The use of mathematical models in policy formulation for the control of pandemics ?

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Mathematical models in health policy formulation – 10th Dec 2014

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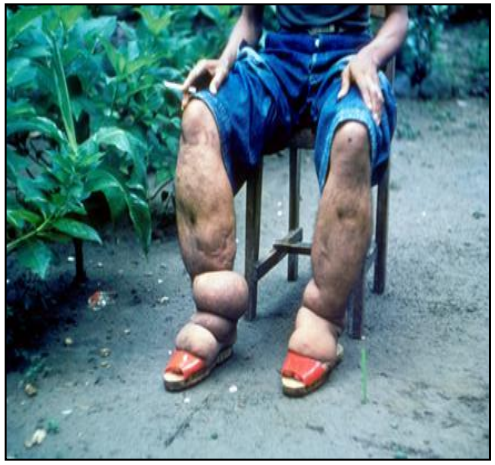
Content

1. Control of the neglected tropical diseases by mass chemotherapy.
2. Influenza A pandemics
3. Ebola virus
4. Conclusions.

The Neglected Tropical Diseases the cause of much morbidity and mortality in large regions of the world

Schistosomiasis



Elephantiasis

- **Protozoan Infections**
  - Leishmaniasis (VL + CL + MCL)
  - African Trypanosomiasis (Sleeping Sickness)
- **Helminth Infections**
  - Soil-transmitted Helminth infections:
    - Ascariasis-Trichuriasis-Hookworm
  - Lymphatic Filariasis (Elephantiasis)
  - Onchocerciasis (River Blindness)
  - Schistosomiasis (Bilharzia)
  - Dracunculiasis (Guinea Worm)
  - Cysticercosis
- **Bacterial Infections**
  - Leprosy
  - Trachoma
  - Buruli Ulcer

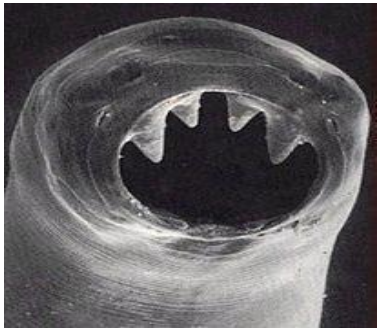
Trachoma

River Blindness

Global distribution of soil-transmitted helminths (STH).

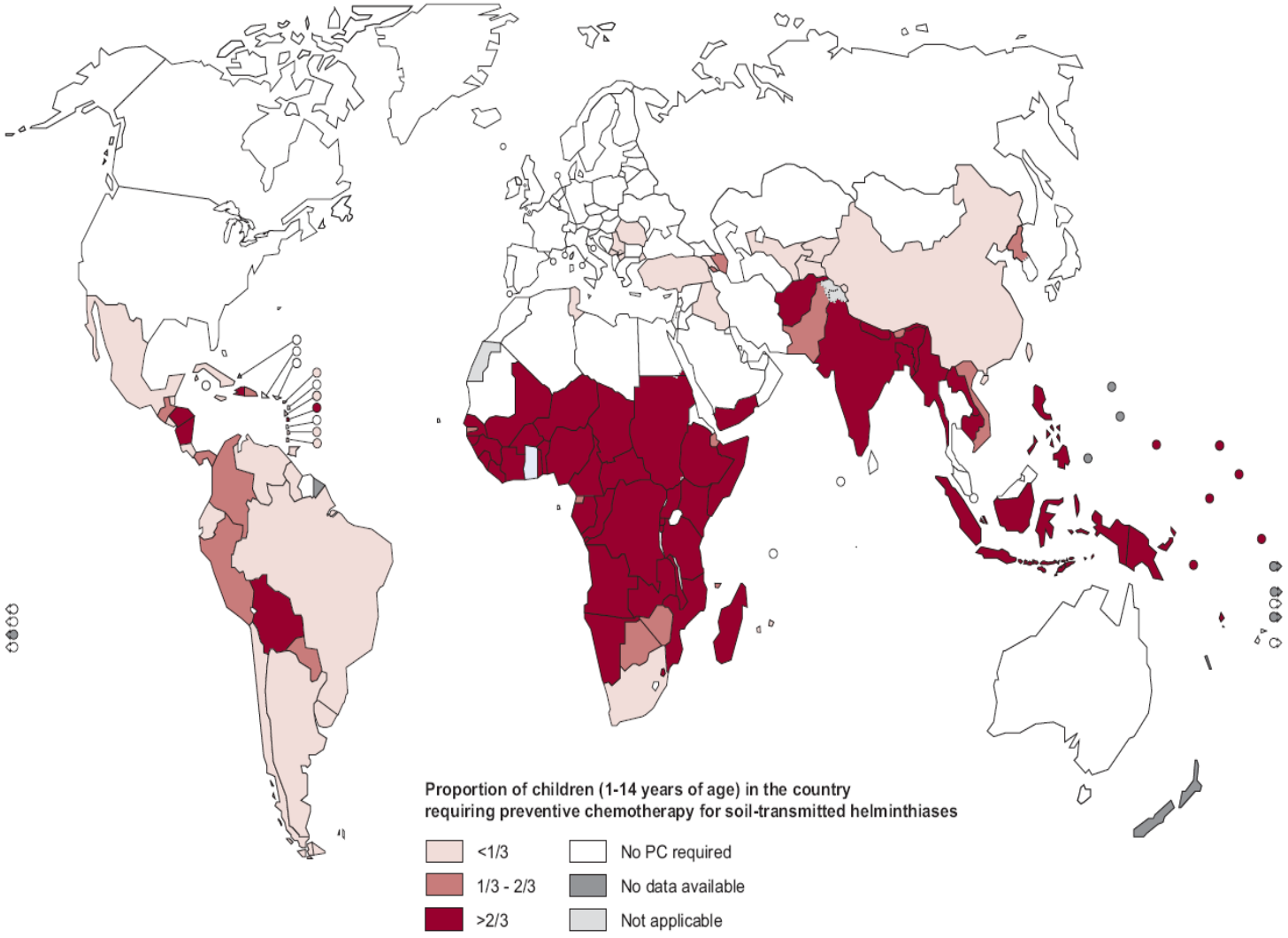
Proportion of children requiring chemotherapy for STH in each country (WHO, 2011)

Trchuris trichuria



Hookworm

Ascaris lumbricoides



Mathematical models underpin community based control designs

1. **Overall aim - to calculate the optimum drug treatment schedules to control or eliminate soil transmitted helminths, (schistosomes and filarial worms).**

2. To define these schedules **for low, medium and high** transmission settings (using WHO criteria for the definition of transmission intensity)

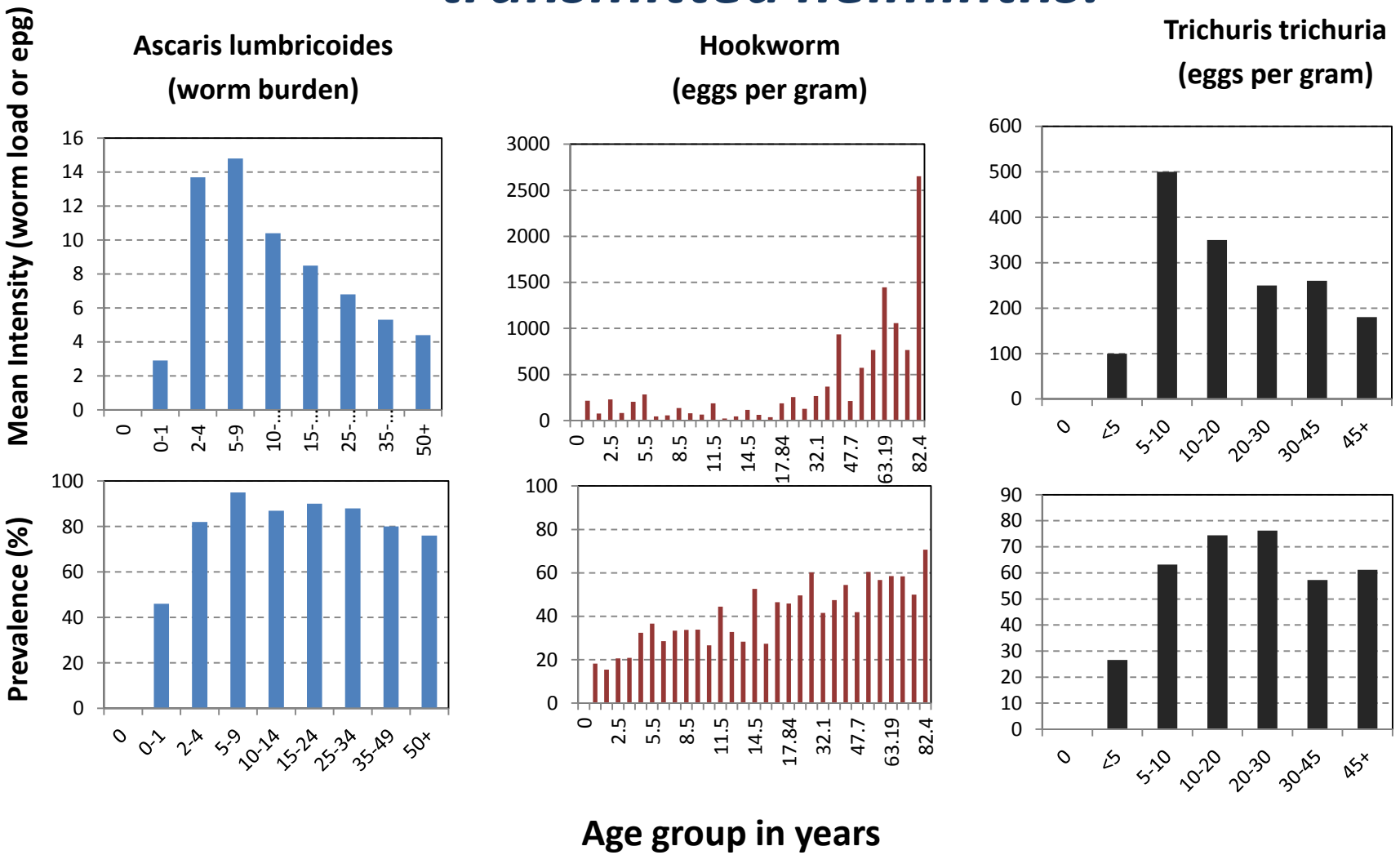
3. To define **who** should be targeted in this programme (pre-school aged children (Pre-SAC), school aged children (SAC) & adults (ADULTS), or what combination of each?

4. To calculate **how long** a given populations based treatment programme should continue (5,10 or 15 years?).

Types of Mathematical Models of Pathogen Transmission and Treatment.

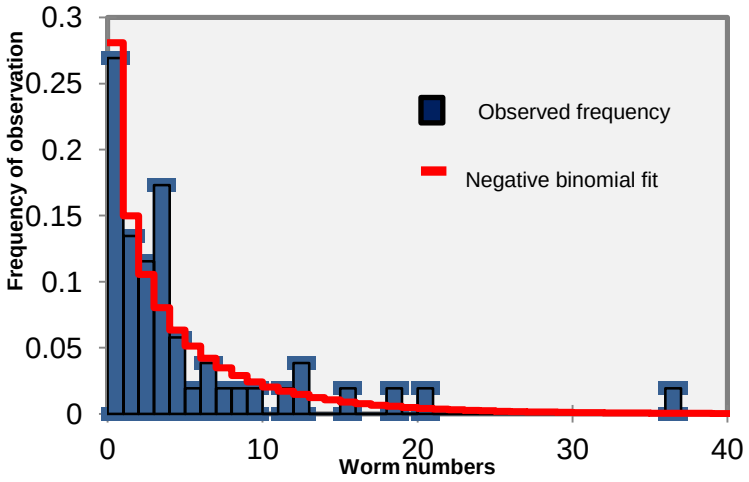
- Simple deterministic – provide analytical insights into what are the major processes influencing observed epidemiological patterns.
- Complex deterministic with age & gender structure, density dependence in parasite survival/reproduction and sexual mating in parasites
- Complex hybrid models (mixed stochastic & deterministic) of transmission dynamics and treatment – age structure, density dependence in parasite survival/reproduction, sexual reproduction and probability distributions of parasite numbers per host.
- Stochastic individual person based models of transmission dynamics and treatment, with spatial structure.
- User friendly software front end to run on PC/laptop

Age-intensity profiles for mean intensity and prevalence (%) for the three major soil transmitted helminths.

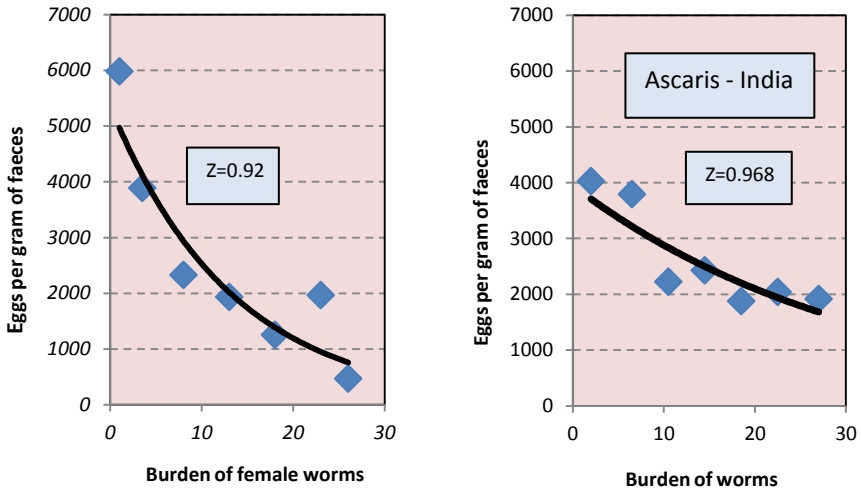


Key epidemiological processes and patterns

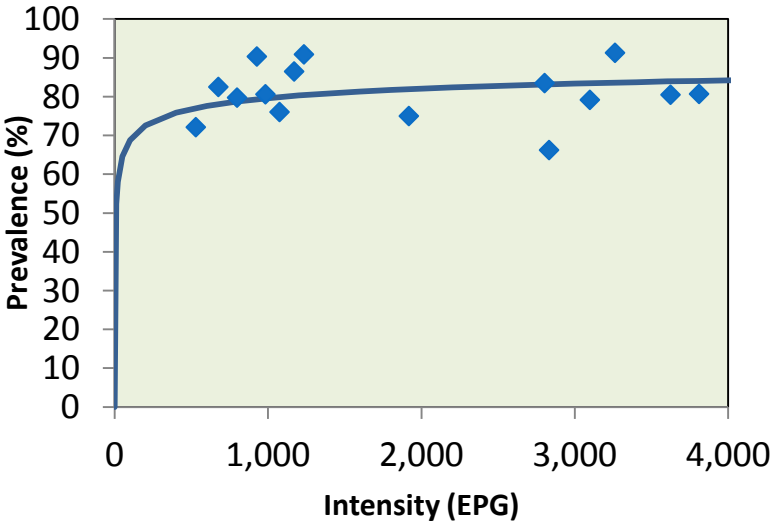
Aggregated distributions of worms numbers per host



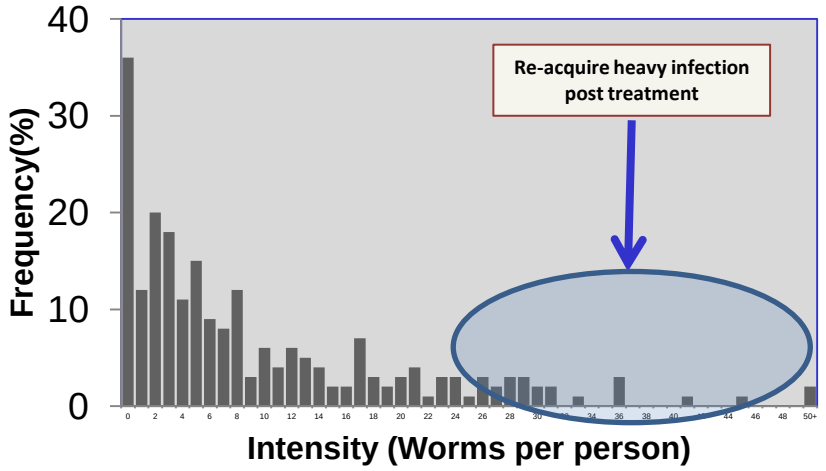
Density dependence in egg production



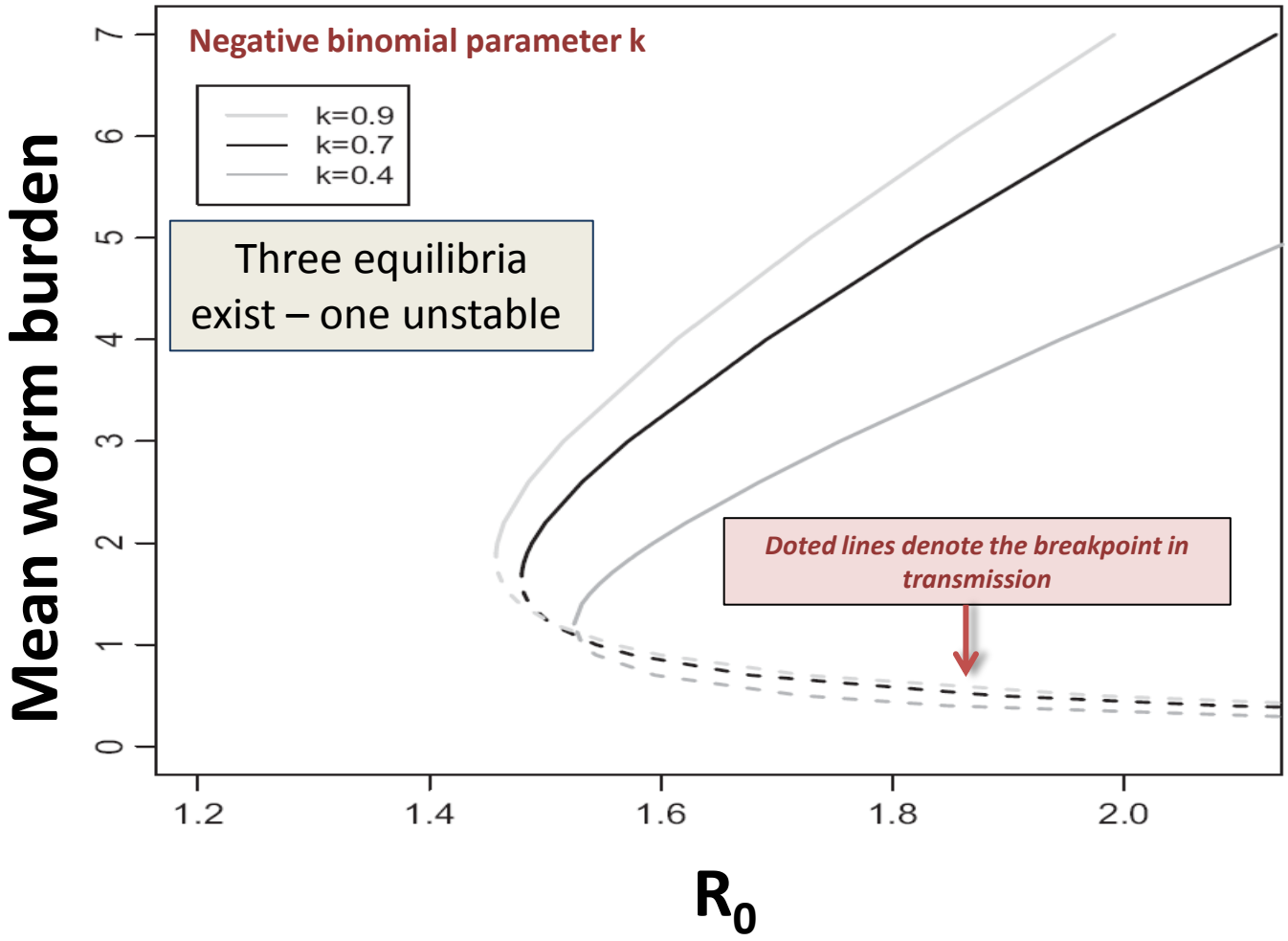
Non-linear relationship between prevalence and intensity



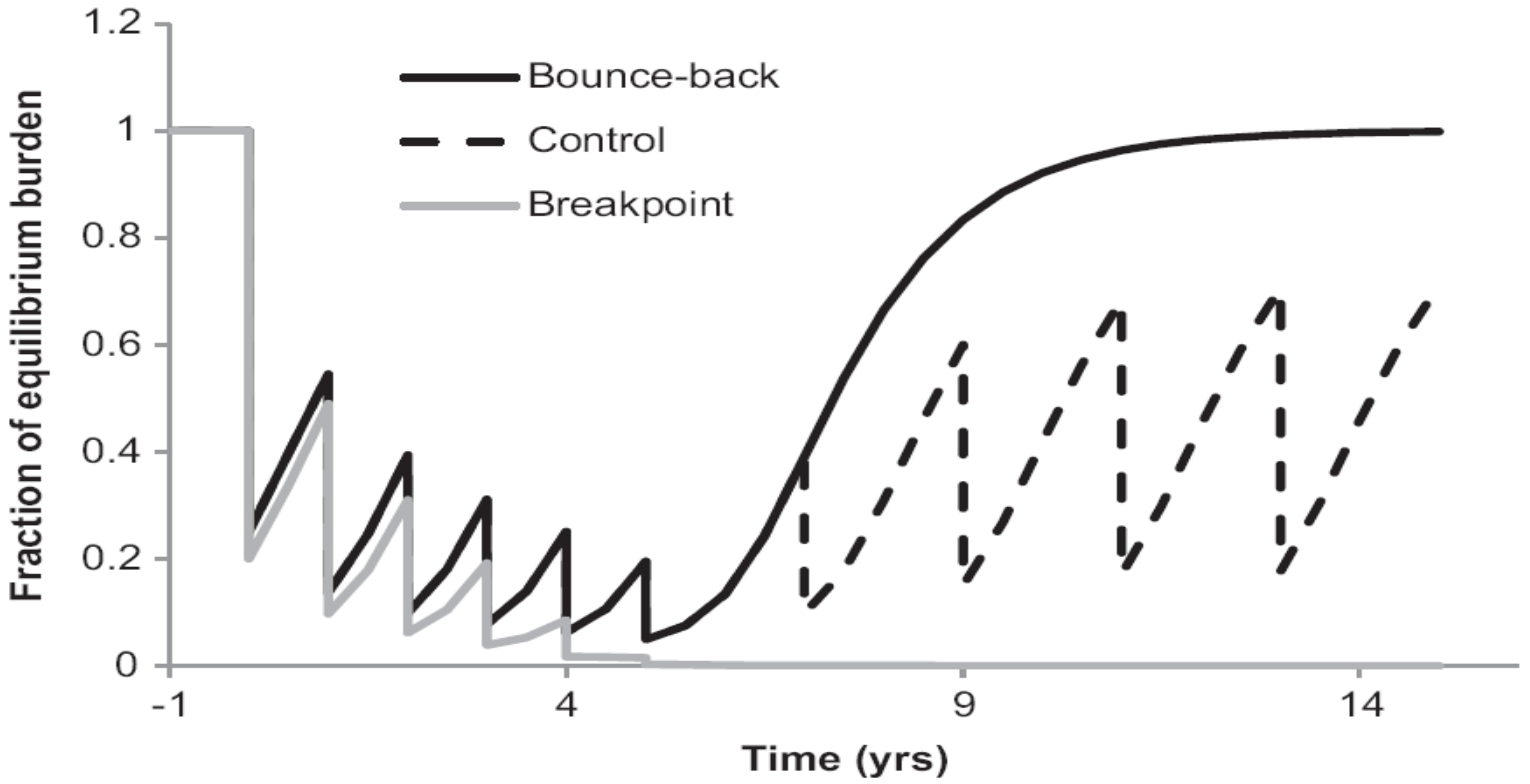
Predisposition to light or heavy infection



Equilibrium worm burden as a function R_0 for simple model and different values of worm distribution shape parameter, k (Ascaris lumbricoides).



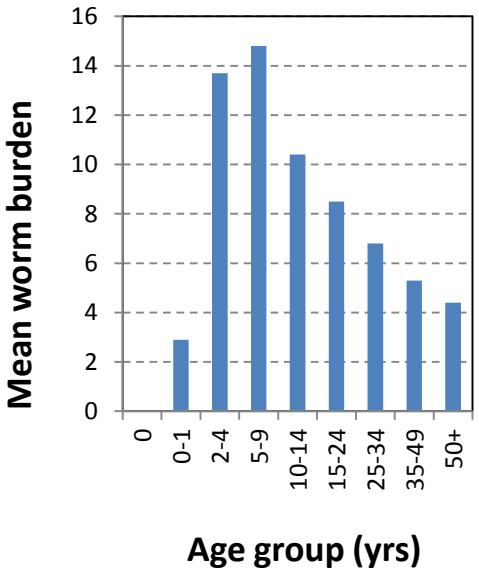
Control of soil-transmitted infections by mass chemotherapy (MDA) – no protective immunity so 'bounce back' always occurs when treatment stops - in the absence of other interventions

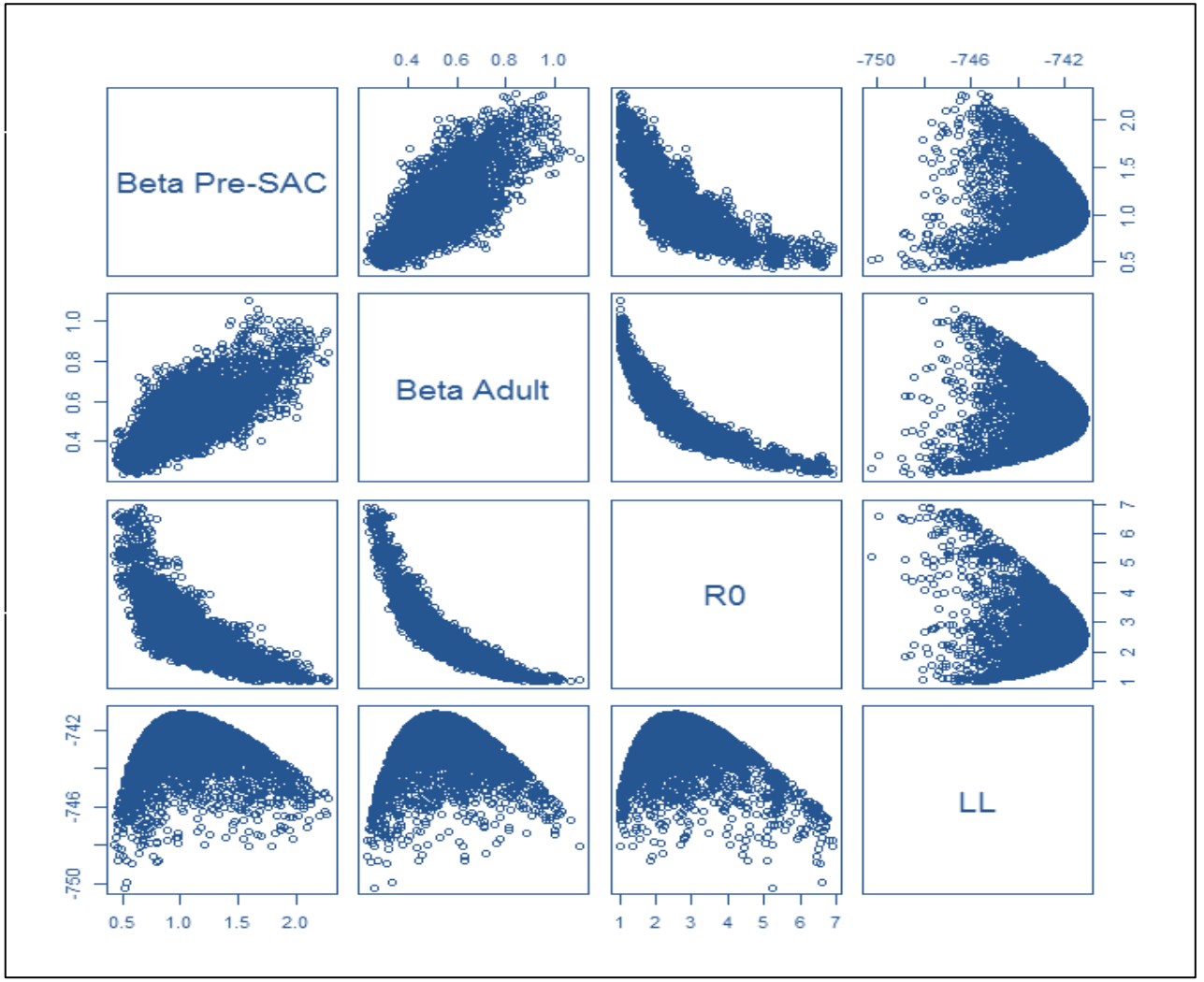


- Frequent treatment can drive burden of infection down
- Lifting treatment typically lead to bounce back
  - How to achieve sustained gains?

Markov Chain Monte Carlo (MCMC) and MLE parameter estimation methods for R_0 and the age group infection weightings (Beta)

[Ascaris – Elkins et al (1986) data from India on re-infection and age intensity worm profiles – k=0.6,L=1, z=0.04, Beta=1,1,0.5,R_0=2.5]



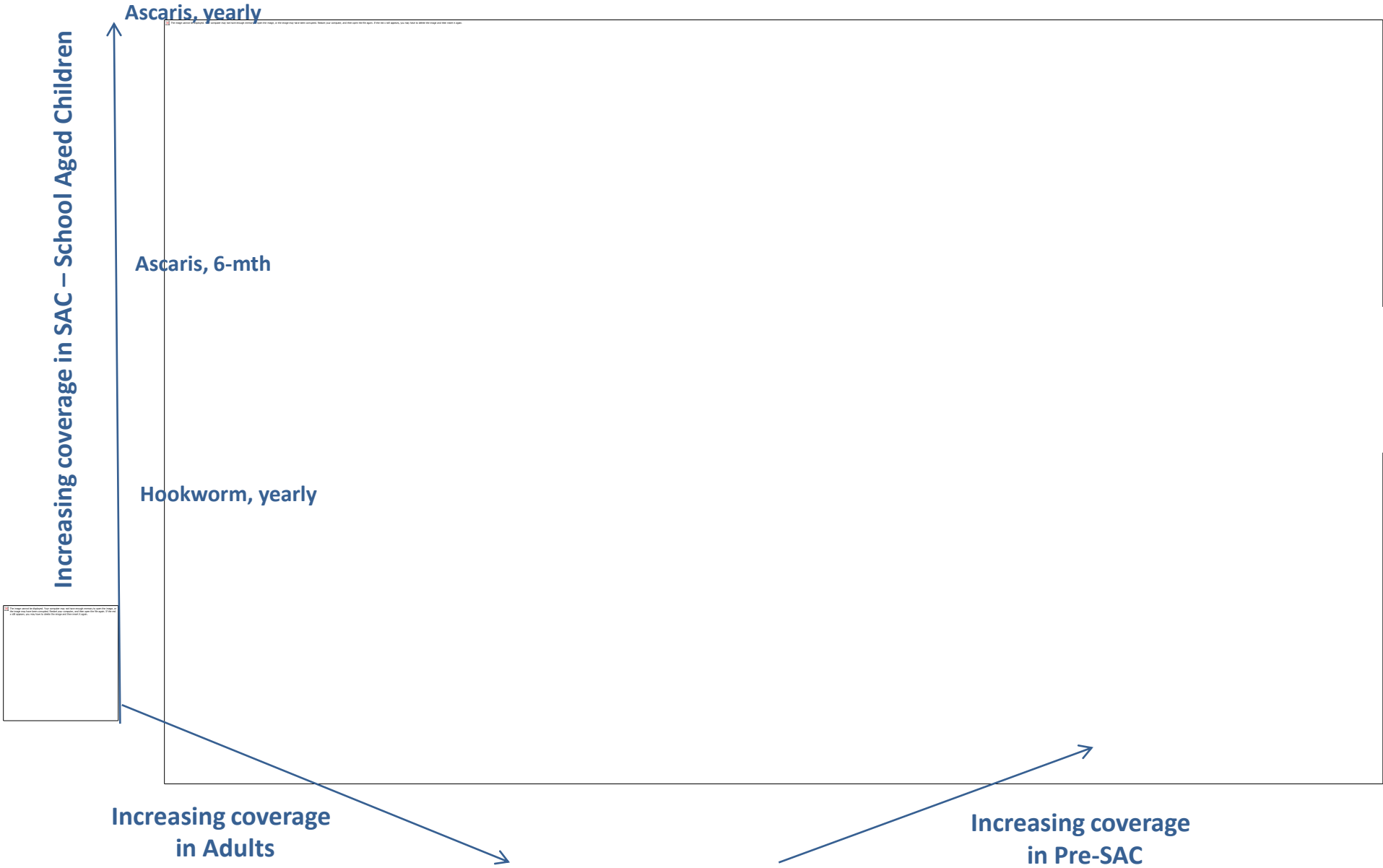


'Breakpoint' surfaces.

Low transmission
R_0=2

Medium transmission
R_0=3

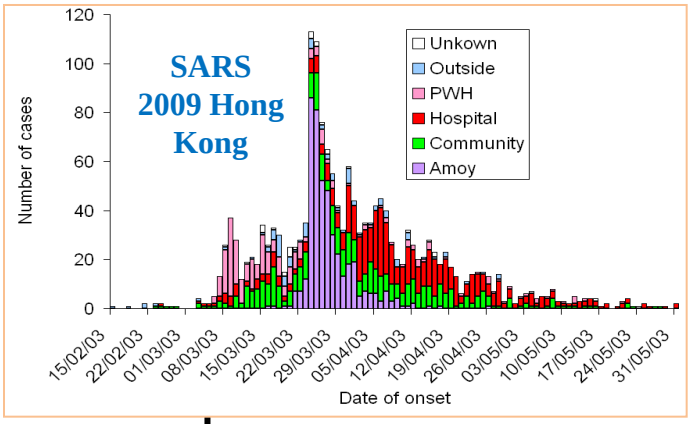
High transmission
R_0=5

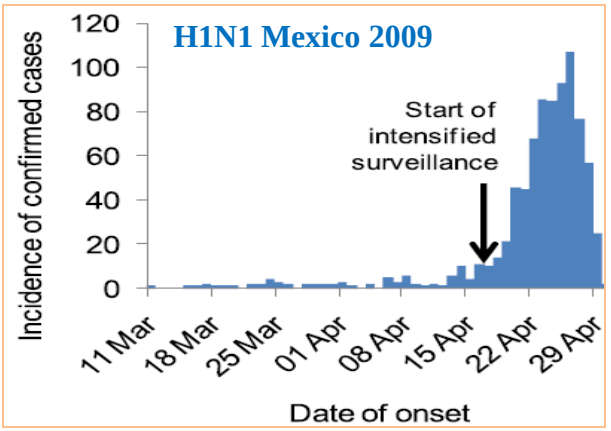


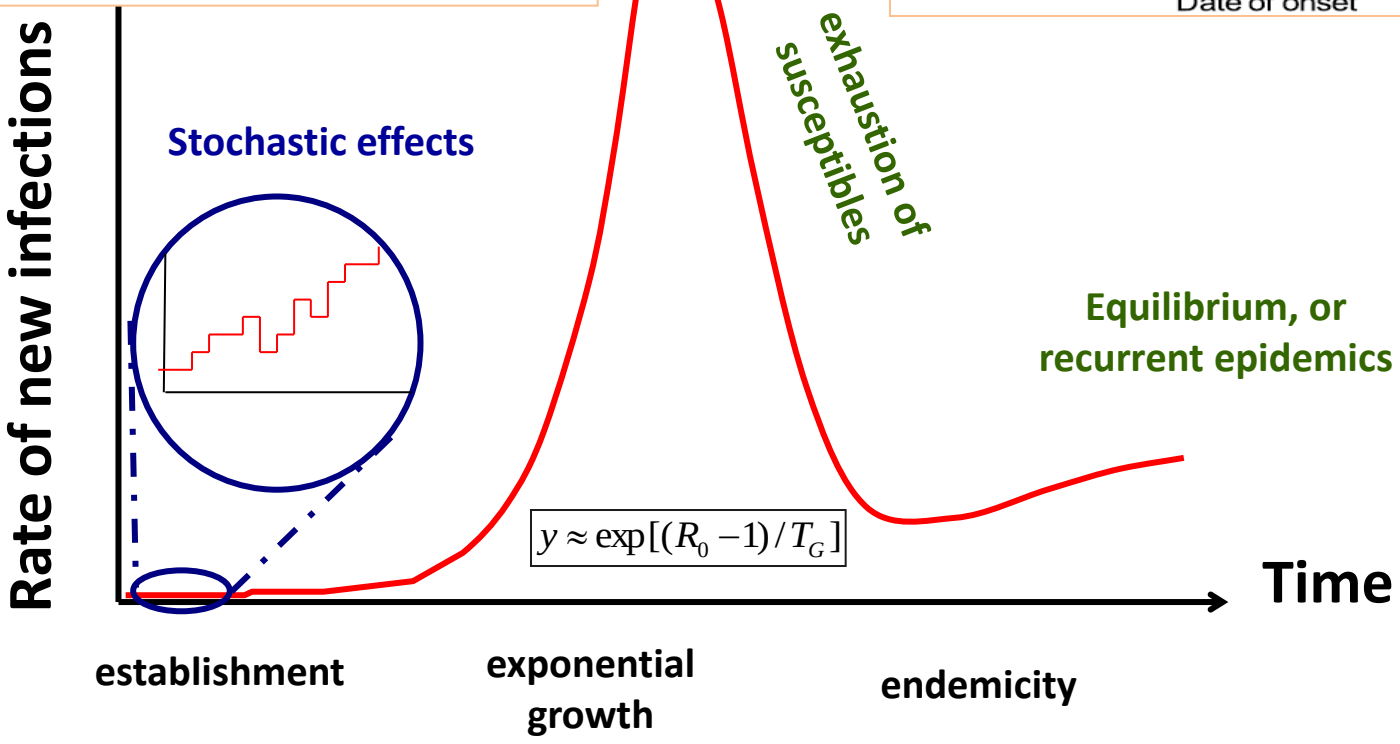
Conclusions – mass drug administration

- Only treating Pre-SAC and or SAC will have little impact in medium and high transmission settings – especially true for hookworm.
- Treatment must be continued for some time (10+ years) to cross breakpoints – if stopped before that – will bounce back to pre-control levels (e.g. LF issue where treatment intensity declining in some areas).
- Tables can be constructed for any given transmission setting to work out how many in each age grouping to treat and at what interval.
- This work can be extended to for a variety of other infections that can be treated by mass chemotherapy.

Epidemic timescales

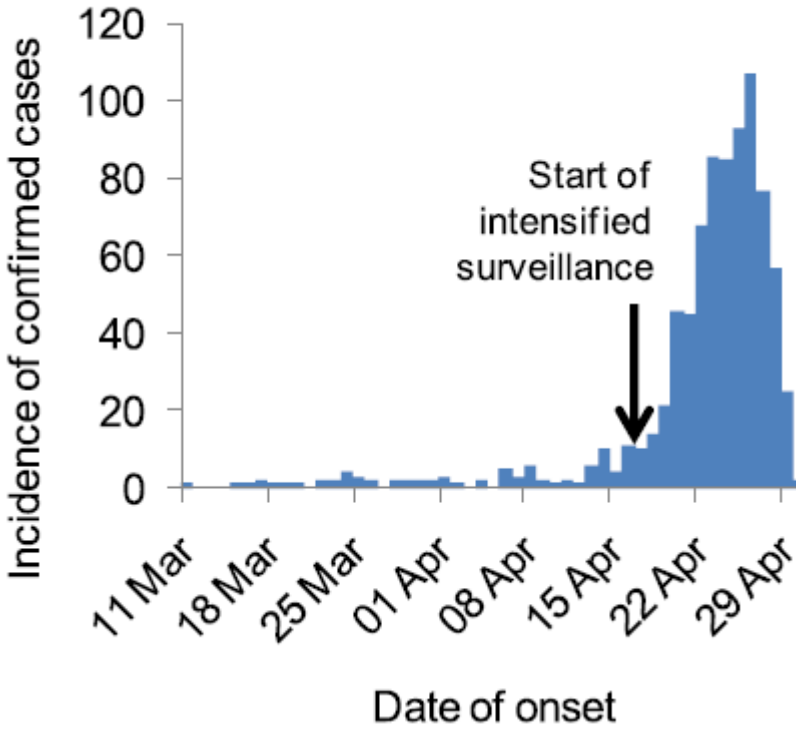


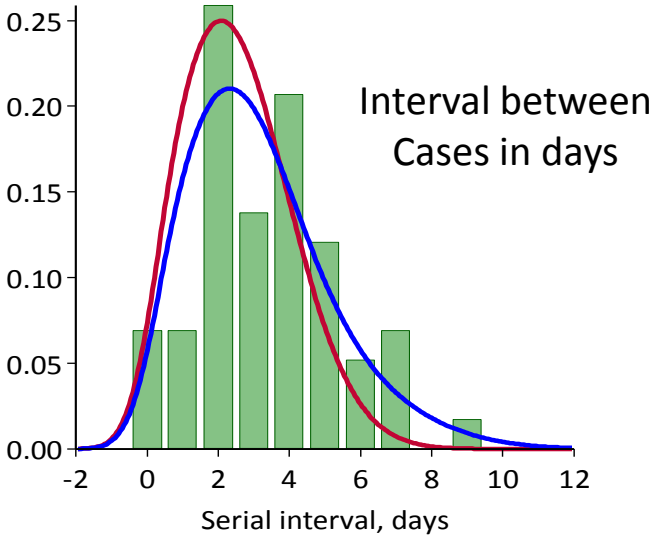




R for Mexico in April-May

(Fraser et al, 2009 Nature)

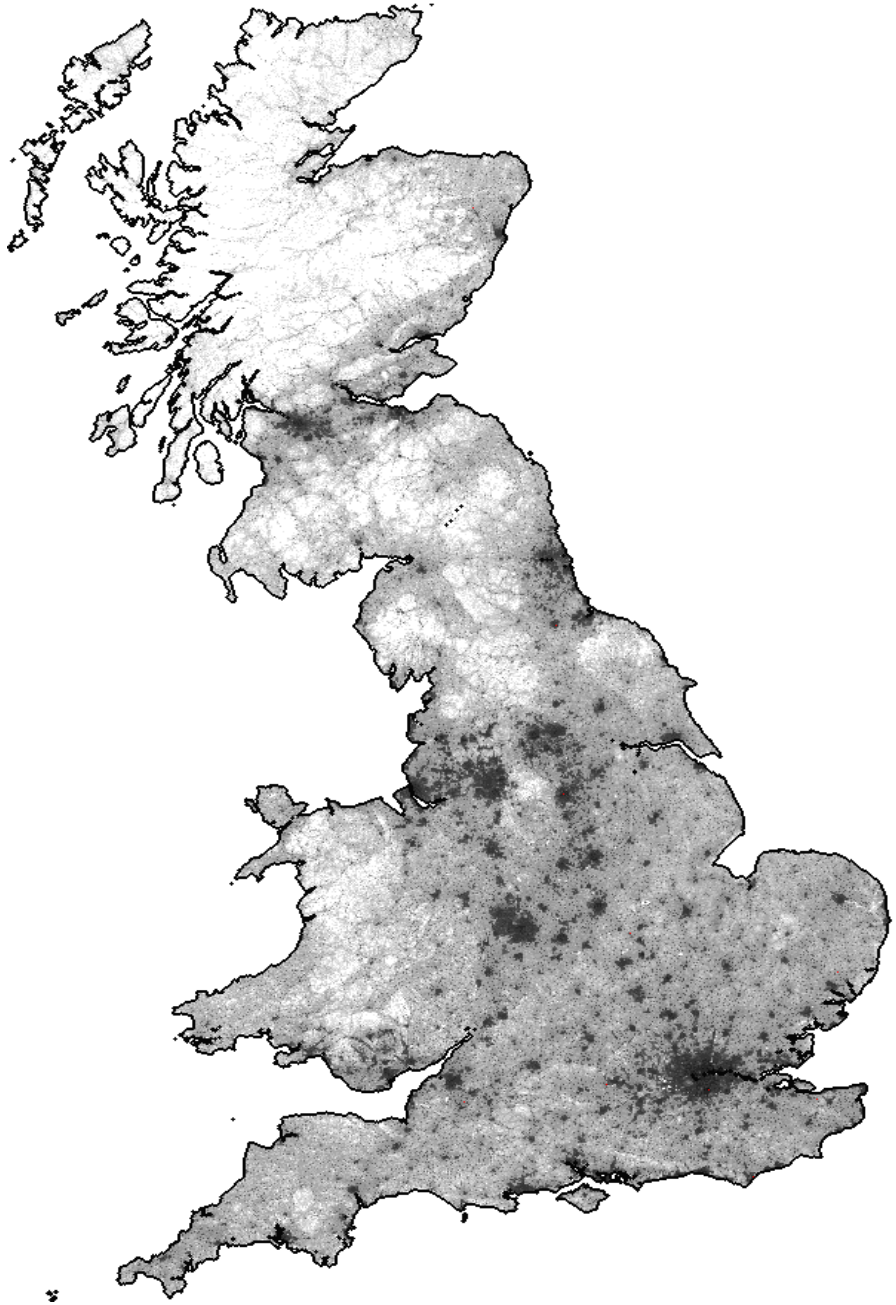


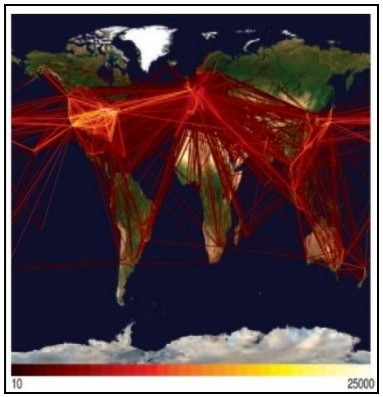


- *R*=1.5 (95% Cr.I.:1.2-1.9) from confirmed case epi curve.
- *R*=1.4 (95% Cr.I.:1.1-1.9) from spatial back-calculation.
- *R*=1.2 (95% Cr.I.:1.1-1.9) from sequence analysis.

Influenza A simulations - England, Scotland and Wales

(1 year compressed Into a few Seconds)





Simulating global spread – Influenza A

(2 years compressed into a few seconds - Ferguson et al, 2009)

- Analysing data from around the world.

Simple theory

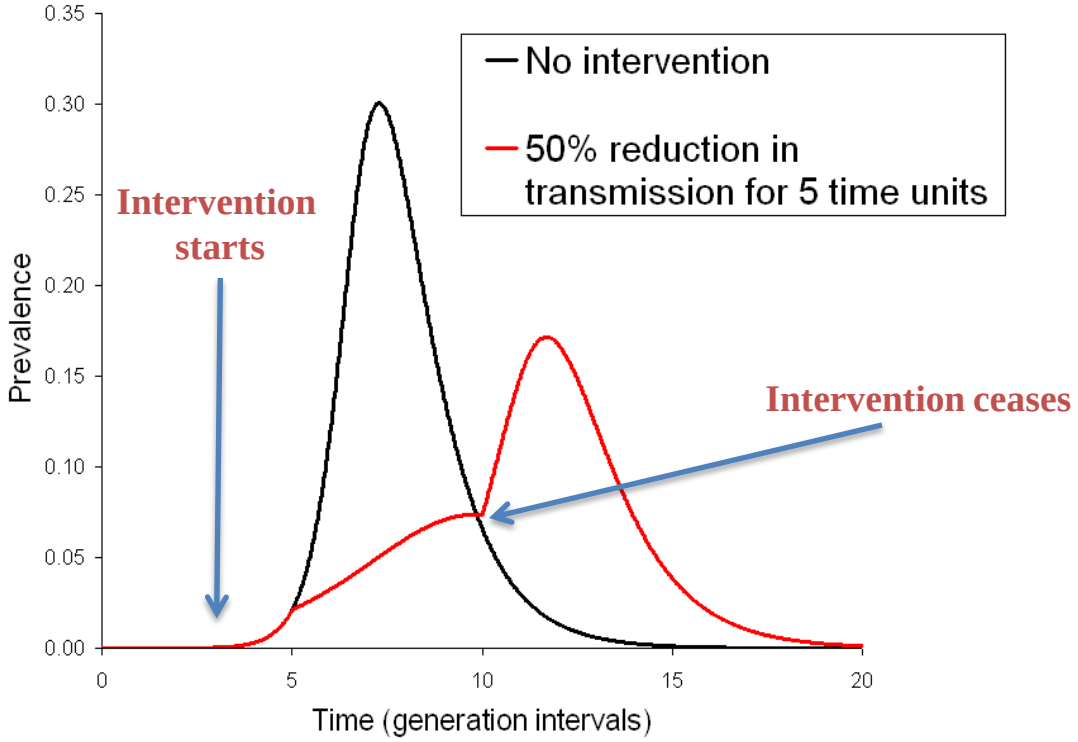
(Hollingsworth, Klinkenberg, Hesterbeck & Anderson, 2011)

- Total epidemic size
- Peak incidence
- Peak prevalence

a = total epidemic size,
T_1 to T_2 = duration of intervention
θ = proportional reduction in transmission
I = cumulative incidence

$$a_{I_{12}} = 1 - \left(\frac{1 - I(T_1)}{1 - I(T_2)} \right)^{\frac{\theta}{1-\theta}} e^{-R_0 a_{I_{12}}}$$

$$dx/dt = -\beta xy$$
$$dy/dt = \beta xy - \sigma y$$



Clear definition of control policy aims & objectives for influenza A

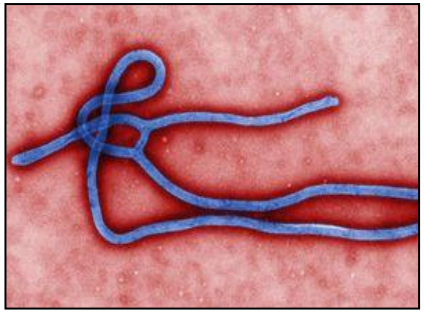
1) Minimize morbidity and mortality – with fixed or variable budget.

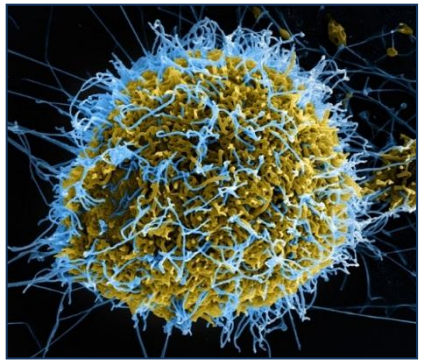
2) Buy as much time as possible to wait for vaccine development.

3) Minimize duration of the epidemic and impact on economy.

4) Minimize peak prevalence below a defined level to avoid collapse of health care systems.

Ebola epidemic – West Africa 2014





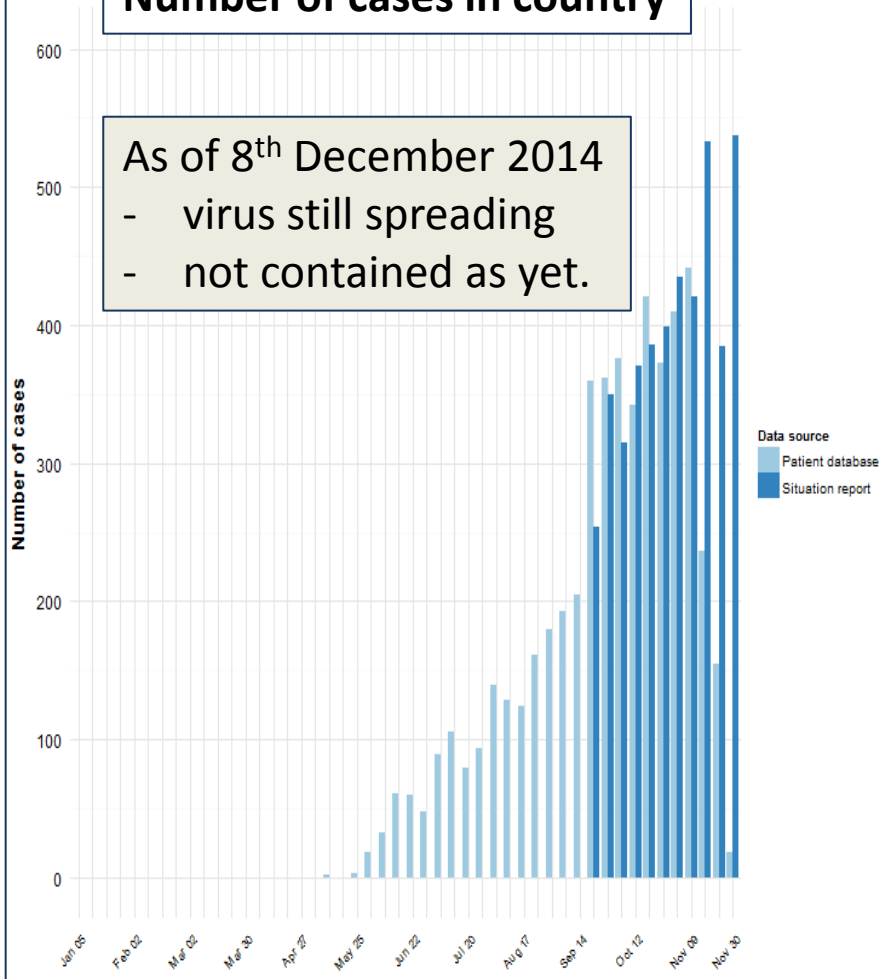
Control options

- Identification, isolation and follow up of contacts.
- Effective contact tracing and isolation of contacts for 21 days post contact essential.
- Stopping within country movements ('lock down') – some impact.
- Border controls usually ineffective.
- Immunotherapy available but very limited supply.
- Vaccine – will be available in 2015

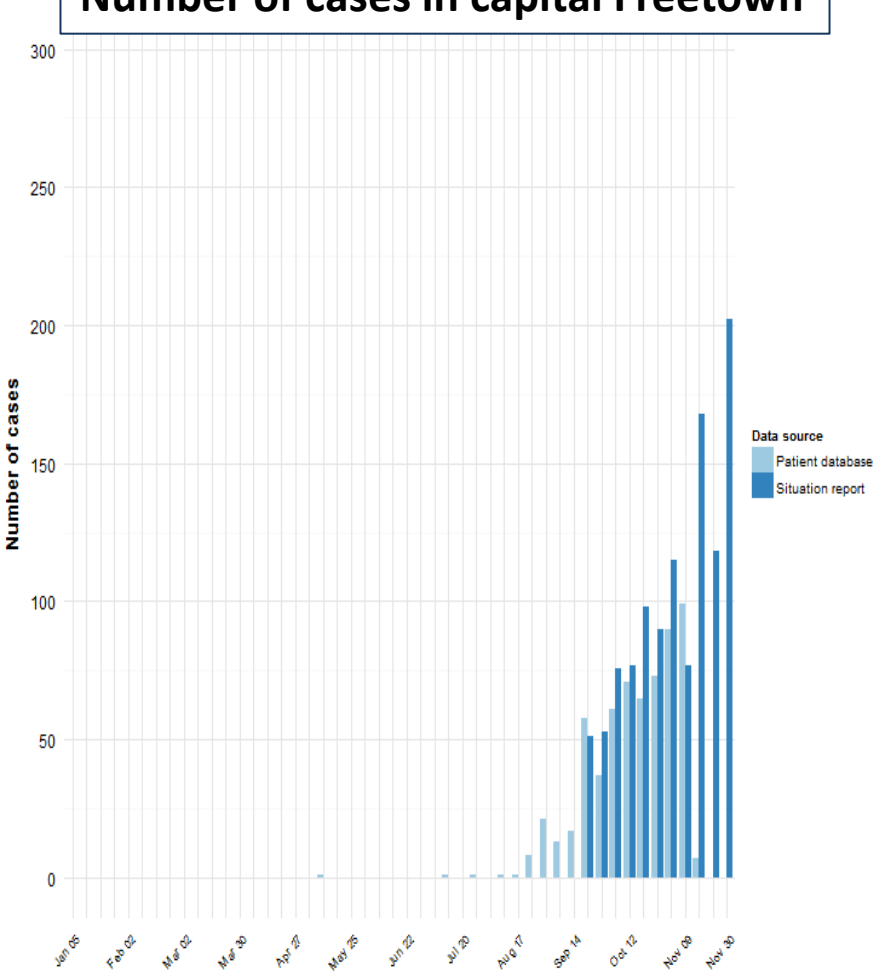
Sierra Leone - end of November 2014

Number of cases in country

As of 8th December 2014
- virus still spreading
- not contained as yet.



Number of cases in capital Freetown



Basic epidemiological parameters – estimated from data and models

(WHO Ebola Response Team and DIDE Imperial College London, New Eng J Med, Sept 2014)

- **Basic reproductive number R_0 1.7-2.1**
- Current reproductive number (December) 0.8 (Liberia)-1.7 (SL)
- Doubling time 15-30 days
- **Case fatality rate 70.8%**
- **Mean incubation period 11.4 days**
- **Range for incubation period 2- 42 days (95% by day 21)**
- Mean time from onset of symptoms to hospitalization 5 days (infectiousness)
- Mean time to death from admission 4.2 days
- Mean time to discharge 11/8 days
- Mean time of stay in hospital 6.4 days

Conclusions – future needs

- Influence in policy formulation – **mathematical models** now regarded by most - as an **essential tool in policy formulation** (e.g. Mass childhood vaccination, AIDS/HIV, Foot and Mouth, BSE, Influenza A, Malaria, NTDs and Ebola)
- **Educate policy makers in their use**.
- **Testing model prediction against observation** – especially in control implementation situations – qualitative and quantitative.
- Data sets – **web based access** – standard data sets with which to test the predictions of different models.
- Complex computer simulations – specification of assumptions – **open access code**.

The End