An Introduction to Deterministic Infectious Disease Models. (n.d.). https://documents1.worldbank.org/curated/en/888341625223820901/pdf/An-Introduction-to-Deterministic-Infectious-Disease-Models.pdf

* Deterministic models are flexible enough to capture complex things, and simple enough to be understood by policy makers
* Can be preferred to stochastic or black-box models
* Used to understand why there are surges and the behaviors of spread early during an outbreak
* Three groups of people: susceptible (not exposed/affected yet), infected (both infected and infectious), and recovered (now immune)
* Going from susceptible to infected depends on disease transmission rate
* The rate of change of either state can be described using differential equations
* In the equations above, is the population, is the transmission rate, and is the recovery rate
* is the product of the average number of contacts at a given time per individual and the probability of transmission between susceptible and infected
* is the inverse of the infections period (i.e., it is the one divided by the average time of being infectious)
* One strategy is to minimize the transmission rate
  + Some examples include reducing contact with others, reducing the probability of transmission, etc.
* Another strategy is to minimize the infectious period, or maximize the recovery rate
* The reproduction ratio (average secondary infections divided by average primary infections) denoted by indicates if an outbreak is likely
  + In other words, we can think about this in terms of the recovery rate and transmission rate such that
  + We can continue to calculate this ratio as time passes, , which describes the outbreak in the current time
  + This reproduction ratio can be derived for many models besides SIR
* Vaccinations effectively move people from the susceptible group directly to the recovered group
  + This changes the initial reproduction ratio since the number of susceptible people at time zero is not equal to the population, hence (in the non-vaccinated case which is why the equation was simplified previously)
* The proportion of people that must be vaccinated to avoid an outbreak can be derived as
  + Alternatively, we can simplify this proportion to
* We can also account for mortality and birth rates, where is the mortality rate and is the birth rate
  + Historically, these things are usually equal
* Considering birth and mortality rates, the updated differential equations are
* And we must consider these new variables with the reproduction rate

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* Note that the number of vaccinated people to avoid an outbreak will be lower (i.e., the ratio of recovered people to the population need not be as big) because the reproduction rate at time zero will be smaller
* In summary, in the most simple form, infectious diseases can be modeled using a framework of three groups (susceptible, infected, and recovered) and a few different rates (reproduction, recovery, mortality, and birth rates), some of which are assumed, and others can be derived from the data itself
* There is s four compartment model called SEIR (susceptible, exposed, infected, and recovered), which has been used to describe COVID-19 and Ebola
* Where is the latent period and

Apolloni, A., Poletto, C., Ramasco, J. J., Jensen, P., & Colizza, V. (2014). Metapopulation epidemic models with heterogeneous mixing and travel behaviour. Theoretical Biology and Medical Modelling, 11(1). https://doi.org/10.1186/1742-4682-11-3

Arias-Reyes, C., Carvajal-Rodriguez, F., Poma-Machicao, L., Aliaga-Raduán, F., Marques, D. A., Zubieta-DeUrioste, N., Accinelli, R. A., Schneider-Gasser, E. M., Zubieta-Calleja, G., Dutschmann, M., & Soliz, J. (2021). Decreased incidence, virus transmission capacity, and severity of COVID-19 at altitude on the American continent. PLOS ONE, 16(3), e0237294. <https://doi.org/10.1371/journal.pone.0237294>

* Infection rate might be lower in people living in high altitude for COVID-19
* Beginning at 1000 meters above sea level, the incidence rate begins to decrease for COVID
* Furthermore, transmission rates are lower at these elevation levels
* Finally, the severity of infections is lower at these altitudes (e.g., death-to-case ratio is lower, recovery percentage is higher, etc.)
* Possible explanations include more drastic changes in temperature between day and night, higher air dryness, higher solar radiation, long-term exposure to barometrical hypoxia (less oxygen at high altitude)
* This study did not consider different risk factors for different groups (e.g., sex, age, comorbidities, etc.)

‌Berkessel, J. B., Ebert, T., Gebauer, J. E., Jonsson, T., & Oishi, S. (2021). Pandemics Initially Spread Among People of Higher (Not Lower) Social Status: Evidence From COVID-19 and the Spanish Flu. Social Psychological and Personality Science, 194855062110399. <https://doi.org/10.1177/19485506211039990>

* Pandemics are thought to spread particularly through lower social status groups
* The hypothesis is that this is true for the later stages of pandemics
* This was analyzed over two studies: first analyzing region-level COVID-19 infection data, and second by analyzing historic data from the 1918 Spanish Flue pandemic
* For both, disease spread more rapidly through people of higher social status first, and in later stages this reverses

‌Colizza, V., Barrat, A., Barthelemy, M., Valleron, A.-J., & Vespignani, A. (2007). Modeling the Worldwide Spread of Pandemic Influenza: Baseline Case and Containment Interventions. PLoS Medicine, 4(1), e13. <https://doi.org/10.1371/journal.pmed.0040013>

* H5N1 avian influenza virus is a potential candidate for a severe pandemic
* Studied spread using metapopulation stochastic epidemic model on a global scale
* Model considers air travel flow among urban areas
* Temporal and spatial evolution with sensitivity analysis
* Compared different containment strategies against a base case (e.g., travel restrictions and antiviral drugs)
* Considering air travel is vital when modeling these epidemics
* Large-scale application of antivirals seems possible and would effectively mitigate some of the spread
* Used metapopulation stochastic epidemic model on a global scale
* Considering airline travel among urban areas
* Compared baseline with containment strategies such as travel restrictions and antiviral drugs
* Considered that not all areas have similar stockpiles of antiviral drugs
  + One scenario is that wealthy nations keep their antiviral medications
  + Another scenario is that these nations collectively allocate smaller stockpiles for global consumption
* Air travel is crucial in assessing the probability of transmission
* Readily available antiviral medication in hit countries could accommodate a reproduction rate of 1.9
* Furthermore, the more cooperative nations are in containment efforts, the more effective the containment is

Cooper, B. S., Pitman, R. J., Edmunds, W. J., & Gay, N. J. (2006). Delaying the International Spread of Pandemic Influenza. PLoS Medicine, 3(6), e212. <https://doi.org/10.1371/journal.pmed.0030212>

* Hypervirulent subtypes of flu are emerging
* Efficient spread through humans would be problematic
* Control would be limited by availability of vaccines
* Key measure would be to delay spread
* Higher international travel could lead to faster global spread than previous pandemics
* Analysis involves stochastic models of the internation spread of influenza based on extensions of coupled epidemic transmission models
* Restrictions on air travel demonstrate little values on delaying the spread of virus
* Only ceasing all travel has a significant impact on preventing the epidemic
* Local transmission control measures are better methods for controlling the spread of disease

Débarre, F. (n.d.). SIR models of epidemics Level 1 module in “Modelling course in population and evolutionary biology.” https://ethz.ch/content/dam/ethz/special-interest/usys/ibz/theoreticalbiology/education/learningmaterials/701-1424-00L/sir.pdf

* We are assuming that we can divide the population into groups
* Also, we assuming that encounters between infected and susceptible individuals occur at a rate proportional to their respective numbers in the population (this is the component)
* We can use this for a “closed” system, meaning there is no immigration or emigration
* It is not necessary to consider death rate since the time scale of influenza pandemics is usually short
* Here is an R script to solve to implement this model:

library("deSolve")

parameters <- list(beta = 1e-3, r = 1e-1)

initial\_conditions <- c(S = 499, I = 1, R = 0)

timepoints <- seq(0, 100, 0.1)

sir\_model <- function(t, x, parameters) {

with(as.list(c(parameters, x)), {

dS <- -beta \* S \* I

dI <- +beta \* S \* I - r \* I

dR <- r \* I

der <- c(dS, dI, dR)

return(list(der))

})

}

sir\_simulation <- as.data.frame(

lsoda(

y = initial\_conditions,

times = timepoints,

func = sir\_model,

parms = parameters

)

)

* Intuitively, a disease-free state is one where there are no members of the infected or recovered state and the susceptible state comprises the entire population
* There are some useful exercise in this paper that might be worthwhile checking out

Eubank, S., Guclu, H., Anil Kumar, V. S., Marathe, M. V., Srinivasan, A., Toroczkai, Z., & Wang, N. (2004). Modelling disease outbreaks in realistic urban social networks. Nature, 429(6988), 180–184. <https://doi.org/10.1038/nature02541>

* Lost of models use differential equations or ad hoc models for the contact process
* This paper uses dynamic bipartite graphs to model physical contact patterns that result from individuals moving from location to location
* Based on large-scale individual-based urban traffic simulations
* Contact patterns are fairly localized
* Placing sensors in travel hub is, therefore, an efficient way of detecting outbreaks early on
* Containment can be achieved through early detection and targeted vaccination
* This was all done within a simulation tool called EpiSims

Ferguson, N. M., Cummings, D. A. T., Cauchemez, S., Fraser, C., Riley, S., Meeyai, A., Iamsirithaworn, S., & Burke, D. S. (2005). Strategies for containing an emerging influenza pandemic in Southeast Asia. Nature, 437(7056), 209–214. https://doi.org/10.1038/nature04017

* Different strains of virus can represent large threats for pandemics, and in the case of this paper the virus examined is H5N1
* The objective is to understand its spreading pattern to identify public health interventions to stop the spread and avoid a pandemic if it were to be human-transmissible
* Specifically, the paper looks at mass use of antiviral medication for prevention (i.e., not using antivirals after infection but before) in targeted locations
* Additionally, the authors consider the use of social distancing measures to limit the contact rate between individuals
* Using these measures, and assuming that the reproduction ratio is less than 1.8, it is feasible that three million courses of antiviral drugs and social distances should be able to curb a pandemic
* This paper modeled the spread of influenza only in southeast Asia, however
* The transmission model was a stochastic, spatially structured, individual-based discrete time simulations
* The authors used rigorous estimates of antiviral estimates (not performed by them) and used parameter estimates from previous flu pandemics
* Sensitivity analysis was used to evaluate how deviating from these parameters would have on a particular policy’s effectiveness
* Infectiousness was modeled as a function rather than a constant (which is what most other approaches do)

Germann, T. C., Kadau, K., Longini, I. M., & Macken, C. A. (2006). Mitigation strategies for pandemic influenza in the United States. Proceedings of the National Academy of Sciences, 103(15), 5935–5940. https://doi.org/10.1073/pnas.0601266103

* Again, H5N1 represents the possibility of having another Spanish influenza pandemic
* Here, authors are using a stochastic model to examine spread patterns in the USA given reproduction ratios between 1.6 to 2.4
* Antiviral agents, vaccination, school closures, social distances, etc. were examined in the modeling to see what impact is on the timing and magnitude of the spread
* Travel restrictions after the outbreak has begun might slow down the spread, but will not impact the final number of infected
* Rapid vaccination can effectively slow and reduce the number of infections even if the vaccines are not particularly suited for the specific strain of influenza for reproduction ratios less than 1.9
* If children are preferentially vaccinated, this will make the outcome of lowered infections more likely
* For relatively low reproduction ratios, antiviral use is an effective method for containing an outbreak, but they must be distributed well based on good contract tracing
* However, for very high reproduction ratios, a combination of strategies is necessary to contain an outbreak

Goldstein, E., Cobey, S., Takahashi, S., Miller, J. C., & Lipsitch, M. (2011). Predicting the Epidemic Sizes of Influenza A/H1N1, A/H3N2, and B: A Statistical Method. PLoS Medicine, 8(7), e1001051. https://doi.org/10.1371/journal.pmed.1001051

* Combined data from CDC ranging from 1997 to 2009
* The magnitude of the pandemic is measured by cumulative incidence proxy (CIP)
* There is a negative association between the CIP and pandemic season (i.e., CIP gets smaller as season progresses? Building immunity?)
* Method for estimating CIP involves looking at the incidence of each strain (or its complement) and see how long it takes for the CIP to reach some threshold
* Early circulation of one strain is associated with a reduced total incidence of the other strains

Johnson, N. P. A. S., & Mueller, J. (2002). Updating the Accounts: Global Mortality of the 1918-1920 “Spanish” Influenza Pandemic. Bulletin of the History of Medicine, 76(1), 105–115. <https://doi.org/10.1353/bhm.2002.0022>

* The Spanish flu had three waves, although this was not universal across the globe
* Recorded statistic
* Figures are likely to be understated; for example, non-registration, missing records, misdiagnoses, and non-medical certification could cause data quality issues
* The degree of data quality issues could vary from location to location
* The 1920 record was 21.5 million deaths; in 1991 the range was 24.7-39.3 million; and this paper concludes 50 million
* Ian Mills established the Indian mortality rate at 18 million, hence the original 1920 estimate is very likely to be an understatement
* On interesting aspect of the Spanish flu was the heavy toll on the young adult population
* The mortality rate of the entire population is estimated between 5-10%
* These figures are not intended to be definitive however
* The method for “recalculating” these figures includes revisiting official records, and recompiling the recorded numbers and considering deaths with different causes
* Part of the problem is that there are parts of the world with little to no information about that time period

LONGINI, I. M., FINE, P. E. M., & THACKER, S. B. (1986). PREDICTING THE GLOBAL SPREAD OF NEW INFECTIOUS AGENTS. American Journal of Epidemiology, 123(3), 383–391. https://doi.org/10.1093/oxfordjournals.aje.a114253

* Most prediction of disease pattern is limited to extrapolation of current data
* Soviet scientists have developed effective techniques for predicting the spread of influenza
* The Soviet model assumes that long-distance movement of the virus requires humans, so knowing how people moving within cities and between cities is sufficient to understanding the spread across major populations
* Global application of these models was first done in 1980
* The original model involved differential equations
  + There are N different cities
  + Cities are connect and there are transportation rates between them
  + Populations are divided into four groups: susceptible, latent/incubating, infectious, and immune
* In other words, this is the SEIR model, with the extension of linking together many cities
* Some argue that the success of these models is due to the fact that Soviet cities are generally far apart and relatively isolated
* For the time period, running these algorithms was computationally expensive, so it was still impractical to use these techniques
* There are six main algorithms:
  + 1: set up the probability distribution of the infectious process among individuals
  + 2: step through the difference equations for the epidemic process in the first city to experience an epidemic
  + 3: estimate the infectious contact rate and the proportion of persons susceptible from morbidity data from the first city to experience an epidemic
  + 4: compute initial conditions for the global model on the basis of the timing of the epidemic in the first city to experience an epidemic
  + 5: move susceptible and latent individuals through the transportation network
  + 6: step through the difference equations for the pandemic process

Longini, I. M., Nizam, A., Xu, S., Ungchusak, K., Hanshaoworakul, W., Cummings, D. A. T., & Halloran, M. E. (2005). Containing Pandemic Influenza at the Source. Science, 309(5737), 1083–1087. https://doi.org/10.1126/science.1115717

Lowen AC, Steel J. 2014. Roles of Humidity and Temperature in Shaping Influenza Seasonality. J Virol 88:.https://doi.org/10.1128/jvi.03544-13

Marshall RJ, Armart P, Hulme KD, Chew KY, Brown ACHansbro PMBloxham CJ, Flint M, Ronacher K, Bielefeldt-Ohmann HGallo LA, Short KR2020.Glycemic Variability in Diabetes Increases the Severity of Influenza. mBio11:10.1128/mbio.02841-19.https://doi.org/10.1128/mbio.02841-19

Md. Samsuzzoha, Singh, M., & Lucy, D. (2013). Parameter estimation of influenza epidemic model. Applied Mathematics and Computation, 220, 616–629. <https://doi.org/10.1016/j.amc.2013.07.040>

* SEIRS and SVEIRS epidemic modes are considered here to capture the main characteristic of transmission of influenzas epidemic
* Least squares (i.e., minimizing the sum of squared differences between the measurements and the model predictions) is used to estimate the unknown parameters
* These tuned models capture the dynamic nature of the data
* Vaccine efficacy and vaccination prevalence are important things to consider in the model

Patterson, K. D., & Pyle, G. F. (1991). THE GEOGRAPHY AND MORTALITY OF THE 1918 INFLUENZA PANDEMIC. Bulletin of the History of Medicine, 65(1), 4–21. https://www.jstor.org/stable/44447656

Sagripanti, J.-L. and Lytle, C.D. (2007), Inactivation of Influenza Virus by Solar Radiation. Photochemistry and Photobiology, 83: 1278-1282. <https://doi.org/10.1111/j.1751-1097.2007.00177.x>

Saunders-Hastings, P., & Krewski, D. (2016). Reviewing the History of Pandemic Influenza: Understanding Patterns of Emergence and Transmission. Pathogens, 5(4), 66. https://doi.org/10.3390/pathogens5040066

* There have been four influenza pandemics in the past one hundred years
* Modern globalization and society have impacted the way that these things develop/spread
* Influenza/pandemics are a product of human development, and we should consider the context for which they spread
* Progress in controlling pandemics can be attributed to pharmaceutical intervention and surveillance
* Persistent challenges include pandemics happen in unpredictable waves and virus jump unpredictable from animals to humans
* Historically, pandemics spread through dominant trade routes, but this is less clear with globalization since there are so many more routes for transmission
* The uncertainty means that we must have flexible policies for handling them when they do occur

Stephens, K. E., Chernyavskiy, P., & Bruns, D. R. (2021). Impact of altitude on COVID-19 infection and death in the United States: A modeling and observational study. PLOS ONE, 16(1), e0245055. https://doi.org/10.1371/journal.pone.0245055

Tan, Y., Cator III, D., Ndeffo-Mbah, M., & Braga-Neto, U. (2021). A stochastic metapopulation state-space approach to modeling and estimating COVID-19 spread. Mathematical Biosciences and Engineering, 18(6), 7685–7710. https://doi.org/10.3934/mbe.2021381

Valle, S. D., Hethcote, H., Hyman, J. M., & Castillo-Chavez, C. (2005). Effects of behavioral changes in a smallpox attack model. Mathematical Biosciences, 195(2), 228–251. <https://doi.org/10.1016/j.mbs.2005.03.006>

Valle, S. Y. D., Mniszewski, S. M., & Hyman, J. M. (2012). Modeling the Impact of Behavior Changes on the Spread of Pandemic Influenza. Modeling the Interplay between Human Behavior and the Spread of Infectious Diseases, 59–77. https://doi.org/10.1007/978-1-4614-5474-8\_4

* Mitigation strategies (e.g., closing schools, limiting air travel, etc.) are some of the only was to address pandemics at the moment
* This is because stockpiles of resources (e.g., antiviral medication) are not likely to be had, nor will vaccines be very prevalent
* Large-scale agent-based model to analyze isolation scenarios (e.g., school closures and fear-based home isolation)
* Certain changes in behavior can be effective at curtailing the spread of disease (e.g., school closures throughout the pandemic can decrease clinical attack rates by 50%)
* Also, stopping intervention/mitigation strategies too soon can lead to a second wave of infection

Weber, T.P. and Stilianakis, N.I. (2008), A Note on the Inactivation of Influenza A Viruses By Solar Radiation, Relative Humidity and Temperature. Photochemistry and Photobiology, 84: 1601-1602. <https://doi.org/10.1111/j.1751-1097.2008.00416.x>