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Pandemic Modelling and Societal Relevance

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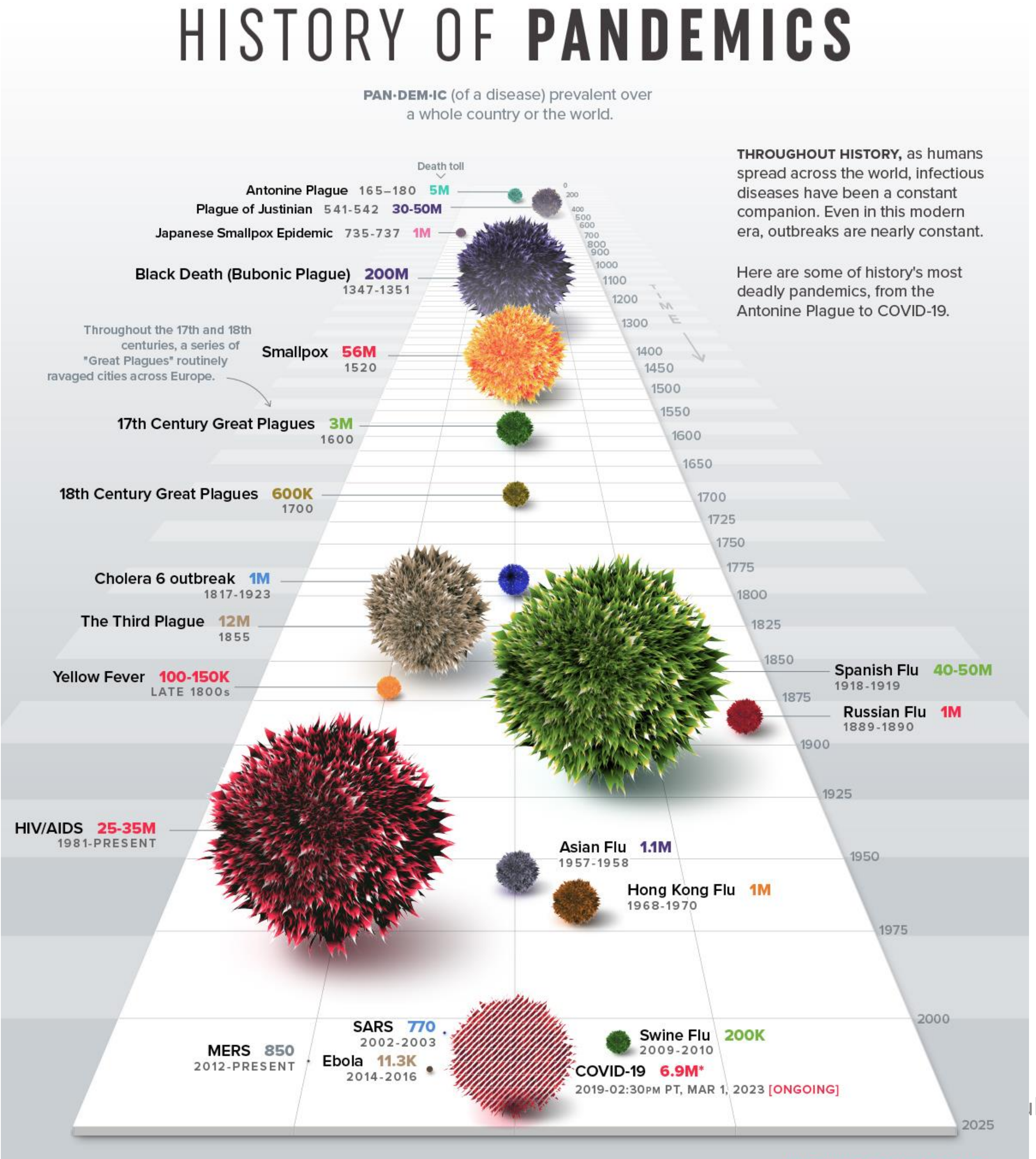
23rd International Conference on Informatics,

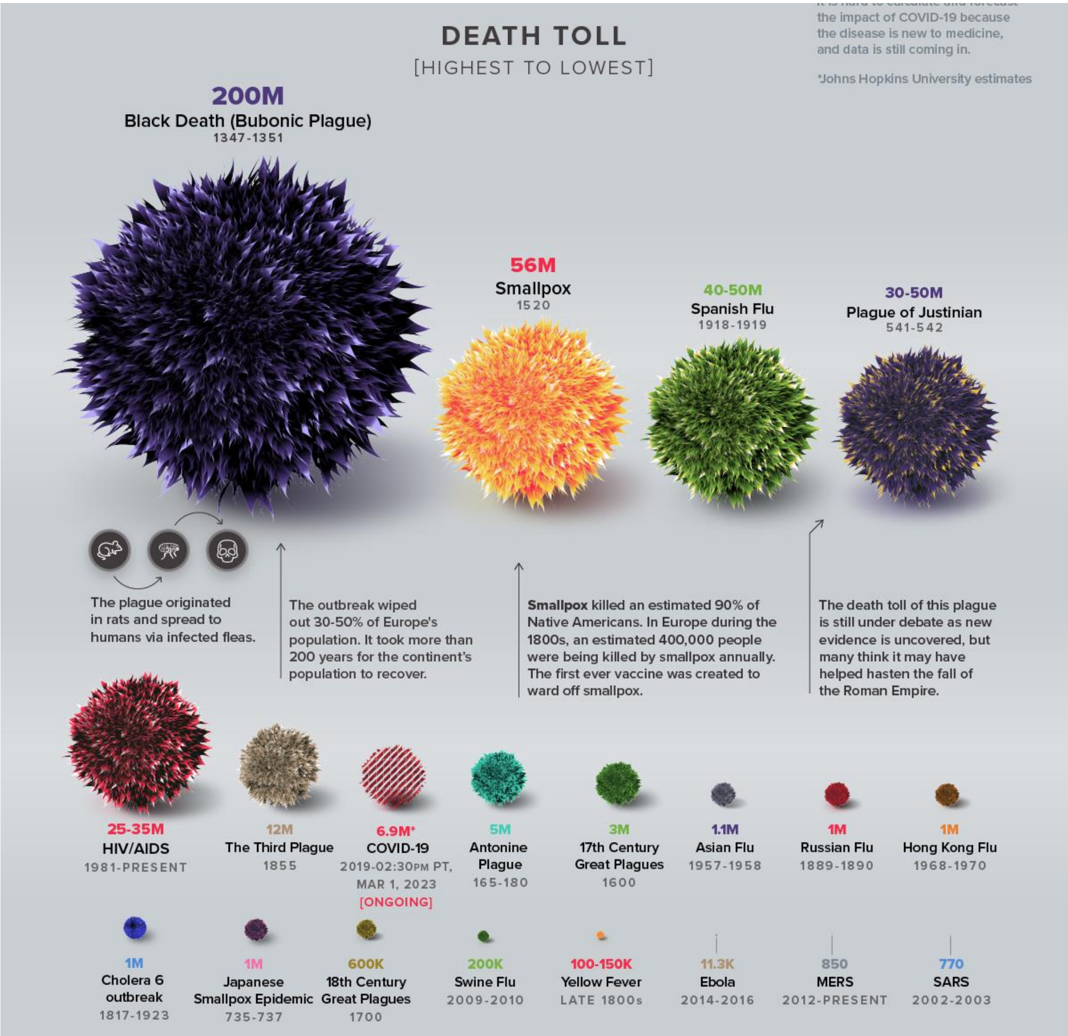
Management, and Technology in Healthcare – 7/5//2025 Athens, Greece

Disclosures

Founded by an unrestricted grant of the Dieter-Schwarz-Foundation, Heilbronn, Germany.

Introduction & Motivation





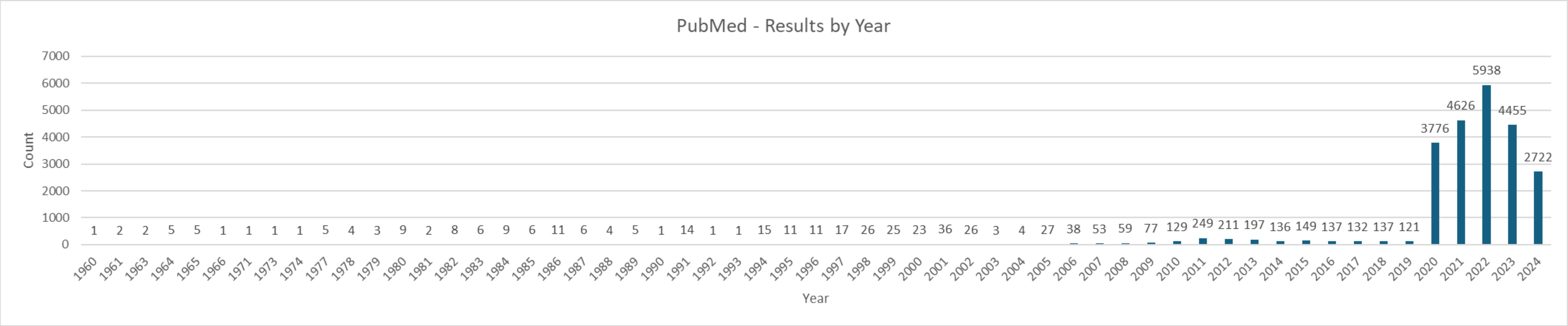
visualcapitalist.com, based on numerous sources, last accessed 3. July 2025

Image by the author.

Unmet Need for Improvement

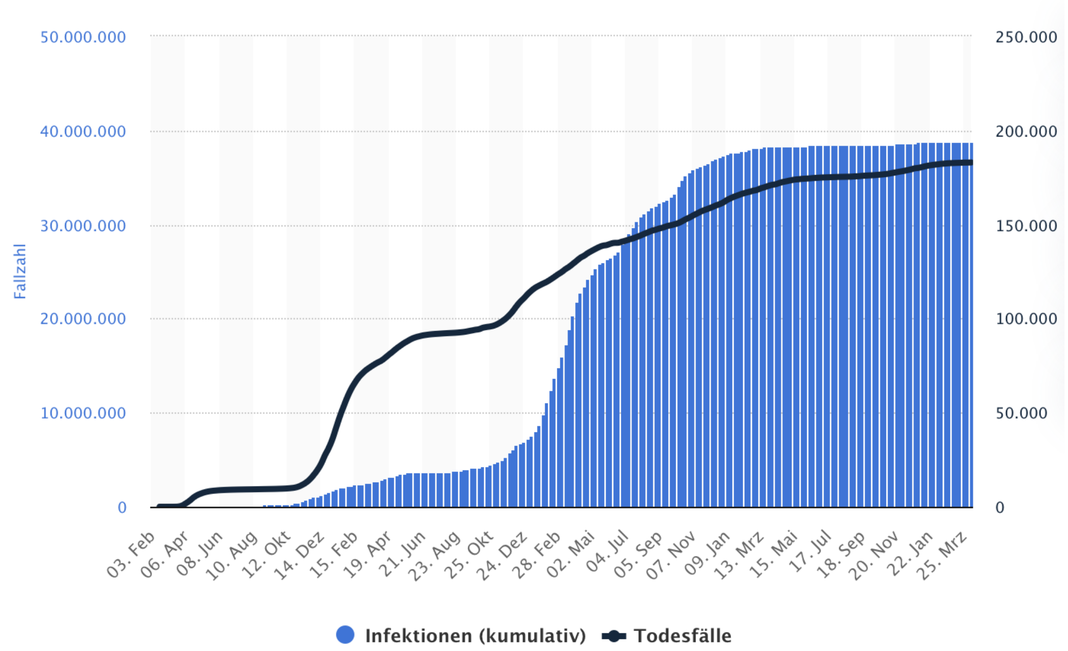
Pandemic Modelling – Historical Evolution

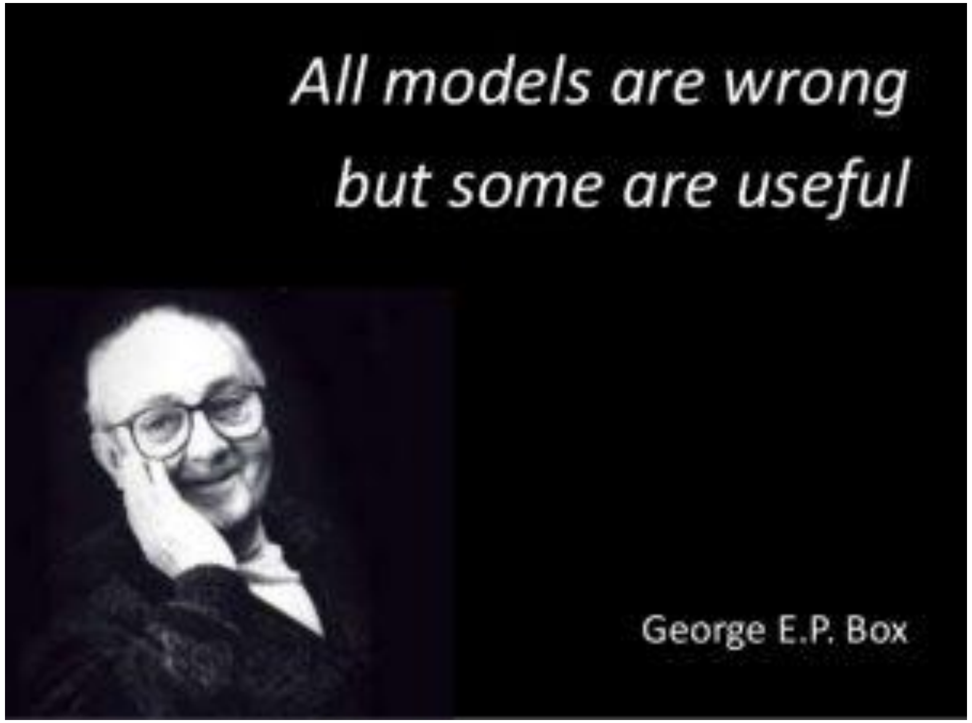
- PubMed Search (30. June 2025)
- Search query: ("Pandemics"[Mesh] OR "Epidemiology"[Mesh]) AND model*[Title/Abstract] → 21,790 results → 2,043 results 1960 - 2019



https://pubmed.ncbi.nlm.nih.gov/?term=(%22Pandemics%22%5BMesh%5D%20OR%20%22Epidemiology%22%5BMesh%5D)%20AND%20model*%5BTitle%2FAbstract%5D&size=200

Will the coronavirus soon be over?





[Statista](); 8. April 2024; last accessed 3. July 2025

- "Disease models describe and simulate on the computer different courses of a disease considering possible intervention strategies and their costs."

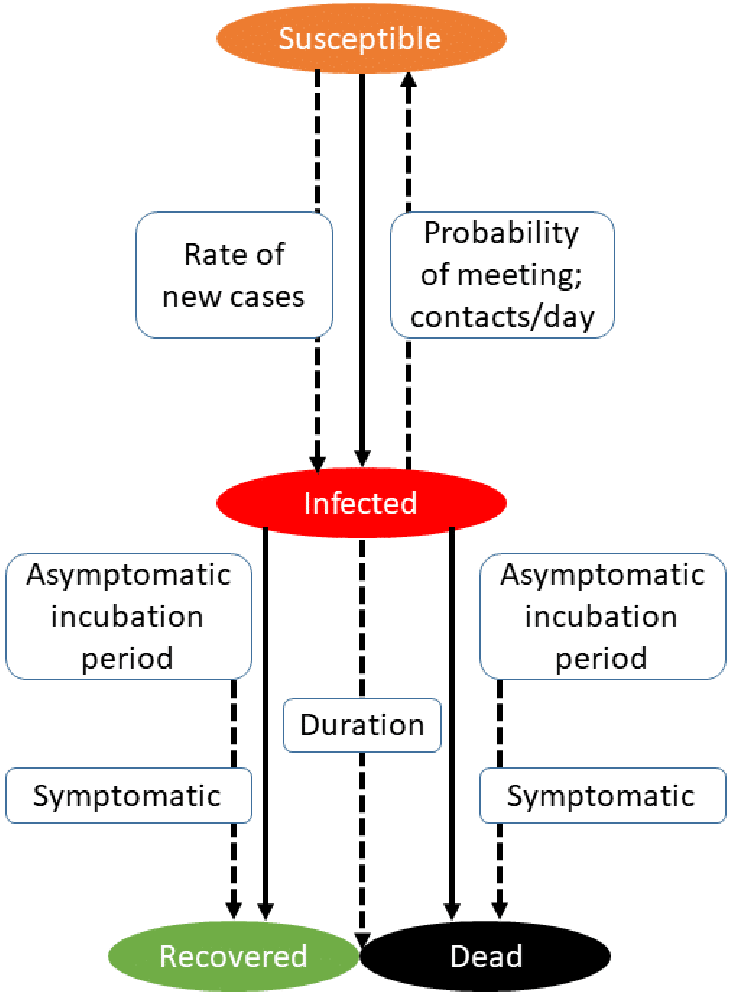
Source: EU Project HARMET 1995

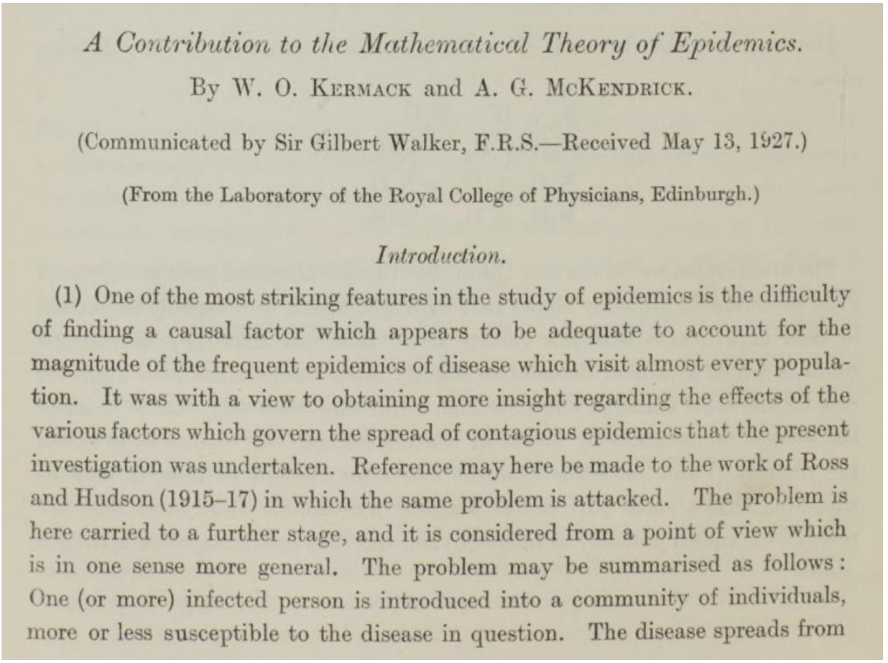
- Models are simplified representations of more complex real systems ("reality").

- Models provide an explanation for the question: "What does today's knowledge about a chronic disease mean for the future …
- … to allow today's decision making

- Models do not forecast the future!
- All models are wrong, but some are useful.

Compartmental Modelling





A Contribution to the Mathematical Theory of Epidemics.

By W. O. Kermack and A. G. McKendrick.

(Communicated by Sir Gilbert Walker, F.R.S.—Received May 13, 1927.)

(From the Laboratory of the Royal College of Physicians, Edinburgh.)

Introduction.

(1) One of the most striking features in the study of epidemics is the difficulty of finding a causal factor which appears to be adequate to account for the magnitude of the frequent epidemics of disease which visit almost every population. It was with a view to obtaining more insight regarding the effects of the various factors which govern the spread of contagious epidemics that the present investigation was undertaken. Reference may here be made to the work of Ross and Hudson (1915–17) in which the same problem is attacked. The problem is here carried to a further stage, and it is considered from a point of view which is in one sense more general. The problem may be summarised as follows: One (or more) infected person is introduced into a community of individuals, more or less susceptible to the disease in question. The disease spreads from

Kermack WO, McKendrick AG. Contribution to the Mathematical Theory of Epidemics. Proc Roy Soc A **1927**; 115: 700-21

Example Ebola Modelling

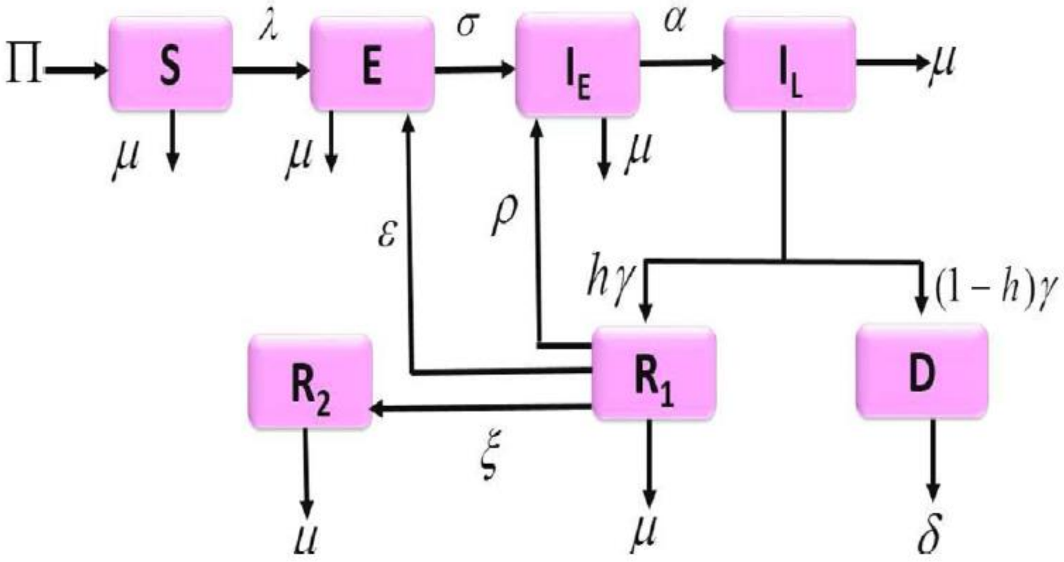


Fig. 1. Flow diagram of the Ebola transmission model.

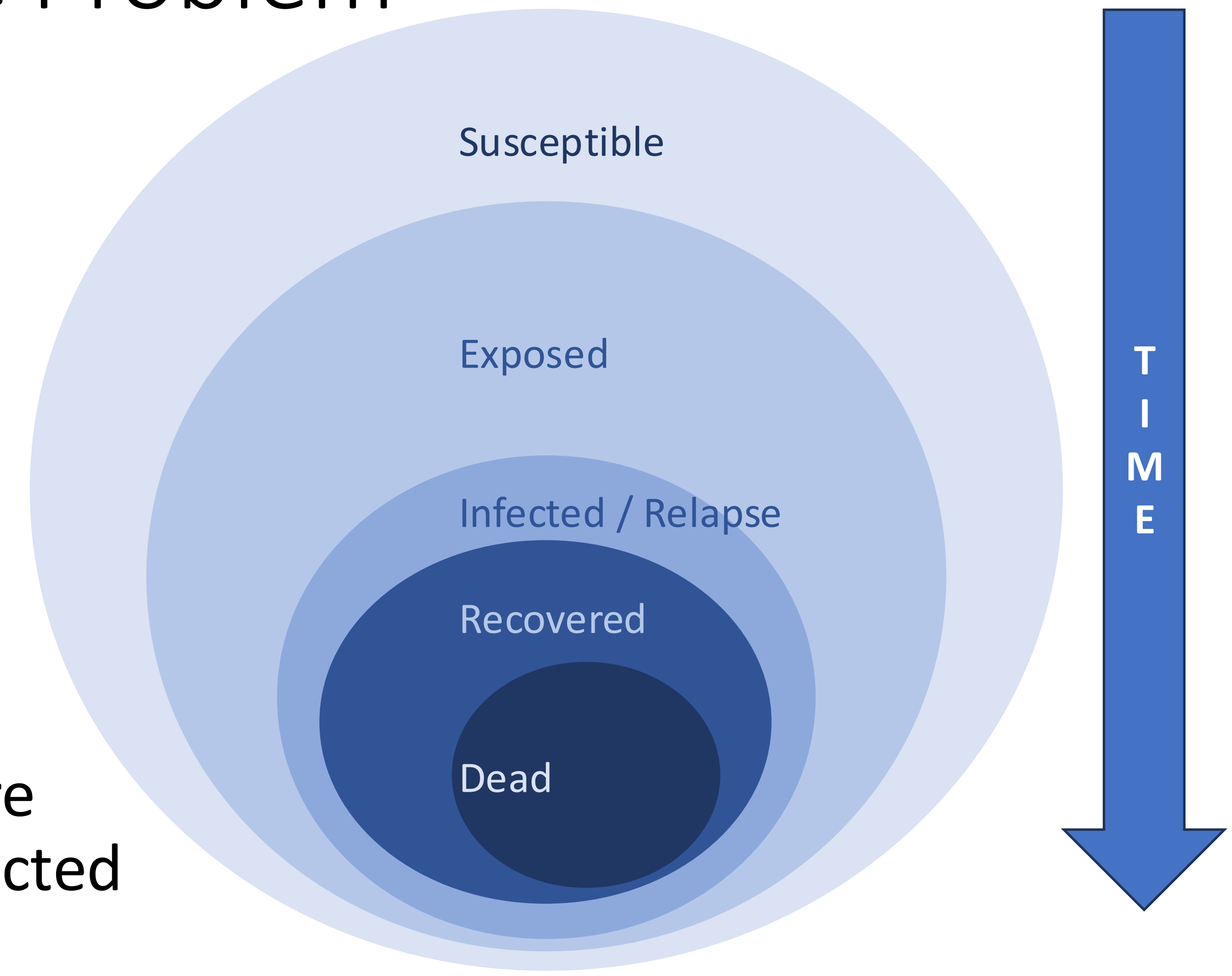
Table 1
Description of the state variables and parameters of the Ebola model (2.1).

Variable	Description
$S(t)$	Population of susceptible individuals
$E(t)$	Population of exposed individuals
$I_E(t)$	Population of symptomatic individuals in the early-stage of EBOV infection
$I_L(t)$	Population of symptomatic individuals in the late-stage of EBOV infection
$R_1(t), R_2(t)$	Population of recovered and immune individuals
$D(t)$	Population of Ebola-deceased individuals
Parameter	Description
β	Effective contact (transmission) rate
Π	Recruitment rate
μ	Natural death rate
τ	Modification parameters for infectiousness
ρ	Infection reactivation rate
σ	Progression rate of symptomatic individuals
α	Progression rate of early-symptomatic individuals
ξ	Progression rate of recovered individuals to immune class
h	Fraction of symptomatic individuals who recovered
ε	Reinfection modification parameters
γ	Recovery rate of symptomatic individuals
δ	Cremation/burial rate of Ebola-deceased individuals

Agusto FB. Mathematical model of Ebola transmission dynamics with relapse and reinfection. *Math Biosci*. 2017;283:48-59. doi:10.1016/j.mbs.2016.11.002

Variants & Pandemic Problem

- SEIR
- SEIRD
- SIRRD
- SEIRRD



- In a Pandemic: most people are Susceptible, Exposed, and Infected

Break Out

- Imagine, you are the health minister of your country and the next pandemic is about to affect the globe.
- What are your most important decision relevant topics for fighting the pandemic?

partici.fi/83336015

Break Out – Potential Answers

- Available Health budget?
- How many doctors available?
- How many nurses available?
- Do we have enough hospital beds?
- Are the ICUs full?

- And many more

IQWIG/G-BA Assessment Categories

		Outcome category			
		All-cause mortality	**Serious *(or severe)* symptoms *(or late complications)* and adverse effects**	***Health-related quality of life***	**Non-serious *(or non-severe)* symptoms *(or late complications)* and adverse effects**
Extent category	**Major** **sustained and great improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator therapy	Major increase in survival time	Long-term freedom or extensive avoidance	*Major improvement*	*Not applicable*
	Considerable **marked improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator therapy	Moderate increase in survival time	Alleviation or relevant avoidance	*Important improvement*	Important avoidance
	Minor **moderate and not only marginal improvement** in the therapy-relevant benefit, which has not previously been achieved versus the appropriate comparator therapy	*Any increase in survival time*	*Any reduction*	*Relevant improvement*	Relevant avoidance

a. Amendments to the ANV in *italics*.
ANV: Arzneimittel-Nutzenbewertungsverordnung (Regulation for Early Benefit Assessment of New Pharmaceuticals)

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Societal Perspectives

Included cost types	Perspective					
	Patient/ household	**Health care payer**	**Health care providers**	**Healthcare sector**	**Health system** (WHO CHOICE definition)	**Societal**
Direct medical costs paid by the patients (i.e., out-of-pocket payments)	Y	N	N	Y	Y	Y
Direct medical costs paid by the health care payer/providers	N	Y (but only those incurred by the payer)	Y	Y	Y	Y
Direct non-medical costs incurred by patients (such as for travel, food, and accommodation)	Y	N	N	N	N	Y
Productivity costs (e.g., monetized productivity losses from patients and their caregivers)	Varies	N	N	N	N	Varies
Non-health sector costs (e.g., spillover impacts affecting other sectors such as education, criminal justice, etc.)	N	N	N	N	Included to the degree that they are a direct component of the intervention intended to improve human health	Depending on whether it is a limited societal or societal perspective*

Sittimart M, Rattanavipapong W, Mirelman AJ, Hung TM, Dabak S, Downey LE, Jit M, Teerawattananon Y, Turner HC. An overview of the perspectives used in health economic evaluations. Cost Eff Resour Alloc. 2024 May 14;22(1):41. doi: 10.1186/s12962-024-00552-1. PMID: 38741138; PMCID: PMC11092188.

Decision Making from a Societal Perspective in a Pandemic

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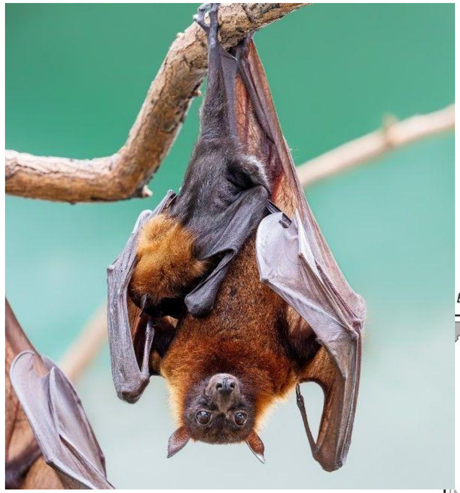
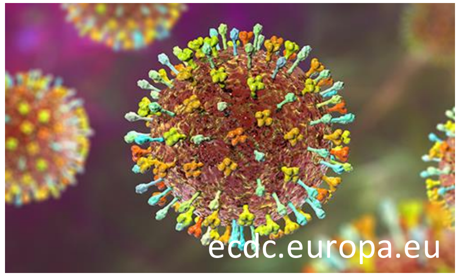
Decision Relevant Topics (select)	Lead questions involved
Diagnosis	Can we detect the pathogen?
Treatment	Are there treatments available for patients?
Prevention	Which measures can prevent or reduce transmission?
Resource allocation	**How to assure that scarce healthcare and other resources are available for the population?**
Societal stability	How to preserve civilian peace in the population?
Economic stability	How to keep up the gross domestic product?
Health budgets	**How to finance the health care of the pandemic?**

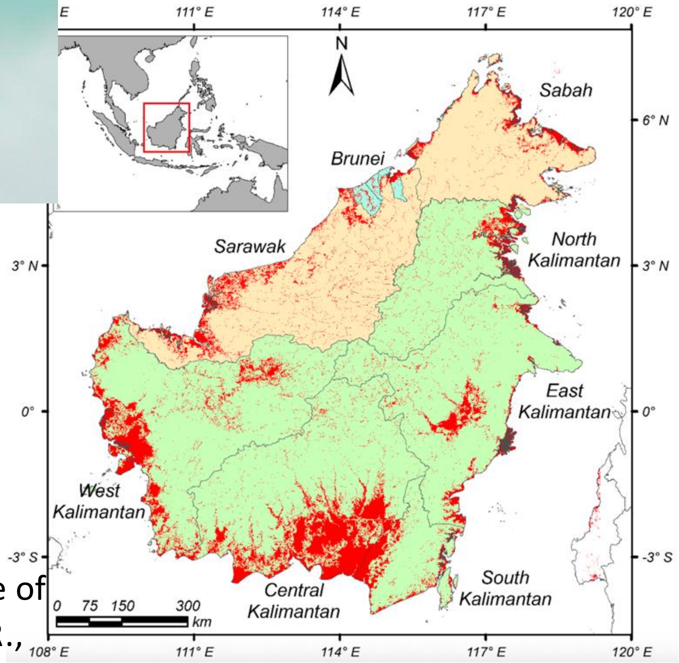
Decision Support – Relevant Aspects

Pandemic Candidate Virus Nipah

- Nipah virus (NiV, *Henipavirus nipahense*) is a zoonotic pathogen
- Pteropus fruit bats are the natural reservoir for NiV
- First outbreak in pig farmers in Malaysia 1998
- 1997 exceptional large wild fires in Borneo, Spread of bats over coastal regions of Asia

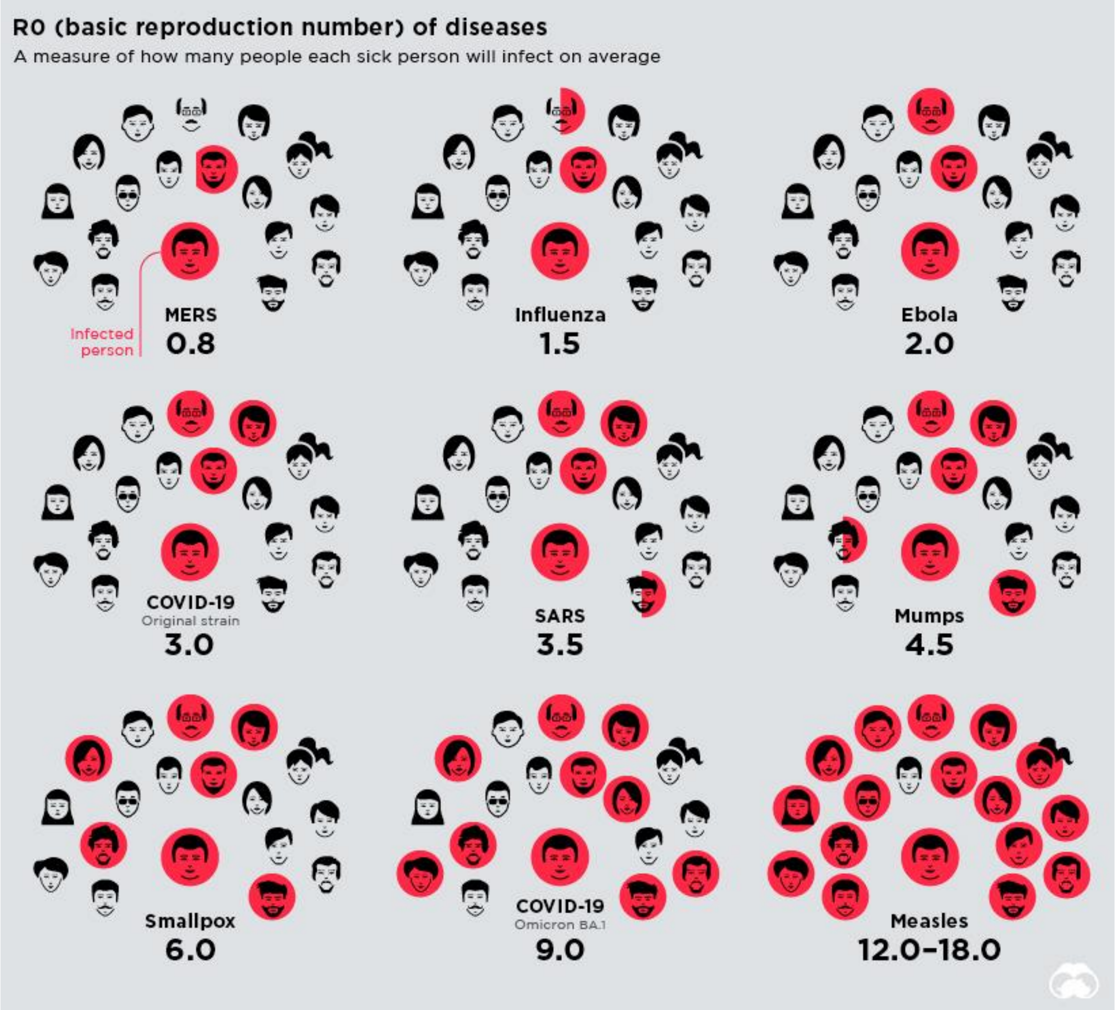




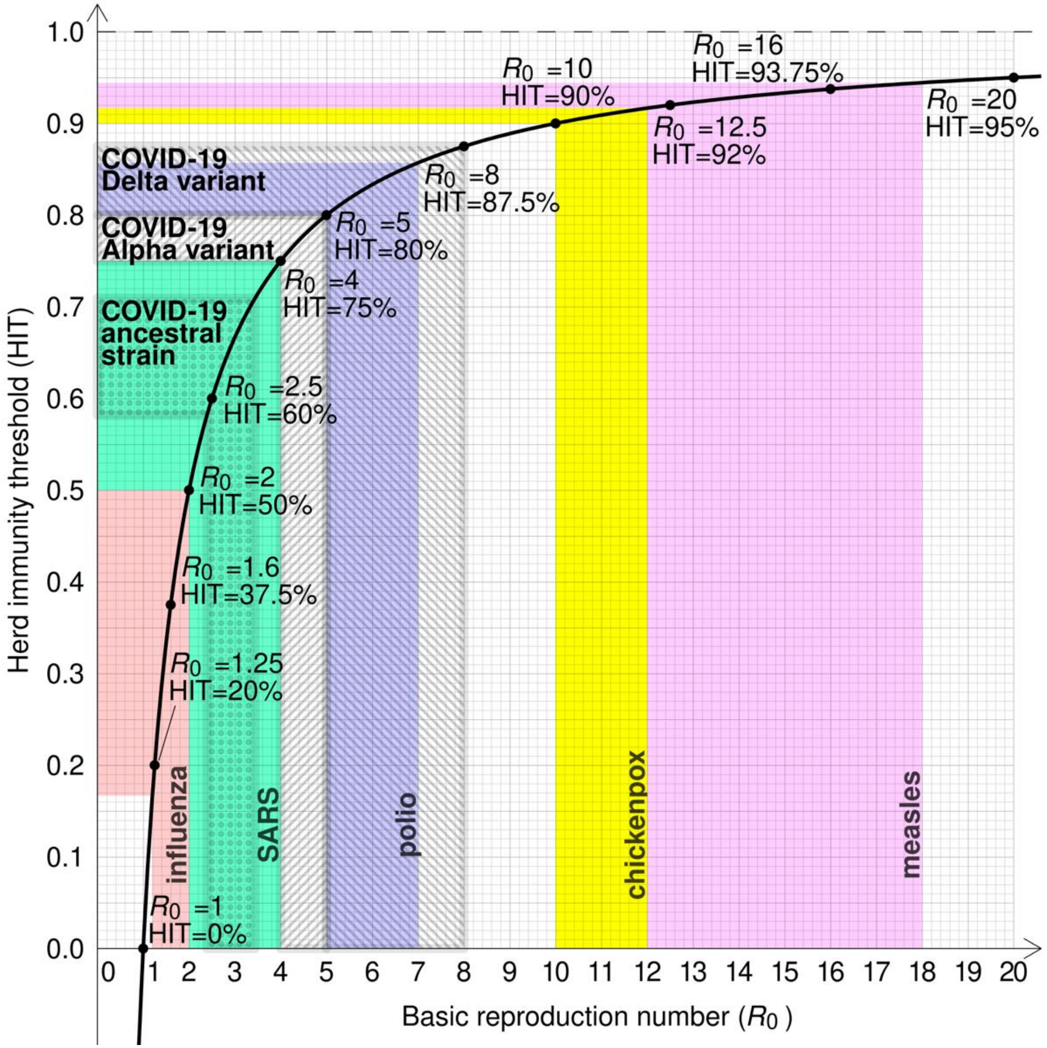


Pulliam JR, Epstein JH, Dushoff J et al. 2012. Agricultural intensification, priming for persistence and the emergence of Nipah virus: a lethal bat-borne zoonosis. Journal of the Royal Society. Interface. 9 (66) 89-101. Shiraishi, T., Hirata, R., Hayashi, M. et al. Carbon dioxide emissions through land use change, fire, and oxidative peat decomposition in Borneo. Sci Rep 13, 13067 (2023). https://doi.org/10.1038/s41598-023-40333-z.

R0 – Basic Reproduction Number



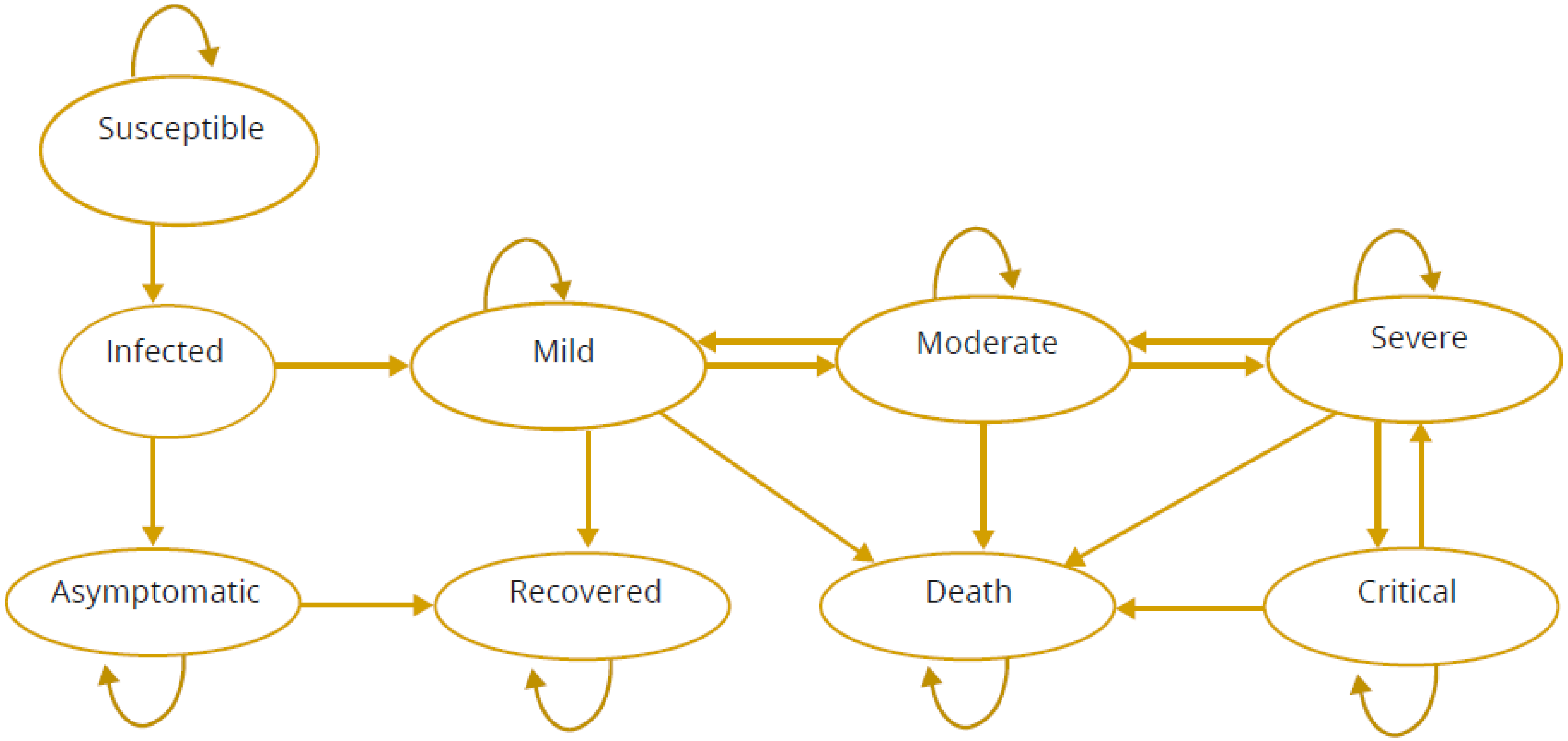
Herd Immunity and R0



Examples of Pandemic Models

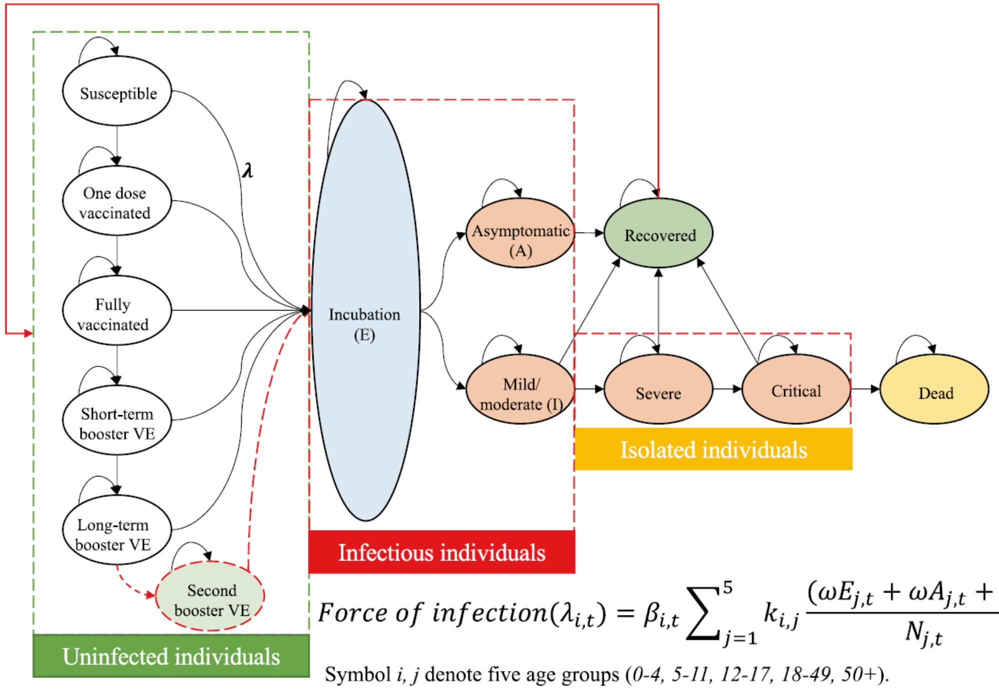
COVID-19 Modelling – Mild Moderate Severe

Figure 1. Markov model structure.



Okafor CE, Keramat SA, Balasooriya NN, Dioji EH. Are Updated COVID-19 Vaccines Still Relevant for All Adult Age Groups? An Economic Evaluation of the Monovalent XBB.1.5 Vaccine in Australia. *Value Health*. 2025;28(5):730-741. doi:10.1016/j.jval.2025.01.014

COVID-19 Modelling - Vaccination



$$Force\ of\ infection(\lambda_{i,t}) = \beta_{i,t} \sum_{j=1}^{5} k_{i,j} \frac{(\omega E_{j,t} + \omega A_{j,t} + I_{j,t})}{N_{j,t}}$$

Symbol *i, j* denote five age groups (*0-4, 5-11, 12-17, 18-49, 50+*).

Fig. 1 Schematic overview of the SEIR-Markov model. The $\lambda_{i,t}$ the parameter of the force of infection to measure the infection risk. The symbols *i,j* denote five age groups (0–4 years, 5–11 years, 12–17 years, 18–49 years, and 50+ years). The $\beta_{i,t}$ denotes the transmission coefficient of five age groups and the $k_{i,j}$ represents the contact metric between age groups

Li R, Lu P, Fairley CK, et al. Cost-Effectiveness of the Second COVID-19 Booster Vaccination in the USA. *Appl Health Econ Health Policy*. 2024;22(1):85-95. doi:10.1007/s40258-023-00844-2

COVID-19 Modelling - Vaccination

- Di Fusco M, Marczell K, Deger KA, et al. Public health impact of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) in the first year of rollout in the United States. *J Med Econ*. 2022;25(1):605-617. doi:10.1080/13696998.2022.2071427

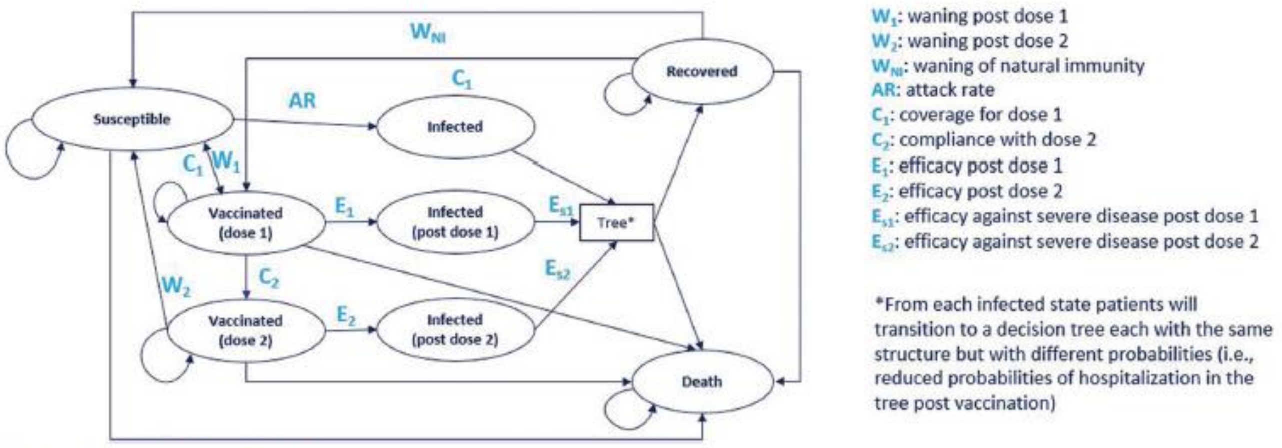


Figure 1. Structure of the Markov model.

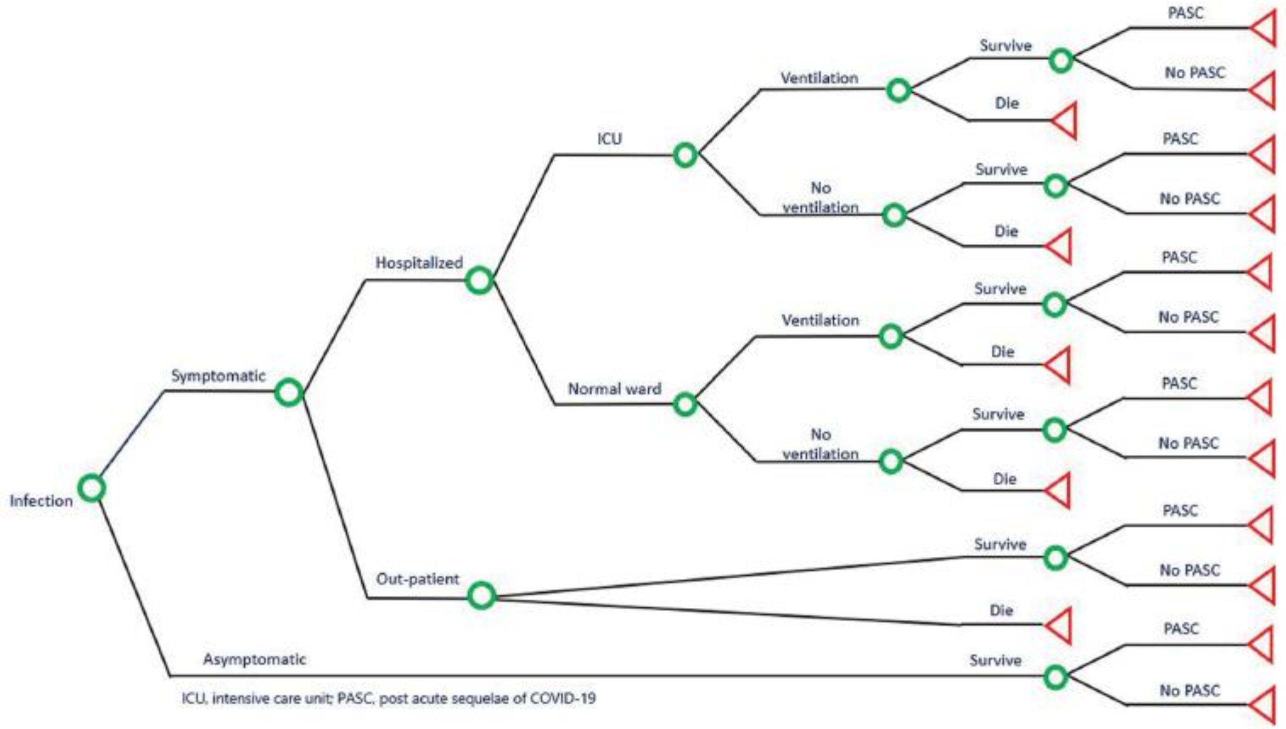


Figure 2. Decision tree for the probabilities of COVID-19 symptoms and sequelae.

COVID-19 Modelling Resource Use

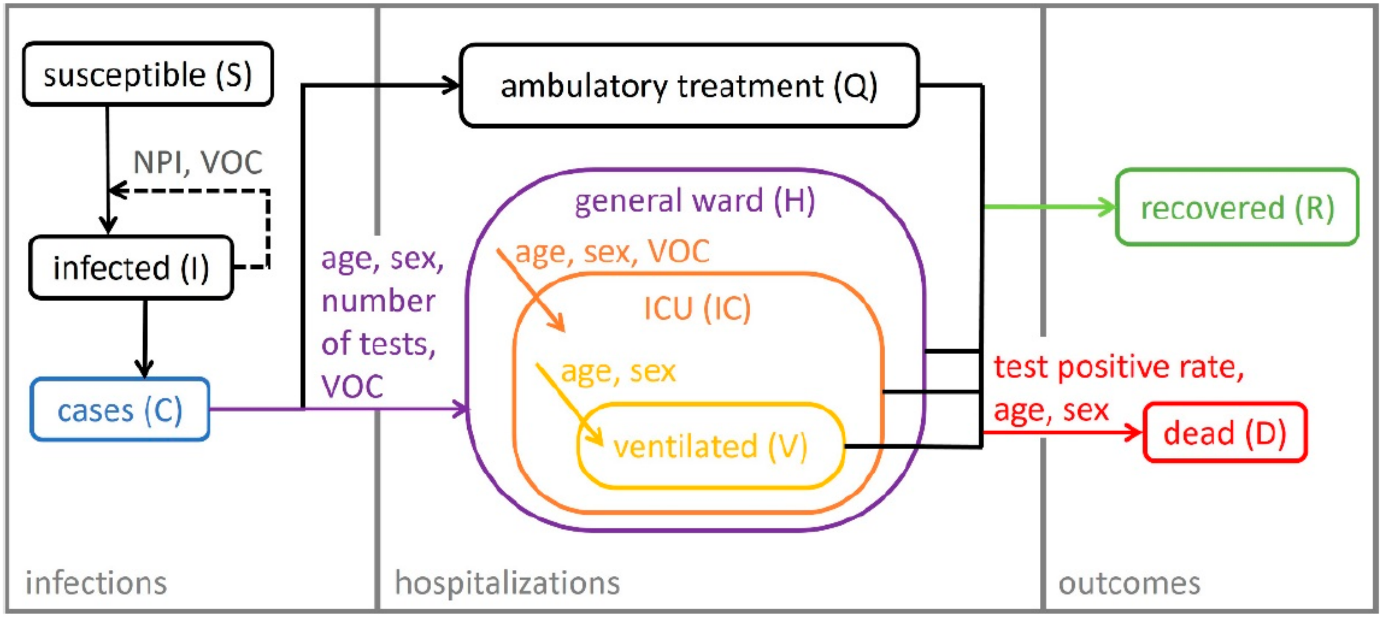


Figure 1. Schematic representation of the epidemiological compartment model. Solid arrows indicate the flow of individuals between compartments during the infection/disease process. Covariates influencing the flow rates are assigned to the respective arrows. Dashed arrows indicate the influence of a compartment value on the rates. NPI: non-pharmaceutical interventions, VOC: fraction of cases infected with the variant of concern B.1.1.7, number of tests: number of weekly performed PCR tests in Germany.

Dings C, Götz KM, Och K, et al. Model-Based Analysis of SARS-CoV-2 Infections, Hospitalization and Outcome in Germany, the Federal States and Districts. *Viruses*. 2022;14(10):2114. Published 2022 Sep 24. doi:10.3390/v14102114

COVID-19 Modelling – Resource Use

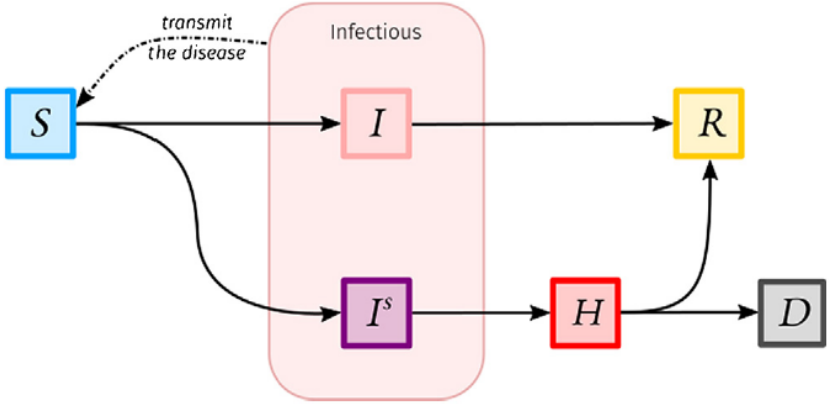


Fig. 1. Illustrative compartmental model to estimate hospital occupancy. Susceptible individuals (*S*compartment) become infected after being in contact with infected individuals. They can develop an asymptomatic or mild version of the disease (*I*) before recovering (*R*), or they can become severely infected (I^s). In the latter, they will transmit the disease as the other infected individuals then end up in the hospital (*H*) before recovery or death (*D*).

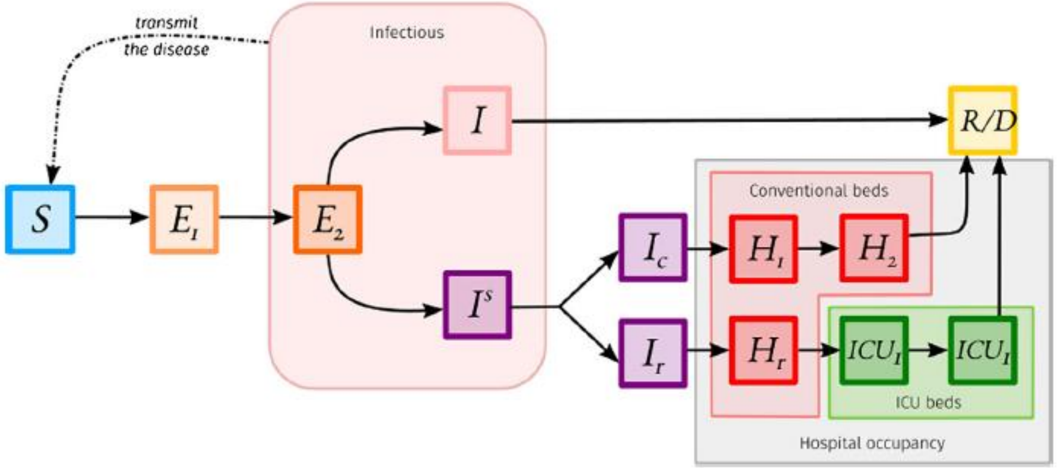


Fig. 3. The model used by Ref. [10] to estimate the hospital conventional beds occupancy and ICU beds occupancy. In this model, individuals can be either susceptible (*S*), exposed (*E*), infected but not hospitalised (*I*), hospitalised in conventional beds (*H*), hospitalised in ICU (*ICU*) or removed (*R*/*D*).

Reyné B, Saby N, Sofonea MT. Principles of mathematical epidemiology and compartmental modelling application to COVID-19. *Anaesth Crit Care Pain Med*. 2022;41(1):101017. doi:10.1016/j.accpm.2021.101017

COVID-19 Modelling Decision Analytic

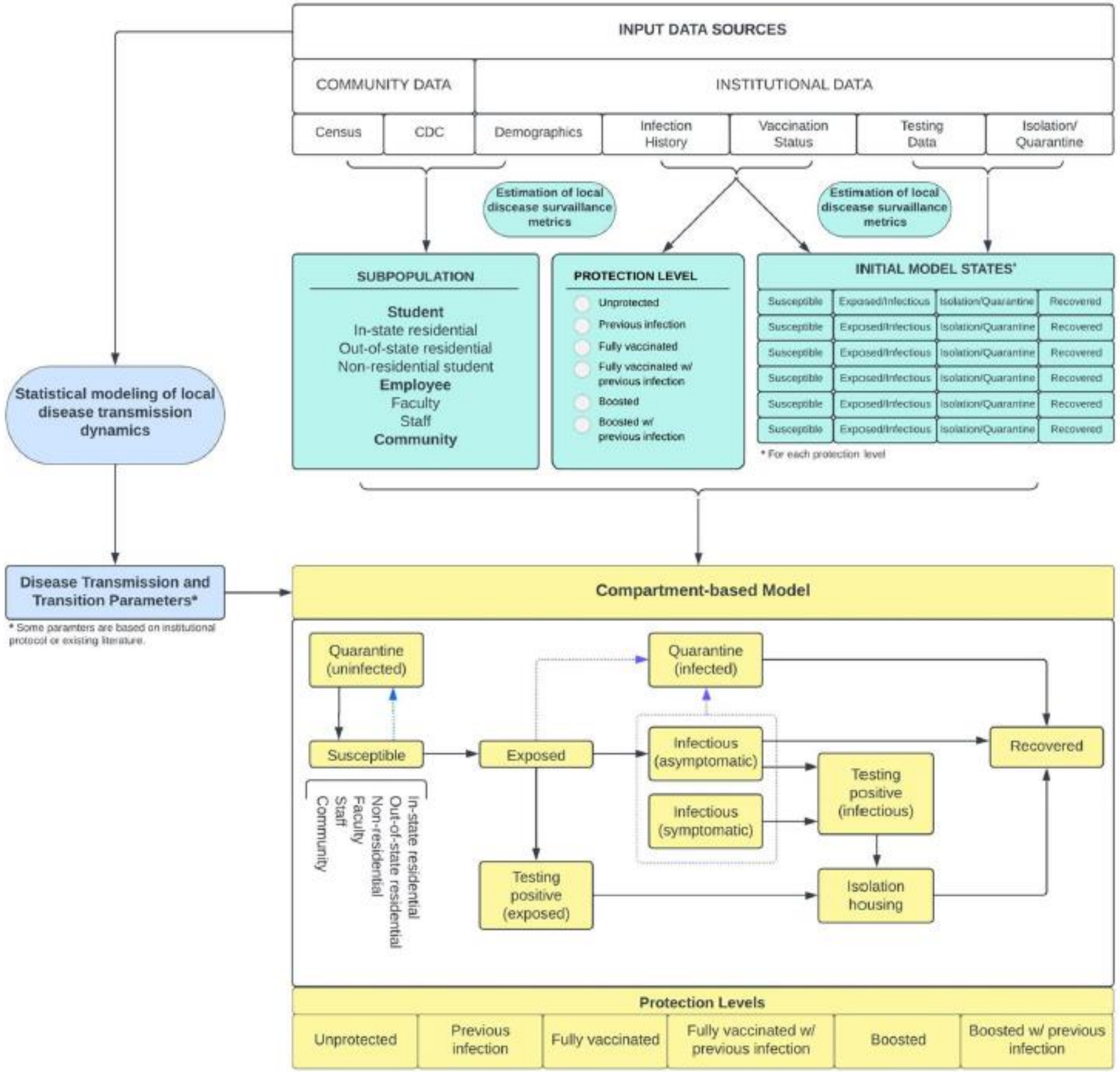
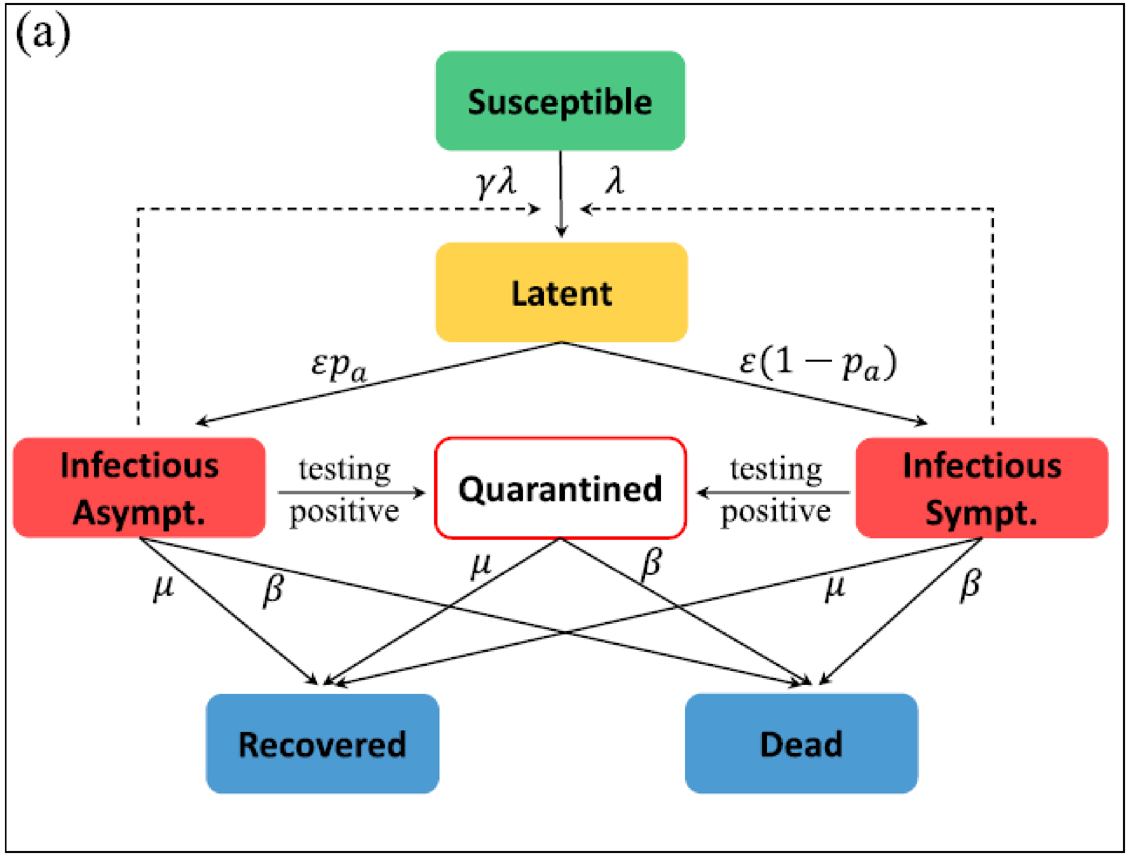


Figure 1. Modeling framework. The modeling framework of the toolkit includes estimating local disease surveillance metrics, statistical modeling of local disease transmission dynamics, and compartment-based modeling framework for Covid-19 prediction based on estimated input parameters and publicly available data.

Ma Z, Rennert L. An epidemiological modeling framework to inform institutional-level response to infectious disease outbreaks: a Covid-19 case study. *Sci Rep*. 2024;14(1):7221. Published 2024 Mar 27. doi:10.1038/s41598-024-57488-y

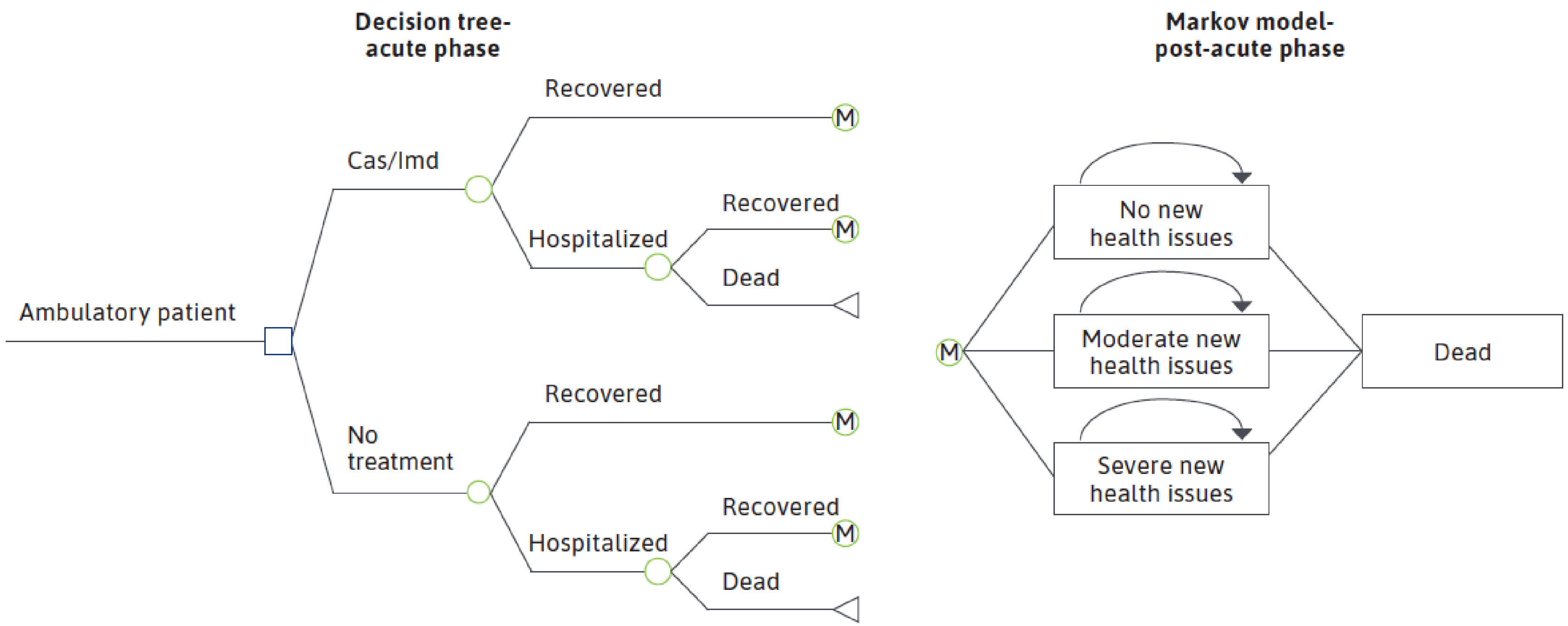
COVID-19 Modelling – Testing & Quarantine



Cui Y, Ni S, Shen S. A network-based model to explore the role of testing in the epidemiological control of the COVID-19 pandemic. *BMC Infect Dis*. 2021;21(1):58. Published 2021 Jan 12. doi:10.1186/s12879-020-05750-9

COVID-19 Modelling – Health Economic

FIGURE 1 Cost-Effectiveness Model Structure



In the base case, the proportion of patients with no health issues is set to 100% in all Markov simulations. In scenario analyses, the proportion of patients with moderate and severe health issues is set at 10% and 10%, respectively, but only in the Markov simulation after hospitalization.

Jovanoski N, Kuznik A, Becker U, Hussein M, Briggs A. Cost-effectiveness of casirivimab/imdevimab in patients with COVID-19 in the ambulatory setting. *J Manag Care Spec Pharm*. 2022;28(5):555-565. doi:10.18553/jmcp.2022.21469

COVID-19 Modelling – Cost Effectiveness

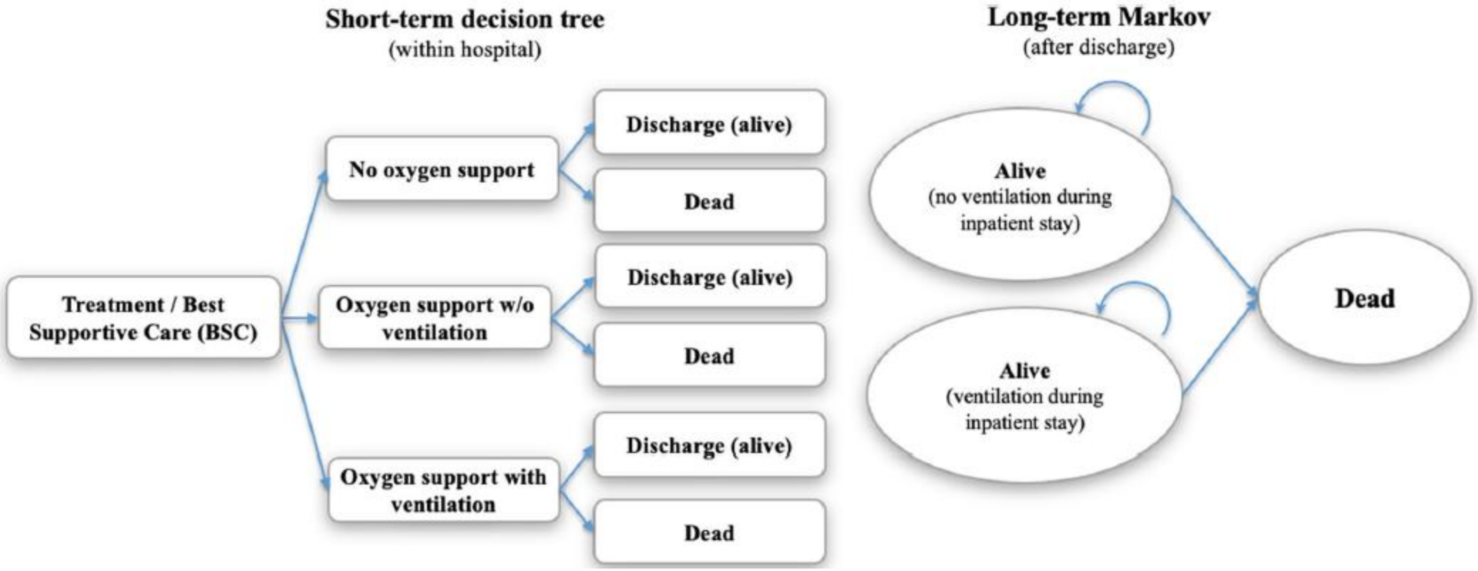


Fig. 1 Model structure. Patients in the 'Alive (no ventilation during inpatient stay)' state comprise patients discharged alive from the 'no oxygen support' and the 'oxygen support without ventilation' states. Patients in the 'Alive (ventilation during inpatient stay)' state represent patients discharged alive from the 'oxygen support with ventilation' state. Ventilation in the model refers to invasive mechanical ventilation. BSC = best supportive care; w/o = without

Sheinson D, Dang J, Shah A, Meng Y, Elsea D, Kowal S. A Cost-Effectiveness Framework for COVID-19 Treatments for Hospitalized Patients in the United States. *Adv Ther*. 2021;38(4):1811-1831. doi:10.1007/s12325-021-01654-5

COVID-19 Modelling – Decision Analytic

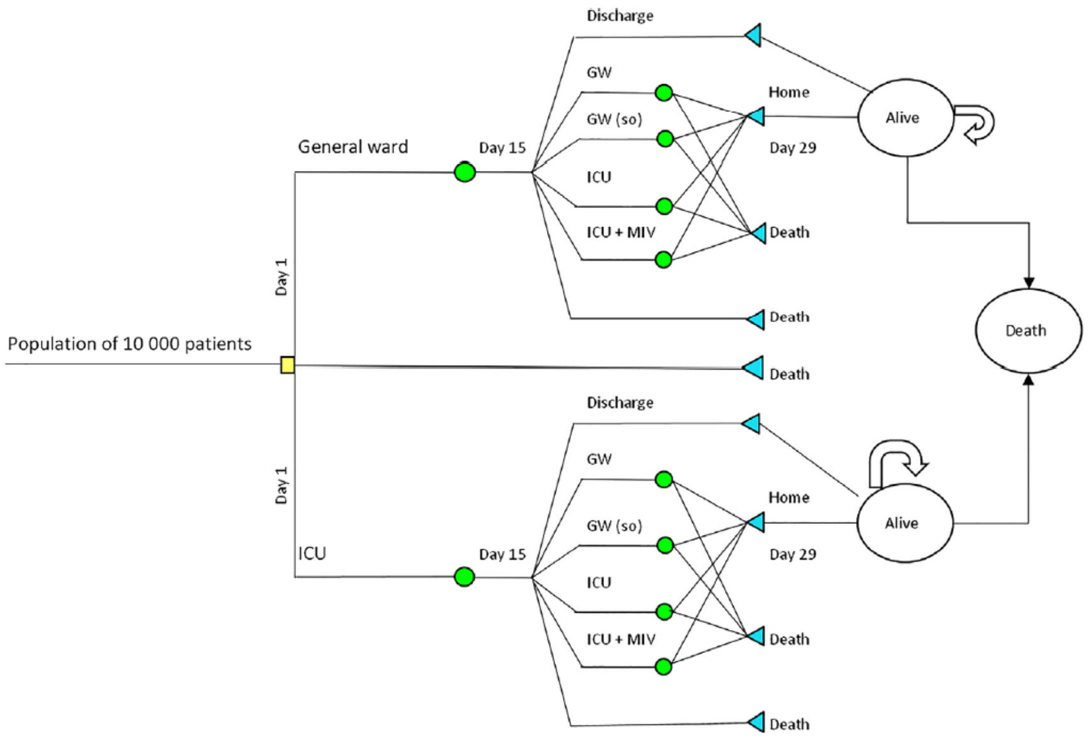
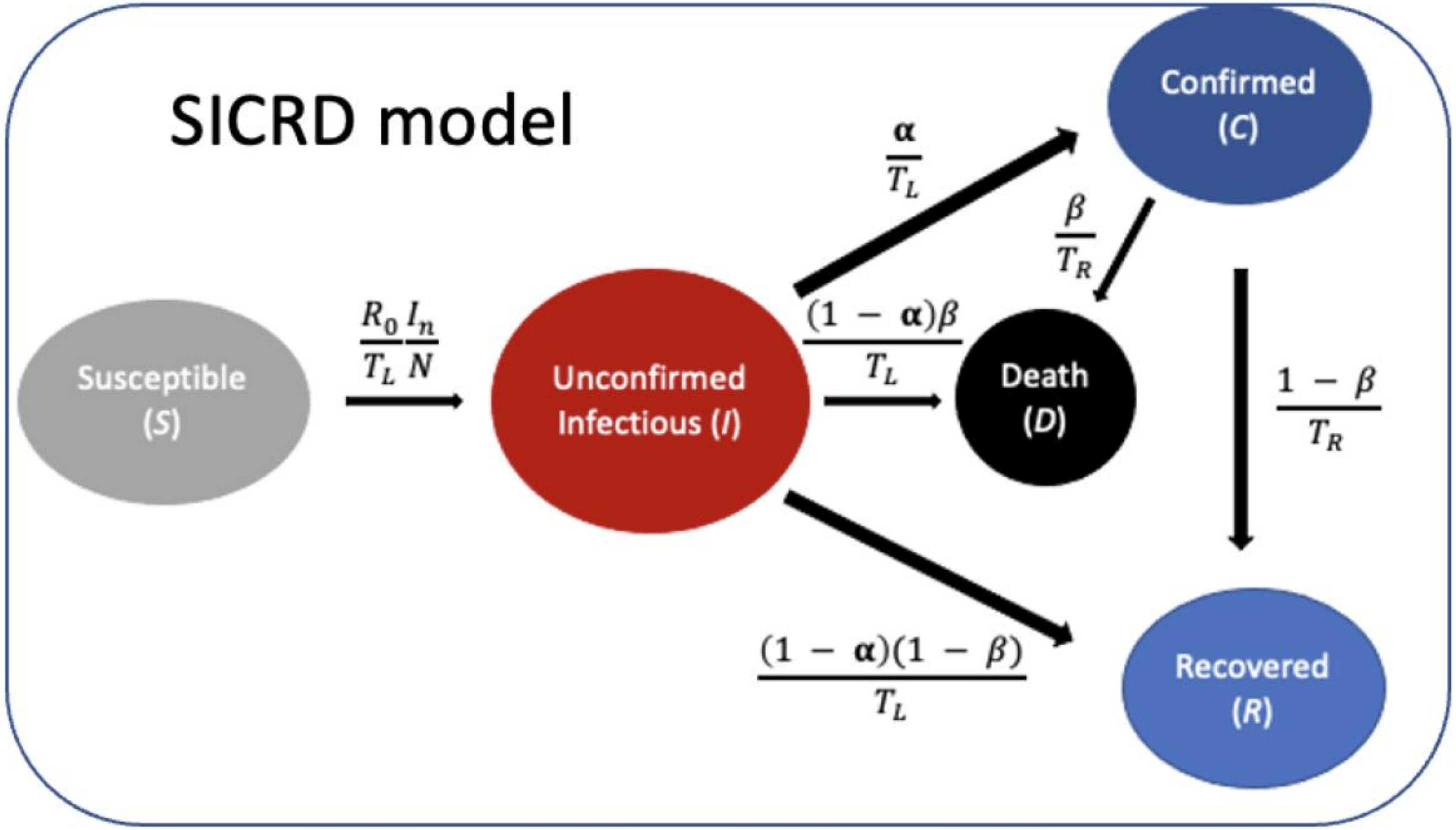


Figure 1. Outline of the model. GW = general ward; ICU = intensive care unit; MIV = mechanical invasive ventilation; so = supplemental oxygen.

Athanasakis K, Zisis K, Tsoulas C, Nomikos N. Cost-effectiveness Analysis and Impact on Length of Hospital Stay of the Introduction of Remdesivir as a Treatment Option for Hospitalized Patients With COVID-19 Requiring Supplemental Oxygen in Greece Versus Standard of Care. *Clin Ther*. 2023;45(12):1244-1250. doi:10.1016/j.clinthera.2023.09.023

Questionable Examples of Pandemic Models ?

SICRD?



Hu H, Kennedy CM, Kevrekidis PG, Zhang HK. A Modified PINN Approach for Identifiable Compartmental Models in Epidemiology with Application to COVID-19. *Viruses*. 2022;14(11):2464. Published 2022 Nov 7. doi:10.3390/v14112464

Quarantine - SQEIAHR?

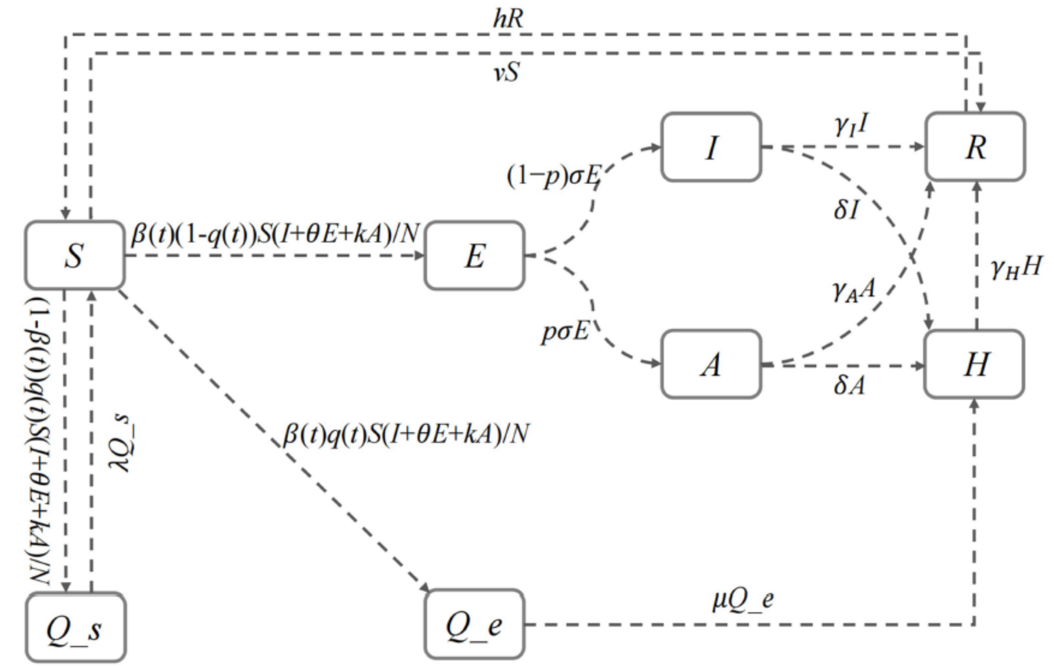


FIGURE 1
The structure of the SQEIAHR model.

TABLE 1 Descriptions of the model compartments and parameters.

	Category	Description
Compartments	S	susceptible individuals
	Q_s	quarantined susceptible individuals
	E	exposed individuals with no symptoms who transmit the virus
	Q_e	quarantined exposed individuals
	I	confirmed cases that show typical clinical symptoms
	A	asymptomatic infections that do not show typical clinical symptoms or corresponding CT imaging manifestations
	H	hospitalized individuals undergoing treatment
	R	recovered individuals who are still at risk of becoming susceptible

Ma Y, Xu S, Luo Y, et al. Epidemiological characteristics and transmission dynamics of the COVID-19 outbreak in Hohhot, China: a time-varying **SQEIAHR** model analysis. *Front Public Health*. 2023;11:1175869. Published 2023 Jun 21. doi:10.3389/fpubh.2023.1175869

Level of Complexity?

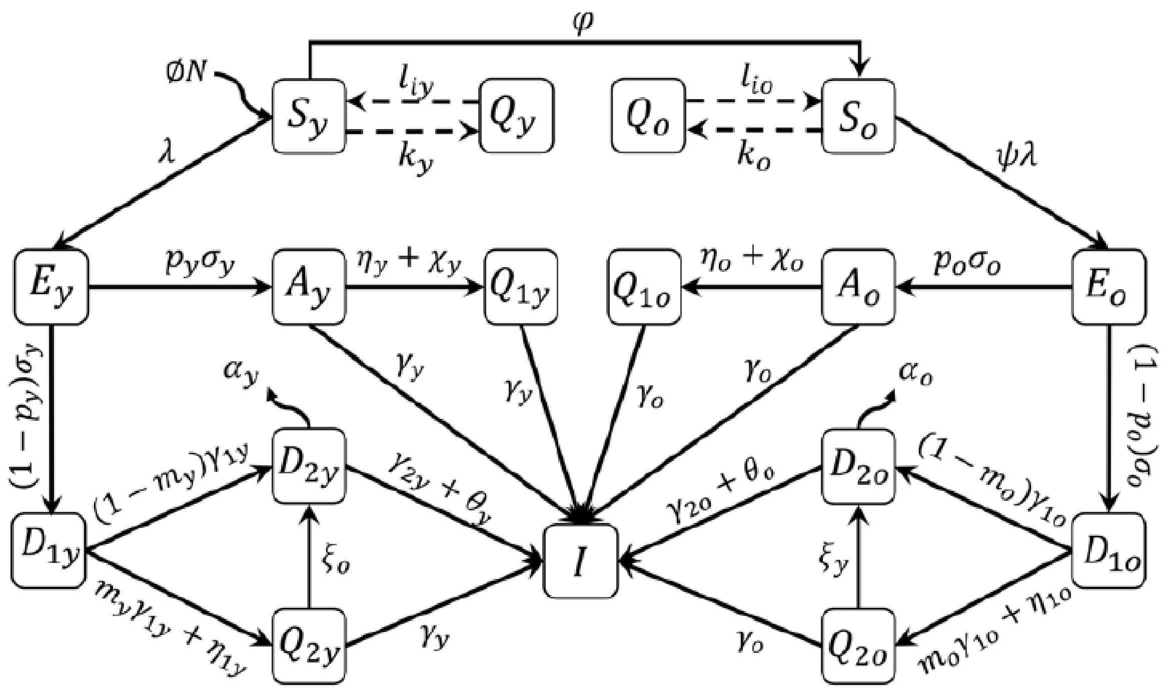


Fig. 1. Flowchart of the new coronavirus transmission model with variables and parameters.

Table 1. Summary of the model variables for young (y)(y) and elder (o) subpopulations

Symbol	Meaning
S_j	Susceptible persons
Q_j	Susceptible persons in isolation
E_j	Incubating new coronavirus persons
A_j	Asymptomatic persons
Q_{1j}	Asymptomatic persons caught by a test in isolation
D_{1j}	Pre-symptomatic (pre-diseased) persons
Q_{2j}	Pre-diseased persons caught by test in isolation
D_{2j}	Severe CoViD-19 persons
I	Immune (recovered) persons

Yang HM, Lombardi Junior LP, Castro FFM, Yang AC. Mathematical model describing CoViD-19 in São Paulo, Brazil - evaluating isolation as control mechanism and forecasting epidemiological scenarios of release. *Epidemiol Infect*. 2020;148:e155. Published 2020 Jul 20. doi:10.1017/S0950268820001600

Artificial Intelligence?

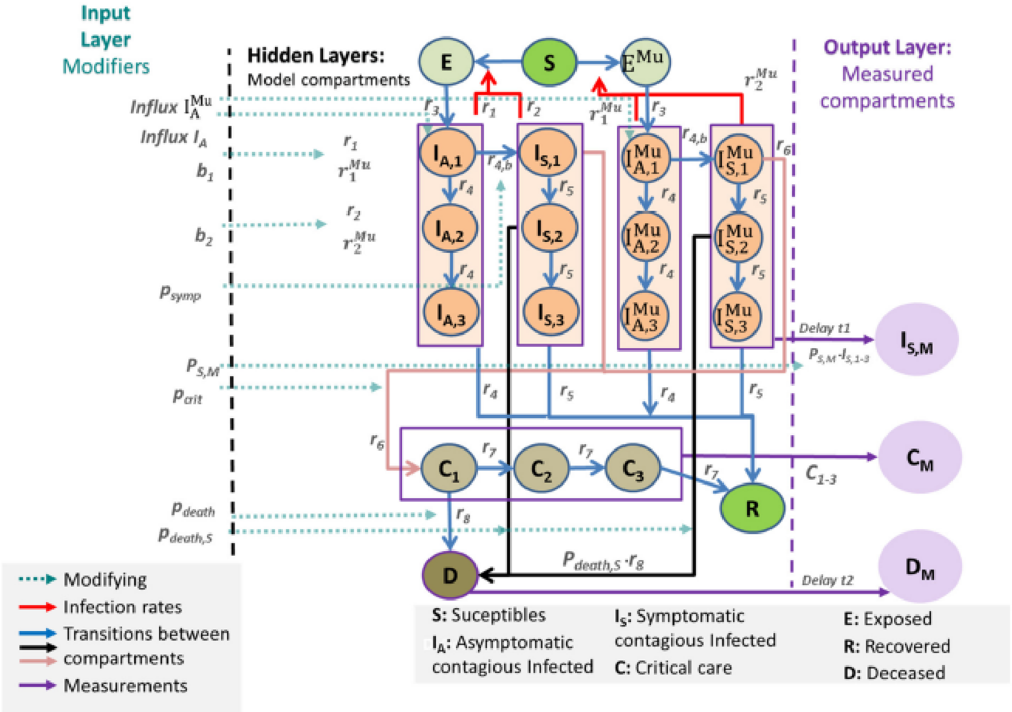


Figure 1. General scheme of our IO-NLDS model. The epidemiologic SECIR model is integrated as a hidden layer. Respective equations are provided in Appendix A. The input layer consists of external modifiers including parameter changes due to changes in testing policy, non-pharamceutical interventions, and age-structures. The output layer is derived from respective hidden layers via stochastic relationships (see later). The output layer is compared with real-world data. The superscript Mu denotes new virus variants.

Kheifetz Y, Kirsten H, Scholz M. On the Parametrization of Epidemiologic Models-Lessons from Modelling COVID-19 Epidemic. *Viruses*. 2022;14(7):1468. Published 2022 Jul 2. doi:10.3390/v14071468

Relevant literature

- Agusto FB. Mathematical model of Ebola transmission dynamics with relapse and reinfection. *Math Biosci*. 2017;283:48-59. doi:10.1016/j.mbs.2016.11.002
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