## **METHODS**

* 1. **SIR Model Structure**

A deterministic SIR model was used to explore the impact of time-limited non-pharmaceutical interventions (NPI) on a simulated UK-based COVID-19 outbreak. *S*, *I* and *R* compartments were used to denote the fraction of susceptible, infected and recovered individuals respectively within the population, with *S + I + R = 1* (**eqn 1.1**). The effects of demography were ignored for this model (births, deaths, migration, etc.). An exposed disease state, *E*, representing a non-infectious latency period, was not considered for this model.

eqn 1.1

Susceptible individuals (*S*) are infected at the time-varying rate *β(t)*, which represents the daily per-capita rate of transmission in a randomly-mixing population. Infected individuals (*I*) recover at rate *γ*, representing the daily per-capita rate of recovery. This rate was taken as the inverse of the average duration of infectiousness. A baseline pre-NPI basic reproduction number (*R0*) of 2.8 and doubling time (*Td*) of 3 days were assumed, in line with reported estimates for COVID-19 transmission in the UK and abroad (**ref**). The generation time was calculated as a function of these two quantities, with a baseline generation time of 7.79 days and a resulting *γ* of 0.128 (**eqn 1.2**).

eqn 1.2

* 1. **Defining the time-varying β(t)**

By setting *β = R0γ*, we define the baseline per-capita transmission rate in the absence of NPIs, *β = 0.359*. To capture the impact of small-scale NPIs (excluding population lockdown), *β* was multiplied by a scaling factor of 0.7, *βscale = 0.252*, with this 30% reduction being roughly in line with estimates of the impact of school-closures, introduction of social distancing and isolation upon COVID-19 symptoms. **– on the transmission dynamics of COVID-19 – explain further provide context. This probably needs a bit more explanation, this was when the government told everybody to self-isolate and use common hygiene like hand-washing, etc. (I’m also not sure if the schools were already closed at that time, better check)**

*β(t)* is defined as the product of *βscale* and a time-varying scaling factor *c(t)*, which reduces *βscale* over the course of the simulation to model the impact of a population lockdown, with *0 ≤ c(t) ≤ 1*. Reductions associated with this scaling factor are introduced on the lockdown trigger day, *tp*. This is defined:

The shape of *c(t)* varies with the different lockdown scenarios explored, with parameter *cmin* describing the minimum value of c(t) during the intervention. This parameter ensures that for each considered intervention scenario, the same minimum value of *c(t)* and therefore *β(t)* is reached. For baseline reductions to β(t) we define *cmin* = 0.4, resulting in *β*(t)= 0.101when the lockdown measures are at its greatest impact*.* Baseline *cmin* was chosen to roughly achieve an effective reproduction number (*Re*) during lockdown, similar to that observed in COVID-19 literature, around *0.7 ≤ Re ≤ 1*, with *Re* defined as *R0S*.

All lockdown interventions were initiated at baseline *tp* = 52 days, equivalent to a total cumulative infected fraction at the initiation of population lockdown, *Ic*(52)= 0.02, in line with model-based COVID-19 UK estimates (**ref**). The model was seeded with an initial infectious fraction, *I*(0) = 0.00001.

* 1. **Single Intervention Population Lockdown**

A time-limited population lockdown was the primary NPI explored in this model, with five different lockdown strategies being explored. Each intervention differed with regards to the shape of *c(t)* and the subsequent *β(t)* reductions being explored over the duration of the lockdown period, defined as *dt* (**Table S1**). The model simulation was run for 400 days.

* Scenario 1 – Immediate and constant reduction to *cmin*.
* Scenario 2 - Immediate reduction to *cmin* followed by a linear increase back to *c(t)* = 1.
* Scenario 3 - Linear decrease to *cmin* followed by an immediate return to *c(t)* = 1.
* Scenario 4 - Linear decrease to *cmin* at *dt*/2, followed by a linear increase back to *c(t)* = 1.
* Scenario 5 - A “pulsing” lockdown with immediate reductions to *cmin* between intervention intervals 0-21, 35-49 and 63-77 days (for an example total intervention duration, *dt* = 84 days).

**Table 1** – Description of the five lockdown interventions.

|  |  |  |
| --- | --- | --- |
| Scenario | *β(t)* during the simulation1 | Definition of *c(t)* scaling parameter |
| 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |

1β(t) plots are shown for baseline parameters, *cmin* = 0.4 and *dt* = 84 days and *dt* = 168 days for scenario 1 and scenario 2, 3, 4 and 5 respectively.

For a total length of lockdown duration, *dt*, the magnitude of *c(t)* scaling reductions over the intervention duration is half for scenario 2, 3, 4 and 5 relative to scenario 1. To maintain comparable overall *β(t)* reductions over the intervention period, *dt* was doubled for scenario 2, 3, 4 and 5 relative to scenario 1 for baseline values. For the baseline analysis, this corresponds to *dt* = 84 days for scenario 1 (12 weeks) and *dt* = 168 days (24 weeks) for all other scenarios in the baseline analysis. An alternative approach was considered by keeping *dt* constant and doubling *cmin* reductions observed in scenario 2, 3, 4 and 5, relative to scenario 1 (**Figure S1 + 2**). Either method is plausible when considering potential intervention scenarios, but we argue that in practice it is more plausible to alter *dt* than it is to alter *cmin* in a public health context.

* 1. **Multiple Intervention Population Lockdown**

To explore the transmission dynamics resulting from multiple time-limited population lockdowns, two interventions were modelled sequentially over the course of the simulation. The generic shape of *c(t)* reductions for the five different lockdown scenarios were kept constant for both intervention 1 and 2 (**Table S2**). We define the lockdown-related *β(t)* scaling factor, lockdown trigger point and duration of the intervention as *c1*(t) and *c2*(t), *tp1* and *tp2*, and *dt1* and *dt2* respectively for intervention 1 and 2. We highlight that *tp2* is defined relative to the end of intervention 1, with the exact start of intervention 2 defined as *t* = *tp1*+*dt1*+*tp2*.

Baseline *dt1*  and *dt2* for multiple interventions were halved relative to the single intervention scenarios to ensure that the dual intervention could occur within the timeframe of the simulated epidemic curve where *I(t)* > 0. Similar to the single intervention scenario, the intervention duration of scenario 2, 3, 4 and 5 were doubled relative to scenario 1 to ensure comparable magnitudes of *β(t)* reductions over the intervention period. Baseline parameter values for the multiple intervention scenario were defined as *dt1* = *dt2* = 42 days (6 weeks) for scenario 1 and *dt1* = *dt2* = 84 days (12 weeks) for scenarios 2, 3, 4 and 5. The model simulation was run for 730 days.

* 1. **Outcome Measures of Interest**

The primary objective of all analyses in this paper was to identify the optimal parameter space for lockdown trigger point (*tp*), duration of lockdown (*dt*) and magnitude of β(t) reductions (cmin) to minimise the values of two outcome measures:

**We define the peak prevalence as the global maxima of the equation, with epidemic peaks defined as the locl maxima occuring uring the trajectory curve. We define the optimal parameter space as the global minima of the parameter space explored in the optimisation analysis**

**Define a suboptimal solution**

* Maximum peak prevalence *I(t): Imax*
* Total cumulative incidence:

1. **Software Used**

All model simulations were carried out using R (v3.6.2) and Rstudio. The “desolve” package was used for all R based simulations.

EXPAND