Modelling, Simulation & Optimisation Literature Review: Understanding the Development and Application of Infectious Disease Epidemic Models

Peter Nolan PGDDA (x22154116@student.ncirl.ie)

***Abstract*—In this short literature review, I look at four papers that show the evolution of epidemiological modelling over the past century. I begin with the 1927 paper by Kermack and McKendrick [1], which formulated the key concepts for a general model of infections and popularised the 'compartmental' approach that is still the basis of the field. I go on to describe the evolution of the 1968 flu pandemic using their SIR models described in [2]. While these were break-throughs in epidemiological modelling, looking at more recent empirical modelling of epidemics by Ferguson and Bootsma [3] and by IEMAG, the Irish epidemic modelling team during the COVID pandemic [4], it becomes clear that the original SIR models presented epidemic behaviour as more stable than it is in reality, were too disconnected from practical interventions and were not supported by realistic estimation. Instead, current practise from the more recent research offers a more useful toolbox for modelers and stakeholders.**

Keywords: infectious disease, public health, epidemics, epidemiology, pandemics, influenza, COVID, SIR, SEIR

I. Introduction

In early 2006, based on articles I wrote for the Irish print media, I appeared on a panel on the show of David McWilliams on Irish television to talk about the threat of bird flu with a politician, a virologist and an ornithologist, saying that my five-person software company had by then done more preparation for a pandemic than the Irish government. A national plan for pandemic preparedness was published late that year and the modelling [5], one aspect of the problem that my work as an economist prepared me for, was seemed both too optimistic and lacking the insights into disease dynamics, interventions or estimation coming from building original models based on clinical experience and on sound mathematical and statistical foundations.

Seldom before has humanity ever been so ruled by models as during the recent pandemic: The language of mathematical epidemiology, R_0, 'flattening the curve', 'herd immunity', has dominated headlines as the disruption and state intervention been larger than for any event since World War 2 [6] [7]. Debate was extremely contentious in Sweden, where I was living at the time, which was something of an outlier in practise, but media and politics everywhere seemed largely disconnected from the epidemic models that produced the headline policies. Also noticeable was a cultural difference between the government in Sweden, whose modellers were much more optimistic in outlook than comparable experts in academia, business and NGOs. For these reasons, since late 2020, I have been investigating the epidemic, albeit from first principles and lacking much of the necessary background in mathematics and statistics, to try to understand how the models were created, and how solidly supported by research and integrated into clinical practise and government policy they are.

II. The Foundation

Graphs showing a bell curve of infection numbers observed over time were drawn for outbreaks of smallpox in England in the 1830s [8], so providing the insight that numbers of infections and deaths, would rise, peak and then fall. However, without an understanding of the factors driving disease dynamics, this was of limited use.

Instead, building on the work of [9], Kermack and McKendrick [1] took a different approach and built a continuous-time dyanamic system, which took a deductive approach, moving from general principles [10] of the behaviour of the epidemic considered as a system rather than inductive, the model emerging from observed behaviour of individual components. Kermack and McKendrick write that their motivation is 'finding a causal factor which appears to be adequate to account for the magnitude of the frequent epidemics of disease' and 'more insight regarding the effects of the various factors which govern the spread' [1](page 700), in other words, discovering dynamics, size of the effects and what factors drive them.

In their model, the whole population, labelled as N people, are divided into one of three distinct compartments representing progressive stages of the disease at time t, namely x_t people being susceptible, not yet infected, may move to y_t infected and infectious to others and then move on to z_t, recovered or dead. By construction, these contain the entire population, so that $N = x_t + y_t + z_t$ (equation 11, page 704). Nowadays, these are labelled as S, I and R and the entire model as SIR [11].

They begin with difference equations, with a time gap of θ between times. Their rate of removal parameter is ψ_θ, the rate of infection by each infected person to a susceptible person ϕ_θ (page 703), nowadays labelled as r and λ_t [11](§3.3) respectively. As $\theta \to 0$, they move to differential equations with the derivatives, $\frac{dx_t}{dt}$, $\frac{dz_t}{dt}$ and y_t, in terms only of t, ψ_t and ϕ_t.

Unable to solve for x_t, as a function only of time, they use a solution like that for solving Volterra's equations. Their spagetti mathematics here is very unclear and hard to follow, and my focus here is on interpreting results; later models and recent textbooks present these same results much more clearly as shown in Section III.

Making a simplifying assumption of constant recovery and infection rates $\psi_t = l$ and $\phi_t = \kappa$, they obtain a solution for the recoveries z in terms of initial susceptibles x_0 and infected y_0 (equation 30). They include some empirical observation, sharing a graph [1](pp.714–715), shown in figure 1, of deaths from a plague epidemic in Mumbai in 1905, symmetric around a central peak, so appearing very similar to the normal distribution. They describe this as the evolution of the time-varying $\frac{dz}{dt}$, rate of change of the number of people recovered, as a function of time t, calculated from their simplified model and fit real observations to the curve constructed by their formula. This model showing how the parameters for infection and recovery over time alone drive the observed path was their first major contribution.

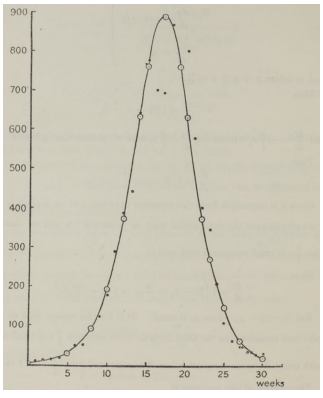

Fig. 1. Observations and the modelled curve [1]

Second, they ask why an epidemic ends (page 702); traditional explanations are inadequate: All susceptible in the beginning have not been infected in our model values, nor do we assume the pathogen is less infectious or lethal. Again from the simple fixed parameter model, the authors calculate the number recovered as $z = \frac{2l}{\kappa x_0}(x_0 - \frac{l}{k})$ (equation 32). By inspection, we can see that the the number of the removed z will be zero if the initial susceptible population $N = x_0 = \frac{l}{k}$ (eqn.32), then this expression for z must be zero and no further numbers of people will move from S to I to R.

Third, more broadly, does the system settle down to an equilibrium around some threshold value, changes around which triggers new

epidemics? It is apparent that the ratio $\frac{l}{\kappa}$ is greater than zero and more people will move through the infection and removal stages of the epidemic: this appears to be the threshold value they seek. However, the concept of the threshold, assumed to be around which the system is stable, is as much an outcome of the limits of these mathematical models and simulation. Whether this stability was hold in practise, they did not explore in detail, but which later research gave deeper insights, as I write in Section IV below.

Fourth, adding some number of people n to the existing population N, would generate a new epidemic with infections = $(2n^2 - \frac{n}{N})$. If $\frac{n}{N}$ is a small proportion of total population, the second term above will be small, the first one increasing the cases with both a multiple and a square term, having a proportionately larger and non-linear effect on infections.

III. Simulating Influenza Epidemics

I want to highlight the definitions, estimation and dynamics seen in a simple SIR epidemic model of the sort described above, showing excess deaths from flu and pneumonia in New York City over winter 1968–69, during a pandemic. I use the description and data from [2] and code based on [12] like our class example `6SIR H3N2 1968`.

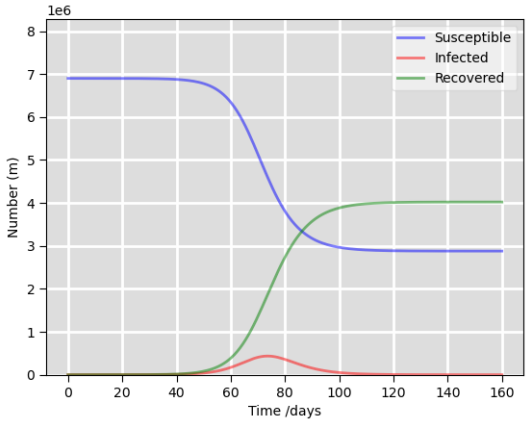

Fig. 2. Simulated S, I and R for Hong Kong flu 1968–69, NY City

The SIR simulation uses the same continuous-time model as [1] with compartments for Susceptible (S), Infectious (I) and Removed (R), so that $N = S + I + R$. The parameter $\lambda(t)$ is defined the rate at which Susceptible individuals become infected per unit time and $\lambda(t) = \beta \times I(t)$. Assuming they mix randomly, and homogenously, independent of age, location or behavioural factors, λ depends on I and also the parameter β, defined as the rate per capita at which two individuals are in infectious contact per unit time [11](§4.2.2). The SIR model is specified by the familiar system of ODEs [11](§3.3):

$$\frac{dS(t)}{dt} = -\lambda(t)S(t) = -\beta I(t)S(t) \tag{1}$$

$$\frac{dI(t)}{dt} = \lambda(t)S(t) - r(t)I(t) \tag{2}$$

$$\frac{dR(t)}{dt} = r(t)I(t) \tag{3}$$

where r is the rate at which the infectious individuals recover per unit time: Assuming the recovery time from flu is 3 days, r would be $\frac{1}{3}$, with the constant rate implying an exponential distribution for r [11](§2.7.2). The infection is assumed immunising, so that once infected, nobody is reinfected, realistic over a limited time of 160 days with one flu strain. Given values of the β and r parameters, these ODEs may be solved by integration to give the values over time of S, I and R.

Numbers of infections over time here show a similar curve as in figure 1 above. Calculations show that infections never reach higher than 6.3% of N, but grow rapidly before leveling off so that around 4 million or over 58% of N have been infected.

The reproduction number measures the number of infections created by adding a single user to a population. This can be the basic reproduction number R_0 at a time where the infection is not yet present in the population and is calculated where β is assumed to be 0.5 to be $R_0 = \beta \times N \times D = \beta \times N \times \frac{1}{r} = \frac{0.5}{\frac{1}{3}} = 1.5$ (assuming a unit N for simplicity), so we can expect growth with each new Infectious individual at the beginning infecting another 1.5 more people, leading to expanding numbers of Infectious. Typical R_0 for flu will be around 2.

The effective reproduction number changes over time as the epidemic progresses. The Herd Immunity Threshold (HIT) is defined as the level of immunity beyond which the number of infections do not grow: This is roughly calculated as $(1 - \frac{1}{R_0})$ [11](§4.3.1) $= \frac{1}{3}$ of the population in our model. In contrast, the effective reproduction number, R_t, which is calculated once the infection is present, as $R_t = R_0 \times S$. The R_t in our model passes below the value of one, so that each infection yields fewer than one additional infection, on day 75 of our model, the same day S falls below 66% of N and I reaches its maximum and thereafter starts to shrink, as we would expect from our HIT calculation.

IV. Flattening the Curve

In my search of the literature, I was unable to find any compartment models published during the 1968 pandemic forecasting its course, or for twenty years afterwards. So, while easier to understand and apply with our data analysis tools of today than the original work, the SIR models in Section III may not have been usable by public health practitioners: One complained in a 1979 review of the literature that epidemic models were either oversimple and too general or overly complex and too hard to estimate [13].

An influential paper by Bootsma and Ferguson [3] brings a contrasting practical focus on public health and brings useful historical data and more realistic modelling. Their study of how excess mortality during the pandemic flu of 1918 was affected by variations in the start date and duration of local measures. The different timing and duration of bans on public gatherings, school closures, mask mandates and quarantine rules across 18 American cities allowed a comparison of the effects of these 'non-pharmaceutical interventions' (NPI) in different places. Their results showed a significant relationship in reducing deaths from having earlier and longer restrictions and fed into later work modelling a pandemic response [14].

One refinement of the SIR model has been to adapt the stages to the progression of different diseases, so representing the life-cycle of the flu virus, SEIR models are used, adding a stage for a phase between Susceptible and Infectious for those infected but not yet infectious [11](§2.4.1), important for flu. Other adaptations may add stages for vaccination or other stages to fit other diseases, such as SI for HIV, which is incurable, or SIS for common colds or gonorrhoea that allow repeated reinfection.

Local factors, which might be hidden in a national or regional or global model, were obviously important also. The R_t was calculated for each city, with the earliest observation being R_0. The models fitted showed that the previous year's all-causes mortality accounting for almost 44% of the variation across the cities. Other environmental factors, total population, density or area of the city, were not found significant. However, the best model fits came from estimates on the

individual city level, rather than on the full population, supporting the view that local factors are important to capture in the epidemic model.

Dynamics are also considered with greater depth and sophistication, going beyond the growth in infections to a peak followed by symmetric decline and the long-term stability around the threshold value in the previous papers. Part of this is a longer time frame for the model, as the 1918 flu pandemic had two to three waves, with different dates around the world [15]. Analysing the control of the flu pandemic with simple SEIR simulations, Ferguson and Bootsma show how early strict NPI could prevent exposure at first, but then increase total deaths and expose the population to a second wave after restrictions ease when most people are still susceptible: They recommend NPI targets that allow the level of infections to reach the herd immunity level of infections first, without leaving enough susceptible people to feed a second wave.

More insight came from more sophisticated modelling techniques: Measles used to show regular seasonality before mass vaccination began in the UK, but it is more recently observed with unpredictable or chaotic dynamics in the timing, size and geographic spread of infection. Endogenous behaviour of SEIR epidemic models with, for example, simple seasonal variations of parameters such as β_t to model the effect of the school year, have been shown to induce this, as can exogenous factors like births adding to the susceptible population [16] [17].

V. Modelling COVID in Ireland

The Irish Epidemic Modelling Advisory Group (IEMAG), a team of academics, was set up in early 2020 and chaired by Prof. Philip Nolan[1] to provide analytical input to the Irish government National Public Health Emergency Team (NPHET). Modelling was divided into three streams. One team looked at health care capacity, likely to be a key part of any future epidemic modelling too. Another subgroup looked at geospatial analysis, reporting and visualisation by city and county.

Building on the literature, the Epidemiology Modelling subgroup built and estimated SEIR models. These were used for reporting historic time-specific effective R_t and forecast cases and deaths over future months under different projected R_t values assumed to follow different lockdown and vaccination scenarios e.g. [18][pp.16–17]. IEMAG published the model specification in two versions [19] updated by [4], SEIR parameter estimates [20] and R_t estimates [21] [22]. Other approaches, such as social network or agent-based models were recommended to the team [23], but not prioritised and were still in progress in October 2020 [24].

IEMAG's first important forecast was given at a crisis meeting of the cabinet on 9 March, of 25–35,000 deaths [25](page 42). I read the published inputs, meeting agendas and summaries from IEMAG and NPHET, but none mention this forecast or how it was calculated. Nevertheless, reverse-engineering with the COVID R_0, which was later estimated empirically as 2.9 and Infection Fatality Rate (IFR) estimate of 1.15% (both from [26]), I estimate the HIT as $(1 - \frac{1}{2.9}) = 65.52\%$, implying 3,275,862 cases and 37,672 resulting deaths. A British report published a week later [14] had more complex logic, building on the paper [3] above, and with an R_0 of 2.4. It estimated over 500,000 deaths in the UK: My estimate would be similar at around $(1 - \frac{1}{2.4}) \times 67.33 \times 10^6$ or 451,672 deaths. All these are assuming no NPIs applied by the government and no change in the public's behaviour that might lower the R_t. Instead, in these calculations the change in the R_t would come about endogenously in the SEIR model through the numbers of susceptible people as a proportion of the population falling over time as $R_t = R_0 \times S_t$.

This sensitivity to small changes, potential for exponential growth, is usually lacking in laypeople without mathematical or statistical understanding, one reason perhaps that in October 2020 rejected advice from its modelling advisors to tighten social-distancing against COVID after the numbers of new infections had tripled over the course of a week [25] (page 175).

To begin with, a log function was used to forecast infections [27], assuming that cases would grow at a constant exponential rate in the first stage of the pandemic. This is a simple, quick and common solution early on. With few cases observed, making parameter estimates for more complex models will be difficult, so this solution, first applied for SARS [11](§4.2.3.1.1), appears reasonable.

Uncertainty in parameter estimates was modelled choosing probability distributions, so the serial interval, the time taken for the pre-infectious (E) and infectious (I) periods, was estimated assuming a gamma distribution with mean 6.5 days, from which the transition rates and R_t can be estimated with data from different COVID testing methods [21]. This estimation methodology is another refinement from more recent mathematical modelling as outlined in [11](Eq 4.17) we should also aim for in future models. Further reflecting the uncertainties in the disease, the model created had 6 distinct pathways from the S to R compartments, including asymptomatic infection, quarantine and testing processes, so the SEIR model had 9 differential equations instead of three. The equations were solved, using an Euler finite difference approach, then fitted to past data using Bayesian estimation to generate estimates of realised values of R_t. Forecasts of new cases are then created for scenarios of R_t. I tried to reproduce the R estimates, but even example data crashed the Bayesian epidemiology packages in [28], my estimates come from ODE integration to calculate β_t while assuming r_t, as used in [29].

Searches on Google Scholar indicate that a doctoral student at TU Dublin who joined IEMAG in September 2020 [30] was the only one who had published previously in epidemiology, in contrast to the UK, which had eight separate modelling groups [26]. This might account for the relative conservatism of the models used, the classic SEIR, and the lack of engagement with criticism such as of the ECDC methodology of [31] by [32] or models of super-spreaders, as is used with HIV [11], when 20% of infected account for 80% of cases, which are needed for COVID also [33]. Controversial as the pandemic measures were, I found it unusual that that there was no critical comment in academic literature and little press comment on the Irish COVID models, perhaps the lack of epidemiologists explains this: Without alternative estimates or forecasts, evaluating IEMAG's work is much more difficult.

VI. Conclusion

In this review, I have traced the development and applications of epidemic models for infectious diseases. I began with the the earliest theoretical work of Kermack and McKendrick [1], the basic compartment model showing the herd immunity threshold, stability around the threshold and non-linear growth in epidemics of the SIR model and demonstrated this with a simple model using data from an historic flu pandemic [2]. I then go on to present a paper by Ferguson and Boomstra [3] that looks at the effectiveness of NPI and present a simulation- rather than theory-driven model of epidemic control. Theoretical work and empirical data [17] [16] shows that the dynamic behaviour assumed by the classic SIR model is oversimple. Finally, looking at the Irish COVID modelling effort, the SIR epidemic models can now run in near real-time, have compartments that track the clinical processes and incorporate uncertainly in estimation, all of which mean that these are now practical tools for epidemiology.

[1]We are not related.

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