Shielding individuals at high risk of COVID-19: a micro-simulation study to inform intervention design

Proposed methods

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Problem statement

One of the proposed interventions for mitigating COVID-19 epidemics is to physically isolate individuals known to be at high risk of developing severe disease and dying if infected with SARS-CoV-2. While compartmental dynamic models indicate that this intervention, commonly denoted as 'shielding', has a substantial potential to reduce mortality and health service pressure, such models do not fully capture the individual-level dynamics of the intervention: in particular, what remains unexplored is the potential harm of inadvertently introducing infection into shielded communities, in scenarios where people are shielded in groups as opposed to individually. Such scenarios would likely be the only feasible modality for implementing this intervention in settings (e.g. low-income urban communities, displaced persons' camps) where individual-level shielding is not possible.

The modelling study proposed here aims to generate quantitative predictions of the potential harm of shielding people together under different scenarios of overcrowding of shielded residents, timing of shielding implementation with respect to local epidemic onset, compliance with physical isolation and interventions to mitigate the risk of outbreaks among shielded communities. Harm here is defined as infection: it is assumed that high-risk individuals, once infected, would have a higher probability of severe disease and death, as described elsewhere. The study is intended to inform options appraisal and potential implementation of the shielding intervention.

Model structure

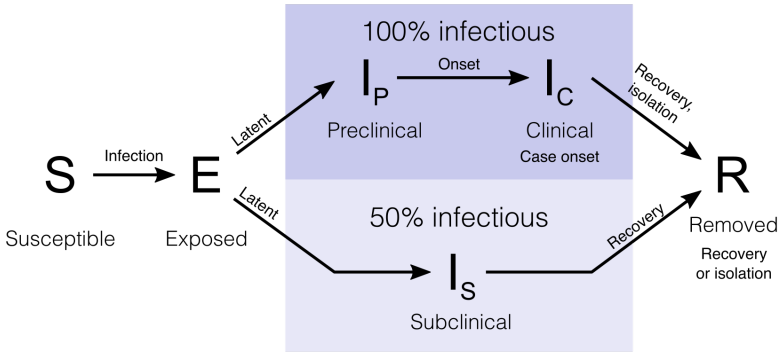
General structure

An individual-based, probabilistic model (IBM) paired with a compartmental, age-structured, stochastic dynamic model (CDM) is proposed. Individuals in both models fall within age strata (where is a given age stratum) with relative proportions . The simulation starts when the population of the CDM is seeded with a sufficient number of infections to establish sustained transmission chains.

The IBM population is divided into households of mean size . The age distribution of household members reflects that of the population. Births, non-COVID-19 deaths, aging and migration are omitted from both the IBM and CDM (this is acceptable given the period of analysis is ≤ 12 months). Because the study's endpoint of interest is infection, the clinical outcome and treatment status of cases is not relevant to this model; infectiousness is assumed to be unaffected by clinical severity.

States and transitions

At any time , individuals within both the IBM and compartmental model are within one of the following classes: (susceptible), (exposed and latent, i.e. infected but not yet infectious), (infectious but pre-symptomatic), (infectious and symptomatic), (infectious and asymptomatic throughout the infection, with infectiousness assumed to be a fraction of the infectiousness of and), and (removed: recovered and assumed to be immune or deceased). The and states are mutually exclusive with as per age-specific probabilities and , i.e. some infections eventually result in symptoms, while some remain asymptomatic until recovery:



The amount of time a given individual spends in states , , , or is drawn from distributions , , and , respectively, giving rise to the following difference equations:

where is the age-specific instantaneous force of infection (incidence) experienced by a susceptible individual, as detailed below.

Transmission dynamics

Over any time unit:

- In the CDM people move from to as discussed in Davies et al. and van Zandvoort et al., based on an age-specific instantaneous force of infection

  where is the probability of transmission per contact and is the matrix of contact rates among individuals of ages and ;
- In the IBM, individuals of any age within each household move from to based on an age- and household-specific instantaneous force of infection

where is the matrix of contact rates within the household among individuals of ages and , while is the corresponding contact matrix outside the household. , i.e. the full contact matrix. In other words, the force of infection is the sum of due to contacts within the household and due to extra-household contacts.

The basic reproduction number is defined as the average number of secondary infections generated by a typical infectious individual in a fully susceptible population and is calculated as the absolute value of the dominant eigenvalue of the next generation matrix (NGM) defined as

where accents indicate the expectation (average) values.

Lastly, is the ratio of this eigenvalue and the value assumed in the simulation (see below).

Shielding and related interventions

Shielding is introduced at time since the simulation's start, by relocating all high-risk individuals within (for simplicity, high risk is defined based solely on an age cut-off, i.e. ≥ 60 years old) into a single shielded residence containing a variable number of high-risk residents.

While shielded, high-risk residents' contact with others remains structured as per the above contact matrices, but is reduced or increased to varying extents as follows:

- contact with unshielded members of the household of origin is reduced by a factor ;
- contact with other unshielded people is reduced by a factor ;
- contact with other high-risk, shielded individuals within is either reduced (if physical distancing and improved hygiene are also maintained within) or increased (if, vice versa, is overcrowded and unsanitary) by a factor .

Accordingly, each shielded individual originally from household experiences a force of infection

Note that, other than by age, no heterogeneity in contact is assumed among shielded individuals (in practice, it is plausible that people might mix preferentially with neighbours or those whom they room most proximately to).

If shielded residents are infected (any or class) at the time of shielding, or become infected while shielded, they may infect other residents. The following interventions to mitigate the occurrence and size of such outbreaks are contemplated in the model:

1. Nothing is done.
2. Varying extent of isolation from people outside , resulting in values of and tending towards 0; for simplicity, we assume .
3. Physical distancing and hygiene improvements within , resulting in a value of ;
4. Symptomatic cases within self-isolate, causing a further reduction in all their contacts;
5. Symptomatic cases within exit the shielded residence with a delay since symptom onset, and return to their households (we assume this is a more likely prospect than hospitalisation in

most low-income settings; either way, the destination on exit has a negligible effect on the model);

6. As soon as a symptomatic case occurs within , all residents exit shielding and return to their households;
7. At the time shielding is introduced, any high-risk individuals who are symptomatic or who live in a household with at least one symptomatic case remain in their households and only join once they and all their household members are recovered.
8. At the time shielding is introduced, all high-risk individuals are tested irrespective of symptoms, and any positive cases do not enter the shielding accommodation. Test sensitivity is assumed to be different depending on and class.
9. Shielding is not implemented at all.

Parameter values

Values for the model parameters are as follows:

Parameter	Description	Value	Applies to	
			CDM	IBM
Model populations and state transitions				
	Number of people in CDM	10,000 (arbitrary, large enough to remove stochasticity)	X	
	Age strata in years	0-4, 5-9,10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75+	X	X
	Proportion of people in each age stratum	From demographic estimates	X	X
	Mean household size	From demographic estimates		X
	Number of people in each household h	~ Poisson(μ =)		X
	Number of people living together within the shielded accommodation	Variable: 2, 4, 8, 16, 32, 64, 128		X
	Number of households			X
	Time step for discrete-time simulation	0.25 days	X	X
	Latent period in days	~ gamma(μ = 4, k = 4)	X	X
	Duration of pre-symptomatic infectiousness in days	~ gamma(μ = 1.5, k = 4)	X	X
	Duration of symptomatic infectiousness in days	~ gamma(μ = 3.5, k = 4)	X	X
	Duration of asymptomatic infectiousness in days	~ gamma(μ = 5, k = 4)	X	X

Parameter	Description	Value	Applies to	
			CDM	IBM
	Probability of becoming a symptomatic case, if infected, for age group	Age-dependent, as estimated in Davies et al.	X	X
Transmission dynamics				
	Basic reproduction number	Variable: 1.5, 2.0, 2.5, 3.0, 3.5, 4.0	X	
	Relative infectiousness of asymptomatic cases	50%	X	X
	Matrix of contacts per within the household among individuals of age and age	Country-specific: Zimbabwe, Somaliland.		X
	Matrix of contacts per outside the household among individuals of age and age	Country-specific: Zimbabwe, Somaliland		X
	Matrix of contacts per within any setting among individuals of age and age		X	
	Probability of transmission per contact with an infectious individual	See text; Computed within CDM, then applied to CDM and IBM	X	X
Shielding interventions				
	Contact between shielded and unshielded individuals, relative to pre-shielding	Variable: 0.0, 0.2, 0.4, 0.6, 0.8, 1.0		X
	Contact among shielded individuals, relative to pre-shielding	Variable: 0.25, 0.50, 1.00, 2.00, 4.00		X
	Contact between symptomatic shielded individuals and other shielded individuals, relative to before becoming symptomatic	Variable: 0.0, 0.2, 0.4, 0.6, 0.8, 1.0		X
	Delay in days between onset of symptoms and exiting the shielded residence	Variable: 0, 2, 4, 6		X
	Sensitivity of SARS-CoV-2 laboratory test among individuals in latent class	?		X
	Sensitivity of SARS-CoV-2 laboratory test among individuals in pre-symptomatic infectious class	?		X
	Sensitivity of SARS-CoV-2 laboratory test among individuals in symptomatic infectious class	?		X
	Sensitivity of SARS-CoV-2 laboratory test among individuals in asymptomatic infectious class	?		X

Analysis

Simulation scenarios

Multiple simulations of the model are run to = 12 months after seeding the CDM with 50 infections. Within each simulation, all parameters are drawn with replacement from their probability distributions. For each simulation, one CDM and nine separate IBMs (one for each of the possible interventions) are run concurrently.

The model will be implemented for

- Two settings: internally displaced persons in Digaale camp, Somaliland and urban Bulawayo, Zimbabwe. Age distribution and an empirical contact matrix are available for both;
- Six scenarios (1.5, 2.0, 2.5, 3.0, 3.5, 4.0).

Analysis outcomes

The model tracks the following outcomes for each [setting,] combination:

- Proportion of simulations in which the shield is breached, i.e. at least one person becomes infected after moving into the shielded residence, by intervention (1-8);
- Cumulative risk of infection among high-risk individuals within , by intervention (1-8); the median and 95% percentile interval of all simulations are presented;
- Cumulative risk of infection among high-risk individuals over , including unshielded and shielded person-time, by intervention (1-9); the median and 95% percentile interval of all simulations are presented;
- Percent reduction in cumulative risk of infection among high-risk individuals within , by shielding mitigation intervention (2-8), compared to no shielding mitigation (1); the median and 95% percentile interval of all simulations are presented;
- Percent reduction in risk of infection among high-risk individuals over , including unshielded and shielded person-time, by shielding intervention (1-8), compared to no shielding (9); the median and 95% percentile interval of all simulations are presented.

Sensitivity analyses

The following parameters are subject to sensitivity analyses:

- , the number of people within the shielded residence;
- , the time at which shielding is implemented, relative the start of the epidemic;
- , the extent to which contacts with people outside the shielded residence are reduced, compared to pre-shielding;
- , the extent to which contacts among shielded residents are reduced, compared to pre-shielding;
- , the extent to which symptomatic cases within further reduce their contacts;
- , the delay with which symptomatic cases exit after developing symptoms.