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unlikely in any

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Modern concepts of epidemic theory originated from the work of William Farr, the first epidemiologist to begin discerning mathematical principles governing the behaviour of infectious diseases. The basic reproduction number of such an infection,  $R_0$ , is defined as 'the number of cases that would result directly from the introduction of a single infectious individual into a susceptible population' and is therefore effectively synonymous with 'transmissibility':

$$R_0 = C \times P \times D$$

In which C represents the average rate of contacts made between an infected individual and susceptible individuals in the population, P is the probability of transmission from each contact and D is the duration of infectiousness. An  $R_0$  value of 1 therefore implies that a single infectious case will cause, on average, one other, whereas an  $R_0$  of less than 1 indicates the disease will eventually disappear, and an  $R_0$  greater than 1 indicates continual spread of infection. Hence, in order to eradicate an infection, we must attempt to alter the host pathogen relationship in such a way that R is decreased below 1.

It is unlikely in any actual population that every single individual will be susceptible to a particular disease, the effective reproductive rate, R, therefore estimates the average number of secondary cases in a given population consisting of both susceptible and non-susceptible individuals.  $R = R_0 \times X$  in which X represents the fraction of the population which is susceptible to the disease. X will be reduced in populations which have previously encountered a disease, and hence a greater proportion of individuals have acquired immunity. This is also seen in public health measures which promote immunization; "When an individual is successfully immunised, not only is there one less person who will ever be infected, there is also one less

person who will be infectious" (McLean, 1992). Vaccination therefore acts to decrease the infectious pool in such a way that it provides protection even to those who have not received the vaccine, known as herd immunity. In order to completely eradicate a disease, the critical level of vaccination (also known as the threshold for herd immunity) can be calculated from  $R_0$ , giving the extent to which the pool of susceptible individuals must be reduced;  $P_c = 1 - 1/R_0$ . The larger  $R_0$ , and hence the greater the transmissibility of a condition, the larger  $P_c$  must be in order to eradicate the disease.

Measles Measles has a high  $R_0$  and therefore a very high proportion of the population must be vaccinated in order to eradicate the disease. The viral disease causes serious complications, including encephalitis and pneumonia as well as suppressing the immune system, increasing the  $P$  value for other epidemics. As a result, measles remains a major cause of death, however, the introduction of a successful vaccine is believed to have decreased child deaths by 1/5th since 1990. The importance in this vaccination program can be seen in the aftermath of the publication of Wakefield's work in a 1998 Lancet paper.

This paper implicated the MMR vaccine in the development of autism in young children, which, despite the paper stating that no causal relationship had been proven, and further studies finding no relationship at all, resulted in a huge decline in confidence in the vaccine, and hence a rise in the number of parents refusing it for their children. This has been implicated as the major cause of the rise seen in measles cases following the paper's publication. In 2008 for example, measles was declared endemic for the first time in 14

years. This illustrates the dramatic effect that may be caused by a seemingly small decline in vaccination rate - it is thought that a 5% fall in MMR vaccine administration may result in a threefold increase in measles cases. The 2008 epidemic was particularly prevalent in festivals, thought to be a result of the increased rate of contact, increasing  $R_0$ ;  $R_0 = \beta B / \gamma$  In which  $B$  is the no. of contacts per unit time which will result in new infections and  $1/\gamma$  the mean infectious period. Smallpox Small pox is also a virus which, in contrast to measles, has a reasonably low  $R_0$  and has therefore been one of the only 2 diseases to be officially declared eradicated (alongside rinderpest in 2011), despite over 15 million cases occurring each year as recently as 1967. Small pox is highly contagious, with a high  $P$  value, however the duration of the infectious phase is short and occurs only following onset of the rash, and with reasonably close contact (within 1.

8m), and hence  $R_0$  is lower than measles and many other viral diseases. The eradication of small pox has been made far easier by the lack of alternative hosts which may provide a reservoir for the disease (for example mosquitoes in malaria) and has relied primarily on widespread vaccination programs and careful surveillance and isolation of outbreaks. HIV One of the most effective methods of reducing the incidence of AIDS, for which there is no vaccine, is to reduce the risk of transmission,  $P$ , by the use of anti-retroviral therapy. By 2020 the joint United Nations program on HIV and AIDS has set a target to ensure 90% of all people infected with HIV are aware of their status, 90% of them are on anti-retroviral therapy and 90% of those on therapy will have full viral load suppression.

This will result in 73% of those who have HIV achieving full viral load suppression, which, if maintained should enable elimination of HIV in 70% of Sub-Saharan countries and reduce  $R_0$  to less than 2 in the remaining 12 countries, compared to the current median  $R_0$  of 4.3. In combination with other high-impact preventative methods such as promotion of condom use and an increase in the availability of Pre-exposure prophylaxis (PrEP) could potentially see the eradication of AIDS. PrEP enables a reduction in the number of susceptible individuals who may come in contact with those which are infectious, and hence a reduction in  $C$  similarly to vaccination.

If taken consistently it has been shown to reduce the risk of infection by up to 92% in high risk individuals. Without treatment, the risk of transmission of HIV from sexual intercourse is considered to be approximately between 0.001 and 0.1 but the use of condoms has been found to reduce this by 80 - 85%. One study found that in 123 discordant couples who consistently used condoms none of the uninfected partners became infected, in comparison to 12 uninfected partners who contracted the disease out of 122 couples using condoms inconsistently. IMMUNITY and mutation? FLU

Childhood diseases  $R_0$  can in fact be estimated from the average age of infection.

This is because there is a greater chance of encountering a disease with a high  $R_0$  (i. e. a high transmission risk and many infectious people) earlier in life. Such infections are commonly termed 'childhood diseases' since the majority of people are infected at a young age, conferring acquired immunity for the remainder of their lives. By this estimation:  $R_0 = 1 + L/A$  In which  $L$  is

the average lifespan and the average age at infection. Chicken pox is one such disease in which early infection is common since the infectious period begins 1-2 days prior to a rash appearing, unlike small pox, preventing cases from being identified and isolated.

This is coupled with a high probability of transmission - studies of transmission have found that over 90% of close, susceptible people in contact with a diseased individual will be infected, resulting of an  $R_0$  value of approximately 11. Generally, contraction of the disease results in immunity to future infection (although latent infection may be reactivated) so outbreaks are rarely seen in adult populations. Pertussis, by comparison, has a much lower  $R_0$ , of approximately 5.5 and as a result is more commonly seen in older populations, as supposed to just the very young. Since the  $R_0$  value of chicken pox is so high, but the symptoms of the disease, particularly in children, are relatively mild in comparison to pertussis, it is not commonly vaccinated against in the UK. Limitations of  $R_0$ :  $R_0$  is always an average value - as not all infected individuals will transmit the disease to exactly the same number of people, therefore if there is great variation in the rate of spread among different subgroups of the population, the average  $R_0$  will be largely meaningless.  $R_0$  is therefore most useful in explaining the dynamics of a disease which is spread broadly among individuals who meet at random.  $R_0$  is difficult to observe and calculate in the field and hence mathematical models are frequently used to estimate its value, however, the true value of  $R_0$  is rarely actually derived from many mathematical models, which instead give a threshold as supposed to the number of secondary infections.

This does have some benefit in determining the viability of an epidemic (with  $R_0 >/< 1$ ) however is of relatively little use in comparing the dynamics of two different disease epidemics.