The Use of Disease Transmission Modelling in Cost-Effectiveness Analyses: Strengths and Weaknesses

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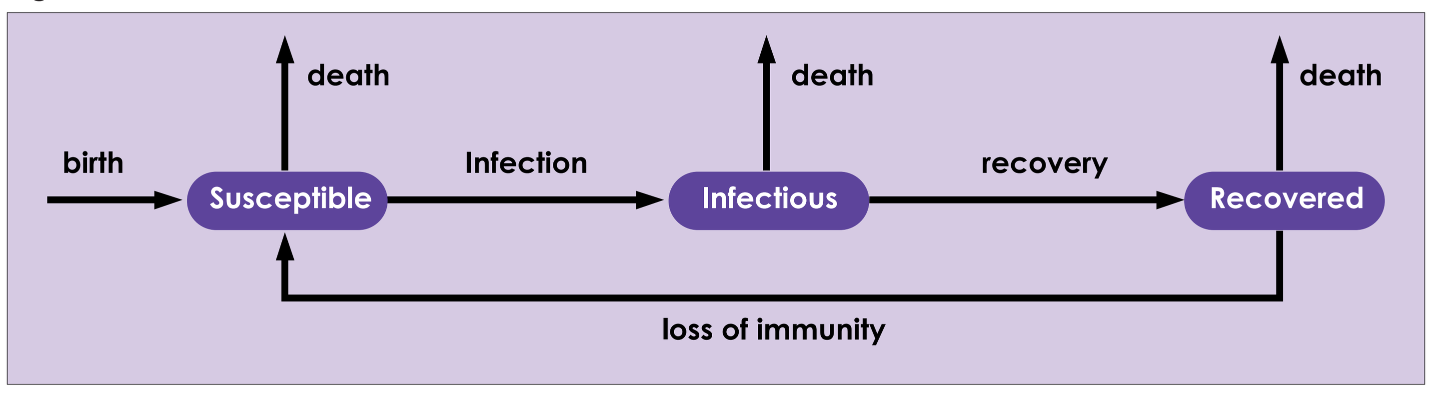
Introduction

The UK National Institute for Health and Clinical Excellence (NICE) recommends[1] that "economic analysis relating to public health guidance should adopt the public health sector, NHS and personal social services perspective." NICE draws on the second Wanless report[2] into the cost effectiveness of improving the health of the whole population which defines public health as "the science and art of preventing disease, prolonging life and promoting health through the organised efforts and informed choices of society, organisations, public and private, communities and individuals." The study presented on this poster outlines some of the reasons why taking a wider population perspective is particularly informative when dealing with infectious diseases and the importance of dynamic transmission models in this approach. The limitations of this approach are also discussed.

Methods

In order to explore the use of dynamic disease transmission modelling in cost-effectiveness analysis, a generalised deterministic compartmental transmission model was developed, Figure 1.

Figure 1



As this is a population based model, new susceptibles arise from the processes of birth and loss of immunity. Individuals may either remain susceptible or become infected. The rate of infection is assumed to be a function of the chance of a susceptible individual meeting someone infectious (population mixing) and of that encounter resulting in transmission of the pathogen (factors dictated by the host and pathogen biology). Once infected, individuals rapidly become infectious, before recovering to an immune state. Infections are assumed not to be fatal. Immunity gradually wanes over time, leaving individuals susceptible once more. All individuals are subject to a natural death rate unrelated to the infection in question. The capacity to account for season fluctuations in transmission was also incorporated into the model (seasonal forcing).

For the purposes of illustration, parameters typical of a directly transmitted close contact disease, such as influenza, were chosen (Table 1).

Table1

Basecase (mean values)	
Cost of falling ill	£36
Weekly cost of treatment	£ 0
Utility of uninfected individuals	1
Utility of untreated symptomatic individuals	0.8
Utility of treated symptomatic individuals	0.8
Duration of infectiousness (weeks)	3
Duration of immunity (years)	6
Treatment curtails the infectious period by (days)	2

The model was integrated using Euler's method, a time step of one day and a time horizon of 10 years. Discounting was applied to both costs and QALYs at an annual rate of 3.5%.

Models were run with and without treatment, recording the incremental cost per QALY gained by including treatment from week 10 following the introduction of a single infectious individual into a susceptible population of 10,000. Outcome was expressed as an incremental cost effectiveness ratio (ICER).

Univariate sensitivity analysis was performed by varying each of the parameters in turn as outlined in Table 2.

Table2

Sensitivity Analysis	Basecase	Low	High
Cost of falling ill	£36	£10	£110
Weekly cost of treatment	£0	£0	£50
Utility of untreated symptomatic individuals	0.8	0.6	0.8
Utility of treated symptomatic individuals	0.8	0.8	0.9
Duration of infectiousness (weeks)	3	2	20
Duration of immunity (years)	6	1	50
Treatment curtails the infectious period by (days)	2	1	20

In order to examine the impact of seasonal variation in the force of infection, the base case parameters were applied, while varying the force of infection using a sine wave with a period of one year and a range between zero and one.

In order to explore the potential for an intervention to influence the pattern of disease dynamics, the duration of immunity was increased to 20 years and treatment effect to a 13 day reduction in the duration of infectiousness.

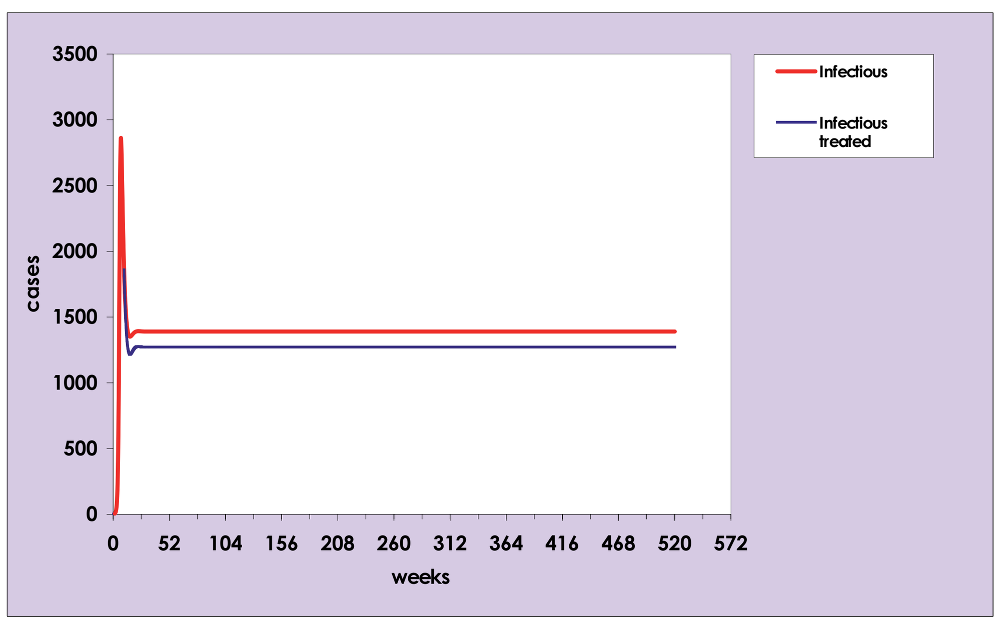
Finally, to illustrate the most extreme form of impact on disease dynamics, an eradication scenario was simulated, using base case parameters with the treatment impact increased to 20 days.

Results

Base case

In the transmission model, after an initial period of fluctuation, the prevalence of infection settles down to a steady endemic level. Reducing the infectious period by 3 days through treatment results in a sustained reduction in this level, Figure 2.

Figure 2



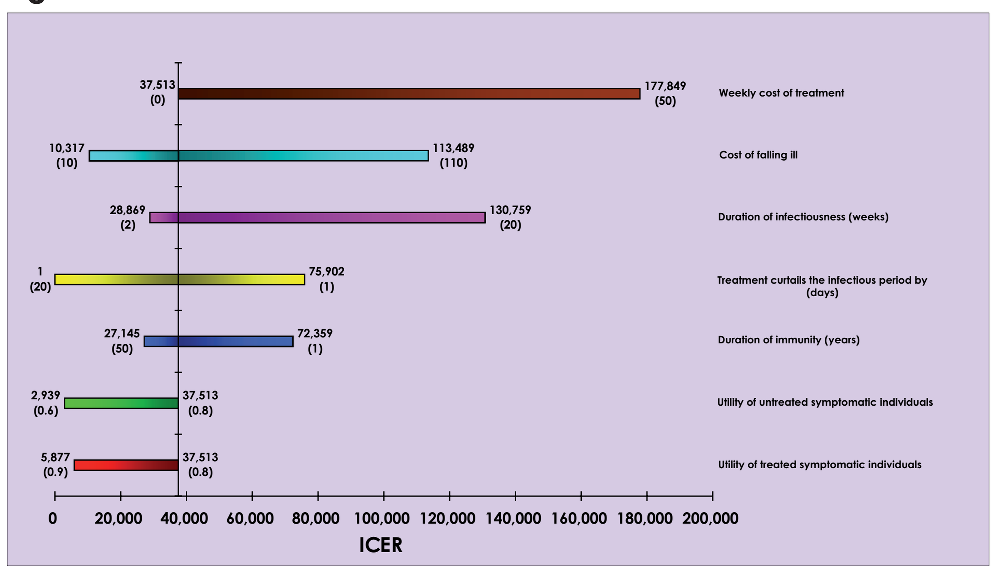
Base case dynamics of disease prevalence following introduction of one infectious individual into a population of 10,000 people.

Over 10 years in a population of 10,000 individuals, treatment resulted in a saving of approximately 390 quality adjusted life years at a cost of £14,640,000. This equates to an incremental cost of £37,513 per QALY, Table 3.

Table3

		No Treatment	Treatment	Increment	ICER
Basecase	QALYs	77933	78323	390	
	Cost	£ -	£14,641,146	£14,641,146	**37,513**
Basecase with seasonal forcing	QALYs	79793	80135	342	
	Cost	£ -	£8,371,079	£8,371,079	**24,505**
Biannual Oscillations	QALYs	81267	82394	1128	
	Cost	£ -	£1,081,151	£1,081,151	**959**
Eradication scenario	QALYs	77933	82523	4590	
	Cost	£ -	£3,771	£3,771	**0.82**

Figure 3.



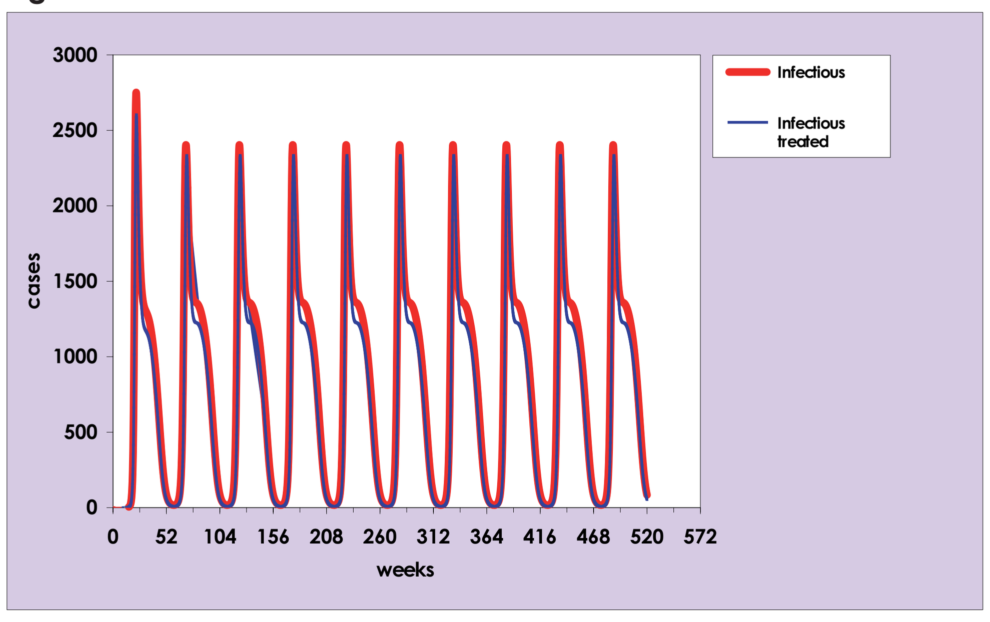
Sensitivity of the estimated incremental cost effectiveness ratio to changes in the value of transmission model parameters.

Sensitivity

The sensitivity of the estimated ICER to changes in each of the parameters is illustrated in a tornado diagrams, Figure 3.

The vertical axis represents the base case ICER with each horizontal bar demonstrating the range of ICERs obtained by varying the parameter named on the right of the diagram. The maximum and minimum ICER value are given, one on each end of the bar, under which is the corresponding parameter value in curly brackets.

Figure 4.

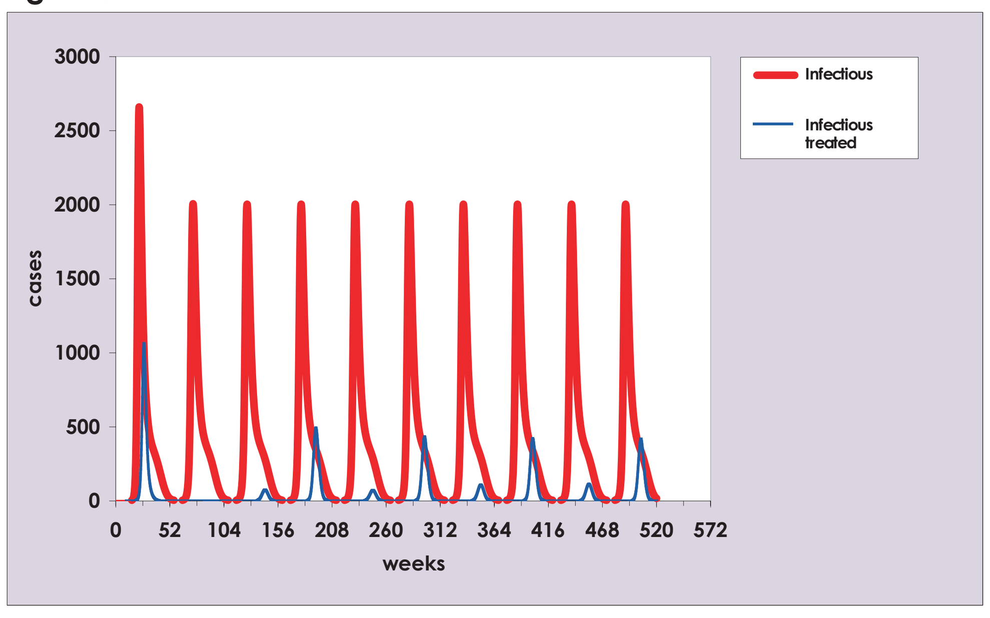


The influence of seasonal fluctuations in the force of infection on the pattern of base case disease prevalence.

Seasonal variation in transmission, when superimposed on the base case, results in annual peaks of disease prevalence, Figure 4.

Such dynamics have a dramatic impact on the estimated population level ICER, reducing it by approximately one third, Table 3.

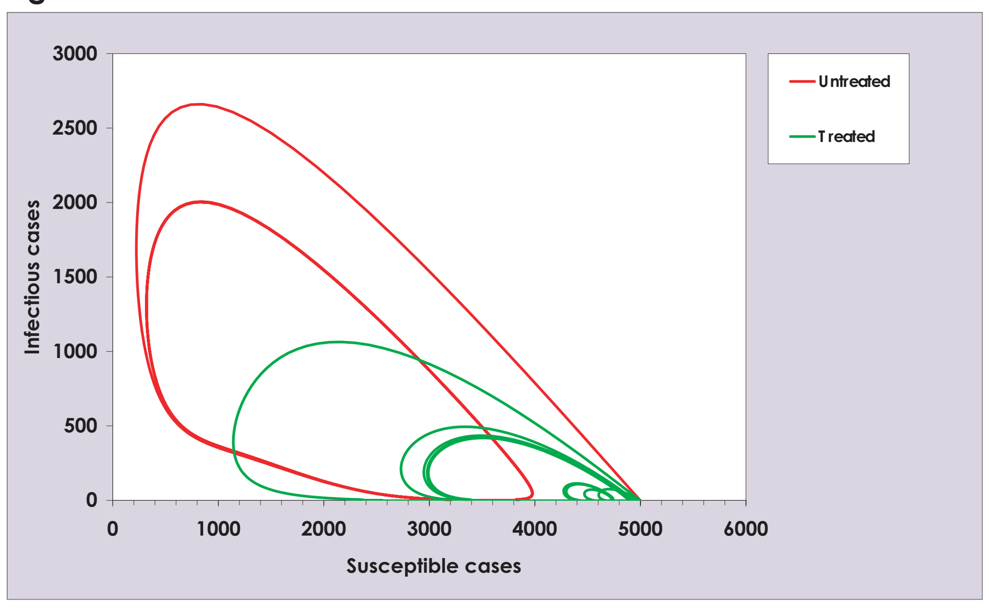
Figure 5.



Interventions can themselves induce changes in the temporal dynamics of disease prevalence. In this case the duration of immunity has been increased to 20 years and the duration of infectiousness reduced by 13 days in the treated population.

Increasing both the duration of immunity to 20 years and the treatment effect to a 13 day reduction in the duration of infectiousness results in an initial suppression of the disease prevalence, followed by alternating high and low annual peaks, Figure 5.

Figure 6.



When the number of susceptible and infectious individuals are plotted against each other, each point of the resulting trace charts the magnitude of these two groups. Time is not represented on the graph. Both treated and untreated populations start with 5000 individuals. The trace of the untreated population settles into a single orbit, while a shift to a two phase pattern in the treated population, with a higher peak every other year, is clear after 4 cycles.

The periodic nature of the peaks is better illustrated by a phase plot, charting the numbers of infectious individuals against the number of susceptibles, Figure 6.

These increases in duration of immunity and treatment effect result in a disproportionate reduction in the population ICER relative to the individual level ICER, Table 3. Increasing the base case treatment effect from 3 to 20 days results in the eradication of the pathogen from the population, reducing the population ICER to near zero.

Discussion

In general, two types of model are used to estimate the cost-effectiveness of interventions aimed at infectious diseases. Static models, in which the probability per unit time of a susceptible person becoming infected (the force of infection) remains constant over time, and dynamic models in which the force of infection is dependent on the number of infectious individuals in the population at each time point.

Some interventions reduce disease transmission across the population, either by reducing the pool of susceptibles (vaccination) or, as in this case, by treatment reducing the duration of infectiousness. This results in fewer new (secondary) cases. Capturing the full value of such an intervention requires a dynamic transmission model.

The processes involved in a dynamic model may be conceptually divided into two; those influencing an infectious individual's recovery and subsequent immune state, and those responsible for generating new infections. Transmission models serve to draw in population level externalities, such as those influencing fluctuations in the force of infection.

The incremental cost effectiveness ratio is sensitive to the parameter values used in the model. This is clearly illustrated in Figure 5 and 6. Accurate parameter estimation is therefore particularly important in the non-linear world of transmission modelling. The benefits of taking account of transmission dynamics are particularly obvious when there are seasonal fluctuations in the force of infection, and hence in the prevalence of disease. Accounting for these reductions can dramatically reduce the ICER for a particular treatment, increasing the probability that it will be deemed cost-effective. The most extreme example of this is where an intervention leads to the eradication of a disease.

The intervention itself may influence the temporal dynamics of a disease. This may have important implications for both health and health service logistics. Increased control may push the pattern of disease prevalence into cyclical oscillations similar to those seen with influenza A and B and respiratory syncytial virus. Reducing the force of infection, may also increase the average age of first infection; an important consideration where the severity of morbidity is a function of age, as is the case for example with rubella and hepatitis A.

Conclusions

1. For interventions that impact on transmission, taking account of the transmission dynamics of an infectious disease can significantly reduce the ICER and increase the probability of the treatment being deemed cost-effective.
2. Non-linear transmission models are sensitive to changes in certain parameter values, necessitating their accurate estimation and require specialist knowledge to construct.
3. Transmission models can take account of a rich diversity of dynamic behaviour, including seasonal variation in prevalence and intervention induced changes in the epidemiology of disease.

References

1. *National Institute for Health & Clinical Excellence (2006) Methods for development of NICE public health guidance.*
2. *Wanless, D. (2004) Securing good health for the whole population. London: HM Treasury.*

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