

Estimating the number of infections and the impact of non-pharmaceutical interventions on COVID-19 in 11 European countries

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Summary

Following the emergence of a novel coronavirus (SARS-CoV-2) and its spread outside of China, Europe is now experiencing large epidemics. In response, many European countries have implemented unprecedented non-pharmaceutical interventions including case isolation, the closure of schools and universities, banning of mass gatherings and/or public events, and most recently, widescale social distancing including local and national lockdowns.

In this report, we use a semi-mechanistic Bayesian hierarchical model to attempt to infer the impact of these interventions across 11 European countries. Our methods assume that changes in the reproductive number – a measure of transmission - are an immediate response to these interventions being implemented rather than broader gradual changes in behaviour. Our model estimates these changes by calculating backwards from the deaths observed over time to estimate transmission that occurred several weeks prior, allowing for the time lag between infection and death.

One of the key assumptions of the model is that each intervention has the same effect on the reproduction number across countries and over time. This allows us to leverage a greater amount of data across Europe to estimate these effects. It also means that our results are driven strongly by the data from countries with more advanced epidemics, and earlier interventions, such as Italy and Spain. We find that the slowing growth in daily reported deaths in Italy is consistent with a significant impact of interventions implemented several weeks earlier. In Italy, we estimate that the effective reproduction number, R_t , dropped to close to 1 around the time of lockdown (11th March), although with a high level of uncertainty.

Overall, we estimate that countries have managed to reduce their reproduction number. Our estimates have wide credible intervals and contain 1 for countries that have implemented all interventions considered in our analysis. This means that the reproduction number may be above or below this value. With current interventions remaining in place to at least the end of March, we estimate that interventions across all 11 countries will have averted 59,000 deaths up to 31 March [95% credible interval 21,000-120,000]. Many more deaths will be averted through ensuring that interventions remain in place until transmission drops to low levels. We estimate that, across all 11 countries between 7 and 43 million individuals have been infected with SARS-CoV-2 up to 28th March, representing between 1.88% and 11.43% of the population. The proportion of the population infected

to date – the attack rate - is estimated to be highest in Spain followed by Italy and lowest in Germany and Norway, reflecting the relative stages of the epidemics.

Given the lag of 2-3 weeks between when transmission changes occur and when their impact can be observed in trends in mortality, for most of the countries considered here it remains too early to be certain that recent interventions have been effective. If interventions in countries at earlier stages of their epidemic, such as Germany or the UK, are more or less effective than they were in the countries with advanced epidemics, on which our estimates are largely based, or if interventions have improved or worsened over time, then our estimates of the reproduction number and deaths averted would change accordingly. It is therefore critical that the current interventions remain in place and trends in cases and deaths are closely monitored in the coming days and weeks to provide reassurance that transmission of SARS-Cov-2 is slowing.

SUGGESTED CITATION

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1 Introduction

Following the emergence of a novel coronavirus (SARS-CoV-2) in Wuhan, China in December 2019 and its global spread, large epidemics of the disease, caused by the virus designated COVID-19, have emerged in Europe. In response to the rising numbers of cases and deaths, and to maintain the capacity of health systems to treat as many severe cases as possible, European countries, like those in other continents, have implemented or are in the process of implementing measures to control their epidemics. These large-scale non-pharmaceutical interventions vary between countries but include social distancing (such as banning large gatherings and advising individuals not to socialize outside their households), border closures, school closures, measures to isolate symptomatic individuals and their contacts, and large-scale lockdowns of populations with all but essential internal travel banned. Understanding firstly, whether these interventions are having the desired impact of controlling the epidemic and secondly, which interventions are necessary to maintain control, is critical given their large economic and social costs.

The key aim of these interventions is to reduce the effective reproduction number, R_t , of the infection, a fundamental epidemiological quantity representing the average number of infections, at time t , per infected case over the course of their infection. If R_t is maintained at less than 1, the incidence of new infections decreases, ultimately resulting in control of the epidemic. If R_t is greater than 1, then infections will increase (dependent on how much greater than 1 the reproduction number is) until the epidemic peaks and eventually declines due to acquisition of herd immunity.

In China, strict movement restrictions and other measures including case isolation and quarantine began to be introduced from 23rd January, which achieved a downward trend in the number of confirmed new cases during February, resulting in zero new confirmed indigenous cases in Wuhan by March 19th. Studies have estimated how R_t changed during this time in different areas of China from around 2-4 during the uncontrolled epidemic down to below 1, with an estimated 7-9 fold decrease in the number of daily contacts per person.^{1,2} Control measures such as social distancing, intensive testing, and contact tracing in other countries such as Singapore and South Korea have successfully reduced case incidence in recent weeks, although there is a risk the virus will spread again once control measures are relaxed.^{3,4}

The epidemic began slightly later in Europe, from January or later in different regions.⁵ Countries have implemented different combinations of control measures and the level of adherence to government recommendations on social distancing is likely to vary between countries, in part due to different levels of enforcement.

Estimating reproduction numbers for SARS-CoV-2 presents challenges due to the high proportion of infections not detected by health systems^{1,6,7} and regular changes in testing policies, resulting in different proportions of infections being detected over time and between countries. Most countries so far only have the capacity to test a small proportion of suspected cases and tests are reserved for severely ill patients or for high-risk groups (e.g. contacts of cases). Looking at case data, therefore, gives a systematically biased view of trends.

An alternative way to estimate the course of the epidemic is to back-calculate infections from observed deaths. Reported deaths are likely to be more reliable, although the early focus of most surveillance systems on cases with reported travel histories to China may mean that some early deaths will have been missed. Whilst the recent trends in deaths will therefore be informative, there is a time lag in observing the effect of interventions on deaths since there is a 2-3-week period between infection, onset of symptoms and outcome.

In this report, we fit a novel Bayesian mechanistic model of the infection cycle to observed deaths in 11 European countries, inferring plausible upper and lower bounds (Bayesian credible intervals) of the total populations infected (attack rates), case detection probabilities, and the reproduction number over time (R_t). We fit the model jointly to COVID-19 data from all these countries to assess whether there is evidence that interventions have so far been successful at reducing R_t below 1, with the strong assumption that particular interventions are achieving a similar impact in different countries and that the efficacy of those interventions remains constant over time. The model is informed more strongly by countries with larger numbers of deaths and which implemented interventions earlier, therefore estimates of recent R_t in countries with more recent interventions are contingent on similar intervention impacts. Data in the coming weeks will enable estimation of country-specific R_t with greater precision.

Model and data details are presented in the appendix, validation and sensitivity are also presented in the appendix, and general limitations presented below in the conclusions.

2 Results

The timing of interventions should be taken in the context of when an individual country's epidemic started to grow along with the speed with which control measures were implemented. Italy was the first to begin intervention measures, and other countries followed soon afterwards (Figure 1). Most interventions began around 12th-14th March. We analyzed data on deaths up to 28th March, giving a 2-3-week window over which to estimate the effect of interventions. Currently, most countries in our study have implemented all major non-pharmaceutical interventions.

For each country, we model the number of infections, the number of deaths, and R_t , the effective reproduction number over time, with R_t changing only when an intervention is introduced (Figure 2-12). R_t is the average number of secondary infections per infected individual, assuming that the interventions that are in place at time t stay in place throughout their entire infectious period. Every country has its own individual starting reproduction number R_t before interventions take place. Specific interventions are assumed to have the same relative impact on R_t in each country when they were introduced there and are informed by mortality data across all countries.

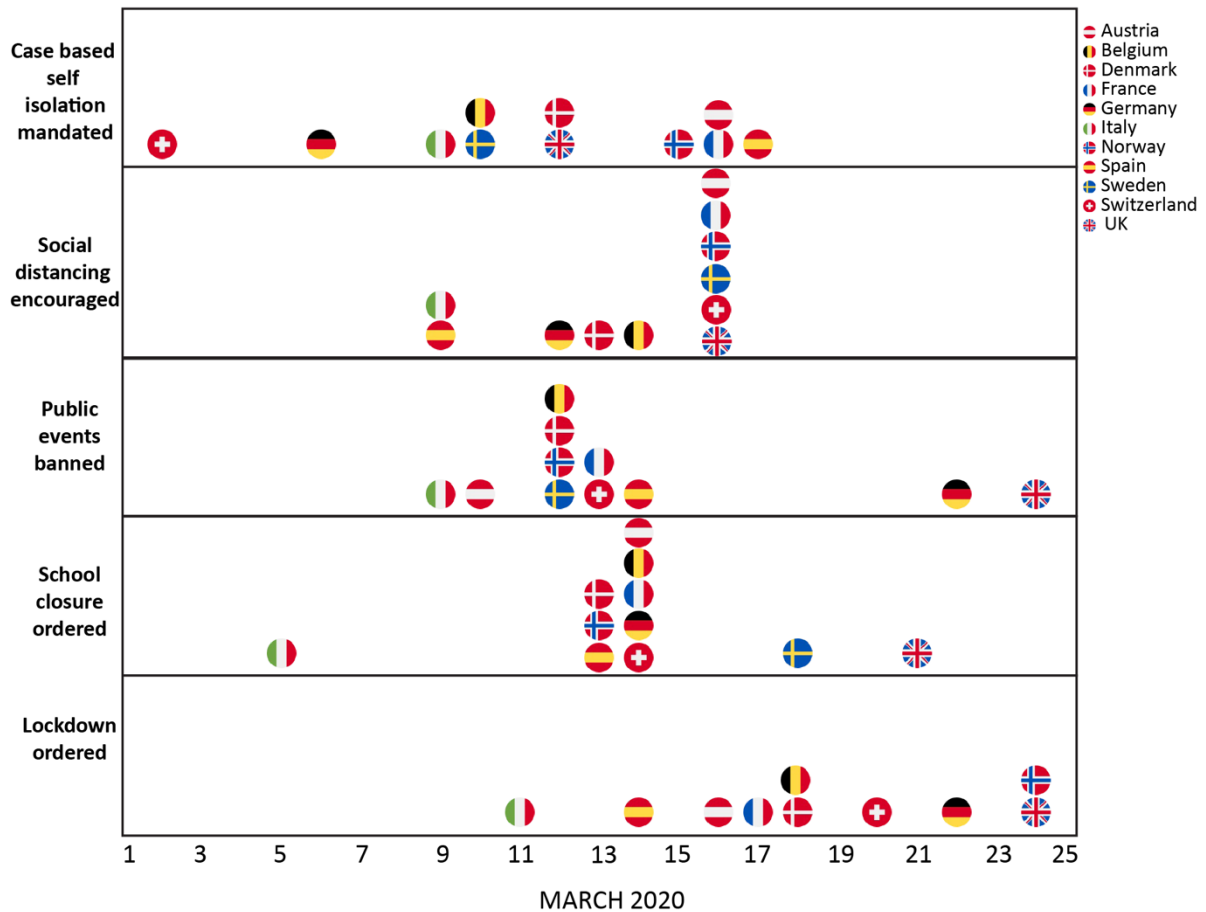


Figure 1: Intervention timings for the 11 European countries included in the analysis. For further details see Appendix 8.6.

2.1 Estimated true numbers of infections and current attack rates

In all countries, we estimate there are orders of magnitude fewer infections detected (Figure 2) than true infections, mostly likely due to mild and asymptomatic infections as well as limited testing capacity. In Italy, our results suggest that, cumulatively, 5.9 [1.9-15.2] million people have been infected as of March 28th, giving an attack rate of 9.8% [3.2%-25%] of the population (Table 1). Spain has recently seen a large increase in the number of deaths, and given its smaller population, our model estimates that a higher proportion of the population, 15.0% (7.0 [1.8-19] million people) have been infected to date. Germany is estimated to have one of the lowest attack rates at 0.7% with 600,000 [240,000-1,500,000] people infected.

Table 1: Posterior model estimates of percentage of total population infected as of 28th March 2020.

Country	% of total population infected (mean [95% credible interval])
Austria	1.1% [0.36%-3.1%]
Belgium	3.7% [1.3%-9.7%]
Denmark	1.1% [0.40%-3.1%]
France	3.0% [1.1%-7.4%]
Germany	0.72% [0.28%-1.8%]
Italy	9.8% [3.2%-26%]
Norway	0.41% [0.09%-1.2%]
Spain	15% [3.7%-41%]
Sweden	3.1% [0.85%-8.4%]
Switzerland	3.2% [1.3%-7.6%]
United Kingdom	2.7% [1.2%-5.4%]

2.2 Reproduction numbers and impact of interventions

Averaged across all countries, we estimate initial reproduction numbers of around 3.87 [3.01-4.66], which is in line with other estimates.^{1,8} These estimates are informed by our choice of serial interval distribution and the initial growth rate of observed deaths. A shorter assumed serial interval results in lower starting reproduction numbers (Appendix 8.4.2, Appendix 8.4.6). The initial reproduction numbers are also uncertain due to (a) importation being the dominant source of new infections early in the epidemic, rather than local transmission (b) possible under-ascertainment in deaths particularly before testing became widespread.

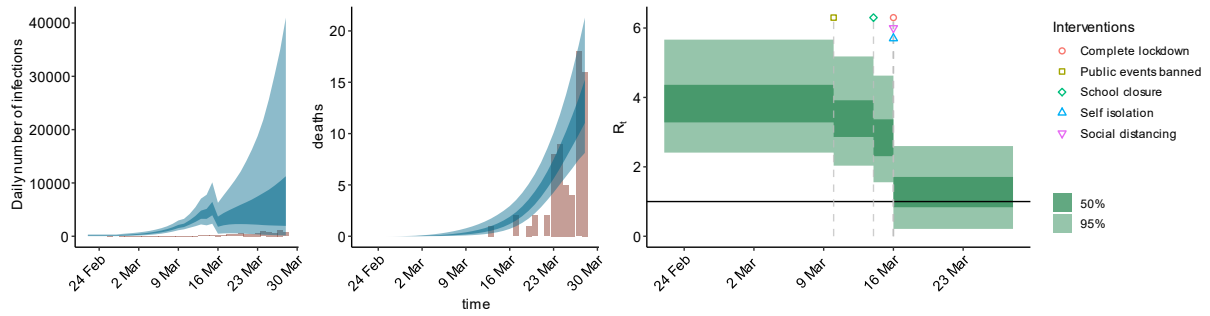
We estimate large changes in R_t in response to the combined non-pharmaceutical interventions. Our results, which are driven largely by countries with advanced epidemics and larger numbers of deaths (e.g. Italy, Spain), suggest that these interventions have together had a substantial impact on transmission, as measured by changes in the estimated reproduction number R_t . Across all countries we find current estimates of R_t to range from a posterior mean of 0.97 [0.14-2.14] for Norway to a posterior mean of 2.64 [1.40-4.18] for Sweden, with an average of 1.43 across the 11 country posterior means, a 64% reduction compared to the pre-intervention values. We note that these estimates are contingent on intervention impact being the same in different countries and at different times. In all countries but Sweden, under the same assumptions, we estimate that the current reproduction number includes 1 in the uncertainty range. The estimated reproduction number for Sweden is higher, not because the mortality trends are significantly different from any other country, but as an artefact of our model, which assumes a smaller reduction in R_t because no full lockdown has been ordered so far. Overall, we cannot yet conclude whether current interventions are sufficient to drive R_t below 1 (posterior probability of being less than 1.0 is 44% on average across the countries). We are also unable to conclude whether interventions may be different between countries or over time.

There remains a high level of uncertainty in these estimates. It is too early to detect substantial intervention impact in many countries at earlier stages of their epidemic (e.g. Germany, UK, Norway). Many interventions have occurred only recently, and their effects have not yet been fully observed due to the time lag between infection and death. This uncertainty will reduce as more data become available. For all countries, our model fits observed deaths data well (Bayesian goodness of fit tests). We also found that our model can reliably forecast daily deaths 3 days into the future, by withholding the latest 3 days of data and comparing model predictions to observed deaths (Appendix 8.3).

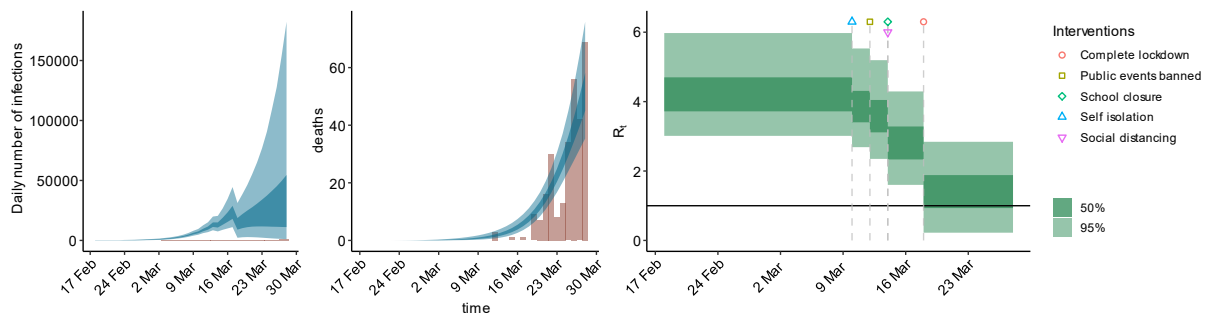
The close spacing of interventions in time made it statistically impossible to determine which had the greatest effect (Figure 1, Figure 4). However, when doing a sensitivity analysis (Appendix 8.4.3) with uninformative prior distributions (where interventions can increase deaths) we find similar impact of

interventions, which shows that our choice of prior distribution is not driving the effects we see in the main analysis.

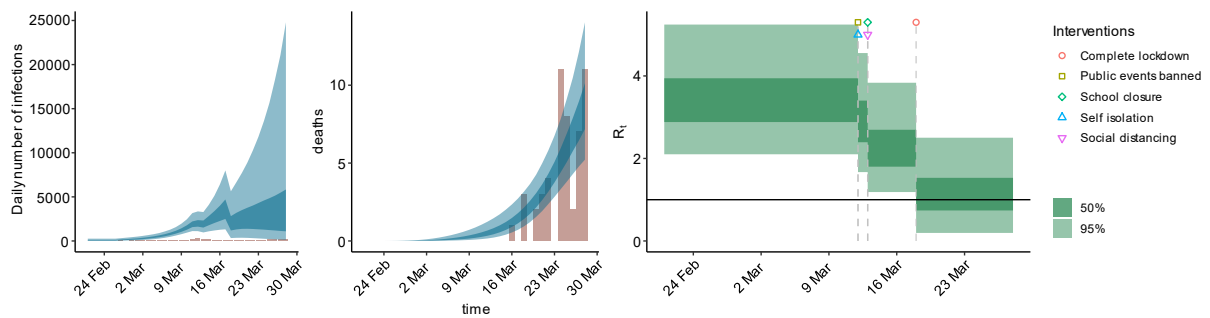
(A) Austria



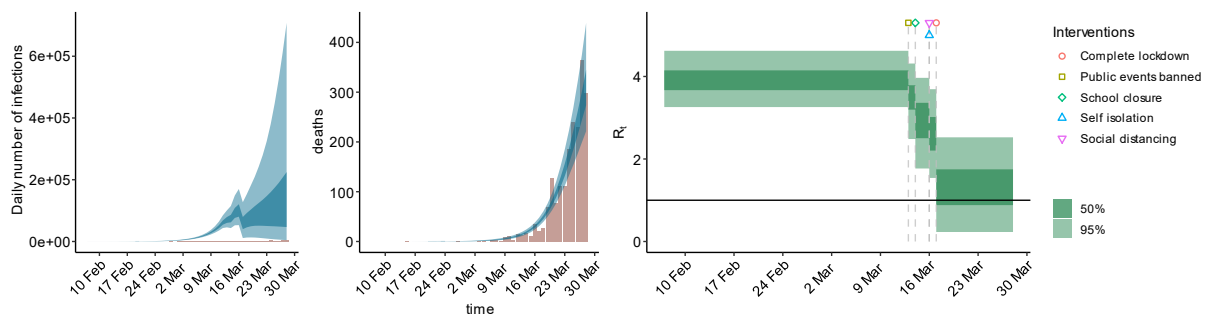
(B) Belgium



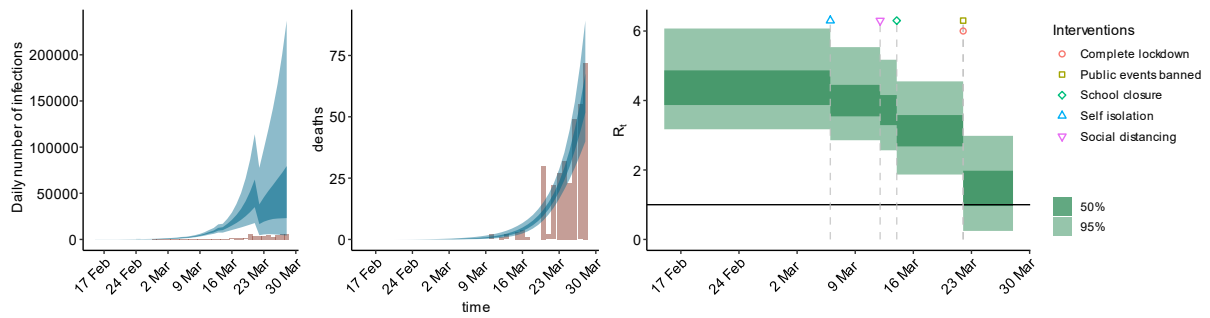
(C) Denmark



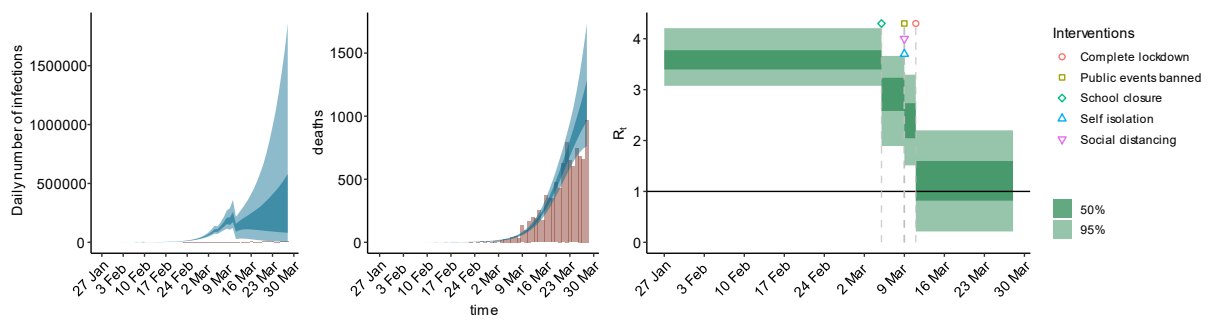
(D) France



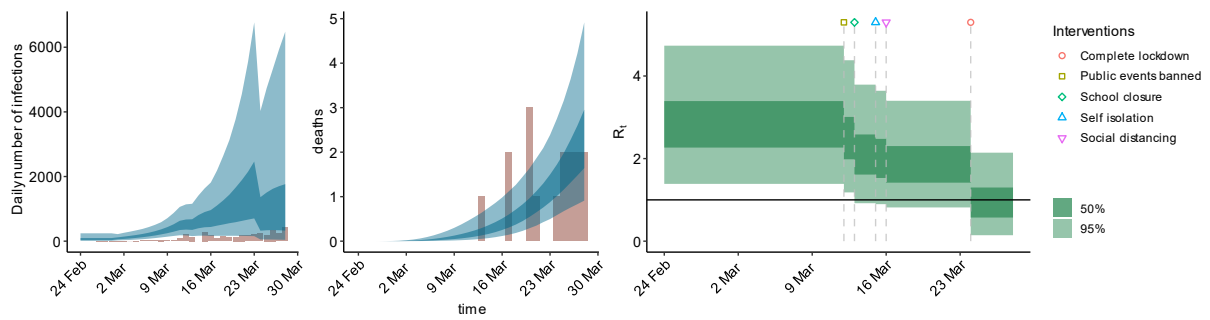
(E) Germany



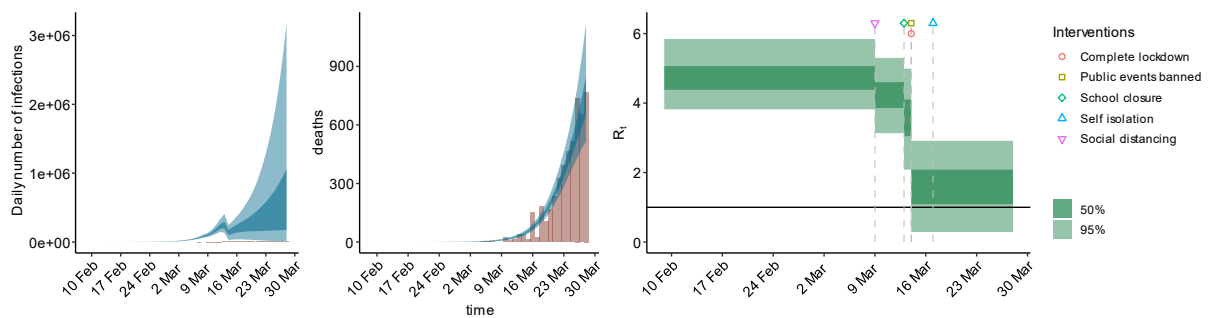
(F) Italy



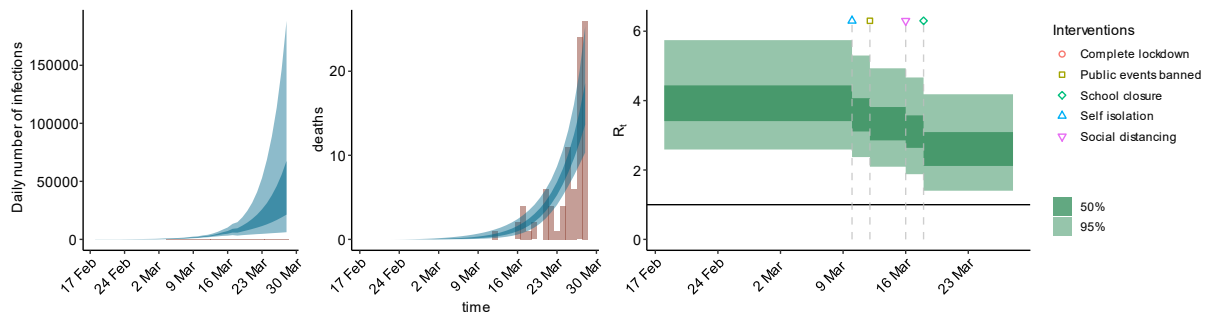
(G) Norway



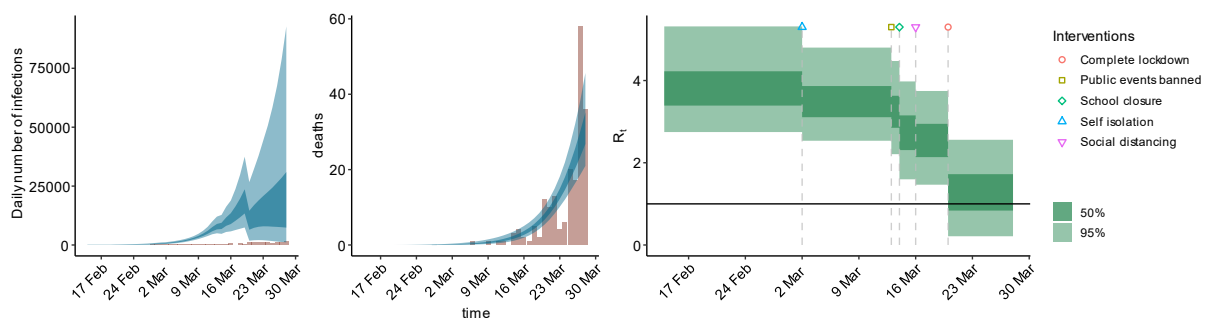
(H) Spain



(I) Sweden



(J) Switzerland



(K) United Kingdom

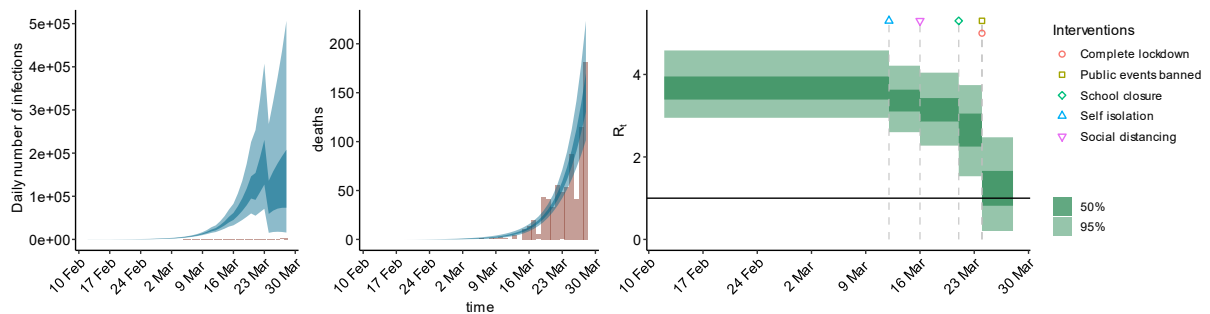


Figure 2: Country-level estimates of infections, deaths and R_t . Left: daily number of infections, brown bars are reported infections, blue bands are predicted infections, dark blue 50% credible interval (CI), light blue 95% CI. The number of daily infections estimated by our model drops immediately after an intervention, as we assume that all infected people become immediately less infectious through the intervention. Afterwards, if the R_t is above 1, the number of infections will start growing again. Middle: daily number of deaths, brown bars are reported deaths, blue bands are predicted deaths, CI as in left plot. Right: time-varying reproduction number R_t , dark green 50% CI, light green 95% CI. Icons are interventions shown at the time they occurred.

Table 2: Total forecasted deaths since the beginning of the epidemic up to 31 March in our model and in a counterfactual model (assuming no intervention had taken place). Estimated averted deaths over this time period as a result of the interventions. Numbers in brackets are 95% credible intervals.

Country	Observed Deaths to 28th March	Model estimated deaths to 28th March	Model estimated deaths to 31 March	Model estimated deaths to 31 March	Model deaths averted to 31 March
	(observed)	(our model)	(our model)	(counterfactual model assuming no interventions have occurred)	(difference between counterfactual and actual)
Austria	68	88 [57 - 130]	140 [88 - 210]	280 [140 - 560]	140 [34 - 380]
Belgium	289	310 [230 - 420]	510 [370 - 730]	1,100 [590 - 2,100]	560 [160 - 1,500]
Denmark	52	61 [38 - 92]	93 [58 - 140]	160 [84 - 310]	69 [15 - 200]
France	1,995	1,900 [1,500 - 2,500]	3,100 [2,300 - 4,200]	5,600 [3,600 - 8,500]	2,500 [1,000 - 4,800]
Germany	325	320 [240 - 410]	570 [400 - 810]	1,100 [570 - 2,400]	550 [91 - 1,800]
Italy	9,136	10,000 [8,200 - 13,000]	14,000 [11,000 - 19,000]	52,000 [27,000 - 98,000]	38,000 [13,000 - 84,000]
Norway	16	17 [7 - 33]	26 [11 - 51]	36 [14 - 81]	9.9 [0.82 - 38]
Spain	4,858	4,700 [3,700 - 6,100]	7,700 [5,500 - 11,000]	24,000 [13,000 - 44,000]	16,000 [5,400 - 35,000]
Sweden	92	89 [61 - 120]	160 [110 - 240]	240 [140 - 440]	82 [12 - 250]
Switzerland	197	190 [140 - 250]	310 [220 - 440]	650 [330 - 1,500]	340 [71 - 1,100]
United Kingdom	759	810 [610 - 1,100]	1,500 [1,000 - 2,100]	1,800 [1,200 - 2,900]	370 [73 - 1,000]
All	17,787	19,000 [16,000 - 22,000]	28,000 [23,000 - 36,000]	87,000 [53,000 - 140,000]	59,000 [21,000 - 120,000]

2.3 Estimated impact of interventions on deaths

Table 2 shows total forecasted deaths since the beginning of the epidemic up to and including 31 March under our fitted model and under the counterfactual model, which predicts what would have happened if no interventions were implemented (and $R_t = R_0$ i.e. the initial reproduction number estimated before interventions). Again, the assumption in these predictions is that intervention impact is the same across countries and time. The model without interventions was unable to capture recent trends in deaths in several countries, where the rate of increase had clearly slowed (Figure 3). Trends were confirmed statistically by Bayesian leave-one-out cross-validation and the widely applicable information criterion assessments – WAIC).

By comparing the deaths predicted under the model with no interventions to the deaths predicted in our intervention model, we calculated the total deaths averted up to the end of March. We find that, across 11 countries, since the beginning of the epidemic, 59,000 [21,000-120,000] deaths have been averted due to interventions. In Italy and Spain, where the epidemic is advanced, 38,000 [13,000-84,000] and 16,000 [5,400-35,000] deaths have been averted, respectively. Even in the UK, which is much earlier in its epidemic, we predict 370 [73-1,000] deaths have been averted.

These numbers give only the deaths averted that would have occurred up to 31 March. If we were to include the deaths of currently infected individuals in both models, which might happen after 31 March, then the deaths averted would be substantially higher.

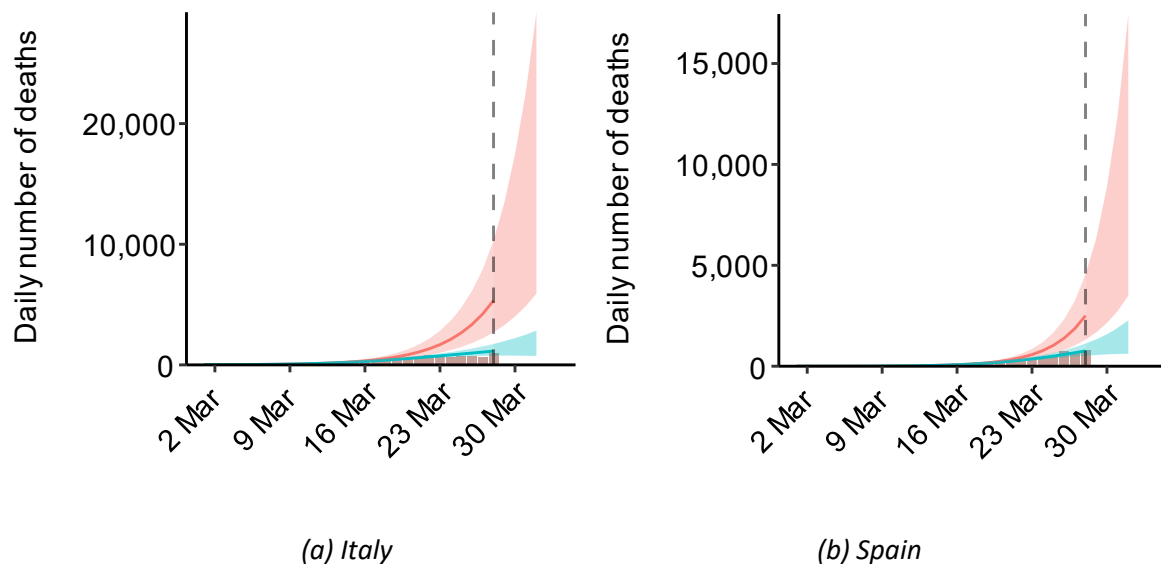


Figure 3: Daily number of confirmed deaths, predictions (up to 28 March) and forecasts (after) for (a) Italy and (b) Spain from our model with interventions (blue) and from the no interventions counterfactual model (pink); credible intervals are shown one week into the future. Other countries are shown in Appendix 8.6.

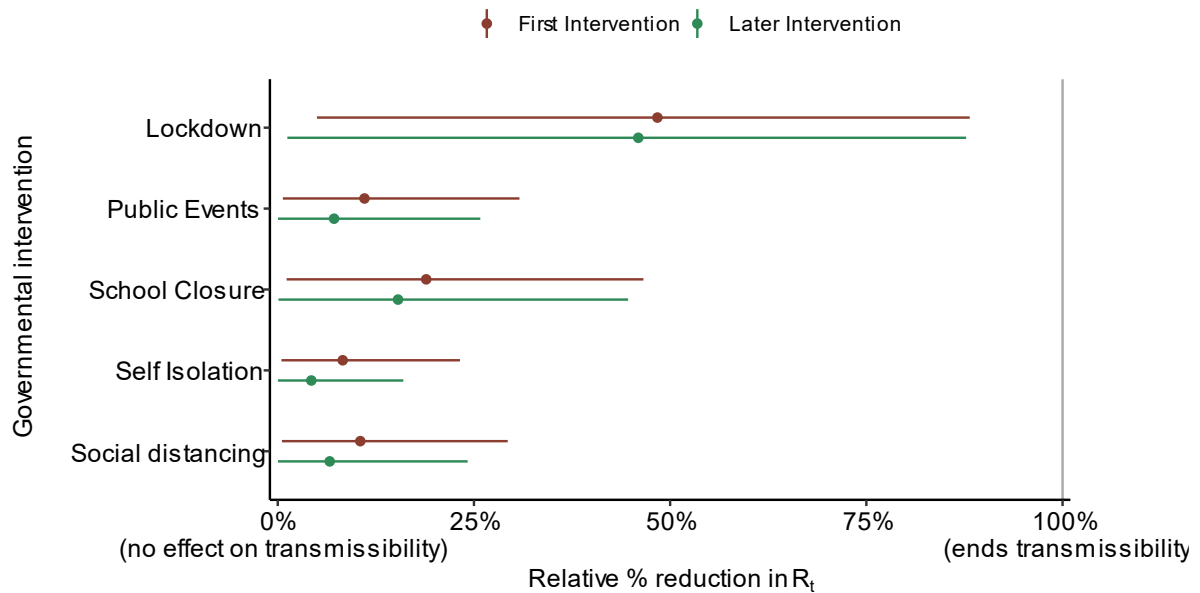


Figure 4: Our model includes five covariates for governmental interventions, adjusting for whether the intervention was the first one undertaken by the government in response to COVID-19 (red) or was subsequent to other interventions (green). Mean relative percentage reduction in R_t is shown with 95% posterior credible intervals. If 100% reduction is achieved, $R_t = 0$ and there is no more transmission of COVID-19. No effects are significantly different from any others, probably due to the fact that many interventions occurred on the same day or within days of each other as shown in Figure 1.

3 Discussion

During this early phase of control measures against the novel coronavirus in Europe, we analyze trends in numbers of deaths to assess the extent to which transmission is being reduced. Representing the COVID-19 infection process using a semi-mechanistic, joint, Bayesian hierarchical model, we can reproduce trends observed in the data on deaths and can forecast accurately over short time horizons.

We estimate that there have been many more infections than are currently reported. The high level of under-ascertainment of infections that we estimate here is likely due to the focus on testing in hospital settings rather than in the community. Despite this, only a small minority of individuals in each country have been infected, with an attack rate on average of 4.9% [1.9%-11%] with considerable variation between countries (Table 1). Our estimates imply that the populations in Europe are not close to herd immunity (~50-75% if R_0 is 2-4). Further, with R_t values dropping substantially, the rate of acquisition of herd immunity will slow down rapidly. This implies that the virus will be able to spread rapidly should interventions be lifted. Such estimates of the attack rate to date urgently need to be validated by newly developed antibody tests in representative population surveys, once these become available.

We estimate that major non-pharmaceutical interventions have had a substantial impact on the time-varying reproduction numbers in countries where there has been time to observe intervention effects on trends in deaths (Italy, Spain). If adherence in those countries has changed since that initial period, then our forecast of future deaths will be affected accordingly: increasing adherence over time will have resulted in fewer deaths and decreasing adherence in more deaths. Similarly, our estimates of the impact of interventions in other countries should be viewed with caution if the same interventions have achieved different levels of adherence than was initially the case in Italy and Spain.

Due to the implementation of interventions in rapid succession in many countries, there are not enough data to estimate the individual effect size of each intervention, and we discourage attributing

associations to individual intervention. In some cases, such as Norway, where all interventions were implemented at once, these individual effects are by definition unidentifiable. Despite this, while individual impacts cannot be determined, their estimated joint impact is strongly empirically justified (see Appendix 8.4 for sensitivity analysis). While the growth in daily deaths has decreased, due to the lag between infections and deaths, continued rises in daily deaths are to be expected for some time.

To understand the impact of interventions, we fit a counterfactual model without the interventions and compare this to the actual model. Consider Italy and the UK - two countries at very different stages in their epidemics. For the UK, where interventions are very recent, much of the intervention strength is borrowed from countries with older epidemics. The results suggest that interventions will have a large impact on infections and deaths despite counts of both rising. For Italy, where far more time has passed since the interventions have been implemented, it is clear that the model without interventions does not fit well to the data, and cannot explain the sub-linear (on the logarithmic scale) reduction in deaths (see Figure 10).

The counterfactual model for Italy suggests that despite mounting pressure on health systems, interventions have averted a health care catastrophe where the number of new deaths would have been 3.7 times higher (38,000 deaths averted) than currently observed. Even in the UK, much earlier in its epidemic, the recent interventions are forecasted to avert 370 total deaths up to 31 of March.

4 Conclusion and Limitations

Modern understanding of infectious disease with a global publicized response has meant that nationwide interventions could be implemented with widespread adherence and support. Given observed infection fatality ratios and the epidemiology of COVID-19, major non-pharmaceutical interventions have had a substantial impact in reducing transmission in countries with more advanced epidemics. It is too early to be sure whether similar reductions will be seen in countries at earlier stages of their epidemic. While we cannot determine which set of interventions have been most successful, taken together, we can already see changes in the trends of new deaths. When forecasting 3 days and looking over the whole epidemic the number of deaths averted is substantial. We note that substantial innovation is taking place, and new more effective interventions or refinements of current interventions, alongside behavioral changes will further contribute to reductions in infections. We cannot say for certain that the current measures have controlled the epidemic in Europe; however, if current trends continue, there is reason for optimism.

Our approach is semi-mechanistic. We propose a plausible structure for the infection process and then estimate parameters empirically. However, many parameters had to be given strong prior distributions or had to be fixed. For these assumptions, we have provided relevant citations to previous studies. As more data become available and better estimates arise, we will update these in weekly reports. Our choice of serial interval distribution strongly influences the prior distribution for starting R_0 . Our infection fatality ratio, and infection-to-onset-to-death distributions strongly influence the rate of death and hence the estimated number of true underlying cases.

We also assume that the effect of interventions is the same in all countries, which may not be fully realistic. This assumption implies that countries with early interventions and more deaths since these interventions (e.g. Italy, Spain) strongly influence estimates of intervention impact in countries at earlier stages of their epidemic with fewer deaths (e.g. Germany, UK).

We have tried to create consistent definitions of all interventions and document details of this in Appendix 8.6. However, invariably there will be differences from country to country in the strength of their intervention – for example, most countries have banned gatherings of more than 2 people when implementing a lockdown, whereas in Sweden the government only banned gatherings of more than 10 people. These differences can skew impacts in countries with very little data. We believe that our uncertainty to some degree can cover these differences, and as more data become available, coefficients should become more reliable.

However, despite these strong assumptions, there is sufficient signal in the data to estimate changes in R_t (see the sensitivity analysis reported in Appendix 8.4.3) and this signal will stand to increase with time. In our Bayesian hierarchical framework, we robustly quantify the uncertainty in our parameter estimates and posterior predictions. This can be seen in the very wide credible intervals in more recent days, where little or no death data are available to inform the estimates. Furthermore, we predict intervention impact at country-level, but different trends may be in place in different parts of each country. For example, the epidemic in northern Italy was subject to controls earlier than the rest of the country.

5 Data

Our model utilizes daily real-time death data from the ECDC (European Centre of Disease Control), where we catalogue case data for 11 European countries currently experiencing the epidemic: Austria, Belgium, Denmark, France, Germany, Italy, Norway, Spain, Sweden, Switzerland and the United Kingdom. The ECDC provides information on confirmed cases and deaths attributable to COVID-19. However, the case data are highly unrepresentative of the incidence of infections due to underreporting as well as systematic and country-specific changes in testing.

We, therefore, use only deaths attributable to COVID-19 in our model; we do not use the ECDC case estimates at all. While the observed deaths still have some degree of unreliability, again due to changes in reporting and testing, we believe the data are of sufficient fidelity to model. For population counts, we use UNPOP age-stratified counts.¹⁰

We also catalogue data on the nature and type of major non-pharmaceutical interventions. We looked at the government webpages from each country as well as their official public health division/information webpages to identify the latest advice/laws being issued by the government and public health authorities. We collected the following:

School closure ordered: This intervention refers to nationwide extraordinary school closures which in most cases refer to both primary and secondary schools closing (for most countries this also includes the closure of other forms of higher education or the advice to teach remotely). In the case of Denmark and Sweden, we allowed partial school closures of only secondary schools. The date of the school closure is taken to be the effective date when the schools started to be closed (if this was on a Monday, the date used was the one of the previous Saturdays as pupils and students effectively stayed at home from that date onwards).

Case-based measures: This intervention comprises strong recommendations or laws to the general public and primary care about self-isolation when showing COVID-19-like symptoms. These also include nationwide testing programs where individuals can be tested and subsequently self-isolated. Our definition is restricted to nationwide government advice to all individuals (e.g. UK) or to all primary care and excludes regional only advice. These do not include containment phase interventions such as isolation if travelling back from an epidemic country such as China.

Public events banned: This refers to banning all public events of more than 100 participants such as sports events.

Social distancing encouraged: As one of the first interventions against the spread of the COVID-19 pandemic, many governments have published advice on social distancing including the recommendation to work from home wherever possible, reducing use of public transport and all other non-essential contact. The dates used are those when social distancing has officially been recommended by the government; the advice may include maintaining a recommended physical distance from others.

Lockdown decreed: There are several different scenarios that the media refers to as lockdown. As an overall definition, we consider regulations/legislations regarding strict face-to-face social interaction: including the banning of any non-essential public gatherings, closure of educational and

public/cultural institutions, ordering people to stay home apart from exercise and essential tasks. We include special cases where these are not explicitly mentioned on government websites but are enforced by the police (e.g. France). The dates used are the effective dates when these legislations have been implemented. We note that lockdown encompasses other interventions previously implemented.

First intervention: As Figure 1 shows, European governments have escalated interventions rapidly, and in some examples (Norway/Denmark) have implemented these interventions all on a single day. Therefore, given the temporal autocorrelation inherent in government intervention, we include a binary covariate for the first intervention, which can be interpreted as a government decision to take major action to control COVID-19.

A full list of the timing of these interventions and the sources we have used can be found in Appendix 8.6.

6 Methods Summary

A visual summary of our model is presented in Figure 5 (details in Appendix 8.1 and 8.2). Replication code is available at <https://github.com/ImperialCollegeLondon/covid19model/releases/tag/v1.0>

We fit our model to observed deaths according to ECDC data from 11 European countries. The modelled deaths are informed by an infection-to-onset distribution (time from infection to the onset of symptoms), an onset-to-death distribution (time from the onset of symptoms to death), and the population-averaged infection fatality ratio (adjusted for the age structure and contact patterns of each country, see Appendix). Given these distributions and ratios, modelled deaths are a function of the number of infections. The modelled number of infections is informed by the serial interval distribution (the average time from infection of one person to the time at which they infect another) and the time-varying reproduction number. Finally, the time-varying reproduction number is a function of the initial reproduction number before interventions and the effect sizes from interventions.

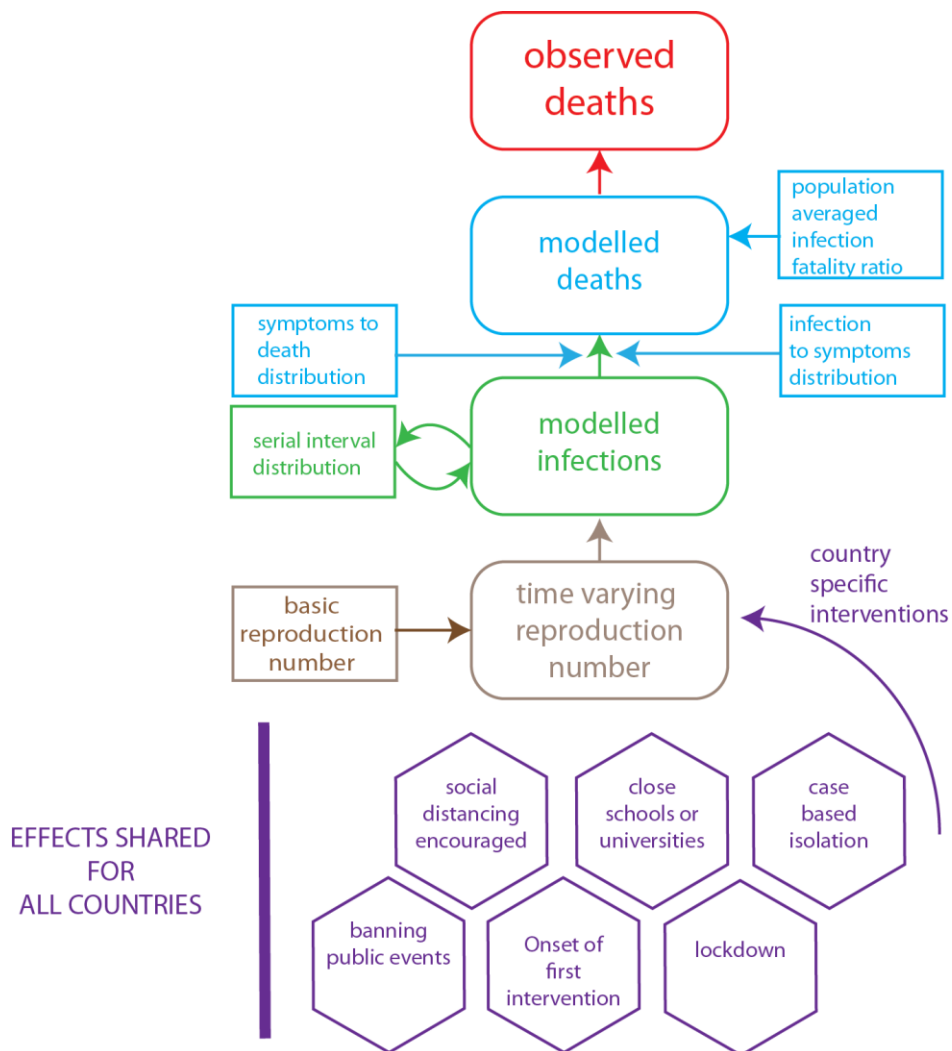


Figure 5: Summary of model components.

Following the hierarchy from bottom to top gives us a full framework to see how interventions affect infections, which can result in deaths. We use Bayesian inference to ensure our modelled deaths can reproduce the observed deaths as closely as possible. From bottom to top in Figure 5, there is an implicit lag in time that means the effect of very recent interventions manifest weakly in current deaths (and get stronger as time progresses). To maximise the ability to observe intervention impact on deaths, we fit our model jointly for all 11 European countries, which results in a large data set. Our model jointly estimates the effect sizes of interventions. We have evaluated the effect of our Bayesian prior distribution choices and evaluate our Bayesian posterior calibration to ensure our results are statistically robust (Appendix 8.4).

7 Acknowledgements

Initial research on covariates in Appendix 8.6 was crowdsourced; we thank a number of people across the world for help with this. This work was supported by Centre funding from the UK Medical Research Council under a concordat with the UK Department for International Development, the NIHR Health Protection Research Unit in Modelling Methodology and Community Jameel.

8 Appendix: Model Specifics, Validation and Sensitivity Analysis

8.1 Death model

We observe daily deaths $D_{t,m}$ for days $t \in 1, \dots, n$ and countries $m \in 1, \dots, p$. These daily deaths are modelled using a positive real-valued function $d_{t,m} = E(D_{t,m})$ that represents the expected number of deaths attributed to COVID-19. $D_{t,m}$ is assumed to follow a negative binomial distribution with mean $d_{t,m}$ and variance $d_{t,m} + \frac{d_{t,m}^2}{\psi}$, where ψ follows a half normal distribution, i.e.

$$D_{t,m} \sim \text{Negative Binomial} \left(d_{t,m}, d_{t,m} + \frac{d_{t,m}^2}{\psi} \right),$$

$$\psi \sim \text{Normal}^+(0,5).$$

The expected number of deaths d in a given country on a given day is a function of the number of infections c occurring in previous days.

At the beginning of the epidemic, the observed deaths in a country can be dominated by deaths that result from infection that are not locally acquired. To avoid biasing our model by this, we only include observed deaths from the day after a country has cumulatively observed 10 deaths in our model.

To mechanistically link our function for deaths to infected cases, we use a previously estimated COVID-19 infection-fatality-ratio *ifr* (probability of death given infection)⁹ together with a distribution of times from infection to death π . The *ifr* is derived from estimates presented in Verity et al¹¹ which assumed homogeneous attack rates across age-groups. To better match estimates of attack rates by age generated using more detailed information on country and age-specific mixing patterns, we scale these estimates (the unadjusted *ifr*, referred to here as *ifr'*) in the following way as in previous work.⁴ Let c_a be the number of infections generated in age-group a , N_a the underlying size of the population in that age group and $AR_a = c_a/N_a$ the age-group-specific attack rate. The adjusted *ifr* is then given by: $ifr_a = \frac{AR_{50-59}}{AR_a} ifr'_a$, where AR_{50-59} is the predicted attack-rate in the 50-59 year age-group after incorporating country-specific patterns of contact and mixing. This age-group was chosen as the reference as it had the lowest predicted level of underreporting in previous analyses of data from the Chinese epidemic¹¹. We obtained country-specific estimates of attack rate by age, AR_a , for the 11 European countries in our analysis from a previous study which incorporates information on contact between individuals of different ages in countries across Europe.¹² We then obtained overall *ifr* estimates for each country adjusting for both demography and age-specific attack rates.

Using estimated epidemiological information from previous studies,^{4,11} we assume π to be the sum of two independent random times: the incubation period (infection to onset of symptoms or infection-to-onset) distribution and the time between onset of symptoms and death (onset-to-death). The infection-to-onset distribution is Gamma distributed with mean 5.1 days and coefficient of variation 0.86. The onset-to-death distribution is also Gamma distributed with a mean of 18.8 days and a coefficient of variation 0.45. ifr_m is population averaged over the age structure of a given country. The infection-to-death distribution is therefore given by:

$$\pi_m \sim ifr_m \cdot (\text{Gamma}(5.1,0.86) + \text{Gamma}(18.8,0.45))$$

Figure 6 shows the infection-to-death distribution and the resulting survival function that integrates to the infection fatality ratio.

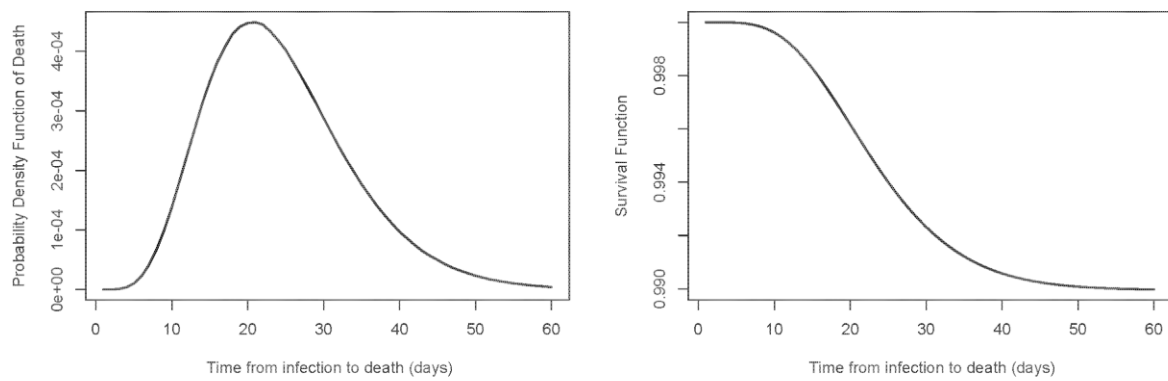


Figure 6: Left, infection-to-death distribution (mean 23.9 days). Right, survival probability of infected individuals per day given the infection fatality ratio (1%) and the infection-to-death distribution on the left.

Using the probability of death distribution, the expected number of deaths $d_{t,m}$, on a given day t , for country, m , is given by the following discrete sum:

$$d_{t,m} = \sum_{\tau=0}^{t-1} c_{\tau,m} \pi_{t-\tau,m}$$

where $c_{\tau,m}$ is the number of new infections on day τ in country m (see next section) and where π_m is discretized via $\pi_{s,m} = \int_{\tau=s-0.5}^{s+0.5} \pi_m(\tau) d\tau$ for $s = 2, 3, \dots$ and $\pi_{1,m} = \int_{\tau=0}^{1.5} \pi_m(\tau) d\tau$.

The number of deaths today is the sum of the past infections weighted by their probability of death, where the probability of death depends on the number of days since infection.

8.2 Infection model

The true number of infected individuals, c , is modelled using a discrete renewal process. This approach has been used in numerous previous studies¹³⁻¹⁶ and has a strong theoretical basis in stochastic individual-based counting processes such as Hawkes process and the Bellman-Harris process.^{17,18} The renewal model is related to the Susceptible-Infected-Recovered model, except the renewal is not expressed in differential form. To model the number of infections over time we need to specify a serial interval distribution g with density $g(\tau)$, (the time between when a person gets infected and when they subsequently infect another other people), which we choose to be Gamma distributed:

$$g \sim \text{Gamma}(6.5, 0.62).$$

The serial interval distribution is shown below in Figure 7 and is assumed to be the same for all countries.

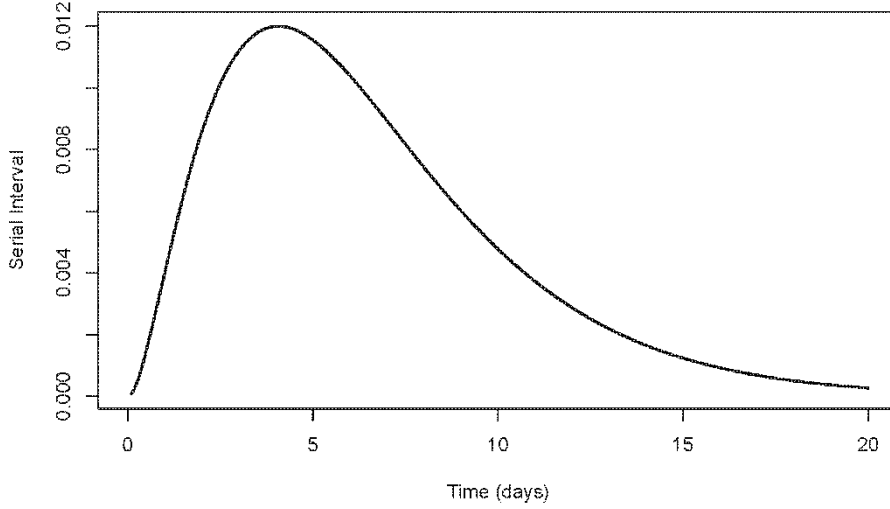


Figure 7: Serial interval distribution g with a mean of 6.5 days.

Given the serial interval distribution, the number of infections $c_{t,m}$ on a given day t , and country, m , is given by the following discrete convolution function:

$$c_{t,m} = R_{t,m} \sum_{\tau=0}^{t-1} c_{\tau,m} g_{t-\tau},$$

where, similar to the probability of death function, the daily serial interval is discretized by

$$g_s = \int_{\tau=s-0.5}^{s+0.5} g(\tau) d\tau \text{ for } s = 2, 3, \dots \text{ and } g_1 = \int_{\tau=0}^{1.5} g(\tau) d\tau.$$

Infections today depend on the number of infections in the previous days, weighted by the discretized serial interval distribution. This weighting is then scaled by the country-specific time-varying reproduction number, $R_{t,m}$, that models the average number of secondary infections at a given time.

The functional form for the time-varying reproduction number was chosen to be as simple as possible to minimize the impact of strong prior assumptions: we use a piecewise constant function that scales $R_{t,m}$ from a baseline prior $R_{0,m}$ and is driven by known major non-pharmaceutical interventions occurring in different countries and times. We included 6 interventions, one of which is constructed from the other 5 interventions, which are timings of school and university closures ($k=1$), self-isolating if ill ($k=2$), banning of public events ($k=3$), any government intervention in place ($k=4$), implementing a partial or complete lockdown ($k=5$) and encouraging social distancing and isolation ($k=6$). We denote the indicator variable for intervention $k \in 1, 2, 3, 4, 5, 6$ by $I_{k,t,m}$, which is 1 if intervention k is in place in country m at time t and 0 otherwise. The covariate “any government intervention” ($k=4$) indicates if any of the other 5 interventions are in effect, i.e. $I_{4,t,m}$ equals 1 at time t if any of the interventions $k \in 1, 2, 3, 4, 5$ are in effect in country m at time t and equals 0 otherwise. Covariate 4 has the interpretation of indicating the onset of major government intervention. The effect of each intervention is assumed to be multiplicative. $R_{t,m}$ is therefore a function of the intervention indicators $I_{k,t,m}$ in place at time t in country m :

$$R_{t,m} = R_{0,m} \exp\left(-\sum_{k=1}^6 \alpha_k I_{k,t,m}\right).$$

The exponential form was used to ensure positivity of the reproduction number, with $R_{0,m}$ constrained to be positive as it appears outside the exponential. The impact of each intervention on $R_{t,m}$ is characterised by a set of parameters $\alpha_1, \dots, \alpha_6$, with independent prior distributions chosen to be

$$\alpha_k \sim \text{Gamma}(.5,1).$$

The impacts α_k are shared between all m countries and therefore they are informed by all available data. The prior distribution for R_0 was chosen to be

$$R_{0,m} \sim \text{Normal}(2.4, |\kappa|) \text{ with } \kappa \sim \text{Normal}(0,0.5),$$

Once again, κ is the same among all countries to share information.

We assume that seeding of new infections begins 30 days before the day after a country has cumulatively observed 10 deaths. From this date, we seed our model with 6 sequential days of infections drawn from $c_{1,m}, \dots, c_{6,m} \sim \text{Exponential}(\tau)$, where $\tau \sim \text{Exponential}(0.03)$. These seed infections are inferred in our Bayesian posterior distribution.

We estimated parameters jointly for all 11 countries in a single hierarchical model. Fitting was done in the probabilistic programming language Stan,¹⁹ using an adaptive Hamiltonian Monte Carlo (HMC) sampler. We ran 8 chains for 4000 iterations with 2000 iterations of warmup and a thinning factor 4 to obtain 2000 posterior samples. Posterior convergence was assessed using the Rhat statistic and by diagnosing divergent transitions of the HMC sampler. Prior-posterior calibrations were also performed (see below).

8.3 Validation

We validate accuracy of point estimates of our model using cross-validation. In our cross-validation scheme, we leave out 3 days of known death data (non-cumulative) and fit our model. We forecast what the model predicts for these three days. We present the individual forecasts for each day, as well as the average forecast for those three days. The cross-validation results are shown in the Figure 8.

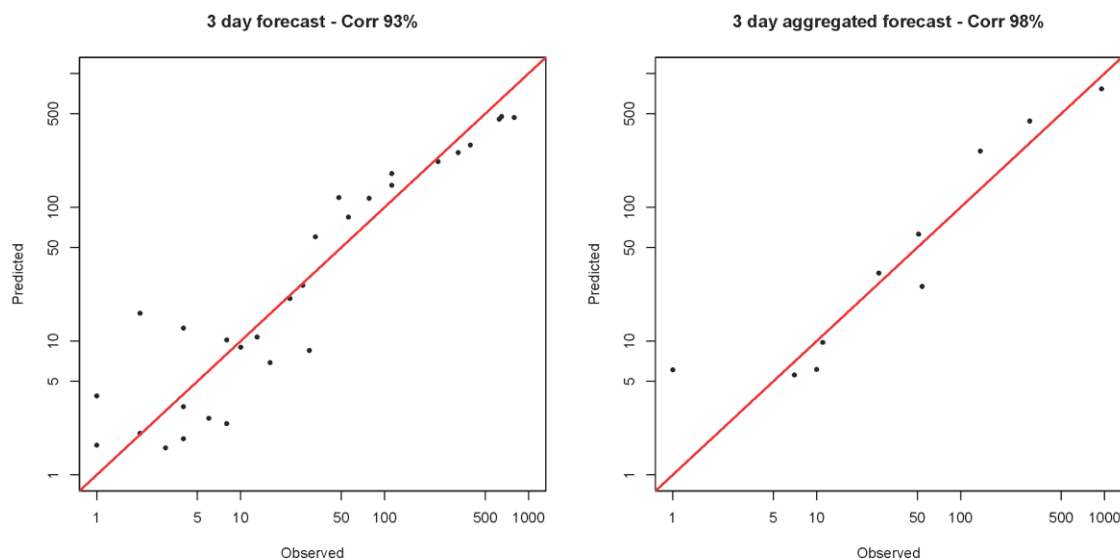


Figure 8: Cross-validation results for 3-day and 3-day aggregated forecasts

Figure 8 provides strong empirical justification for our model specification and mechanism. Our accurate forecast over a three-day time horizon suggests that our fitted estimates for R_t are appropriate and plausible.

Along with from point estimates we all evaluate our posterior credible intervals using the Rhat statistic. The Rhat statistic measures whether our Markov Chain Monte Carlo (MCMC) chains have

converged to the equilibrium distribution (the correct posterior distribution). Figure 9 shows the Rhat statistics for all of our parameters

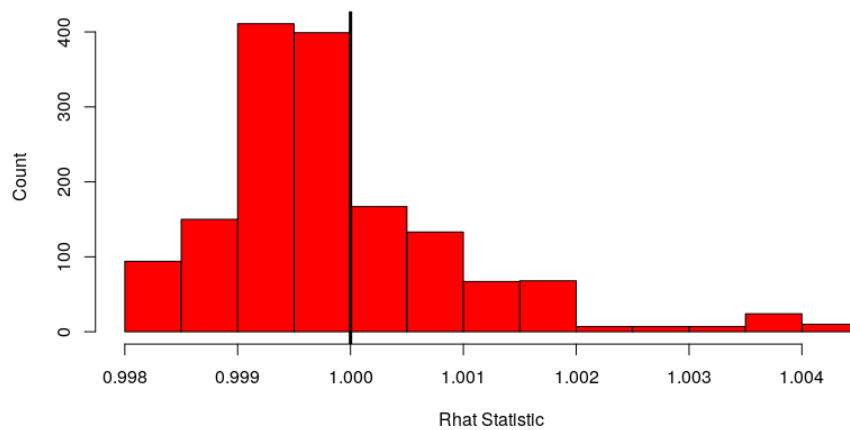


Figure 9: Rhat statistics - values close to 1 indicate MCMC convergence.

Figure 9 indicates that our MCMC have converged. In fitting we also ensured that the MCMC sampler experienced no divergent transitions - suggesting non pathological posterior topologies.

8.4 Sensitivity Analysis

8.4.1 Forecasting on log-linear scale to assess signal in the data

As we have highlighted throughout in this report, the lag between deaths and infections means that it takes time for information to propagate backwards from deaths to infections, and ultimately to R_t . A conclusion of this report is the prediction of a slowing of R_t in response to major interventions. To gain intuition that this is data driven and not simply a consequence of highly constrained model assumptions, we show death forecasts on a log-linear scale. On this scale a line which curves below a linear trend is indicative of slowing in the growth of the epidemic. Figure 10 to Figure 12 show these forecasts for Italy, Spain and the UK. They show this slowing down in the daily number of deaths. Our model suggests that Italy, a country that has the highest death toll of COVID-19, will see a slowing in the increase in daily deaths over the coming week compared to the early stages of the epidemic.

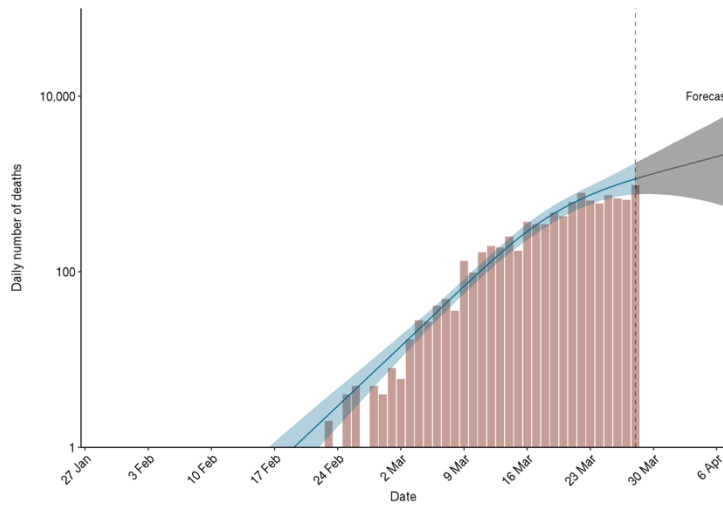


Figure 10: 7-day-ahead forecast for Italy.

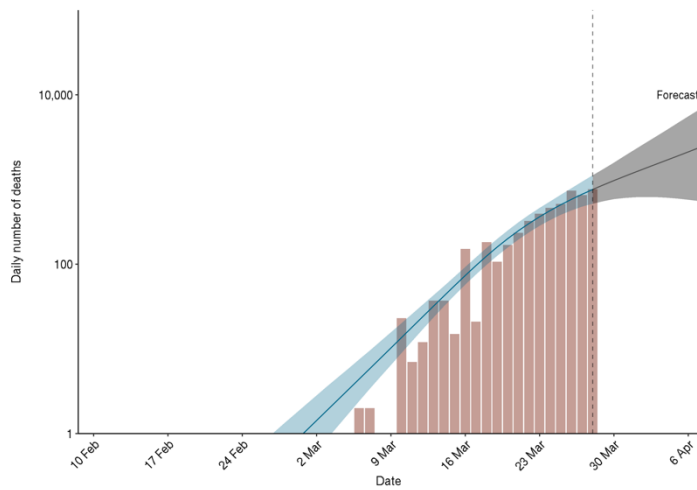


Figure 11: 7-day-ahead forecast for Spain.

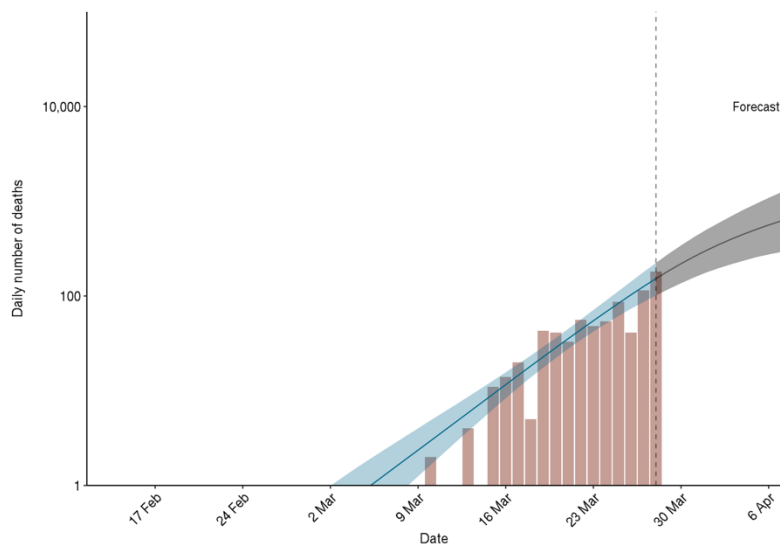


Figure 12: 7-day-ahead forecast for the UK.

8.4.2 Serial interval distribution

We investigated the sensitivity of our estimates of starting and final R_t to our assumed serial interval distribution. For this we considered several scenarios, in which we changed the serial interval distribution mean, from a value of 6.5 days, to have values of 5, 6, 7 and 8 days.

In Figure 13, we show our estimates of R_0 , the starting reproduction number before interventions, for each of these scenarios. The relative ordering of the $R_{t=0}$ in the countries is consistent in all settings. However, as expected, the scale of $R_{t=0}$ is considerably affected by this change – a longer serial interval results in a higher estimated $R_{t=0}$. This is because to reach the currently observed size of the epidemics, a longer assumed serial interval is compensated by a higher estimated R_0 .

Additionally, in Figure 14, we show our estimates of R_t at the most recent model time point, again for each of these scenarios. The serial interval mean can influence R_t substantially, however, the posterior credible intervals of R_t are broadly overlapping.

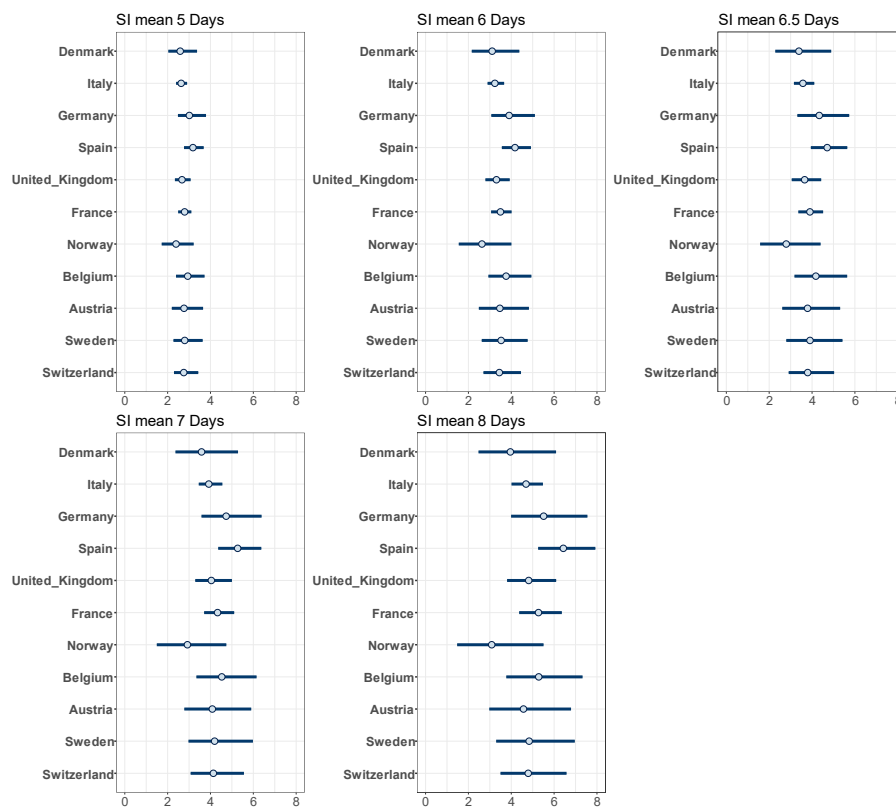


Figure 13: Initial reproduction number R_0 for different serial interval (SI) distributions (means between 5 and 8 days). We use 6.5 days in our main analysis.

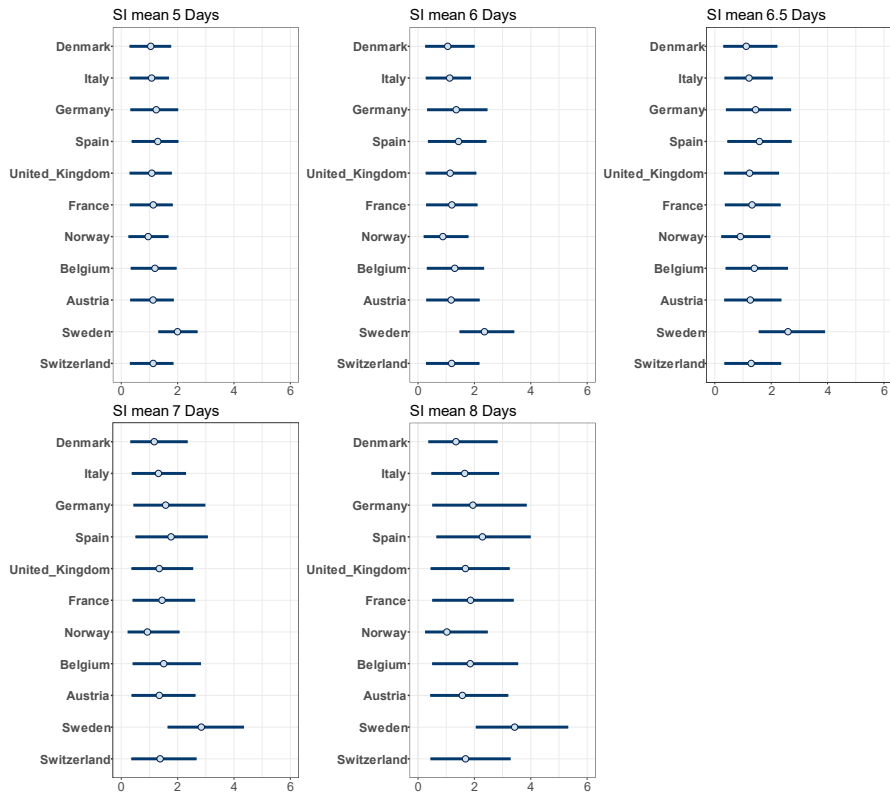


Figure 14: R_t on 28 March 2020 estimated for all countries, with serial interval (SI) distribution means between 5 and 8 days. We use 6.5 days in our main analysis.

8.4.3 Uninformative prior sensitivity on α

We ran our model using implausible uninformative prior distributions on the intervention effects, allowing the effect of an intervention to increase or decrease R_t . To avoid collinearity, we ran 6 separate models, with effects summarized below (compare with the main analysis in Figure 4). In this series of univariate analyses, we find (Figure 15) that all effects on their own serve to decrease R_t . This gives us confidence that our choice of prior distribution is not driving the effects we see in the main analysis. Lockdown has a very large effect, most likely due to the fact that it occurs after other interventions in our dataset. The relatively large effect sizes for the other interventions are most likely due to the coincidence of the interventions in time, such that one intervention is a proxy for a few others.

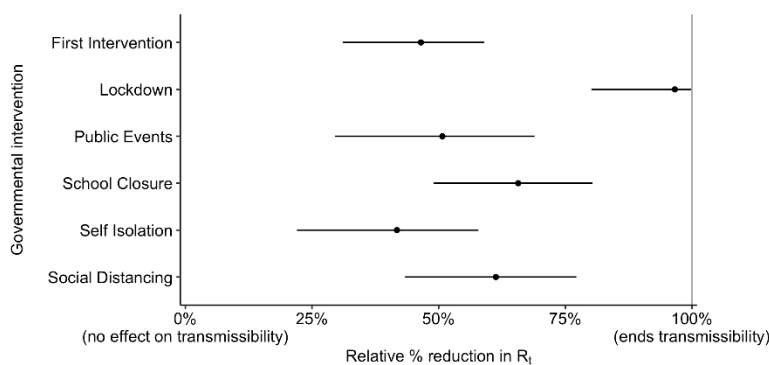


Figure 15: Effects of different interventions when used as the only covariate in the model.

8.4.4 Nonparametric fitting of R_t using a Gaussian process:

To assess prior assumptions on our piecewise constant functional form for R_t we test using a nonparametric function with a Gaussian process prior distribution. We fit a model with a Gaussian process prior distribution to data from Italy where there is the largest signal in death data. We find that the Gaussian process has a very similar trend to the piecewise constant model and reverts to the mean in regions of no data. The correspondence of a completely nonparametric function and our piecewise constant function suggests a suitable parametric specification of R_t .

8.4.5 Leave country out analysis

Due to the different lengths of each European countries' epidemic, some countries, such as Italy have much more data than others (such as the UK). To ensure that we are not leveraging too much information from any one country we perform a "leave one country out" sensitivity analysis, where we rerun the model without a different country each time. Figure 16 and Figure 17 are examples for results for the UK, leaving out Italy and Spain. In general, for all countries, we observed no significant dependence on any one country.

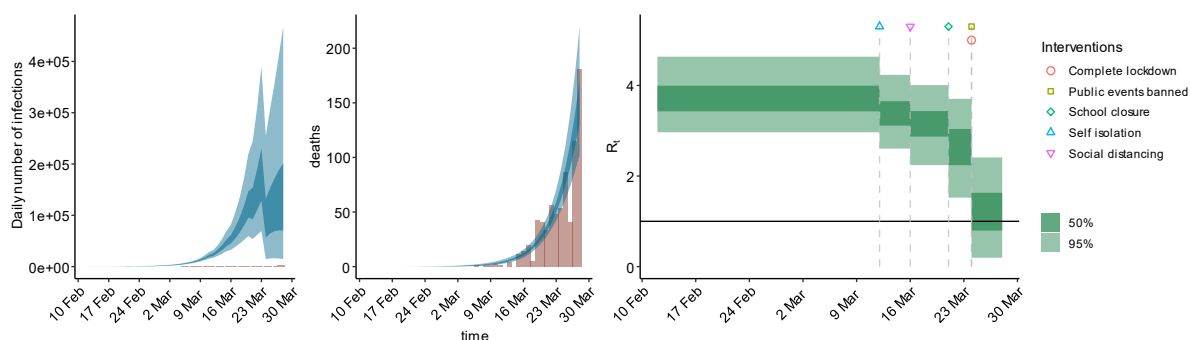


Figure 16: Model results for the UK, when not using data from Italy for fitting the model. See the caption of Figure 2 for an explanation of the plots.

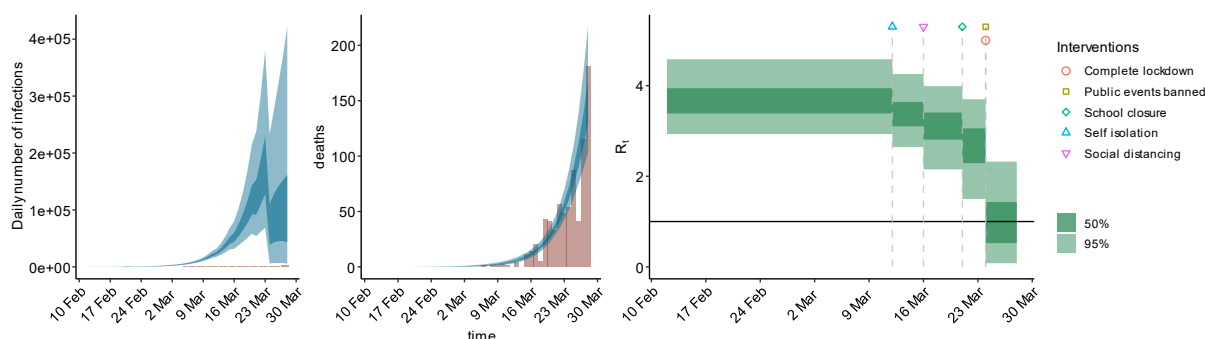


Figure 17: Model results for the UK, when not using data from Spain for fitting the model. See caption of Figure 2 for an explanation of the plots.

8.4.6 Starting reproduction numbers vs theoretical predictions

To validate our starting reproduction numbers, we compare our fitted values to those theoretically expected from a simpler model assuming exponential growth rate, and a serial interval distribution mean. We fit a linear model with a Poisson likelihood and log link function and extracting the daily growth rate r . For well-known theoretical results from the renewal equation, given a serial interval distribution $g(\tau)$ with mean m and standard deviation s , given $a = m^2/s^2$ and $b = m/s^2$, and

subsequently $R_0 = \left(1 + \frac{r}{b}\right)^a$. Figure 18 shows theoretically derived R_0 along with our fitted estimates of $R_{t=0}$ from our Bayesian hierarchical model. As shown in Figure 18 there is large correspondence between our estimated starting reproduction number and the basic reproduction number implied by the growth rate r .

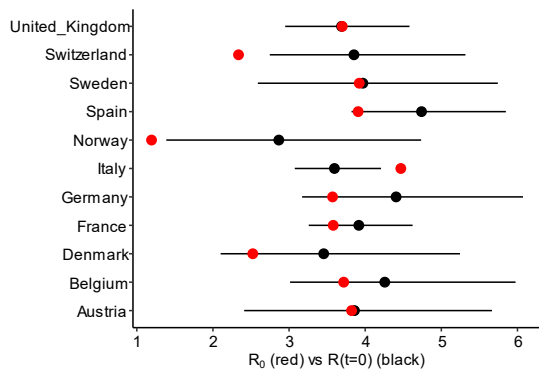
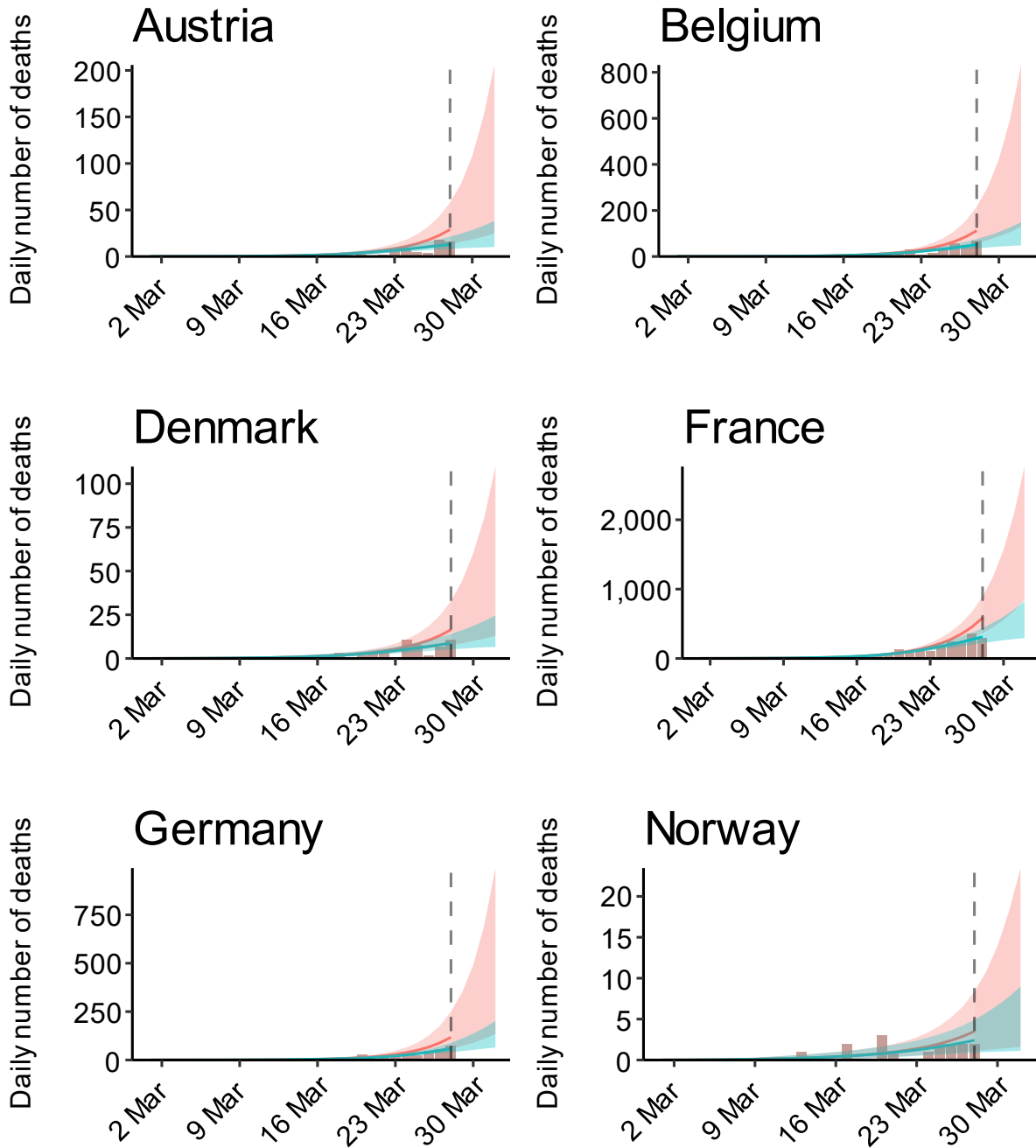


Figure 18: Our estimated R_0 (**black**) versus theoretically derived R_0 (**red**) from a log-linear regression fit.

8.5 Counterfactual analysis – interventions vs no interventions

Figures in this section are all country-specific plots equivalent to Figure 3 which only shows Italy and Spain.



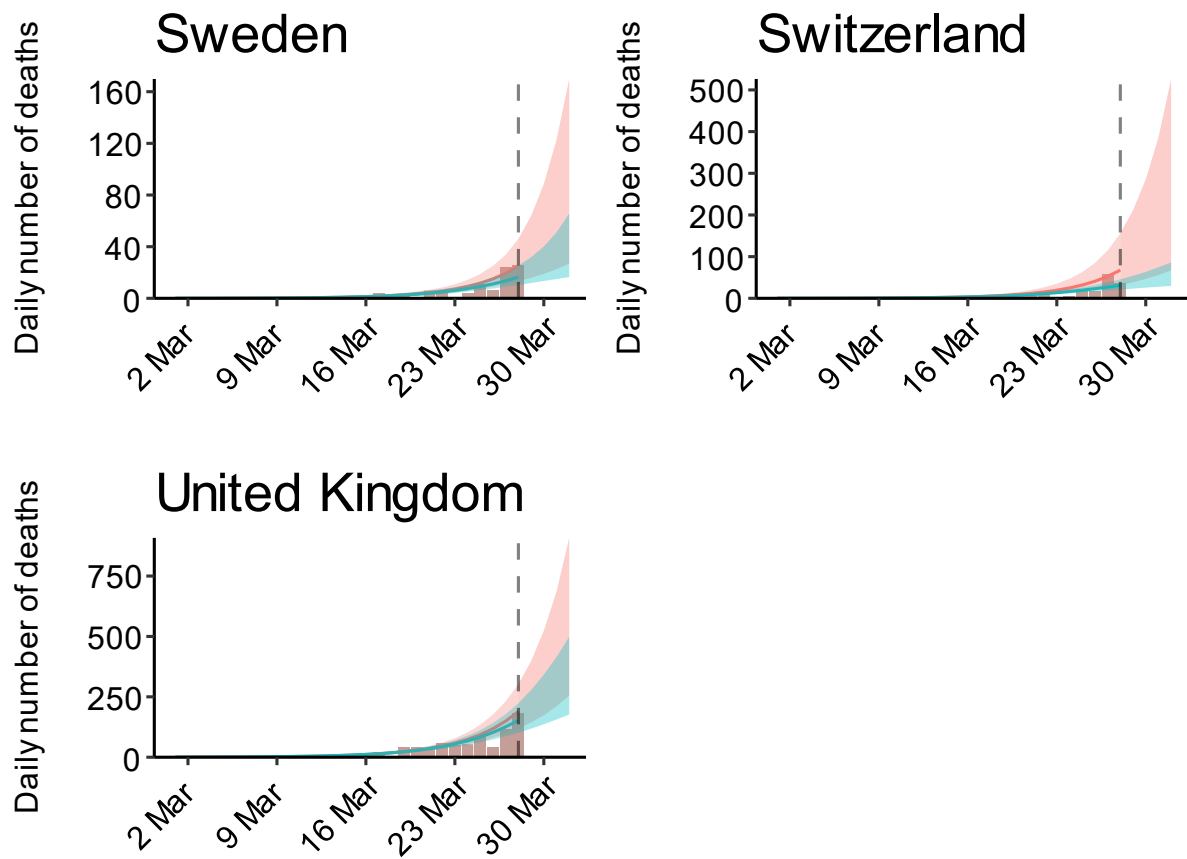


Figure 19: Daily number of confirmed deaths, predictions (up to 28 March) and forecasts (after) for all countries except Italy and Spain from our model with interventions (blue) and from the no interventions counterfactual model (pink); credible intervals are shown one week into the future.

8.6 Data sources and Timeline of Interventions

Figure 1 and Table 3 display the interventions by the 11 countries in our study and the dates these interventions became effective.

Table 3: Timeline of Interventions.

Country	Type	Event	Date effective
Austria	School closure ordered	Nationwide school closures. ²⁰	14/3/2020
	Public events banned	Banning of gatherings of more than 5 people. ²¹	10/3/2020
	Lockdown ordered	Banning all access to public spaces and gatherings of more than 5 people. Advice to maintain 1m distance. ²²	16/3/2020
	Social distancing encouraged	Recommendation to maintain a distance of 1m. ²²	16/3/2020
	Case-based measures	Implemented at lockdown. ²²	16/3/2020
Belgium	School closure ordered	Nationwide school closures. ²³	14/3/2020
	Public events banned	All recreational activities cancelled regardless of size. ²³	12/3/2020
	Lockdown ordered	Citizens are required to stay at home except for work and essential journeys. Going outdoors only with household members or 1 friend. ²⁴	18/3/2020
	Social distancing encouraged	Public transport recommended only for essential journeys, work from home encouraged, all public places e.g. restaurants closed. ²³	14/3/2020
	Case-based measures	Everyone should stay at home if experiencing a cough or fever. ²⁵	10/3/2020
Denmark	School closure ordered	Secondary schools shut and universities (primary schools also shut on 16th). ²⁶	13/3/2020
	Public events banned	Bans of events >100 people, closed cultural institutions, leisure facilities etc. ²⁷	12/3/2020
	Lockdown ordered	Bans of gatherings of >10 people in public and all public places were shut. ²⁷	18/3/2020
	Social distancing encouraged	Limited use of public transport. All cultural institutions shut and recommend keeping appropriate distance. ²⁸	13/3/2020
	Case-based measures	Everyone should stay at home if experiencing a cough or fever. ²⁹	12/3/2020

France	School closure ordered	Nationwide school closures. ³⁰	14/3/2020
	Public events banned	Bans of events >100 people. ³¹	13/3/2020
	Lockdown ordered	Everybody has to stay at home. Need a self-authorisation form to leave home. ³²	17/3/2020
	Social distancing encouraged	Advice at the time of lockdown. ³²	16/3/2020
	Case-based measures	Advice at the time of lockdown. ³²	16/03/2020
Germany	School closure ordered	Nationwide school closures. ³³	14/3/2020
	Public events banned	No gatherings of >1000 people. Otherwise regional restrictions only until lockdown. ³⁴	22/3/2020
	Lockdown ordered	Gatherings of > 2 people banned, 1.5 m distance. ³⁵	22/3/2020
	Social distancing encouraged	Avoid social interaction wherever possible recommended by Merkel. ³⁶	12/3/2020
	Case-based measures	Advice for everyone experiencing symptoms to contact a health care agency to get tested and then self-isolate. ³⁷	6/3/2020
Italy	School closure ordered	Nationwide school closures. ³⁸	5/3/2020
	Public events banned	The government bans all public events. ³⁹	9/3/2020
	Lockdown ordered	The government closes all public places. People have to stay at home except for essential travel. ⁴⁰	11/3/2020
	Social distancing encouraged	A distance of more than 1m has to be kept and any other form of alternative aggregation is to be excluded. ⁴⁰	9/3/2020
	Case-based measures	Advice to self-isolate if experiencing symptoms and quarantine if tested positive. ⁴¹	9/3/2020
Norway	School closure ordered	Norwegian Directorate of Health closes all educational institutions. Including childcare facilities and all schools. ⁴²	13/3/2020
	Public events banned	The Directorate of Health bans all non-necessary social contact. ⁴²	12/3/2020
	Lockdown ordered	Only people living together are allowed outside together. Everyone has to keep a 2m distance. ⁴³	24/3/2020
	Social distancing encouraged	The Directorate of Health advises against all travelling and non-necessary social contacts. ⁴²	16/3/2020
	Case-based measures	Advice to self-isolate for 7 days if experiencing a cough or fever symptoms. ⁴⁴	15/3/2020

Spain	School closure ordered	Nationwide school closures. ⁴⁵	13/3/2020
	Public events banned	Banning of all public events by lockdown. ⁴⁶	14/3/2020
	Lockdown ordered	Nationwide lockdown. ⁴³	14/3/2020
	Social distancing encouraged	Advice on social distancing and working remotely from home. ⁴⁷	9/3/2020
	Case-based measures	Advice to self-isolate for 7 days if experiencing a cough or fever symptoms. ⁴⁷	17/3/2020
Sweden	School closure ordered	Colleges and upper secondary schools shut. ⁴⁸	18/3/2020
	Public events banned	The government bans events >500 people. ⁴⁹	12/3/2020
	Lockdown ordered	No lockdown occurred.	NA
	Social distancing encouraged	People even with mild symptoms are told to limit social contact, encouragement to work from home. ⁵⁰	16/3/2020
	Case-based measures	Advice to self-isolate if experiencing a cough or fever symptoms. ⁵¹	10/3/2020
Switzerland	School closure ordered	No in person teaching until 4th of April. ⁵²	14/3/2020
	Public events banned	The government bans events >100 people. ⁵²	13/3/2020
	Lockdown ordered	Gatherings of more than 5 people are banned. ⁵³	2020-03-20
	Social distancing encouraged	Advice on keeping distance. All businesses where this cannot be realised have been closed in all states (kantons). ⁵⁴	16/3/2020
	Case-based measures	Advice to self-isolate if experiencing a cough or fever symptoms. ⁵⁵	2/3/2020
UK	School closure ordered	Nationwide school closure. Childminders, nurseries and sixth forms are told to follow the guidance. ⁵⁶	21/3/2020
	Public events banned	Implemented with lockdown. ⁵⁷	24/3/2020
	Lockdown ordered	Gatherings of more than 2 people not from the same household are banned and police enforceable. ⁵⁷	24/3/2020
	Social distancing encouraged	Advice to avoid pubs, clubs, theatres and other public institutions. ⁵⁸	16/3/2020
	Case-based measures	Advice to self-isolate for 7 days if experiencing a cough or fever symptoms. ⁵⁹	12/3/2020

9 References

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