Supplementary online material
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Measles outbreaks in a population with declining vaccine uptake

Methods

We described the disease dynamics using a continuous time stochastic SIR model. Susceptibles become infected with probability $\beta I/N$ per unit of time, where S (I) is the number of susceptible (infected) individuals, N is the size of the population and β the transmission parameter. With a probability γ per unit of time an infected individual recovers from the disease and becomes immune.

To illustrate the effect of decreased vaccine uptake we simulated the number of cases of measles following repeated importations. Over time large outbreaks become increasingly likely (Figure S1a). If the reproductive number exceeds one, then outbreaks that affect a large part of the population become a possibility, but not necessarily immediately. If the reproductive number is less than one, limited outbreaks of the disease are possible due to stochastic effects following the importation of the disease.

We calculated the outbreak size distribution by assuming that the population is sufficiently large so that an outbreak does not have a significant effect on the fraction of susceptibles. The use of the outbreak size distributions to estimate a reproductive number smaller than one is given in (1). However, the distribution used in (1) is based on the unnecessary assumption of non-overlapping generations (see also ($2,3$)).

Let the fraction of the population that is immunised be c. The total number of susceptibles is approximately $S=(1-c)N$ and the reproductive number is $R=(1-c)\beta/\gamma$. We reduced the continuous time branching process by only considering the probability of transitions but not the time between them. The probability that the next event is recovery is given by $\gamma I/(\beta I(1-c)+\gamma I)=1/(R+1)$ and the probability that the next event is infection is $\beta I(1-c)/(\beta I(1-c)+\gamma I)=R/(R+1)$. This defines a simple random walk. We calculated $p(I,T)$, the probability of having I infected individuals in the population after T events. At $T=0$ all probabilities are 0 except $p(1,0)=1$. We found

that $p(I,T)=T!I\dfrac{(R+1)^{-T}}{(\frac{1}{2}(T+I+1))!}\dfrac{R^{\frac{1}{2}(T+I-1)}}{(\frac{1}{2}(T-I+1))!}$ if T-I-1>0 and if T-I-1 is even, $p(I,T)=0$ otherwise.

To calculate the outbreak size distribution suppose that the outbreak stops after T events and has size x. Therefore at T-1 the number of infected individuals has to be one and (T-1)/2 of the past events must have been infections. Therefore $x=1+(T$-1)/2 and $T=2x$-1. For the outbreak to stop after $2x$-1 events the last event has to be a recovery and the probability that the total size of the outbreak is x is

$q(x)=\dfrac{1}{R+1}p(1,2x-2)=\dfrac{R^{x-1}}{(R+1)^{2x-1}}\dfrac{(2x-2)!}{x!(x-1)!}$. If R<1 the average outbreak size is 1/(1-R). The average outbreak size for outbreaks of 2 or larger, m, is

$$m = \frac{1/(1-R) - 1/(R+1)}{1 - 1/(R+1)} = \frac{2}{1-R}$$ and hence the reproductive number can be estimated as

$R=1-2/m$.

The probability of an outbreak of size n or larger is visualised in Fig S1b. Note that if R is slightly smaller than one very large outbreaks are possible even though population-size outbreaks (upper bar) are not. If R tends to one the probability of having an outbreak of at

least n cases is given by $\sum_{x=n}^{\infty} 2^{1-2x} \frac{(2x-2)!}{x!(x-1)!} = \frac{\Gamma(n-\frac{1}{2})}{2\sqrt{\pi}\,\Gamma(n)}$ which in the limit for large n

tends to $\frac{n^{-\frac{1}{2}}}{\sqrt{\pi}}$ $(4, 5)$.

References

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Figure S1a: The number of cases of measles that followed an importation into a population of 1,000,000 with a decreased vaccine uptake. The model uses the branching process as described in the text, but to which we added a vaccine uptake rate of vS and death rate $\mu(S+I)$. Dead individuals are immediately replaced by newborn susceptibles so that the population size remains constant. Parameters are β=500.133, γ=50, v=0.075 and μ=1/75 which will eventually result in a vaccine coverage of 85%. At time zero we started with vaccine coverage of 94%. The diagram was constructed by introducing single cases of measles at different points in time and counting the number of cases that this importation caused within a year. The red line gives the percentage of the population that is immunised, at the dashed line the reproductive number is one. Outbreak sizes of 300 and larger are represented on a logarithmic scale. **Figure S1b**: The probability of an outbreak of certain size or larger. On the abscissa is the reproductive number, R, on the ordinate is the size of the outbreak. The bar across the top is the probability of a large, population-size outbreak. The bar on the right is the colour index. The vertical line indicates R=1.