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Supplementary information

The impact of uncertainty on predictions of the CovidSim epidemiological code

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Supplementary Information

The Impact of Uncertainty on Predictions of the CovidSim Epidemiological Code

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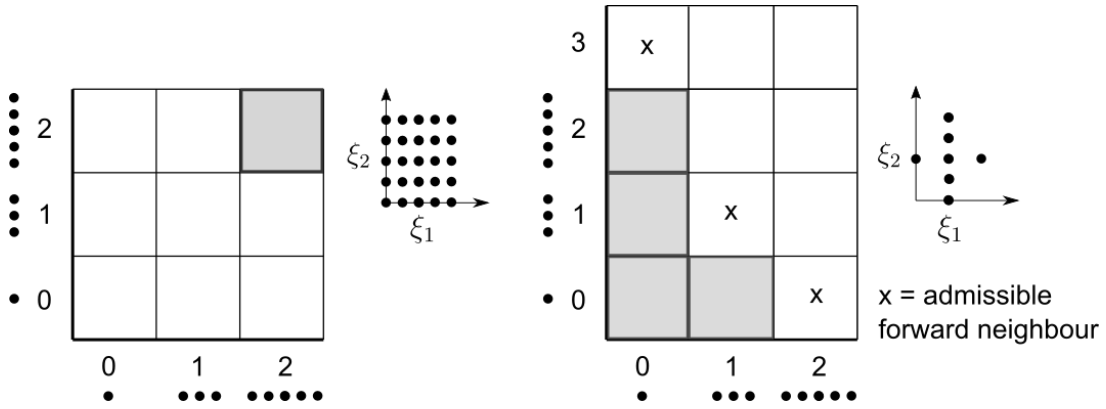


Supplementary Figure 1: **Sampling plans.** Two-dimensional example of building sampling plans with one-dimensional quadrature rules of different orders. Left shows a standard method, where for both inputs a 2nd-order quadrature rule is selected, leading to a dense sampling plan. Right displays a dimension-adaptive example at the 4-th iteration. The first iteration always contains the 0-th order rule for all inputs, i.e. $\Lambda = \{(0,0)\}$ in this two-dimensional case. A possible sequence which results in the setup shown above could be $(0,0) \to (1,0) \to (0,1) \to (0,2)$, and the 5-th multi index to be added to Λ must be selected from one of the admissible forward neighbors. Note that $(1,2)$ is not an admissible forward neighbour, since its backward neighbour $(1,1)$ is not in Λ (the gray squares). The displayed sampling plan is built from a linear combination of tensor products, using the quadrature orders in Λ.

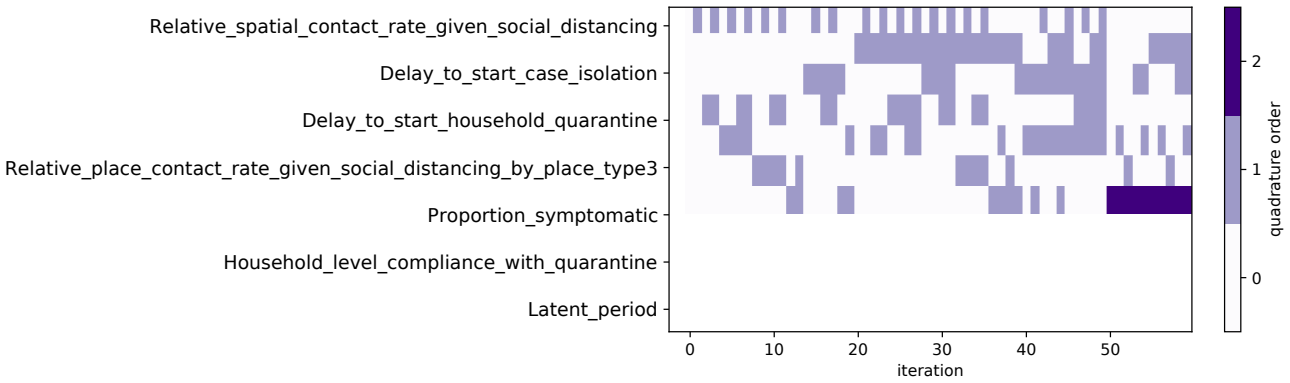
1 Introduction

The Supplementary Information contains results which provides further information on aspects of the uncertainty in the CovidSim code, along with details on the parameter refinement we performed.

2 Parameter refinement

The dimension-adaptive method iteratively builds a sampling plan, using a linear combination of points from quadrature rules of different order, as the locations on which to evaluate CovidSim. All parameters are initialized with quadrature order zero, and refinement is achieved by anisotropically increasing the quadrature order of (combinations of) parameters within a given iteration of the algorithm, based on a suitable error metric, see Supplementary Figure 1 for an illustration.

Consider Supplementary Figure 2, which shows the colour-coded refinement per iteration. Specifically, each column shows the quadrature orders that were used to refine the sampling plan. The first column is fully white, as all parameters are initialised to a zero-order rule. In the second column one parameter is refined to first order, and from there on different (combinations) of parameters are refined. Clearly, during roughly the first 50 iterations, the



Supplementary Figure 2: **Iterative refinement of sampling.** Colour-coded refinements per iteration of the dimension-adaptive algorithm. For the sake of clarity, not all iterations are shown. These results were obtained for $\mathcal{S}_1$.

algorithm refines many *combinations* of important parameters to a first-order quadrature rule, before the first parameter is refined to second order. That is, it focuses on interaction effects between different parameters, and in doing so it creates a relatively dense sampling plan in the hypercube spanned by the important parameters.

3 Parameter distributions

Table 1 contains the 19 parameters which were included in the final UQ campaign. All were prescribed with uniform distributions with ranges displayed in Table 1, along with their default values as found in the Report 9 parameter input files [1].

The 'Relative spatial contact rates by age power' is not a direct input parameter to CovidSim. It is part of a parametrization for the 'Relative spatial contact rates by age array' input, which is defined for a number of age groups with the default values of $[0.6, 0.7, 0.75, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 0.75, 0.5]$. There is a clear structure to this array, and it does not make sense to vary each entry independently form the others. Therefore, since these values lie between 0 and 1, we apply a simple power law to the default values, where 'Relative spatial contact rates by age power' is the exponent that we vary. This is implemented via a custom EasyVVUQ encoder, see [2] for the software.

4 Tuning ICU triggers

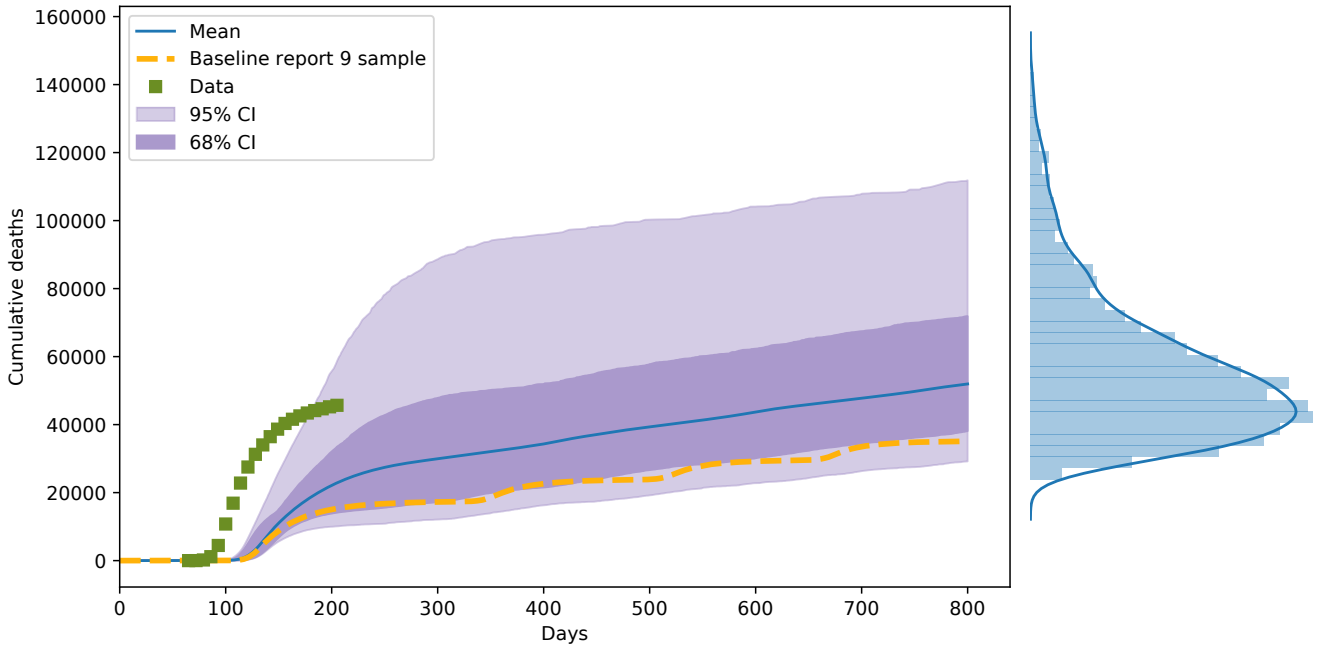
In this section we present the results for a third UQ campaign, at $R_0 = 2.6$, and ICU trigger values which are fitted to data. We use two data sources, the first detailing the 7 day rolling average of the the new ICU admissions as a percentage of new hospital admissions [3]. With data for the 7 day rolling average of new hospital admissions from [4], we can therefore obtain an estimate for the number of weekly new ICU admissions, which are the required values for

Parameter name	default	min	max	group
Relative household contact rate after closure	1.50	1.20	1.80	I
Household level compliance with quarantine	0.50	0.50	0.90	I
Relative spatial contact rate given social distancing	0.25	0.15	0.35	I
Delay to start household quarantine	1.00	0.50	3.50	I
Length of time households are quarantined	14.00	11.50	16.50	I
Delay to start case isolation	1.00	0.50	3.50	I
Duration of case isolation	7.00	4.50	9.50	I
Symptomatic infectiousness relative to asymptomatic	1.50	1.00	2.00	D
Proportion symptomatic	0.66	0.40	0.80	D
Latent period	4.59	3.00	6.00	D
Household attack rate	0.14	0.10	0.19	D
Relative spatial contact rates by age power	1.00	0.25	4.00	D
Residual place contacts after household quarantine	0.25	0.20	0.30	SG
Relative place contact rate given social distancing by place type2	0.75	0.60	0.90	SG
Relative place contact rate given social distancing by place type3	0.75	0.60	0.90	SG
Relative rate of random contacts if symptomatic	0.50	0.40	0.60	SG
Relative level of place attendance if symptomatic1	0.25	0.20	0.30	SG
Relative level of place attendance if symptomatic2	0.50	0.40	0.60	SG
Relative level of place attendance if symptomatic3	0.50	0.40	0.60	SG

Supplementary Table 1: The parameters, with their default values and uncertain range, which were included in the final UQ campaign. Variables ending with a number are part of a vector with the same name. The 'group' column indicates the group from which the parameter was selected, namely the intervention (I), disease (D) of spatial/geographic (SG) group. A description of these parameters can be found in our 'parameter list' folder in [2].

the ICU triggers.

Next we try to match CovidSim's 'on' and 'off' events to reality. By March 25, all NPIs were in place in the UK. We then extract the rolling average of new hospital admissions (1987) and the percentage which moves to the ICU from the data at that date (12%), such that our estimate for the 'on' trigger is $1987 \times 0.12 \approx 238$. It is not possible to match CovidSim's 'off' event to actual events. The model relaxation of NPIs consists of turning off both place closure of schools and universities (PC) and general social distancing (SD) [5]. A simultaneous relaxation of PC and SD did not occur in the UK. The stay-at-home order ended on May 13, which we will use instead, giving an 'off' trigger of $928 \times 0.05 \approx 46$ new



Supplementary Figure 3: **Cumulative death predictions with tuned ICU triggers.** The mean cumulative death prediction for the scenario with tuned ICU triggers, plus confidence intervals (CI), and at the right of the figure, the pdf of the total death count after 800 days. These results were obtained using a computational budget of 3000 CovidSim evaluations per scenario. Day 0 corresponds to January 1st, 2020. In addition, we plot the observed cumulative death count data for the UK (green squares), obtained from [7]. The first data point is at March 6th 2020, which corresponds to day 66. The striped line is a single sample from CovidSim (current release), run with the baseline parameter values of Report 9.

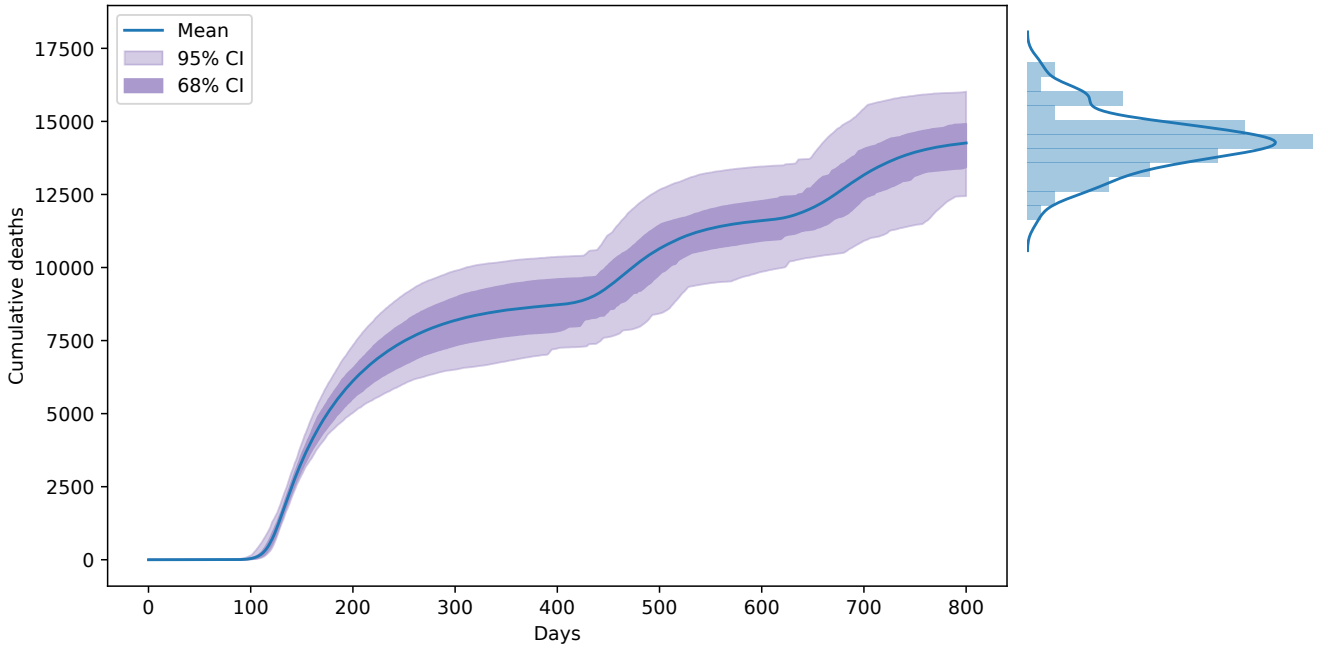
weekly ICU cases.

The confidence intervals obtained in this way are shown in Supplementary Figure 3. Note that these do not deviate from the Results section of the main manuscript in any significant (qualitative) way. We therefore conclude that tuning other scenario parameters, such as R_0 and the initial condition as done in [6], is more effective if one wishes to remove the bias of the mean prediction with respect to the validation data.

5 Random seeds

CovidSim is stochastic, with 4 random seeds, specified via the command line. Two random seeds are used in the creation of the network of individuals mentioned in the Introduction. The remaining seeds affect the interactions between individuals, controlling how they become infected and propagate infection. The role of the random seeds in the code is of some significance, but they do not play as large a role as the dominant parameters shown in the

preceding section. Specifically, we varied the 4 random seeds, keeping all other parameters fixed, and compared the amount of output variance we obtain compared to varying the parameters with fixed seeds. The uncertainty due to the seeds is significantly smaller, see Supplementary Figure 4. In light of these results, we do not vary the random seeds in our parametric uncertainty analysis. We do note however, that the large number of infections in the population could damp the effect of stochastic dynamics. For diseases with low prevalence, like measles, stochastic dynamics may well prove to be an important source of uncertainty. In this case one may use recently developed uncertainty-quantification techniques, designed specifically for stochastic simulators [8].



Supplementary Figure 4: **Cumulative death predictions with varying random seeds.** The confidence intervals (CI) for the predicted cumulative deaths under scenario $\mathcal{S}_1$, varying the random seeds only. The seeds were sampled on a standard tensor grid sampling plan of 81 points. The variance is significantly smaller than in Figure 1 of the main article, in which 19 input parameters were varied.

6 Model structure uncertainty

We also reiterate that there is uncertainty in the model structure $\mathcal{M}$, as a different model might have given a better fit to the data, while still conditioned on the same scenario of the preceding section. For instance, during the pandemic it has become apparent that the COVID-19 spread in hospitals and care homes constituted a significant fraction of the overall spread, particularly in the UK [1]. The spread in these locations, which is not explicitly

modelled in CovidSim, may also be a reason why the number of cases initially forecast with CovidSim was lower than the number that occurred in reality. Although precautions have been taken to reduce this spread, and the availability of personal protective equipment has improved, incorporating these factors will still be important for those models that need to be validated against data from the start of the pandemic.

Other missing epidemiological processes which might become important for future predictions are face masks and contact tracing. In March 2020, the beneficial effects of wearing face masks was still heavily contested [9]. However, research is now available that suggests that wearing a face mask reduces viral spread when coughing [10], and that it correlates on the population level with a reduced case incidence [11].

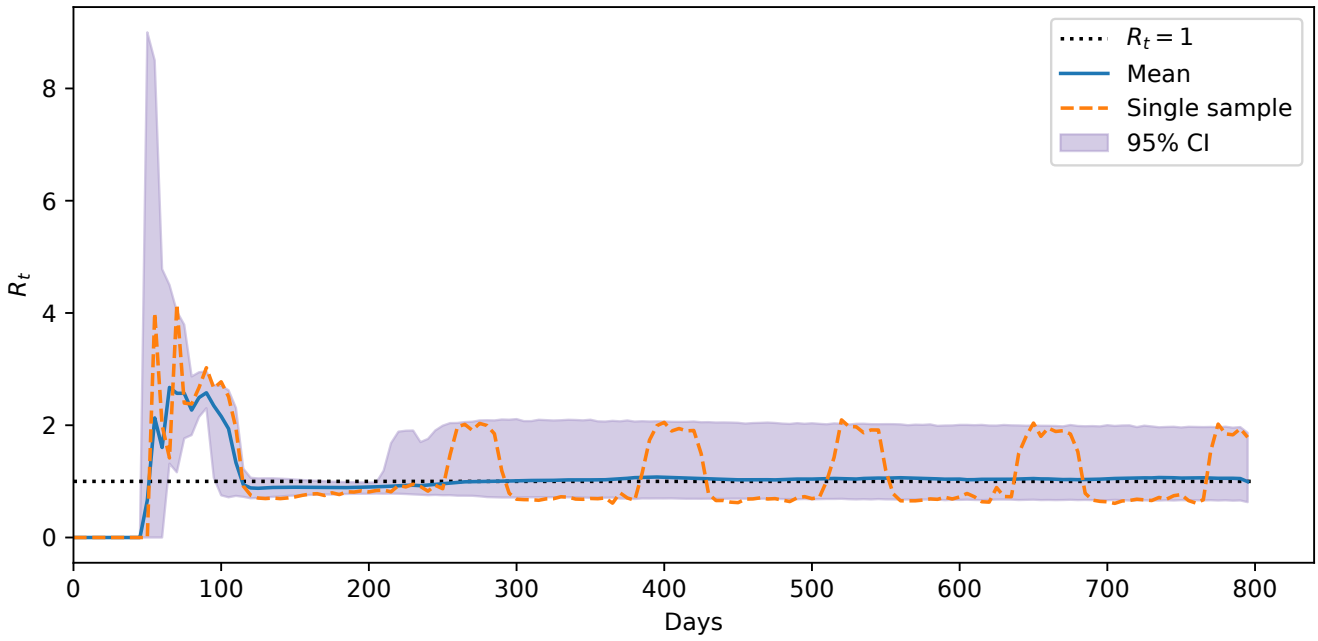
In many countries with low case prevalence, contact tracing is used to reduce the spread of COVID-19. Contact tracing capability was very limited in the UK during March 2020, but it has now improved and could be incorporated in future models. Here, the quality and extent of contact tracing are important, as imperfect contact tracing has a strongly reduced benefit [12].

One might also think of a ban on public events, i.e. limiting gatherings to below a specified number of people, as a missing process. This is often one of the first NPIs to be implemented; see [13] for a time line. However, the argument can be made that general social distancing implicitly takes this into account.

Some practical issues may arise in regard to validating new model components. One would need hard data on the effect of face masks or contact tracing in order to directly validate the new model components. Alternatively, indirect data might be used, e.g. to see if the inclusion of these new model structures reduces the bias between the mean cumulative death prediction and the validation data. Another sensible recourse would be to treat new components as probabilistic, and perform a UQ study on the model structure uncertainty [14, 15].

7 Other quantities of interest

We have thus far only focused on cumulative death predictions. Here we will briefly show the confidence intervals for R_t, i.e. the effective reproduction number as a function of time t. We will focus on the scenario with the tuned ICU triggers from Section 4. The results are depicted in Supplementary Figure 5. After an initial transient part, the 95% confidence intervals are bounded between an R_t value of 2.0 and 0.7. These bounds are generated by the sawtooth pattern of individual model outputs, of which we show a random example as well. Interestingly, the actual R value has not fallen below 0.7 in the UK [16], so it seems that CovidSim predicts this quite well. The straight dotted line marks $R_t = 1$, which practically overlaps with the mean prediction after the initial transient part.



Supplementary Figure 5: **The mean and 95% confidence interval for R_t.** A single sample is also shown, whose sawtooth pattern clearly indicates the effect of the on/off ICU triggers. After the initial transient part, the upper and lower 95% confidence intervals are located at approximately 2.0 and 0.7. The dotted line indicates $R_t = 1$.

8 Other Sobol indices

The main article only showed the Sobol indices for the three most influential inputs for scenario $\mathcal{S}_1$ and $\mathcal{S}_2$. Instead, Supplementary Figure 6 displays the first-order Sobol indices for all 19 input parameters and both scenarios. The results for $\mathcal{S}_1$ and $\mathcal{S}_2$ are fairly similar, as for instance the three most dominant parameters are the same. For the less influential parameters the ranking starts to differ between $\mathcal{S}_1$ and $\mathcal{S}_2$.

By definition, the contribution of the least influential parameters are clumped together near zero, making it poorly visible. Consider therefore Supplementary Figure 7 as well, which shows a bar chart depicting their time-averaged values. For this set, 'Relative place contact rate given social distancing by place type3', 'Proportion symptomatic', 'Delay to start household quarantine' and 'Household level compliance with quarantine' are dominant for both $\mathcal{S}_1$ and $\mathcal{S}_2$, although the order does differ.

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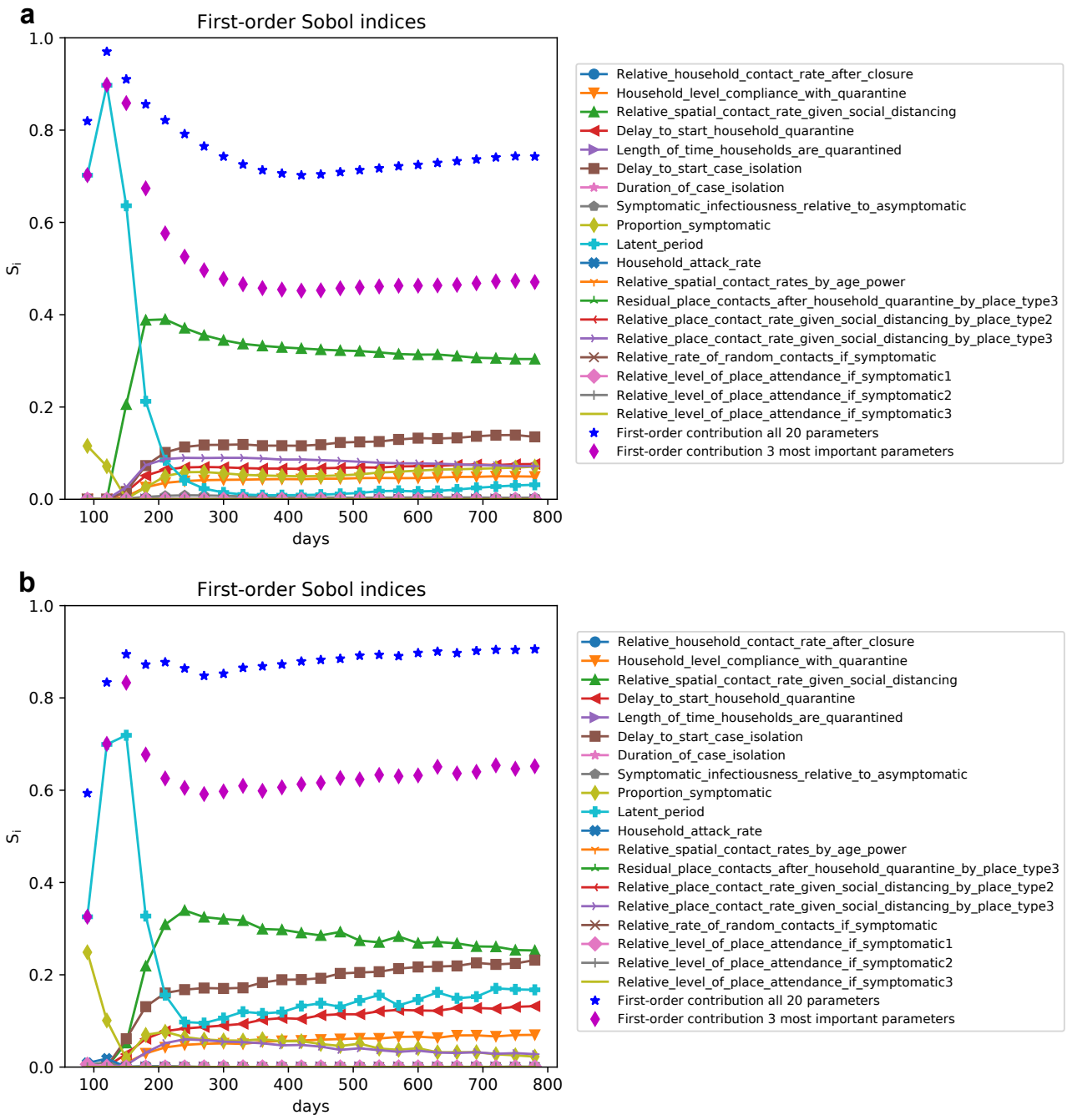
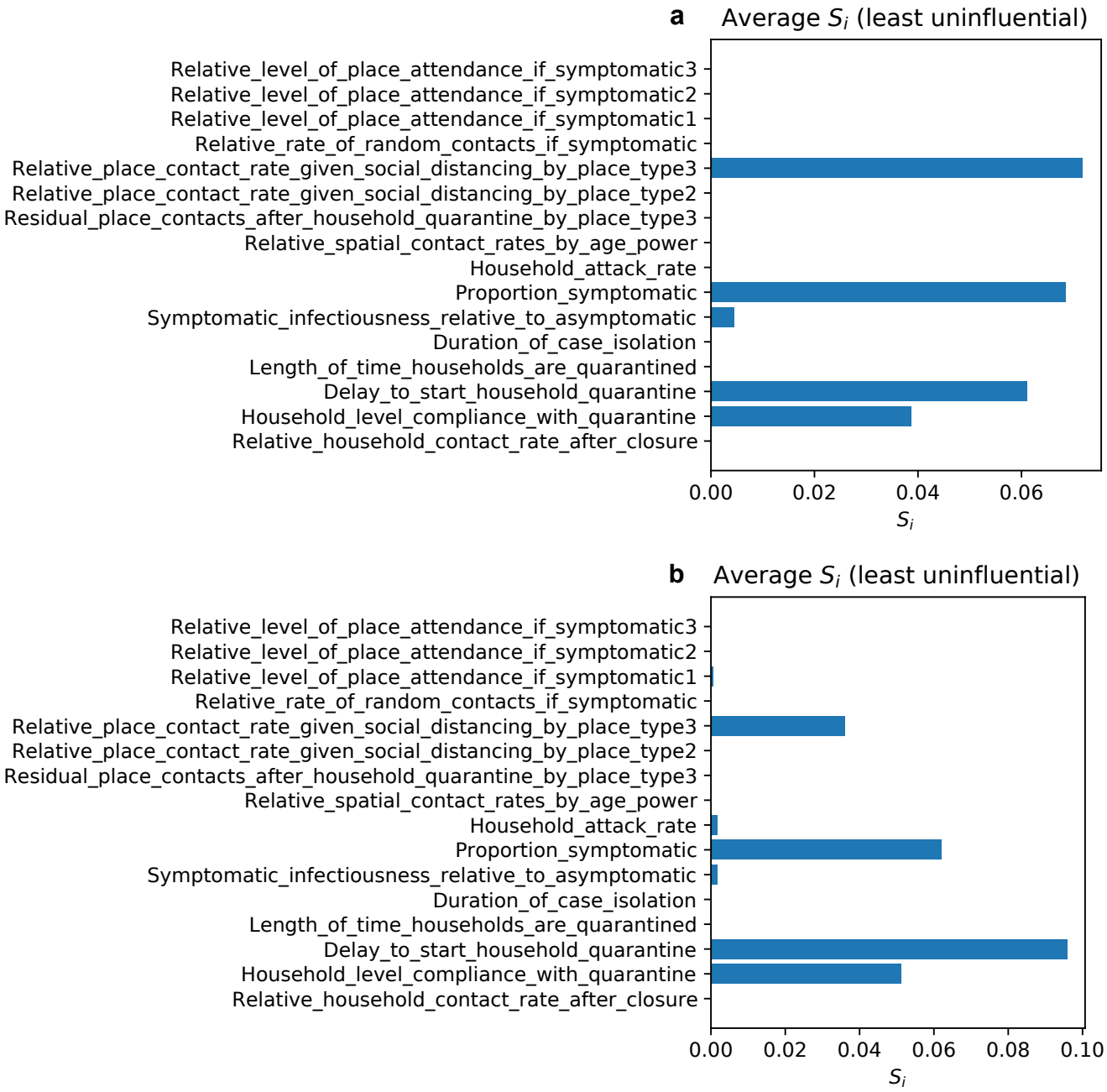


Supplementary Figure 6: **Sobol indices for all parameters within the two scenarios.** The first-order Sobol indices for all parameters and two scenarios (**a**: $\mathcal{S}_1$, **b**: $\mathcal{S}_2$), plotted against time at one month intervals. It shows the fraction of the variance that each parameter is responsible for, over time. In addition, we show the sum of all 19 first-order indices (blue stars). The sum of the 3 most dominant parameters is also shown (red diamonds).



Supplementary Figure 7: **Time-averaged sobol indices for least influential parameters within the two scenarios.** The time-averaged first-order Sobol indices for the 16 least influential parameters, for both scenarios (**a**: $\mathcal{S}_1$, **b**: $\mathcal{S}_2$). Parameters which were never refined do not contribute to the variance.

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