Irish Epidemiology Modelling Advisory Group to NPHET

Technical Notes

Note from Prof. Philip Nolan, IEMAG Chair

The Irish Epidemiological Modelling Advisory Group (IEMAG) was formed on 11 March 2020 to provide statistical and mathematical modelling support and advice to the Chief Medical Officer and the National Public Health Emergency Team (NPHET). The remit of IEMAG includes:

- gathering evidence and monitoring the epidemiological characteristics of the COVID-19 outbreak in Ireland and the pandemic internationally; and
- developing epidemiological models to forecast the COVID-19 outbreak in the Republic of Ireland, monitoring the impact of public health interventions, and modelling probable scenarios for numbers of new cases of COVID-19 over time.

IEMAG is now publishing a set of technical notes to inform other scientists, epidemiologists statisticians and mathematicians of our approach, and to help refine and enhance our techniques and models. These notes are of necessity technical in nature.

A mathematical model of an epidemic is a tool to help us better understand the epidemic as it evolves, to forecast possible scenarios for strategic and operational planning, and to support risk assessment and public health decisions. Statistical and modelling approaches have significant and important limitations. These limitations are well understood by NPHET and key decision makers.

The central model used is a population-based SEIR model[1]. This is a robust, widely-utilised and well-understood approach to modelling infectious disease, and as such could be developed and deployed quickly. The model divides the population into compartments, starting with those *susceptible* to the virus (the S compartment); at the outset, for a novel virus where there is no immunity in the population, the entire population is susceptible. The model is seeded with a small number of individuals who are infected with the virus and as a result some of the population become exposed to the virus and are assigned to the *exposed* (E) compartment. These individuals are not yet infectious: the virus is replicating in their bodies, but they are not yet shedding virus. However, after the latent period (3-4 days) the individual becomes infectious and is assigned to the *infectious* (I) compartment for the duration of the infectious period (the model assumes an average infectious period of 5-9 days, which is typical, though individuals may remain infectious for up to 14 days and sometimes longer). Finally, at the end of the infectious period the individual is *removed* from the model (to the R compartment) on the basis that they are immune to further infection.

The dynamics of the model are driven by the dynamics of viral transmission, expressed as a set of differential equations, and in particular the *reproduction number* (R). An intuitive way to think of R is as the average number of infections caused from each new case. Of course some cases will lead to many secondary infections, and some may lead to none. The quoted average can be useful, since values bigger than 1 indicate a situation where we expect

substantial growth in the future number of cases, whereas values close to zero indicate that it is expected to see many fewer future cases than currently are incident.

It is important to distinguish between basic reproduction number (R_0) and effective reproduction number (R)

- The basic reproduction number, R_0, is the expected number of additional cases that are generated, on average, by a single but typical case, over the course of its infectious period, in an otherwise uninfected population, where the entire population is susceptible and no public health interventions are in place. It is characteristic of the early phase of an unmitigated epidemic of a new emerging virus where there is no prior immunity in the population.
- The effective reproduction number, R, is a dynamic estimate of the average number of secondary cases generated by a single but typical case, over the course of its infectious period, in a population where an outbreak is ongoing and there are changes in the level of contact between people or the level of immunity in the population.

Reproduction number is a characteristic of the virus *and* the population. The number of other people likely to be infected by any given infectious individual is proportional to:

- the number of close contacts between the infectious individual and susceptible contacts;
- the probability that any given contact leads to infection;
- the duration of the infectious period.

Reproduction number, and hence the rate at which a virus spreads through a population, can be reduced by reducing the number of contacts, by reducing the probability that a contact leads to infection (by hygiene, distancing, or barriers), and through early identification and isolation of infected individuals. Reproduction number is an important parameter in SEIR models of disease transmission*, and estimates of effective reproduction number are valuable in monitoring our progress in mitigating or suppressing the epidemic.

The usefulness of a model of an infectious disease depends heavily on assumptions about how the virus is transmitted from person to person and how the disease develops and propagates. SARS- CoV-2 is a new virus, and COVID-19 a novel disease. IEMAG immediately established an epidemiological parameters sub-group to review and critique the available research as it emerged, providing very high-quality evidence in a timely manner on the dynamics of viral transmission and the nature of the disease. The technical note[2] is a summary of this work, evaluating current research on the epidemiology of COVID-19 and providing best estimates of the important parameters, which were then used to inform the development of the mathematical models and their calibration.

* The relevant parameter in the SEIR model is β. R is the average number of other individuals infected by a typical infectious case over the full course of the infectious period. β is the average number of other individuals infected *per unit time*. R = β.D where D is the duration of the infectious period.

The overall model used by IEMAG is summarised in diagrammatic form in Figure 1. The outputs of the SEIR model are used to estimate demand for hospital and critical care, and mortality, based on data from the European Centres for Disease Control and calibrated against the experience of the epidemic in Ireland.

Finally, we present technical notes on the approaches used to estimated effective reproduction number over the course of the epidemic. This is a difficult parameter to estimate, and we are currently using three approaches to cross-check and triangulate. The SEIR model can be used to infer R; the technique developed by Wallinga and Teunis (2004)[3] provides an estimate of time-dependent reproduction number[4], as does the approach introduced by Flaxman *et al.* (2020)[5] to examine the effect of interventions on reproduction number[6].

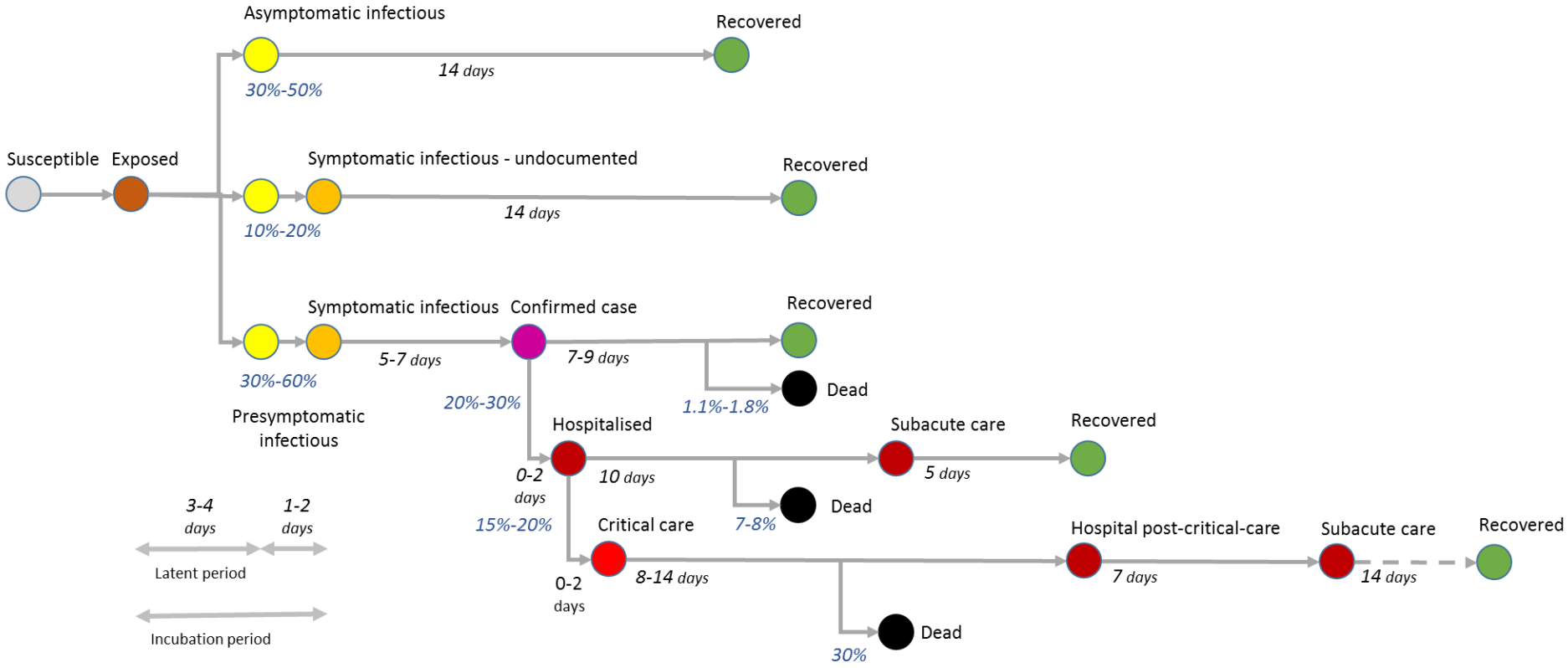

Figure 1: Model of disease and care: The parameters here are clinical, and used to estimate healthcare demand from the outputs of the SEIR model. The SEIR model uses wider and in some cases different estimates for these parameters.

References

[1] A population-based SEIR model for COVID-19 scenarios. IEMAG Technical Note 1, 11 May 2020.

[2] COVID-19 Epidemiological parameters – summary note. IEMAG Technical Note 2, 13 May 2020

[3] Wallinga J, Teunis P: Different epidemic curves for severe acute respiratory syndrome reveal similar impacts of control measures. Am J Epidemiol. 2004, 160: 509-10

[4] Time-Series Based Estimation of the Effective Reproduction Number (Rt). IEMAG Technical Note 4, 21 May 2020

[5] Flaxman, S et al. Estimating the number of infections and the impact of non-pharmaceutical interventions on COVID-19 in 11 European countries. MRC Centre for Global Infectious Disease Analysis COVID-19 Report 13. 30 March 2020

[6] Estimation of the effective reproduction number (Rt). IEMAG Technical Note 3, 20 May 2020