Introduction

There are two primary classes methods of estimating R(t) from case count data that are used in most R software packages. The first class of methods assumes there is a formulaic relationship between infections and reproduction number, a relationship known as the renewal equation.10 These infections are then assumed to result in (some fraction of) the observed cases. A second class of methods involves empirically calculating a quantity that approximates the latent quantity represented by a reproduction number by fitting a curve to the case count time-series and finding the time-varying slope in log space (and then performing other transformations). Empirical calculations are discussed in detail below in our examination of ways in which R(t) is constrained over time.

Renewal equation estimates of R(t)

The renewal equation relates R(t) and infections on day t, I(t), using a third parameter known as the generation interval. The generation interval, , is the time between infection in the infector and infection in the infectee, and assuming independence is the linear combination of incubation time, the time between infection and symptom onset in an individual, and transmission time, the time between symptom onset in the infector and infection of the infectee.11 A similar parameter to the generation interval is the serial interval, which is the time between symptom onset in the infector and symptom onset in the infectee. The serial interval and generation interval are interchangeable if the incubation time is independent from the transmission time, and some formulations of the renewal equation use generation interval. In this paper we use the generation interval described by a probability mass function with non-zero values from day 1 (assuming that disease incubation takes at least 1 day) to a maximum day s, i.e., the longest interval between symptom onset in infector and infectee. Taking care to note that R(t) is undefined on day 0 since there has been no transmission yet (and assuming the initial infections are I(0)), the formulation of the renewal equation is thus:

I(t)=R(t) _(i=max(1, t-s+1))^t (i) I(t-i) (Eq.1)

For brevity, we write the inner sum of (Eq.1) as:

Λ(t)= _(i=max(1, t-s+1))^t (i) I(t-i) (Eq.2)

The assumptions of this formulation, as per Green et. al. 2022,12 are that incident infections can be described deterministically within each window of t [t-s+1,t] and that the generation interval distribution does not change over the modeling time. A common reframing of the renewal equation is to equate R(t) with an exponential growth rate, r. Under specific conditions and within a small time window (t [t-s+1,t]), infections can be assumed to grow exponentially at a constant rate (r).12–14 Using Eq. 1 in the time window t [t- s+1,t] and assuming some initial infections k, R(t) for t [t- s+1,t] can be inferred from only r and : I(t)=ke^rt,t [t-s+1,t] (Eq.3) R(t)=[_(i=max(1, t-s+1))^t (i) e^(-ri)]^(-1) ,t [t- s+1,t] (Eq.4) Again, we will omit the writing the bounds for time in remaining formulae. A single R(t) value, say R_0, can also be put in the form of an infection attack rate, z,15 or in the final size equation,16 to estimate the proportion of all individuals that were affected by a disease with this R_0:

z=1-exp(-R_0 z) (Eq.5)

The attack rate function and others are implemented in the package epigrowthfit.17 The major difference between calculating R(t) from a renewal equation or an exponential growth rate equation is whether I(t) is used. If for a given time window both r and can be estimated independently, then R(t) can be inferred without infection data. Otherwise, infection data are needed to estimate R(t).

Using the renewal equation (Eq. 1) and given that I(t) and are known, R(t) can be solved for algebraically starting with R(t=1) and iterating forwards in time. However, this will produce highly volatile estimates of R(t) that recover the incidence curve directly. This is undesirable for several reasons: real-world infectivity likely does not vary dramatically from day to day, and real-world infection data are rarely complete, especially in an emerging epidemic, meaning that a certain amount of uncertainty must be incorporated into any estimation framework. In addition, infection incidence, I(t), are the data of interest but it is impossible to observe, so many calculations instead may use the observed reported cases, C(t), which requires some additional processing to incorporate into calculations of R(t). Therefore, a variety of constraints on R(t) are added in the inferential process: using distributions on key variables, placing restrictions on how R(t) varies through time, and with additional data sources and delay distributions. These choices dictate which estimation framework is used, which can add additional constraints.