Supplementary Information: COVID SA

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In this supplementary information we include details of the extended SIR model. All code is freely available at `www.github.com/FredHutch/COVID_modeling`.

To model SARS-CoV-2 epidemiological dynamics we have applied a dynamical systems approach which uses an SIR model extended in several key ways. In general each state variable is now a tensor whose dynamics are given by its properties, distinguished as age group a, vaccination status V, and depending on the infecting strain q. The model extensions are detailed in Table S1 and a schematic cartoon is provided in Fig S1.

variable	values	definition
a	[0-19,20-49,50-69,70+]	age group (years)
V	[0, 1]	vaccination status, 1 = vaccinated
q	[current, B117]	infecting strain
σ_t	continuous, time-dependent	% reduction in contacts due to social/physical distancing

Table S1: Variables describing extensions to SIR model.

Force of infection. Perhaps the most important equation for the model summarizing the dynamics is the 'force of infection'. Here we show the value of the force of infection for each subset of state variables. The force of infection depends on the state of the infected individual (X) and the strain-specific infectivity $\beta_X(q)$. It also depends on a time-dependent reduction in contacts mediated by social/physical distancing σ_t. Finally, we use the empirically derived contact matrix to adjust the force of infection on a certain age group from transmitters in each other age groups (denoted by a_T, and calculated using the adjacency matrix $\mathcal{A}(a, a_T)$). Finally, we have the force of infection for an individual in age group a, exposed to strain q, with vaccination status V, and with ongoing social distancing level σ_t:

$$\lambda[a, V, q|\sigma(a,t)] = (1 - \mathrm{VE}_{\mathrm{INF}}(V)) \sum_{a_T} \frac{\mathcal{A}(a, a_T)}{N(a_T)} \sum_{X \in \mathcal{X}} [1 - \sigma(a,t)]\beta_X(q)X(a_T, V, q) \quad \text{(S1)}$$

where $\mathcal{X} = \{A, P, I, C_A, C_I\}$ is the set of all potentially infectious states. Note it is assumed that hospitalized individuals do not contribute to transmission ($\beta_H = 0$). Naturally, susceptible, exposed, recovered, and deceased individuals also do not contribute to ongoing infection.

The total number of individuals (across age, vaccination, and strain) in each compartment can then be calculated as a sum over the variables as

$$X = \sum_{a,V,q} X(a, V, q) \quad \text{(S2)}$$

Assumptions on asymptomatic infection. We assume that 20% of infections are asymptomatic and that asymptomatic people are as infectious as symptomatic individuals but missing the highly infectious pre-symptomatic phase. As a result, the relative infectiousness of individuals who never develop symptoms is 56% of the overall infectiousness of individuals who develop symptomatic COVID-19. This conservative estimate falls between the 35% relative infectiousness estimated in recent review based on 79 studies[1] and the current best estimate of 75% suggested by the CDC in their COVID-19 pandemic planning scenarios.

Dynamic social distancing. An attribute that sets our model apart from most others is a notion of dynamical social distancing related to the current diagnosed cases. We include a time-varying, age-stratified vector $\sigma(a,t)$ that governs social distancing (non-pharmaceutical interventions) including reduced contacts through personal choices and/or mandated partial lockdowns, as well as reductions in exposure contacts due to mask wearing or physical distancing. $\sigma(a,t)$ varies from 0, indicating pre-pandemic levels of societal interactivity and no masking, to 1, indicating complete lockdown with no interactions. This function is parameterized by 4 values: the maximum C_{max} and minimum C_{min} number of cases and the partial-lockdown and reopened social distancing values $\sigma_{PL}(a)$ and $\sigma_{min}(a)$ (see Supp Fig 1B). Thus we have

$$\sigma(a,t) = \begin{cases} \sigma_{PL}(a) & \langle C(t)\rangle_T > C_{max} \\ \sigma_{PL}(a) - 0.1T & \langle C(t)\rangle_T < C_{min} \\ \sigma_{min}(a) & \sigma_{max}(a) - 0.1T < \sigma_{min}(a) \end{cases} \tag{S3}$$

where the time average of cases $\langle C(t)\rangle_T$ is taken over $T = 2$ week intervals in the current simulation. Thus, the system triggers lockdown if the average cases rises over the max threshold and distancing immediately becomes $\sigma_{PL}(a)$ which is 40% of prepandemic levels in non-seniors and 20% in seniors. Then, once cases drop below the release threshold C_{min}, 10% of the distancing is removed every T weeks until reaching the minimum social distancing $\sigma_{min}(a)$. This value is not necessarily zero because we expect persistent features such as masking, work from home and avoidance of large social gatherings will continue to limit the number of interpersonal contacts relative to pre-pandemic levels.

Vaccination mechanisms. The possibility of vaccination is further complicated by inclusion of 3 mechanisms. The vaccine can completely block infection ($\mathrm{VE_{SUSC}}$), adjust the fraction of infections that are symptomatic ($\mathrm{VE_{SYMP}}$), and/or decrease the possibility of onward transmission after infection ($\mathrm{VE_{INF}}$). Each vaccine efficacy ranges from 0-1.

The number of individuals in each age group $N(a)$ is calculated at each step as

$$N(a) = \sum_{V,q} \sum_{X \in \mathcal{X}} X(a,V,q) \tag{S4}$$

where $\mathcal{X} = \{S, E, A, P, I, C_A, C_I, H, R\}$ is all non-deceased states. We also sum over the vaccinated and unvaccinated individuals, and over infecting strains.

[1] Buitrago-Garcia *et al.* PLOS Medicine (2020) doi:10.1371/journal.pmed.1003346.

Vaccination program. The vaccination program is implemented to best-mimic the current practice of vaccinating mostly elderly first, and then adult age groups, but never children. Vaccination distribution follows a daily rate r. Thus we allow 80% of vaccines to go to elderly each day $S(a = 70+, V = 1) = 0.8rt$ and the remaining 20% to adults $S(20 < a < 70, V = 1) = 0.2rt$. We set a maximum coverage V_{max} that roughly models vaccine uptake and compliance. Once the coverage is reached in the elderly, all vaccines are distributed to adults.

The whole set of equations thus is

$$\begin{aligned}
\dot{\mathbf{S}} &= -\sum_q \lambda[a, V, q|\sigma(a,t)](1 - \mathrm{VE}_{\mathrm{SUSC}}(V))\mathbf{S} \\
\dot{\mathbf{E}} &= \lambda[a, V, q|\sigma(a,t)](1 - \mathrm{VE}_{\mathrm{SUSC}}(V))\mathbf{S} - \gamma\mathbf{E} \\
\dot{\mathbf{A}} &= [1 - \pi(a)(1 - \mathrm{VE}_{\mathrm{SYMP}}(V))]\gamma\mathbf{E} - (\rho_A + \Delta_A)\mathbf{A} \\
\dot{\mathbf{P}} &= \pi(a)(1 - \mathrm{VE}_{\mathrm{SYMP}}(V))\gamma\mathbf{E} - (\zeta + \Delta_P)\mathbf{I} \\
\dot{\mathbf{I}} &= \zeta\mathbf{P} - \Delta_I(a,t)\mathbf{I} - [1 - \mu(a)]\eta_I(a)\mathbf{I} - \mu(a)\rho_I\mathbf{I} \\
\dot{\mathbf{H}} &= [1 - \mu(a)]\eta_I(a)\mathbf{I} + \eta_C(a)\mathbf{C_I} - \rho_H\mathbf{H} - \delta\mathbf{H} \\
\dot{\mathbf{F}} &= \delta_H\mathbf{H} + \delta_I(a)\mathbf{I} \\
\dot{\mathbf{R}} &= \rho_A[\mathbf{A} + \mathbf{C_A}] + \mu(a)\rho_I\mathbf{I} + \rho_C(a)\mathbf{C_I} + \rho_H\mathbf{H}
\end{aligned} \tag{S5}$$

and equations for diagnosed cases follow

$$\begin{aligned}
\dot{\mathbf{C_A}} &= \Delta_A\mathbf{A} - \rho_A\mathbf{C_A} \\
\dot{\mathbf{C_I}} &= \Delta_P\mathbf{P} + \Delta_I(a,t)\mathbf{I} - \eta_C(a)\mathbf{C_I} - \rho_C\mathbf{C_I}
\end{aligned} \tag{S6}$$

Comments on diagnosed cases. In addition to the main set of differential equations (Eq. S5), we also track the equations that govern the accumulating diagnosed cases (C_X, Eq. S6). Diagnosed cases can reenter the main equation set above because of hospitalizations due to diagnosed cases. We use the total diagnosed cases $C = C_A + C_I$ to fit caseload data. A nuance is that diagnosis rates $\Delta_X(a,t)$ are explicitly time dependent, which is used to incorporate data on number of individuals in each age group that are seeking testing. Importantly, diagnosed individuals may behave differently, so they are separated in the model for this reason too.

Initial conditions and model parameters. We use the state of the pandemic in October 2020 as derived in our prior publication [2] to initialize and parameterize the simulations in this manuscript.

Initial conditions are tabulated in Table S2. Fixed parameters are tabulated in Table S3, and estimated parameters are tabulated in Table S4.

[2] Swan, D. A. et al. Vaccines that prevent SARS-CoV-2 transmission may prevent or dampen a spring wave of COVID-19 cases and deaths in 2021. medRxiv 133, 323–57 (2020)

State	Initial condition			
	Children	Young Adults	Adults	Seniors
S	471690	950078	493341	169429
E	1175	1973	925	297
A	469	634	300	107
P	624	932	423	139
I	1763	2260	1139	509
C_A	217	805	248	5
C_I	43	158	46	0.73
H	3	25	34	85
R	26183	40004	18032	5115
F	0	19	162	609

Table S2: Initial conditions, no vaccinated individuals and no new strain, i.e. $V = 0$ and q=current for all entries.

Variable	Value	Definition	Reference
θ	7 days	Duration of infectious period	Cevik et al. Lancet Microbe 2021
γ	1/3 day^{-1}	Inverse of first part of estimated incubation period, the rate of transition from exposed to next stage of infection (either presymptomatic or asymptomatic)	McAloon et al. BMJ 2020, Lauer et al. Annals Int Med 2020
ζ	1/2 day^{-1}	Inverse of second part of incubation period progression from pre-symptomatic to symptomatic infection	Qin et al. Science Adv
π	0.8	Proportion of infections that are symptomatic infection.	Buitrago-Garcia et al. PLOS Medicine 2020
η_I	1/6 day^{-1}	Hospitalization rate from symptomatic state, from median days to hospitalization	CDC
ρ_H	1/14 day^{-1}	Recovery rate from hospitalized	CDC
δ_I	1/24 day^{-1}	Fatality rate from symptomatic, inverse of median days from symptom onset to death	CDC
δ_H	1/20 day^{-1}	Fatality rate from hospitalized, this assumes no overwhelming of healthcare system ICU capacity	CDC

Table S3: Fixed parameters.

variable	value	definition
$\beta^*(q)$	0.21 person^{-1} day^{-1}	Infectivity by SARS-CoV-2 strain
β_{C_A}, β_{C_I}	0.63β^*	Infectivity of diagnosed cases, less than undiagnosed
$\Delta_X(a)$	0.015, 0.042, 0.026, 0.0011 day^{-1}	Diagnosis rates from each age group, currently each state (presymptomatic, asymptomatic, symptomatic) has the same diagnosis rate
$\eta_I(a)$, $\eta_C(a)$	$f_H(a)\times$ [0.02, 0.046, 0.028, 0.05] day^{-1}	Hospitalization rate from severe cases, uses a monthly smoothed average of the fraction of cases f_H resulting in hospitalization from WA Department of Health
β_A, β_I	β^*	Infectivity of asymptomatic and symptomatic individuals are identical.
β_P	2.75β^*	Infectivity of presymptomatic individuals, calculated from result that f_P=44% of infections are presymptomatic $\beta_P = \frac{f_P}{1-f_P}\theta\zeta$
ρ_I, ρ_A, ρ_C	1/7 day^{-1}	Recovery rate from symptomatic, asymptomatic, and diagnosed cases that are mild and do not require hospitalization; calculated as $1/\theta$
$\delta_H(a)$	1/ $f_H\times$ [0 0 2.5$\times10^{-4}$, 5.5$\times10^{-3}$] day^{-1}	Fatality rate from hospitalized cases, uses the case fatality ratio from the WA department of health as well as the fraction

Table S4: Estimated and inferred parameters.