Reproducibility and potential application of modeling study on maintaining face mask use before and after achieving different COVID-19 vaccination coverage levels

Background

Fack mask policy is one of an important non-pharmaceutical intervention against spreading of COVID-19 (1–3). However, the question on how long we need to maintain face mask for our population would be challenge for public health authorities to advise the public (4–7). Previous studies show that face mask can be effectively prevent (reduce number of) COVID-19 outbreaks when vaccine is not wildly available for population (1–3). On the other hand, when the population has already achieved the target of vaccine coverage and the number of severe cases and death from COVID-19 trended to be decrease, we may need to re-evaluate the cost-benefit of maintaining face mask use in different levels of vaccination coverage. A simulation-based study could be one approach for answering this question.

Recently, Bartsch et al have proposed the simulation model study to estimate cost-effectiveness of maintaining face masks use according to different scenarios of COVID-19 vaccination coverage in the USA (8). They used a system dynamics model to estimate the number of symptomatic infections based on difference intervention scenarios, then used a decision (probability) tree to estimate the number of patients for each clinical outcome. Finally, they calculated an incremental cost-effectiveness ratio (ICER) to compare the cost-benefit for maintaining face mask use in different scenarios and timeline in the US population. Thus, the object of this study is to reproduce and develop the simulation models proposed by Bartsch et al and to identify the potential application of this model to another country as a tool for policy maker.

Methods

Model specification:

A disaggregate system dynamics model was reproduced using the diagram provided in the appendix of Bartsch et al publication. The cohort was stratified into five age group including 0-17 years, 18-44 years, 45-64 years, 65-84 years, and >=85 years. There were seven stocks including susceptible (S), susceptible and vaccinated (Sv), exposed (E), exposed and vaccinated (Ev), infected and symptomatic (Is), infected and asymptomatic (Ia), recovery (R). The maximum length of time was 600 days with 1 day step. The overall stock and flow model was shown in Figure 1A (8).

The number of symptomatic infections from each scenario generated from the system dynamics model were turned through the similar decision tree with probability parameters (Figure 2A) (8) to get the number of each clinical outcomes in every 10 days of time point. Then vaccination costs including medical costs (hospital admission and

treatment) and intervention costs (face mask use) were calculated for each scenario. Finally, ICER was calculated to compare the ratio of the incremental costs of face mask use and the incremental health effects measured in quality-adjusted life years (QALYs). All parameters and their distribution were provided by Bartsch et al (8). The costs with societal perspective including direct and indirect costs (i.e., productivity losses caused by absenteeism and presenteeism) were excluded from presented study to keep the simplicity of cost calculation.

Calibration and validation:

Calibration could not be directly done as the original article, because some parameters including effective reproductive number (i.e., for each pair of age-stratum, fixed reproductive number, seasonal reproductive number), initial number of populations for each stock, and vaccination force (referred to a factor of daily vaccination rate in the article) in the original article were not well defined. Bartsch et al mentioned that the effective reproductive number were estimated from the shape of the pandemic curve from March 2020 to October 2021 and summarized in the seasonality scaling factor for effective reproductive number but did not provide the details on how to substitute these parameters into the system dynamics model. Thus, the reproductive number for this project was set to be 1.66 (9) and the initial number of populations for each stock were identified from census data (10) and reported number of COVID-19 cases in the first week of March 2020 provided by the Centers for Disease Control and Prevention (11). Then the vaccination force was calibrated to get the closest number of total symptomatic infection through October 2021 (579 days) as reported in the appendix of original paper which calculated by the total number of prevalence cases per day divided by average duration of disease (7 days). Initial model validation was done by consulting the subject matter expert on modeling.

Main experiment:

The main experiment of this study was an interventional evaluation of face mask cost-effectiveness by comparing the patterns of ICER in every-10-day time points. The means and 95% confidence limits (2.5^{th} and 97.5^{th} percentile) of ICERs for each time point and sensitivity scenario were calculated from the 1,000 times of simulation (Mote Caro simulation) using the distributions of each parameter for ICER calculation provided by the original article, see Table 1A. The visualization of ICER estimates were generated to access sensitivity and flexibility of the model by range of the parameters including reproductive number (1.35 – 2.11; from a study) (9), vaccination force (0.016 – 0.025; +/- 20%), and initial vaccine coverage (0.6 – 0.8; assumption).

The simulations and data analysis were conducted using R program. The application for simulation model was created by R Shiny to verify the model flexibility and potential model application to various scenario in other countries. Additional options including initial

vaccine coverage for each age group and parameter adjustments were added into the Shiny application.

Results

The preliminary version of reproduced model with ICER calculation for the U.S. population were created. The code could be found on the GitHub repository link: https://github.com/AnupongSiri/Face_mask_ICER_US
and the Shiny application could be run through R program using command: library(shiny); runGist("cd7daf9661d390dd24640840b8737723")

After calibration, the vaccination force was set to be 0.021, and the reproduced model could simulation the pattern of epidemic in the U.S. population with number of symptomatic infected as showed in Table 1.

The higher variation of ICER estimates were observed when the different of number of symptomatic infected between population who use face mask and those without facemask was high which was the peak of epidemic of each population (Figure 1). When the face mask was implemented, the number of infected cases were decrease and the curve was flattened comparing to no face mask scenario (Figure 2).

Thus, the conclusion in cost-effectiveness of face mask use based on the cut-off ICER up to 50,000 USD per QALY could vary by timing of the epidemic (at the peak or decreasing trend) and several factors in the sensitivity analysis including reproductive number (Figure 3), vaccination force (Figure 4), and initial vaccine coverage (Figure 5). The preliminary model seems to be flexible enough to handle the range of parameters.

Discussion

The preliminary model has showed the possibility of model reproducibility from the original article. The results generated form the simulations in this study do not intent to be interpreted as the policy guidance nor prediction for current situation. Because the original code was not publicly available (8), and some model specifications were unclear. The coding and calculation for this study is prone to be different from the original version as well as the errors of the model could be found. This study also simplified some calculation parts of the original article by excluding the societal costs.

The major point of model specification that prone to be error is that vaccination force which depends on the daily vaccination rate as presented in the original article (8). It is hard to estimate and model the vaccination rate where the vaccination policy trends be change over the time and vary across the age-group and underlying disease conditions (12,13). This study used number of symptomatic cases provided by the original article to calibrate vaccination force which seemed to be inappropriate because the vaccine uptake rate in

simulated cohort was too fast and seemed to be unrealistic for the beginning of COVID-19 pandemic. In the future, the assumptions on timing and the variation of vaccination uptake by age-group may need to be considering in the future development of this system dynamics model.

Other potential improvements for the system dynamics model including: 1.) additional stocks (death, quarantine) and flows (recovery to vaccination) to reflect more realistic scenarios of the epidemic (14–16). 2.) using more flexible reproductive numbers for each pair of age group to reflex the age-dependent mixing pattern. The contact rate for each pair of age group could be estimated (17) then apply the probability of infection to get the pair-wise transmission parameters (18). 3.) recategorization of age-group to reflex the realistic policy implementations such as face mask, and vaccine coverage (12,13,19–21).

As we can observed from the results, the system dynamics model could only capture one epidemic peak for cohort population. This is the limitation of the model that could not handle the complex epidemic of different strains and prolong pandemic which occurs in a real-world situation. More complex and flexible system dynamics model may need to be considered regarding to trade-off for overfitting (22–24). On the other hand, another potential and simpler approaches for ICER calculation may need to be applied including using proportion of symptomatic infected form the system dynamic model and accounting for inflation rate. In addition, a stage transitional model (25) and agent based model (26) may be other options for cost-effectiveness analysis however these model approached also require the identification of additional parameters than presented in the original article as well as additional assumptions.

Finally, the results showed the flexibility of the model that could be applied to other country setting by updated the population structure and some parameters including age-specific contact rate, control measures (vaccine coverage, face make use), costs (medical, vaccination, face mask) and utility weights.

Conclusion

The disaggregated system dynamics model with probability tree approach proposed by Bartsch et al could potentially be reproduced. The conclusion on cost-effectiveness analysis of face mask use may vary depend on timing and parameters related to the epidemic. The further development to other population could be achieved by model modification and updating some parameters.

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Table 1. Number of COVID-19 symptomatic infected cases from March 2020 to October 2021

	Model-generated	Bartsch et al†	CDC data‡
All ages	101,117,879	100,073,580	35,502,419
0 - 17 years	23,704,301	22,451,302	5,279,186
18 - 44 years	29,116,108	35,920,131	18,859,138
45 - 64 years	25,291,072	25,664,557	6,842,295
≥ 65	19,016,045	16,037,590	4,521,800

†Model-generated number by Bartsch et al (original article)

‡Centers for Disease Control and Prevention data as published in Bartsch et al article

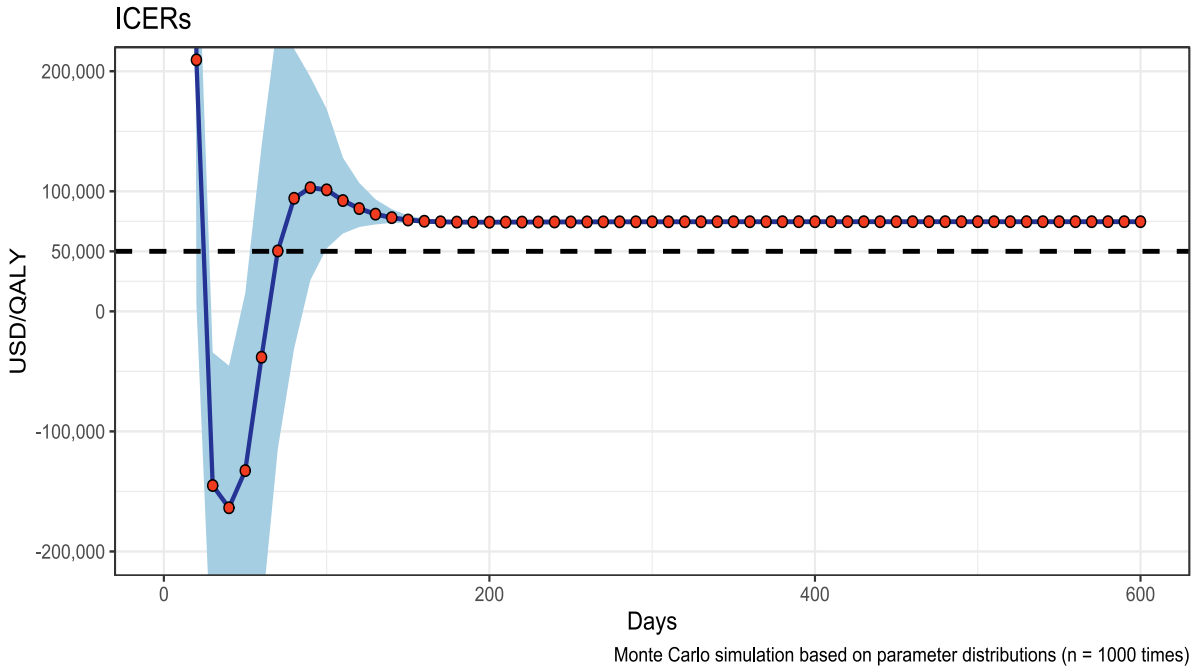

Figure 1. Simulated incremental cost-effectiveness ratio (ICER) for every-ten-day time points with 95% confidence interval band: reproductive number = 1.66, vaccination force = 0.021, and initial vaccine coverage for every age group = 0

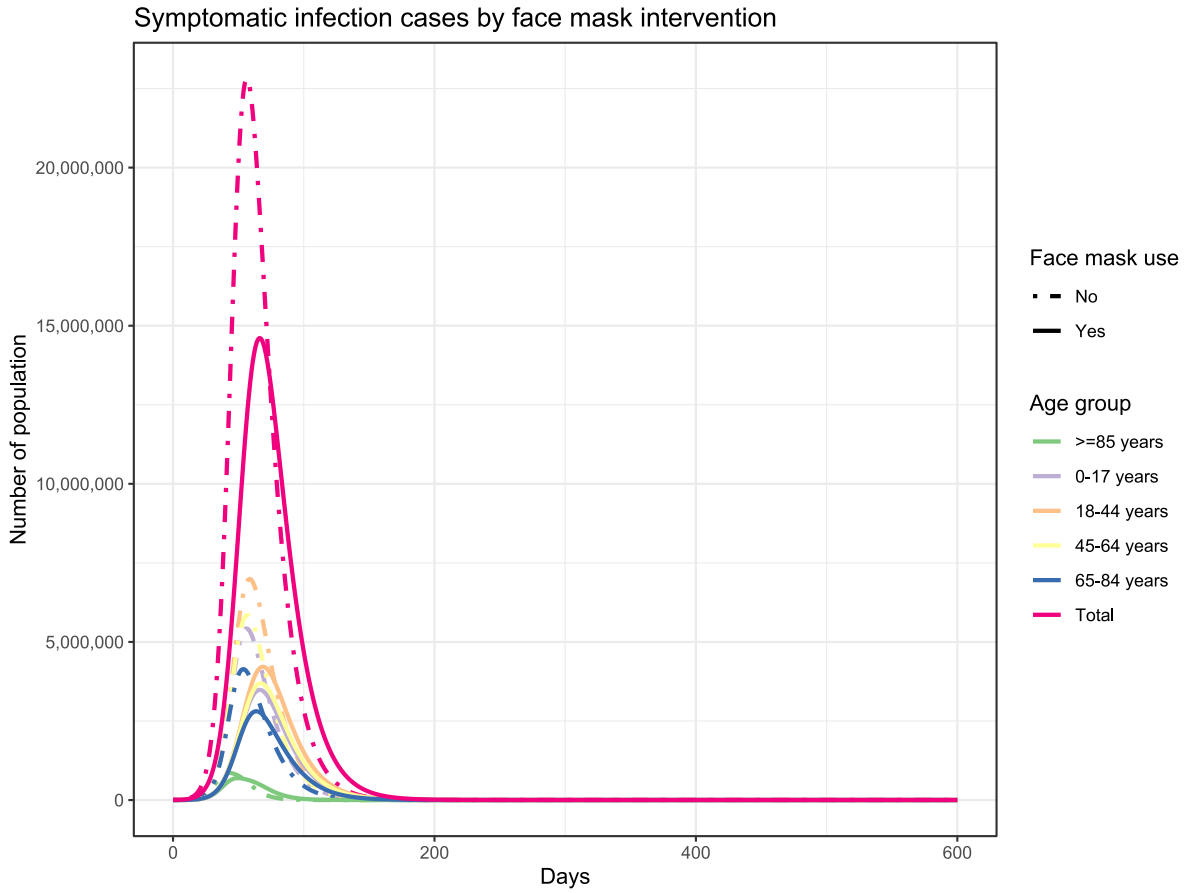

Figure 2. Number of simulated symptomatic infected cases (prevalence cases) by face mask use and age group: reproductive number = 1.66, vaccination force = 0.021, and initial vaccine coverage for every age group = 0

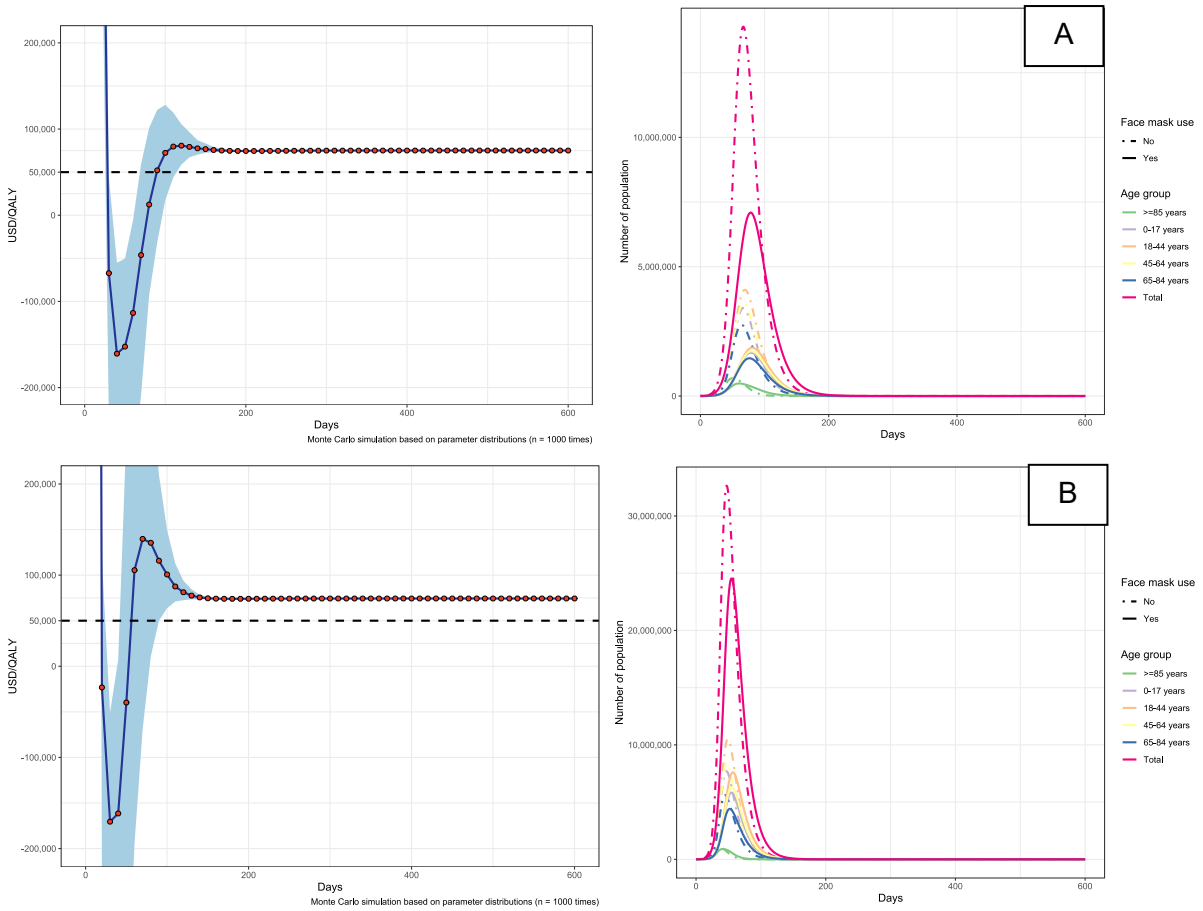

Figure 3. Simulated incremental cost-effectiveness ratio (ICER) and number of simulated symptomatic infected cases (prevalence cases) by face mask use and age group; A) reproductive number = 1.35, vaccination force = 0.021, and initial vaccine coverage for every age group = 0; B) reproductive number = 2.11, vaccination force = 0.021, initial vaccine coverage for every age group = 0

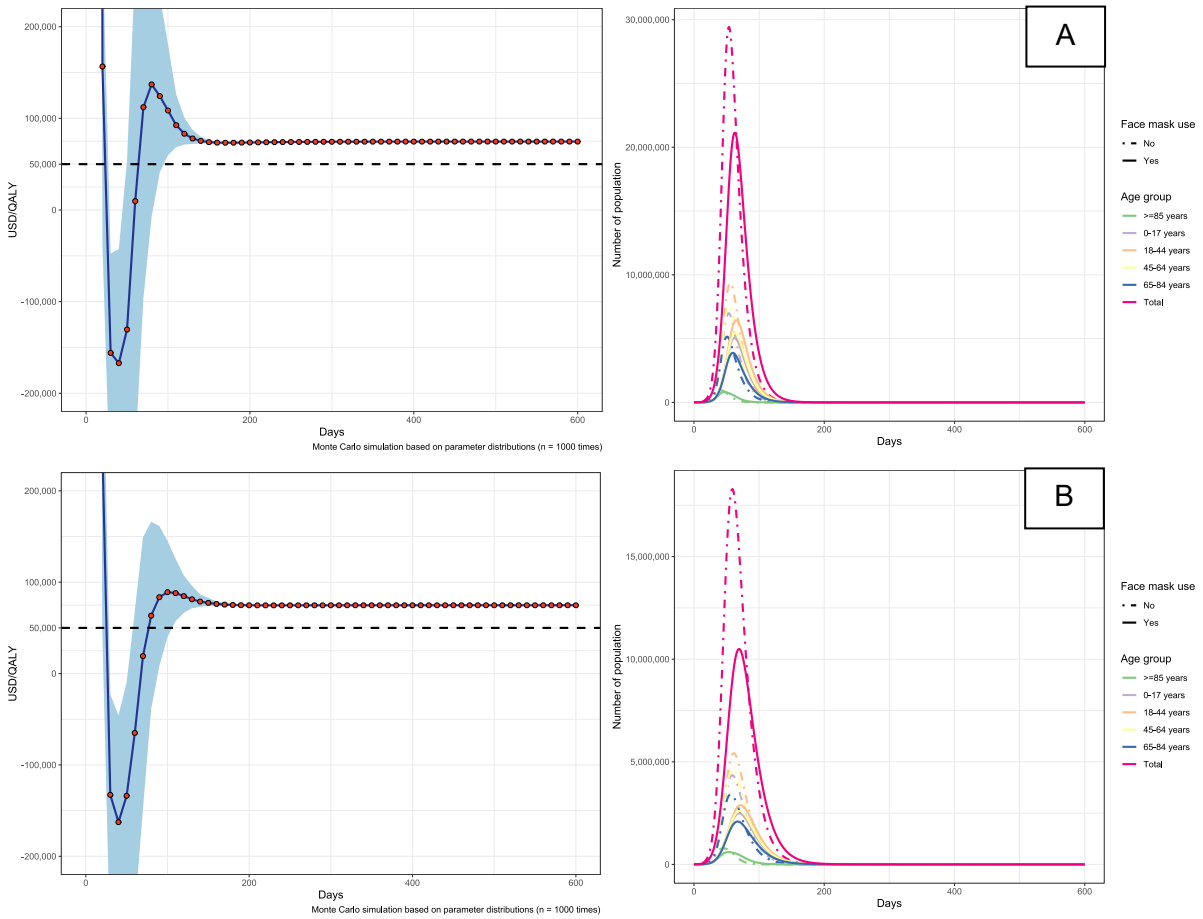

Figure 4. Simulated incremental cost-effectiveness ratio (ICER) and number of simulated symptomatic infected cases (prevalence cases) by face mask use and age group; A) reproductive number = 1.66, vaccination force = 0.016, and initial vaccine coverage for every age group = 0; B) reproductive number = 1.66, vaccination force = 0.025, and initial vaccine coverage for every age group = 0

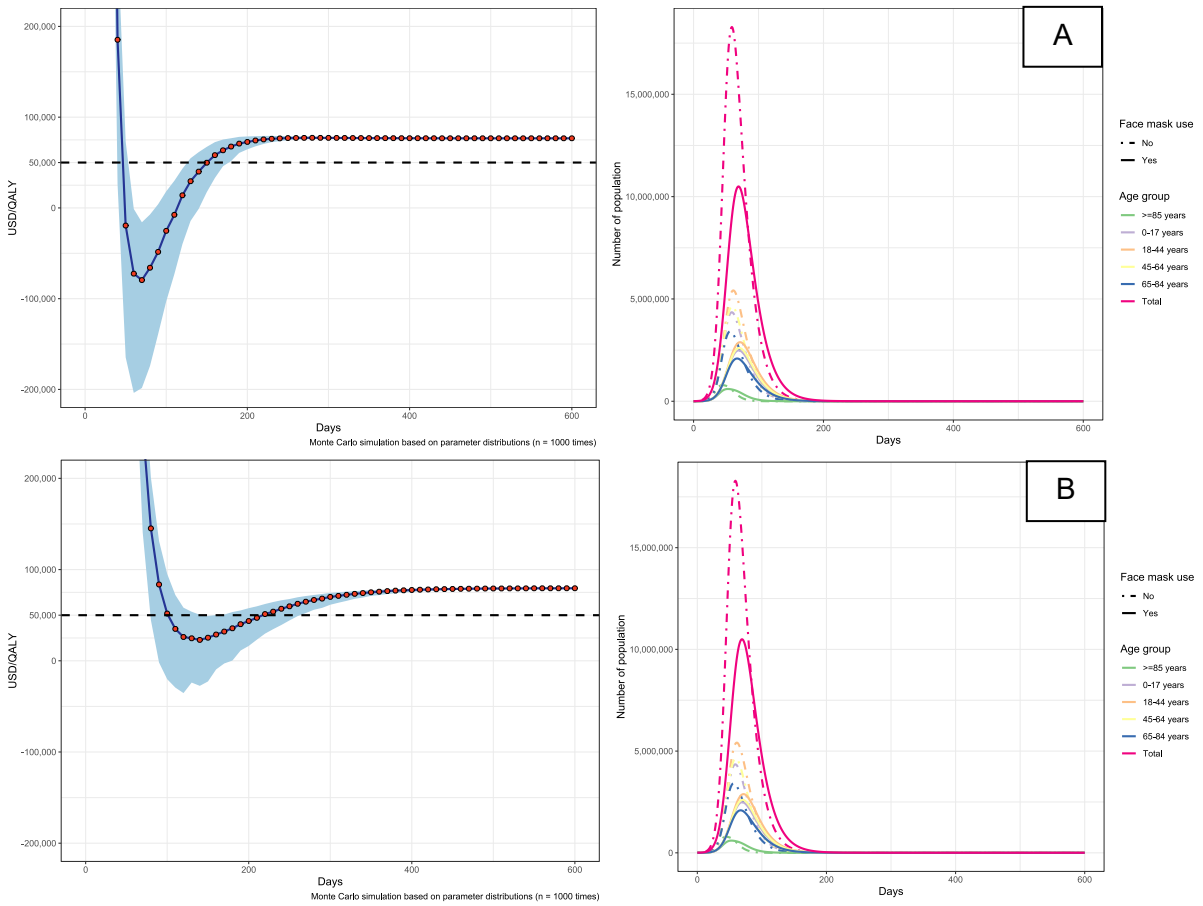

Figure 5. Simulated incremental cost-effectiveness ratio (ICER) and number of simulated symptomatic infected cases (prevalence cases) by face mask use and age group; A) reproductive number = 1.66, vaccination force = 0.021, and initial vaccine coverage for every age group = 0.6; B) reproductive number = 1.66, vaccination force = 0.021, and initial vaccine coverage for every age group = 0.8

Appendix

Table A1. Parameters as provided in Bartsch et al article

Parameter	Label†	Distribution Type	Mean or Median	Standard Error or Range	Source‡
Spring and fall Rt	-	Point Estimate	0.659	-	22
Summer Rt	-	Point Estimate	0.318	-	22
Winter Rt	-	Point Estimate	1.000	-	22
Latent period (days)	D_lat	Triangular	5.200	4.1 - 7.0	23
Infectious period (days)	D_inf	Uniform	-	4 - 15	24-27
Surgical face mask	c_sx_m	Point Value	0.08	0.16 - 0.24	2
N95 face mask	c_n95_m	Point Value	0.50	1 - 1.5	2
Cloth face mask	c_cl_m	Point Value	2.50	0 - 7.5	Assumption
Washing cloth face mask (per day)	c_cl_m_w	Point Value	0.007	-	4, 6, 7
COVID-19 vaccine (per dose)	c_vacc	Point Value	20	-	28
Vaccination administration (per dose)	c_vacc_adm	Point Value	40	-	30
Annual wages	-	Point Value	42,223.00	21950 - 104403 (95% CI)	31
Ambulatory care visit	c_ambu	Uniform	-	110.43 - 148.33	32
Over counter medications, daily: 0-12 years	c_med_A	Gamma	3.990	2.1	33
Over counter medications, daily: >=13 years	c_med_B	Gamma	0.470	0.17	33
Hospitalization for pneumonia: 0-17 years	c_pneu1_A	Gamma	12,877.37	1,508.04	34
Hospitalization for pneumonia: 18-44 years	c_pneu1_B	Gamma	10,945.96	1,045.06	34
Hospitalization for pneumonia: 45-64 years	c_pneu1_C	Gamma	14,129.68	1,238.76	34
Hospitalization for pneumonia: 65-84 years	c_pneu1_D	Gamma	12,632.32	478.4	34
Hospitalization for pneumonia: >=85 years	c_pneu1_E	Gamma	11,312.21	518.29	34
Hospitalization for severe non-pneumonia, all age	c_pneu0	Gamma	7,093.13	1,182.99	34

Hospitalization for sepsis: 0-17 years	c_seps_A	Gamma	23,375.13	1,861.33	34
Hospitalization for sepsis: 18-44 years	c_seps_B	Gamma	45,091.74	5,382.40	34
Hospitalization for sepsis: 45-64 years	c_seps_C	Gamma	39,896.27	2,725.10	34
Hospitalization for sepsis: 65-84 years	c_seps_D	Gamma	31,217.54	1,367.91	34
Hospitalization for sepsis: >=85 years	c_seps_E	Gamma	23,375.13	1,861.33	34
Hospitalization for ARDS: 0-17 years	c_ards_A	Gamma	43,621.10	4,198.97	34
Hospitalization for ARDS: 18-44 years	c_ards_B	Gamma	26,997.29	1,558.61	34
Hospitalization for ARDS: 45-64 years	c_ards_C	Gamma	20,459.90	453.92	34
Hospitalization for ARDS: 65-84 years	c_ards_D	Gamma	19,280.11	335.69	34
Hospitalization for ARDS: >=85 years	c_ards_E	Gamma	17,056.54	754.12	34
Hospitalization for myocarditis	c_myoc	Gamma	35,289.60	2,222.34	34
Hospitalization for pericarditis	c_peri	Gamma	16,002.76	291.16	34
Hospitalization for allergic reaction/anaphylaxis	c_anap	Tringular	7,753.38	6,774.80 - 8,280.31 (+/- 10% mean/median)	34
Face mask effectiveness	ME	Beta Pert	0.18	0.16 - 0.20 (95% CI)	35
Using surgical masks	p_sx_m	Point Estimate	0.20	-	8
Using N95 masks	p_n95_m	Point Estimate	0.345	-	8
Using cloth masks	p_cl_m	Point Estimate	0.455	-	8
Developing immunity after infection (seroconversion)	p_imm	Point Estimate	0.91	-	36, 37
Vaccine efficacy against COVID-19 hospitalization	VE	Beta Pert	0.86	0.82 - 0.89 (95% CI)	38
Side effect due to vaccination: Minor	-	Uniform	-	0.33 - 0.42	39-41
Side effect due to vaccination: Severe myocarditis/pericarditis	p_card	Uniform	0.000023	0.0000156 - 0.000027 (95% CI)	42
Side effect due to vaccination: Severe-allergic reaction/anaphylaxis	p_anap	Triangular	-	0.000003 - 0.000011	

Asymptomatic infection	q_symp	Triangular	0.45	0.305-0.495 (+/-10% mean/median)	45, 46
Relative infectiousness of asymptomatic infection	-	Point Estimate	1	-	46
Missing work/school	-	Point Estimate	1	-	Assumption
Ambulatory care	p_ambu	Triangular	0.150	0.06 - 0.26	1
Hospitalization given infection: 0-17 years	p_hosp_A	Beta Pert	0.0092	0.0081 - 0.0101 (+/-10% mean)	12
Hospitalization given infection: 18-44 years	p_hosp_B	Beta Pert	0.0081	0.0073 - 0.0089 (+/-10% mean)	12
Hospitalization given infection: 45-64 years	p_hosp_C	Beta Pert	0.0826	0.0744 - 0.909 (+/-10% mean)	12
Hospitalization given infection: >=65 years	p_hosp_D	Beta Pert	0.2570	0.2314 - 0.2828 (+/-10% mean)	12
ICU admission, given hospitalization: 0-17 years	p_icu_A	Beta Pert	0.1710	0.154 - 0.1881 (+/-10% mean)	47
ICU admission, given hospitalization: 18-44 years	p_icu_B	Beta Pert	0.2380	0.214 - 0.262 (+/-10% mean)	48
ICU admission, given hospitalization: 45-64 years	p_icu_C	Beta Pert	0.3610	0.325 - 0.397 (+/-10% mean)	48
ICU admission, given hospitalization: >=65 years	p_icu_D	Beta Pert	0.3530	0.318 - 0.388 (+/-10% mean)	48
Mortality, given hospitalization: 0-17 years	p_die_A	Beta Pert	0.0061	0.0055 - 0.0067 (+/-10% mean)	12, 49
Mortality, given hospitalization: 18-44 years	p_die_B	Beta Pert	0.0890	0.0801 - 0.0979 (+/-10% mean)	12, 49
Mortality, given hospitalization: 45-64 years	p_die_C	Beta Pert	0.0580	0.0520 - 0.0635 (+/-10% mean)	12, 49
Mortality, given hospitalization: >=65 years	p_die_D	Beta Pert	0.1550	0.1392 - 0.1702 (+/-10% mean)	12, 49
Pneumonia, given hospitalization	p_pneu	Beta	0.790	0.711 - 0.869 (IQR)	50
ARDS, requiring ventilator use in ICU	p_ards	Beta	0.771	0.053	51-55
Reduced work productivity (presenteeism) due to long COVID	-	Triangular	0.452	0.429 - 0.472	56
Get vaccinated in any setting (hours)	D_vac	Uniform	-	0.1 - 2	57
Minor side effects	-	Uniform	-	1- 2	Assumption
Ambulatory care	d_ambu	Point Estimate	0.500	-	Assumption
Duration of symptoms with mild illness	-	Triangular	7	3 - 17	26, 58, 59
Duration of symptoms prior to hospital admission	-	Triangular	7	3 - 9 (10% - 90%)	60, 61

Hospitalization, not admitted to ICU: 0-49 years	d_hosp_A	Beta Pert	3	2 - 5 (IQR)	48
Hospitalization, not admitted to ICU: 50-64 years	d_hosp_C	Beta Pert	4	2 - 7 (IQR)	48
Hospitalization, not admitted to ICU: >=65 years	d_hosp_D	Beta Pert	6	3 - 10 (IQR)	48
Hospitalization, ICU (all ages)	d_icu	Gamma	9	4 - 17 (IQR)	53-55, 62
Hospitalization, ventilator use	-	Gamma	9	5 - 12 (IQR)	53, 54, 63
Hospitalization, myocarditis	d_myoc	Gamma	5.9	0.28	34
Hospitalization, pericarditis	d_peri	Gamma	4.8	0.06	34
Hospitalization, allergic reaction/anaphylaxis	d_anap	Gamma	2.3	2.1-2.5	34
Reduced productivity (presenteeism) due to long COVID	-	Point Estimate	182	-	56
Cloth mask per person	n_cl_m	Point Estimate	2	-	4
Disposable masks per day (average)	n_dis_m	Point Estimate	0.515	0.62 - 0.77	3
Healthy QALY: <17 years	qaly_A	Point Estimate	1.00	-	64
Healthy QALY: 18-64 years	qaly_B	Point Estimate	0.92	-	64
Healthy QALY: >=65	qaly_D	Point Estimate	0.84	-	64
Mild non-specific symptoms	qaly_ls	Beta	0.648	0.103	65-74
Hospitalized, non-pneumonia symptoms	qaly_pneu0	Beta	0.514	0.089	67, 74, 75
Pneumonia	qaly_pneu1	Beta	0.496	0.170	76-80
Sepsis	qaly_seps	Beta	0.467	0.180	80-86
ARDS	qaly_ards	Triangular	0.100	0.08 - 0.15	87

†Generated labels for coding in this study, no label means non-used parameters for this study

‡Sources as referred in the original article by Bartsch et al

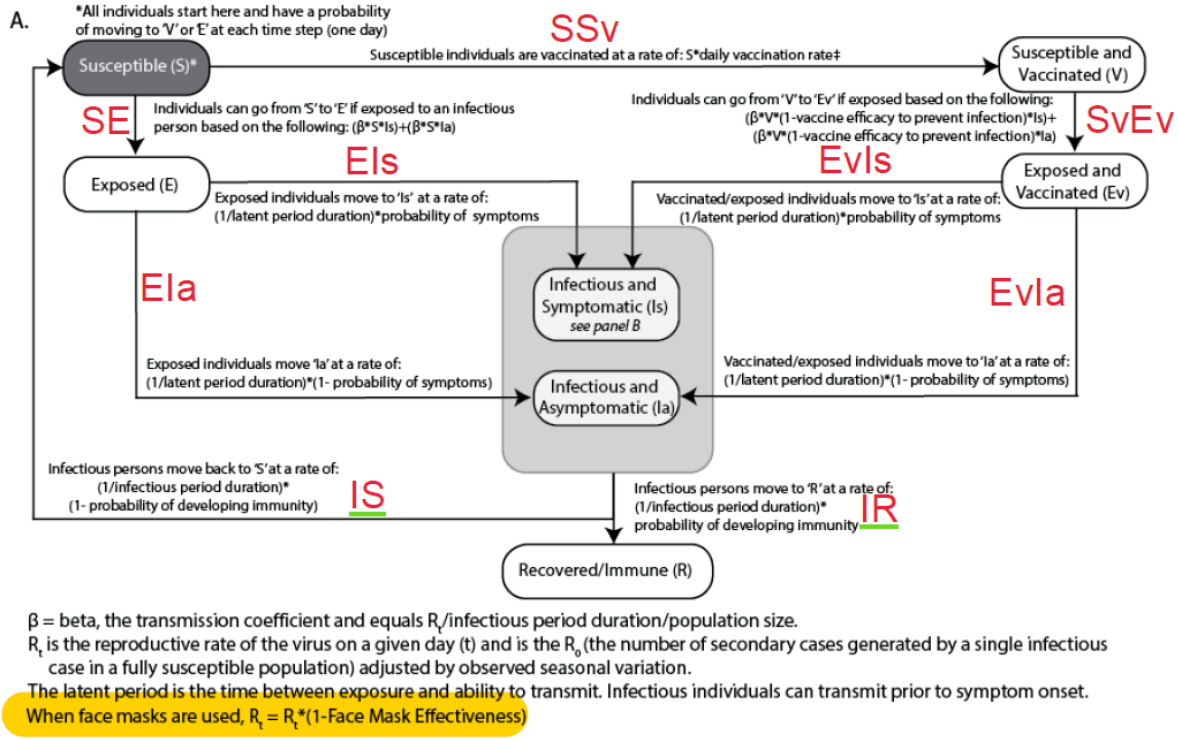

Figure 1A. Augmented system dynamics model diagram from the original article by Bartsch et al

SSv = flow from susceptible to susceptible and vaccinated

SE = flow from susceptible to exposed

SvEv = flow from susceptible and vaccinated to exposed and vaccinated

EIs = flow from exposed to infectious and symptomatic

EvIs = flow from exposed and vaccinated to infectious and symptomatic

EIa = flow from exposed and symptomatic to infectious and asymptomatic

EvIa = flow from exposed and vaccinated to infectious and asymptomatic

IS = flow from infectious (symptomatic & asymptomatic) to susceptible

IR = flow from infectious (symptomatic & asymptomatic) to recovery

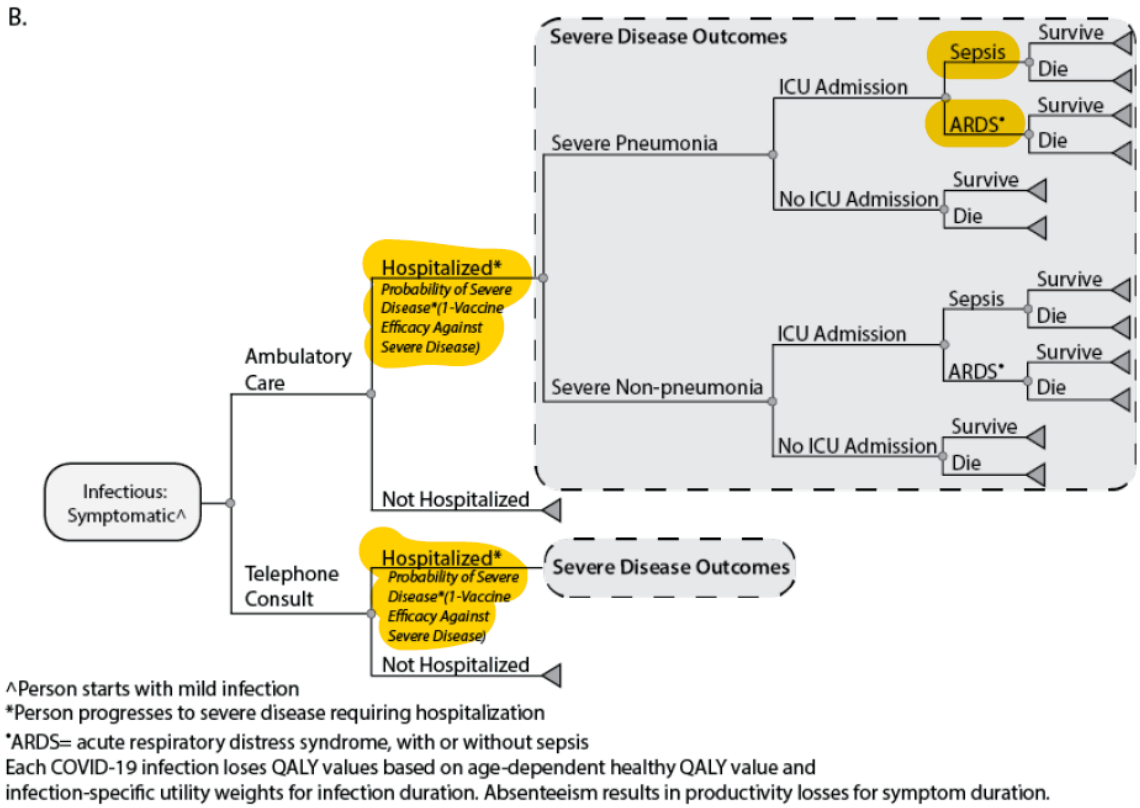

Figure 2A. Probability tree of outcomes that infectious and symptomatic persons travel through, source Bartsch et al