Mathematical models used to inform study design or surveillance systems in infectious diseases: a systematic review

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Introduction

The value of mathematical models for infectious diseases is widely recognized in various fields such as ecology and epidemiology.

In addition to improving our understanding of infectious diseases and helping decision making, mathematical models may also help in informing design of studies. The current use of mathematical models in planning studies has to our knowledge never been systematically summarized.

Objective

To determine to what extent mathematical models have been incorporated into the process of planning studies and hence inform study design for infectious diseases transmitted between humans and/or animals.

Methods

- We systematically searched Ovid Medline and two trial registry platforms (Cochrane, WHO) using search terms related to infection, mathematical model, and study design from the earliest dates to October 2016.
- Inclusion criteria: mathematical models (compartmental, individual-based, or Markov) which were described and used to inform the study design of infectious disease studies.
- Information about the investigated infection, population, model characteristics, design outcomes, research questions, and study design were extracted.

Table 1: Description of the design outcomes.

Design outcomes	Description
Follow-up	The model was used to determine/inform the follow-up time of the study.
Timing of sampling	The model was used to determine/inform at which time point(s) sampling should be performed.
Frequency	The model was used to determine/inform the frequency at which sampling has to be collected (over time) during the study.
Number	The model was used to determine/inform the number of sampling to collect over time during the study.
Monitoring	The model was used to identify parameters or indicators that should be monitored during the study.
Sample size	The model was used to determine/inform the sample size.
Whom	The model was used to determine/inform which subgroups of the population studied should be sampled.
Power	The model was used to perform statistical power calculations.

Results

- Among the 23 publications that used compartmental or individual-based models, 12 were observational or surveillance studies and 11 were clinical trials.
- Infections studied were equally animal and human infectious diseases for the observational/surveillance studies, while all but one between humans for clinical trials.

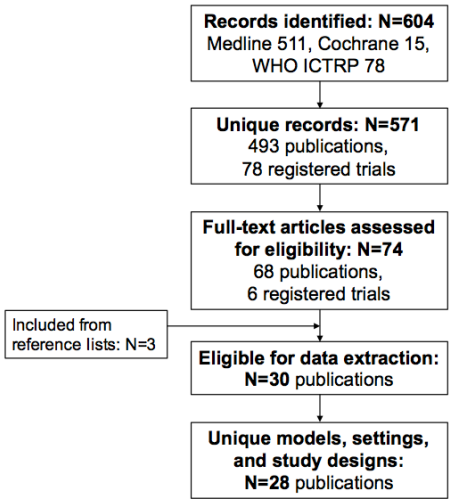

Figure 1: Simplified flow diagram of included and excluded publications and registered trials.

- About a third of the publications reported the software in which the mathematical model was implemented but code is available in only two publications.
- The mathematical models were mostly used to inform the required sample size (n=16), the statistical power (n=9), the frequency at which samples should be taken (n=6), and from whom (n=6).
- Research question categories identified among the studies included: detect infection early, estimate epidemiological parameters, compare different trial arms, include potentially good responders in a trial, follow trial progression, detect changes in infection values over time, and determine appropriate time point(s) to estimate a parameter.

Conclusion

Despite the fact that mathematical models have been advocated to be used at the planning stage of studies or surveillance systems, our results show that they are used scarcely.

With only one exception, the publications described theoretical studies, hence, not being utilized in real studies.

Further research is needed to make mathematical models available to help informing the design of future infectious disease studies.

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