COVID-19 Epidemic and Health System Impact Modelling

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Outline

- Introduction
  - Motivation
  - Problem Statement
- Historical Model Development
  - Use of Penn-CHIME
  - SIHAUDR model
- Stochastic SIHAUDR model with sub-networks
  - Network allocation
  - Transmission model
- Future Directions

Introduction
Motivation

- COVID-19 has caused more than 250,000 deaths worldwide, with many more hospitalizations

- Expectation was that NHS hospitals across the UK would be overloaded due to exponential spread of COVID-19

- Several critical issues with regards to planning:

  - **No estimates of general COVID-19 demand for individual hospitals**

  - **No way of estimating effect of social distancing policies**

  - **No estimates of ICU usage or ventilator usage**

- In the case of hospitals being overloaded: field hospitals would have needed to have been set up, and extra staff needed

- Though COVID-19 is currently in decline in UK, there are fears of subsequent waves of infections

Introduction
Problem Statement

- Aim to assess demand for a specific hospital's resources from COVID-19:
  - General ward beds (non-ICU),
  - ICU beds,
  - Deaths (for mortuary)

- Resources broken down by age group also desired

- Require a model to predict hospitalization time-series with following requirements:
  - It must reflect the transmission dynamics of the disease
  - It must take into account observed hospital data: from length of stay data to observed hospitalization time series

Remarks:

- Many classical epidemic models (SIR, SEIR etc) do not explicitly include hospital pathways, instead (often poorly) deriving hospitalization time series from infection curves

- Hospitalization length of stay distributions are observably non-exponential

- There is no solid knowledge of when first UK case was, given the existence of mild COVID-19 cases

- **Number of cases cannot be used reliably to assess infection rates**

The Penn-CHIME model
https://penn-chime.phl.io/

- Penn-CHIME is a modification of a deterministic SIR model

- Hospitalisation time-series are constructed directly by re-scaling and shifting infection curve

- Also includes one social distancing parameter at a specific case, changing the rate of transmission

- Used in early stages to produce forecasts

Admitted Patients (Census)

Projected **census** of COVID-19 patients, accounting for arrivals and discharges.

key
- ● Hospitalized Census ● ICU Census ● Ventilated Census

The Penn-CHIME model

https://penn-chime.phl.io/
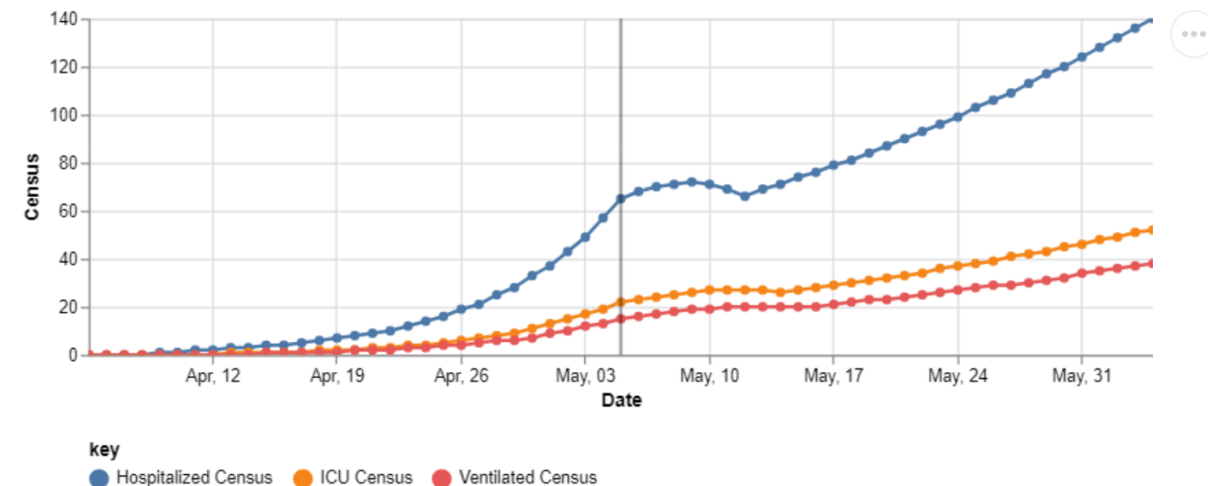
Several issues:

- Simple re-scaling and shifting of the curve not reflective of the dynamics

- Computed the β parameter for SIR model via a "doubling time", doesn't hold outside the exponential growth phase

- Can only model one social distancing policy implemented at one date

- Couldn't fit the model or integrate the software easily with systems

- After some days working with the tool, we dropped the model and looked to developing own software and models

SIHAUDR Model
High-level description

- There was a need to expand SIR to include more states to:
  - Length of stay
  - Reflect hospital pathways correctly
  - Include deaths

- Result is the SIHAUDR (**S**usceptible-**I**nfected-**H**ospitalised-**A**fter-ICU-IC**U**-**D**ead-**R**ecovered) model

- The model is a deterministic, discrete time model, taken in time steps of $\Delta t = 1$ day
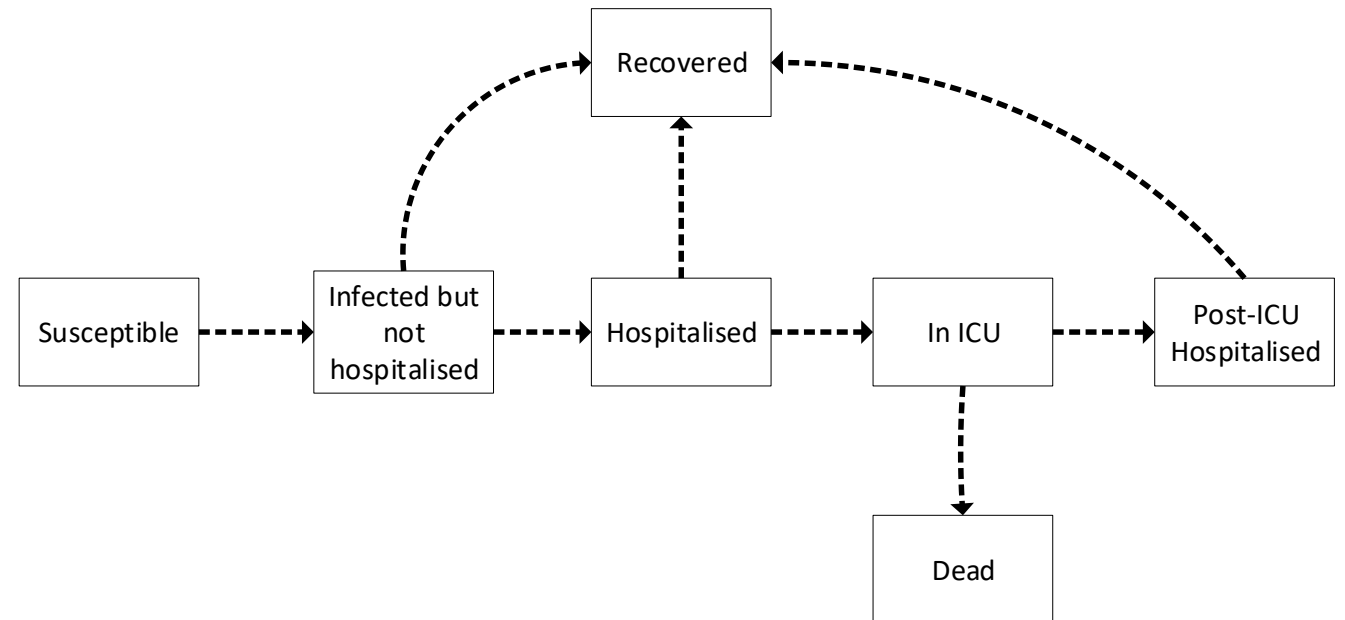
SIHAUDR Model
Deterministic discrete-time equations

$$\Delta S = -\frac{\beta(t)SI}{N}$$

$$\Delta I = \frac{\beta(t)SI}{N} - (1 - p_{IH})\gamma_{IR}\,I - p_{IH}\gamma_{IH}\,I$$

$$\Delta H = p_{IH}\gamma_{IH}\,I - (1 - p_{HU})\gamma_{HR}\,H - p_{HU}\gamma_{HU}\,H$$

$$\Delta U = p_{HU}\gamma_{HU}\,H - (1 - p_{UD})\gamma_{UA}\,U - p_{UD}\gamma_{UD}\,U$$

$$\Delta A = (1 - p_{UD})\gamma_{UA}\,U - \gamma_{AR}\,A$$

$$\Delta D = p_{UD}\gamma_{UD}\,U$$

$$\Delta R = (1 - p_{IH})\gamma_{IR}\,I + (1 - p_{HU})\gamma_{HR}\,H + \gamma_{AR}\,A$$

- S = susceptible
- I = infected but not hospitalised
- H = hospitalised
- U = In ICU
- A = After-ICU hospitalised
- D = dead
- R = recovered
- γ_{AB} = reciprocal of average time it takes to go from state A to state B
- p_{AB} = proportion of population going from state A to state B
- $\beta(t)$ = contact parameter piecewise constant function of time according to government interventions
- There are 7 gamma parameters and 3 proportion parameters

SIHAUDR Model
Implementation & use case

- Implemented using Python 3

- Parameters are human-parseable:
    - Using average time-in-state for gamma parameters
    - R0 to determine contact parameters
    - Proportion of population susceptible to hospitalisation, ICU usage and death

- Use SIHAUDR to simulate at *region level* and extract specific hospitalisations for given hospital

Prominent parameters are:

- R0: the basic reproduction number before social distancing policies enacted

- Social distancing: list of dates of government interventions and proportion reduction in R0 enacted at that date.

- We assume a time lag between government announcement and public adoption

SIHAUDR Model

Fitting and projection scenario – University Hospitals Southampton Trust

- Suppose we are interested in evaluating the effect of a new social distancing policy that was enacted 27/04/2020 to examine the effect of either:

  - Natural reduction in social distancing due to behavioural fatigue

  - Stricter (or reduced) enforcement of current social distancing measures

- This must be conducted *in addition* to already existing policies

- To evaluate this, we must:

  - Fit the hospitalisations curve, **not case numbers**, to previous data

  - Correctly implement past social distancing factors

  - Vary the social distancing factor for the policy at 27/04/2020

SIHAUDR Model
Fitting and projection scenario – University Hospitals Southampton Trust

- Fitting the infections curve directly is ill-advised for a few reasons:

  - Testing rates are an unknown function of time; multiple sources of uncertainty:

    - Availability of tests varies with time

    - Social dynamics: though who develop symptoms may not necessarily test

  - Self-isolation of mild cases are unrecorded

  - In short, signal-to-noise ratio is very low

- Hospitalisations, ICU usage and deaths are much more reliable for fitting:

  - Clinically guided data: patients can be more rigorously tested

  - Percentage of COVID-19 hospitalisations likely to be a fixed percentage of a region's demography
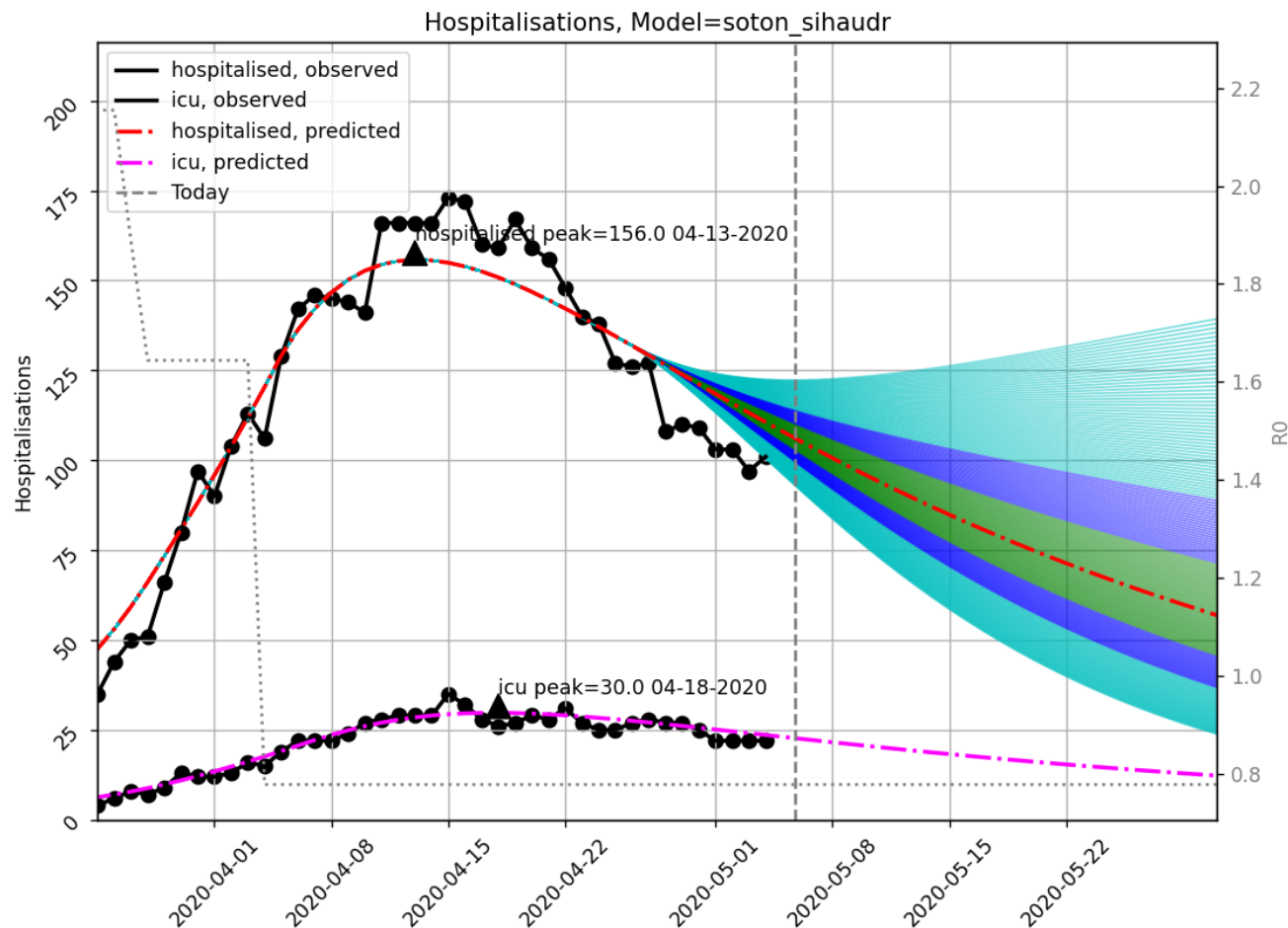
SIHAUDR Model
Fitting and projection scenario – University Hospitals Southampton Trust

- We receive data from University Hospitals Southampton Trust giving us

  - COVID-19 hospitalisations each day: daily admissions, discharges, total in hospital

  - ICU beds used for COVID-19: daily admissions, discharges, total in hospital

- This can be used to fit the model via least-squares regression

- The gamma parameters for internal hospital states are fixed using publicly available data for length of stay of COVID-19 patients (e.g. ICNARC)

- Parameters governing the population: the number of people, hospital catchment determined by NHS Clinical Commissioning Groups

- We leave R_0, γ_{IR}, γ_{IH}, the date of first hospitalisation, and the last social distancing policy as free parameters to be determined

SIHAUDR Model

Fitting and projection scenario – University Hospitals Southampton Trust

Hospitalisations, Model=soton_sihaudr

Social Distancing
- 17/02/2020, 0% (R0 2.3) – Date of first hospitalisation
- 16/03/2020, 3% (R0 2.25) – Non-essential businesses close
- 22/03/2020, 15% (R0 1.97)– Schools close
- 23/03/2020, 26% (R0 1.72)– Poor SD compliance
- 30/03/2020, 65% (R0 0.81)– Good SD compliance
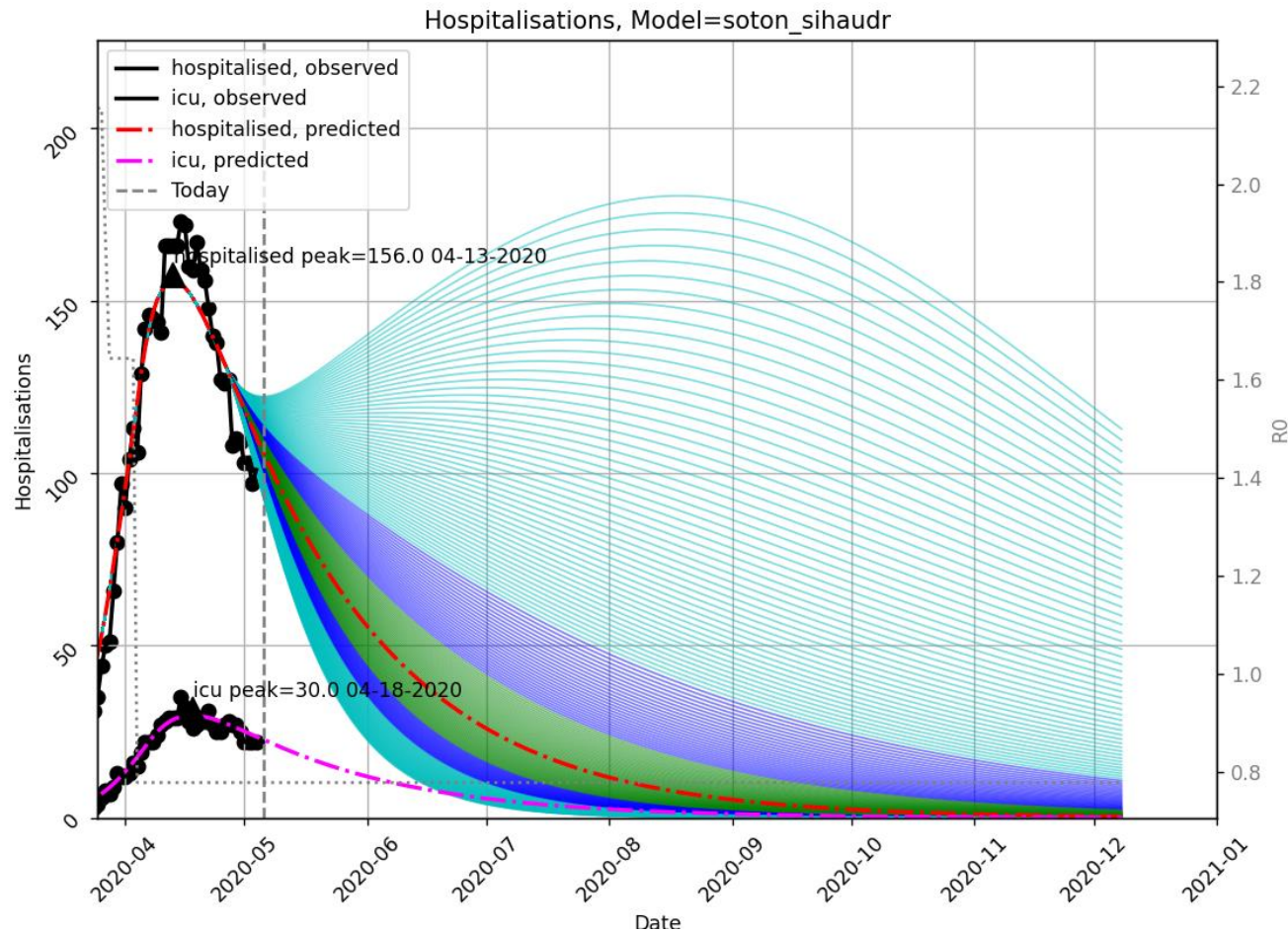
Social distancing sensitivity from 27/04/2020
- Cyan: +/- 15%
- Blue: +/- 10%
- Green: +/- 5%

Note
- Last few data points have greater uncertainty, skewing the fitting slightly

SIHAUDR Model

Fitting and projection scenario – University Hospitals Southampton Trust

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SIHAUDR Model

Fitting and projection scenario – University Hospitals Southampton Trust

- There are multiple sources of uncertainty in the data:

  – Coding errors between "suspected" and "actual" COVID-19 patients (random errors)

  – Changes in the way COVID-19 hospitalisations are reported (systematic errors)

  – Delays in COVID-19 reporting of admissions and discharges (random errors)

- There are sources of uncertainty in the fitting:

  – For early times, difficult to identify COVID-19 patients

  – Fitting is a gradient descent algorithm, and therefore good initial guess is important

  – The type of regularisation to use for effective fitting

SIHAUDR Model
Shortcomings

Shortcomings

- No social resolution: still assumes each individual across the region has equal probability of interaction

- Doesn't represent non-exponential distributions of length of stay

- Deterministic: no assessment of variance at each time point!

Solutions

-> Use individual-based simulation: assign attributes to individuals based on demographics, networks

-> Individual timelines can be generated with non-exponential distributions

-> Make individual state transitions stochastic

Stochastic SIHAUDR Model with Sub-Networks

High-level description

- Monte-Carlo simulation of synthetic individuals interacting in sub-networks

- The model based on two parts:

    - Allocation model: how individuals are assigned to contact networks

    - Transmission model: how the disease is carried and transmitted by individuals
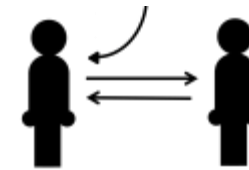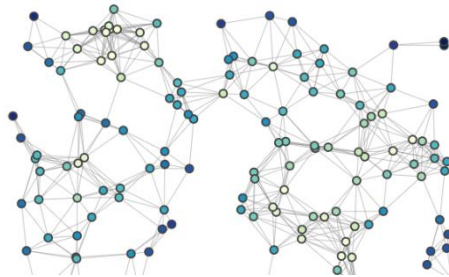
- Simulation can include

    - Individual probabilities for different disease-related outcomes, such as hospitalisation and death

    - Incorporate known distributions of incubation periods, and hospital length of stay

Stochastic SIHAUDR Model with Sub-Networks

Why include networks?

- UK government interventions based on controlling out-of-household contact rates:

  – Closure of social spaces with known high contact rates: schools, workplaces, restaurants, pubs etc

  – Controlled entry and enforcement of social distancing in supermarkets

  – Only essential travel allowed: to shop for food or go to work if an essential worker

- Need to estimate the effect of "easing" various aspects of lockdown policy. Various scenarios:

  – Allowing non-essential travel => increase in contacts in wider community

  – Re-opening of schools shortly before summer => increase in contact among school-children

  – Partial re-opening of non-essential workplaces => increase in contact among working adult population

Stochastic SIHAUDR Model with Sub-Networks

Overall model assumptions

- Each individual i has a set of networks, A_i which they interact in*

- Each network has a corresponding type, governing the frequency of interaction between individuals

- Frequency of interaction changes in each network with time corresponding to social distancing policies

- Simulation time evolves in distinct time steps $\Delta T = 1$ day, with simulation time

* Network generation is network-focused, not individual-focused: aim to model average interactions in social spaces, not individual interactions

- Assumptions:
  - Individuals interact in *fixed* networks, i.e., the networks do not evolve in time
  - Each individual has an equal chance of interaction with other individuals in their respective networks
  - Individual disease progression unaffected by other individuals in networks
  - Assume hospitalised and ICU patients *do not interact with anyone while hospitalised*
  - Assume recovered and dead patients are immune
  - Assume there is no transition between "hospitalised" and "dead" states

Stochastic SIHAUDR Model with Sub-Networks
Allocation Model

- Allocation of individuals to sub-networks is critical for implementing future social distancing policies: re-opening of schools and workplaces should be explicitly modelled

- Possibilities:

  - Explicit modelling of high person-density areas: schools, workplaces, households, shopping centres, hospitals

  - Location-based networks: interactions based on distance between cells

  - Demographic-based networks: social interaction types differ by age

- Development of this model in-progress

Stochastic SIHAUDR Model with Sub-Networks

Transmission Model

- Probability of infection for individual i in each time step ΔT is*:

$$P\left(I_i^f = 1 \mid t\right) = 1 - \exp\left(-\Delta T \sum_{j \in A_i} \beta_{\tau(j)}(t) \frac{I_j(t)}{N_j}\right)$$

- I_i^f is the indicator that individual i is infected

- A_i is the set of networks allocated to individual i

- $\tau(j)$ is the type of network j

- $\beta_{\tau(j)}(t)$ is the beta parameter for network j at time t, with units day^{-1}

- $I_j(t)$ is the total number of infected in network j at the time t

- N_j is the total number of individuals in network j

* Assume individual time to infection is exponentially distributed. For each time step, we assume an approximate constant survival rate for the duration of the time step. The probability is then derived from the CDF of the exponential distribution.

Stochastic SIHAUDR Model with Sub-Networks

Transmission Model

- After infection, individual timeline is unaffected by the presence of other individuals

- Each individual timeline is generated by sampling from distributions governing:

  - Probability of hospitalisation, ICU, and death

  - Infectious period

  - Length of stay in wards:

    - Non-ICU patients

    - ICU patients that recover

    - ICU patients that do not recover

    - Post-ICU patients

Stochastic SIHAUDR Model with Sub-Networks
Transmission Model

- Individual timelines are then aggregated to produce aggregated statistics for the expected value and variance of:

  – Hospitalisations

  – ICU beds

  – Post-ICU beds

  – Deaths

- Model can then be fit with a maximum-likelihood estimator, where PDF is estimated from MC simulations

Future Directions

- Build allocation model based on known distributions derived from sociological datasets: school sizes, age distributions, workplace sizes, household distributions

- Check influence of ΔT on predictions: smaller ΔT reflects Kolmogorov equations more accurately, but how much?

Network-based directions:

- Investigate effect of changing degree distribution within social space networks

- Is it possible to determine an approximation of the number of contacts per day per individual through micro simulations of social spaces?

YOUR QUESTIONS