Pan American Health Organization

World Health Organization
REGIONAL OFFICE FOR THE Americas

Dengue modeling

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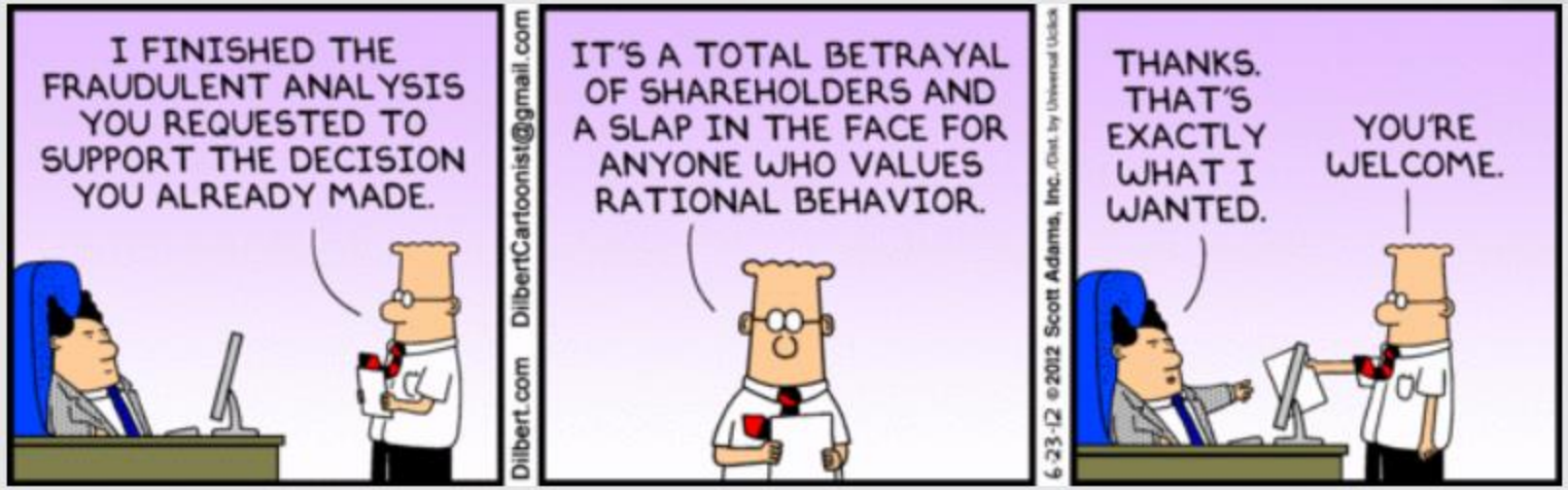
Outline

- Framing modeling within policy cycle
- Purposes of infectious disease modeling
- Overview of dengue modeling
- Final considerations

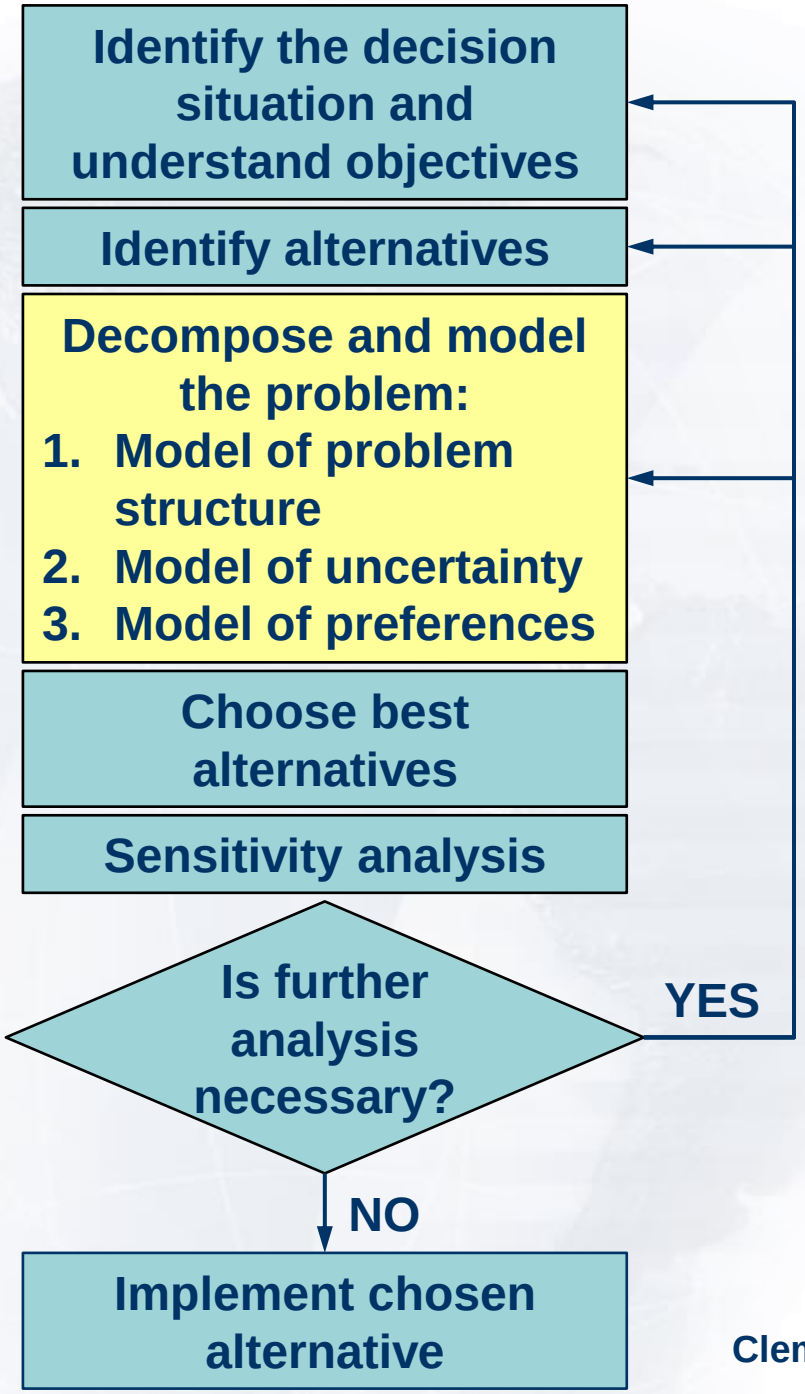

I FINISHED THE FRAUDULENT ANALYSIS YOU REQUESTED TO SUPPORT THE DECISION YOU ALREADY MADE.
Dilbert.com DilbertCartoonist@gmail.com
IT'S A TOTAL BETRAYAL OF SHAREHOLDERS AND A SLAP IN THE FACE FOR ANYONE WHO VALUES RATIONAL BEHAVIOR.
6-23-12 ©2012 Scott Adams, Inc./Dist. by Universal Uclick
THANKS. THAT'S EXACTLY WHAT I WANTED.
YOU'RE WELCOME.

Five stages of a policy cycle

Agenda setting	Problem recognition
Policy formulation	Proposal of solution
Decision-making	Choice of solution
Policy implementation	Putting solution into effect
Policy evaluation	Monitoring results

Howlett & Ramesh, Studying public policy: Policy cycles and policy subsystems, 1995

A decision-analysis process flowchart



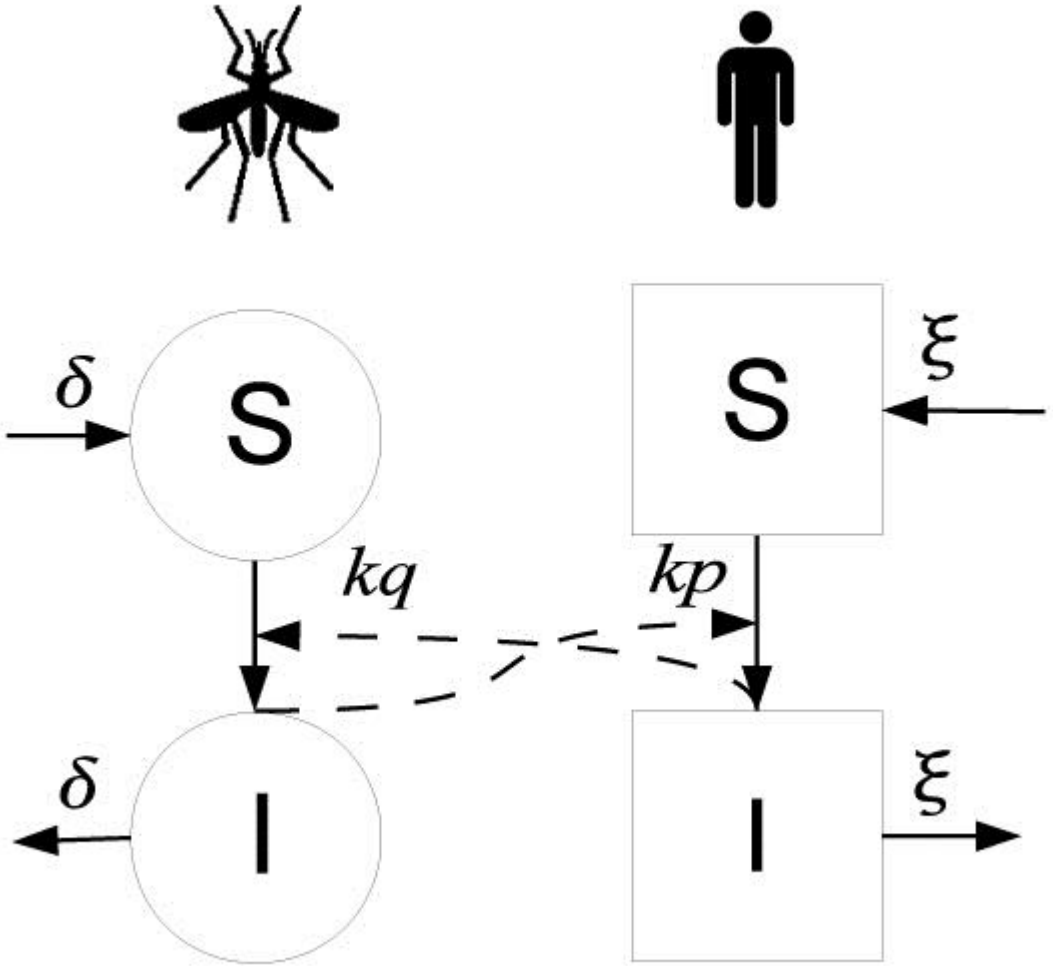
Clemen and Reilly, Making hard decisions, 2002.

Main purposes of infectious disease modeling

- To understand fundamental driving forces of disease ecology and epidemiology
- To measure epidemiological parameters that cannot be directly measured with field or laboratory data
- To make predictions of future disease incidence under specified conditions
- To forecast impact of different prevention/control measures and their combination

Adapted from: WHO-VMI Dengue Vaccine Modeling Group, PLoS Negl Trop Dis 2012, 6:e1450

Classical Ross-Macdonald model for malaria transmission (1)



Classical Ross-Macdonald model for malaria transmission (2)

$$R_0 = \frac{m\, a^2\, b\, c}{\gamma\, \mu} \exp^{-\mu\tau}$$

Description of model parameters

m: Number of female mosquitoes per human host

a: Number of bites per mosquito per unit time

b: Probability of transmission of infection from infectious mosquitoes to humans per bite

c: Probability of transmission of infection from infectious humans to mosquitoes per bite

μ: Death rate of mosquitoes

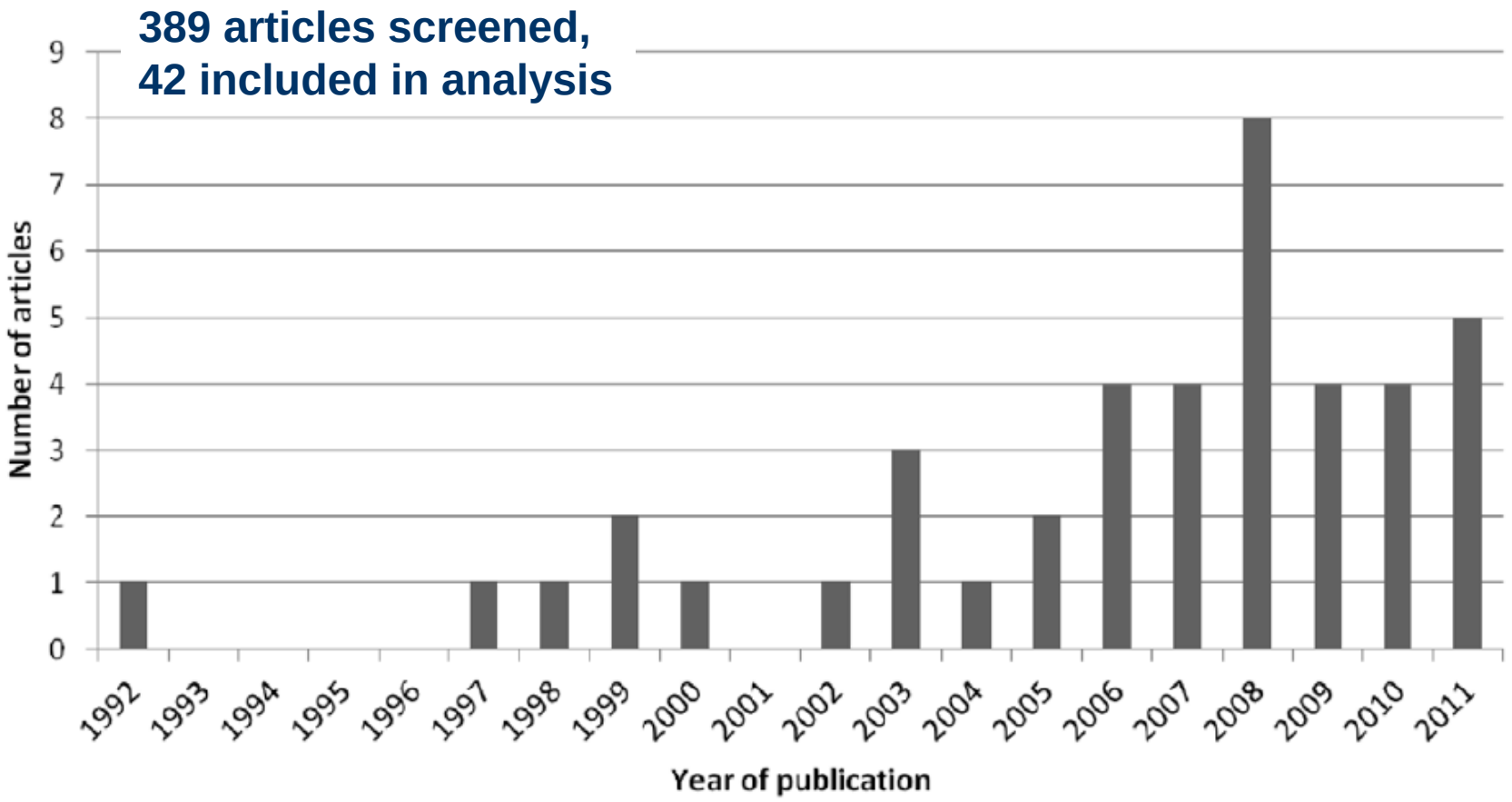
γ: Recovery rate of humans

τ: Extrinsic incubation period

"The 'Ross-Macdonald' model has played the classical role of a scientific theory; it is a deliberately simplified set of concepts that serves as a basis for studying mosquito-borne pathogen transmission. Like other theories, it has formed the starting point for a dialogue about methods, for defining what should be emphasized and measured, and for building new models of mosquito-borne disease transmission."

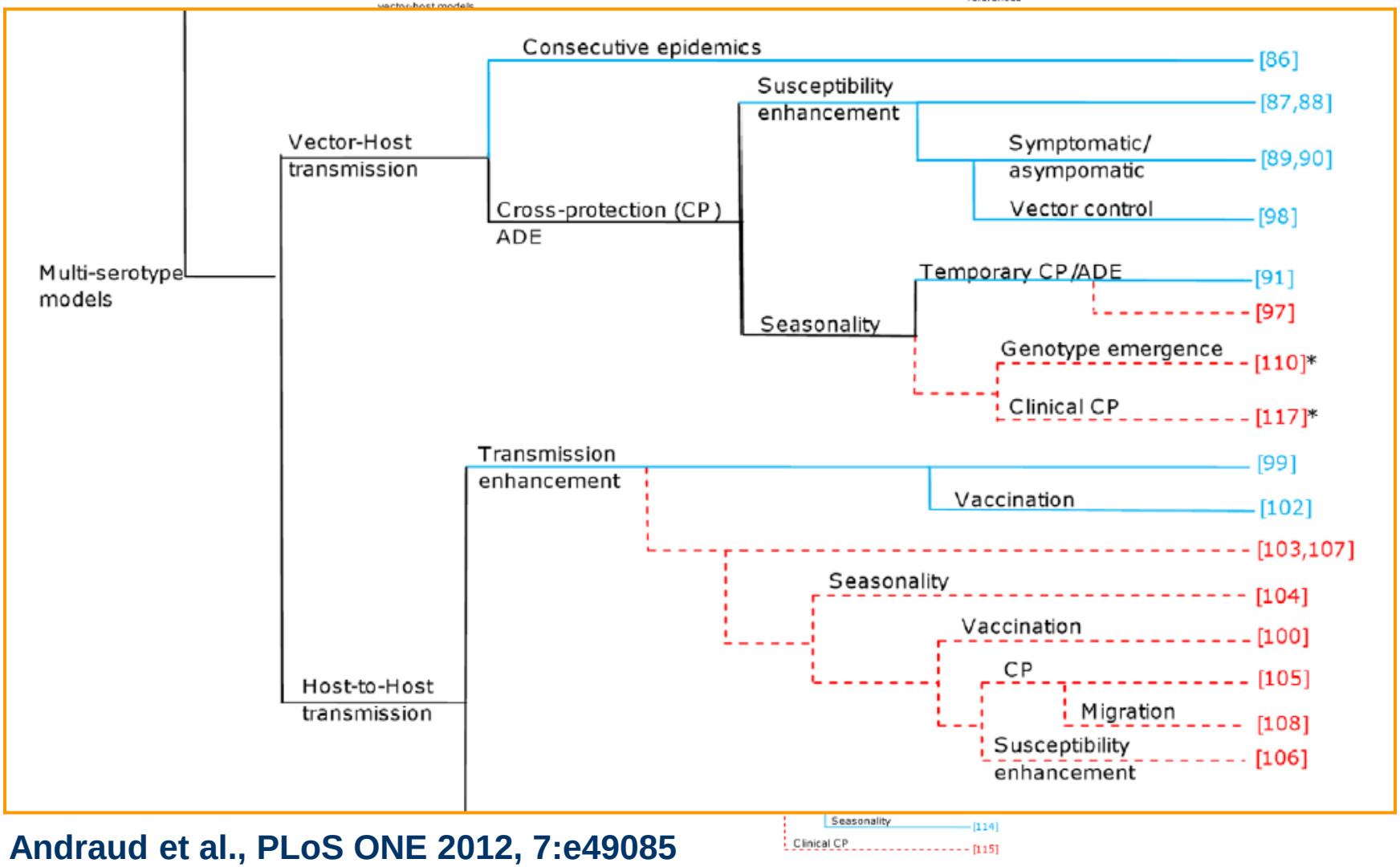
Smith et al., PLoS Pathog 2012, 8:e1002588

Published deterministic models for dengue transmission, 1992–2011



Andraud et al., PLoS ONE 2012, 7:e49085

Structural characteristics of published dengue deterministic models, 1992–2011



Andraud et al., PLoS ONE 2012, 7:e49085

http://www.vaccinemodeling.org/

OPEN ACCESS Freely available online

PLoS NEGLECTED TROPICAL DISEASES

Policy Platform

Assessing the Potential of a Candidate Dengue Vaccine with Mathematical Modeling

WHO-VMI Dengue Vaccine Modeling Group*¶

Background

Dengue viruses are single-stranded positive-sense RNA viruses (genus *Flavivirus*, family Flaviviridae) that are the etiological agents of dengue fever (DF). More than 2 billion people live in dengue-endemic areas [1–3], and dengue virus infections account for an estimated 500,000 episodes of severe disease each year [4]. A recent review suggests that these may be underestimates [5]. Despite the fact that the virus has been expanding in geographic range over the past four decades [6–12], there are still no licensed drugs or vaccines and no consistently effective vector interventions to combat dengue. DF is caused by four antigenically distinct viral serotypes. Each type gives rise to both life-long serotype-specific immunity and short-term cross-protective immunity against the other serotypes thought to last between 2 and 9 months [13]. The spectrum of disease ranges from asymptomatic infection to life threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome

chimeric yellow fever dengue vaccine—commenced Phase II and Phase IIB clinical trials in 2009, and Phase III trials in December of 2010 [17–21]. Preliminary results have demonstrated significant immunogenicity in all age groups after three vaccine doses over a 12-month period. Immunogenicity increased steadily with each dose and was higher in individuals with previous flavivirus immunity [21]. A tetravalent dengue vaccine (TDV) candidate is currently the preferred formulation of a dengue vaccine, as it should prevent infection by all serotypes, thereby eliminating the potential risk of severe infections associated with pre-existing immunity [22].

In line with the theory behind ADE, subneutralizing antibody concentrations—theoretically occurring when immunity is waning or between vaccine doses—represent a potential risk of severe dengue to patients infected with wild-type virus during this critical period. This individual-level risk can be evaluated

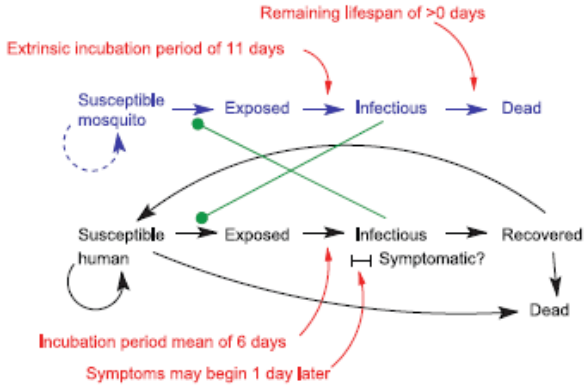
Although there is no evidence that vaccine-derived immunity could lead to increased severity or transmissibility upon infection, given the immunopathogenesis of dengue, this possibility should be planned for.

Population-level effects, whether related to ADE or not, can be analyzed with mathematical models. Since it is not feasible to enroll and randomize populations to dengue vaccine or placebo, mathematical models may provide the only environment where multiple types of population-wide dengue strategies can be evaluated. Models allow for assessment of multiple intervention and evaluation strategies. They can be used to understand the specific population-level mechanisms by which vaccines reduce incidence and can aid in the design of evaluation studies. The World Health Organization (WHO) has recommended that mathematical models be used to assess and inform various methods of new vaccine introductions [24,25].

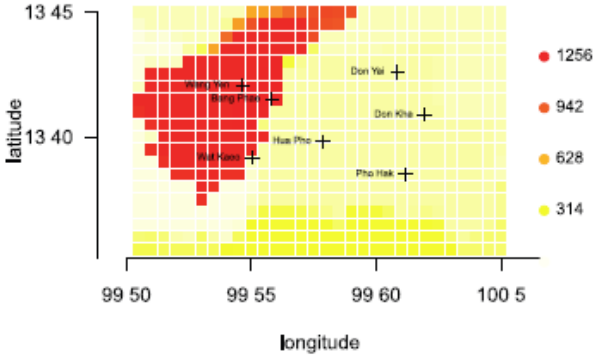
WHO-VMI Dengue Vaccine Modeling Group, PLoS Negl Trop Dis 2012, 6:e1450

Simulation of dengue control with vaccine in a Thai locality

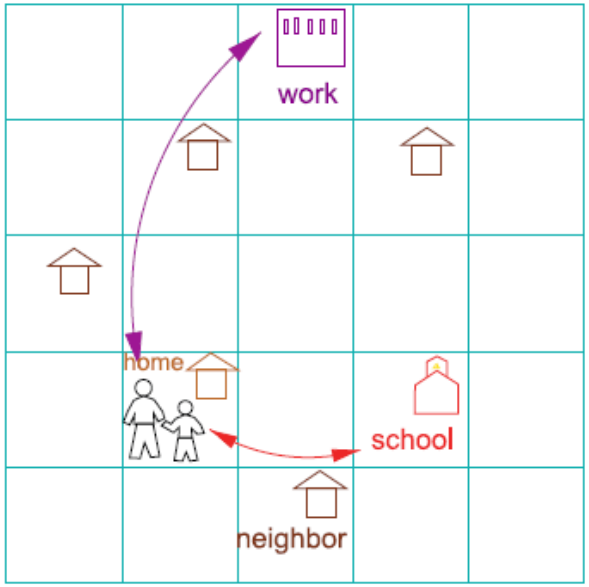
A Natural history



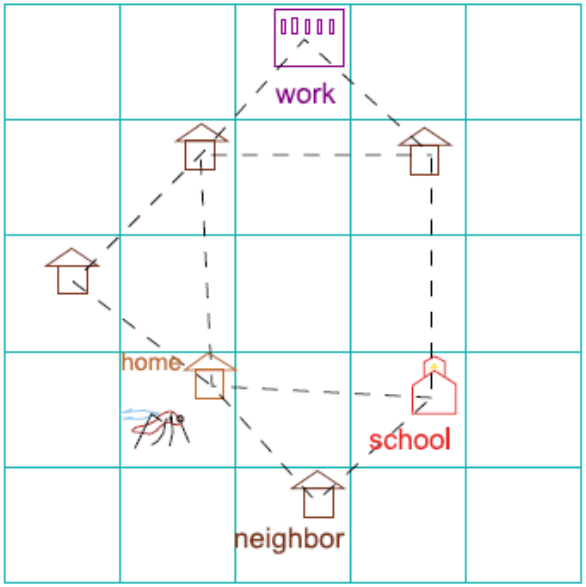
B Human population density



C Human movement

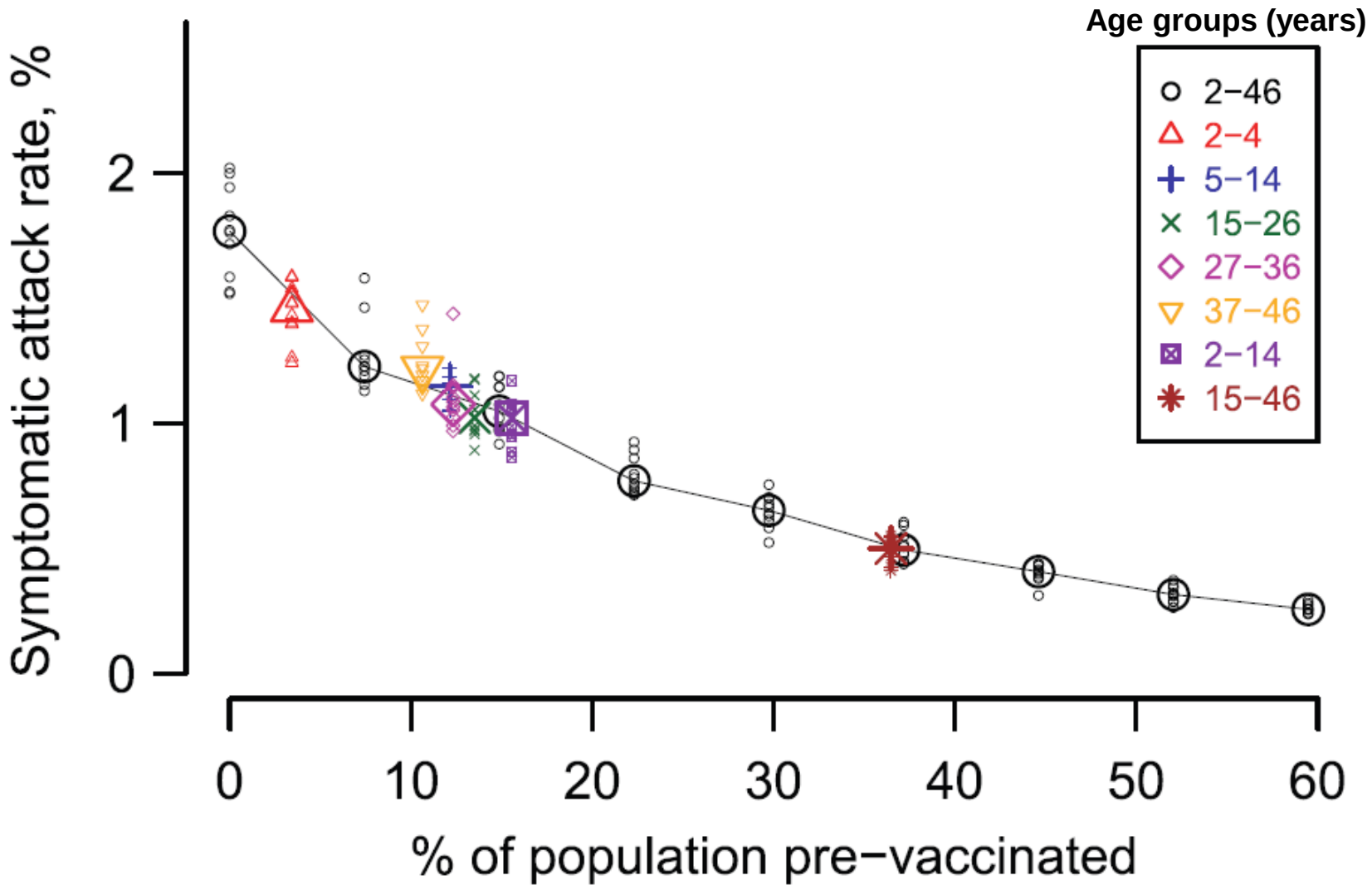


D Vector movement



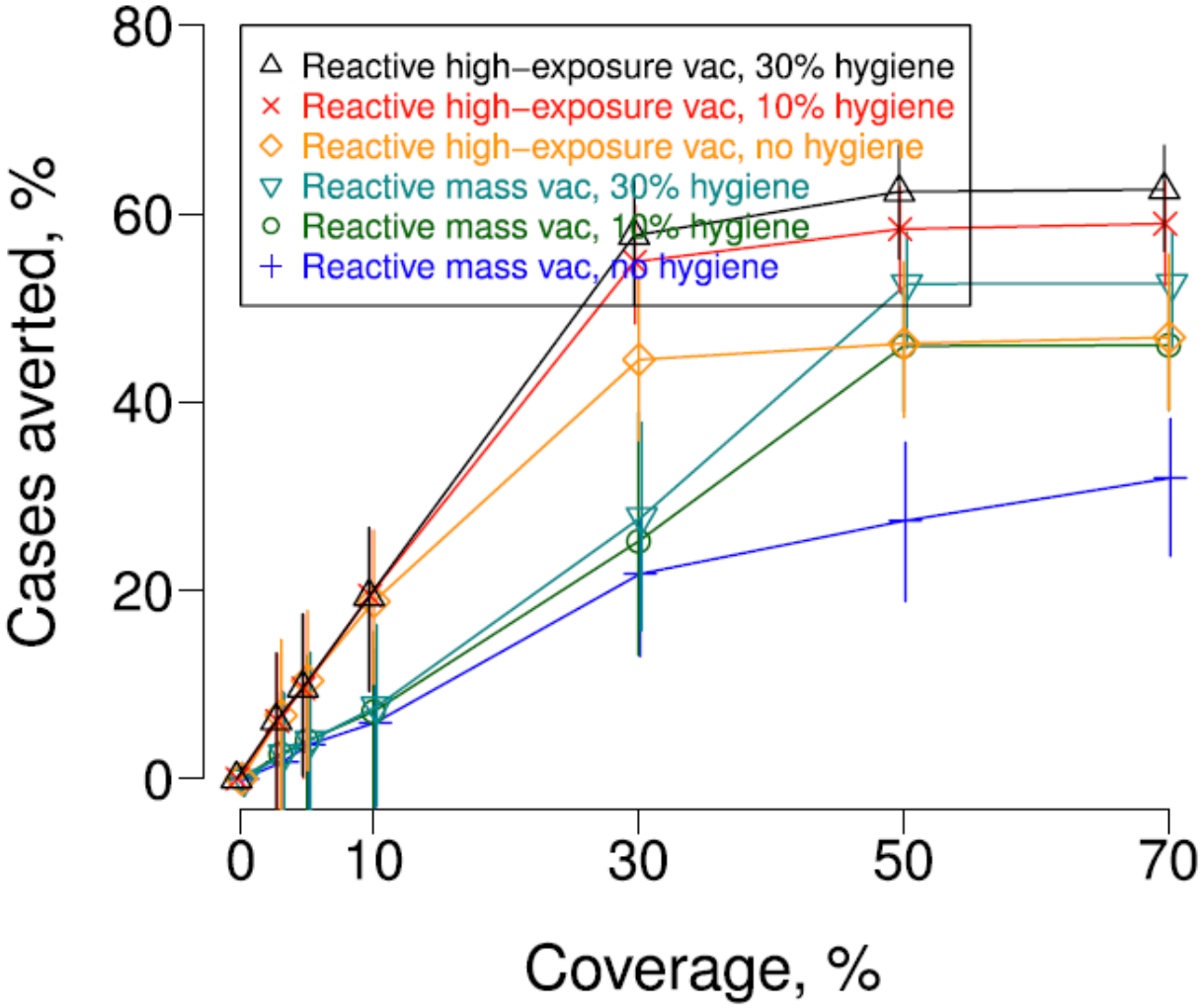
Chao et al., PLoS Negl Trop Dis 2012, 6:e1876

Simulated impact of dengue vaccination in a Thai locality, by vaccinated age group



Chao et al., PLoS Negl Trop Dis 2012, 6:e1876

Simulated effects of vaccination during first 6 months of Haitian cholera outbreak



Chao et al., Proc Natl Acad Sci USA 2011, 108:7081–7085

Final considerations

- Modeling can be a key input to structured decision-making
- Several initiatives on dengue modeling (e.g., WHO-VMI, DVI) are ongoing
- Researchers drive current development and decision-makers are largely not involved
  - Focus on simulation rather than model structure; variability and uncertainty mixed
  - Unrealistic assumptions and scenarios
  - Sensitivity analyses not always done

WHO-VMI Dengue Vaccine Modeling Group: 2014 plans

- Consensus meeting on dengue vaccine impact modelling planned for last quarter of 2014
  - Sharing of best practices by vaccine and vector control modelers
  - Discussion and consensus on key parameters, assumptions and key public health outcomes
- Comparative review of models is on hold because most modeling groups associated with only one vaccine developer

Possible PAHO role

- Outline role of modeling within decision-making process
- Forster conjoint work of modelers and decision-makers
  - Reasonable assumptions and realistic scenarios
  - Centered on affordability and long-term sustainability
- Stimulate models that integrate vaccination and vector control as complementary measures (not mutually exclusive)

Thank you

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