

SUPPLEMENTARY MATERIAL

Additional explanation of intervention scenarios

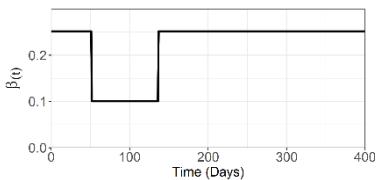
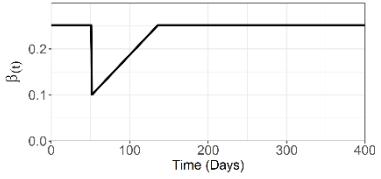
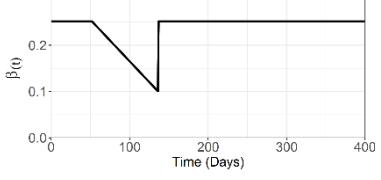
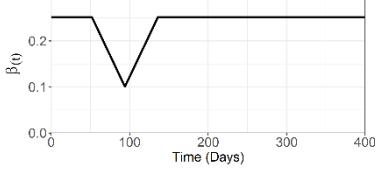
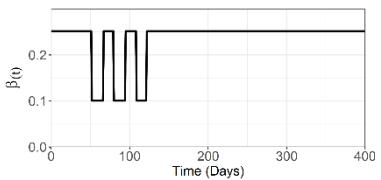
Scenario	$\beta(t)$ during the simulation	Real-world Parallels
1	 <p>A classic interpretation of NPIs such as lockdown measures, a flat constant reduction to transmission which is sustained until the cessation of the intervention. Used in a variety of models considering the effects of NPIs (1-4).</p>	
2	 <p>“Ramping down” strategy, an initial strong intervention is followed by a gradual reduction in the strength of the intervention. Can draw parallels to the gradual re-opening strategies adopted by countries after having instituted strong NPIs. The purpose of this strategy is to slowly reinvigorate the economy and allow greater levels of population movement following a restrictive NPI (3, 5, 6).</p>	
3	 <p>A “ramping up” strategy, uses a slow deliberate introduction of harsher NPI measures over time, with the intervention reaching its greatest magnitude as the intervention is finishing. After this point, NPI restrictions are lifted. Due to the riskier nature of this intervention scenario, evidence of this intervention scenario is not common in epidemiological or modelling literature. However we envisage a scenario where policy makers attempt to reactively increase the strength of interventions over time to mitigate potential economic effects of NPI measures, as opposed to an instantaneous population lockdown in response to new cases .</p>	
4	 <p>A hybrid of scenario 2 and 3, involving a ramping up and ramping down of intervention measures. Real-world parallels to this strategy are rare, but could involve a scenario where a policy-maker ramps up outbreak response and deems the situation controlled enough to initiate a controlled ramping down of measures after the peak of the outbreak has passed.</p>	
5	 <p>The pulsed intervention scenario has parallels with hypothetical interventions aiming to control COVID-19. Two types of pulsed measures have been theorised, either a “triggered” pulse measure in response to epidemiological threshold being met (ICU bed capacity or incidence), or an “open loop” pulse which uses fixed timings, independent of the epidemiological situation, to introduce the intervention (4, 5, 7-9).</p>	

Table S1 – Parameters for the Single Intervention Scenario

Parameter Description	Notation	Baseline Value	References
Doubling Time	t_d	3 Days	(10, 11)
Baseline Basic Reproduction Number	R_0	2.8 (baseline) - used to calculate gamma	(9, 12-14)
Generation Time	G	7.8 days	Calculated from eqn 1.2 (15)
Per capita rate of recovery from COVID-19 infection	γ	0.128	Calculated from $1/G$
Per capita rate of COVID-19 transmission (Baseline)	β	0.359	Calculated from $R_0\gamma$
Scaled per capita rate of COVID-19 transmission (reflects the impact of small-scale NPIs on transmission)	β_{scale}	0.2513 (30% reduction to baseline β)	(9, 14, 16)
Minimum value of the lockdown-related scaling factor $c(t)$	c_{min}	0.4 (60% reduction to β_{scale})	(9, 14, 16)
Length of Intervention	Scenario 1	d_t	84 days (12 weeks)
	Scenario 2, 3, 4 and 5		168 days (24 weeks)
Intervention Trigger Point	t_p	Day 52 ($I_c(52) = 0.02$)	Calculated from Model

Table S2 – Parameters for the Multi Intervention Scenario

Parameter Description	Notation	Baseline Value	References
Doubling Time	T_d	3 Days	(10, 11)
Baseline Basic Reproduction Number	R_0	2.8 (baseline) - used to calculate gamma	(9, 12-14)
Generation Time	G	7.8 days	Calculated from eqn 1.2 (15)
Per capita rate of recovery from COVID-19 infection	γ	0.128	Calculated from $1/G$
Per capita rate of COVID-19 transmission (Baseline)	β	0.359	Calculated from $R_0\gamma$
Scaled per capita rate of COVID-19 transmission (reflects the impact of small-scale NPIs on transmission)	β_{scale}	0.2513 (30% reduction to baseline β)	(9, 14, 16)
Minimum value of the lockdown-related scaling factor $c(t)$ – Intervention 1	c_{min1}	0.4 (60% reduction to β_{scale})	(9, 14, 16)
Minimum value of the lockdown-related scaling factor $c(t)$ – Intervention 2	c_{min2}	0.4 (60% reduction to β_{scale})	(9, 14, 16)
Length of Intervention – Intervention 1	Scenario 1	d_{t1}	42 days (6 weeks)
	Scenario 2, 3, 4 and 5		84 days (12 weeks)
Length of Intervention – Intervention 2	Scenario 1	d_{t2}	42 days (6 weeks)
	Scenario 2, 3, 4 and 5		84 days (12 weeks)
Intervention Trigger Point – Intervention 1	t_{p1}	Day 52 ($I_c(52) = 0.02$)	Calculated from Model
Intervention Trigger Point – Intervention 2	t_{p2}	Day 52 ($I_c(52) = 0.02$)	Calculated from Model

Software and R Packages Used

R packages used to run model ODEs, plotting and data manipulation are as follows: “desolve” ((17)), “ggplot2” (18) and “reshape2” (19).

Table S3 – Optimal parameter values for the main text model sensitivity analyses

Sensitivity Analysis	Scenario	Value of the optimised outcome measure		Optimal Value of Parameter 1		Optimal Value of Parameter 2	
		I_{max}	$I_c(t_{max})$	I_{max}	$I_c(t_{max})$	I_{max}	$I_c(t_{max})$
Single-intervention (t_p) (Figure 1B)	1	0.055	0.503	72	86		
	2	0.035	0.504	67	85		
	3	0.035	0.517	7	24		
	4	0.037	0.508	38	53		
	5	0.059	0.516	32/53/74	79		
Single-intervention (c_{min}) (Figure 1B)	1	0.051	0.067	0.72	0.77		
	2	0.055	0.648	0.56	0.62		
	3	0.087	0.545	0.00	0.00		
	4	0.044	0.671	0.00	0.41		
	5	0.052	0.573	0.27	0.47		
Single-intervention (d_t) (Figure 1B)	1*	0.131	0.774	328	N/A		
	2	0.041	0.601	400	400		
	3	0.054	0.565	60	97		
	4	0.044	0.506	100	174		
	5	0.058	0.500	104/175	270		
Single-intervention (t_p/d_t) (Figure 2)	1*	0.065	0.426	70	80	250	250
	2	0.031	0.415	66	80	250	250
	3	0.033	0.471	0	0	184	221
	4	0.033	0.432	22	31	248	250
	5	0.057	0.474	42	79	244	250
Multi-intervention (t_{p1}/t_{p2}) (Figure 3A)	1	0.038	0.505	68	86	22	9
	2	0.046	0.512	39	80	0	0
	3	0.037	0.515	38	50	0	0
	4	0.041	0.511	54	65	0	0
	5	0.054	0.521	34	70	0	0
Multi-intervention (c_{min1}/c_{min2}) (Figure 3B)	1	0.049	0.514	0.26	0.52	0.62	0.00
	2	0.095	0.515	0.64	0.01	0.00	0.00
	3	0.044	0.495	0.00	0.23	0.00	0.00
	4	0.048	0.546	0.54	0.00	0.00	0.00
	5	0.070	0.515	0.49	0.01	0.00	0.00

*Note that scenario 1 d_t sensitivity analyses were used a transformed relative scale for d_t to allow for comparison across scenarios, with the relative scale of $0 \leq d_t \leq 400$ being equal to an absolute d_t range of $0 \leq d_t \leq 200$.

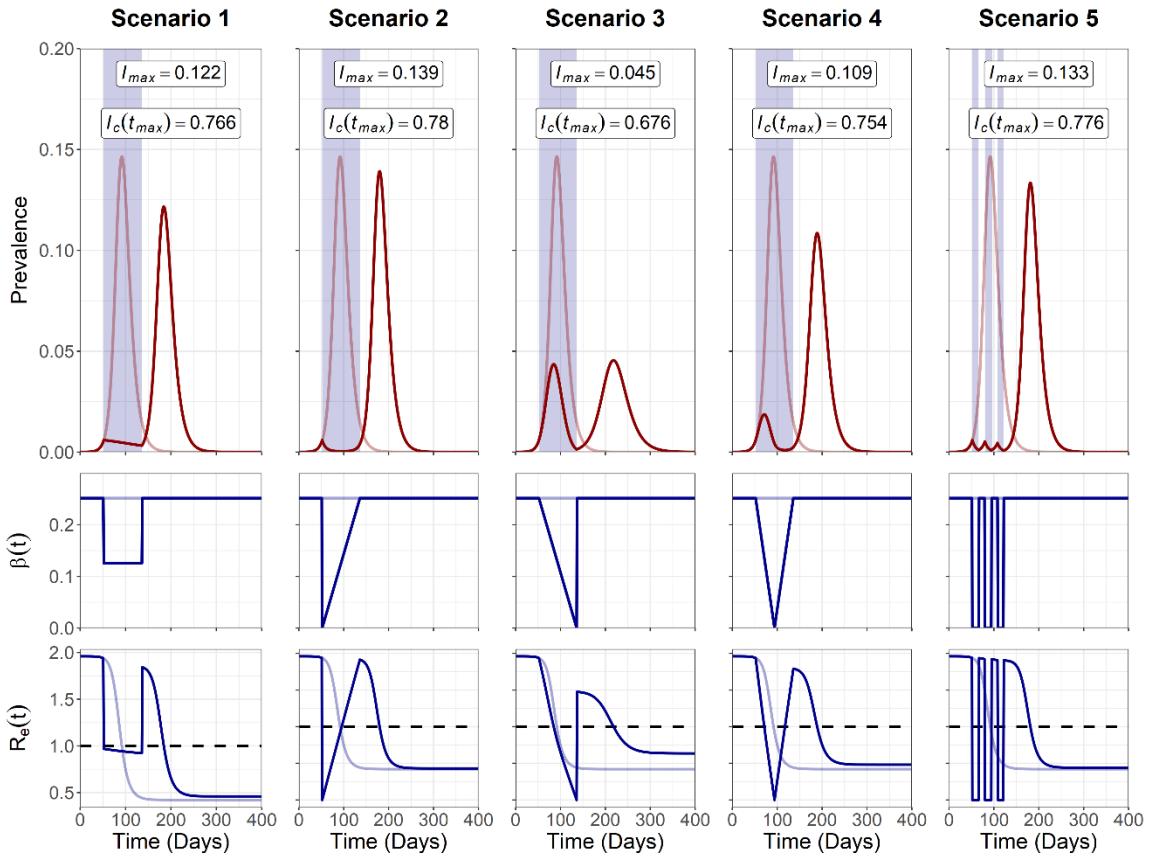


Figure S1. Trajectory plots for the single intervention epidemic curve, $\beta(t)$ reductions and $R_e(t)$ for the alternative methodology to double c_{min} to ensure similar magnitude of intervention across the intervention durations for scenario 2, 3, 4 and 5. Note that for A) opaque red and blue lines in the trajectory plot depict unmitigated epidemic curve dynamics. Blue shading indicates the period of the intervention. Dotted line on the $R_e(t)$ plot denotes the threshold for sustained epidemic growth. I_{max} and $I_c(t_{max})$ values are annotated for each scenario. Scenario 1 was set at $c_{min} = 0.5$ to allow for scenario 2, 3, 4 and 5 to be set at $c_{min} = 0$ (double the intervention magnitude).

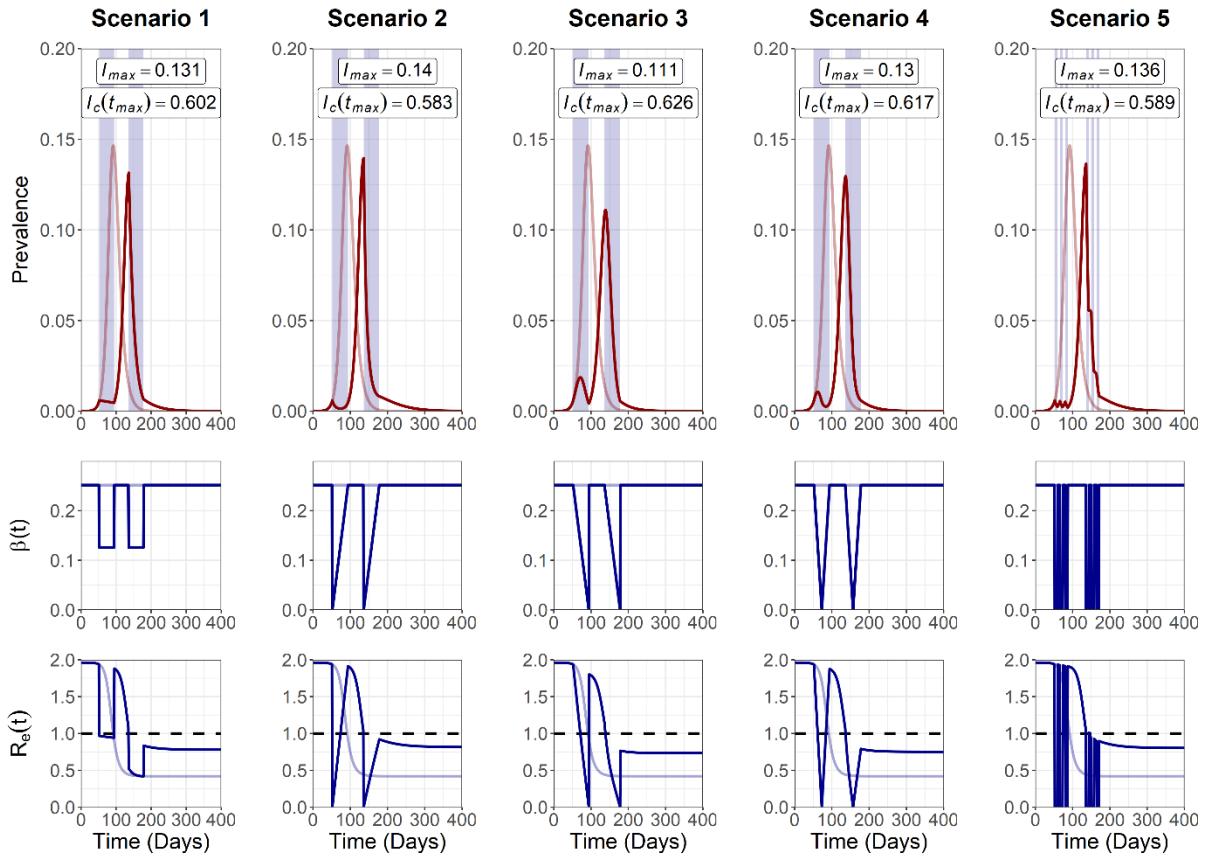


Figure S2. Trajectory plots for the multiple intervention epidemic curve, $\beta(t)$ reductions and $R_e(t)$ for the alternative methodology to double c_{min} to ensure similar magnitude of intervention across the intervention durations for scenario 2, 3, 4 and 5. Note that for A) opaque red and blue lines in the trajectory plot depict unmitigated epidemic curve dynamics. Blue shading indicates the period of the intervention. Dotted line on the $R_e(t)$ plot denotes the threshold for sustained epidemic growth. I_{max} and $I_c(t_{max})$ values are annotated for each scenario. Scenario 1 was set at $c_{min} = 0.5$ to allow for scenario 2, 3, 4 and 5 to be set at $c_{min} = 0$ (double the intervention magnitude).

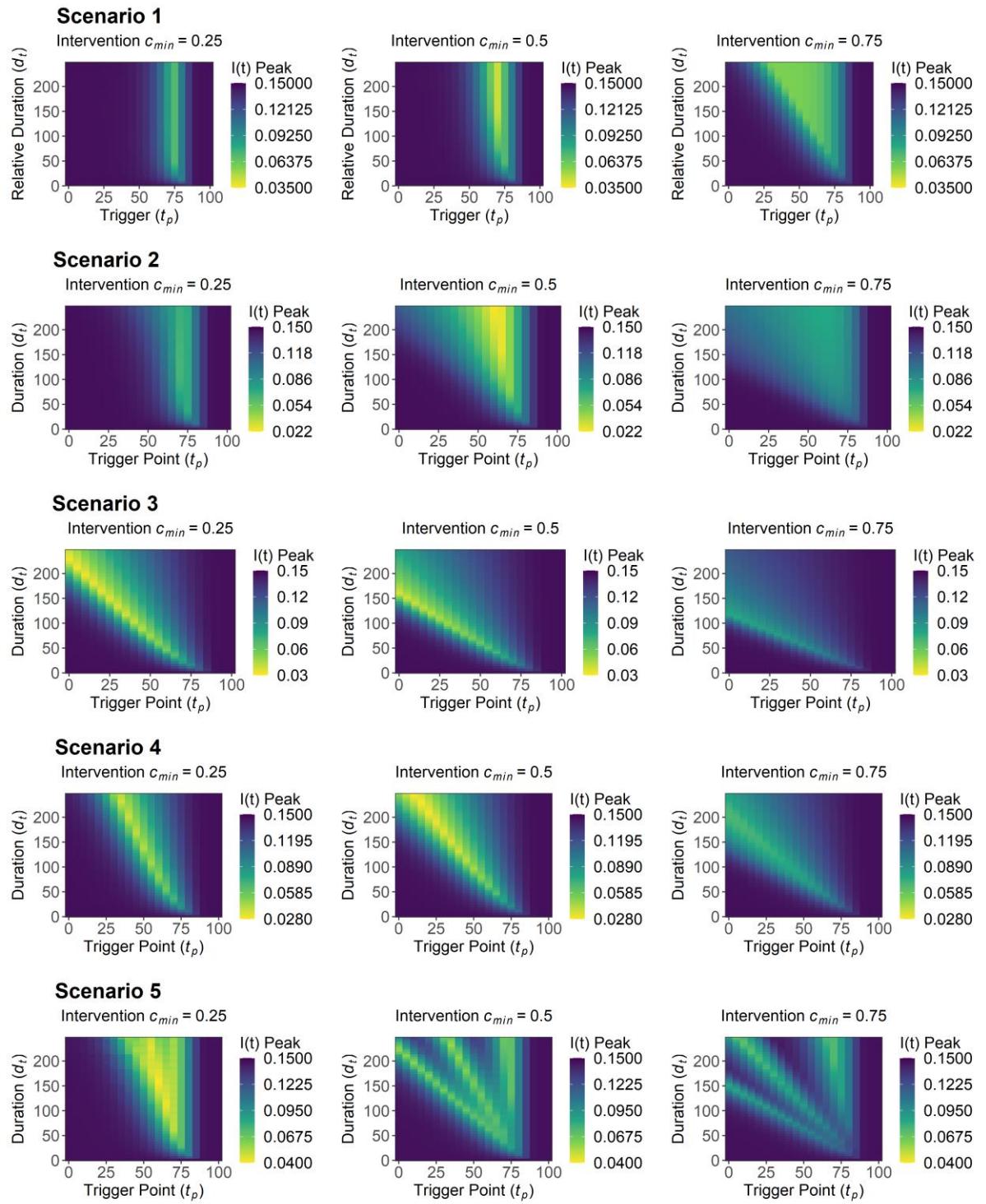


Figure S3. Sensitivity analysis for maximum $I(t)$ peak, I_{max} for intervention trigger day, t_p , and the intervention duration, d_t , explored for varying values of c_{min} . Note that the scenario 1 d_t axis was transformed into a relative axis to allow for comparison across scenarios, with the relative axis of $0 \leq d_t \leq 400$ being equal to an absolute d_t range of $0 \leq d_t \leq 200$.

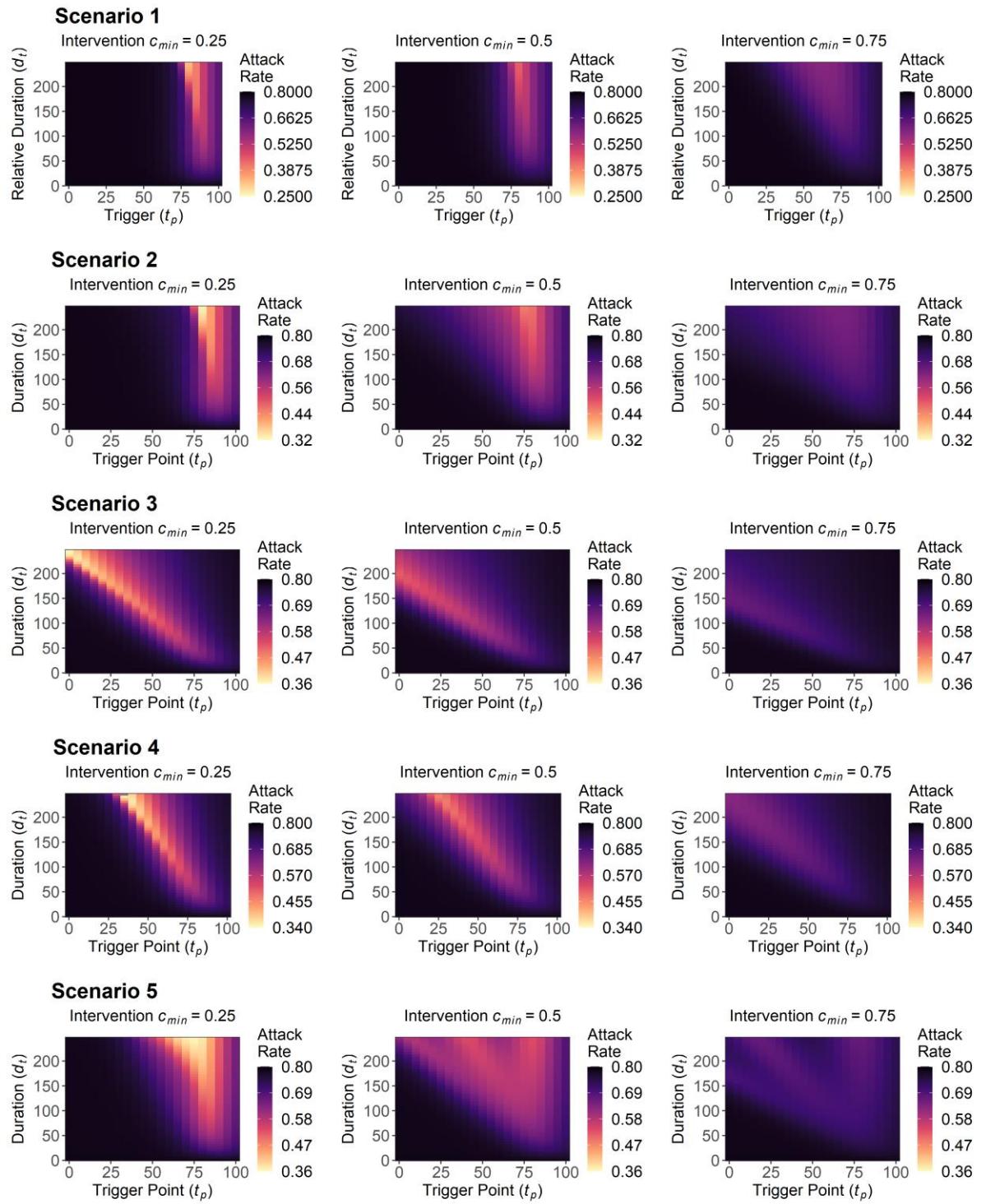


Figure S4. Sensitivity analysis for the attack rate, $I_c(t_{max})$ for intervention trigger day, t_p , and the intervention duration, d_t , explored for varying values of c_{min} . Note that the scenario 1 d_t axis was transformed into a relative axis to allow for comparison across scenarios, with the relative axis of $0 \leq d_t \leq 400$ being equal to an absolute d_t range of $0 \leq d_t \leq 200$.

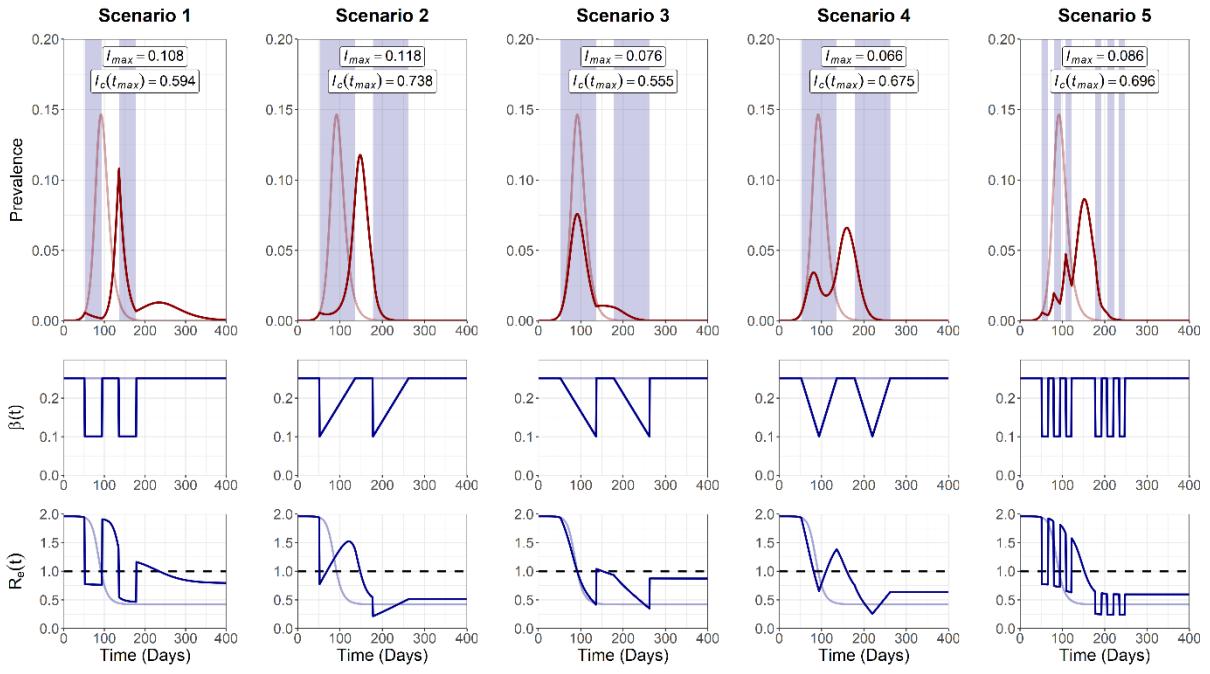


Figure S5. Trajectory plots for the epidemic curve, intervention associated $\beta(t)$ reductions and $R_e(t)$, for the five multi-intervention scenarios. Opaque red and blue lines depict unmitigated epidemic curve dynamics. Blue shading on the trajectory plot indicates the period of the intervention. Dotted line denotes the $R_e(t)$ threshold for sustained epidemic growth. I_{max} and $I_c(t_{max})$ values are annotated for each scenario.

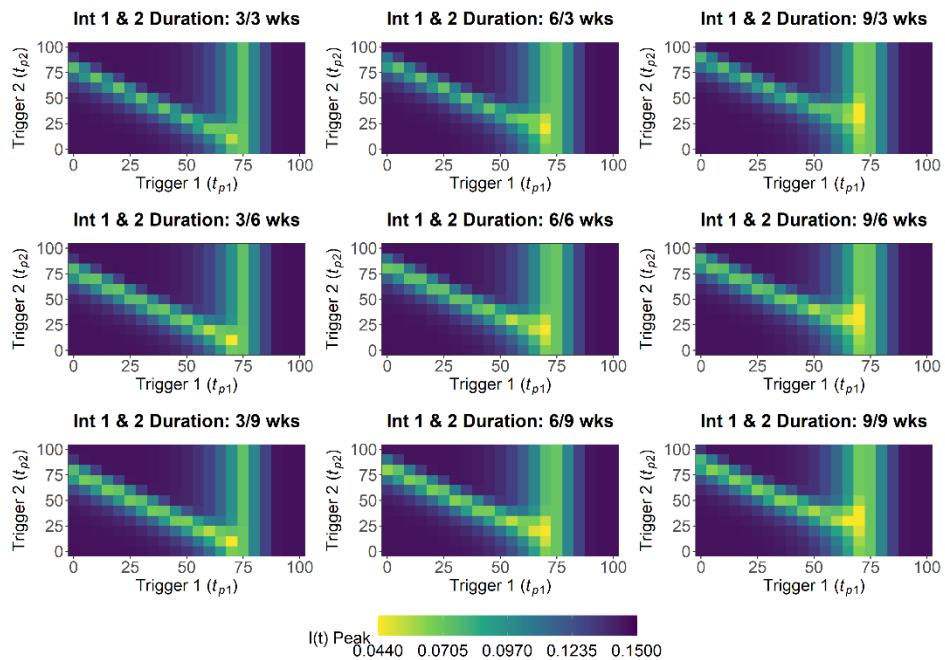
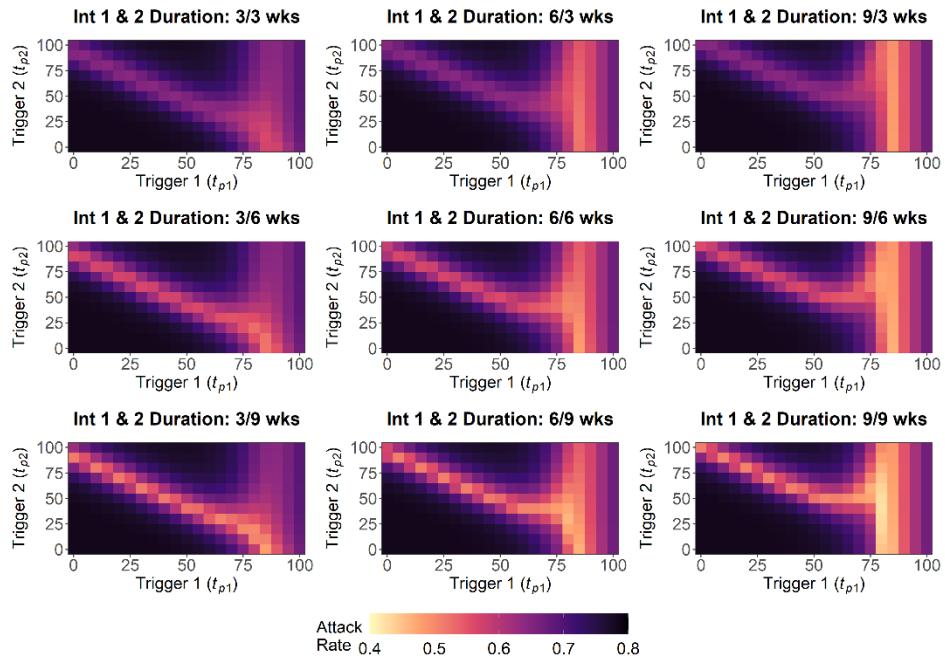
A**B**

Figure S6. Scenario 1 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) attack rate, $I_c(t_{max})$, for intervention 1 trigger date, t_{p1} , and intervention 2 trigger date, t_{p2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 3/6/9$ weeks were explored in this sensitivity analysis.

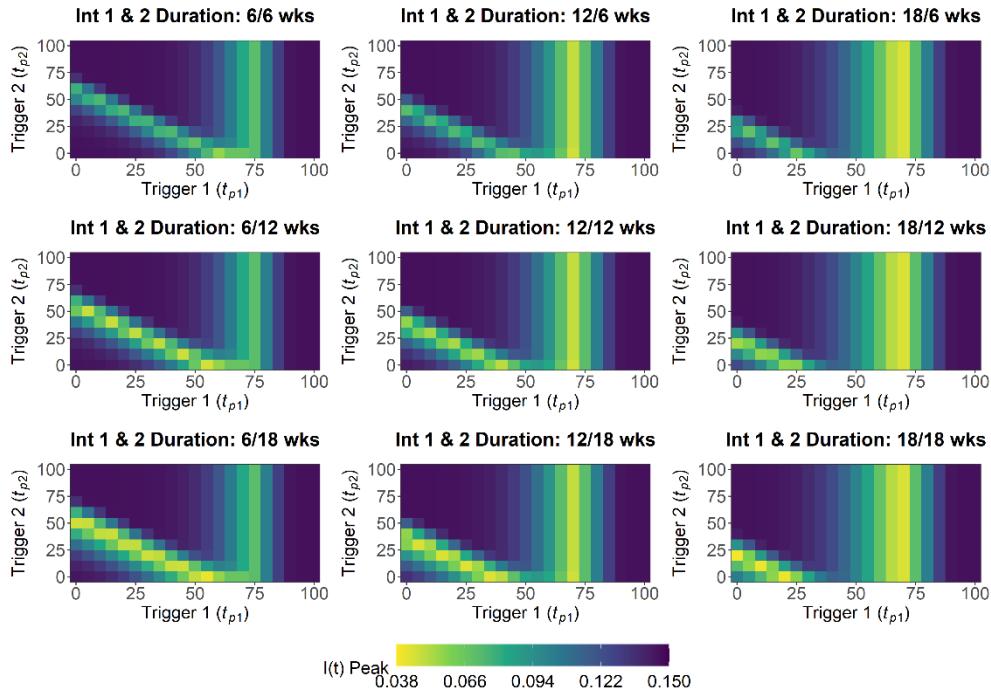
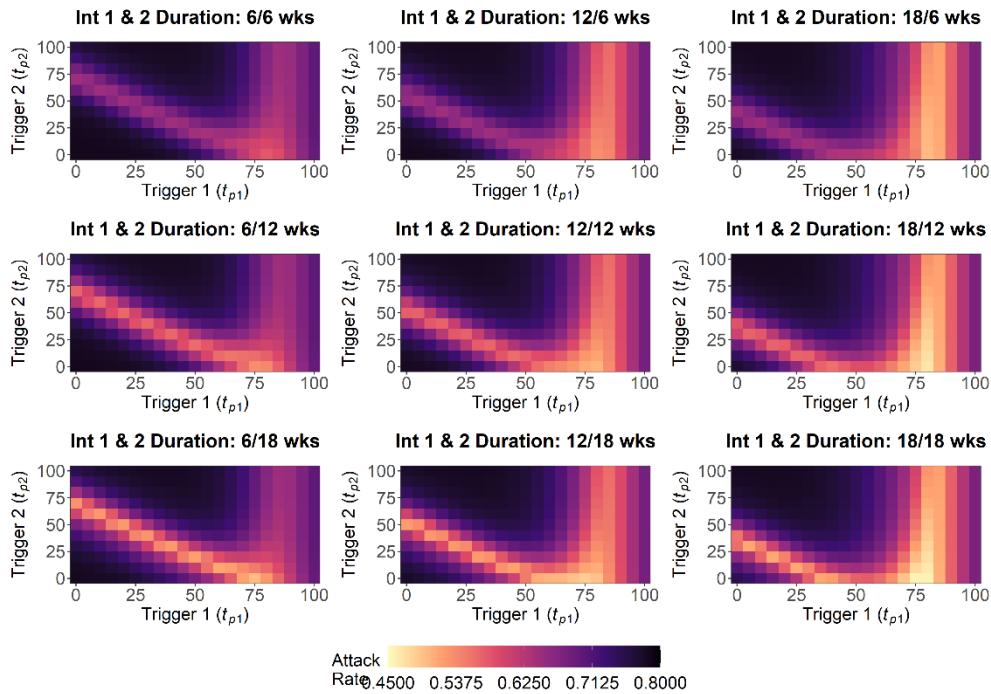
A**B**

Figure S7. Scenario 2 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) attack rate, $I_c(t_{max})$, for intervention 1 trigger date, t_{p1} , and intervention 2 trigger date, t_{p2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 3/6/9$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

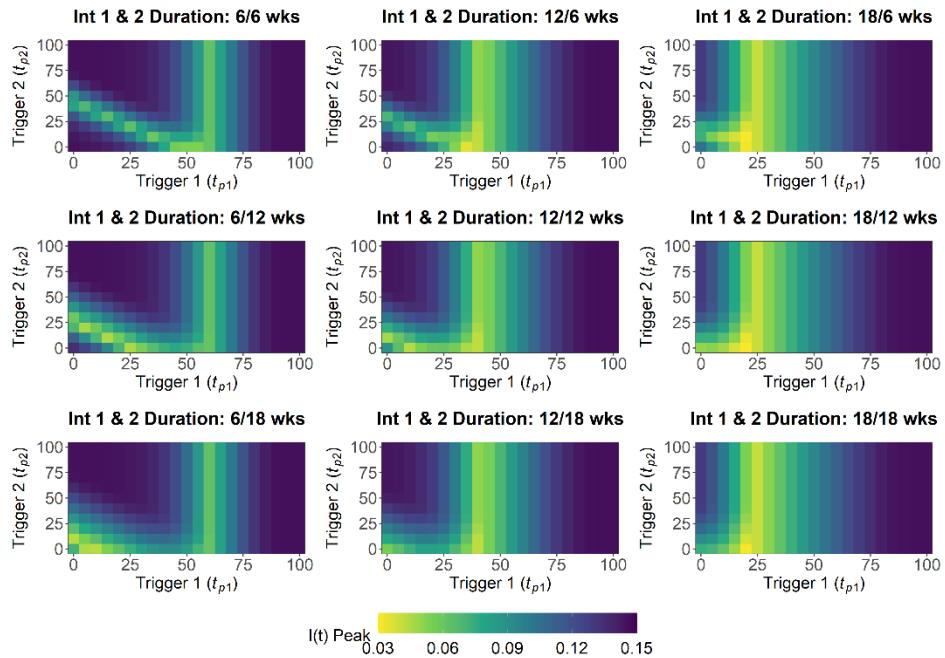
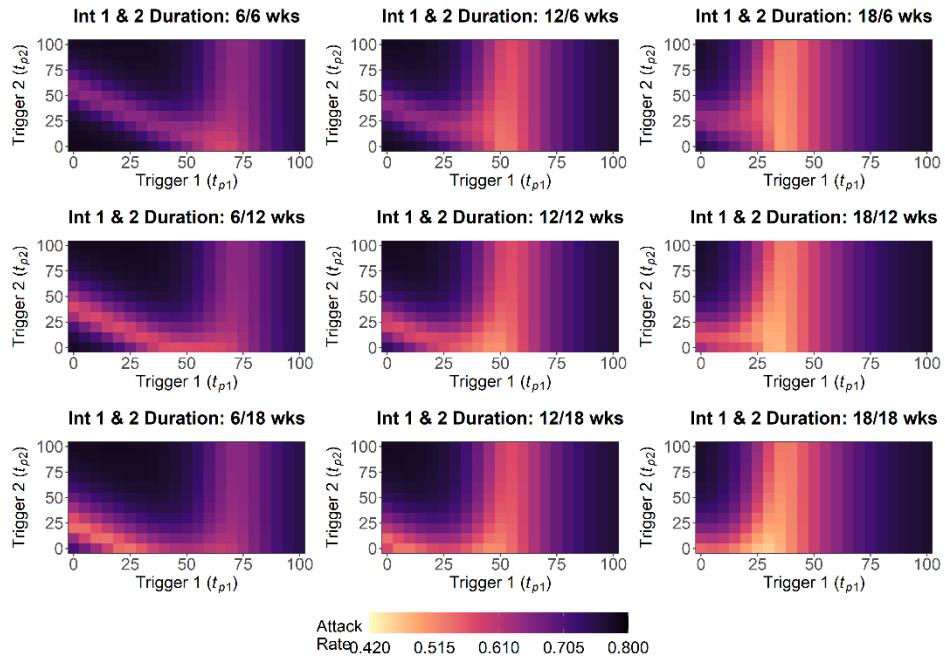
A**B**

Figure S8. Scenario 3 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) attack rate, $I_c(t_{max})$, for intervention 1 trigger date, t_{p1} , and intervention 2 trigger date, t_{p2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

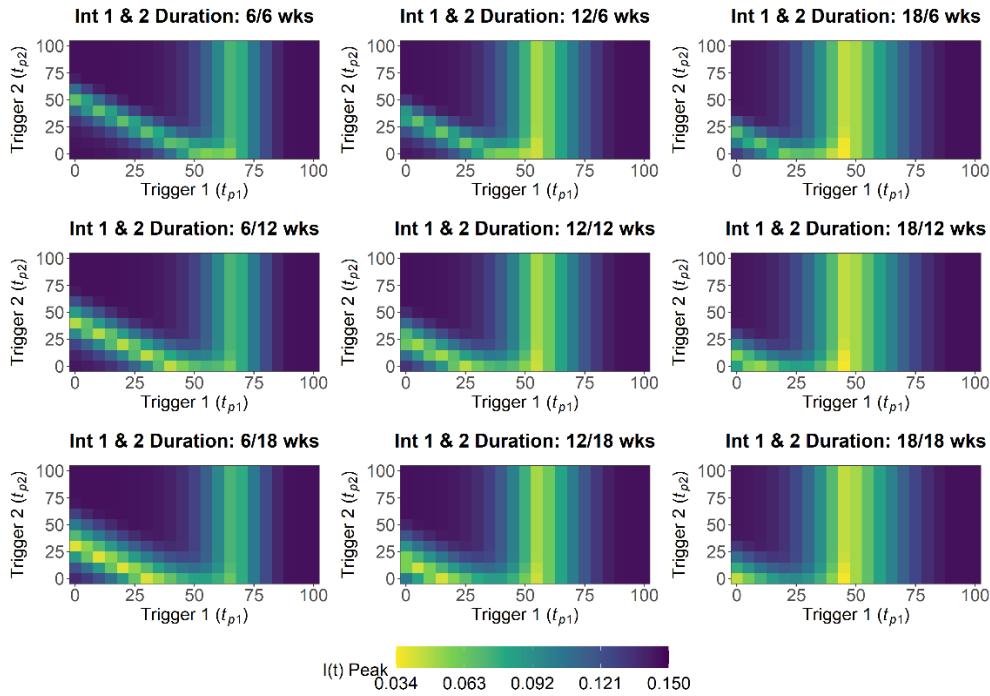
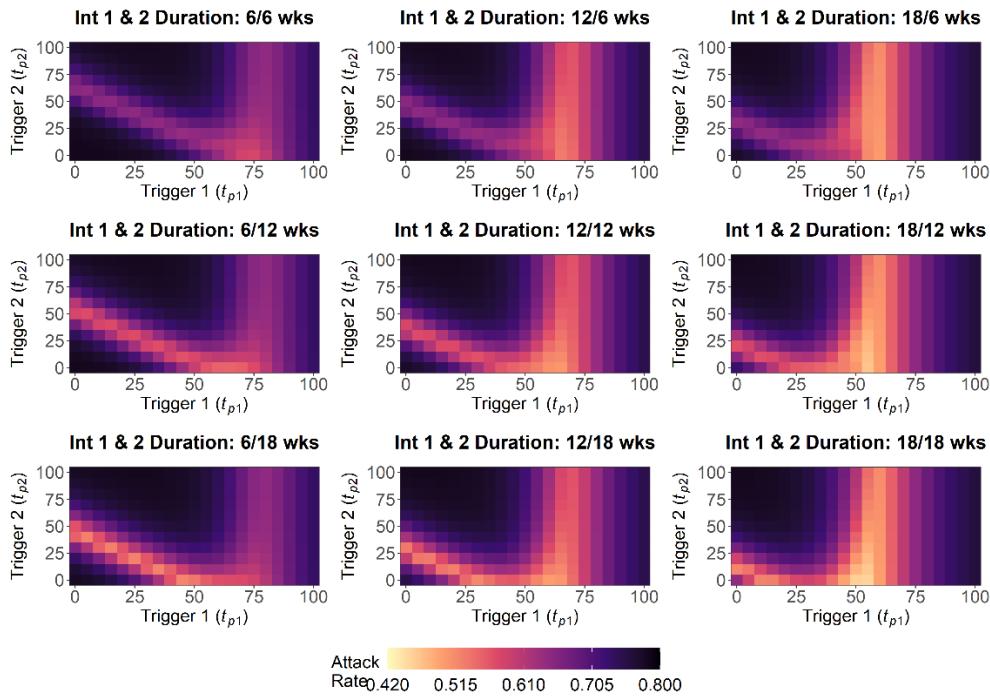
A**B**

Figure S9. Scenario 4 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) attack rate, $I_c(t_{max})$, for intervention 1 trigger date, t_{p1} , and intervention 2 trigger date, t_{p2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

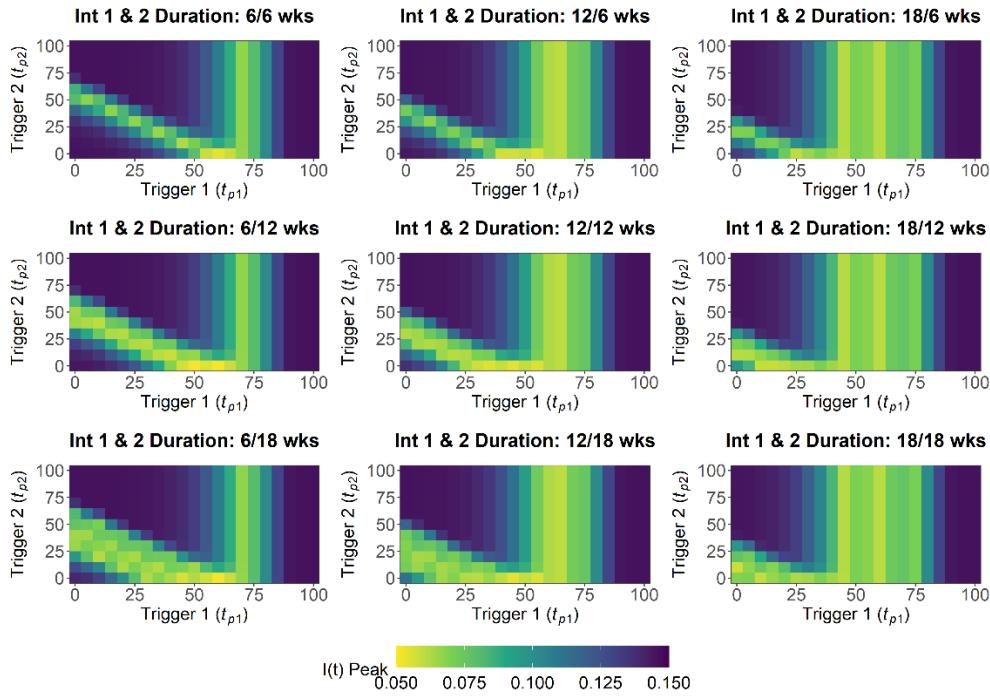
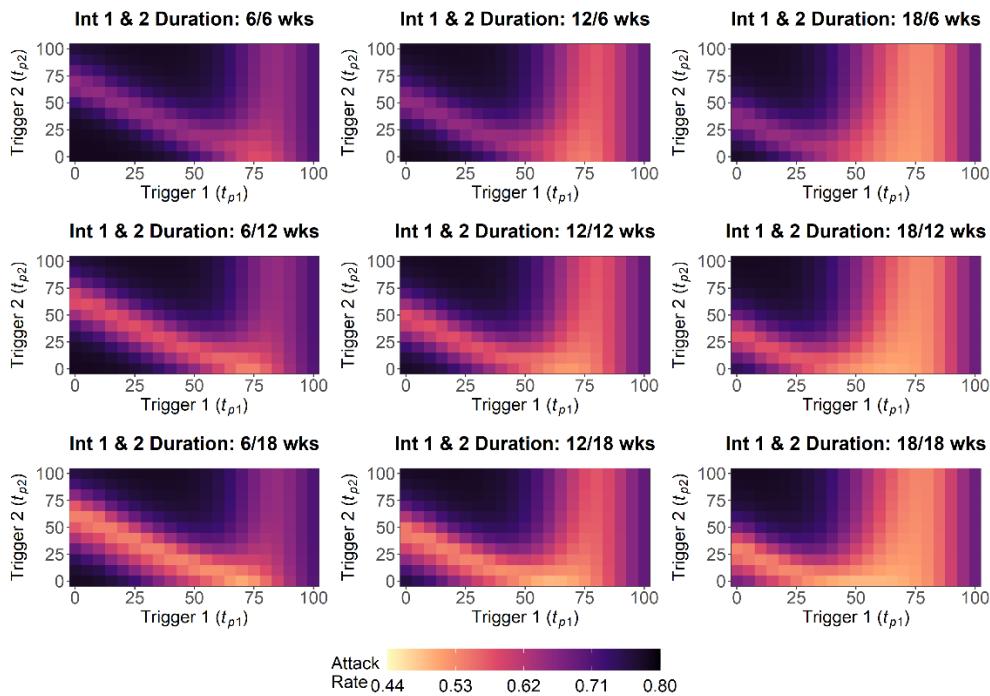
A**B**

Figure S10. Scenario 5 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) attack rate, $I_c(t_{max})$, for intervention 1 trigger date, t_{p1} , and intervention 2 trigger date, t_{p2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

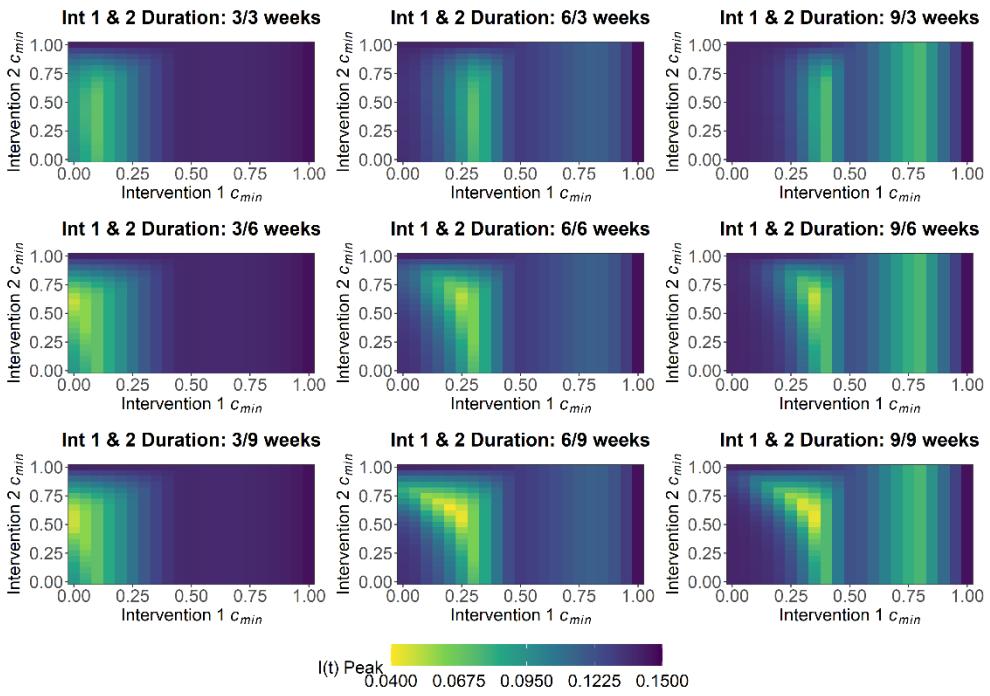
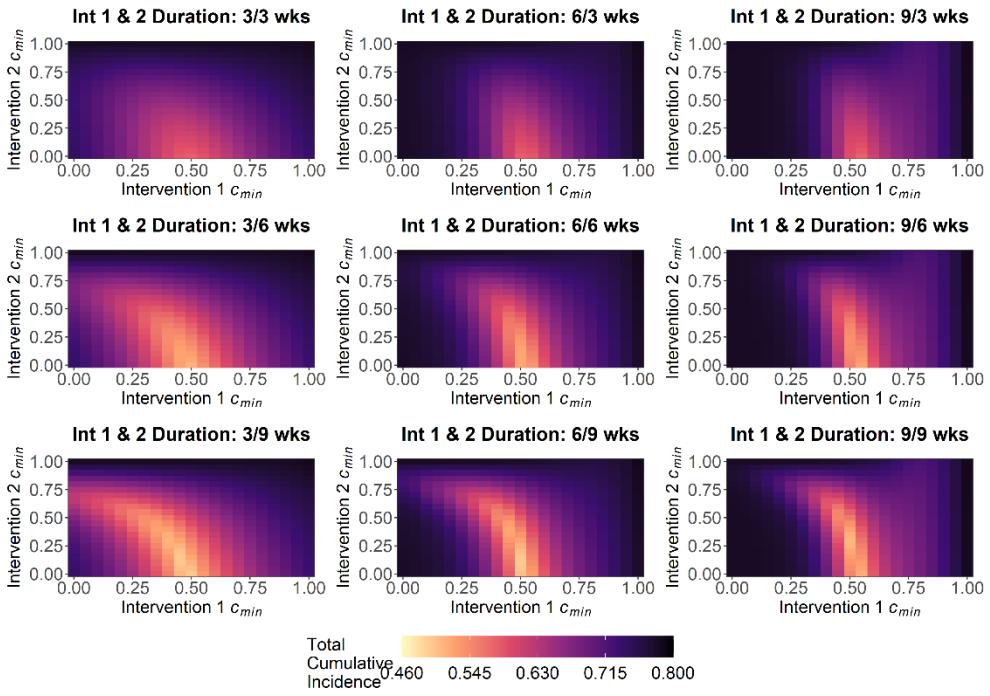
A**B**

Figure S11. Scenario 1 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) the attack rate, $I_c(t_{max})$, for the minimum value of scaling factor $c(t)$ for intervention 1, c_{min1} , and intervention 2, c_{min2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 3/6/9$ weeks were explored in this sensitivity analysis.

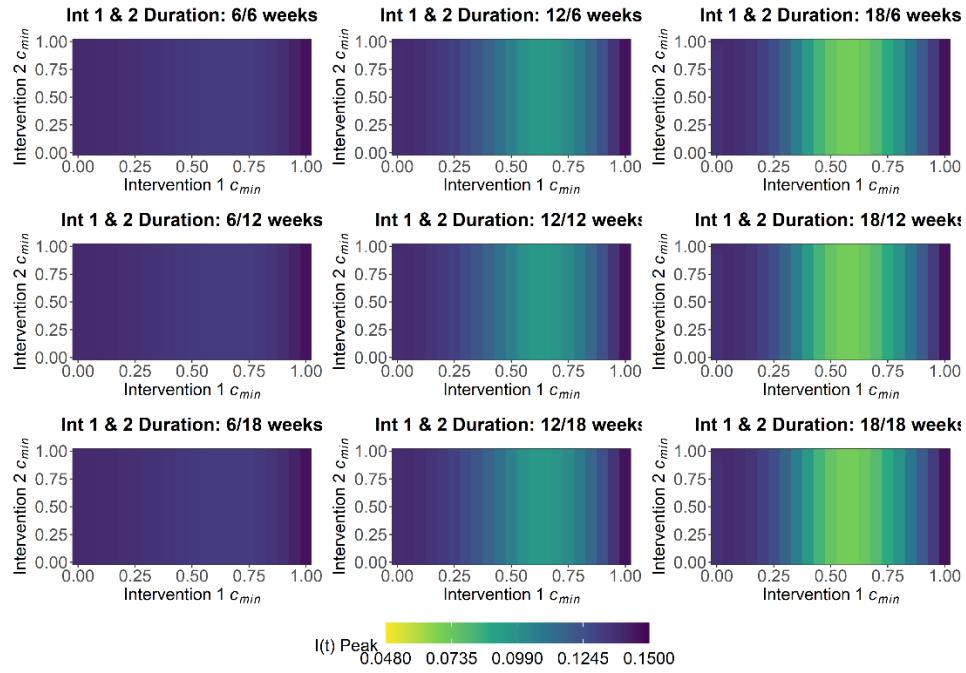
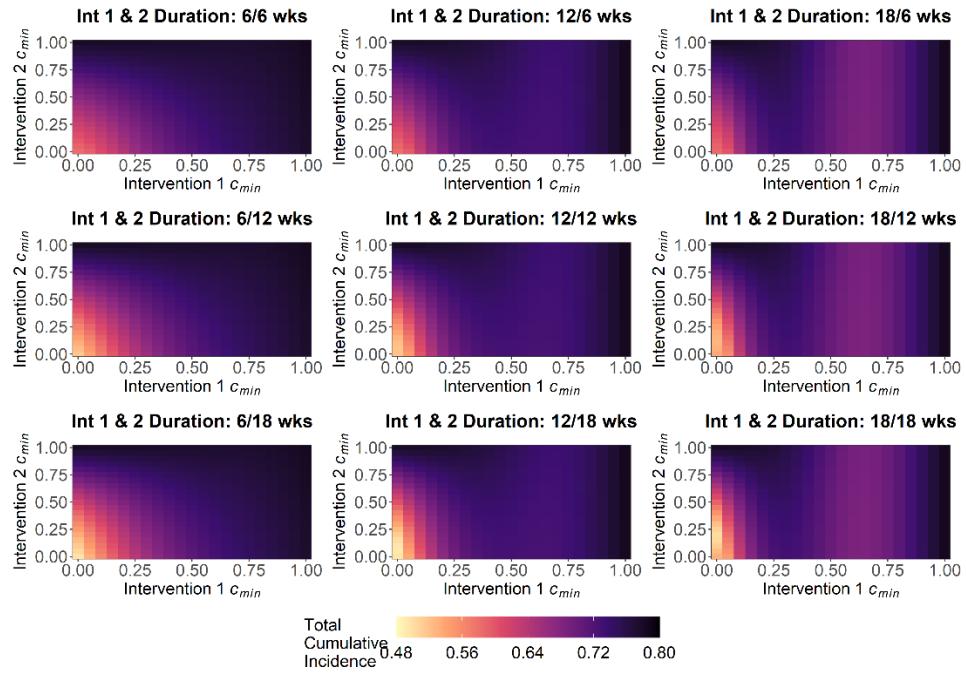
A**B**

Figure S12. Scenario 2 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) the attack rate, $I_c(t_{max})$, for the minimum value of scaling factor $c(t)$ for intervention 1, c_{min1} , and intervention 2, c_{min2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

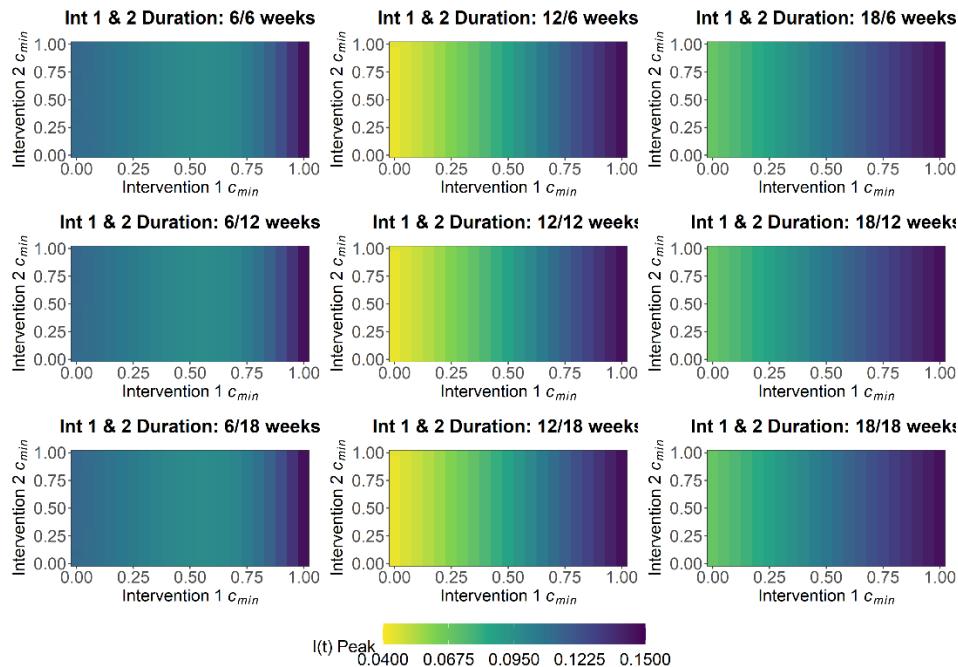
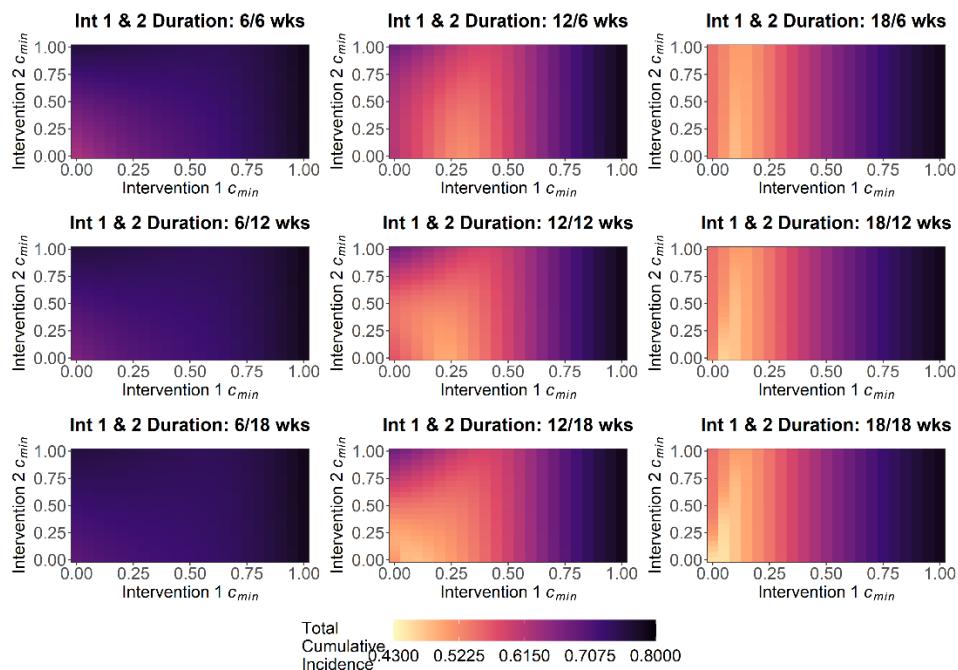
A**B**

Figure S13. Scenario 3 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) the attack rate, $I_c(t_{max})$, for the minimum value of scaling factor $c(t)$ for intervention 1, c_{min1} , and intervention 2, c_{min2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

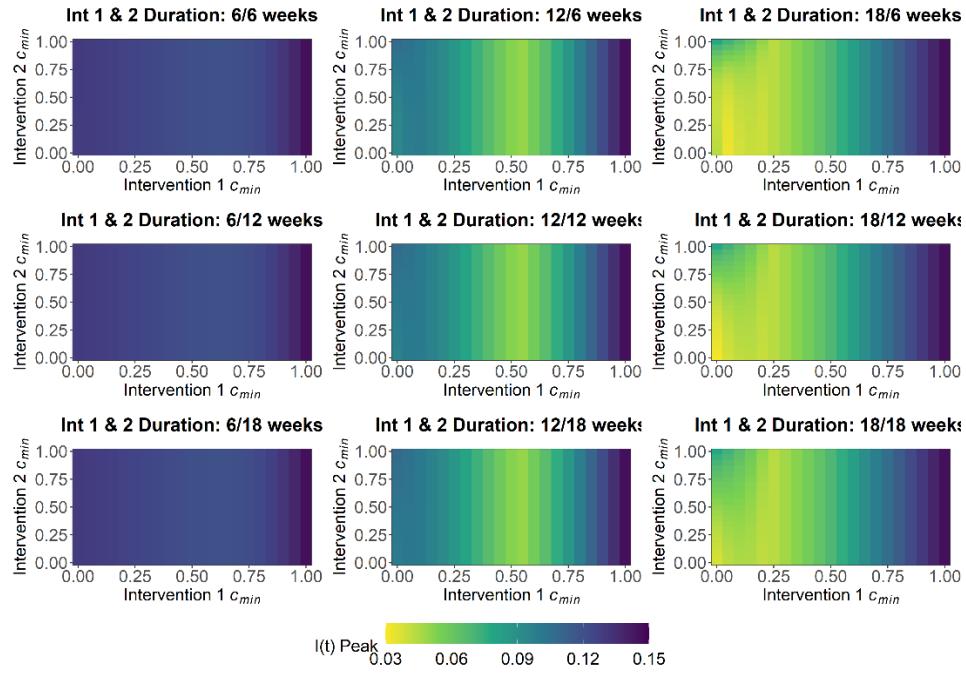
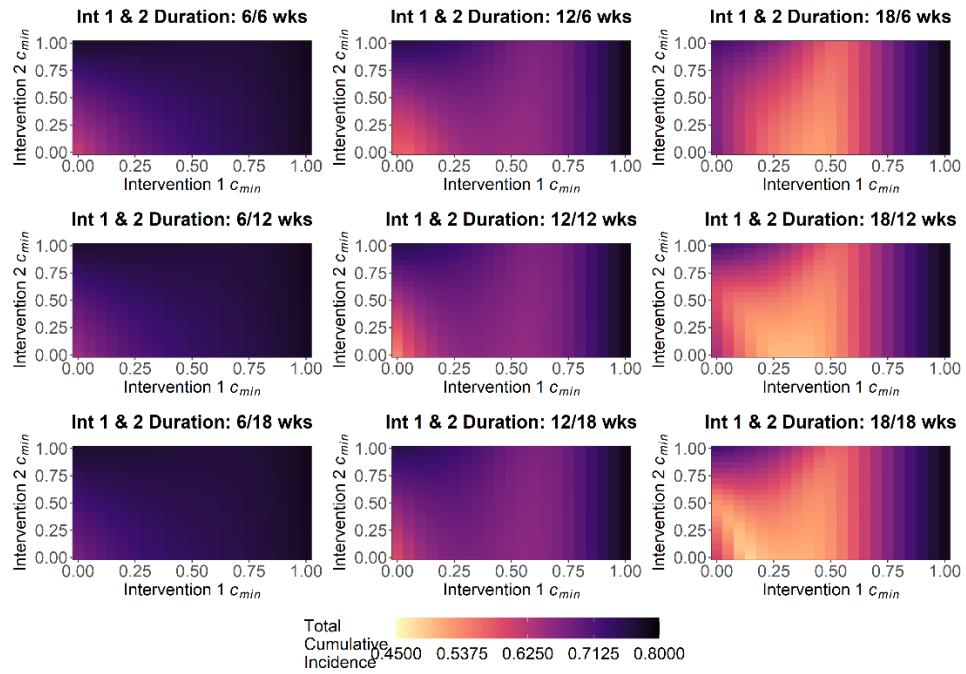
A**B**

Figure S14. Scenario 4 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) the attack rate, $I_c(t_{max})$, for the minimum value of scaling factor $c(t)$ for intervention 1, c_{min1} , and intervention 2, c_{min2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

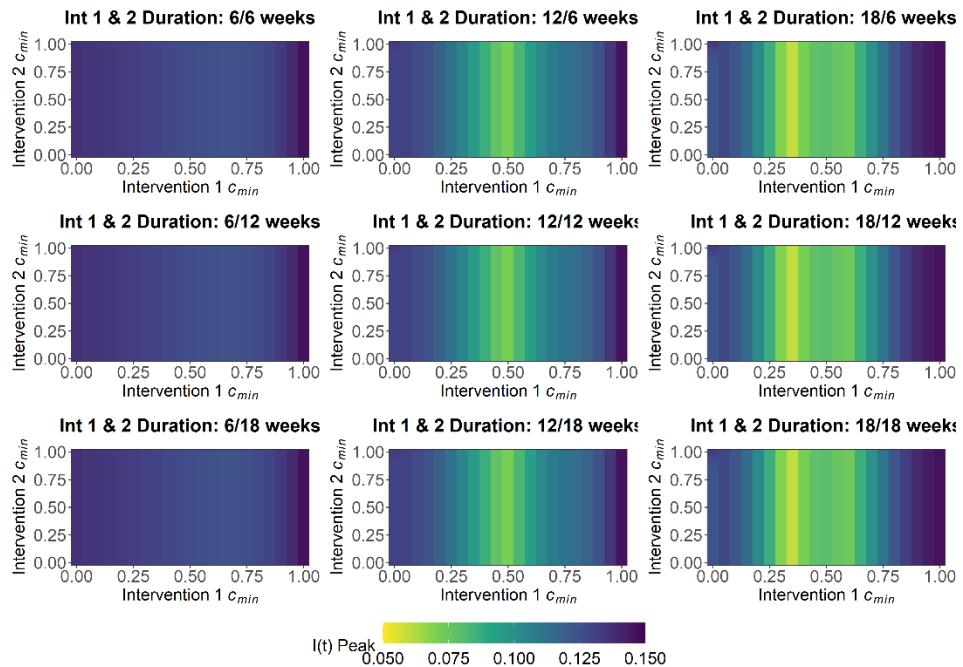
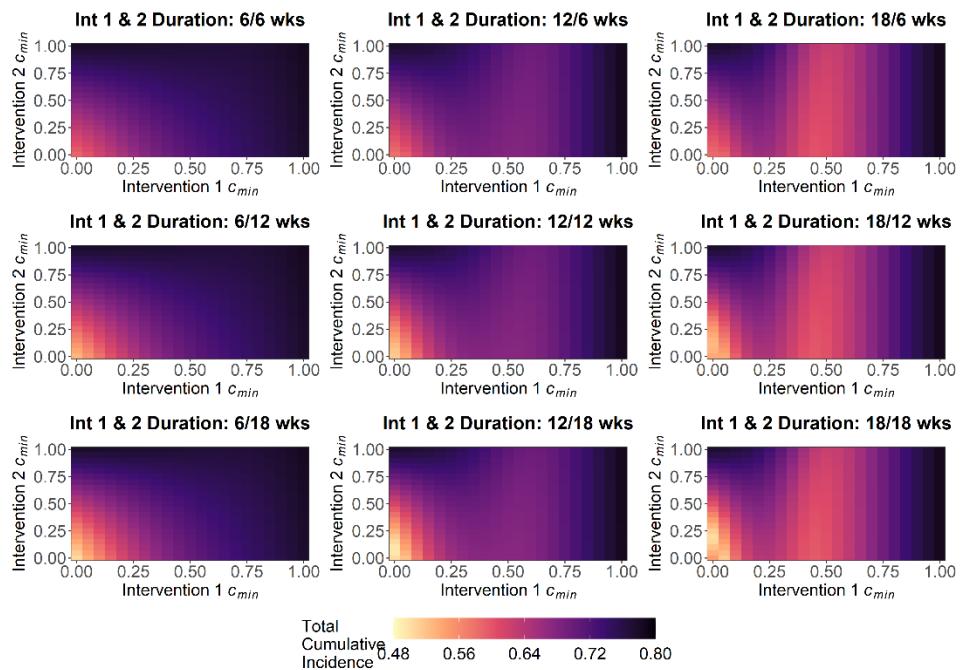
A**B**

Figure S15. Scenario 5 sensitivity analysis for A) maximum $I(t)$ peak, I_{max} , and B) the attack rate, $I_c(t_{max})$, for the minimum value of scaling factor $c(t)$ for intervention 1, c_{min1} , and intervention 2, c_{min2} , explored for varying combinations of the duration of intervention 1, d_{t1} , and intervention 2, d_{t2} . Combinations of $d_{t1} = d_{t2} = 6/12/18$ weeks were explored in this sensitivity analysis. Note that explored d_{t1}/d_{t2} values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for d_{t1}/d_{t2} in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.

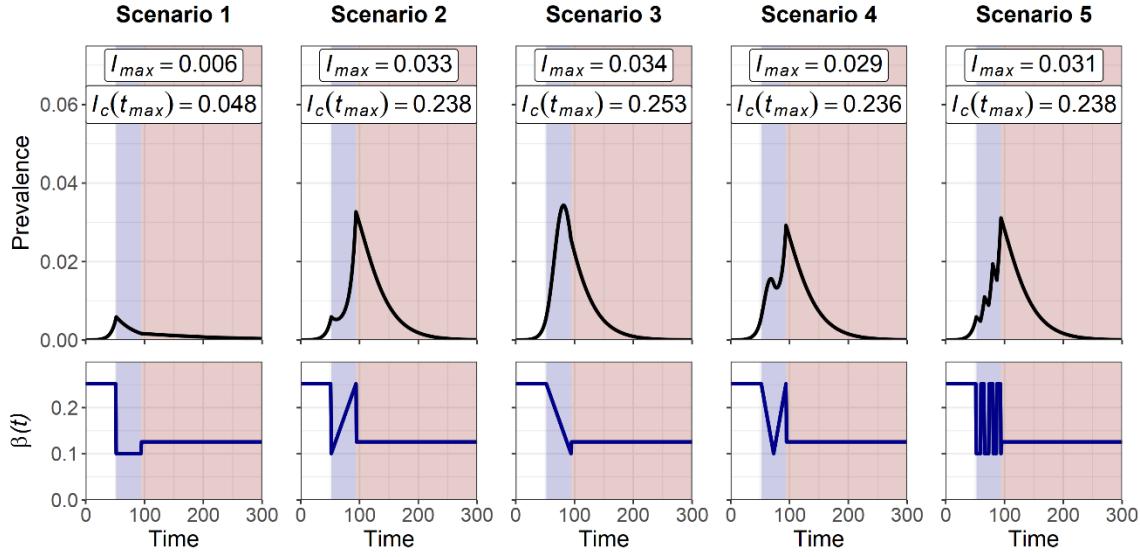
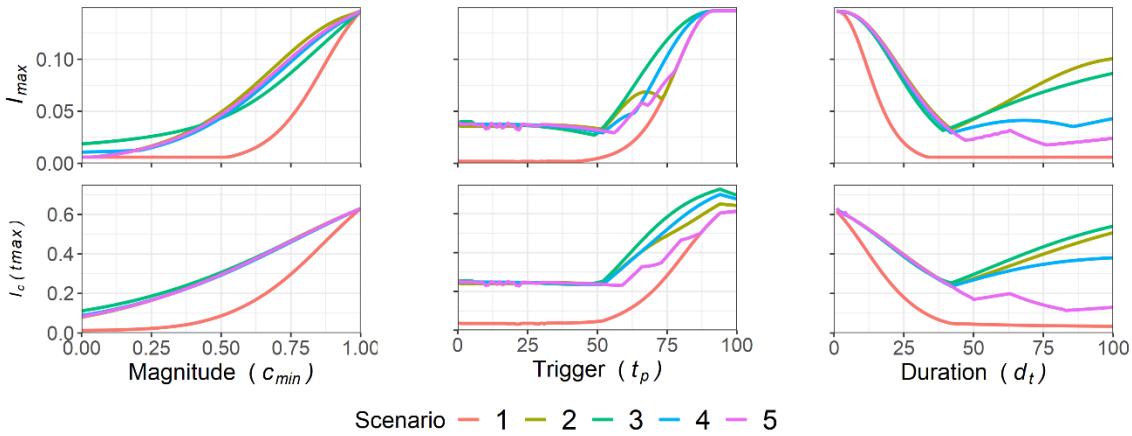
A**B**

Figure S16. A) Trajectory plots and changes in $\beta(t)$ for the multi-intervention scenario, with intervention 1 allowed to change and with intervention 2 indefinitely set at a scenario 1 $c(t)$ profile with $c_{min2} = 0.5$. B) Sensitivity analysis for intervention trigger day (t_p), magnitude of lockdown measures (c_{min}) and intervention duration (d_t) to minimise maximum $I(t)$ peak, I_{max} , and the attack rate, $I_c(t_{max})$. The purpose of this analysis was to represent the optimisation of an initial intervention, with the introduction of more sustainable reductions in transmission (test, track and trace capacity) modelled through indefinite reductions to transmission in intervention 2. Note that for A) blue shading indicates the period of intervention 1 and red shading indicates period of intervention 2. I_{max} and $I_c(t_{max})$ values are annotated for each scenario. As t_{p2} was set at $t = 100$, it was not possible to compensate for differing intervention magnitudes over the intervention duration for scenario 2, 3, 4 5, with all scenarios set at $d_{t1} = 42$ days (6 weeks). Therefore the scenario 1 trajectory plot and sensitivity analysis was not comparable to all other scenarios.

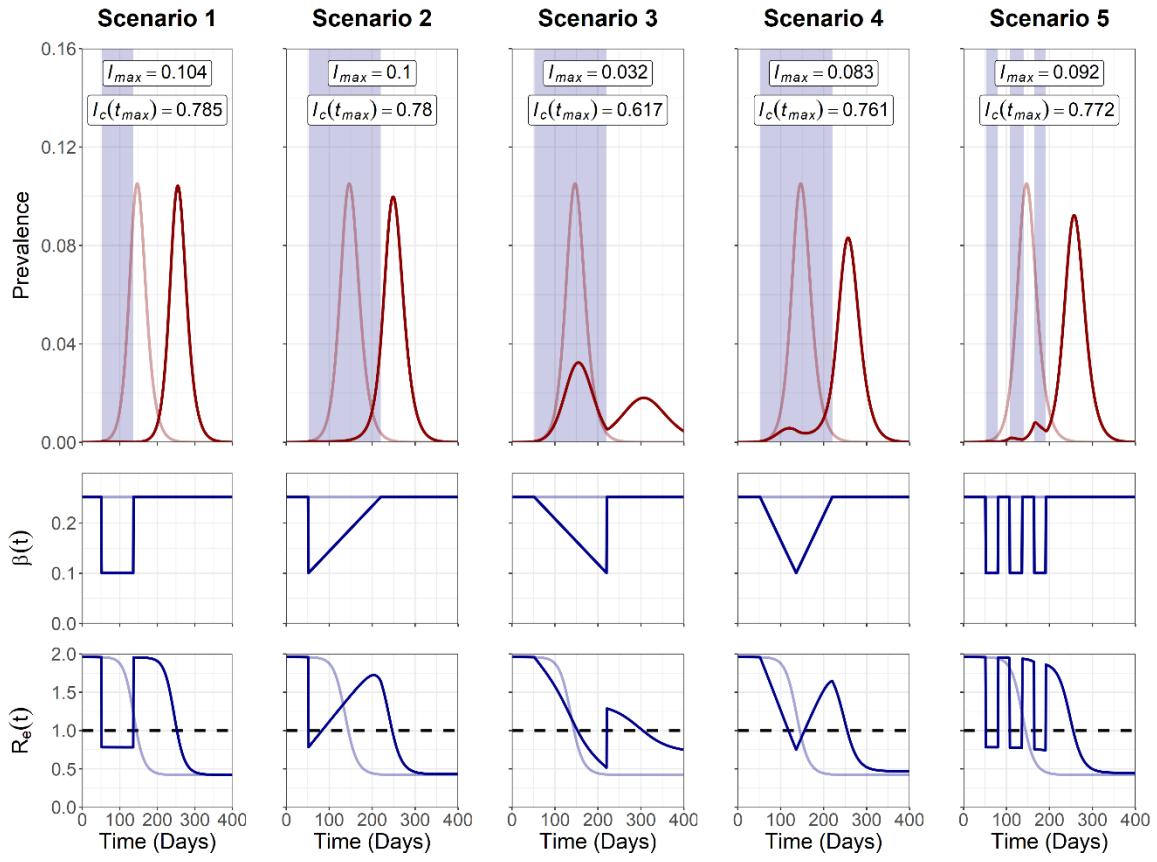


Figure S17. Trajectory plots, changes in $\beta(t)$ and $R_e(t)$ for the single-intervention SEIR model for all five scenarios. Note that parameter $t_p = 90$, corresponding to $I_c(90) = 0.0206$. The transition rate from exposed-to-infected, equivalent to the reciprocal of the average duration spent in the COVID-19 incubation period, was set at $\sigma = 1/3$. I_{max} and $I_c(t_{max})$ values are annotated for each scenario.

Appendix References

1. Di Lauro F, Kiss IZ, Miller J. The timing of one-shot interventions for epidemic control. *medRxiv*. [Preprint]. 2020. Available from: <https://doi.org/10.1101/2020.03.02.20030007>.
2. Morris DH, Rossine FW, Plotkin JB, Levin SA. Optimal, near-optimal, and robust epidemic control. *arXiv*. [Preprint]. 2020. Available from: <https://arxiv.org/abs/2004.02209>.
3. Gevertz J, Greene J, Tapia CHS, Sontag ED. A novel COVID-19 epidemiological model with explicit susceptible and asymptomatic isolation compartments reveals unexpected consequences of timing social distancing. *medRxiv*. [Preprint]. 2020. Available from: <https://doi.org/10.1101/2020.05.11.20098335>.
4. Ferguson N, Laydon D, Nedjati Gilani G, Imai N, Ainslie K, Baguelin M, et al. Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand. [Report]. Imperial College London. 2020. Available from: <https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-9-impact-of-npis-on-covid-19/>.
5. Rawson T, Brewer T, Veltcheva D, Huntingford C, Bonsall MB. How and when to end the COVID-19 lockdown: an optimization approach. *Frontiers in Public Health*. 2020; 8:262.
6. Dickens BL, Koo JR, Lim JT, Park M, Quaye S, Sun H, et al. Modelling lockdown and exit strategies for COVID-19 in Singapore. *The Lancet Regional Health-Western Pacific*. [Internet]. 2020. e100004. Available from: <https://doi.org/10.1016/j.lanwpc.2020.100004>.
7. Bin M, Cheung P, Crisostomi E, Ferraro P, Lhachemi H, Murray-Smith R, et al. On fast multi-shot covid-19 interventions for post lock-down mitigation. *arXiv*. [Preprint]. 2020. Available from: <https://arxiv.org/abs/2003.09930v5>.
8. Sadeghi M, Greene J, Sontag E. Universal features of epidemic models under social distancing guidelines. *bioRxiv*. [Preprint]. 2020. Available from: <https://doi.org/10.1101/2020.06.21.163931>.
9. Davies NG, Kucharski AJ, Eggo RM, Gimma A, Edmunds WJ, Centre for the Mathematical Modelling of Infectious Diseases C-wg. Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study. *Lancet Public Health*. 2020; 5(7):e375-e85.
10. Pellis L, Scarabel F, Stage HB, Overton CE, Chappell LH, Lythgoe KA, et al. Challenges in control of Covid-19: short doubling time and long delay to effect of interventions. *arXiv*. [Preprint]. 2020. Available from: <https://doi.org/10.1101/2020.04.12.20059972>.
11. Zhou L, Liu JM, Dong XP, McGoogan JM, Wu ZY. COVID-19 seeding time and doubling time model: an early epidemic risk assessment tool. *Infect Dis Poverty*. 2020; 9(1):76.
12. Pan A, Liu L, Wang C, Guo H, Hao X, Wang Q, et al. Association of Public Health Interventions With the Epidemiology of the COVID-19 Outbreak in Wuhan, China. *JAMA*. 2020; 323(19):1915-1923.
13. Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, et al. Comparing SARS-CoV-2 with SARS-CoV and influenza pandemics. *Lancet Infect Dis*. [Internet]. 2020; S1473-3099(20)30484-9. Available from: [https://doi.org/10.1016/S1473-3099\(20\)30484-9](https://doi.org/10.1016/S1473-3099(20)30484-9).
14. Flaxman S, Mishra S, Gandy A, Unwin HJT, Mellan TA, Coupland H, et al. Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*. 2020; 584: 257–261.
15. Anderson RM, May RM. *Infectious diseases of humans: dynamics and control*. Oxford University Press. 1991.
16. Flaxman S, Mishra S, Gandy A, Unwin H, Coupland H, Mellan T, et al. Report 13: Estimating the number of infections and the impact of non-pharmaceutical interventions on COVID-19 in 11 European countries. [Report]. 2020. Available from: <https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/report-13-europe-npi-impact/>.
17. Soetaert KE, Petzoldt T, Setzer RW. Solving differential equations in R: package deSolve. *Journal of statistical software*. 2010; 33(9).
18. Wickham H. ggplot2: elegant graphics for data analysis. *Journal of Statistical Software*. 2017; 77(2).
19. Wickham H. Reshaping data with the reshape package. *Journal of Statistical Software*. 2007; 21(12):1-20.