## **SUPPLEMENTARY MATERIAL**

**Appendix Material Explanation of Scenarios**

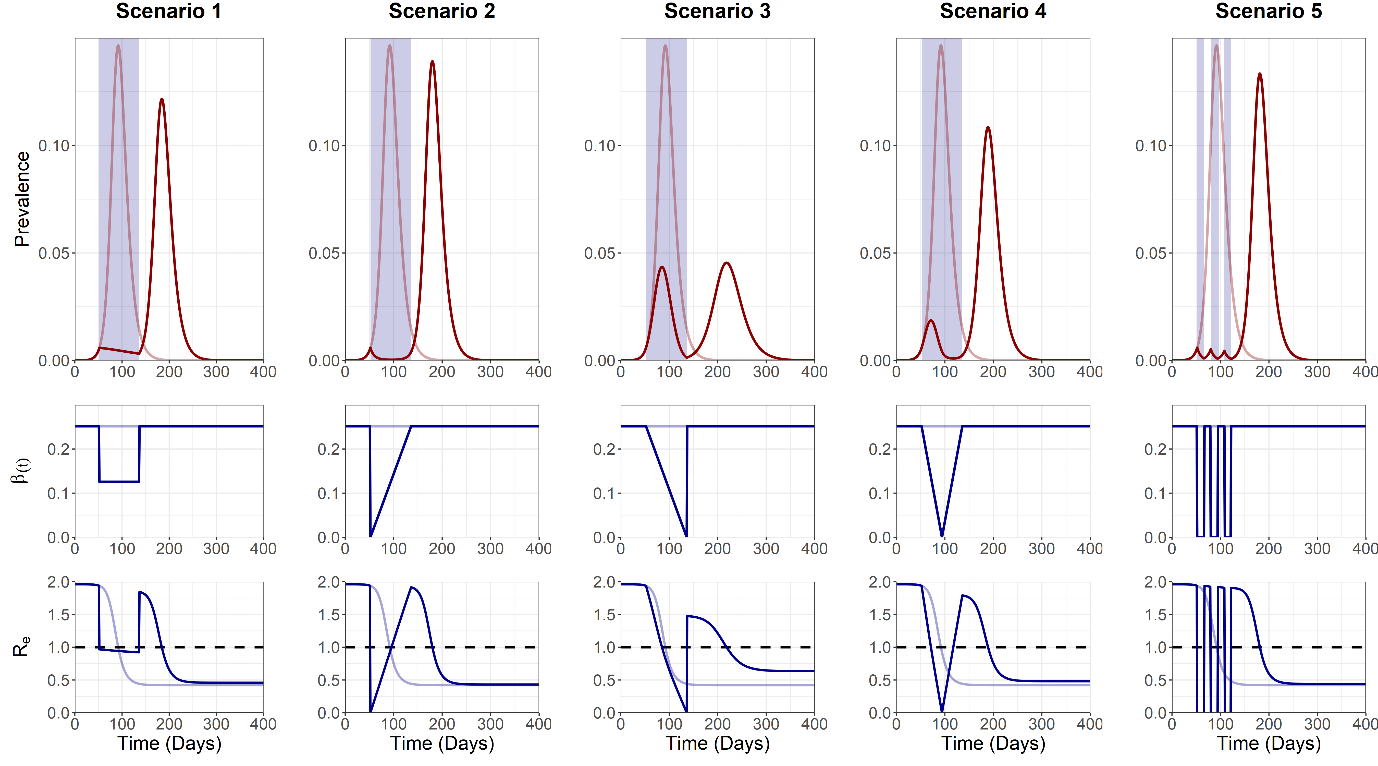
|  |  |  |  |
| --- | --- | --- | --- |
| Scenario | | *β(t)* during the simulation | Real-world Parallels |
| 1 |  | | A classic interpretation of NPIs such as lockdown measures, a flat constant reduction to transmission which is sustained until the cessation of the intervention. Used in a variety of models considering the effects of NPIs (1-4). |
| 2 |  | | “Ramping down” strategy, an initial strong intervention is followed by a gradual reduction in the strength of the intervention. Can draw parallels in 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). |
| 3 |  | | A “ramping down” 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, it is not well represented in epidemiological 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 . |
| 4 |  | | 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 policy-makers 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. |
| 5 |  | | 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). |

**Table S1 – Parameters for the Single Intervention Scenario**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter Description** | | **Notation** | **Baseline Value** | **References** |
| Doubling Time | | *td* | 3 Days | (10, 11) |
| Baseline Basic Reproduction Number | | *R0* | 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 *R0γ* |
| Scaled per capita rate of COVID-19 transmission (reflects the impact of small-scale NPIs on transmission) | | *βscale* | 0.2513 (30% reduction to baseline *β*) | (9, 14, 16) |
| Minimum value of the lockdown-related scaling factor *c(t)* | | *cmin* | 0.4 (60% reduction to *βscale*) | (9, 14, 16) |
| Length of Intervention | Scenario 1 | *dt* | 84 days (12 weeks) | N/A |
| Scenario 2, 3, 4 and 5 | 168 days (24 weeks) | N/A |
| Intervention Trigger Point | | *tp* | Day 52 (*Ic(52)* = 0.02) | Calculated from Model |

**Table S2 – Parameters for the Multi Intervention Scenario**

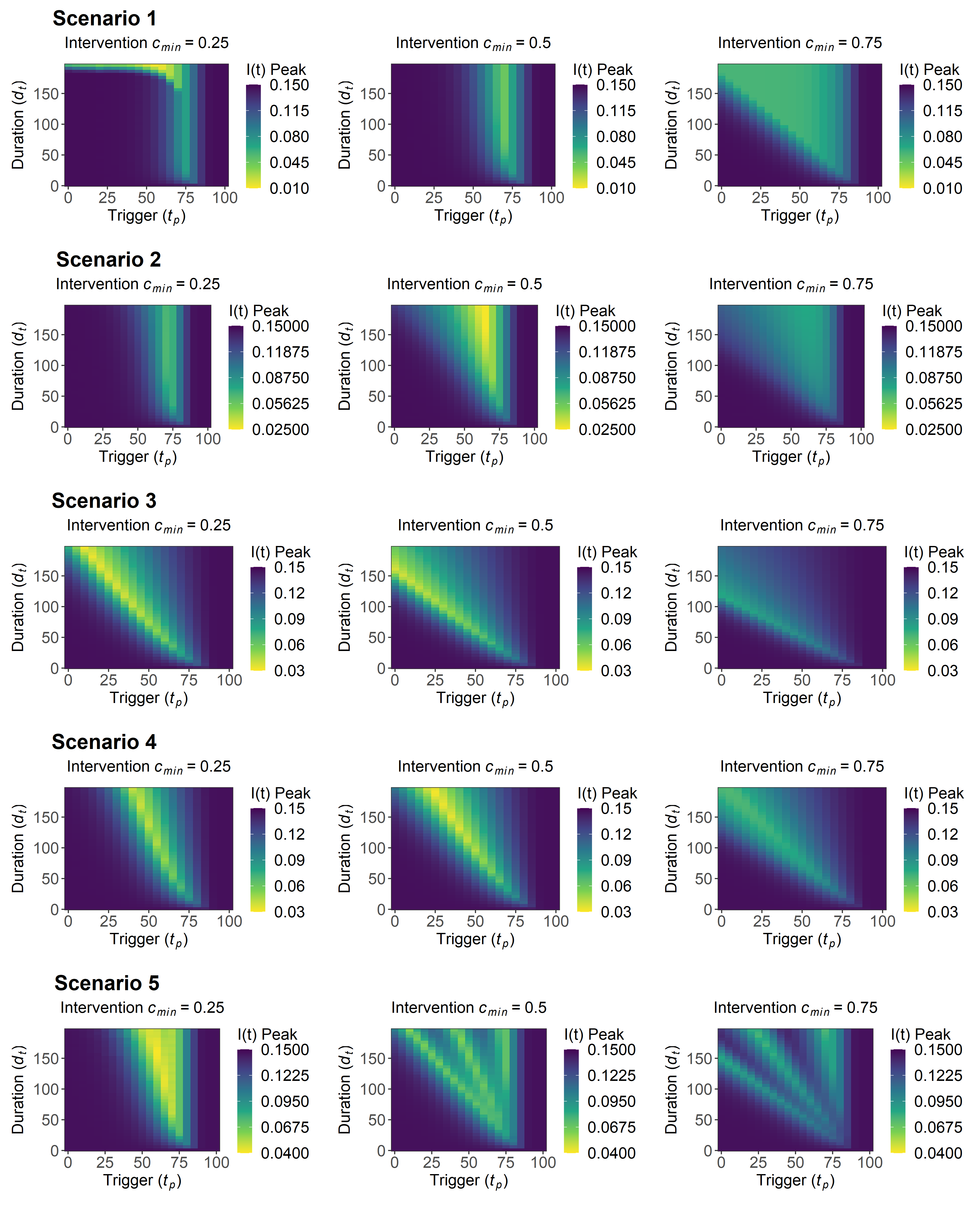
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter Description** | | **Notation** | **Baseline Value** | **References** |
| Doubling Time | | *Td* | 3 Days | (10, 11) |
| Baseline Basic Reproduction Number | | *R0* | 2.8 (baseline) - used to calculate gamma | (9, 12-14) |
| Generation Time | | *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 *R0γ* |
| Scaled per capita rate of COVID-19 transmission (reflects the impact of small-scale NPIs on transmission) | | *βscale* | 0.2513 (30% reduction to baseline *β*) | (9, 14, 16) |
| Minimum value of the lockdown-related scaling factor *c(t)* – Intervention 1 | | *cmin1* | 0.4 (60% reduction to *βscale*) | (9, 14, 16) |
| Minimum value of the lockdown-related scaling factor *c(t)*– Intervention 2 | | *cmin2* | 0.4 (60% reduction to *βscale*) | (9, 14, 16) |
| Length of Intervention – Intervention 1 | Scenario 1 | *dt1* | 42 days (6 weeks) | N/A |
| Scenario 2, 3, 4 and 5 | 84 days (12 weeks) | N/A |
| Length of Intervention – Intervention 2 | Scenario 1 | *dt2* | 42 days (6 weeks) | N/A |
| Scenario 2, 3, 4 and 5 | 84 days (12 weeks) | N/A |
| Intervention Trigger Point – Intervention 1 | | *tp1* | Day 52 (*Ic(52)* = 0.02) | Calculated from Model |
| Intervention Trigger Point – Intervention 2 | | *tp2* | Day 52 (*Ic(52)* = 0.02) | Calculated from Model |



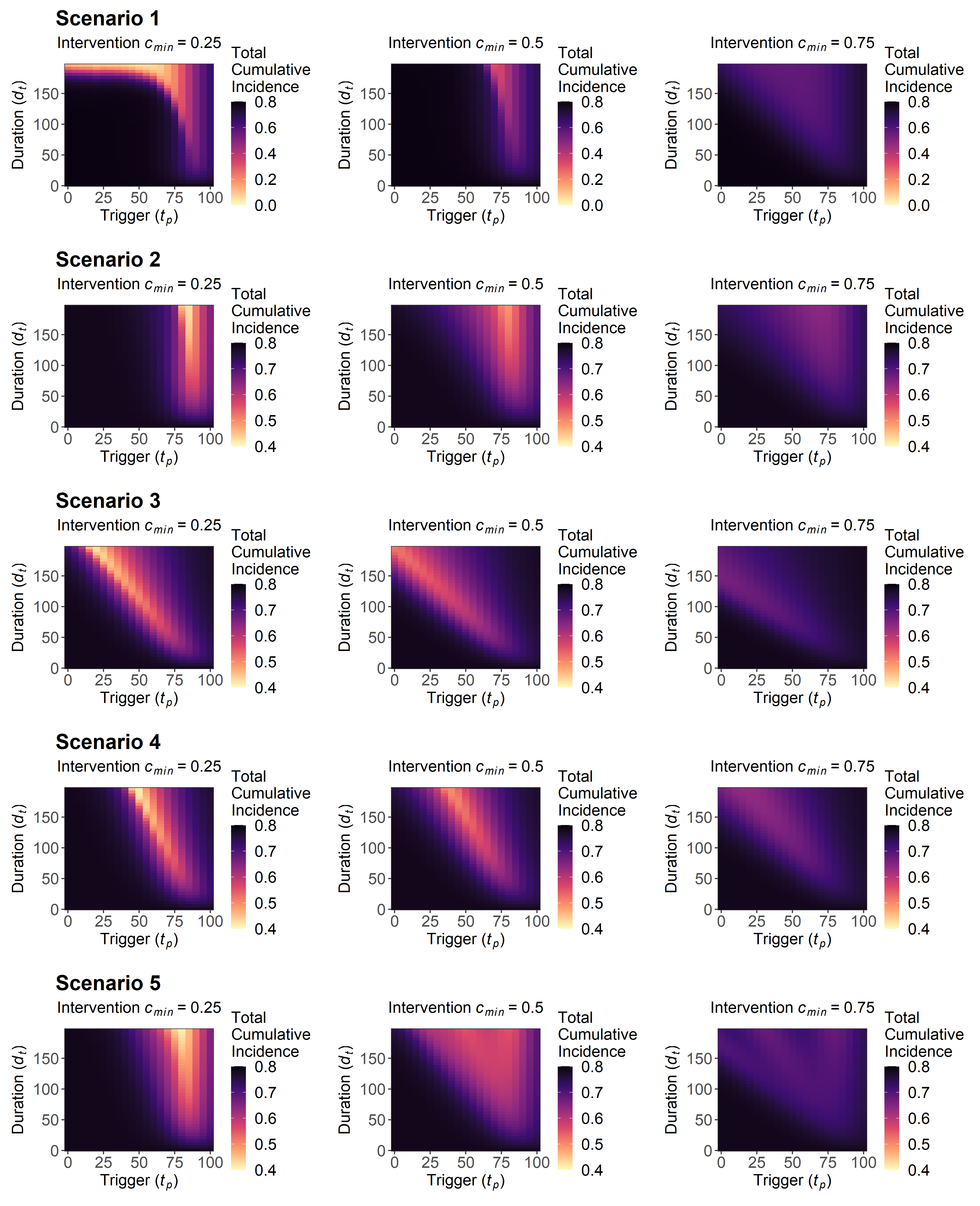
**Figure S1. Trajectory plots for the single intervention epidemic curve, *β(t)* reductions and *Re* for the alternative methodology to double *cmin* to ensure similar magnitude of intervention across the intervention durations for scenario 2, 3, 4 and 5.** Note that for A) opaque red and blue lines in the trajectory plot depict unmitigated epidemic curve dynamics. Blue shading indicates the period of the intervention. Dotted line on the *Re* plot denotes the threshold for sustained epidemic growth. Scenario 1 was set at *cmin* = 0.5 to allow for scenario 2, 3, 4 and 5 to be set at *cmin* = 0 (double the intervention magnitude).



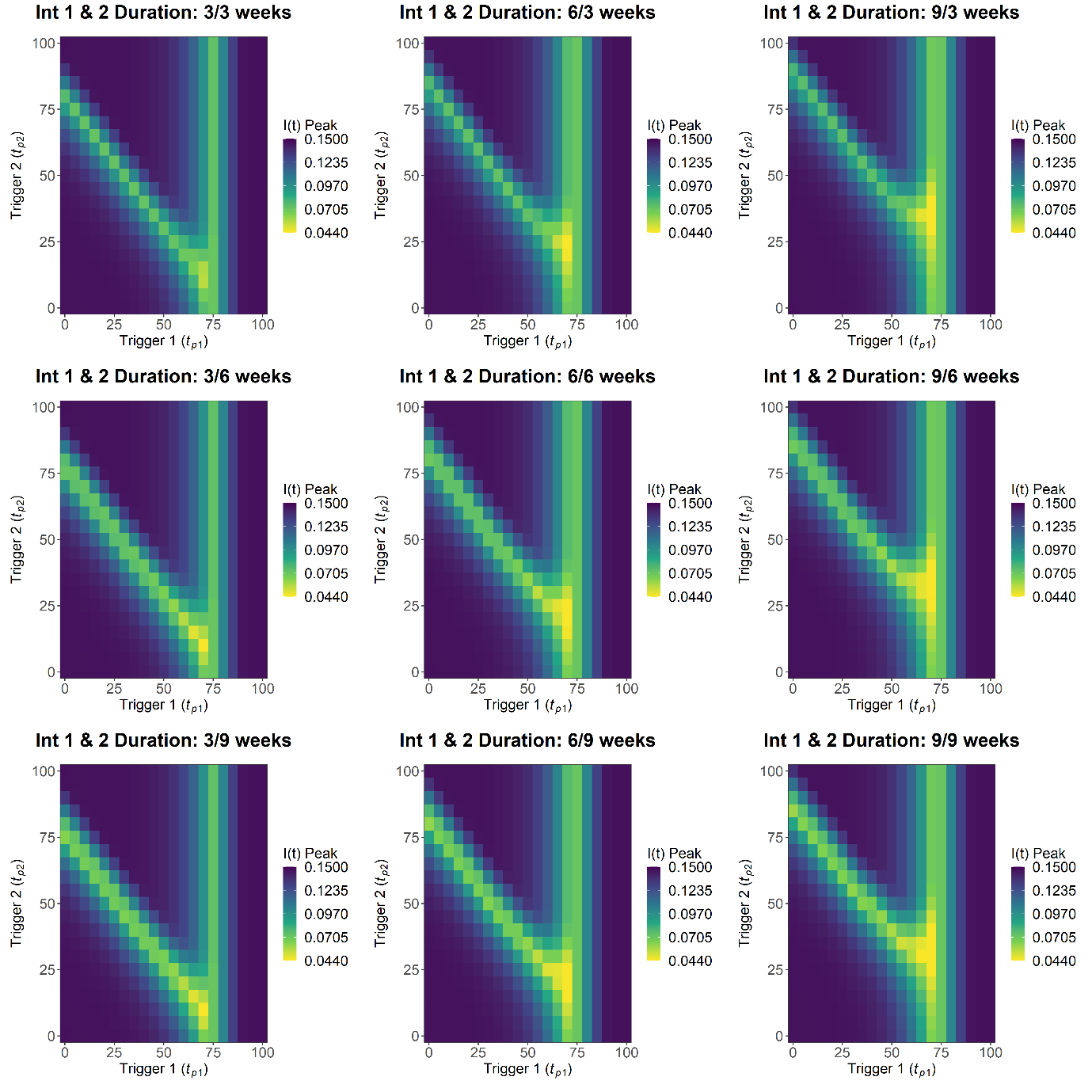
**Figure S2. Trajectory plots for the multiple intervention epidemic curve, *β(t)* reductions and *Re* for the alternative methodology to double *cmin* to ensure similar magnitude of intervention across the intervention durations for scenario 2, 3, 4 and 5.** Note that for A) opaque red and blue lines in the trajectory plot depict unmitigated epidemic curve dynamics. Blue shading indicates the period of the intervention. Dotted line on the *Re* plot denotes the threshold for sustained epidemic growth. Scenario 1 was set at *cmin* = 0.5 to allow for scenario 2, 3, 4 and 5 to be set at *cmin* = 0 (double the intervention magnitude).



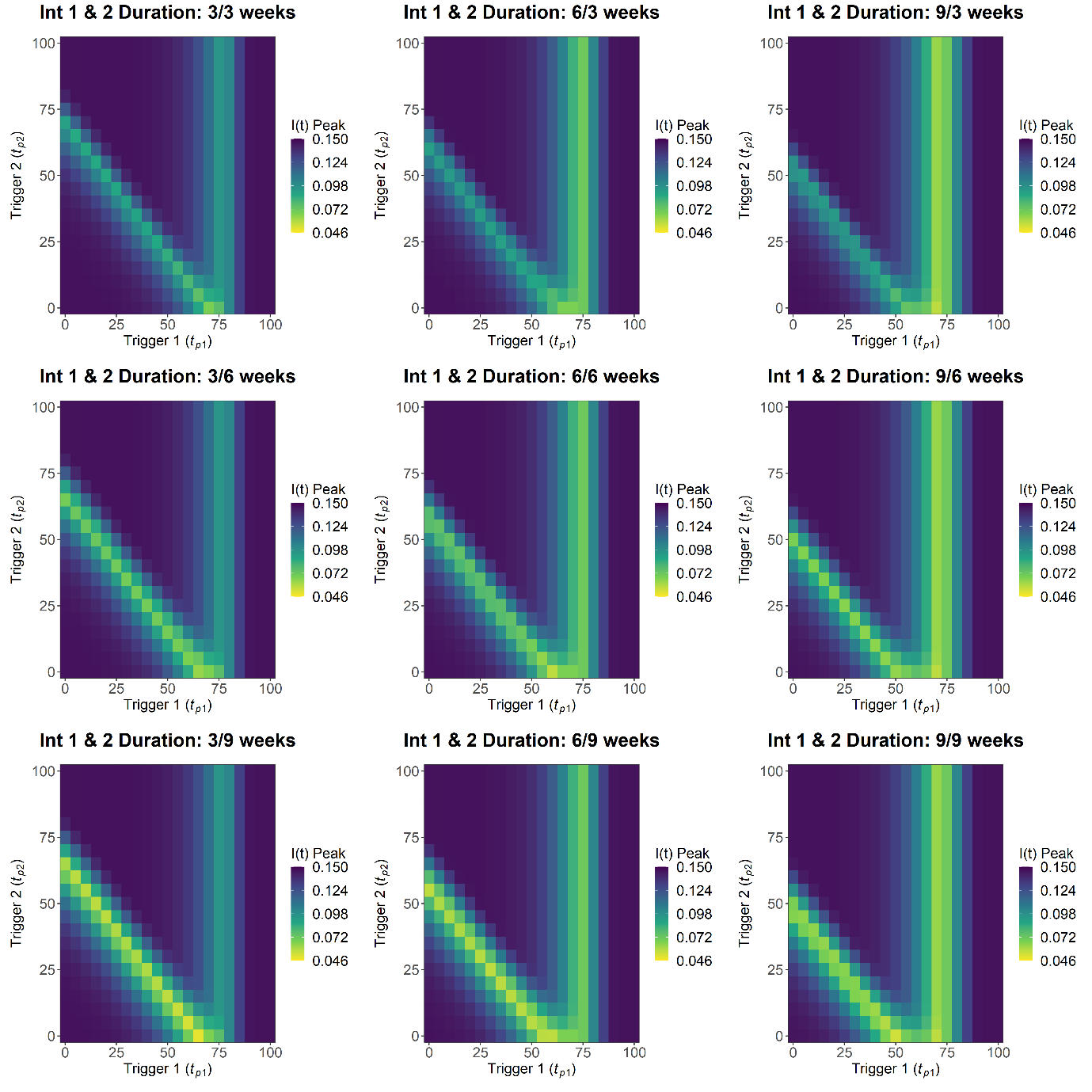
**Figure S3. Sensitivity analysis for maximum *I(t)* peak, *Imax* for intervention trigger day, *tp*, and the intervention duration, *dt*, explored for varying values of *cmin*.** Note that for a specific value of *dt*, scenario 1 is not comparable with scenario 2, 3, 4 and 5 due to the need to double *dt* for the latter scenarios to ensure a comparable intervention magnitude over the intervention duration. This is not possible for this sensitivity analysis with *dt* being a fixed explored parameter and heatmap legends will therefore differ across scenarios.



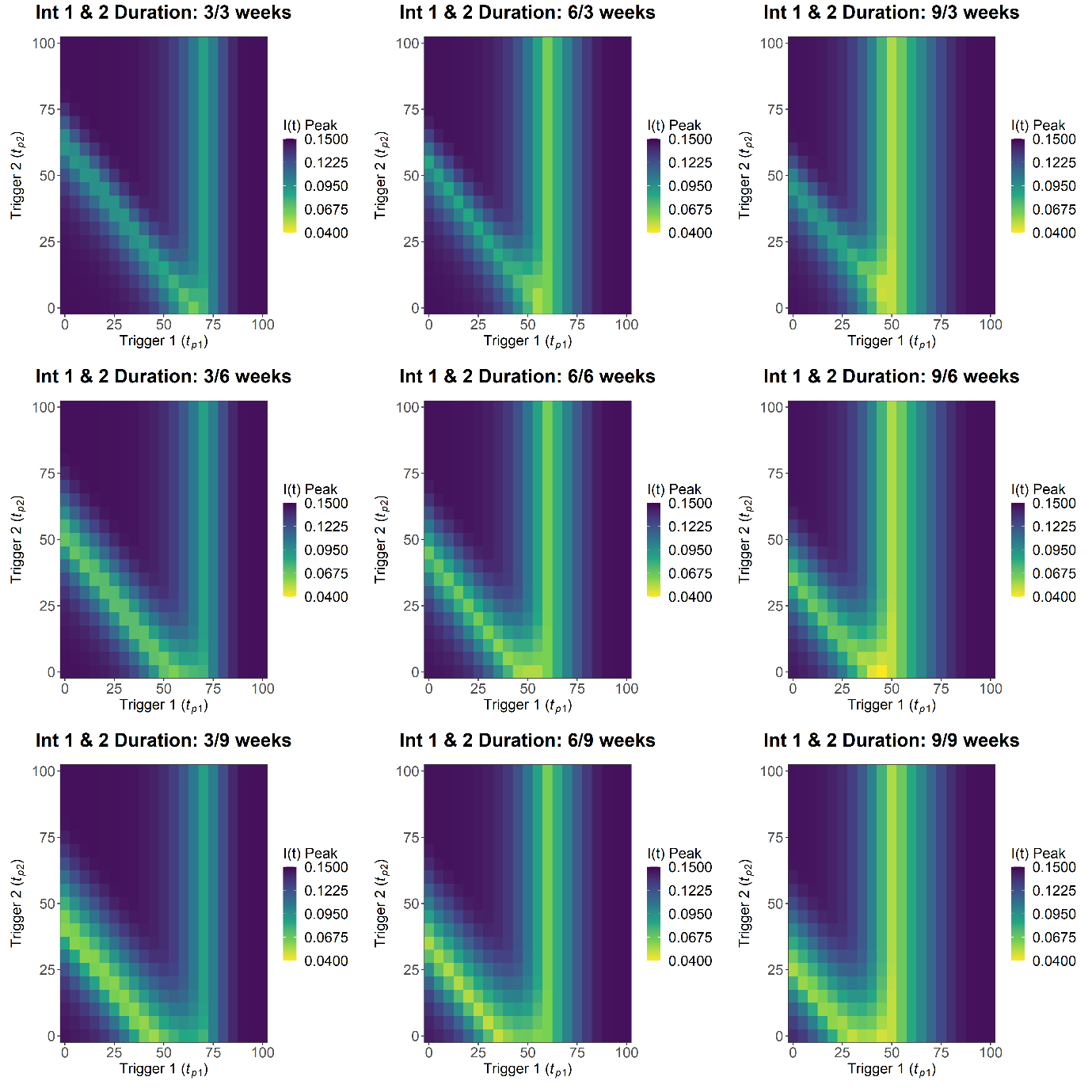
**Figure S4. Sensitivity analysis for total cumulative incidence, *Ic(∞)* for intervention trigger day, *tp*, and the intervention duration, *dt*, explored for varying values of *cmin*.** Note that for a specific value of *dt*, scenario 1 is not comparable with scenario 2, 3, 4 and 5 due to the need to double *dt* for the latter scenarios to ensure a comparable intervention magnitude over the intervention duration. This is not possible for this sensitivity analysis with *dt* being a fixed explored parameter and heatmap legends will therefore differ across scenarios.



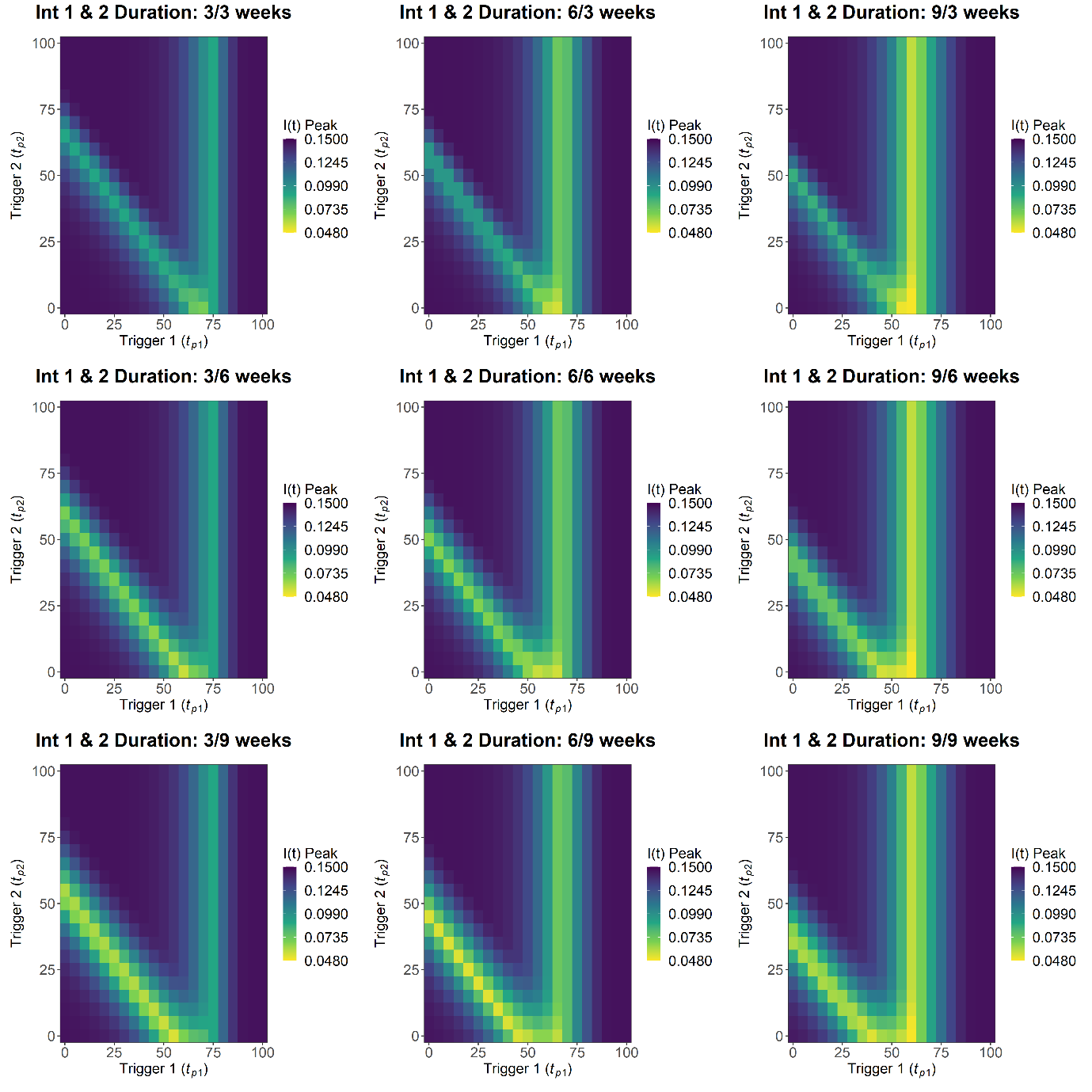
**Figure S5. Scenario 1 sensitivity analysis for maximum I(t) peak, *Imax*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 3/6/9 weeks were explored in this sensitivity analysis.



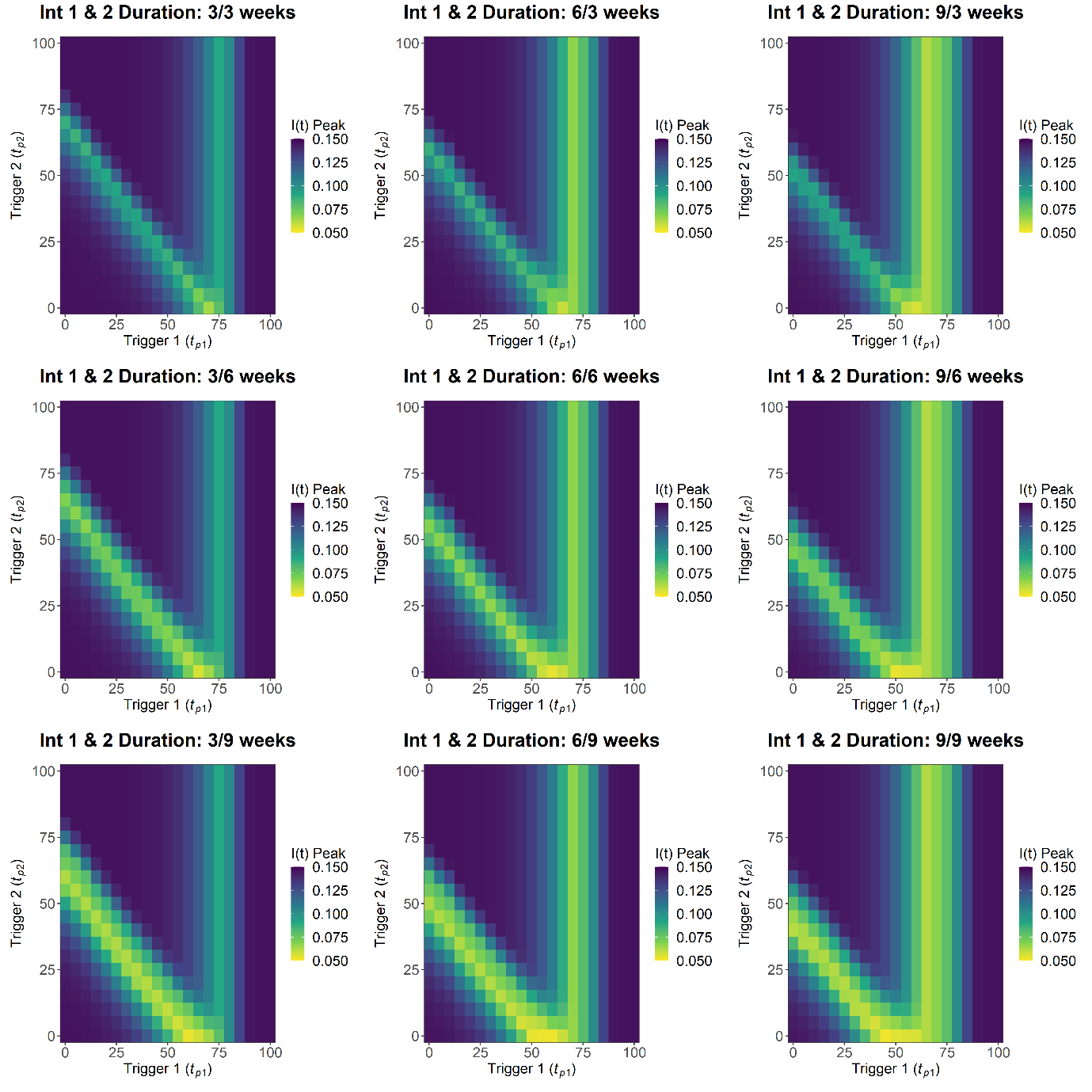
**Figure S6. Scenario 2 sensitivity analysis for maximum I(t) peak, *Imax*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



**Figure S7. Scenario 3 sensitivity analysis for maximum I(t) peak, *Imax*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



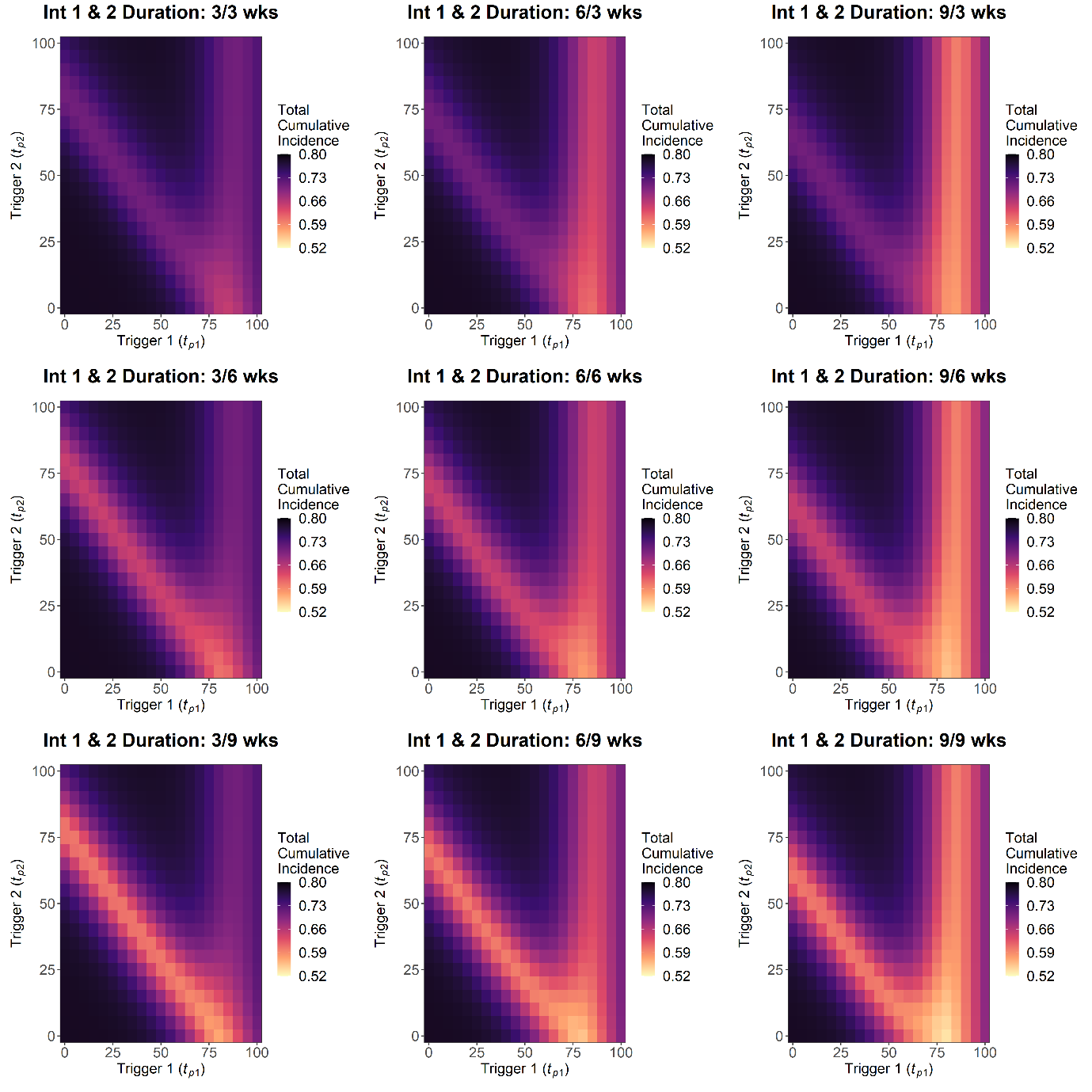
**Figure S8. Scenario 4 sensitivity analysis for maximum I(t) peak, *Imax*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



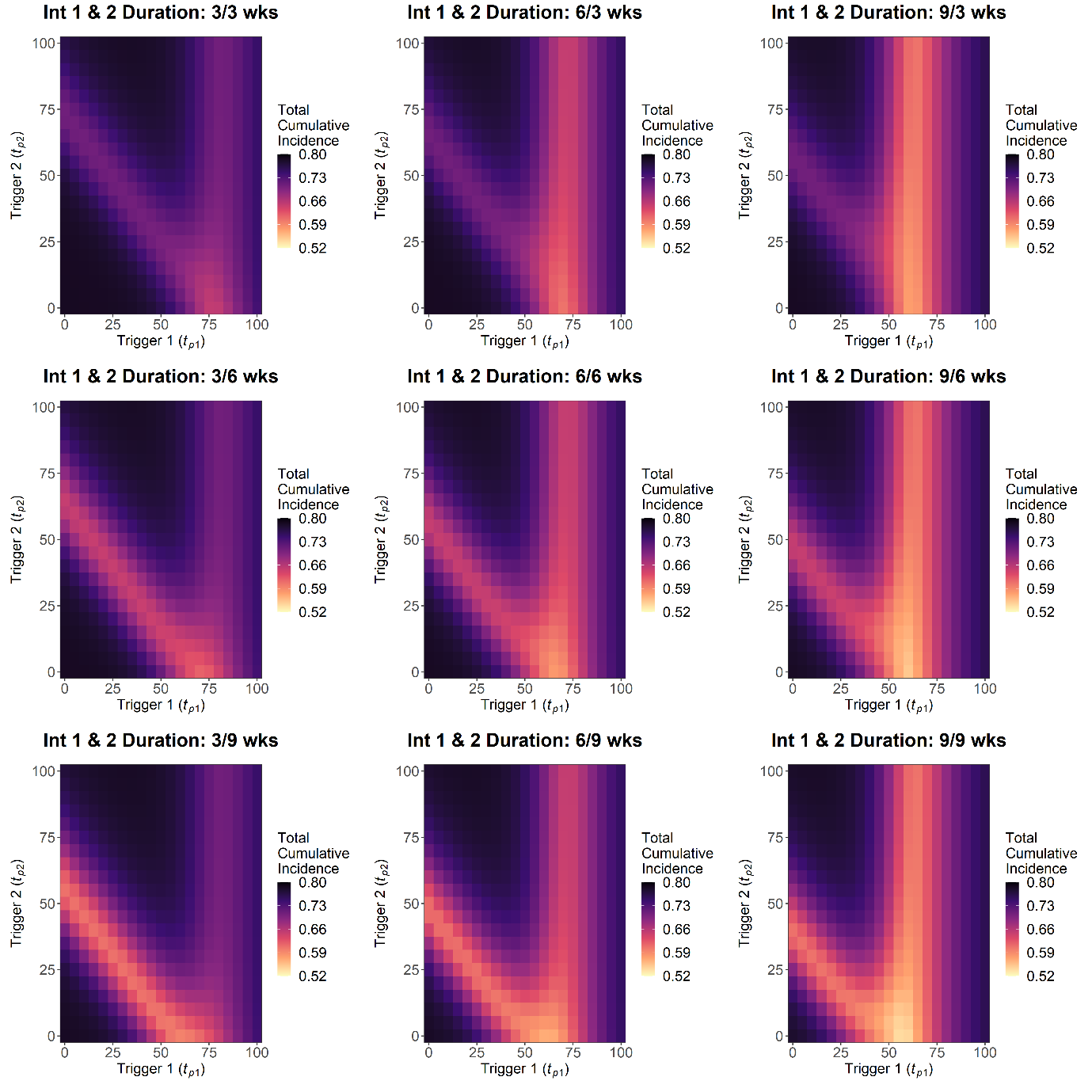
**Figure S9. Scenario 5 sensitivity analysis for maximum I(t) peak, *Imax*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S5), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



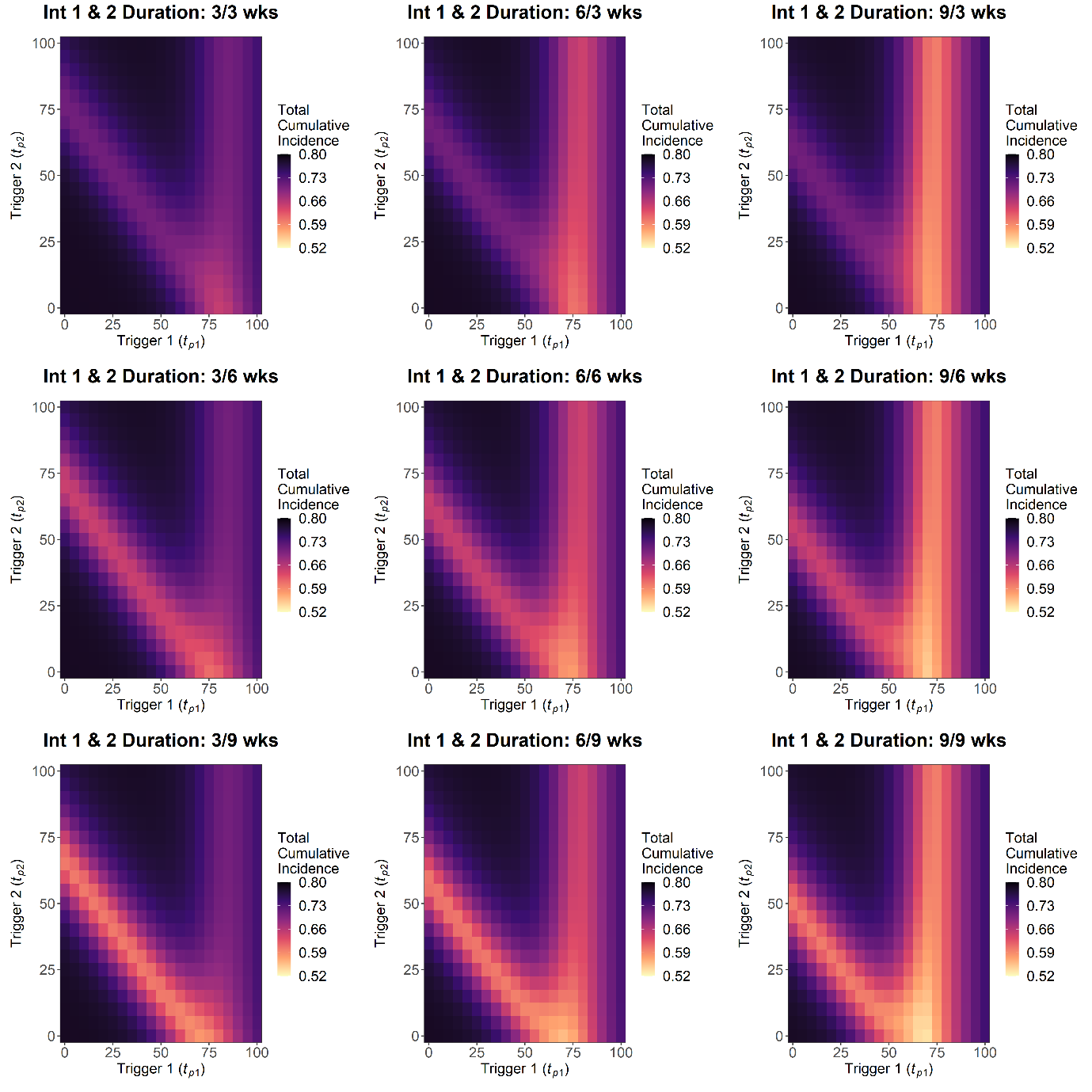
**Figure S10. Scenario 1 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 3/6/9 weeks were explored in this sensitivity analysis.



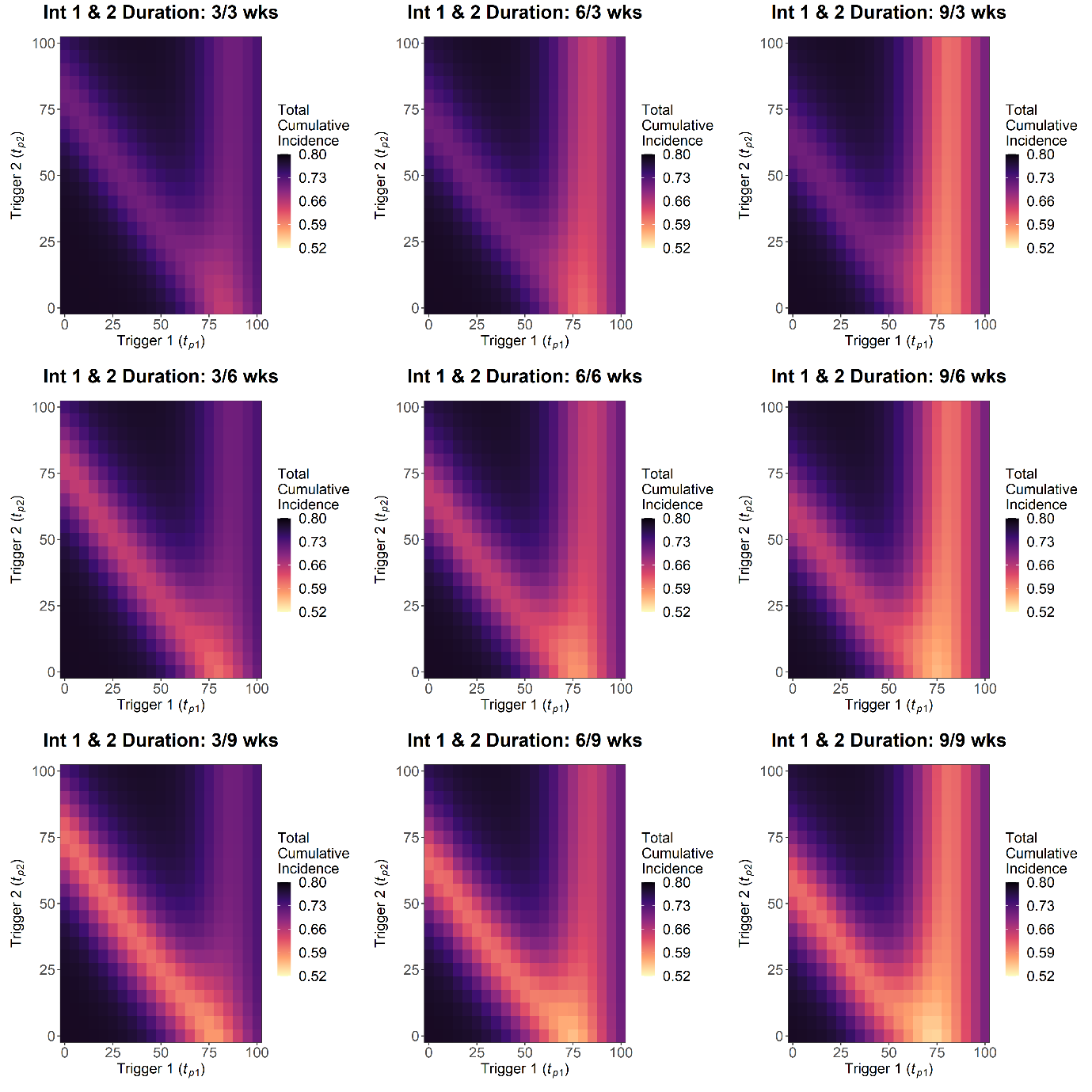
**Figure S11. Scenario 2 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S10), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



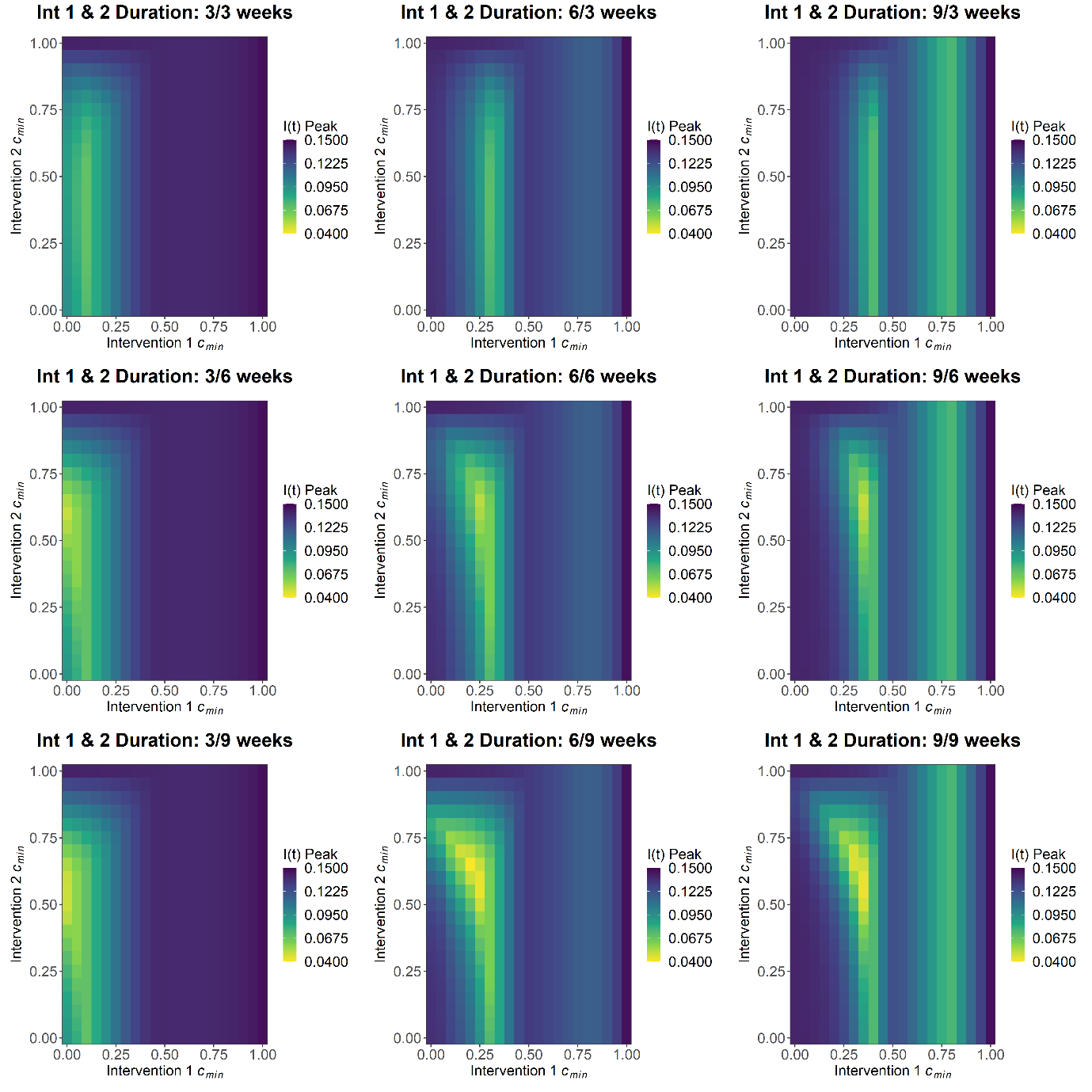
**Figure S12. Scenario 3 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S10), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



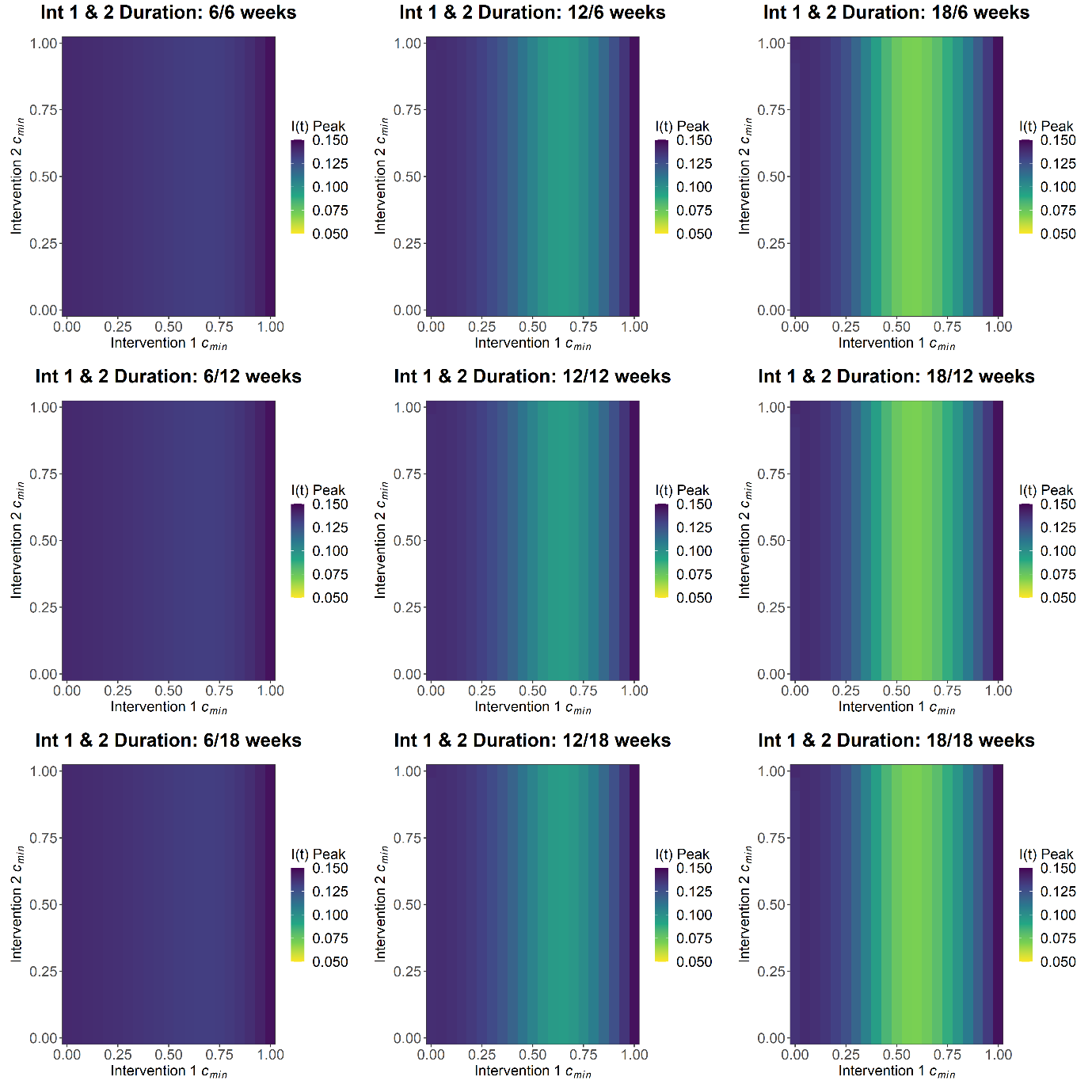
**Figure S13. Scenario 4 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S10), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



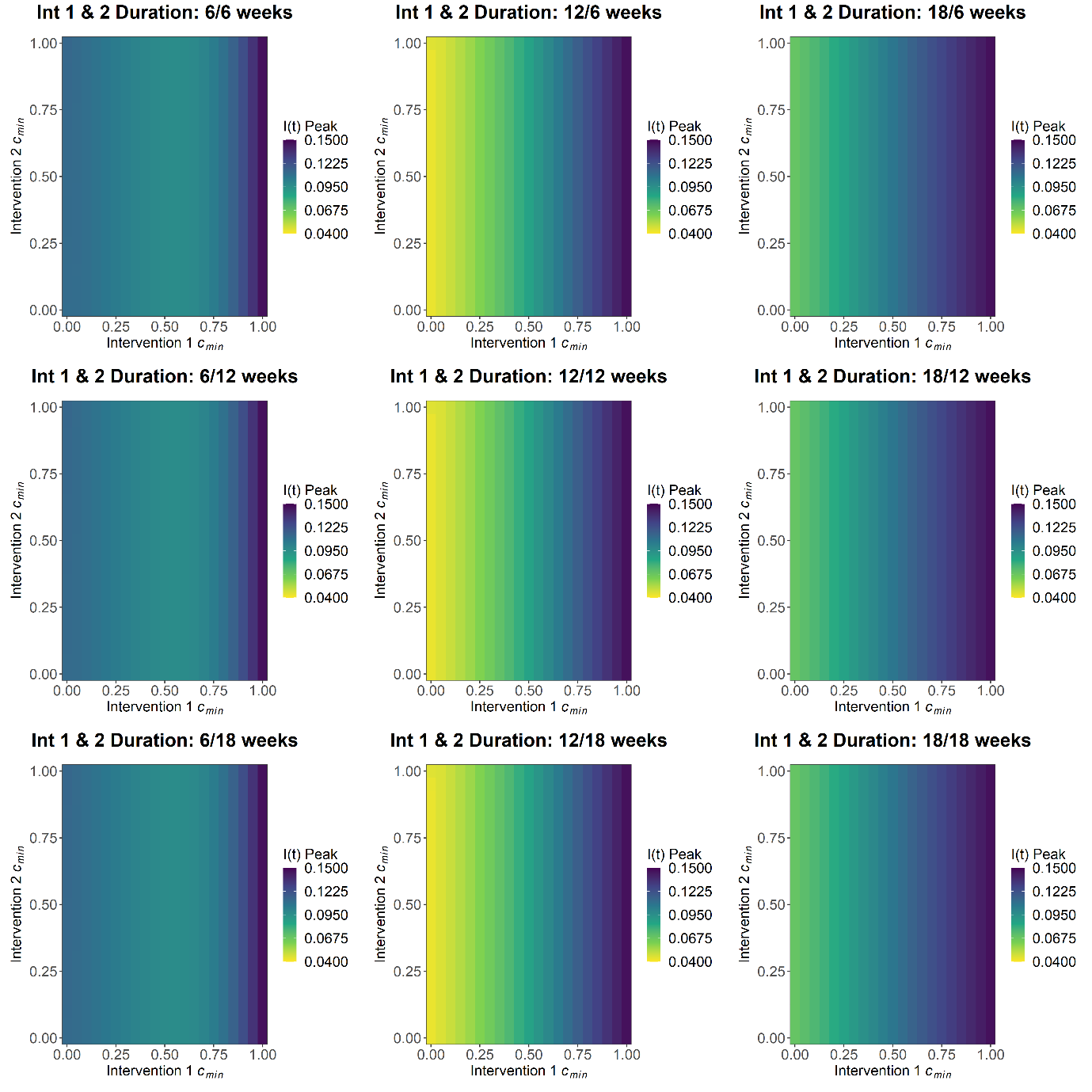
**Figure S14. Scenario 5 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for intervention 1 trigger date, *tp1*, and intervention 2 trigger date, *tp2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S10), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



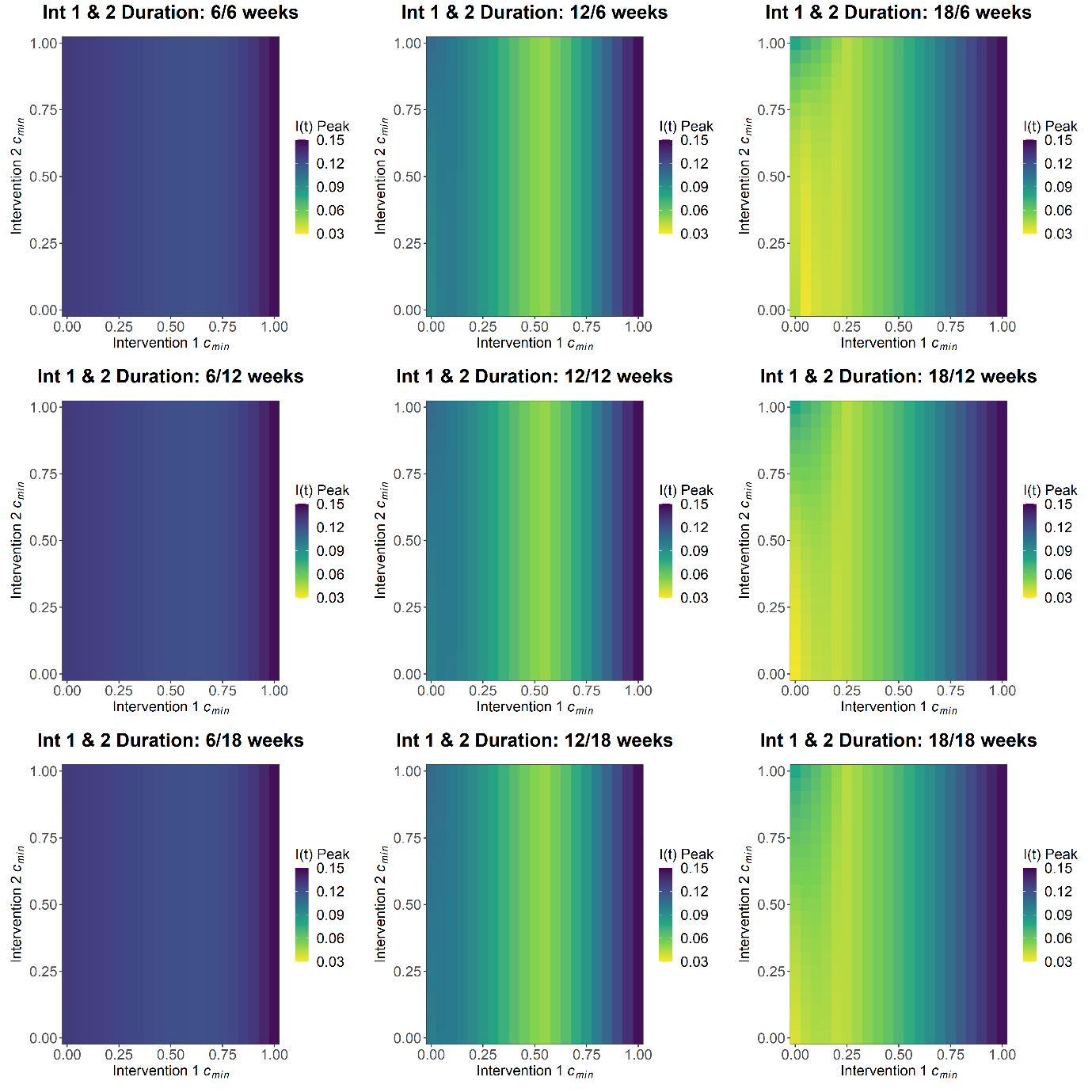
**Figure S15. Scenario 1 sensitivity analysis for the maximum I(t) peak, *Imax*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 3/6/9 weeks were explored in this sensitivity analysis.



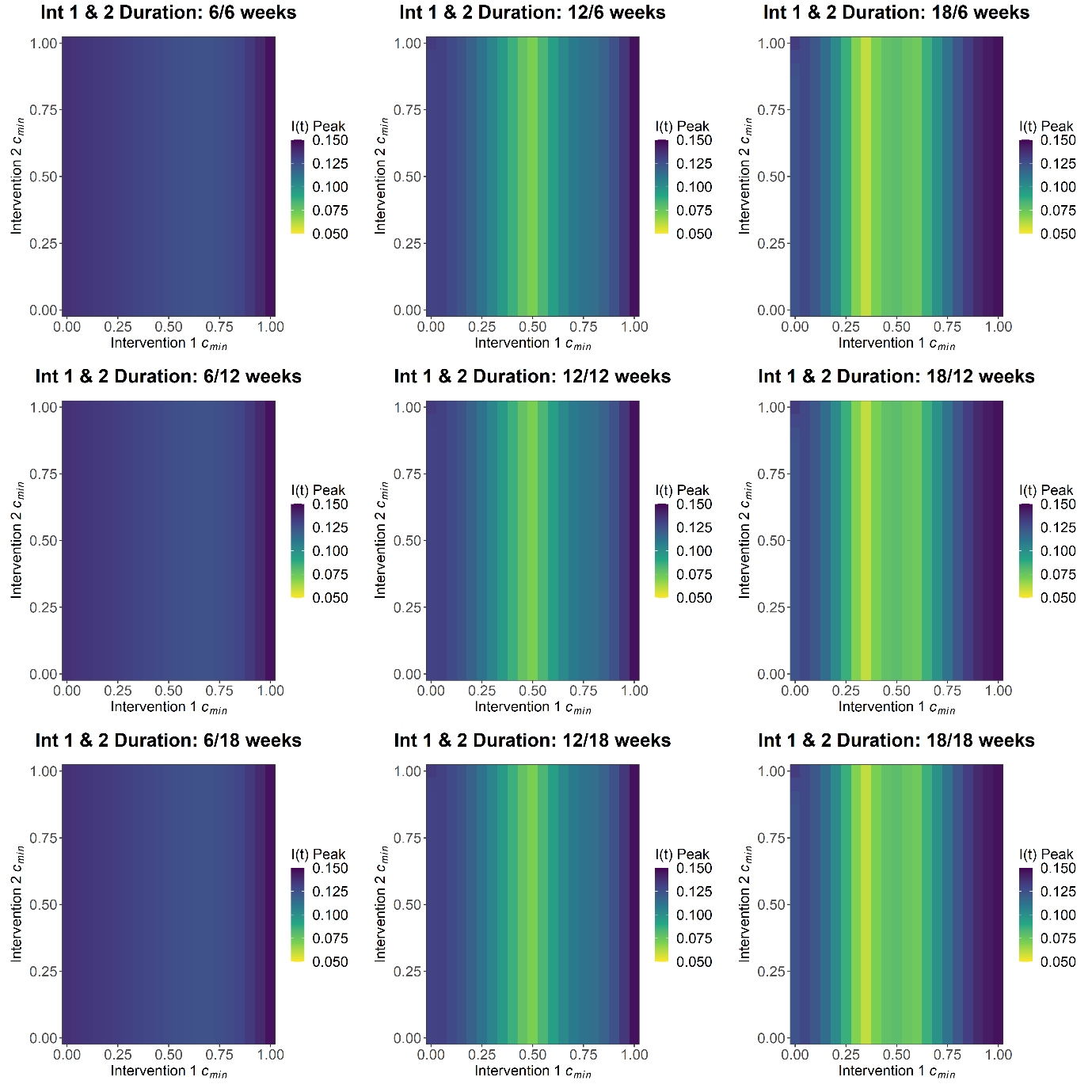
**Figure S16. Scenario 2 sensitivity analysis for the maximum I(t) peak, *Imax*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



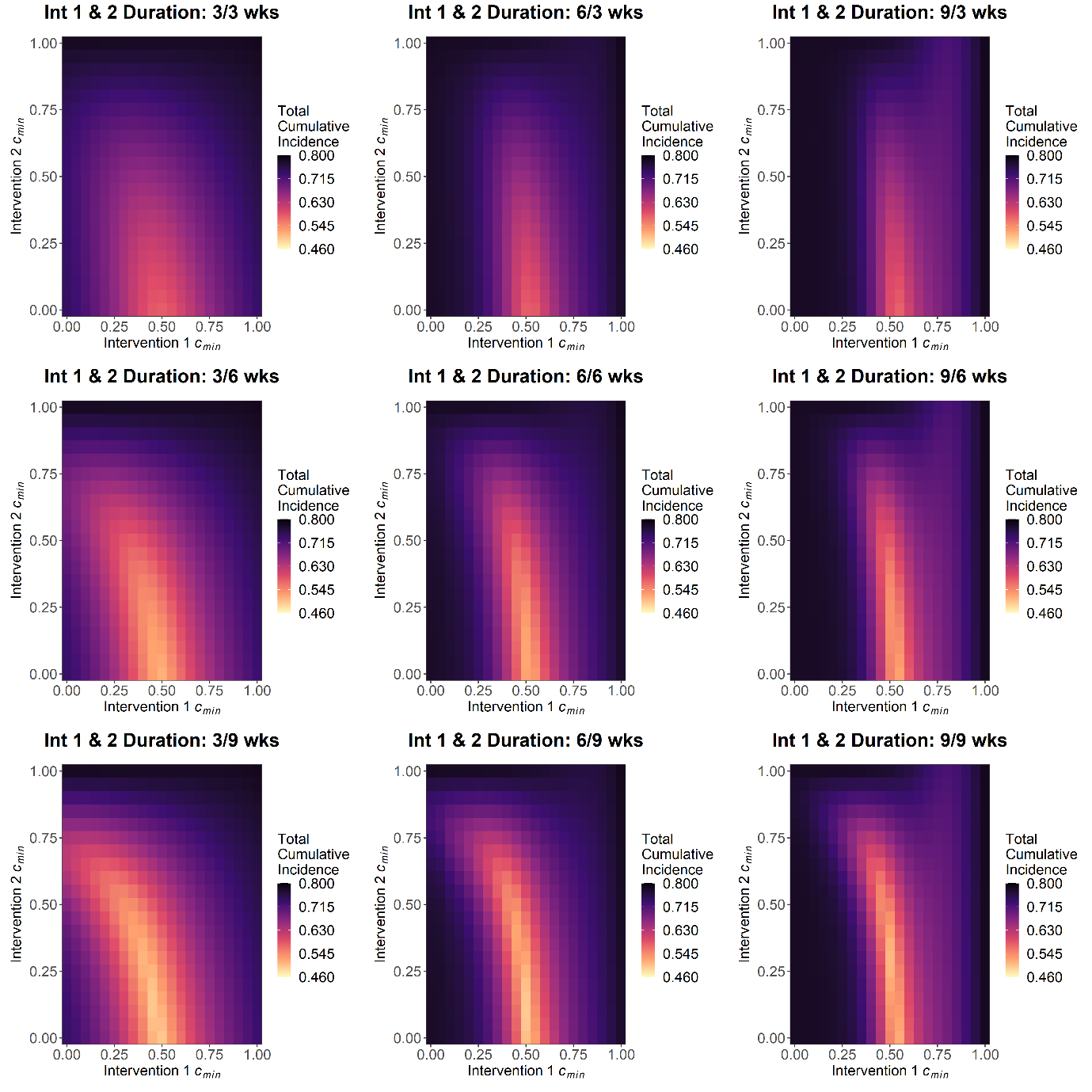
**Figure S17. Scenario 3 sensitivity analysis for the maximum I(t) peak, *Imax*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



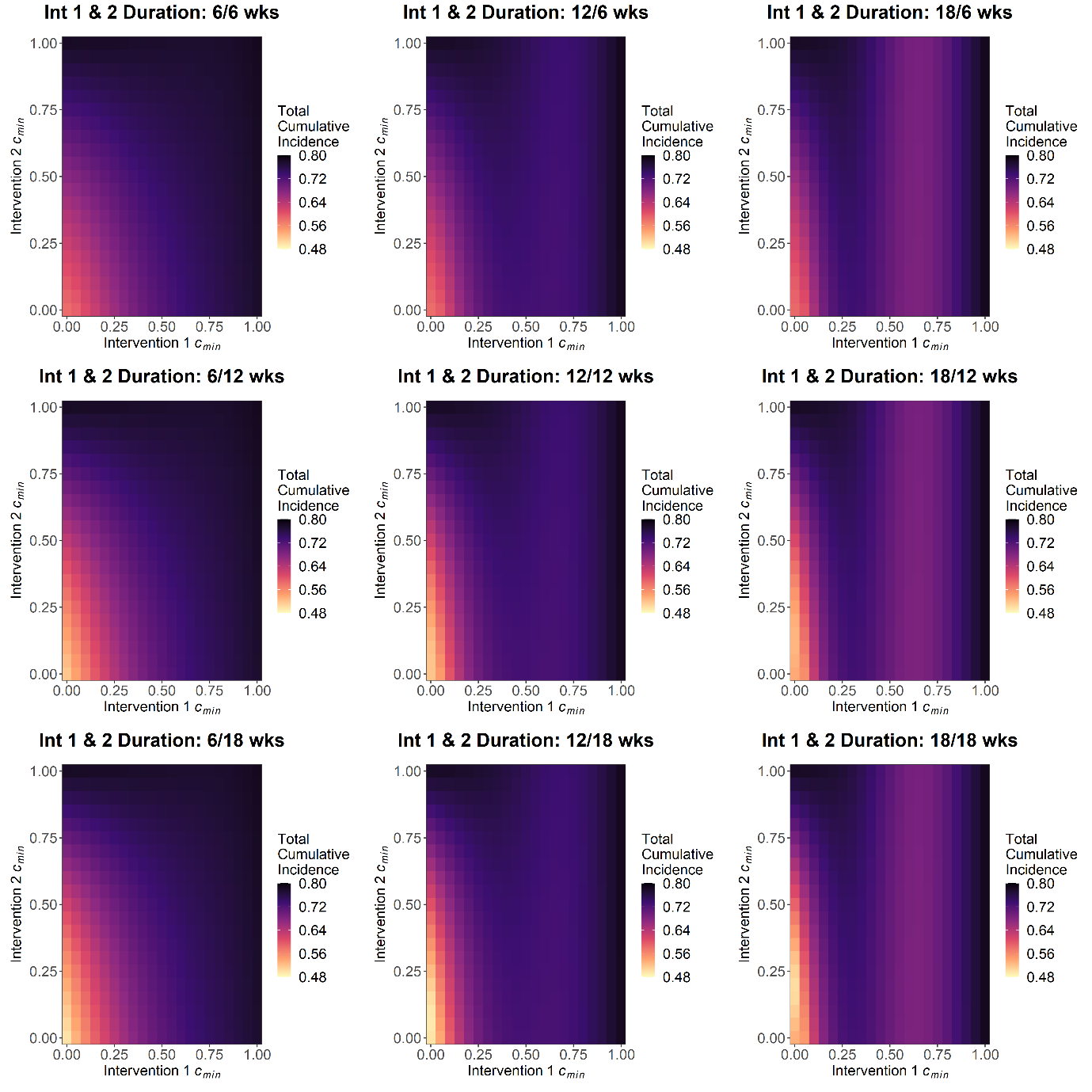
**Figure S18. Scenario 4 sensitivity analysis for the maximum I(t) peak, *Imax*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



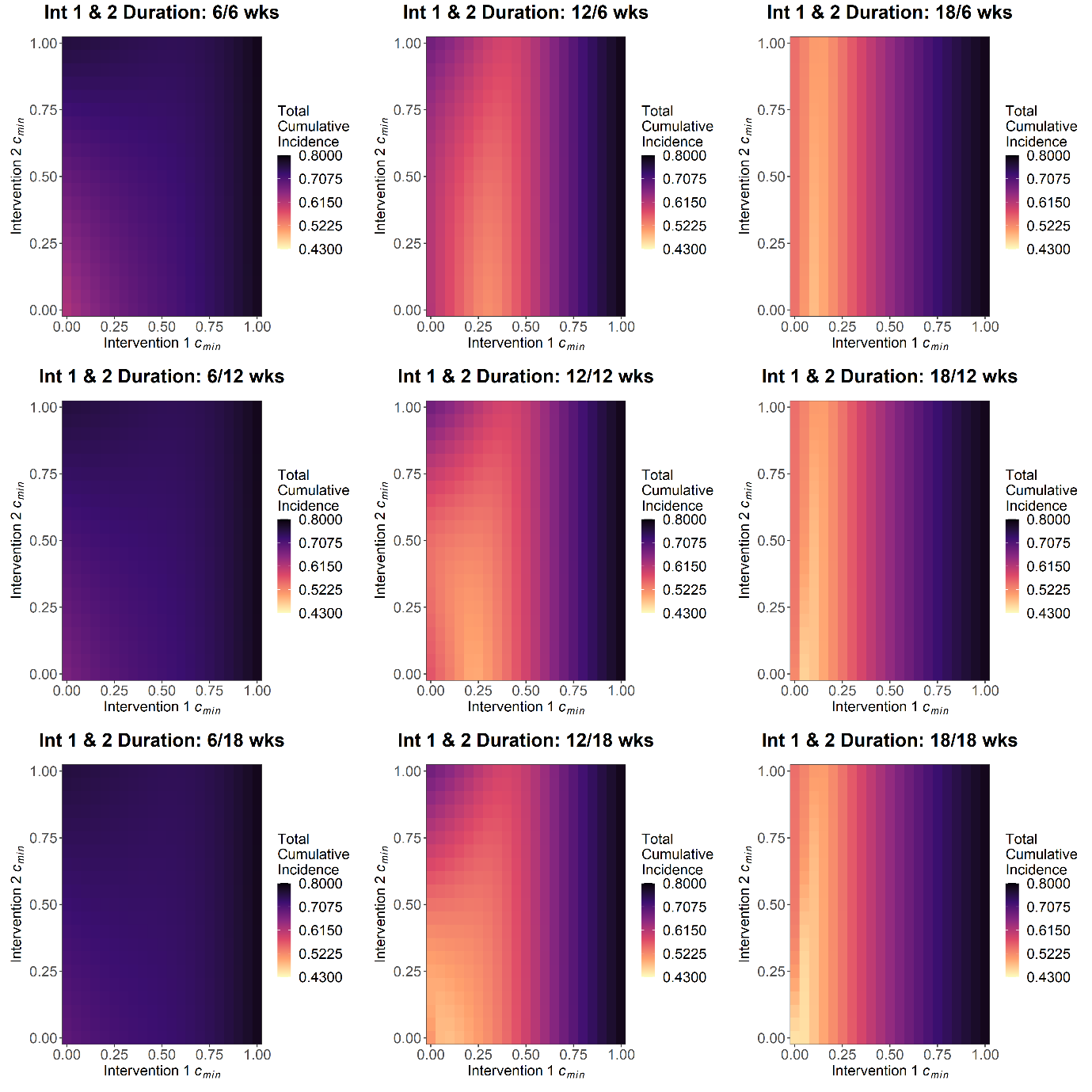
**Figure S19. Scenario 5 sensitivity analysis for the maximum I(t) peak, *Imax*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S15), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



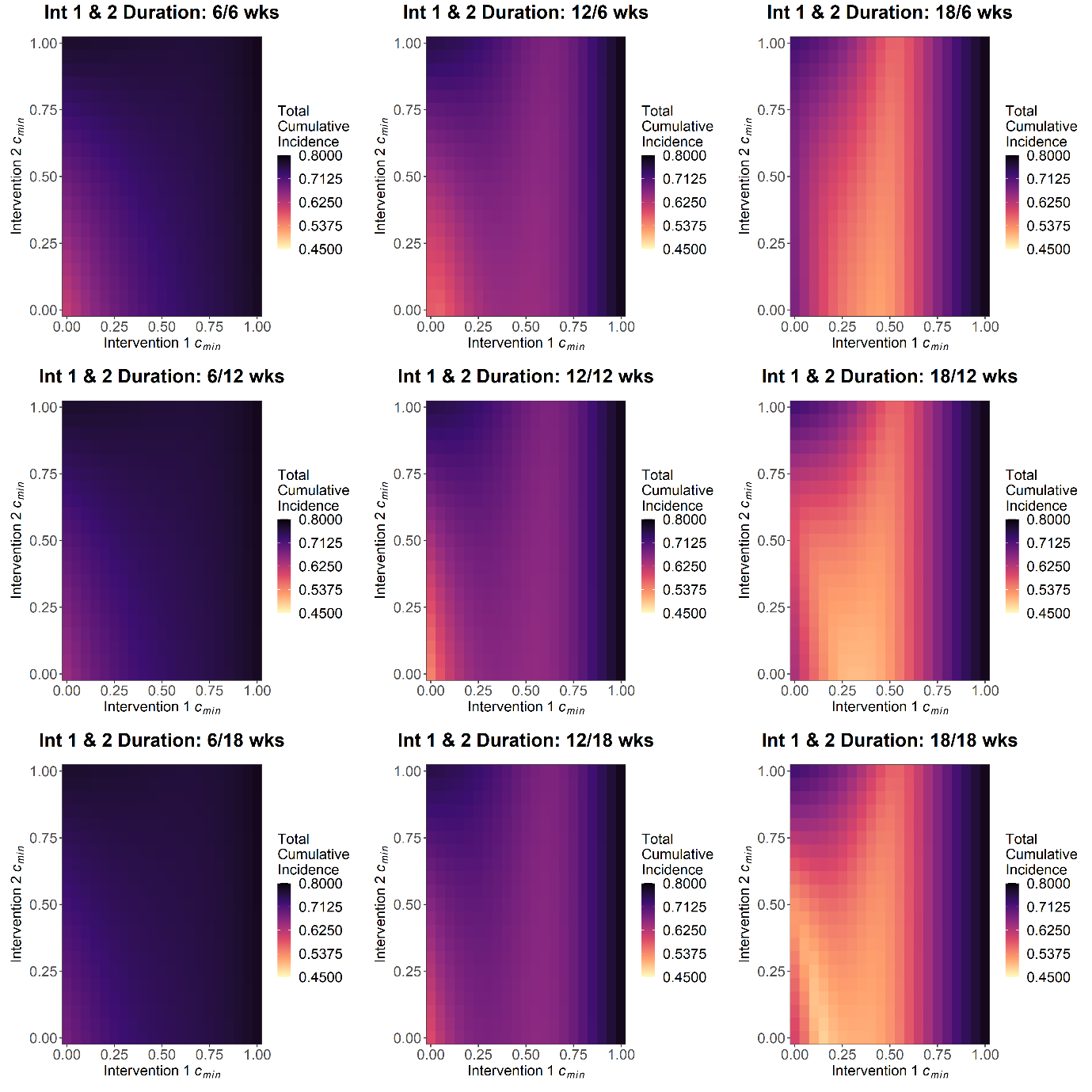
**Figure S20. Scenario 1 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 3/6/9 weeks were explored in this sensitivity analysis.



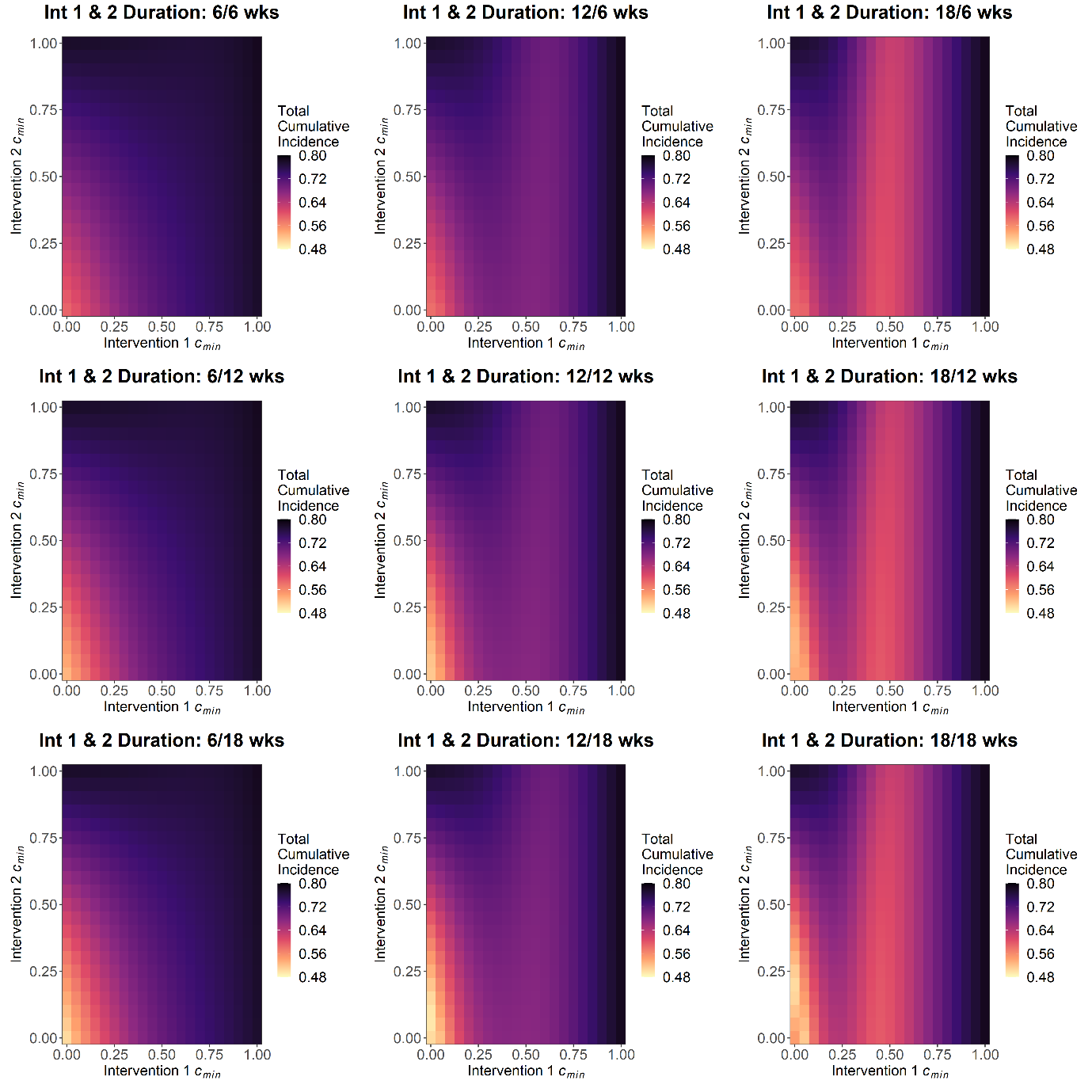
**Figure S21. Scenario 2 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S20), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



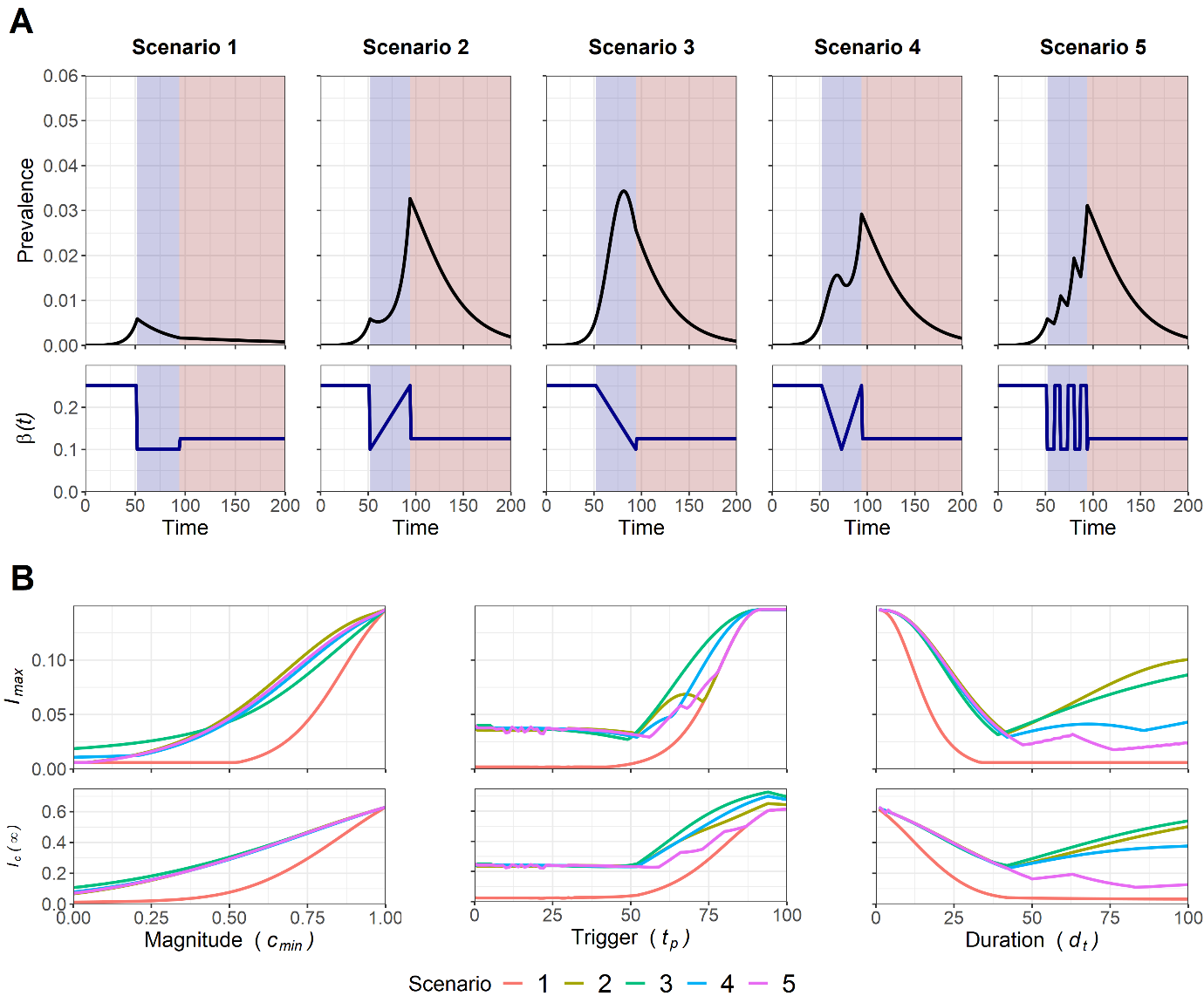
**Figure S22. Scenario 3 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S20), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



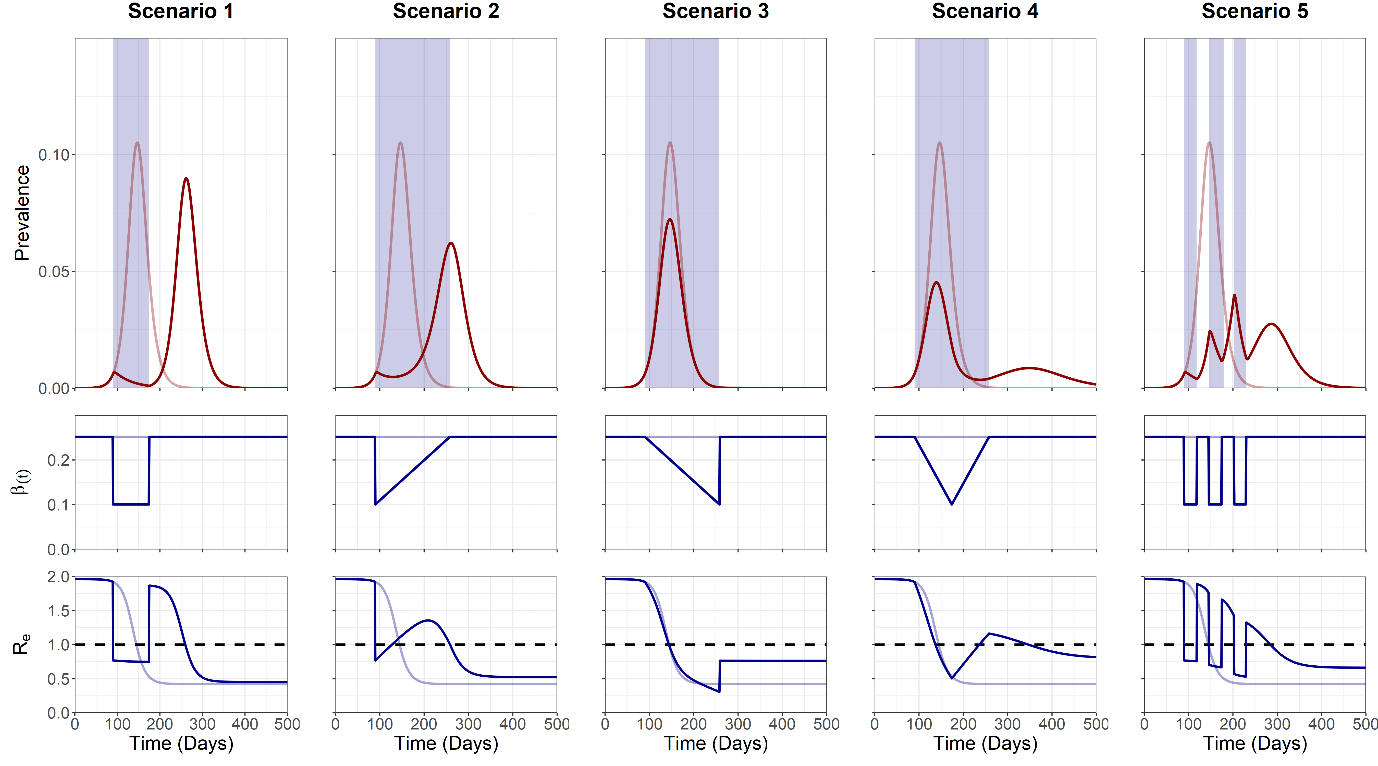
**Figure S23. Scenario 4 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S20), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



**Figure S24. Scenario 5 sensitivity analysis for total cumulative incidence, *Ic(∞)*, for the minimum value of lockdown-related scaling factor *c(t)* for intervention 1, *cmin1*, and intervention 2, *cmin2*, explored for varying combinations of the duration of intervention 1, *dt1*, and intervention 2, *dt2*.** Combinations of *dt1* = *dt2* = 6/12/18 weeks were explored in this sensitivity analysis. Note that explored *dt1*/*dt2* values were doubled relative to scenario 1 (Figure S20), this was to explore the parameter range for *dt1*/*dt2* in the baseline analysis (Figure 4) where scenario 2, 3, 4 and 5 were doubled relative to scenario 1.



**Figure S25. A) Trajectory plots and changes in *β(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 *cmin2* = 0.5. B) Sensitivity analysis for Intervention trigger day (*tp*), magnitude of lockdown measures (*cmin*) and intervention duration (*dt*) to minimise maximum *I(t)* peak, *Imax*, and total cumulative incidence, *Ic(∞)*.** 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. As *tp2* 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 *dt1* = 42 days (6 weeks). Therefore the scenario 1 trajectory plot and sensitivity analysis was not comparable to all other scenarios.



**Figure S26. Trajectory plots and changes in *β(t)* for the single-intervention SEIR model for all five scenarios.** Note that parameter *tp* = 90, corresponding to *Ic(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 *σ* = 1/3.

**Appendix References**

1. Di Lauro F, Kiss IZ, Miller J. The timing of one-shot interventions for epidemic control. medRxiv. 2020:2020.03.02.20030007.

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