Spatio-temporal and Network Modelling of Diseases Rottenburg/Tubingen, 21^{st} - 25^{th} October 2008

On age-dependent branching models for surveillance of infectious diseases controlled by additional vaccination

M. Slavtchova-Bojkova



UNIVERSITY OF SOFIA, BULGARIA

Faculty of Mathematics and Informatics

Rottenburg/Tubingen (Germany) October 2008



Outline





• Epidemic Modelling





- Epidemic Modelling
 - ► Model
 - Infectious period
 - ► Vaccination policies
 - Elimination





- Epidemic Modelling
 - ► Model
 - Infectious period
 - ► Vaccination policies
 - Elimination

• Sevast'yanov's Age-Dependent Branching Processes





- Epidemic Modelling
 - ► Model
 - Infectious period
 - Vaccination policies
 - Elimination
- Sevast'yanov's Age-Dependent Branching Processes
 - Stochastic monotony property
 - Continuity property





- Epidemic Modelling
 - ► Model
 - Infectious period
 - Vaccination policies
 - Elimination

- Sevast'yanov's Age-Dependent Branching Processes
 - Stochastic monotony property
 - Continuity property

• An Example with real data of Avian influenza in Vietnam



 Some monographs on Epidemic Modelling are Daley and Gani (1999), Andersson and Briton (2000) or Mode and Sleeman (2000), Andersson and May (1991).



- Some monographs on Epidemic Modelling are Daley and Gani (1999), Andersson and Briton (2000) or Mode and Sleeman (2000), Andersson and May (1991).
- Ball and Donnelly (1995), Farrington and Grant (1999), Farrington, Kanaan and Gay (2003), Dietz (1993)



- Some monographs on Epidemic Modelling are Daley and Gani (1999), Andersson and Briton (2000) or Mode and Sleeman (2000), Andersson and May (1991).
- Ball and Donnelly (1995), Farrington and Grant (1999), Farrington, Kanaan and Gay (2003), Dietz (1993)
- Different types of stochastic models have been used to model the evolution of an infectious disease into a population: branching processes.



• Branching processes approach is appropriate when the number of infected individuals is small in relation to the total population size (see Ball (1997)).



- Branching processes approach is appropriate when the number of infected individuals is small in relation to the total population size (see Ball (1997)).
- We shall use Sevast'yanov's age-dependent branching processes because the infection time might be more accurately controlled than using discrete-time processes.



- Branching processes approach is appropriate when the number of infected individuals is small in relation to the total population size (see Ball (1997)).
- We shall use Sevast'yanov's age-dependent branching processes because the infection time might be more accurately controlled than using discrete-time processes.
- Infectious period consists of two parts: an incubation or latency part and comparatively very short contact part. Different levels of severity depend on the length of incubation period





• Let us assume that three types of individuals may exist in the population: infected; healthy but susceptible to catch the infection (susceptible individuals); healthy and immune to the disease



- Let us assume that three types of individuals may exist in the population: infected; healthy but susceptible to catch the infection (susceptible individuals); healthy and immune to the disease
- The disease is spreading when an infected individual is in contact with susceptible individuals.



- Let us assume that three types of individuals may exist in the population: infected; healthy but susceptible to catch the infection (susceptible individuals); healthy and immune to the disease
- The disease is spreading when an infected individual is in contact with susceptible individuals.
- We denote by $p_{\alpha,k}(u)$, u > 0 the probability that one infected individual at age u contacts k healthy individuals, $k \ge 0$, where α $(0 \le \alpha \le 1)$ is the proportion of immunized individuals into the population.



• Following this spreading scheme along time, infected individuals pass on the disease to other susceptible individuals and so on. We model the number of infected individuals in the population by Sevast'yanov's age-dependent branching process: $\{Z_{\alpha}(t)\}_{t\geq 0}$

A possible path





- Life-length: G(t)
- Family of reproduction laws: $\{p_{\alpha,k}(u)\}_{k\geq 0}$, u > 0, $m_{\alpha}(u)$ is the mean of contacts of infected individual at age u when the level of immunized individuals is α
- $m_{\alpha} = \int_0^{\infty} m_{\alpha}(u) dG(u).$

Intuitively: By life-length we mean the infectious period (measured in real time) till one infected individual infects susceptible individuals or the disease disappears in this individual



1) To suggest vaccination policies based on the mean of the infection period.



- 1) To suggest vaccination policies based on the mean of the infection period.
- 2) To investigate the distribution of the duration time of the infection depending on the proportion of immunized individuals into the population.



- 1) To suggest vaccination policies based on the mean of the infection period.
- 2) To investigate the distribution of the duration time of the infection depending on the proportion of immunized individuals into the population.

Extinction Time: $T_{\alpha} = \inf_{t \ge 0} \{ Z_{\alpha}(t) = 0 \}$ $v_{\alpha}(t) = P(T_{\alpha} \le t)$



- 1) To suggest vaccination policies based on the mean of the infection period.
- 2) To investigate the distribution of the duration time of the infection depending on the proportion of immunized individuals into the population.

Extinction Time: $T_{\alpha} = \inf_{t \ge 0} \{ Z_{\alpha}(t) = 0 \}$ $v_{\alpha}(t) = P(T_{\alpha} \le t)$

Intuitively: T_{α} is the maximal time that the infection survives into the population when the proportion of immune individuals is α



Epidemic Modelling: Infection Extinction Time

Stochastic Monotony: If $\alpha_1 < \alpha_2$, then $v_{\alpha_1}(t) \leq v_{\alpha_2}(t)$, $t \geq 0$.



Epidemic Modelling: Infection Extinction Time

Stochastic Monotony: If $\alpha_1 < \alpha_2$, then $v_{\alpha_1}(t) \leq v_{\alpha_2}(t)$, $t \geq 0$.



Intuitively, it is clear that the greater is the proportion of the immune individuals, the more probable is that the infectious disease disappears faster



• Mean of the infection extinction time T_{α}

$$\mu_{\alpha} = E[T_{\alpha}] = \int_0^\infty (1 - v_{\alpha}(t))dt$$



• Mean of the infection extinction time T_{α}

$$\mu_{\alpha} = E[T_{\alpha}] = \int_0^\infty (1 - v_{\alpha}(t))dt$$

• Continuity property: For each $\varepsilon > 0$ there exist $\eta = \eta(\varepsilon, \alpha) > 0$ such that for all α^* with $m_{\alpha^*} \leq 1$ and $|\alpha - \alpha^*| \leq \eta$,

$$\sup_{t\geq 0} |v_{\alpha}(t) - v_{\alpha^*}(t)| \leq \varepsilon.$$



• Mean of the infection extinction time T_{α}

$$\mu_{\alpha} = E[T_{\alpha}] = \int_0^\infty (1 - v_{\alpha}(t))dt$$

• Continuity property: For each $\varepsilon > 0$ there exist $\eta = \eta(\varepsilon, \alpha) > 0$ such that for all α^* with $m_{\alpha^*} \leq 1$ and $|\alpha - \alpha^*| \leq \eta$,

$$\sup_{t\geq 0} |v_{\alpha}(t) - v_{\alpha^*}(t)| \leq \varepsilon.$$

• If
$$\alpha_1 < \alpha_2 \leq 1$$
, then $\mu_{\alpha_2} \leq \mu_{\alpha_1}$



• We try to control the spread of the disease by immunizing some proportion of susceptible individuals.



- We try to control the spread of the disease by immunizing some proportion of susceptible individuals.
- This proportion of susceptible individuals to be vaccinated depends on the time that we allow the infectious disease to survive after vaccination.



- We try to control the spread of the disease by immunizing some proportion of susceptible individuals.
- This proportion of susceptible individuals to be vaccinated depends on the time that we allow the infectious disease to survive after vaccination.
- Assume that at an arbitrary time t_0 after the infection occurred, we want to vaccinate a proportion α of susceptible individuals. We suppose that the vaccination process finishes at time t_1 . Therefore, $t_1 - t_0$ is the period of time that is taken for immunization, called the vaccination period. We suppose that vaccination period is fixed a priori and does not depend on α .



• Optimal proportion of vaccinated individuals:

For fixed τ , we are looking for vaccination policies, which guarantee that the average time to extinction of an infection after vaccination period t_1 , is less than or equal to $t_1 + \tau$.

$$\alpha_{opt} = \inf\{\alpha : \alpha \le 1, \mu_{\alpha} \le \tau\}$$



• Optimal proportion of vaccinated individuals:

For fixed τ , we are looking for vaccination policies, which guarantee that the average time to extinction of an infection after vaccination period t_1 , is less than or equal to $t_1 + \tau$.



$$\alpha_{opt} = \inf\{\alpha : \alpha \le 1, \mu_{\alpha} \le \tau\}$$





To apply the simulation method based on the mean of the extinction time

1) d.f. G(.) is of a gamma distribution



To apply the simulation method based on the mean of the extinction time

- 1) d.f. G(.) is of a gamma distribution
- 2) $\{p_{\alpha,k}(u)\}_{k\geq 0}$ follows a Poisson distribution with parameter λu (Intuitively, λ represents the power of the virus.)



To apply the simulation method based on the mean of the extinction time

- 1) d.f. G(.) is of a gamma distribution
- 2) $\{p_{\alpha,k}(u)\}_{k\geq 0}$ follows a Poisson distribution with parameter λu (Intuitively, λ represents the power of the virus.)
- 3) incubation period for avian influenza virus is estimated between 3 and 7 days (IDSA, 2007) \implies mean of gamma is 5 and the shape is 16, which guarantee that the survival period in 90% of individuals is between 3 and 7 days





Data for infected domestic birds detected between 7^{th} December 2006 and 14^{th} January 2007 in South Vietnam









(ii) first outbreak (in 7^{th} December) = 80



- (ii) first outbreak (in 7^{th} December) = 80
- (iii) after incubation period (in 13^{th} and 14^{th} December) = 413



- (ii) first outbreak (in 7^{th} December) = 80
- (iii) after incubation period (in 13^{th} and 14^{th} December) = 413
- (iv) m = 413/80 (Lotka's estimator)



- (ii) first outbreak (in 7^{th} December) = 80
- (iii) after incubation period (in 13^{th} and 14^{th} December) = 413
- (iv) m = 413/80 (Lotka's estimator)
- (v) The number of individuals incubating the virus at 19^{th} December we estimate by 2132 = 413 * (413/80)



(ii) first outbreak (in 7^{th} December) = 80

(iii) after incubation period (in 13^{th} and 14^{th} December) = 413

(iv) m = 413/80 (Lotka's estimator)

(v) The number of individuals incubating the virus at 19^{th} December we estimate by 2132 = 413 * (413/80)

(vi) $\alpha_{opt}(30, 2132) = 0.97.$





Histogram of simulated extinction times for $\alpha = 0.97$.





Epidemic Modelling: Avian influenza in Vietnam conclusion



(i) Control measures applied in Vietnam correspond to a vaccination level close to 1 ($\alpha = 0.97$)



- (i) Control measures applied in Vietnam correspond to a vaccination level close to 1 ($\alpha = 0.97$)
- (ii) The optimal vaccination level does not depend on the initial number of individuals incubating the virus (sensitivity analysis)



Establishing a threshold in terms of the total progeny of infected individuals.

Establishing a threshold in terms of the total progeny of infected individuals.

2) How to model the vaccination period?

Establishing a threshold in terms of the total progeny of infected individuals.

How to model the vaccination period? By age-dependent branching processes in varying environments.



ECDC for financial support

This is a part of the joint work in progress with M. Gonzales and R. Martinez, both at University of Extremadura, Spain. Special thanks for the helpful discussion to C. P. Farrington. Research is partially supported by the NSFI, grant VU-MI-105/2005, Bulgaria.



- Anderson R. M. and May, R. M., (1991) *Infectious diseases of Humans: Dynamics and Control.* Oxford University Press.
- Ball, F. (1997) The thresholds behaviour of stochastic epidemics. Series in Mathematical Biology and Medicine 6, 407-424. A.D. Axelrod and M. Kimmel (eds.). World Scientific.
- Ball, F., Donnelly, P., (1995) Strong Approximation for epidemic models. *Stochastic processes and Appl.*, 55, 1-21.
- Daley, D.J. and Gani, J. (1999). *Epidemic Modelling.* Cambridge University Press.



- Dietz, K.(1993), The estimation of the basic reproduction number for infectious diseases. *Statistical Methods in Medical Research* 2, 23-41.
- Farrington, C., Grant, A., (1999). The distribution of the time to extinction in subcritical branching processes: applications to outbreaks of infectious disease. *J. Appl. Probab.* 36. 771-779.
- Farrington, C., Kanaan M. N. and Gay N. J. (2001). Estimation of the basic reproduction mean for infectious diseases from agestratified serological survey data. *Applied Statistics* 50, 251-292.
- Mode, C.J. and Sleeman, C.K. (2000). Stochastic Processes in Epidemiology. World Scientific.

THANK YOU FOR YOUR ATTENTION!