 50% relaxation, though occurring later than the modelled

relaxation. In the US, the numbers increased dramatically, well above the first peak and in line with a 25% relaxation. The number of cases for Italy and the UK in figure 2 are more in line with the no relaxation results.

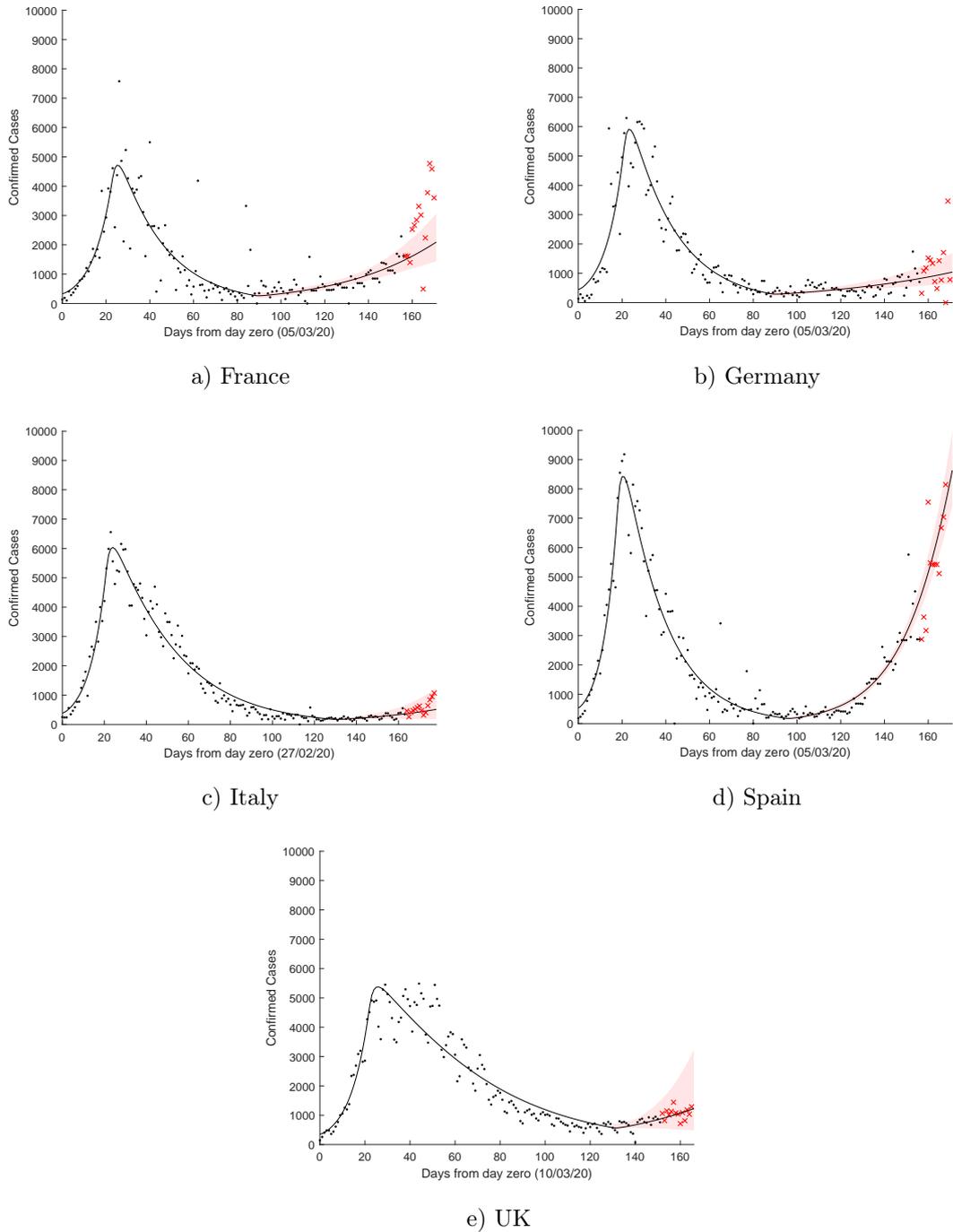


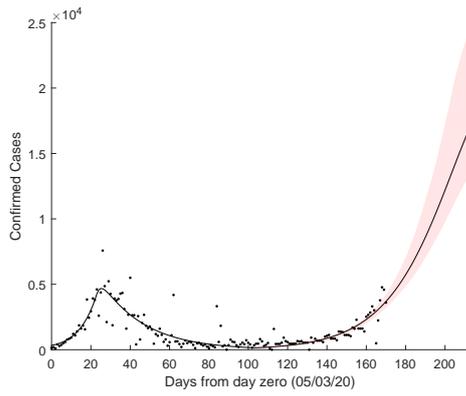
Figure 3: Results obtained by applying the three-stage model to learn the parameters for the time and degree of relaxation from data up to 08/08/20 (●) and compared with subsequent numbers of cases up to 22/08/20 (x). Shaded regions represent 95% confidence intervals.

However, when more data up until 22nd August 2020 are taken into account, it becomes clear (see figure 3) that there have been increases in the numbers of cases in all of the European countries as well

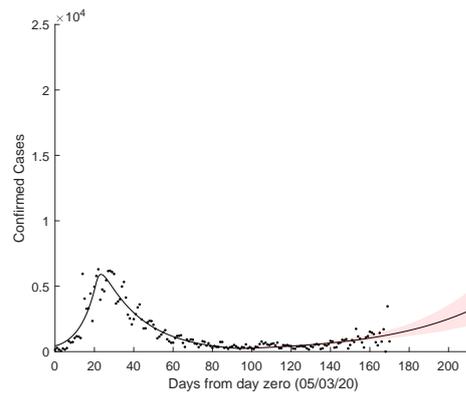
as in the US. (The US will be considered in detail later.) Figure 3 presents results obtained by applying the three-stage model to all five European countries. In contrast to figure 2, where relaxations were introduced arbitrarily at a given point in time to illustrate how this could affect the number of cases, the results in figure 3 were obtained by estimating the time at which the relaxation took effect, t_{relax} , and the resulting reproductive number, R_0^{Relax} . This was achieved by first applying the two-stage model to find $t_{lockdown}$ based on data up to 1st June 2020 (and using a value of ρ based on data to that point) and then applying the three-stage model to find t_{relax} , R_0^{Pre} , R_0^{Post} and R_0^{Relax} based on data up to 8th August (and the corresponding value of ρ). The results are compared with the most recent data up to 22nd August (indicated by red crosses in figure 3) and in general agreement is good with most of the recent data points lying within or close to the 95% confidence interval. The situation in France and Spain is particularly concerning, with numbers of cases already at a similar level to those at the first peak, but the upward trend is also evident in Germany, Italy and the UK.

The above procedure was then repeated using all the available data up to 22nd August 2020 to learn the parameters of the three-stage model. Results corresponding to those in figure 3, but based on the more recent data and extended for a period of six weeks up to 3rd October, are shown in figure 4. The results indicate the potential during this period for dramatic increases in France and Spain with numbers of cases much higher than at the first peak in these countries. These results are extended over a much longer period of time in section S9 of supplementary material together with corresponding results when ρ , the ratio of confirmed to unconfirmed cases, is assumed to increase linearly over time to represent increased levels of testing, rather than kept fixed as it is here. Figure S3 in supplementary material shows that over the period of time shown in figure 4, there is very little difference between the results irrespective of whether ρ is kept fixed or increases over time, but for longer periods of time the latter approach results in much higher peaks. While a lot of caution is needed with results over longer timescales, they do nevertheless indicate the potential for second waves in all five European countries. In all cases, the results suggest second waves that last longer than the first one with peaks that are significantly higher in terms of the number of cases. These higher numbers are partially due to increased testing levels, but even taking that into account (see the discussion in supplementary material), the results suggest significant increases in levels of transmission. It is important to emphasise that these results assume that current trends continue without any further restrictions (or relaxations) being introduced. Needless to say, new restrictions would be implemented if numbers of cases rise significantly. In fact, the hope would be that restrictions such as those reintroduced in France [36] and Spain [37] will bring about a reduction in the number of cases.

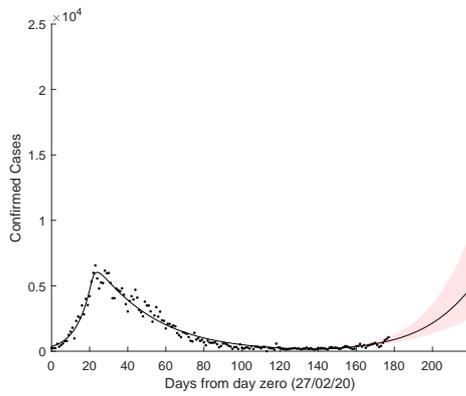
The estimated parameters on which these results are based are presented in table 5. Note that in all five cases, the percentage relaxation is found to be above 30% with R_0^{Relax} values ranging from 1.19 in Germany to 1.52 in Spain. The effective date of the relaxation ranges from 5th June 2020 for Germany to 17th July for the UK. It needs to be borne in mind that identifying the relaxation to a single date is an artefact of the general approach adopted here of having a fixed reproductive number in each period (before lockdown, after lockdown but before relaxation, and after relaxation). Nevertheless, it should give some indication of the time when relaxing the lockdowns started to give rise to increases in numbers



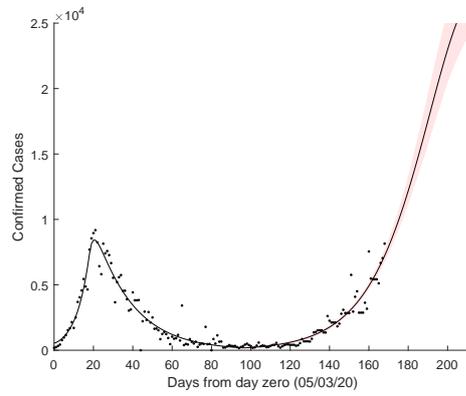
a) France



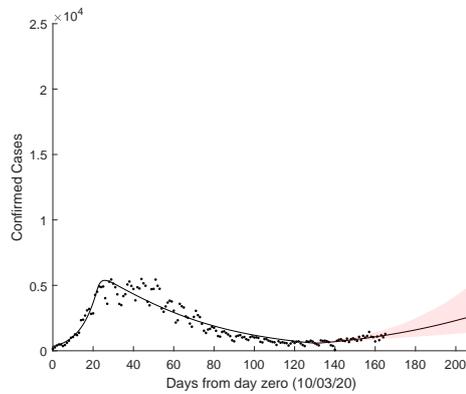
b) Germany



c) Italy



d) Spain



e) UK

Figure 4: As for figure 3, but now parameters are learned from data up to 22/08/20 and results are presented over the following six weeks up to 3/10/20.

of cases (taking into account a time lag which is typically around 10 days, see supplementary material) and hence potentially of relaxation measures that might need to be reconsidered. Again, it should be noted that these results are based on a fixed value of ρ , but similar values of t_{relax} and percentage relaxation are found when increasing values of ρ are used (see section S9 in supplementary material for discussion).

It should be noted that these results depend not only on ρ , but also on other parameters used in

Table 5: Parameter estimates for the application of the three-stage model on data up to 22/08/20.

	t_{relax}	R_0^{Relax}	% relaxation
France	15/06/20	1.46 (1.40-1.52)	57
Germany	05/06/20	1.19 (1.14-1.23)	35
Italy	12/07/20	1.49 (1.40-1.57)	49
Spain	08/06/20	1.52 (1.49-1.55)	47
UK	17/07/20	1.28 (1.20-1.36)	31

the model. Sensitivity analysis of the results involved considering different values for the parameters for the latent period, infectious period and mortality rate and results are presented in section S8 of supplementary material. These results confirm the general picture presented here. However, once again the peaks of the second waves can depend a lot on the mortality rate, which is not surprising since the mortality rate affects the numbers of people modelled as having had the virus, and hence also the number who remain susceptible. Further calculations suggest that the peak is often about twice as high when the mortality rate is doubled from 0.66% to 1.32% and about half as high when it is reduced to 0.33%. So a lot of caution is needed when it comes to the peaks of second waves, but the possibility of second waves is robust with the changes in parameters that were considered.

For some of the European countries, it is only with the most recent data that the trend becomes clearer. By contrast, a second surge occurred in the US much earlier. By fitting the three-stage model to data up to 22nd June 2020, t_{relax} is found to be 92 days after day zero, i.e. 6th June, and the estimated value for the reproductive number is $R_0^{Relax} = 1.33$ (95% CI: 1.24-1.41), which corresponds to a 29% relaxation. Results are presented in figure 5a, which also includes subsequent data up to 8th August (indicated by red crosses). It is evident that there was good agreement with the data for a period of over a month with the data points lying within or very close to the confidence interval.

However, it is also clear that the data shown in figure 5a indicate that the number of cases in the US had already peaked for a second time. This is consistent with restrictions having been reintroduced in various US states [38]. In principle it should be possible to identify the time at which these restrictions took effect by the same approach used in the two-stage model to identify the time of the initial lockdown. To investigate this, the model was extended further, essentially to a four-stage model. The two-stage model was used to identify $t_{lockdown}$ and then the three-stage model for t_{relax} , before using these values as input into the four-stage model to identify the time new restrictions relating to the second peak became effective. Using data up to 8th August 2020, the resulting date from this approach is 129 days after day zero, i.e. 13th July, which would correspond with restrictions being introduced around the beginning of July. The results also give a R_0^{Relax} value after this peak of 0.99 (95% CI: 0.97-1.01), which is very similar to the result obtained for R_0^{Post} after the first peak. Projected results until 3rd October 2020 (corresponding to the results in figure 4) are shown in figure 5b and are in agreement with the most recent data points from 9th to 22nd August (indicated by red crosses).

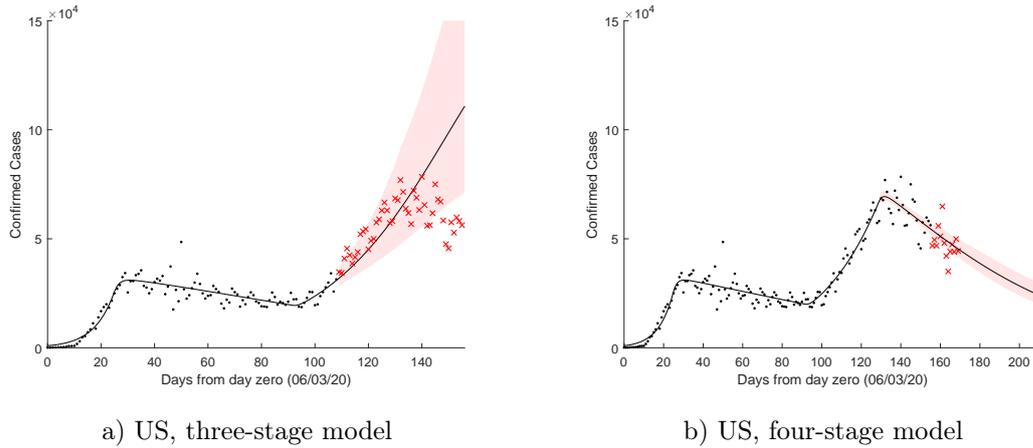


Figure 5: a) Results obtained by applying the three-stage model to US data on the number of cases up to 22/06/20 (\bullet) and then compared with data up to 08/08/20 (\times). b) Results from applying the four-stage model to US data up to 08/08/20 (\bullet) and compared with data up to 22/08/20 (\times), with results presented over the following six weeks up to 3/10/20.

Clearly, caution is needed when attempting to model the number of cases of COVID-19 in future weeks and months, particularly when it comes to details of the second waves. More caution is needed with the results for the European countries for two reasons. First of all, at time of writing the daily number of deaths is much lower in the European countries than in the US, so the increased number of cases could partly be due to other factors such as changes in testing rates, for example (though see section S9 in supplementary material). However, any such change would occur in data on number of deaths later than in the number of cases and the most recent data on numbers of deaths show increases in France and Spain. Second, some of the increases could be due to local factors and may not necessarily reflect what is going on in a country as a whole. Nevertheless, there is a clear upward trend in all of the European countries, which is a cause for concern, especially given the scale of the increases in France and Spain and the potential for significant second waves in all the countries.

More generally, the results highlight the ability of the three-stage model to investigate not only lockdowns, but also relaxations of them, including the ability to detect relaxations of a certain degree. Furthermore, the results suggest that if the current levels of relaxation in European countries were to continue unchecked, the consequences could be very serious.

4 Discussion

The two-stage model has a single reproductive number before lockdown and another one afterwards and it does not divide the population into separate subgroups (e.g. spatially or by age). As such, the simplicity of the model has advantages, but also limitations. In terms of fitting the model to the data and extending it to the three-stage version to make predictions, it has advantages because it is able to keep the number of parameters to a minimum. This can help avoid overfitting the model to the data, which can occur if too many parameters need to be estimated, or else having to specify too many parameters

that may be difficult to justify.

However, an important limitation also arises from the simplicity of the approach since it cannot be used to model interactions between different age groups within society or specific relaxations such as allowing pubs and restaurants to re-open. Instead, it models society as a whole and so would need to be complemented by other work that provides more detailed models of society [2, 8, 39]. This point is also closely related to the way in which relaxations have been modelled as a percentage increase in the transmission rate. While this gives a general idea about the potential impact of relaxations and can be easily interpreted since it relates to the levels of interactions in society, it is also interesting to explore how it might relate to specific measures.

Of course, even with more detailed models, it is difficult to estimate the impact of specific measures since many assumptions need to be made. However, contact matrices can be constructed to represent the interactions that occur between different age groups in society including interactions in the household, school, workplace and community [2, 8, 39]. Based on estimates about the relative impact on these matrices of different intervention strategies, simulations can then be carried out to explore the consequences. For example, in their study of interventions in the UK, Davies *et al* [2] estimate that the combined effect of various measures including school closures, physical distancing, shielding of older people and self-isolation just before the lockdown would have had no effect on household contacts, but would have reduced school contacts to zero, and work contacts and other community contacts to slightly under 50% (25% for those over 70 years old and 50% for others) of their baseline level. They also estimate that the lockdown would have further reduced work contacts and other community contacts to 10% of the baseline level.

Suppose we were to consider relaxing all the other components of the lockdown, but keep the specific restrictions mentioned above in place. Typically about one third of transmission is assumed to occur in the household, a further third in schools and workplaces and a final third in the community [39]. Since there is no difference between the lockdown and proposed relaxation scenario in terms of household contacts, we can focus on schools, workplaces and the community, so let us assume that 75% of the relevant transmission is due to workplaces and community contacts. Based on the estimates that have been noted, the contacts would increase from 10% to almost 50% in each of these categories. This corresponds to an increase of around 30% with respect to the baseline in terms of contact rates. (An increase from 10% to 50% would be an increase of $40/90$ compared to the baseline for these components, which are assumed to constitute 75% of the relevant transmission, and so it would be a $75\% \times 4/9 = 33.3\%$ increase with respect to the baseline.)

However, recall that the current approach does not involve relaxations relative to the baseline (before any measures were in place), but relative to the situation for several weeks prior to the lockdown. In terms of workplace and the community, many of the measures were not introduced until about a week before the lockdown in the UK and schools were only closed on the Friday before the lockdown. Assuming that the contacts in the workplace and community were reduced to 75% of baseline over the pre-lockdown period, then the proposed relaxation would correspond to a relaxation of over 40%. While this is a very rough estimate, it is similar to the levels of relaxation found in the various European countries here (see

table 5). This is consistent with the finding in the earlier study that stricter measures were necessary to bring R_0 near or below one [2], while other work showed that the early termination of strict social distancing measures in the US could also lead to a second wave [40]. Other relaxation scenarios could be considered, but the discussion here gives an indication of how percentage relaxations can be related to more specific proposals.

The assumption in the discussion so far has been that relaxations consist in removing or easing restrictions that have been introduced to some degree. However, other mitigation strategies could give rise to more scope for relaxation. For example, a study of contact tracing explored different percentages of contacts traced to investigate the effectiveness of the approach in containing COVID-19 for different levels of transmission before symptom onset, delays from symptom onset to isolation, and R_0 values [41]. While that work was in the context of a new outbreak, it would be interesting to explore to what extent higher degrees of success in contact tracing might permit higher degrees of relaxation.

Despite the challenges of relating percentage lockdowns to specific measures, the application of the three-stage version of the model to the six countries here suggests that a more data-driven approach may be the best way to proceed. The model can be used to detect the percentage relaxation in a given country and the date at which it started to take effect. Consequently, it should be possible to relate these measures to specific relaxations that were introduced. For example, the dates identified for the relaxations in France and the UK (see table 5) appear to correspond to significant relaxations, including the opening of pubs and restaurants, introduced in early June [42] and early July [43] respectively, allowing for a time lag. Clearly, more work would be needed to explore possible factors across a number of countries.

This provides one direction for future research. Other directions include developments to address limitations of the current model. The model has been fitted to the data for numbers of confirmed cases, numbers of deaths or numbers of hospital patients, allowing for time delays, but these delays could be included explicitly in the model to allow, for example, for variation in time between confirmation and death when fitting to the number of deaths. Also, while the results based on the number of deaths and hospital patients provide a useful comparison since they are less likely to be affected by changing levels of testing, for example, it would also be interesting to integrate all the data to obtain a single estimate. Another direction concerns the modelling of asymptomatic cases. While the current model distinguishes between confirmed and unconfirmed cases, it does not do so between symptomatic and asymptomatic cases. As discussed in section 2, this does not play a major role when the ratio of confirmed to unconfirmed cases is kept fixed, but it does become more important when this ratio increases with time. This issue is addressed in section S9 of supplementary material, where two different values of α are considered to see the effect of lower transmission for the unconfirmed group. However, future work could apply such values only to a distinct asymptomatic group and potentially also consider a different value of γ for asymptomatic cases. Another limitation arises from the fact that the model does not consider vital dynamics or migration. While this is reasonable for short term applications of the model, such factors would be important when the model is applied over longer periods of time. Furthermore, given the importance of vaccination in the context of COVID-19, it would be interesting to include vaccination at

various levels of availability and efficacy into the model.

5 Conclusion

A two-stage SEIR model has been fitted to data on the daily numbers of confirmed cases of COVID-19 in France, Germany, Italy, Spain, the UK and the US. According to the results, while the lockdowns in all six countries were successful to greater or lesser extents, Spain saw the greatest reduction in the reproductive number. Validation of the model was carried out by applying it to data on the number of deaths (and numbers of hospital patients with COVID-19 in the UK) and its predictive performance was evaluated using time series cross-validation.

The model was extended to a three-stage version that was used to investigate various levels of relaxation. Results based on data up to 12th May 2020 suggested a 50% relaxation could lead to large second waves in each country if no further measures were put in place, while a 25% relaxation could lead to a second wave in the US and could halt the decline in numbers in other countries. However, more recent data show that the number of cases has increased in all six countries. Applying the three-stage model to each country, data from August 2020 have been shown to correspond to results from models learned from earlier data. The results indicate that relaxations took effect in terms of increasing numbers of cases with dates ranging from early June in some countries to mid-July in other countries. For the European countries, results suggest relaxations ranging from 31% to 57% are underway and if current trends continue unchecked could lead to significant second waves that last longer than the corresponding earlier waves. In the case of the US, where the number of cases has already peaked for a second time, an extended version of the model suggests that the level of transmission may now be similar to that after the first peak.

While caution is needed with some of the results, particularly when it comes to modelling second waves, the results from the US highlight the serious consequences if levels of relaxation are too high. The results presented in this paper suggest that this is now the case in the European countries that have been considered and that lower levels of transmission are needed. Also, since the model applies to society as a whole, particular measures would need to be kept in place to protect more vulnerable groups. More generally, however, a lot of caution is needed if further waves are to be avoided.

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Appendix A. Supplementary material

Supplementary material related to this article can found online at <https://doi.org/10.1016/j.mbs.2020.108472>.

References

- [1] W. O. Kermack and A. G. McKendrick, “A contribution to the mathematical theory of epidemics,” *Proceedings of the Royal Society of London A*, vol. 115, pp. 700–721, 1927.
- [2] N. G. Davies, A. J. Kucharski, R. M. Eggo, A. Gimma, W. J. Edmunds, T. Jombart, K. O’Reilly, A. Endo, J. Hellewell, E. S. Nightingale, *et al.*, “Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study,” *The Lancet Public Health*, 2020. doi: [https://doi.org/10.1016/S2468-2667\(20\)30133-X](https://doi.org/10.1016/S2468-2667(20)30133-X).
- [3] Y. Fang, Y. Nie, and M. Penny, “Transmission dynamics of the COVID-19 outbreak and effectiveness of government interventions: A data-driven analysis,” *Journal of Medical Virology*, vol. 92, no. 6, pp. 645–659, 2020.
- [4] A. J. Kucharski, T. W. Russell, C. Diamond, Y. Liu, J. Edmunds, S. Funk, R. M. Eggo, F. Sun, M. Jit, J. D. Munday, *et al.*, “Early dynamics of transmission and control of COVID-19: a mathematical modelling study,” *The Lancet Infectious Diseases*, 2020.
- [5] R. Li, S. Pei, B. Chen, Y. Song, T. Zhang, W. Yang, and J. Shaman, “Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (sars-cov-2),” *Science*, vol. 368, no. 6490, pp. 489–493, 2020.
- [6] Q. Lin, S. Zhao, D. Gao, Y. Lou, S. Yang, S. S. Musa, M. H. Wang, Y. Cai, W. Wang, L. Yang, and D. He, “A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action,” *International Journal of Infectious Diseases*, vol. 93, pp. 211–216, 2020.
- [7] K. Y. Ng and M. M. Gui, “Covid-19: Development of a robust mathematical model and simulation package with consideration for ageing population and time delay for control action and resusceptibility,” *Physica D: Nonlinear Phenomena*, vol. 411, p. 132599, 2020.
- [8] K. Prem, Y. Liu, T. W. Russell, A. J. Kucharski, R. M. Eggo, N. Davies, S. Flasche, S. Clifford, C. A. B. Pearson, J. D. Munday, *et al.*, “The effect of control strategies to reduce social mixing on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study,” *The Lancet Public Health*, 2020. doi: [https://doi.org/10.1016/S2468-2667\(20\)30073-6](https://doi.org/10.1016/S2468-2667(20)30073-6).
- [9] B. Tang, X. Wang, Q. Li, N. L. Bragazzi, S. Tang, Y. Xiao, and J. Wu, “Estimation of the transmission risk of the 2019-ncov and its implication for public health interventions,” *Journal of Clinical Medicine*, vol. 9, no. 2, 2020.

- [10] J. T. Wu, K. Leung, and G. M. Leung, “Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study,” *The Lancet*, vol. 395, no. 10225, pp. 689 – 697, 2020.
- [11] Z. Yang, Z. Zeng, K. Wang, S.-S. Wong, W. Liang, M. Zanin, P. Liu, X. Cao, Z. Gao, Z. Mai, *et al.*, “Modified SEIR and AI prediction of the epidemics trend of COVID-19 in China under public health interventions,” *Journal of Thoracic Disease*, vol. 12, no. 3, 2020.
- [12] M. A. Acuña-Zegarra, M. Santana-Cibrian, and J. X. Velasco-Hernandez, “Modeling behavioral change and COVID-19 containment in Mexico: A trade-off between lockdown and compliance,” *Mathematical Biosciences*, vol. 325, p. 108370, 2020.
- [13] S. Flaxman, S. Mishra, A. Gandy, H. J. T. Unwin, T. A. Mellan, H. Coupland, C. Whittaker, H. Zhu, T. Berah, J. W. Eaton, *et al.*, “Estimating the number of infections and the impact of nonpharmaceutical interventions on COVID-19 in Europe,” *Nature*, 2020. doi: <https://doi.org/10.1038/s41586-020-2405-7>.
- [14] O. Diekmann, J. Heesterbeek, and M. Roberts, “The construction of next-generation matrices for compartmental epidemic models,” *Journal of the Royal Society, Interface / the Royal Society*, vol. 7, pp. 873–85, 11 2009.
- [15] S. A. Lauer, K. H. Grantz, Q. Bi, F. K. Jones, Q. Zheng, H. R. Meredith, A. S. Azman, N. G. Reich, and J. Lessler, “The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application,” *Annals of Internal Medicine*, 2020. doi: <https://doi.org/10.7326/M20-0504>.
- [16] Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, R. Ren, K. S. Leung, E. H. Lau, J. Y. Wong, *et al.*, “Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia,” *New England Journal of Medicine*, vol. 382, no. 13, pp. 1199–1207, 2020.
- [17] N. Linton, T. Kobayashi, Y. Yang, K. Hayashi, A. Akhmetzhanov, S.-M. Jung, B. Yuan, R. Kinoshita, and H. Nishiura, “Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: A statistical analysis of publicly available case data,” *Journal of Clinical Medicine*, vol. 9, no. 2, p. 538, 2020.
- [18] C. G. McAloon, A. Collins, K. Hunt, A. Barber, A. Byrne, F. Butler, M. Casey, J. M. Griffin, E. Lane, D. McEvoy, *et al.*, “The incubation period of covid-19: A rapid systematic review and meta-analysis of observational research,” *medRxiv*, 2020. doi: [10.1101/2020.04.24.20073957](https://doi.org/10.1101/2020.04.24.20073957).
- [19] P. Yu, J. Zhu, Z. Zhang, and Y. Han, “A Familial Cluster of Infection Associated With the 2019 Novel Coronavirus Indicating Possible Person-to-Person Transmission During the Incubation Period,” *The Journal of Infectious Diseases*, vol. 221, pp. 1757–1761, 02 2020.
- [20] G. Qian, N. Yang, A. H. Y. Ma, L. Wang, G. Li, X. Chen, and X. Chen, “COVID-19 Transmission Within a Family Cluster by Presymptomatic Carriers in China,” *Clinical Infectious Diseases*, 03 2020. ciaa316.

- [21] A. W. Byrne, D. McEvoy, A. Collins, K. Hunt, M. Casey, A. Barber, F. Butler, J. Griffin, E. Lane, C. McAloon, K. O'Brien, P. Wall, K. Walsh, and S. More, "Inferred duration of infectious period of sars-cov-2: rapid scoping review and analysis of available evidence for asymptomatic and symptomatic covid-19 cases," *medRxiv*, 2020. doi: 10.1101/2020.04.25.20079889.
- [22] F. Brauer, C. Castillo-Chavez, and Z. Feng, *Mathematical Models in Epidemiology*. New York: Springer-Verlag, 2019.
- [23] M. Casey, J. Griffin, C. G. McAloon, A. W. Byrne, J. M. Madden, D. McEvoy, A. B. Collins, K. Hunt, A. Barber, F. Butler, *et al.*, "Estimating pre-symptomatic transmission of covid-19: a secondary analysis using published data," *medRxiv*, 2020. doi: 10.1101/2020.05.08.20094870.
- [24] X. He, E. Lau, P. Wu, X. Deng, J. Wang, X. Hao, Y. Lau, J. Y. Wong, Y. Guan, X. Tan, X. Mo, Y. Chen, B. Liao, W. Chen, F. Hu, Q. Zhang, M. Zhong, Y. Wu, L. Zhao, and G. Leung, "Temporal dynamics in viral shedding and transmissibility of covid-19," *Nature Medicine*, vol. 26, pp. 672–675, 2020.
- [25] H.-Y. Cheng, S.-W. Jian, D.-P. Liu, T.-C. Ng, W.-T. Huang, H.-H. Lin, *et al.*, "High transmissibility of covid-19 near symptom onset," *medRxiv*, 2020. doi: 10.1101/2020.03.18.20034561.
- [26] J. M. Griffin, A. B. Collins, K. Hunt, D. McEvoy, M. Casey, A. W. Byrne, C. G. McAloon, A. Barber, E. A. Lane, and S. J. More, "A rapid review of available evidence on the serial interval and generation time of covid-19," *medRxiv*, 2020. doi: 10.1101/2020.05.08.20095075.
- [27] R. Verity, L. C. Okell, I. Dorigatti, P. Winskill, C. Whittaker, N. Imai, G. Cuomo-Dannenburg, H. Thompson, P. G. T. Walker, H. Fu, *et al.*, "Estimates of the severity of coronavirus disease 2019: a model-based analysis," *The Lancet Infectious Diseases*, 2020.
- [28] R. Hyndman and G. Athanasopoulos, *Forecasting: principles and practice*. OTexts: Melbourne, Australia, 3rd ed., 2019. OTexts.com/fpp3. Accessed on 06/06/20.
- [29] Wikipedia, "National responses to the COVID-19 pandemic," 2020. https://en.wikipedia.org/wiki/National_responses_to_the_COVID-19_pandemic, Last accessed: 06/06/2020.
- [30] Independent, "Coronavirus: France imposes 15-day lockdown and mobilises 100,000 police to enforce restrictions," 2020. <https://www.independent.co.uk/news/world/europe/coronavirus-france-lockdown-cases-update-covid-19-macron-a9405136.html>, Last accessed: 28/07/20.
- [31] BBC News, "Coronavirus: Germany tightens curbs and bans meetings of more than two," 2020. <https://www.bbc.co.uk/news/world-europe-51999080>: Last accessed: 28/07/2020.
- [32] CNN, "All of Italy is in lockdown as coronavirus cases rise," 2020. <https://edition.cnn.com/2020/03/09/europe/coronavirus-italy-lockdown-intl/index.html>, Last accessed: 28/07/20.

- [33] Politico, “Spain goes into lockdown,” 2020. <https://www.politico.eu/article/coronavirus-spain-lockdown/>, Last accessed: 28/07/20.
- [34] Gov.UK, “Prime Minister’s statement on coronavirus (COVID-19): 23 March 2020,” 2020. <https://www.gov.uk/government/speeches/pm-address-to-the-nation-on-coronavirus-23-march-2020>, Last accessed: 28/07/20.
- [35] D. H. Glass, “European lockdowns and the consequences of relaxation during the covid-19 pandemic,” *medRxiv*, 2020. doi: 10.1101/2020.05.19.20106542, version 1, <https://www.medrxiv.org/content/10.1101/2020.05.19.20106542v1.full.pdf>.
- [36] Independent, “Coronavirus: France escalates response as outbreak hits ‘tipping point’,” 2020. <https://www.independent.co.uk/news/world/europe/coronavirus-france-cases-deaths-covid-tipping-point-a9666846.html>, Last accessed: 25/08/20.
- [37] Politico, “Spain bans smoking, shuts nightclubs under new coronavirus restrictions,” 2020. <https://www.politico.eu/article/spain-bans-smoking-shuts-nightclubs-under-new-coronavirus-restrictions/>, Last accessed: 25/08/20.
- [38] CNN, “Some US states return to previous restrictions to slow surge of coronavirus cases,” 2020. <https://edition.cnn.com/2020/06/29/health/us-coronavirus-monday/index.html>, Last accessed: 28/07/20.
- [39] N. M. Ferguson, D. Laydon, G. Nedjati-Gilani, *et al.*, “Impact of non-pharmaceutical interventions (NPIs) to reduce COVID-19 mortality and healthcare demand,” 2020. Imperial College London (16-03-2020), doi: <https://doi.org/10.25561/77482>.
- [40] C. N. Ngonghala, E. Iboi, S. Eikenberry, M. Scotch, C. R. MacIntyre, M. H. Bonds, and A. B. Gumel, “Mathematical assessment of the impact of non-pharmaceutical interventions on curtailing the 2019 novel Coronavirus,” *Mathematical Biosciences*, vol. 325, p. 108364, 2020.
- [41] J. Hellewell, S. Abbott, A. Gimma, N. I. Bosse, C. I. Jarvis, T. W. Russell, J. D. Munday, A. J. Kucharski, W. J. Edmunds, F. Sun, *et al.*, “Feasibility of controlling covid-19 outbreaks by isolation of cases and contacts,” *The Lancet Global Health*, vol. 8, no. 4, pp. e488–e496, 2020.
- [42] France 24, “France begins ‘Phase II’ of easing lockdown measures as coronavirus abates,” 2020. <https://www.france24.com/en/20200602-france-lifts-more-covid-19-restrictions-what-you-need-to-know-for-phase-ii>, Last accessed: 25/08/20.
- [43] Insitute for Government, “Coronavirus lockdown rules in each part of the UK,” 2020. <https://www.instituteforgovernment.org.uk/explainers/coronavirus-lockdown-rules-four-nations-uk>, Last accessed: 25/08/20.