# **OPTIMISING THE EFFICACY OF TIME-LIMITED INTERVENTIONS FOR EPIDEMIC CONTROL**

## **DISCUSSION – (1500-2000) words**

**Description of Results**

This work builds on previous epidemiological modelling to explore the optimal parameter space to minimise maximum peak prevalence (*Imax*) and total cumulative incidence (*Ic(∞)*) across five different intervention scenarios (**Morris et al, Lauro et al**). This was explored in the context of a simulated COVID-19 outbreak. We note that there is no single intervention strategy that can be considered the most optimal approach, with each scenario capable of minimizing both *Imax* and *Ic(∞)* for a given set of unique parameter values.

The optimal parameter space to minimise *Imax*, and to a lesser extent *Ic(∞)*, for each intervention scenario can be attributed to two key characteristics: 1) Intervention peak timing and 2) Intervention *cmin* balance. Matching the timing of an intervention to the epidemic peak is not a novel concept and has been explored previously (**Lauro et al**). However, we demonstrate that it is also necessary to match the timing of the epidemic peak with the greatest extent of the intervention (*cmin*/*cmin1*/*cmin2*) if reductions to *β(t)* are allowed to vary. This can be intuitively observed by comparing scenario 2 (*cmin* at *tp*) and scenario 3 (*cmin* at *tp* + *dt*) (**Figure 3**), with scenario 2 being optimal at a later trigger day to coincide with the early *cmin* reduction and scenario 3 optimal with an earlier intervention trigger to coincide with the later *cmin* reduction. Additionally, as highlighted by previous modelling (**Lauro et al**), it is also necessary to balance the intervention strength, to prevent an unmitigated epidemic due to an insufficient intervention, or the maintenance of population susceptibility due to an intervention that is too strong.

As highlighted by previous research, achieving these optimums in practice is likely to be difficult. A combination of narrow parameter optimums, imperfect disease surveillance, confounding parallel interventions, public compliance, an inability to fine tune the strength of an intervention and a lag between the introduction of an intervention and observable alterations in the disease prevalence, would likely prevent policy makers from micromanaging the course of a COVID-19 outbreak to minimise *Imax* and *Ic(∞)*. It is therefore more relevant to focus on the viability of suboptimal interventions, to identify a generic intervention course that can still somewhat minimise *Imax* and *Ic(∞)*.

We note that for a single time limited intervention, the most effective suboptimal strategy to reduce *Imax* and *Ic(∞)* can be achieved by intervening stronger and for long than what is considered optimal. While for multiple time-limited interventions, it is more beneficial to focus efforts on managing the initial intervention, with subsequent interventions only able to compensate for a suboptimal initial intervention under a narrow range of circumstances. Increasing the strength and introducing this initial intervention earlier was found to provide the greatest reductions to *Imax* and *Ic(∞)* under suboptimal circumstances.

Intervention measures such as population lockdown are widely recognised as unsustainable, with detrimental economical, physical and mental health impacts. As evidenced by the ongoing COVID-19 outbreak, these measures are often not considered a primary approach, instead used as an integral part of a wider strategy to drive down the level of infection and buy time for the development introduction of more sustainable measures, such as test, track and trace or vaccination. We note that in this context, it universally more optimal across all scenarios to introduce the initial intervention earlier, more strongly and for as long as necessary for the introduction of the more sustainable secondary intervention. While we note that this corroborates some of the suboptimal strategies to minimise *Imax* and *Ic(∞)*, there are also substantial differences. This highlights the importance of identifying the questions posed by policy makers when considering either suboptimal or optimal epidemic control.

**Caveats + Limitations**

In contrast to the SIR model structure used by this study, we note that an SEIR framework could be considered more accurate to describe the epidemiological characteristics of SARS-COV-2. This model structure alteration would manifest as a delay between the intervention and observed effects in *I(t)*. However, this was considered unnecessary, with the aim of this study to describe the existence and patterns of intervention optimums, and not describe the exact timing. We also note that the addition of this compartment would likely increase the number of assumptions underlying the model, with both the infectious and an incubation period possessing implicitly assumed exponentially distributed waiting times. However, we note that this could be resolved through the use of Erlang or gamma distributed waiting times in future analyses.

An assumption of life-long immunity was also assumed following SARS-COV-2 infection. This choice was made due to the large amount of uncertainty regarding the immunological characteristics of the virus, which is currently under debate. A relatively simple disease metric was also used for this study, with an optimal intervention able to reduce maximum peak prevalence, *Imax*, and total cumulative incidence, *Ic(∞)*. While outside of the scope of this study, the use of more epidemiologically relevant outcome measures such as occupied ICU capacity or deaths per 100,000 population may be of interest when investigating optimal COVID-19 interventions in a more policy-relevant context. This could also be complemented by an exploration into the impact of individual or population level variation of risk on intervention optimisation. For example, investigating intervention optimisation in the context of a realistic age-structured population or with regards to the impact of individual-level overdispersion in transmission.

**Summary**

While we describe the possibility of optimising various intervention strategies throughout this study, it was not the intention to propose this as a singular solution for COVID-19 epidemic control. The results described in this study are highly nuanced, with narrow intervention optimums and a number of other factors likely preventing the trajectory of an epidemic conforming uniformly to the dynamics observed in this study. Instead, it is of greater interest to identify potential benefits from more easily achievable suboptimal interventions that can still successfully minimise epidemiologically relevant outcome measures. This has the additional benefit of being a risk-averse approach, which is often favourable during the initial stages of the outbreak, where the potential impact of risky public health policy can lead to disastrous consequences. Finally, we note that the evidence from this study should be taken into context with the work tirelessly undertaken by the wider epidemiological and modelling community. It is only through this collaboration and synthesis where effective and humanistic public health policy can be generated to combat the COVID-19 pandemic.