Published: November 2017

A decade of individual-based transmission models: why, what and how?

Lander Willem - Modeller, Centre for Health Economic Research and Modelling Infectious Diseases, University of Antwerp, Belgium.

Decades of prevention and control programmes for infectious diseases are more and more challenged by the combination of increased global reach of both infectious diseases and vaccine controversies. Historical examples exist where misperceptions on vaccine-related side effects have lowered vaccine coverage substantially, opening a window for outbreaks, re-emergence and sustained prevalence. For instance, a vaccine scare in 1998 linking MMR vaccination and autism has significantly decreased the coverage in England and Wales from around 92% in 1995 to around 80% in 2003 (1). In addition, low incidence of vaccine-preventable diseases often leads to the public perception of reduced severity and susceptibility, which increasingly leads to people delaying or refusing vaccinations (2). These events threaten the high historical immunization coverage in many countries. So-called herd immunity that results from high immunization coverage is extremely important as it indirectly protects risk groups who cannot be vaccinated due to age or medical reasons (e.g. very young children or immunocompromised individuals). The options to adjust current programmes to prevent the (re)emergence of pathogens are endless and require continuous evaluation using different methods. Mathematical models provide a powerful set of tools in this process as timely, budgetary or ethically feasible alternatives are often lacking. For example, modelling stochastic transmission events of vaccine-preventable childhood diseases in highly immunized populations with (clustered) heterogeneity in susceptibility can benefit from an individual-level approach using individual-based models. These models work bottom-up, with population-level behaviour emerging from the interactions between autonomous individuals and their environment. Individual-based models allow a high degree of heterogeneity for the creation, disappearance and movement of a finite collection of discrete interacting individuals.

Different terminology has been used in the literature for individual-level or individual-based models (IBM) including agent-based models, cellular automata, micro-simulation as well as more generic terms such as computer simulations and complex adaptive systems (3). A distinction in nomenclature can be designated by whether the simulation is based on nodes of a grid (as in a cellular automata), or based on agents that are self-contained programs that collect information from their surroundings and have the autonomy and capacity to learn and adapt (as in agent-based models). These terms have been used inter-changeably in the literature and this inconsistency curtails efficient knowledge transfer. The standard incorporation of the over-arching term "individual-based model" in the abstract or keywords would greatly improve current and future systematic searches in large electronic databases. Henceforth, we will use the overall term "IBM" to refer to the individual-level approach.

Current and future IBM applications

A systematic review of a decade (2006-2015) of disease transmission modelling (3) showed that most papers elaborate on unspecified close-contact infections or influenza, though IBMs for other air-, saliva-, vector-borne and sexually transmitted infections are emerging. Methods for vector-borne diseases have been described for malaria and dengue and could guide future research. IBM applications on chikungunya and zika are expected over the next decade given the growing geographical expansion of their common vectors. Also screening and (non-)pharmaceutical intervention strategies have not been fully explored with IBMs yet. The combination of targeted screening and vaccination strategies with economic evaluations is promising for the near future. Relatively few papers have used an IBM to model stochastic outbreak analysis under high vaccination coverage for vaccine-preventable childhood diseases. However, for measles it has been shown that stochastic fluctuations around the endemic equilibrium in populations with high vaccination coverage could cause recurrent epidemics (4). The three main reasons cited in the reviewed papers for choosing an IBM are: [a] to model heterogeneous between-host interactions regarding social mixing behaviour, age, compliance to mitigation strategies and spatial distribution; [b] to model heterogeneous within-host processes in combination with between-host interactions; [c] to obtain stochastic individual-level information on the disease burden to inform economic analysis or other post-processing.

The lowest-level entity in each model was a "person" and the minimum characteristic was the health state. Depending on the research questions, also heterogeneity for age, gender, spatial location, social mixing behaviour, compliance to reactive strategies, serotype carriage and cellular mediated immunity were incorporated. Social mixing behaviour and transmission events were modelled

in one unified population and/or within specific social contact clusters such as households, schools, workplaces and communities, sometimes in combination with occasional long distance trips.

How to execute IBMs

To implement an IBM, there are different simulation platforms. Firstly, software environments for statistical computing (e.g. R) enable many embedded features and are user-friendly but currently lack specific modules for IBMs. Secondly, there are integrated platforms such as Netlogo (5), which can be practical and straightforward but might not fulfil all requirements of the inherent heterogeneity and computational burden of IBMs. A third option are low-level programming languages such as C++, which enable high-performance code but require high-level programming skills.

Computational performance is an important aspect of a simulator's usefulness. The evaluation and update of each unique individual in an IBM requires more processing and data access compared to population-aggregate models. Although runtimes and memory requirements are inherent to model implementation and computer hardware, the endless options with an IBM come at a price. The memory access and data movement slows down simulation runs especially. Given the high programming burden, transparent reuse of models increases confidence in their approach and generated results. Making IBM code open-source (e.g. FluTE, FRED, STRIDE) is useful to validate model outcomes, to inspire future modelling projects and to expand model exploration. Consistent "branding" of the IBM, with a proper acronym, is practical to link studies and consolidate intellectual ownership of freely accessible source code.

In conclusion, IBMs are suited to combine heterogeneous within-and between-host interactions and offer many opportunities, especially to analyse targeted interventions for endemic infections and to model host behaviour. The latter has a major impact on disease transmission and policy interventions. There is an increasing interest to incorporate behaviour change in response to disease-related information (6). To facilitate this expansion, we advocate the exchange of (open-source) platforms and stress the need for consistent". IBMs come at a computational cost but offer a very powerful and flexible framework to analyse disease transmission in depth and ultimately to inform policy making in decades to come.

Lander Willem *- Modeller, Centre for Health Economic Research and Modelling Infectious Diseases, University of Antwerp, Belgium. Areas of interest: transmission models for airborne diseases, parameter estimation, social contact patterns and computational efficiency.*
lander.willem@uantwerpen.be

References:

1. Bauch CT, Bhattacharyya S. Evolutionary game theory and social learning can determine how vaccine scares unfold. PLoS Comput Biol. 2012:8(4): e1002452.
2. Larson HL, de Figueiredo A, Xiahong Z, et al. The state of vaccine confidence 2016: global insights through a 67-country survey. EBioMedicine. 2016: 12: 295-301.
3. Willem L, Verelst F, Bilcke J, Hens N, Beutels P. Lessons from a decade of individual-based models for infectious disease transmission: a systematic review (2006-2015). BMC Infectious Diseases. 2017:17(1):612.
4. Marguta R, Parisi A. Impact of human mobility on the periodicities and mechanisms underlying measles dynamics. J R Soc Interface. 2015;12(104):20141317.
5. Railsback SF, Grimm V. Agent-based and individual-based modeling: a practical introduction. New Jersey: Princeton University Press; 2011.
6. Verelst F, Willem L, Beutels P. Behavioural change models for infectious disease transmission: a systematic review (2010–2015). J R Soc Interface. 2016;13(125):20160820.