1   **Article Summary Line:** Imposing mask usage requirements, group size restrictions, duration

2   limits, and social distancing policies can have additive, and in some cases multiplicative

3   protective effects on SARS-CoV-2 infection risk during indoor events.

4   **Running Title:** Indoor SARS-CoV-2 Transmission Interventions

5   **Keywords:** aerosol, airborne, agent-based model, COVID-19, coronavirus, droplet, indoor

6   transmission, respiratory pathogen, SARS-CoV-2

7

8   **Title:** Assessing the efficacy of interventions to control indoor SARS-Cov-2 transmission: an

9   agent-based modeling approach

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14

15   **Abstract – 149 words**

16   Intervention strategies for minimizing indoor SARS-CoV-2 transmission are often based on

17   anecdotal evidence because there is little evidence-based research to support them. We

18   developed a spatially-explicit agent-based model for simulating indoor respiratory pathogen

19   transmission, and used it to compare effects of four interventions on reducing individual-level

20   SARS-CoV-2 transmission risk by simulating a well-known case study. We found that imposing

21   movement restrictions and efficacious mask usage appear to have the greatest effects on reducing

22   infection risk, but multiple concurrent interventions are required to minimize the proportion of

23   susceptible individuals infected. Social distancing had little effect on reducing transmission if

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24   individuals move during the gathering. Furthermore, our results suggest that there is potential for

25   ventilation airflow to expose susceptible people to aerosolized pathogens even if they are

26   relatively far from infectious individuals. Maximizing rates of aerosol removal is the key to

27   successful transmission-risk reduction when using ventilation systems as intervention tools.

28

29   **Main Text – 3499 words**

30   *1. Introduction*

31   Understanding transmission mechanisms is necessary to generate evidence-based guidance

32   for controlling infectious diseases. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-

33   CoV-2), the causative agent of Coronavirus Disease 2019 (COVID-19), is primarily spread

34   through infectious respiratory droplets and aerosols of varying size (*1, 2, 3, 4, 5*). These media

35   are expelled when an individual speaks, coughs, sneezes, or otherwise expectorates (*6, 7*).

36   Pathogen transmission can occur when these virion-containing particles are inhaled by, or

37   otherwise come into contact with the mucosae or conjunctiva (i.e., mouth, nasal membranes, or

38   eyes) of a susceptible person (*5*). Aerosol transmission is emerging as an important transmission

39   pathway, particularly for large clusters associated with superspreading events (*2, 8, 9, 10*). van

40   Doremalen et al. (2020) (*11*) found that SARS-CoV-2 can remain viable in aerosolized droplets

41   for at least 3 hours post expectoration. While these results may not accurately represent SARS-

42   CoV-2 stability outside of laboratory conditions (*5*), their findings are in line with case reports of

43   viral-RNA detection in air collected from hospital rooms housing COVID-19 patients (*12, 13,*

44   *14, 15*).

45   Transmission of SARS-CoV-2 is more likely in indoor settings than outdoors (*8, 9*).

46   Households are the most common venue linked to transmission, but healthcare facilities,

47   religious venues, food processing plants or prisons are also likely to be associated with large

48   clusters of COVID-19 cases (*9*). Recommended interventions to reduce indoor transmission

49   include: social distancing, use of face coverings, increased ventilation, and reduced group sizes

50   (*1*). U.S. state government recommendations and restrictions for group size limits in indoor

51   gatherings range from 10 to 100 people or 10 – 75% of a locale's original capacity (*16*). There is

52   little evidence-based research to support specific group size restrictions, however, and few

53   studies have sought to identify the most-effective strategy for limiting indoor SARS-CoV-2

54   transmission.

55   Some mathematical models have been built to support individual-level risk assessment of

56   indoor transmission and analyze aerosol contributions to past outbreaks. Chande et al. (2020)

57   (*17*) created a tool to assess the U.S. county level probability that someone infected with SARS-

58   CoV-2 will attend events of varied sizes. Their tool is useful for estimating the probability that

59   SARS-CoV-2 transmission could occur during any gathering, but provides no direct measure of

60   transmission risk from infectious individuals during events and no way to assess the impact of

61   intervention strategies other than reducing group sizes. Other models have sought to determine

62   the role that aerosolized infectious droplets play in indoor SARS transmission relative to larger

63   droplets that are unlikely to be inhaled, and quantify the transmission risk attributable to aerosols

64   in varied environments (*18, 19, 20, 21, 22*). These models are primarily based on Wells-Riley

65   equations for estimating aerosol-attributable risk, which assume homogenous spatiotemporal

66   mixing of air constituents and exposure to infectious agents (*23*). Mathematical indices and

67   parameter values in these models can be adjusted to simulate effects of intervention strategies

68   like social distancing (*22*) and increased ventilation rates (*18, 20, 21, 22*), but are insufficient for

69   capturing or accounting for any behavior- or environment-mediated spatiotemporal heterogeneity

70   in transmission risk. Shao et al. (2021) (*24*) used a fluid dynamics model to simulate ventilation

71   effects on SARS-CoV-2 transmission while allowing for heterogenous droplet movement

72   behaviors. Their findings highlight the need to account for within-room spatial heterogeneity

73   when studying indoor transmission risk, as phenomena like ventilation can increase infection risk

74   to individuals in one area of a room or building while simultaneously mitigating risk in another.

75   Here, we present a spatially-explicit agent-based model (ABM) for simulating within-room

76   respiratory pathogen transmission to inform policy-making decisions aiming to mitigate indoor

77   transmission and implementing individual-level interventions. By simulating spatiotemporal

78   droplet dynamics (e.g., emission of varying droplet size and subsequent distribution in the

79   environment) as well as allowing for dynamic movement and positioning of infectious and

80   susceptible individuals, our model allows virion exposure rates to vary within indoor settings.

81   We use our model to estimate effects of proposed COVID-19 intervention strategies for indoor

82   environments (i.e., increased airflow, limiting contact durations, wearing masks, and increased

83   interpersonal spacing). For benchmarking purposes, we simulate the outbreak that took place

84   during a choir practice in Skagit County, WA in March 2020 (*2*). Additionally, we further

85   investigate potential drivers of superspreading events, like the Skagit County example, by

86   characterizing and comparing how different aspects of indoor gatherings (i.e., population

87   density, duration, quanta production by infectious individuals, and ventilation effects) impact

88   transmission risk. Through these analyses we provide guidance for minimizing SARS-CoV-2

89   transmission during indoor gatherings.

90   *2. Methods*

91   *2.1 Model Description*

92   We developed a spatially-explicit, stochastic ABM to simulate both direct-droplet and

93   airborne respiratory pathogen transmission in indoor settings. This model was created and

94   executed using the open-source modeling software, NetLogo (Ver. 6. 1. 1) (*25*) and is available

95   for download at https://github.com/lanzaslab/droplet-ABM. In Appendix S1 we provide a

96   detailed description of our model in accordance with ODD (Overview, Design concepts, Details)

97   standards outlined by (*26*). We present a limited summary of the model design below. When

98   describing infectious media in our model, we use the term "droplet" to refer to respiratory

99   droplets of any size.

100   Agents in our model represent people congregating in a fixed space (e.g., students in a

101   classroom, diners in a restaurant, etc.). Patches (i.e., grid cells in the NetLogo model interface)

102   represent 1 x 1 m^2 areas, and the spatial extent can range from 1 to ∞ m^2. The model time step is

103   1 minute. Droplets ranging from 3 to 750 μm in diameter are expelled by infectious agents.

104   Subsequently, droplets can be inhaled, fall out, diffuse to nearby patches, move via directed

105   airflow, and decay at fixed rates over the course of a simulation. Infection in our model is driven

106   by exposure to virions contained in these droplets, and the number of virions per droplet scales

107   with droplet size. The rate at which droplets fall out (i.e., are removed from circulating air flows)

108   of the simulation is based on the calculated terminal velocity falling speed for droplets, and

109   therefore varies with droplet size. Droplet sizes incapable of settling on the ground within one

110   minute are allowed to move between patches via ventilation- and diffusion-induced airflow.

111   Thus, risk of exposure and subsequent infection for susceptible individuals varies by space and

112   time during the simulation (Figure 1). We recognize that the ability of forced air ventilation

113   systems to reduce local respiratory pathogen transmission is linked to their ability to move

114   aerosolized droplets away from susceptible individuals in three dimensions (*18, 24*). Though this

115   effect is not explicitly tied to airflow inputs in our model, which only allows airflow in two

116   dimensions, we can effectively simulate ventilation-induced aerosolized droplet movement to

117   heights outside of individuals' inhalation ranges by increasing the decay rate when ventilation

118   effects are simulated. In addition to controlling the number of individuals present and the size of

119   the simulated world, users can dictate infectiousness parameters and other scenario-specific

120   variable values (e.g., number of infectious individuals, probability that infectious individuals are

121   asymptomatic, cough frequency, number virions per mL of droplet fluid, risk of infection given

122   exposure to 1 virion, etc.), ventilation parameters (e.g., direction and speed of airflow, droplet

123   filtration probability, etc.), and adherence to transmission-risk-reduction guidelines (e.g., mask

124   usage, local social distancing, etc.).

125   *2.2 Testing SARS-CoV-2 transmission reduction strategies*

126   *2.2.1 Case scenario and model inputs*

127   In March 2020, there was a probable SARS-CoV-2 superspreading event during a choir

128   practice taking place at a church in Skagit County, Washington, USA (*2*). Sixty-one people were

129   in attendance, one attendee was experiencing flu-like symptoms at the time and later tested

130   positive for COVID-19 (*2*). This individual likely infected 53 other attendees over the course of

131   the event (*2*). We briefly describe our rationale for setting scenario-specific input values to

132   simulate this case in our model below, but more-detailed explanations for input and parameter

133   values are given in Appendix S2, and Appendix S3 describes how sensitive simulated infection

134   risk is to variations in select model parameters.

135   We know from (*2*) that the choir practice lasted 150 minutes in total, split into 4 distinct time

136   intervals. In our simulations, we decided to rearrange agents in our model after 40, 90, and 105

137   minutes to recreate mixing associated with changing time intervals. At timestep 105, individuals

138   moved back to their initial placements, representing their adherence to assigned seating during

139   interval 4 (i.e., minutes 105 – 150). The seating chart has not been shared due to privacy

140   concerns (*21*) however, we can assume that a maximum of 2 people could be within 1-m^2

141   patches in this scenario. We set the inhalation rate for simulated individuals to 0.023 m^3 air/min,

142   a rate consistent with adults participating in light activity (*27*). Because it is uncertain whether or

143   not the forced-air system was turned on during the choir practice (*21*), we decided to run our

144   simulations in two sets: ventilation-on (i.e., both forced-air effects and natural diffusion moved

145   droplets between patches) and ventilation-off (i.e., only natural diffusion moved droplets

146   between patches).

147   In addition to model the baseline scenario, we modulated values of model inputs related to

148   group-level risk-reduction strategies (i.e., limited population, limited contact durations, mask

149   usage, and meter-level social distancing) between simulations in order to assess the efficacy of

150   each strategy on reducing the number of susceptible individuals infected. Regarding mask usage,

151   we assumed face coverings have both source-prevention and wearer-protection effects, and

152   reduced global droplet exposure/exhalation rates by 0%, 25%, 50%, 75% and 90%. The upper

153   range here is intended to simulate the use of N95 and simple surgical masks, which are estimated

154   to reduce aerosol emission rates by approximately 90% and 74%, respectively (*28, 29*). Lower

155   values are intended to simulate the use of single- and multi-layered fabric masks, for which a

156   wide range of aerosol-filtration efficacies have been reported (*30*). When simulating mask usage,

157   we assumed that all individuals were wearing masks and that all masks had the same efficacy.

158   Table 1 outlines the model input values for our superspreading-scenario simulations.

159   *2.2.2 Running simulations and analyses*

160 We set up a factorial simulation run within the NetLogo BehaviorSpace using our specified

161 input levels. We ran 1000 replicates of all input set combinations, ultimately resulting in

162 1,080,000 simulations. Simulations were aggregated into a single data set prior to analysis.

163 We used a beta regression model with a fixed unknown precision parameter, ϕ, (*31*) to

164 estimate effects of interventions on the mean proportion of susceptible individuals infected in our

165 full simulation set, μ. Beta regression models are employed to analyze proportion data (*31, 32*).

166 We chose to use this method because the potential number of infected individuals in each

167 simulation was limited by the simulated group size, which was a predictor variable of interest,

168 and because preliminary analysis suggested that fitting our data to a beta distribution better

169 explained observed variation than other regression models. We therefore determined it was more

170 appropriate to evaluate effect sizes in terms of the relative proportion of susceptible people

171 infected rather than their total number. We fit our data to the model:

172 $\ln\left(\dfrac{\mu}{1-\mu}\right) = \beta_0 + \beta_1(\text{Gathering duration}) + \beta_2(\text{Mask use}) + \beta_3(\text{Mask efficacy})$

173    $+ \beta_4(\text{Group size}) + \beta_5(\text{Social distancing}) + \beta_6(\text{Ventilation}) + \beta_7(\text{Movement})$

174    $+ \beta_8(\text{Mask use} * \text{Group size}) + \beta_9(\text{Mask use} * \text{Social distancing})$

175    $+ \beta_{10}(\text{Group size} * \text{Social distancing})$

176    $+ \beta_{11}(\text{Mask use} * \text{Group size} * \text{Social distancing}),$

177 where "Gathering duration," "Mask efficacy," and "Group size" are intervention-strategy

178 variables relating to: minutes of simulated interaction between individuals, the efficacy of worn

179 face masks for reducing expectoration and inhalation of infectious droplets, the simulated

180 population size, and attempted meter-level social distancing in each realized simulation,

181 respectively. The variables "Mask use," "Movement," and "Ventilation" are known confounders

182 related to: reduced droplet spread distance from expectorating infectious individuals wearing

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183   masks, the number of times individuals were rearranged within simulations to reflect mixing of

184   event attendees, and movement of infectious aerosols throughout the simulated space due to a

185   forced-air ventilation system, respectively. "Mask use" is a binary variable taking the value of 1

186   when simulated individuals are masked (i.e., "Mask efficacy" > 0), and 0 when they are not.

187   "Movement" takes any one value within the range of 1-to-4, dependent on "Gathering duration."

188   "Ventilation" is a binary variable taking the value of 1 for simulations in the "ventilation-on"

189   subset, and 0 for those in the "ventilation-off" subset.

190   Because beta regression procedures assume all dependent variable values fall between 0 and

191   1, we used the data transformation procedure described by (*33*) to reconstruct our proportion data

192   without these extremities. All analysis and plotting was carried out using functions from the

193   "betareg" R package (*32*) in RStudio (v. 1.1.463) (*34*) running R (v. 3.6.2) (*35*). We calculated a

194   pseudo-R^2 (*31*) to assess goodness of fit for our regression model

195   *2.3 Evaluating drivers of transmission in indoor gatherings*

196   To assess the relative contribution of environmental conditions to SARS-CoV-2 transmission

197   risk, we conducted a sensitivity analysis to ascertain relative effects of population density,

198   gathering duration, quanta production by infectious individuals, and ventilation on SARS-CoV-2

199   infection risk beyond the conditions tested in the Skagit County case. In addition, we quantified

200   the ability of different ventilation system aspects (i.e., air-change rate, filtration rate, and

201   effective three-dimensional droplet removal rate) to reduce SARS-CoV-2 transmission risk.

202   Table 2 describes the model input values for these indoor-gathering-risk-assessment simulations.

203   We set up a factorial simulation run within the NetLogo BehaviorSpace using our specified

204   input levels. We ran 1000 replicates of each parameter set combination when the "Forced air"

205   parameter was set to "on" and when it was "off." We ran these sets separately in order to save

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206 computation time as there were many inputs that only changed when forced airflow was

207 simulated. Ultimately, we produced 144,000 "off" simulations, and 20,160,000 "on" simulations.

208 In both sets, we identified simulations when transmission occurred (i.e., simulations where ≥ 1

209 person was infected), and recorded this occurrence as the binary variable y_i so that

210
$$y_i = \begin{cases} 1 & \text{if transmission was observed} \\ 0 & \text{if no transmission occurred,} \end{cases}$$

211 for each realized simulation, i.

212 We aggregated simulation data into a single data set and carried out a logistic regression

213 analysis to estimate effects of variable inputs on observed differences in the probability of

214 observing ≥ 1 infections. We fit our data to the model:

215
$$\ln\left(\frac{\Pr(y_i = 1)}{\Pr(y_i = 0)}\right) = \beta_0 + \beta_1(\text{Population density}) + \beta_2(\text{Gathering duration}) +$$

216
$$\beta_3(\text{Quanta per hour}) + \beta_4(\text{Excess droplet removal rate}) + \beta_5(\text{Air change rate}) +$$

217
$$\beta_6(\text{Air filtration rate}),$$

218 where "Population density" is given by $\frac{n}{\text{m}^2}$, and the "Excess droplet removal rate" (%/min)

219 represents the increased removal of aerosols due to ventilation-induced 3-dimensional droplet

220 movement. It is given by the equation: (Virion decay rate $-$ 1.05). The 1.05 here represents the

221 general SARS-CoV-2 decay rate (i.e., 1.05%/min) as reported by (*11*). Subtracting this baseline

222 value from the simulated Virion decay rate gives us an excess removal rate that we use as a

223 proxy for 3-dimensional droplet removal attributable to forced airflow movement. When no

224 forced airflow is simulated, excess droplet removal, air change, and filtration rates all equal 0.

225 We calculated the Tjur (*36*) pseudo-R^2 for our logistic regression model to assess goodness of fit.

226 *3. Results & Discussion*

10

227   We presented a stochastic ABM for studying indoor individual-level respiratory pathogen

228   transmission, and used it to demonstrate the potential effectiveness of multiple intervention

229   strategies for reducing SARS-CoV-2 transmission in an indoor group setting mimicking that of a

230   known superspreading event. We were able to effectively recreate the empirical proportion of

231   susceptible individuals likely infected during the Skagit County superspreading event by

232   simulating the gathering without implementing any intervention strategies (Figure 2).

233   Our beta regression model for estimating intervention efficacy had a pseudo-R^2 of ≈ 0.43.

234   Given the number of stochastic processes in our ABM, the explanatory power of the model is

235   acceptable. Duration limits and efficacious mask usage appear to have the greatest effects on

236   reducing the proportion of susceptible individuals infected, but multiple concurrent interventions

237   are required to minimize the proportion of susceptible individuals infected (Table 3, Figure 3).

238   However, it is important to note that observed proportional differences are more meaningful for

239   relatively large groups than for smaller ones. The effectiveness of limiting the duration of

240   gatherings for reducing the proportion of infected individuals appears to largely result from

241   reducing the confounding movement effect that increases over time, thereby reducing the

242   probability that susceptible individuals will move from uncontaminated space to areas with

243   greater concentrations of infectious aerosols or nearby to infectious individuals where they may

244   be exposed to large virion-containing droplets (Table 3). We show that simply by limiting the

245   time spent rehearsing that night to 40 min, reducing random mixing between attendees by ending

246   the event prior to splitting into disparate groups (*2*), the proportion of people infected could have

247   been reduced by 70 – 88% even without implementing any other intervention strategies.

248   Therefore, imposing movement restrictions could be a more effective intervention than strict

249   duration limits.

11

250   We found that mask usage and social distancing interventions are relatively more effective

251   for reducing proportional infection rates in small groups than in large ones. Our findings suggest

252   that in the Skagit County choral case, duration limits with implied movement restrictions and

253   mask usage would have been the most-effective intervention strategies for reducing SARS-CoV-

254   2 infection rates, but multiple interventions would have needed to be deployed simultaneously to

255   reach near-zero rates (i.e., mean rate < 0.5 people / gathering duration). Infection rates generally

256   increased with group size and decreased with mask efficacy, and we found that when movement

257   rates were minimized (i.e., gathering durations ≤ 40) we could minimize infection rates with

258   relatively-low mask efficacy or even no mask usage in some cases. Our results support recent

259   evidence suggesting that even wearing masks with relatively low droplet-filtering abilities

260   around others can help to reduce exposure to infectious agents (*30, 37*). Attempted social

261   distancing up to 3 m had little effect on transmission rates relative to other intervention

262   strategies. That said, because social distancing generally had a greater effect on proportional

263   infection rates when group size was limited to 10 people, and 2-m social distances reduced the

264   mean number of infections in larger groups, we can intuit that the relatively small overall effect

265   of social distancing was likely due to the presence of physical barriers (e.g., edges of the

266   simulated world) or the physical arrangement of nearby individuals impeding agents' attempts to

267   social distance, rather than due to far-reaching droplet spread that makes social distancing

268   irrelevant.

269   Conclusions regarding social distancing effects are further supported by our logistic

270   regression model results that describe the relative effects of population density, gathering

271   duration, quanta production, and ventilation on the probability of indoor SARS-CoV-2

272   transmission from a single infectious individual (Table 4). This model had a pseudo-R^2 value of

12

273   0.25 and demonstrated that among the considered variables, population density was the most-

274   important contributor to SARS-CoV-2 transmission risk. Additionally, increases in gathering

275   duration, infectious aerosol production, and horizontal air movement all escalate the probability

276   that transmission will occur during gatherings, though the effect is much lesser than that of

277   increasing population density. The relatively small effects of quanta production and duration on

278   transmission risk suggest that once individuals are exposed to infectious agents, they are likely to

279   become infected quickly. Thus, minimizing susceptible people's exposure to infectious media is

280   of paramount importance for controlling COVID-19 incidence.

281   Regarding observed effects of ventilation in our beta and logistic regression models, our

282   results suggest that in spite of some evidence that forced-air ventilation systems can reduce risk

283   of respiratory pathogen infection from indoor aerosols (*38, 39*), there is potential for forced

284   airflow to expose susceptible people to aerosolized pathogens even if they are relatively far from

285   infectious individuals, and therefore increase transmission risk. We show that, though filtering

286   re-circulated air can lower transmission risk (Table 4), increasing this effect is unlikely to

287   compensate for the elevated risk attributable to increased horizontal air-change rates (Tables 3 &

288   4). It appears that maximizing rates of three-dimensional aerosol removal is the key to successful

289   transmission-risk reduction when using forced-air ventilation systems as intervention tools. Our

290   results are therefore consistent with the findings of (*18*), who advise that "displacement"

291   ventilation systems, those designed to vertically stratify indoor air by temperature and remove

292   warmer air, are likely able to reduce local SARS-CoV-2 transmission risk. "Mixing" ventilation

293   systems, designed to distribute temperature and aerosols equally throughout the space, are likely

294   insufficient for preventing transmission and may even facilitate it (*18*).

13

295   Given our findings, we maintain that in areas where COVID-19 prevalence remains high,

296   holding events associated with relatively-increased mixing rates between individuals (e.g., social

297   gatherings, sporting events, etc.) should be avoided even if attendance rates are presumed to be

298   low. Such events are likely to be associated with SARS-CoV-2 transmission if ≥ 1 infectious

299   individual(s) were to attend, the probability of which increases linearly with group size (*17*). It is

300   important to note however, that though our results provide insight into mechanisms for reducing

301   SARS-COV-2 transmission rates, given the effect that model parameters can have on simulation

302   outcomes (*see* Appendix S3), our findings may not be reasonably extrapolated to accurately

303   predict transmission in scenarios dissimilar from those we modeled here (e.g., ≥ 2 infectious

304   individuals, fewer aerosolized virions produced during expectorations, etc.). Regardless, we can

305   still conclude that imposing mask usage requirements, group size restrictions, duration limits,

306   and social distancing policies have additive, and in some cases multiplicative protective effects

307   on individual-level SARS-CoV-2 infection risk during gatherings, and can be particularly

308   efficacious interventions when deployed simultaneously.

309   **Acknowledgments**

311   **Author Bio**

312   Trevor S. Farthing is a PhD candidate in the Comparative Biomedical Sciences program at

313   North Carolina State University. His work combines ecological and epidemiological analyses

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315   transmission in varied pathogen-host systems.

316   Dr. Cristina Lanzas is an Associate Professor of Infectious Disease at North Carolina State

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318　animal and human populations. Her work combines data science, epidemiological analysis and

319　mathematical models to study transmission mechanisms, and to identify and design effective

320　control measures to reduce the public health burden associated with infectious diseases.

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454   **Tables**

455   Table 1. Parameter descriptions for simulations of the Skagit County, WA March 2020 SARS-

456   CoV-2 transmission case study.

Parameter/Model Input	Value(s)	Reference(s)
Infectiousness parameters		
Cough frequency (coughs/min)	0.19	*40*
Droplet count (droplets/expectoration)	$9.7e^5$ $(3.9e^5)^\dagger$	*21,* Appendix S2
Droplet spread angle – coughing (º)	35	*41*
Droplet spread angle – not coughing (º)	63.5	*41*
Droplet travel distance – coughing (m)	$5 (0.256)^\dagger$	*42*
Droplet travel distance – not coughing (m)	$0.55 (0.068)^{\dagger\S}$	*43*
Scenario environment and individual behavior inputs		
Area (m^2)	180^*	*2*
Expectoration height (m)	1.7	*44*
Inhalation rate (m^3 air/min)	0.023	*27*

Maximum people in a single 1-m^2 patch (people)	2	*2*
Number of symptomatic individuals (people)	1	*2*
Scenario virion behavior inputs		
Virion count (virions/mL fluid)	2.35e^9	*45*
Virion decay rate (%/min)	1.05	*11*
Virion infection risk (%/inhaled virion)	6.24	Appendix S2
Scenario airflow inputs		
Diffusion rate (m^3/min)	1.5e^{-3}	*46*
Forced air	on, off	–
Forced air direction	North-to-South, East-to-West	–
Air change rate (%/min)	4.3	*21*
Re-circulated air filtration (%/min)	90	*21*
Scenario intervention inputs		
Attempted social distancing (m)	0, 1, 2, 3	–
Contact duration (min)	20, 40, 60, 90, 105, 150	–
Mask efficacy (%)	0‡, 25, 50, 75, 90	*28, 29*
Population (people)	10, 50, 61	*2, 16*

457 *Simulated worlds were 10 m X 18 m. †Standard deviations are given in parentheses. ‡Zero-

458 percent mask efficacy is equivalent to no mask use. §Das et al. (2020) (*45*) estimated the average

459 travel distance of a 100-micrometer droplet expelled from a height of 1.7 m at a velocity of 0.5

460 m/s to be 0.55 m. They also found that the majority of 100-μm droplets will fall 0.55-2.35 m

461 away from the expelling individual, depending on initial velocity, but droplets may settle up to

462 3.2 m away very rarely. a random draw of 10,000,000 samples from a log-normal distribution

463 parameterized using 1.7-m and 0.2095-m droplet spread distance mean and standard deviation

464 values, respectively, generated a distribution in line with this finding. The standard deviation we

465 use in simulations for non-coughing expectoration is proportionate to the one used in this random

466 draw.

467

468 Table 2. Parameter descriptions for ventilation-system effect evaluations.

Parameter/Model Input	Value(s)	Reference(s)
Infectiousness parameters		
Cough frequency (coughs/min)	0.19	*40*
Droplet count (droplets/expectoration)[†]	1,000 (0)[‡], 9.7e^5 (3.9e^5)[‡]	*21,* Appendix S2
Droplet spread angle – coughing (º)	35	*41*
Droplet spread angle – not coughing (º)	63.5	*41*
Droplet travel distance – coughing (m)	5 (0.256)[‡]	*42*
Droplet travel distance – not coughing (m)	0.55 (0.068)[‡§]	*43*
Scenario environment and individual behavior inputs		
Area (m^2)[*]	9, 36, 81	–
Expectoration height (m)	1.7	*44*
Inhalation rate (m^3 air/min)	0.023	*27*
Maximum people in a single 1-m^2 patch (people)	2	*2*
Number of infectious individuals (people)	1	–

23

Proportion of infectious individuals that are symptomatic (%)	0, 100	–
Scenario virion behavior inputs		
Virion count (virions/mL fluid)	$2.35e^9$	*45*
Virion decay rate (%/min)	1.05, 5¶, 10¶, 25¶, 50¶, 75¶, 90¶	*11*
Virion infection risk (%/inhaled virion)	6.24	Appendix S2
Scenario airflow inputs		
Diffusion rate (m³/min)	$1.5e^{-3}$	*46*
Forced air	on, off	–
Forced air direction**	East-to-West	–
Air change rate (%/min)	0#, 1¶, 5¶, 10¶, 25¶, 50¶	–
Re-circulated air filtration (%/min)	0#, 1¶, 5¶, 90¶, 100¶	–
Scenario intervention inputs		
Attempted social distancing (m)	0	–
Contact duration (min)	10, 30, 60	–
Mask efficacy (%)	0††	–
Population density (people/m²)‡‡	0.333, 0.667, 1, 1.667	–

469

470   *All simulated worlds were square-shaped. †Based on linear modeling described in Appendix S2,

471   these values equate to 1 (SD = 0) and 970 (SD = 390) quanta/hr. ‡Standard deviations are given

472   in parentheses. §Das et al. (2020) (*45*) estimated the average travel distance of a 100-micrometer

473   droplet expelled from a height of 1.7 m at a velocity of 0.5 m/s to be 0.55 m. They also found

474   that the majority of 100-μm droplets will fall 0.55-2.35 m away from the expelling individual,

475   depending on initial velocity, but droplets may settle up to 3.2 m away very rarely. a random

476   draw of 10,000,000 samples from a log-normal distribution parameterized using 1.7-m and

477   0.2095-m droplet spread distance mean and standard deviation values, respectively, generated a

478   distribution in line with this finding. The standard deviation we use in simulations for non-

479   coughing expectoration is proportionate to the one used in this random draw. ¶These parameter

480   values were only used when the "Forced air" parameter value was set to "on." #These parameter

481   values were only used when the "Forced air" parameter value was set to "off." **All patches on

482   the east side of the simulated world acted as supply vents. All patches on the west side acted as

483   return vents. ††Zero-percent mask efficacy is equivalent to no mask use. ‡‡Instead of specifying a

484   fixed number of individuals in simulations, we scaled the simulated population with world size.

485

486   Table 3. Logit scale estimates associated with 1-unit increases in covariate values given by our

487   beta-regression model for evaluating intervention effects. Wald 95% confidence intervals are

488   given in parentheses.

Coefficient	Estimate	p
Intercept	-2.927 (-2.940, -2.914)	–
ϕ	5.808 (5.791, 5.824)	–
Gathering duration (min)	0.012 (0.012, 0.012)	< 0.001
Mask efficacy (%)	-0.015 (-0. 015, -0.015)	< 0.001
Mask use	-0.949 (-0.964, -0.935)	< 0.001
Movement (No. rearrangements)	0.491 (0.485, 0.497)	< 0.001
Group size (people)	0.001 (0.001, 0.001)	< 0.001

Social distancing (m)	-0.250 (-0.256, -0.243)	< 0.001
Ventilation	0.898 (0.895, 0.902)	< 0.001
Mask use : Group size	0.014 (0.013, 0.014)	< 0.001
Mask use : Social distancing	-0.018 (-0.025, -0.010)	< 0.001
Group size : Social distancing	0.004 (0.004, 0.004)	< 0.001
Mask use : Group size : Social distancing	$1.923e^{-4}$ ($3.039e^{-5}$, $3.542e^{-4}$)	0.020

489

490 Table 4. Logit scale estimates associated with 1-unit increases in covariate values given by our

491 logistic-regression model for evaluating effect on SARS-CoV-2 transmission risk during an

492 indoor gathering. Wald 95% confidence intervals are given in parentheses.

Coefficient	Estimate	Odds ratio	*p*
Intercept	-0.146 (-0.151, -0.140)	–	–
Population density (people/m^2)	2.766 (2.761, 2.771)	15.891 (15.813, 15.968)	< 0.001
Gathering duration (min)	0.015 (0.015, 0.015)	1.015 (1.015, 1.015)	< 0.001
Quanta (quanta/hr)	0.002 (0.002, 0.002)	1.002 (1.002, 1.002)	< 0.001
Excess droplet removal rate (%/min)	-0.024 (-0.024, -0.024)	0.976 (0.976, 0.976)	< 0.001
Air change rate (%/min)	0.017 (0.017, 0.017)	1.02 (1.02, 1.02)	< 0.001
Air filtration rate (%/min)	-0.005 (-0.005, -0.005)	0.995 (0.995, 0.995)	< 0.001

493

494 **Figures**

495
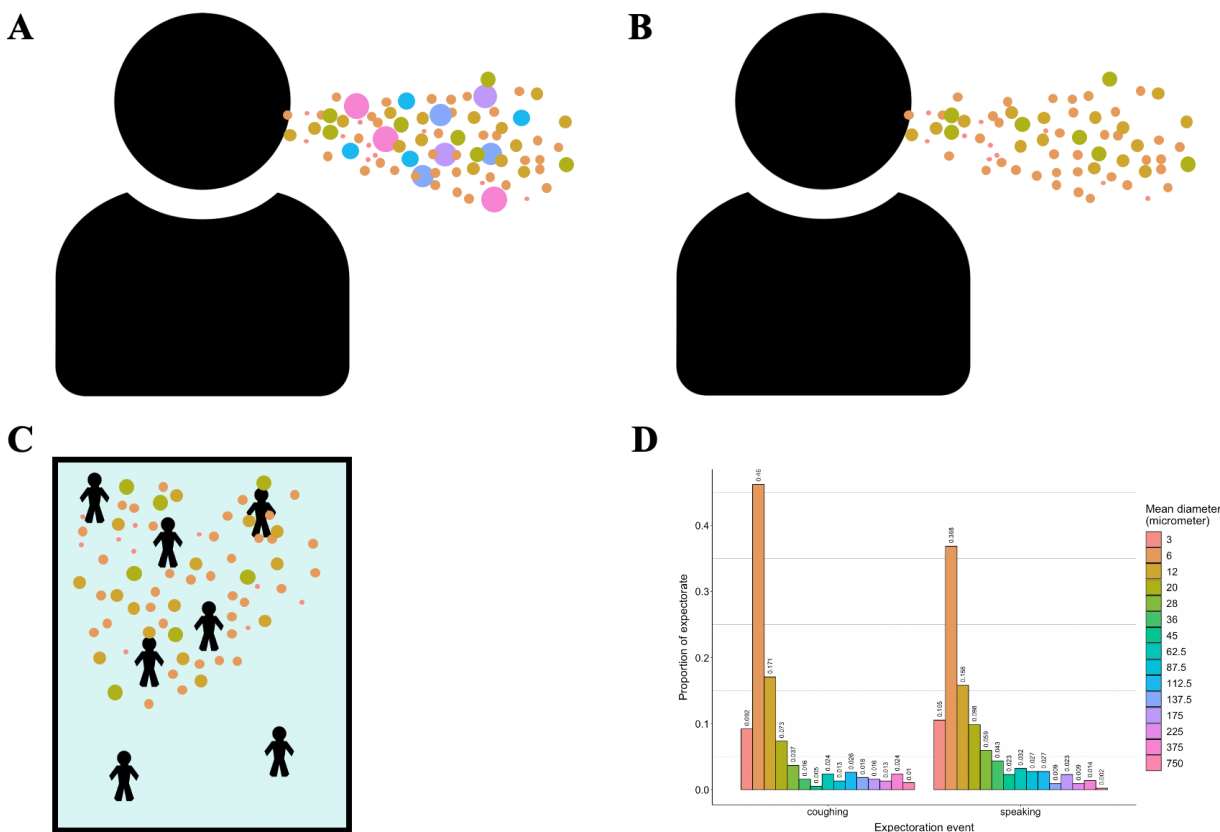
Figure 1. Model droplet dynamics. A) Infectious individuals expel droplets of different sizes. B) Relatively large droplets fall out of the air quickly post expectoration. C) Smaller droplets remain aerosolized for longer time periods and move throughout the simulated room via diffusion and forced airflow effects. D) Distribution of droplet sizes during expectoration events. Distributions of size classes during coughing and speaking events are based on findings of (*47*), and represent mean observed droplet-size measurements they recorded 60 mm away from individuals' mouths immediately following these activities.
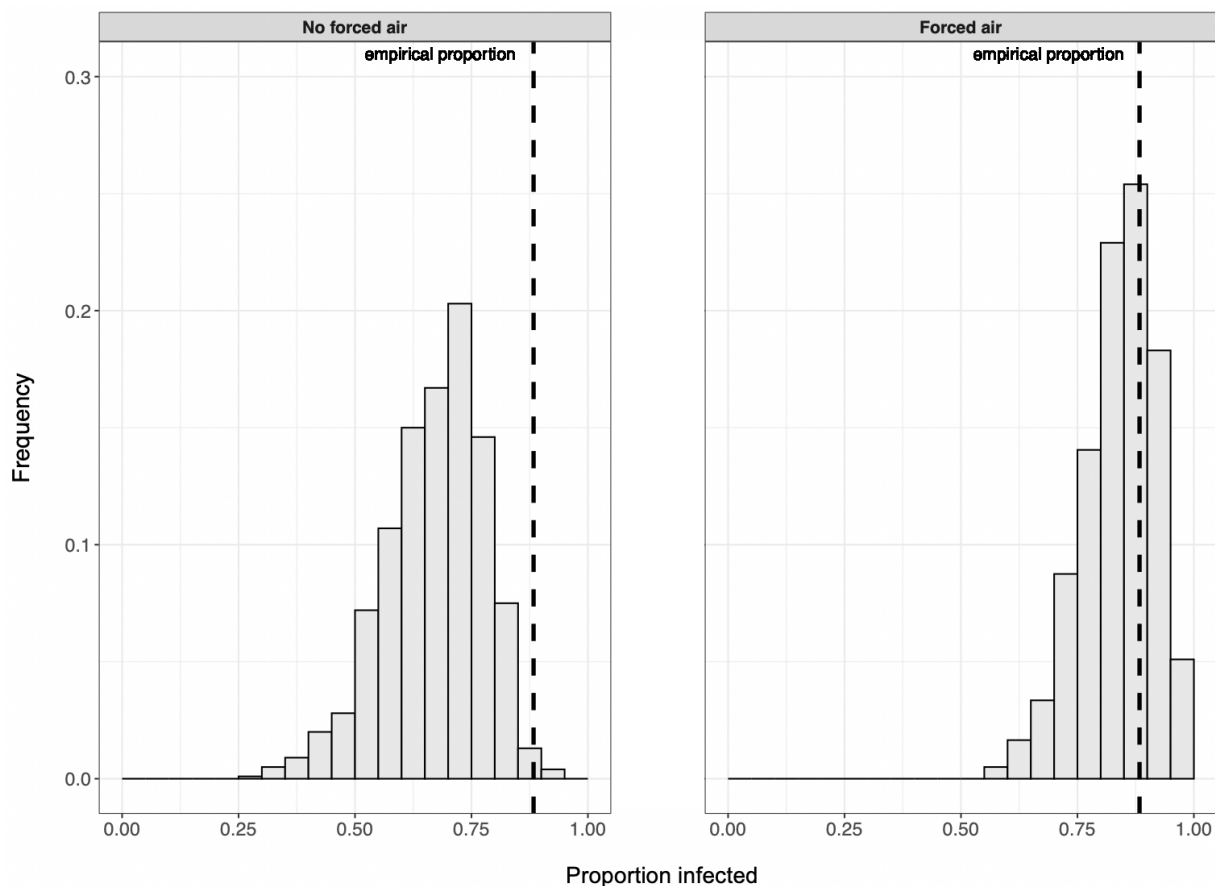
503

504 Figure 2. In the absence of interventions to reduce transmission risk, the proportion of

505 susceptible people infected in simulations can reflect the case study value (i.e., 0.88) and is more

506 likely to do so when forced airflow is included.

507
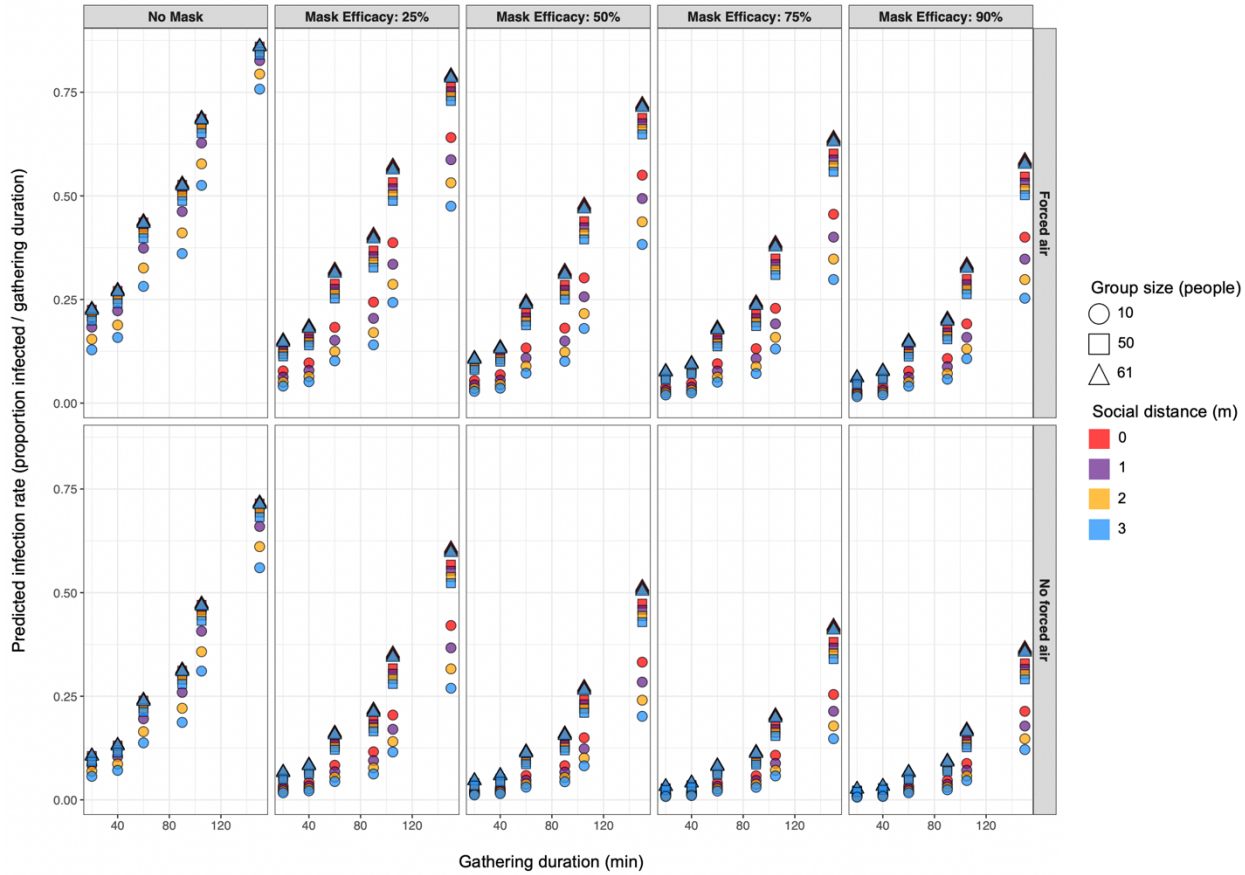
Figure 3. Predicted proportion of susceptible populations infected with SARS-CoV-2 for varied

parameter sets suggest that concurrent deployment of multiple interventions is required to

achieve near-zero transmission rates.

29