J. theor. Biol. (2000) **203,** 51–61
doi:10.1006/jtbi.1999.1064, available online at http://www.idealibrary.com on IDEAL®

Individual-based Perspectives on R_0

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(*Received on* 4 *August* 1999, *Accepted in revised form on* 24 *November* 1999)

Without doubt the basic reproductive ratio, R_0, is the most widely used quantity in epidemic theory. Standard compartmental models show how R_0 is related to the average age of infection, vaccination thresholds for eradication and equilibrium solutions. However, many of the basic formulae for R_0 break down when we consider transmission of infection to be a stochastic process involving discrete individuals. This paper clarifies why and when these differences arise and predicts when individual-based considerations are likely to be important in modelling infection dynamics.

Introduction

The basic reproductive ratio, R_0, is the most fundamental parameter used by epidemiologists. For microparasites it is defined as "the average number of secondary cases caused by an infectious individual in a completely susceptible population" (Anderson & May, 1992). As such, it provides an important tool for understanding the behaviour of infectious diseases (MacDonald, 1952; Dietz, 1975) and has been much studied by both theoretical and empirical researchers (Mollison, 1977; Grenfell & Anderson, 1985; Diekmann *et al*., 1990; Mollison *et al*., 1993; Green-halgh & Dietz, 1994; Sanchez & Blower, 1997; Knell *et al*., 1998).

The main use of R_0 is in the calculation of an invasion threshold for the infection. The introduction of a disease into a population is one of the most studied and well-understood forms of biological invasions in ecology (Kornberg & Williamson, 1987). In the past ten years, there has been a proliferation of research into individual-based systems (DeAngelis & Gross, 1992; Judson, 1994; Bolker *et al*., 1997) and stochastic systems (Casdagli, 1991; Hiebeler, 1997; Wilson, 1998); here we consider the changes to R_0 as a generic method of understanding the effects of individual-based modelling.

When R_0 is greater than one, infections can invade a totally susceptible population and persist in the short term; long-term persistence is a more complex, stochastic phenomenon (Keeling, 1997). Upon vaccinating against a disease, the effective reproductive ratio is reduced to a level below R_0 (Anderson & May, 1992). For successful eradication, it is necessary that the level of vaccination forces the effective R_0 below one; the disease then dies out and cannot re-invade if vaccination is maintained. Thus, understanding R_0 is important from both a theoretical and control perspective.

There are discrepancies however between the definition of R_0, its usual mathematical formulation and estimation from field data. These discrepancies only become apparent when individual level behaviour is considered and we

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0022–5193/00/050051 + 11 $35.00/0

relax the assumptions of mean-field (homogeneously mixed) models. Epidemiology has been at the forefront of work pioneering the use of individual-based, stochastic models to study population dynamics (Mollison *et al*., 1993; Bolker & Grenfell, 1995; Levin & Durrett, 1996; Swinton *et al*., 1998), yet the general understanding and use of R_0 still focuses on the mean-field paradigm. This paper attempts to unify the various approaches to the calculation of R_0 for microparasites, starting from the most basic of definitions; these calculations are then compared to the standard mean-field results (Anderson & May, 1992). This section of the work concentrates exclusively on the invasion of a susceptible population, this means that we can ignore the spatial correlations that develop during the epidemic for which there is little quantitative data. As epidemiology is a data-driven subject, we next consider how the individual-based assumptions affect the estimation of R_0 from sero-positive data, this forces the consideration of the endemic disease. Finally, the work leads to a means of quantifying the relative strengths of the individual-based to mean-field-type behaviour.

Theoretical Calculation of R_0

Throughout this work, we shall consider the simple SIR epidemic, without births or deaths (Kermack & McKendrick, 1927; Anderson & May, 1992), from an individual-based stochastic perspective. Although R_0 can be calculated for more complicated scenarios (Diekmann *et al*., 1990), this reduced model is used since it simplifies the algebra and is ideal for illustrating the differences between mean-field and stochastic, individual-based approaches. In many cases, R_0 is used to identify situations when a disease can invade a population, in which case the dynamics of host births and deaths are largely irrelevant (Anderson & May, 1992). The deterministic differential equations governing the SIR system are then given as

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\beta SI,$$

$$\frac{\mathrm{d}I}{\mathrm{d}t} = \beta SI - gI, \qquad (1)$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = gI,$$

where S, I and R are the proportions of susceptible, infectious and recovered individuals, β is the contact rate and $1/g$ is the mean infectious period (Anderson & May, 1979, 1992). These "mean-field" or homogeneous equations assume that each infectious individual interacts weakly with an infinite set of other individuals, thus ignoring the discrete nature of the population (Durrett & Levin, 1994; Wilson, 1996, 1998; Bolker *et al*., 1997).

INDIVIDUAL-BASED RESULTS

To incorporate an individual-based component, we suppose that each infectious individual on average comes in contact with—and could transmit the disease in isolation to—exactly n susceptible individuals. (In Appendix A the argument has been generalized to the case where the mixing is non-uniform.) It is important to realize that although the average number of susceptible neighbours will change during the progression of an epidemic, for the calculation of R_0 we are only interested in the initial spread of infection in a susceptible population. Similarly, we can ignore most of the complications of spatial structure that develop as the epidemic progresses.

We now consider in detail how n, the potential number of susceptible neighbours, is related to the average neighbourhood size N. For the first infectious individual landing in a totally susceptible population, it is clear that n must be equal to N. However, for all subsequent cases, as they must have been infected by one of their neighbours, $n \leqslant N - 1$. In general, for the vast majority of contact networks we find that within a few generations the relationship between n and N achieves its asymptotic limit (Keeling, 1999; cf. Bolker & Pacala, 1997). The precise form of this relationship can only be calculated by knowing the exact contact network, but in general, networks with predominantly long-range connections (such as the random graph) initially have $n \approx N - 1$, whereas networks with many local connections (such as lattice-based models or small world networks) have far lower n [see Andersson (1998) for the treatment of R_0 on

a random graph]. These local networks have reduced n for two reasons: firstly infectious individuals are aggregated so each infectious case has fewer susceptibles in its neighbourhood, and secondly, some susceptibles are shared between many sources of infection again reducing the potential n. Although we could calculate n from the contact network, as is effectively done in Keeling (1999), there is only limited data from which to estimate this network; therefore it is far simpler to use n as an underlying epidemiological parameter.

From probabilistic considerations, we can average over all possible numbers of new infections produced, to calculate the expected number of the n individuals who contract the disease; this is the average number of secondary cases an infectious individual causes, or R_0. The constant decay rate, g, of infection in eqn (1) introduces the assumption that infectious periods are exponentially distributed, giving

$$R_0 = n \int_0^\infty g\, \mathrm{e}^{-pg}(1 - \mathrm{e}^{-\tau p})\, \mathrm{d}p$$

$$= n \frac{\tau}{\tau + g}, \tag{2}$$

where τ is the rate at which disease is transmitted across a contact. Here, R_0 is calculated as the integral over all infectious periods, of the probability of having that length infectious period times the expected number of the n susceptibles that will get infected.

On the other hand, for many diseases it is more appropriate to assume that every individual is infectious for a fixed time, exactly $1/g$ (cf. Keeling & Grenfell, 1997), this leads to

$$R_0 = n(1 - \mathrm{e}^{-\tau/g}). \tag{3}$$

The derivation of these two forms is presented in Appendix A; notice that the constant infectious period model has a larger R_0 in this discrete neighbourhood approach than its exponential counterpart (Fig. 1). This is because in the exponential period model, the few individuals who are infectious for a long time rapidly use up all their neighbouring susceptibles, whereas for the constant period model this is less of a problem (Keeling & Grenfell, 1997).

COMPARISON WITH THE TRADITIONAL APPROACH

Most modellers calculate the basic reproductive ratio using the underlying mean-field equations (1), taking R_0 to be the rate of change in the number of cases per infectious individual times the average infectious period. Hence, defining R_0' to be the basic reproductive ratio using this method, we find

$$R_0' = \beta \times \frac{1}{g}. \tag{4}$$

An important difference is that any probabilistically estimated R_0 must lie between 0 and n, whereas R_0' can take arbitrarily large values. This difference comes from the fact that the probabilistic approach considers the number of susceptible neighbours to be reduced every time an infection event occurs; therefore the number of susceptible contacts of an infectious individual decreases with time. Under the mean-field assumptions, the contact rate does not vary as the number of neighbours is assumed to be infinite.

To compare the individual approach given above with the mean-field model, we set $\tau = \beta/n$ and hence preserve the initial infection rate. This means that as the number of neighbours increases so the strength of the contact with each neighbour decreases, we could envisage this as implying that as the number of contacts increases so less time can be spent with each contact. As expected, if we allow $n \to \infty$, while keeping β constant, the above three formulae for the basic reproductive ratio (2)–(4) are equivalent. However, for finite values of n (and particularly for n small), the value from the deterministic equations (R_0') is greater than that from the probabilistic definition (R_0). As shown in Appendix A, this result is true for all assumptions about mixing and infectious periods.

We illustrate these results by finding the relationship between τ, n and g when R_0 (or R_0') is unity, and we are at the invasion threshold (Table 1). Figure 1 shows the estimated basic reproductive ratio for the above three cases (mean-field, constant decay rate and fixed infectious period). In graph (a), we fixed $n = 2$ and

TABLE 1

From eqns (2)–(4), *the relationship between the individual level parameters* (τ, n and g) *when the estimated basic reproductive ratio is unity. These relationships clearly show that* R_0 *for the fixed period model lies between the deterministic and exponential period estimates*

Exponential period	Fixed period	Deterministic model
$g = (n-1)\tau$	$g = \dfrac{-\tau}{\ln\left(1-\dfrac{1}{n}\right)} \approx (n-\frac{1}{2})\tau$	$g = n\tau$

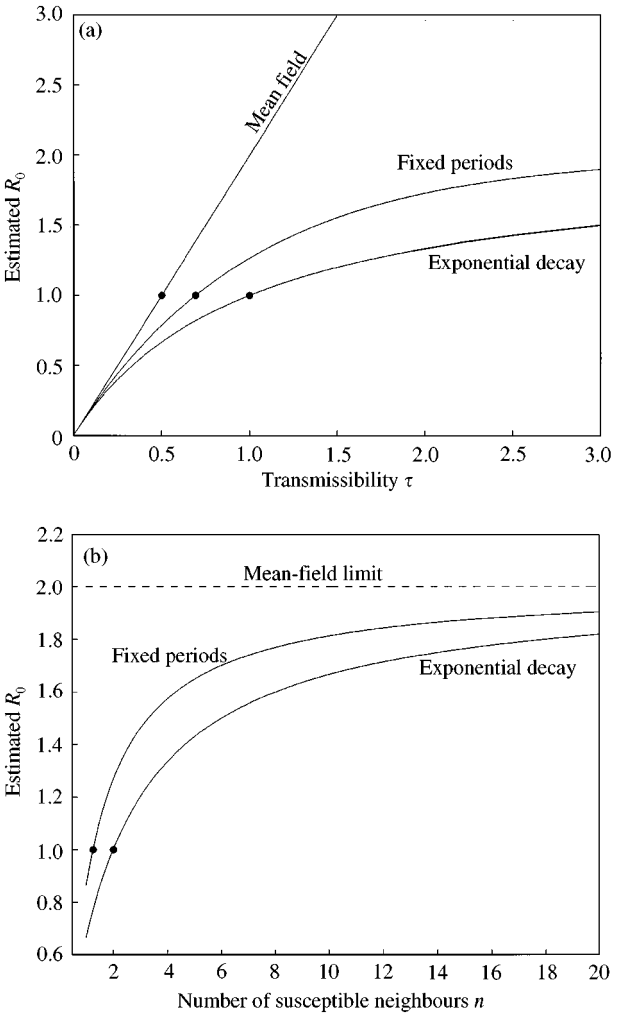

FIG. 1. The value of R_0 for the two assumptions of fixed infectious periods and exponentially distributed periods, and the value of R_0' derived from the deterministic equations. Notice that R_0' is always greater than R_0. In graph (a) the average number of susceptible neighbours $n = 2$ and τ (and hence $\beta = n\tau$) is varied. Note that although $n = 2$ the actual neighbourhood size could be far bigger. As $\tau \to \infty$ we find that R_0 asymptotes to n whereas R_0' tends to infinity. For graph (b), the contact rate $\beta = 5$ and n and also $\tau = \beta/n$ are varied. The mean-field estimate R_0' is unaffected by changes in n; the discrete models asymptote to the mean-field limits as $n \to \infty$. The dots on both graphs the position of the invasion threshold where the basic reproductive ratio is estimated to be one.

vary τ and hence β as well; for graph (b) the contact rate is fixed at $\beta = 2$, but n and hence τ is varied. The graphs also indicate the points where R_0 is estimated as one (the invasion threshold). The greatest discrepancies between the curves occur when n is small and τ is large.

Even at the fundamental level of calculating whether a disease will spread, the standard modelling approach is not consistent with the true probabilistic argument, and our assumptions about the infectious period have a strong effect. Therefore, for a finite neighbourhood, it is possible for the deterministic model to predict incorrectly the successful spread of the disease despite the fact that in reality each infectious individual triggers less than one new case—this is commonly found for disease models on a lattice (Mollison, 1977).

Estimation of R_0 from Data

In practical situations, R_0 is usually estimated from the proportion of susceptibles at equilibrium, S^* (Anderson & May, 1992),

$$R_0 = \frac{1}{S^*}. \tag{5}$$

This formulation means that the long-term endemic behaviour of the disease must be considered, so many of the simplifying assumptions are used for invasion break-down. For endemic diseases many new facets arise which can complicate the analysis and make quantitative predictions difficult. Instead, this section focuses on the estimation of R_0 from the proportion of susceptibles and considers the qualitative effects of each new complication.

Equation (5) relies on the three major assumptions about the distribution of cases,

(1) The total number of infectious cases is small, so that each susceptible individual has at most one infectious neighbour.
(2) At any one instant each infectious individual on average triggers exactly one further case, so that the infection is at equilibrium.
(3) The number of susceptibles around an infectious individual is reduced to exactly a fraction S^* of the value when the entire population was susceptible. That is, the distribution of infectious and susceptible individuals is uncorrelated.

From Appendix B, it is clear that under these assumptions this basic formula (5) still holds even when we consider the number of neighbours, n, to be finite. However, as mentioned above some new questions need to be addressed if we are to fully understand this formula in a stochastic spatial context. Below, we examine these issues and suggest how they affect the estimation of R_0.

What happens if the number of infectious cases is not small? When there are many infectious cases, or the infectious cases are highly aggregated, it is highly likely that a susceptible individual is surrounded by more than one infectious neighbour. Hence, because some of the susceptibles are shared, the effective number of susceptibles per infectious individual is reduced. This phenomenon can be viewed as a functional response, with infectious individuals in competition for a limited amount of susceptibles (Heesterbeek & Metz, 1993; de Jong *et al*., 1995). As the effective number of neighbouring susceptibles is lower than the standard estimated value, we will consequently underestimate the value of R_0.

How is this calculation affected by temporal fluctuations in the number of susceptibles? One of our assumptions was that the population was at equilibrium; we next consider the effects of both deterministic and stochastic fluctuations. Let $S(t)$ be the average proportion of susceptibles surrounding an infectious individual; S is assumed slowly varying compared to the generation time of the disease. Over a long period of time the geometric mean of the number of cases produced per infectious individual must be one if the disease is to remain extant and bounded. As detailed in Appendix B, from this long-term behaviour we obtain

$$R_0 = \left\langle \frac{1}{S(t)} \right\rangle, \tag{6}$$

where $\langle \cdot \rangle$ represents the long-term geometric average value. Thus, simply taking the arithmetic mean of the susceptibles leads to an underestimate of R_0. This underestimate is greatest when there are large fluctuations and the level of susceptibles drops to low values.

It is interesting to consider the non-ergodicity of this problem, that is, temporal and spatial variations lead to different averages. To find S at a point in time, we necessarily take the arithmetic spatial average of the susceptibles across the population. However, eqn (6) reveals that temporal fluctuations should be treated as geometric averages. This may lead to complications when we come to consider populations with large-scale spatial heterogeneity—as the spatial scale over which we aggregate will affect the size of the temporal fluctuations. We find that averaging over large-scale spatial heterogeneities within the system will lead us to further underestimate R_0.

How is this calculation affected by local heterogeneities? The final assumption was that each infectious individual interacted, on average, with $nS(t)$ susceptible individuals and that it could infect these in isolation. This is generally not true due to the presence of spatial correlations between susceptible and infectious individuals. Much of the research on the spread of disease using lattice-based models (Mollison, 1977; Durrett, 1992; Rhodes and Anderson, 1996; Levin & Durrett, 1996) displays striking spatial patterns, indicating strong spatial correlations. Pair-wise approximations for the spread of a disease through a network show analytically that, during the initial spread of a disease, infectious and susceptible individuals become negatively correlated in space, while infectious individuals are highly aggregated (Altmann, 1995; Keeling *et al*., 1997; Keeling, 1999). Once again, the standard approach has overestimated the potential susceptible neighbours per infection source—and hence underestimated R_0. Although many different models have been used to examine the

development of spatial correlations, it has become clear that without a detailed description of the network of contacts quantitative predictions cannot be made. Contact networks with large amounts of local structure and few connections per individual lead to the strongest correlations, and hence the largest errors in our estimation of R_0 (Keeling, 1999).

All the above errors act in the same direction: the standard estimate of R_0 is always an underestimate of the true value. As well as being of theoretical importance there is also a practical advantage in knowing the value of R_0 accurately. The precise value of R_0 is most commonly used for parameter estimation and hence the calculation of vaccination thresholds. As we have underestimated R_0, we will also underestimate the level of vaccination required to eradicate the disease and prevent it from re-invading. This could potentially have very important public health implications. Our underestimate of the vaccination threshold is likely to be greatest when there is a large number of infectious individuals; each individual can only spread the disease to a few near neighbours and there are large deterministic fluctuations in the number of cases.

There is seldom sufficient data to correct for all of the above complexities; however, by combining observations at the individual and population levels we can predict the strength of the individual-based nature on the dynamics.

Minimum Effective Neighbourhood

If we can find the values of the individual level parameters (τ and g) from detailed observations (for example at the family level; Hope-Simpson, 1952), then the underestimated value of R_0 can also be used to provide a lower bound to the size of the effective local neighbourhood. To achieve this, we define a new quantity, the minimum effective neighbourhood (MEN) as "the number of (potentially susceptible) neighbours n, which, together with the individual level parameters, produces the estimated value of R_0". This value of n is clearly an underestimate of the actual number of neighbours because it contains the effects of spatial correlations, fluctuations and many infectious individuals.

As shown in Fig. 1, the mean-field approach works well for large neighbourhood sizes, but differs greatly from the more accurate individual-based estimation for small values of n (cf. Diekmann *et al.*, 1998). Therefore, a large MEN generally implies that the mean-field limit models are more accurate; each infectious individual interacts with a larger environment and hence the effects of stochasticity should be weaker and local spatial correlations should be smaller and slower to develop. This lower bound can therefore be used to determine the reliability of the standard models when individual-based stochastic approaches are necessary. We would expect the MEN to be far lower for a sexually transmitted disease than for airborne diseases which have far more potential contacts; hence airborne infections are more rapidly modelled by mean-field equations.

AN EXAMPLE—TRANSMISSION OF CHILDHOOD VIRAL INFECTIONS

We consider three childhood diseases in developed countries: measles, chickenpox and mumps (parameter estimates from Anderson & May, 1992; Hope-Simpson, 1952). In primary infections, all these diseases closely follow the susceptible, infectious, recovered paradigm (Anderson & May, 1979; Grenfell & Dobson, 1992). Table 2 shows the estimated values of basic epidemiological parameters (R_0, the infectious period $1/g$ and the transmission probability or infectiousness T). The transmission probability is defined as the proportion of susceptible contacts who catch the disease; this is an increasing

TABLE 2

Basic epidemiological parameters and the minimum effective neighbourhood for three common childhood infections

	Measles	Chickenpox	Mumps
Estimated R_0	11–15	7–12	11–14
Infectious period (d)	7	11	6
Transmission prob. T	0.75	0.6	0.3
Estimated τ	0.198	0.083	0.059
Minimum effective neighbourhood	15–20	12–20	37–47

function of the transmissibility and the infectious period. The transmission probability and the infectious period ($1/g$) are estimated from detailed observations of transmissions within families (Hope-Simpson, 1952; Bailey, 1956) and hence provide parameterization at the level of the individual. Note that as the transmission probability, T, is calculated from within-family observations where contacts are strong, it is likely to be an overestimate of the true value, leading to an even larger underestimate of n.

Considering the chance of catching the disease from a single contact, for the fixed infectious period model we find

$$T = (1 - e^{-\tau/g}).$$

Therefore, from R_0, T and g we can estimate τ and MEN,

$$\tau = -g \ln(1 - T) \quad \text{and} \quad \text{MEN} = \frac{R_0}{T}.$$

From the values in Table 2, we should expect measles and chickenpox to behave less like their mean-field counterparts than mumps, which has a far larger MEN. Mumps has a lower transmission probability than the other two diseases, therefore it requires far more potential contacts to achieve the estimated levels of R_0. Before vaccination, measles, chickenpox and mumps were all predominantly spread by school children of about the same age, which would suggest the same contact network for all three diseases (Edmunds *et al.*, 1997). However, as mumps has a larger MEN, we suggest that either mumps is spread by a larger proportion of the adult population (i.e. a different contact matrix), or that mumps can survive for longer out of the human body, both of which will act to increase the effective neighbourhood size.

Figure 2 shows how the minimum effective neighbourhood (MEN) varies with R_0 and the transmission probability, T. The ranges of the three childhood diseases, measles, chickenpox and mumps, are given for comparison. As R_0 increases and the transmission probability decreases, MEN get larger and the system approaches the mean-field, homogeneously mixed limit.

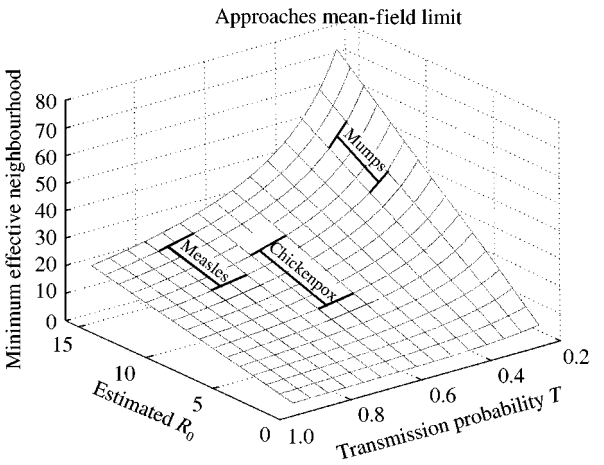

FIG. 2. Relationship between the transmission probability T, R_0 and the minimum effective neighbourhood (MEN). The dark lines show where the three childhood diseases, measles, chickenpox and mumps occur in parameter space. As the transmission probability decreases and R_0 increases the minimum effective neighbourhood becomes larger and we approach the mean-field limit.

Discussion

This paper has highlighted how the discrete nature of a population can alter our conclusions about basic epidemiological processes. The results underline a fundamental idea in ecology—that part (though not all) of our methodology, derived from deterministic models, breaks down when individuals with stochastic behaviour are considered (Durrett & Levin, 1994; Levin & Durrett, 1996; Wilson, 1998). For many systems, mean-field models provide a robust means of understanding the behaviour, yet for others it is necessary to consider the individual nature of the population. By introducing the minimum effective neighbourhood (MEN) which links local individual-based observations with global behaviour, we are beginning to develop a means to assess the likely validity of the standard homogeneous models. The existence of small contact neighbourhoods has two important implications, each individual experiences large fluctuations in its local environment (Keeling & Rand, 1999) and strong local correlations are likely to develop (Keeling *et al.*, 1997).

Fundamental to this work is the assumption that the contact rate β is composed of a transmission rate τ and a potential susceptible

neighbourhood of size n, hence enabling us to scale between individual-based and mean-field limits. Calculating R_0 from its basic definition by a probabilistic approach shows that the value derived from the mean-field equations is always an overestimate. The error in the mean-field estimate (and hence the error in the mean-field equations) increases for small numbers of interactions, for long periods of contact (g small) and when the transmission rate, τ, is large. This would imply that the standard mean-field models are most accurate at capturing the spread of diseases such as measles (where the number of potential transmissions per individual is large), but fail to describe the behaviour of sexually transmissible diseases in a predominantly monogamous population (Dietz & Hadeler, 1988). Even with simple respiratory diseases problems may still occur if the transmission rate is high and therefore the spread of infection becomes limited by the number of contacts. For many childhood diseases, spread within a small family group is considered to be vitally important to the dynamics (Becker & Dietz, 1995; Keeling, 1997) so the individual nature of the system again becomes important.

Recent work using pair-wise models for disease spread through a network provides a robust method of capturing the dynamics when the number of contacts is limited (Sato *et al*., 1994; Altmann, 1995; Keeling *et al*., 1997; Keeling, 1999). These pair-wise models predict the same invasion threshold as the probabilistic calculation of R_0, but also allow us to consider the spread of infection when there is a high degree of local spatial structure, which further reduces R_0.

Separating the contact rate β into two components leads to a novel interpretation of the seasonal forcing of childhood infections. Although we may expect some variation in the transmission rate τ, due to changes in the environment, it is the potential neighbourhood size n which contains the majority of the seasonal (term-time) forcing. Results from a stochastic SEIR-type model (Keeling & Grenfell, 1997) indicate that for measles the MEN varies by a factor of two between term time and school holidays. Therefore, the accuracy with which mean-field models predict the local dynamics varies greatly throughout the year.

The use of the minimum effective neighbourhood has also highlighted another important ecological consideration. An individual-based or stochastic approach is often only adopted when a population is considered small. However, the MEN shows that an individual-based approach may be necessary for all population sizes if the number of interactions per individual is limited.

The standard method of estimating R_0 from the density of susceptibles at equilibrium has been shown to consistently underestimate the value. Although it is possible to describe mathematically the errors in the estimation process, a more reliable estimate cannot be produced without detailed information about the individual transmission rates, network of contacts and correlation of susceptible and infectious individuals. Such information is currently unavailable. The underestimation of R_0 from the proportion of susceptible individuals (obtained from serological data) leads to an underestimate for the vaccination threshold necessary to eradicate a disease. This could be a potential problem when planning a vaccination strategy, as the level of vaccination required may be far higher than the level predicted. The inclusion of discrete individuals and finite neighbourhoods means that the (aggregation) of susceptibles and vaccinated individuals should ideally also be taken into account. Successful vaccination strategies must not only treat a high proportion of the population, but must achieve an even coverage—pockets of susceptible individuals will allow a disease to re-invade (Keeling, 1999).

In general, this work has demonstrated the difficulties in ecological modelling with linking individual-based parameters and probabilistic arguments with global parameters and deterministic equations. For many ecological and epidemiological problems the discreteness of individuals plays a major role—understanding these effects and knowing when they must be considered is still an open problem. It is therefore essential to have good, quantitative measurements for both the global dynamics and the local behaviour if these two very different modelling approaches are to be reconciled.

This research was motivated by discussions and work with David Rand. Thanks also go to Pej Rohani

and Håkan Andersson for their many helpful comments. This work was supported by the Wellcome Trust (BTG) and the Royal Society (MJK).

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APPENDIX A

Let $d(m, p)$ be the proportion of individuals who are in contact with m susceptible neighbours for a period p while they are infectious—note that a single individual can be in contact with various numbers of neighbours for different amounts of time. For the SIR model the contact parameter β is given by

$$\beta = \sum_{m=0}^{\infty} \int_0^{\infty} mp\tau g\, d(m, p)\, \mathrm{d}p.$$

For a fixed number of susceptibles m around an infectious individual and assuming that the infection process is random, the number of neighbours that are infected by this primary case is binomially distributed. To calculate R_0, we need to sum this binomial distribution over all possible neighbourhoods and periods of contact,

$$\begin{aligned} R_0 &= \sum_{m=0}^{\infty} \int_0^{\infty} d(m, p) \\ &\quad \times \sum_{i=0}^{m} \binom{m}{i} i(1 - \mathrm{e}^{-\tau p})^i (\mathrm{e}^{-\tau p})^{m-i}\, \mathrm{d}p \\ &= \sum_{m=0}^{\infty} \int_0^{\infty} d(m, p)\, m(1 - \mathrm{e}^{-\tau p})\, \mathrm{d}p. \end{aligned} \tag{A.1}$$

However, the calculation of the basic reproductive ratio from the underlying mean-field equations as the rate of change in the number of cases per infectious individual times the average infectious period, gives

$$R_0' = \sum_{m=0}^{\infty} \int_0^{\infty} d(m, p) mp\tau\, \mathrm{d}p.$$

As $p\tau$ is always greater than $1 - \exp(-p\tau)$, R_0' is greater than R_0 for all possible distributions of neighbourhoods and times.

In both of the above calculations, if it can be assumed that the number of susceptible neighbours and the contact period are independent, such that

$$d(m, p) = N(m)P(p),$$

then the integral and sum in the above forms can be naturally separated,

$$R_0 = n \int_0^{\infty} P(p)(1 - \mathrm{e}^{-\tau p})\, \mathrm{d}p,$$

$$R_0' = n \int_0^{\infty} p\tau\, P(p)\, \mathrm{d}p,$$

where n is the average number of neighbours or $\sum mN(m)$.

Two main assumptions can be made about the infectious period (cf. Keeling & Grenfell, 1997). The first is the more natural fixed infectious period, and the second is the mathematically simpler constant decay rate.

For the fixed period assumption, $d(m, p)$ is only non-zero when $m = n$ and $p = 1/g$. Thus,

$$R_0 = n(1 - \mathrm{e}^{-\tau/g}).$$

The constant decay rate g, assumed by the SIR model, means that infection periods are exponentially distributed, hence,

$$d(m, p) = \begin{cases} g\mathrm{e}^{-pg} & \text{when } m = n, \\ 0 & \text{otherwise.} \end{cases}$$

So we find that

$$R_0 = n\frac{\tau}{\tau + g}.$$

APPENDIX B

If we assume that susceptibles are randomly distributed with density S^*, then this adds an extra factor to the binomial distribution of eqn (A.1). The probabilistic approach to calculating the effective reproductive ratio now has to consider the probability that an individual is susceptible and then the probability that it is infected. Given that we are at equilibrium, the average number of secondary cases produced by

an infectious individual must be one, so that the number of infectious individuals remains constant. Therefore,

$$\begin{aligned}1 &= \sum_{m=0}^{\infty} \int_0^{\infty} d(m, p) \\ &\quad \times \sum_{i=0}^{m} \binom{m}{i} i(S^*[1 - e^{-\tau p}])^i \\ &\quad \times (1 - S^*[1 - e^{-\tau p}])^{m-i} \, dp \\ &= \sum_{m=0}^{\infty} \int_0^{\infty} d(m, p) m S^* (1 - e^{-\tau p}) \, dp \\ &= S^* R_0 \\ \Rightarrow R_0 &= \frac{1}{S^*}.\end{aligned}$$

This is the same formula as from the mean-field model.

When the number of susceptibles has temporal fluctuations the calculation is more complex. For the infectious process to remain extant and bounded in the long term, the geometric average of the number of secondary cases produced should tend to one. We require a geometric average because infection acts multiplicatively with successive number of cases growing or decaying exponentially if the geometric average is not equal to one. Assuming that the number of susceptibles is slowly varying, that each infectious individual has on average $S(t)n$ susceptible individuals that it alone can infect, and taking logarithms, we find

$$\begin{aligned}0 &= \lim_{T \to \infty} \frac{1}{T} \int_0^T \ln \left[\sum_{m=0}^{\infty} \int_0^{\infty} d(m, p) \, m \, S(t) \right. \\ &\qquad \left. \times (1 - e^{-\tau p}) \, dp \right] dt, \\ 0 &= \lim_{T \to \infty} \frac{1}{T} \int_0^T \ln[S(t) R_0] \, dt \quad \text{as } m = n, \\ \Rightarrow \ln[R_0] &= \lim_{T \to \infty} \frac{1}{T} \int_0^T \ln \left[\frac{1}{S(t)} \right] dt.\end{aligned}$$

Thus, under these assumptions, R_0 is given by the geometric average of the inverse of the proportion of susceptible individuals.