Modelling the transmission dynamics of nosocomial pathogens with data of a recent VRE-outbreak at a University Hospital

Wolkewitz M[1], Dettenkofer M[2], Huebner J[3] and Schumacher M[1]

[1]Institute of Medical Biometry and Informatics,
[2]Institute of Environmental Medicine and Hospital Epidemiology,
[3]Division of Infectious Diseases,
University Medical Center Freiburg

wolke@fdm.uni-freiburg.de

11 Sept 2006

Background
- Hospital-acquired pathogens
- Outbreak in University Medical Center Freiburg

Methods

Results

Discussion

Hospital-acquired pathogens

- Multi-resistent pathogens like e.g. vancomycin-resistent enterococci (**VRE**) are a major infection control problem
- increasing costs and prolonging the length of stay in hospitals
- intervention strategies are essential to control the outbreak
- mathematical modelling can help to understand the transmission dynamics
- recent VRE-outbreak at the University Medical Center Freiburg, where more than 100 patients were colonised or infected
- data-based estimates will be used for model parameters

Outbreak in University Medical Center Freiburg

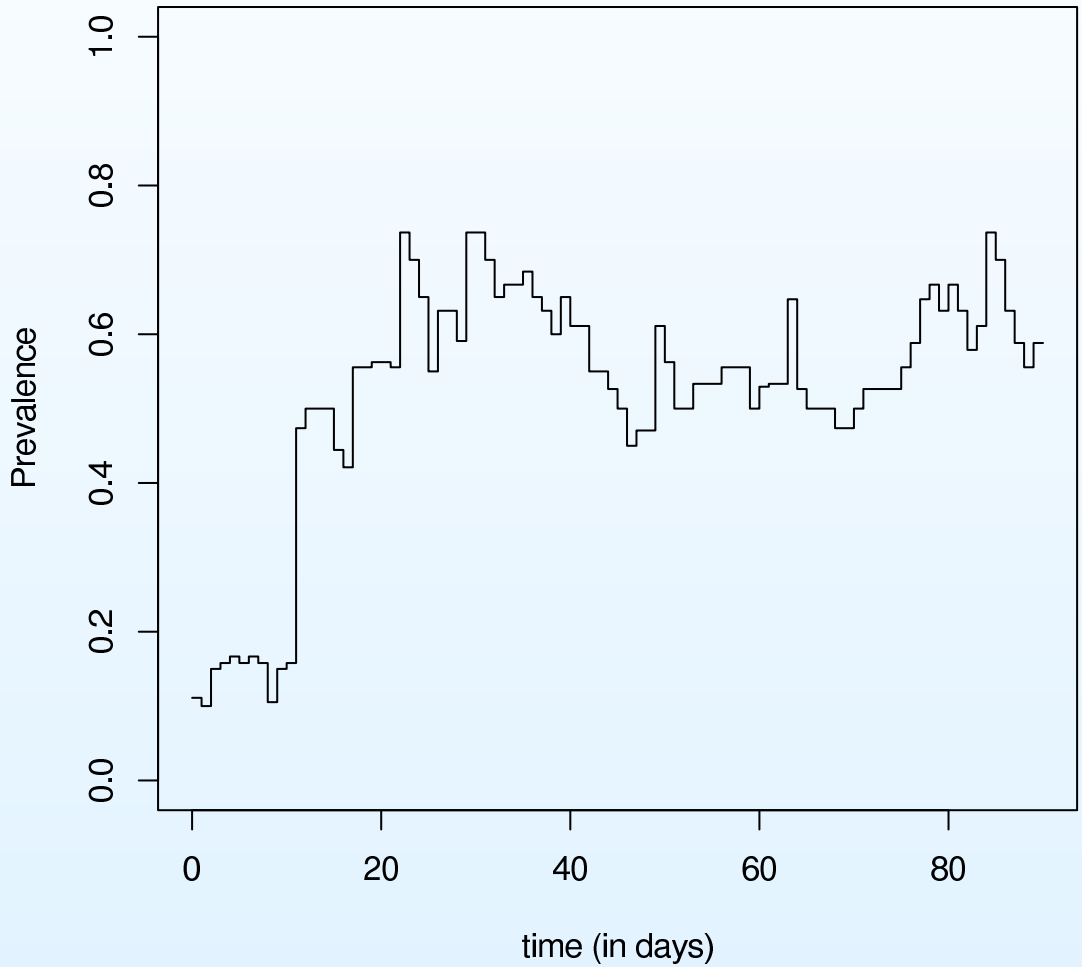
Background
- Hospital-acquired pathogens
- Outbreak in University Medical Center Freiburg

Methods

Results

Discussion

Prevalence of VRE-positive patients per day in hematological / oncological ward (19 beds), 11/2004 - 1/2005



Parameters for hematological / oncological ward

Background
Methods
- Parameters
- Modelling
- Stochastic simulations

Results
Discussion

Data based estimation and expert guesses (literature)

Parameter	Meaning	Value
N_p	number of beds	19
N_s	number of med.staff	7
a	contact rate (/med.staff/patient/day)	6.9
n	nursing-staff proportion	0.7
$\hat{\phi}$	admission colonisation prevalence	0.16
$\hat{\gamma}$	uncolonised discharge rate	0.08
$\hat{\gamma}'$	colonised discharge rate	0.04
$1/\mu$	duration of contamination	1 h
b_s	contamination probability	0.4
b_p	colonisation probability	0.06
$1/\kappa$	duration of contamination of the envir.	10 days
β_{e_s}	transmission from med. staff to envir.	0.15
β_{e_p}	transmission from colon. patient to envir.	2

Ross-Macdonald model (applied for ICU's)

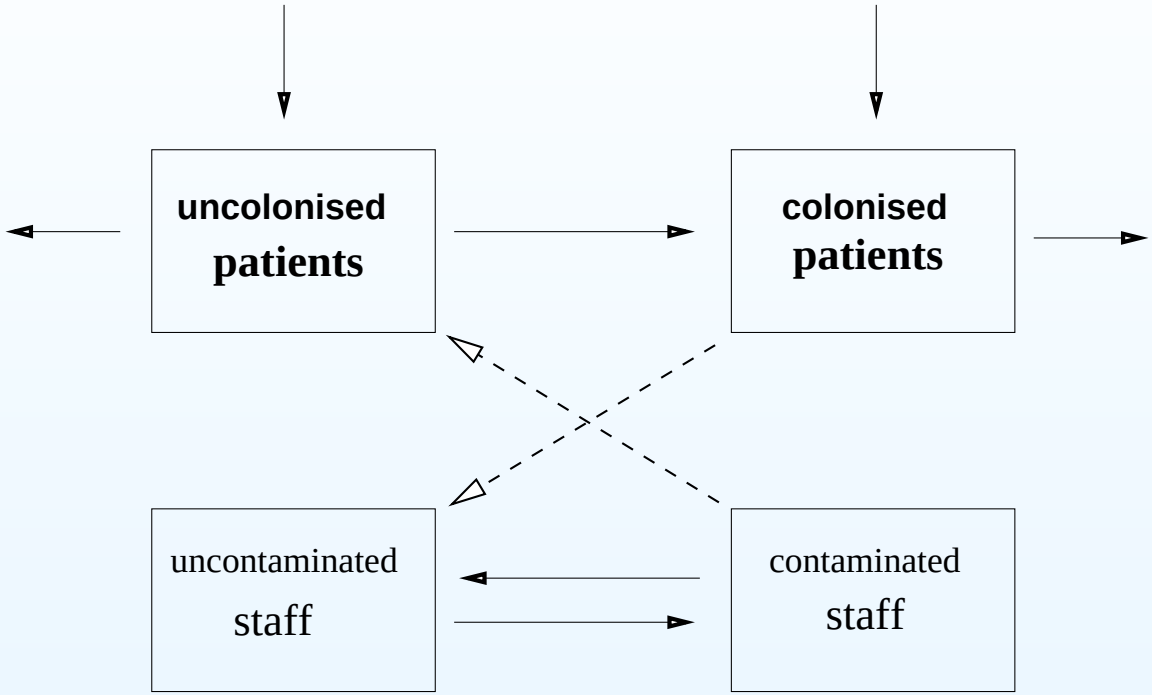
Background

Methods

- Parameters
- Modelling
- Stochastic simulations

Results

Discussion



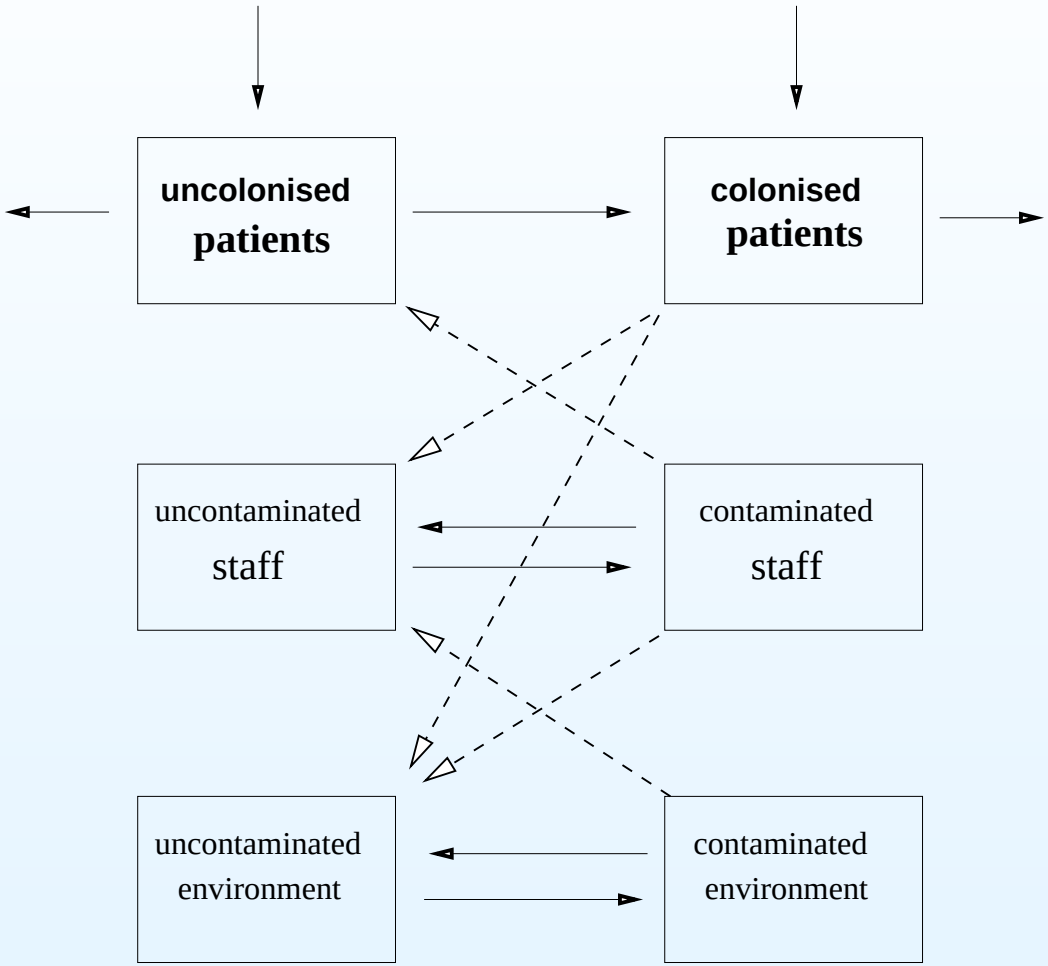
$$\frac{dY_p(t)}{dt} = \Lambda\phi + ab_p\frac{Y_s(t)}{N_s}X_p(t) - \gamma' Y_p(t)$$

$$\frac{dY_s(t)}{dt} = ab_s\frac{Y_p(t)}{N_p}X_s(t) - \mu Y_s(t)$$

Extension: Additional route via contaminated environment

Background
Methods
- Parameters
- Modelling
- Stochastic simulations

Results
Discussion



Mathematical Modelling: Stochastic model

Background
Methods
- Parameters
- Modelling
- Stochastic simulations

Results
Discussion

Event		Rate
colon. admission	$Y_p \rightarrow Y_p + 1$	$\Lambda\phi$
transmission	$Y_p \rightarrow Y_p + 1$	$ab_p \frac{Y_s(t)}{N_s} X_p(t)$
removal	$Y_p \rightarrow Y_p - 1$	$\gamma' Y_p(t)$
med. staff cont.	$Y_s \rightarrow Y_s + 1$	$ab_s(\frac{Y_p(t)}{N_p} + \frac{Y_e(t)}{N_e})X_s(t)$
med. staff decont.	$Y_s \rightarrow Y_s - 1$	$\mu Y_s(t)$
ENVIR cont.	$Y_e \rightarrow Y_e + 1$	$(\beta_{e_s} \frac{Y_s(t)}{N_s} + \beta_{e_p} \frac{Y_p(t)}{N_p})X_e(t)$
ENVIR decont.	$Y_e \rightarrow Y_e - 1$	$\kappa Y_e(t)$

Remarks

- true mass action ('/N.')
- Reed-Frost assumption ('Y.X.') instead of Greenwood ('X.')
- solution of ODE's only yields the mean, but without any variation
- stochastic simulations are essential for small populations
- time to next event is assumed to be exponentially distributed

Background
Methods
- Parameters
- Modelling
- Stochastic simulations

Results
Discussion

Simulations of the Poisson process

- initializations
  - choose parameter values
  - choose initial values
- iteration
  - sum up all rates of change:
    $\sum = \lambda_1(t) + \lambda_2(t) + \lambda_3(t) + \lambda_4(t) + \lambda_5(t) + \lambda_6(t) + \lambda_7(t)$
  - next event occurs after random time $T \sim exp(\sum)$
  - the conditional probability that single event i, $(i \in \{1, ..., 7\})$ happens is proportional to the corresponding rate of change: e.g. at T a colonised admission happens with probability $\lambda_1 / \sum$
  - calculate new $\sum$

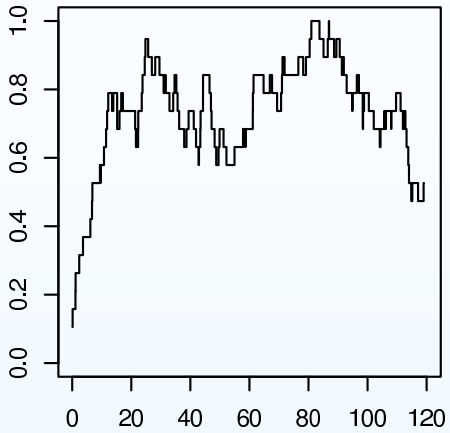
Monte-Carlo simulations of the stochastic process

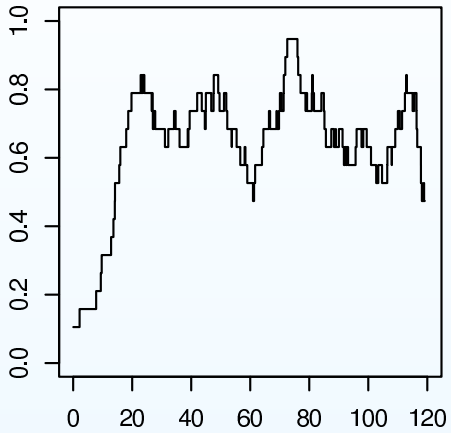
Background

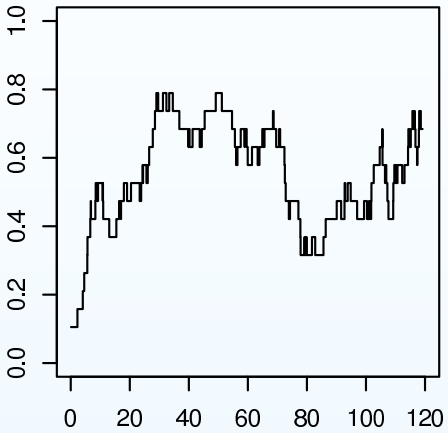
Methods

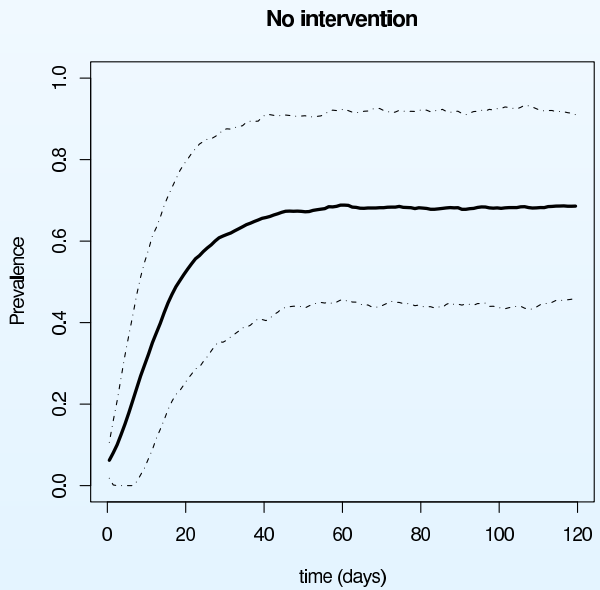
Results
- Intervention strategies
- Effect of intervention strategies

Discussion









1000 simulations: mean with 95% pointwise confidence band

Intervention strategies

Background
Methods
Results
- Intervention strategies
- Effect of intervention strategies

Discussion

Intervention

1. hand-washing, use of gloves (compliance 50%)
2. specific cleaning of contaminated environment (3 times a day)
3. patient isolation or one-to-one nursing (cohorting prob. 80%)
4. screening on admission (isolation of VRE-positve)
5. restricting antibiotics (RR=3, reduction of 50%)

Monte-Carlo simulations

- 20 days after the outbreak: intervention
- simulations might show the effect of the intervention

Effect of one intervention strategy (after 20 days)

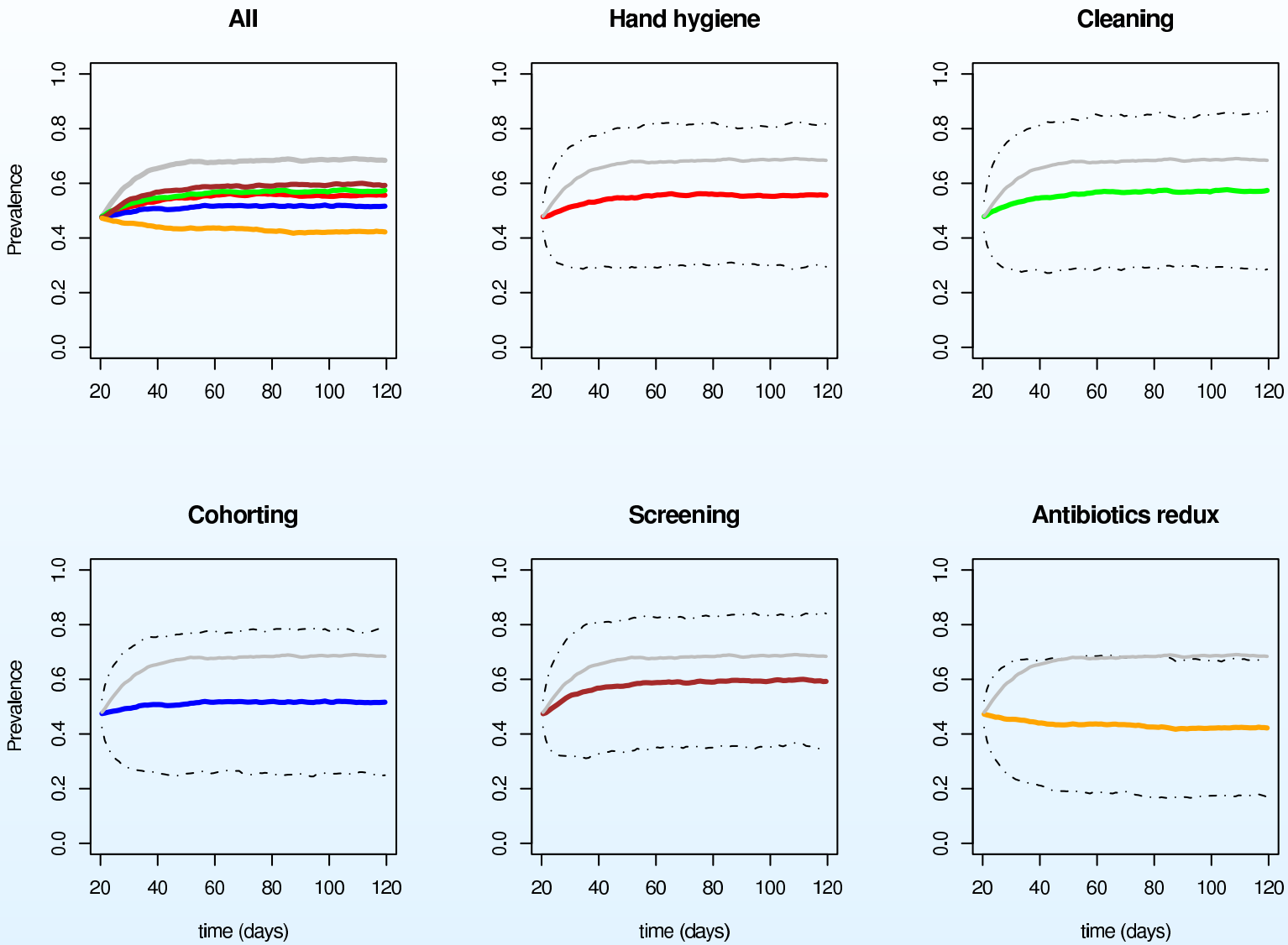
Background

Methods

Results

- Intervention strategies
- Effect of intervention strategies

Discussion

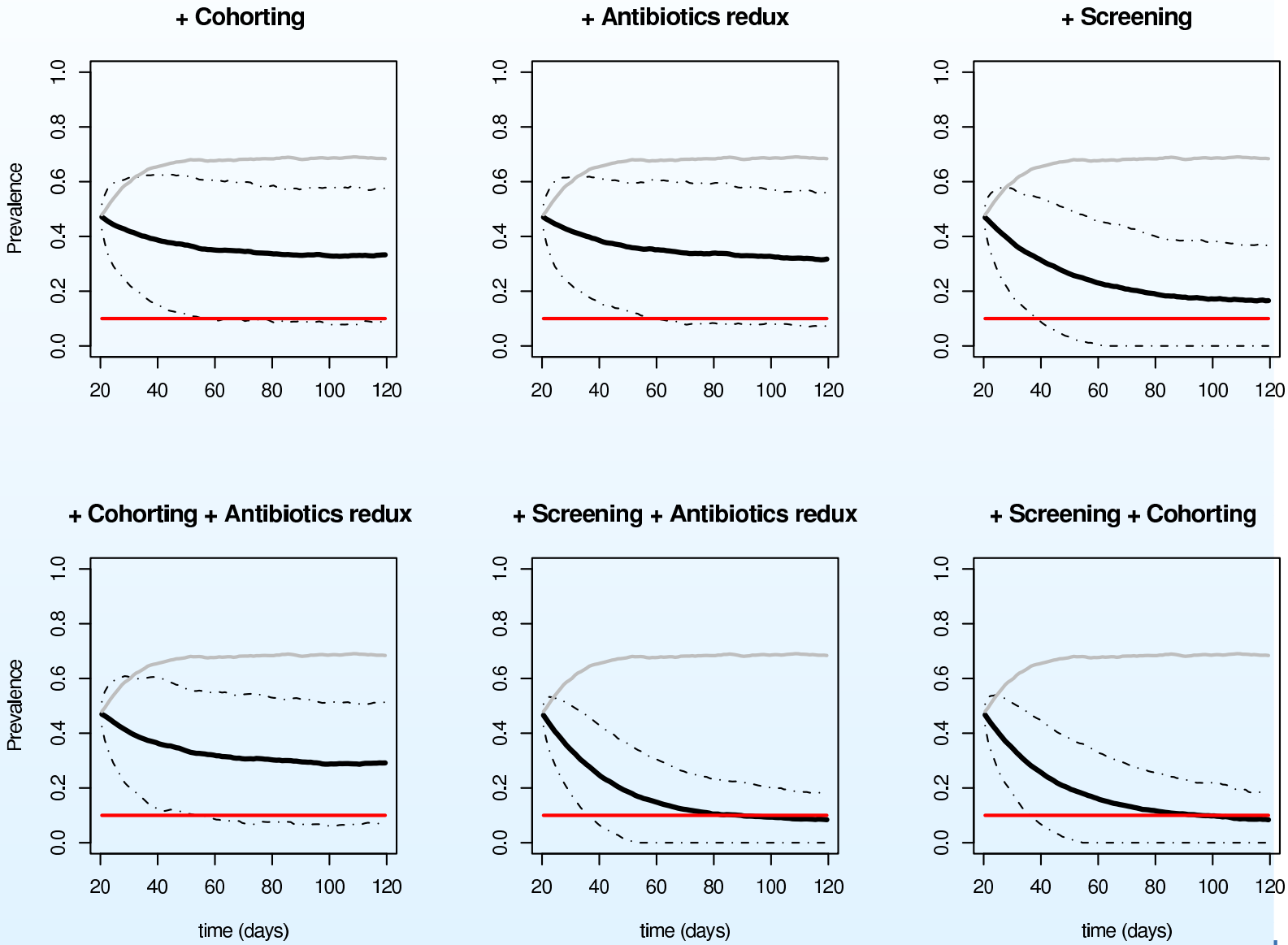


Effect of combined intervention strategies

Background
Methods
Results
- Intervention strategies
- Effect of intervention strategies

Discussion

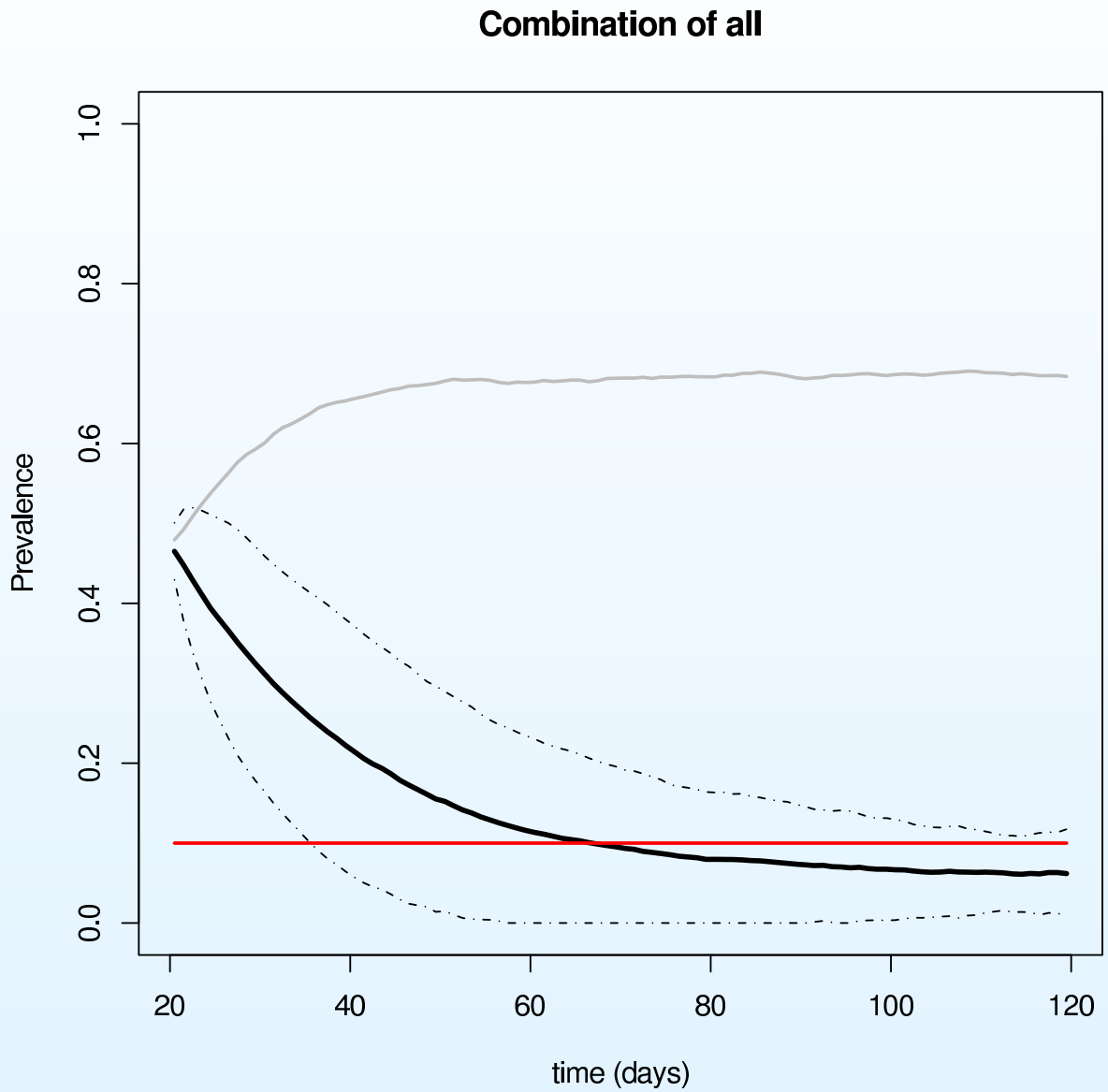
Hand hygiene, cleaning and ...



Effect of combined intervention strategies

Background
Methods
Results
- Intervention strategies
- Effect of intervention strategies

Discussion



Background
Methods
Results
Discussion
- Summary
- Limitations and outlook

Summary

- Modelling
  - extension of established methods: additional routes
  - stochastic simulations of the Poisson process
- Findings
  - expected prevalence 30 days after outbreak: $\sim$ 65-70%
  - only combination of several interventions might control VRE
  - then one can expect that it would last about 40-100 days to eliminate VRE

Background
Methods
Results
Discussion
- Summary
- Limitations and outlook

Limitations and outlook

Limitations:

- more realistic, but overfitted ?
- parameters partly judged by expert guess rather than estimated from data
- constant rates assumed, but e.g. transmission rate probably changes with time after interventions

Outlook:

- combining deterministic modelling with statistical analysis methods
- parameter estimation via martingale theory
- estimating time-dependent rates

Background
Methods
Results
Discussion
- Summary
- Limitations and outlook

Acknowledgement and Reference

Data collection: Thanks to C. Scheiber, M. Bussmann

- Anderson RM and May RM (1991) Infectious Diseases of Humans: Dynamics and Control (Oxford Univ. Press, Oxford)
- Renshaw (1991) Modelling Biological Populations in Space and Time (Cambridge University press)
- McBryde ES and McElwain LS. The Journal of Infectious Diseases 2006;193:1472-3
- Austin DJ, Bonten MJM, Weinstein RA, Slaughter S, Anderson R. Vancomycin-resistant enterococci in intensive-care hospital settings: transmission dynamics, persistence, and the impact of infection control programs. Proc Natl Acad Sci USA 1999; 96:6908-13.
- Grundmann H, Hori S, Winter B, Tami A, Austin DJ. Risk Factors for the Transmission of Methicillin-Resistant Staphylococcus aureus in an Adult Intensive Care Unit: Fitting a Model to the Data. The Journal of Infectious Diseases 2002;185:481-488