

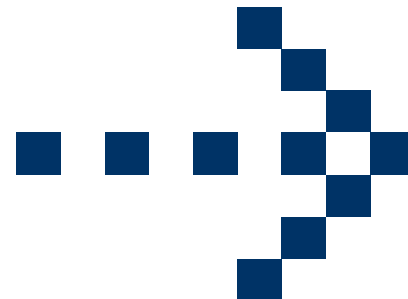
Using simulation to model the transmission and control of MRSA in hospital wards

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Acknowledgements

- ▣ Funding from the Department of Health, England
- ▣ Collaborators University of Birmingham and Warwick Medical School: Peter Hawkey, Katie Hardy, Ala Szczepura, Charlotte Bean and others
- ▣ The ward staff at Heartlands Hospital

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Thursday April 12, 2007

By Victoria Fletcher

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Bacteria tests reveal how MRSA strain can kill in 24 hours

- Cases of drug-resistant PVL likely to rise in Britain
- Fear that GPs will not recognise lethal infection


Ian Sample, science correspondent
 Friday January 19, 2007
[The Guardian](#)

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Scientists have unravelled the workings of a deadly superbug that attacks healthy young people and can kill within 24 hours.

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PVL-producing MRSA, a highly-virulent strain of the drug-resistant superbug, methicillin-resistant staphylococcus aureus, has spread around the world and caused deaths in the UK, Europe, the US and Australia. PVL or panton-valentine leukocidin toxin destroys white blood cells and usually causes



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IS THERE A CURE OUT THERE?
 Published: Monday October 15, 2007 by PHILLS

“ I am due to be admitted to an NHS hospital to have my eye operated on. I have worries about CDiff and MRSA within the NHS. I read the Express headline story on the young soldier and among the expert interviewees, the contribution of Prof. Enright in London. It is strange that Prof Enright did not mention published in 2006 on a new compound that had killed all the MRSA strains had tested, including MRSA/VISA/MSSA. He states in the paper that he had tested all 213 isotopes tested from around the world. I wonder if he had heard and read Prof. Enright responses to questions on Superbugs. No interviewer has asked him about his research on the BBC that the alcohol based handwashes are not effective in this apply in MRSA too? He suggested soap and water treatment.”



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Everyday objects could spread MRSA
 Last updated at 12:14pm on 13th September 2005

Everyday objects used frequently in hospitals such as pens, patient notes and computer keyboards could be helping the spread of the MRSA superbug, an expert has warned.

A study by University College London Hospitals NHS Foundation Trust found charts, case notes, bins, pens and keyboards on an intensive care unit were contaminated with MRSA.

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Problem

- ❑❑❑ Resistant strain of staphylococcus called methicillin resistant staphylococcus aureus (MRSA);
 - ❑❑ Colonises patients;
 - ❑❑ Infects surgical wounds.
- ❑❑❑ Secondary infections called nosocomial cases.
- ❑❑❑ 3% to 7% of admissions are colonised and a similar % of nosocomial cases.

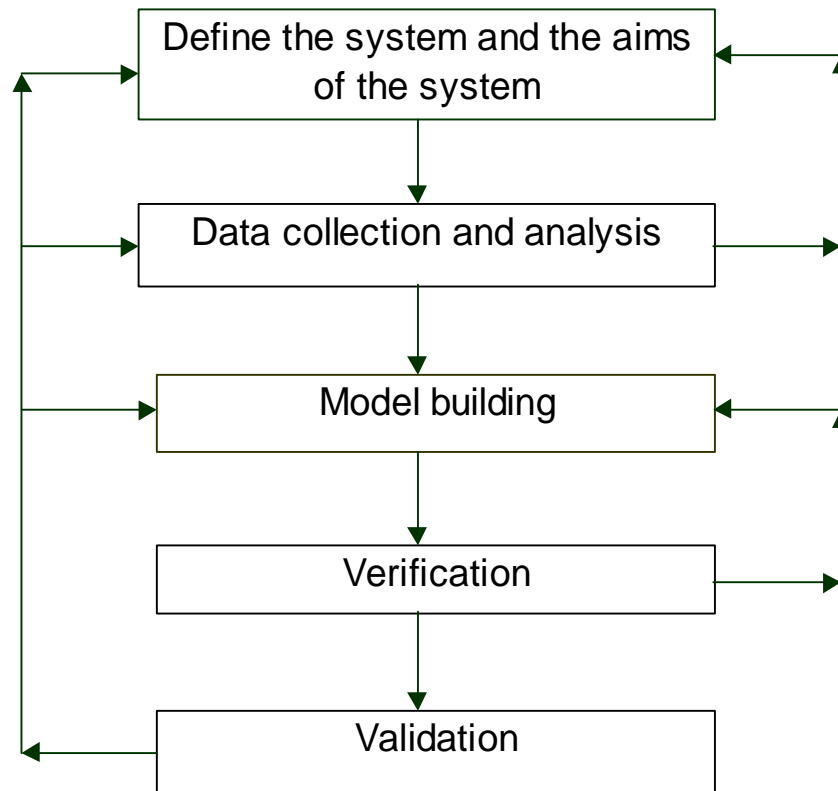
Context

- ▣▣▣ DoH funded control trial of a new rapid molecular test to see if nosocomial cases fall;
- ▣▣▣ 7 wards – cross-over after 8 months
- ▣▣▣ Response to MRSA infection
 - ▣▣▣ Put in isolation ward if available;
 - ▣▣▣ Group together if possible;
 - ▣▣▣ Label;
 - ▣▣▣ Decolonise.

Objectives of the Modelling Exercise

- ▣ Evaluate the potential effectiveness of a rapid molecular test and other MRSA interventions in reducing nosocomial MRSA transmission.
- ▣ Advise the Department of Health about appropriate interventions

Process of modelling - overview



Simulation

- ⌘ Using logic to model (usually complex) processes
- ⌘ Different techniques available
 - ⌘ Stochastic representation of mathematical models
 - ⌘ System dynamics
 - ⌘ Discrete event
 - ⌘ Agent based
- ⌘ An aid to decision-making: cannot make the decisions itself

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Based on individuals



Agent-based simulation

☐☐☐ **Key features**

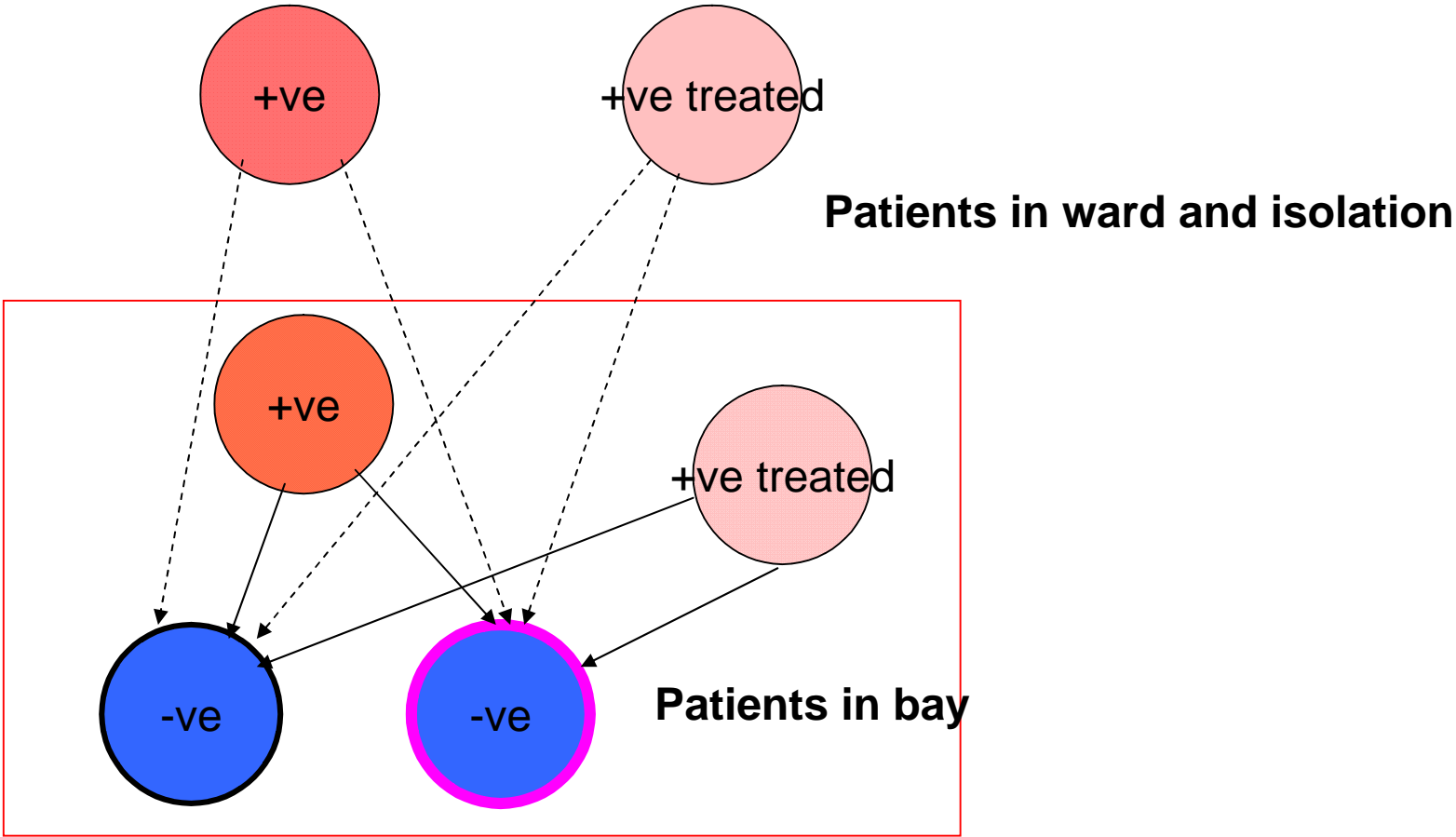
- ☐☐☐ Heterogeneous agents can interact and change the future of the remaining agents
- ☐☐☐ 'Bottom-up' modelling approach. System behaviour emerges from interactions of individual agents among themselves and with the overall environment.


Simulation software

- ☐☐☐ Anylogic™

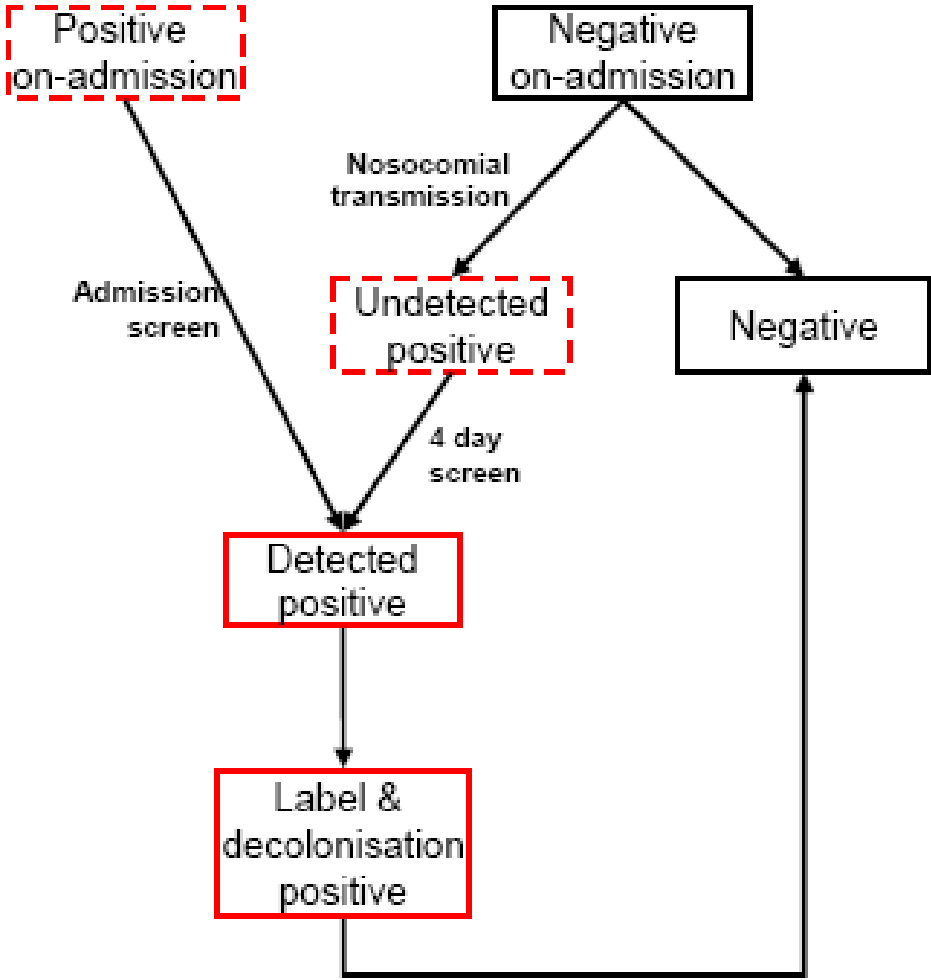
Previous MRSA modelling

- ⌘ Most existing MRSA models are stochastic mathematical models and Monte Carlo simulations of such models: Cooper, Robotham, Bootsma.
- ⌘ We validated agent-based simulation models against existing studies: Cooper *et al.* (1999) and Robotham *et al.* (2006) and produced comparable results.

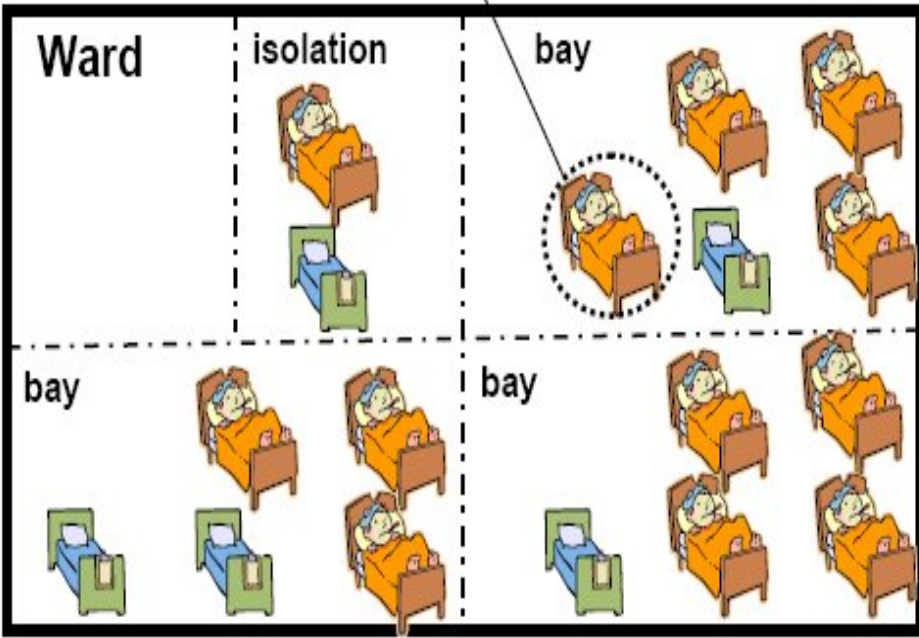


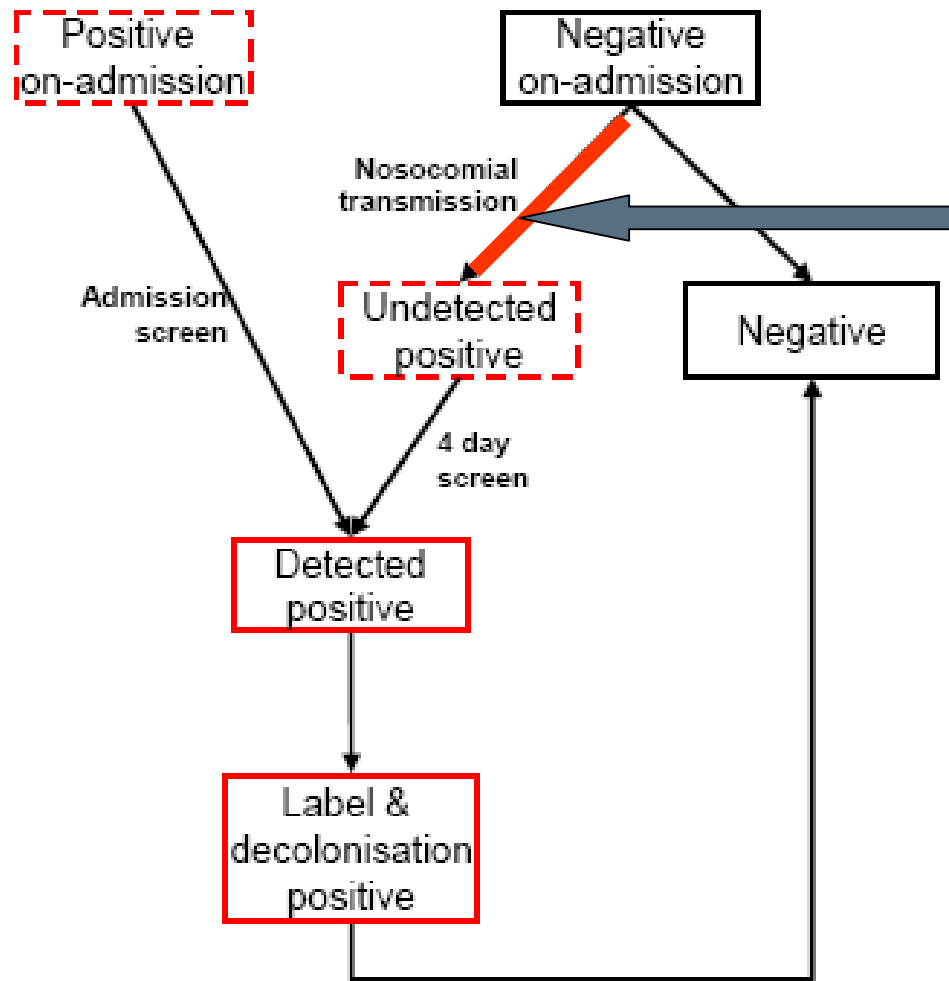
 Patients at high risk eg inserted device

Patient transitions



Attributes: length of stay, age, vulnerability
 Behaviour: MRSA dynamics (MRSA status change, get infected, contaminate environment...),
 Movement dynamics (inter-bay movement, move to and from isolation)





Key transition

Transition negative to positive

$$\begin{aligned} & \text{Probability of colonisation per day} = \\ & \text{Basic Transmission Coeff (per day)} * \text{Vulnerability} * \\ & \left[\frac{K (\text{No. undetected} + b * \text{No. detected on bay})}{(\text{Total patients in bay} - 1)} \right. \\ & \left. + (1-K) \frac{(\text{No. undetected} + b * \text{No. detected on ward})}{(\text{Total patients in ward} - 1)} \right] \end{aligned}$$

K and b are constants between 0 and 1

Vulnerability of (-ve patient) = V

V is a constant = 1 for regular patients and >1 for high risk

Negative patients will be evaluated for the transmission risk when they are admitted to the ward and when:

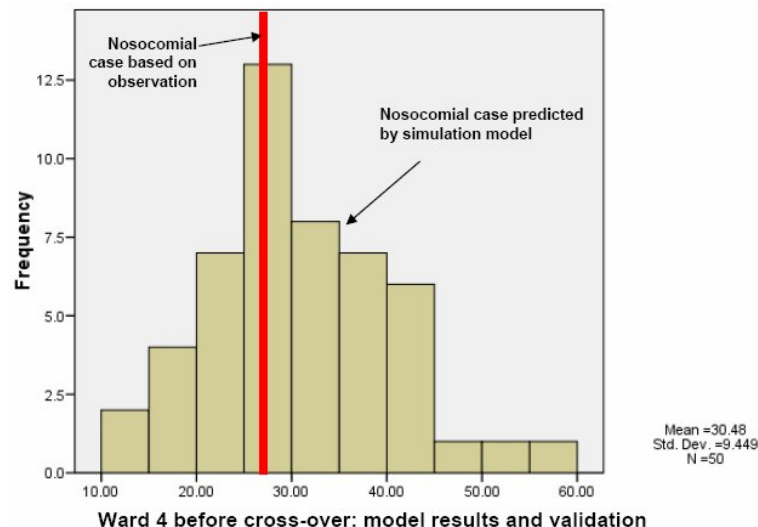
- Positive patient enters or leaves the ward
- New nosocomial cases in the ward
- The status of existing positive patient changes

Data

- ▣ From the data collected for the study;
 - ▣ Length of stay distributions
 - ▣ Admission rate
 - ▣ Timing of pathology tests (in practice)
 - ▣ Results of pathology tests
 - ▣ Timing of treatments
 - ▣ Patients on ITU, with inserted devices
- ▣ From the literature and clinical expertise;
 - ▣ Transmission coefficient
 - ▣ Effect of cleanliness (labelling) and decolonisation
 - ▣ Presence of infection after patient has left
 - ▣ Additional risks from factors such as ITU treatment.

Model validation

- ▣ Model is validated against all 14 scenarios.
- ▣ Model runs 30 replications for each scenario.
- ▣ Number of nosocomial case based on observation is compared with number of nosocomial case (mean, 1st and 3rd quantile, 10 and 90 percentile) predicted by the model.



Model validation summary (14 scenarios)

	count	%
Good fit (within 1st and 3rd quantile)	6	42.9%
Moderate Fit (within 10 and 90 percentile)	6	42.9%
Poor fit (outside 10 and 90 percentile)	2	14.3%
Smaller than simulation mean	6	42.9%
Larger than simulation mean	8	57.1%

Effectiveness of rapid molecular test (interim results)

⌘ The comparison is based on the validated model.

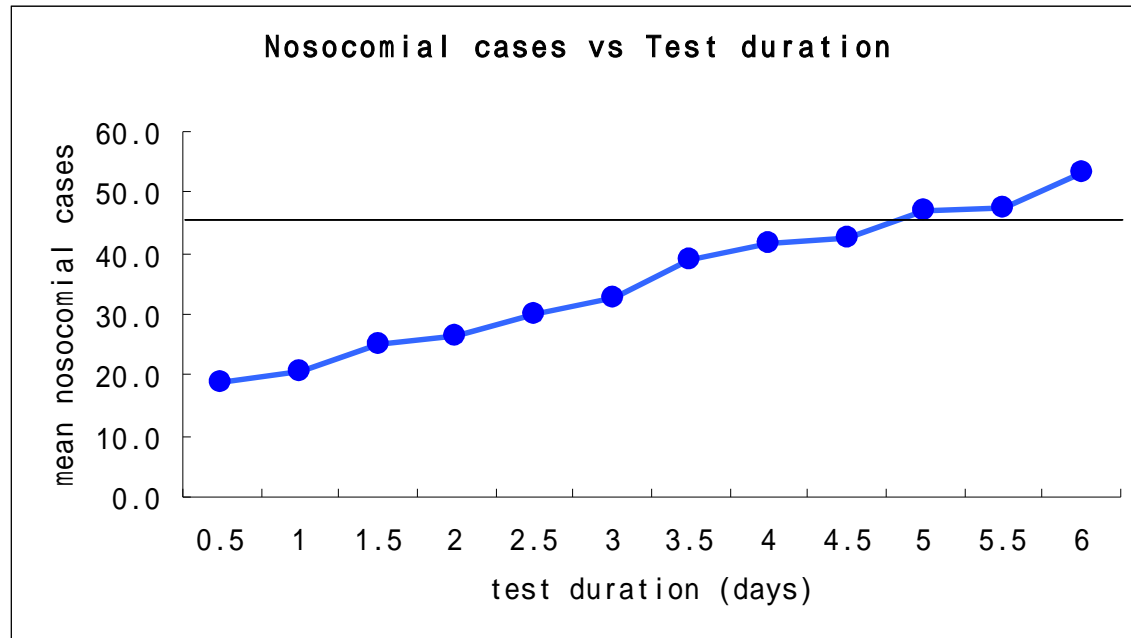
Table: Effectiveness of rapid molecular test over conventional culture

Ward	Transmission ratio under culture test (mean)	Transmission ratio under rapid test (mean)	Absolute reduction	Relative reduction	P-value
Ward 4	1.36 (std 0.77)	0.56 (std 0.18)	0.8	143%	<0.0001
Ward 5	0.46 (std 0.22)	0.34 (std 0.16)	0.12	35%	<0.0001
Ward 10	0.90 (std 0.53)	0.46 (std 0.18)	0.45	98%	<0.0001
Ward 11	0.96 (std 0.28)	0.42 (std 0.14)	0.54	126%	<0.0001
Ward 12	0.76 (std 0.24)	0.45 (std 0.18)	0.31	69%	<0.0001
Ward Beech	1.05 (std 0.51)	0.76 (std 0.55)	0.39	51%	<0.0001
Ward Rowan	0.96 (std 0.56)	0.49 (std 0.40)	0.47	96%	<0.0001

⌘ A significant reduction of transmission ratio is expected for all scenarios. The extent of the reduction is different for different wards.

What-if analysis: time to response to test (interim results)

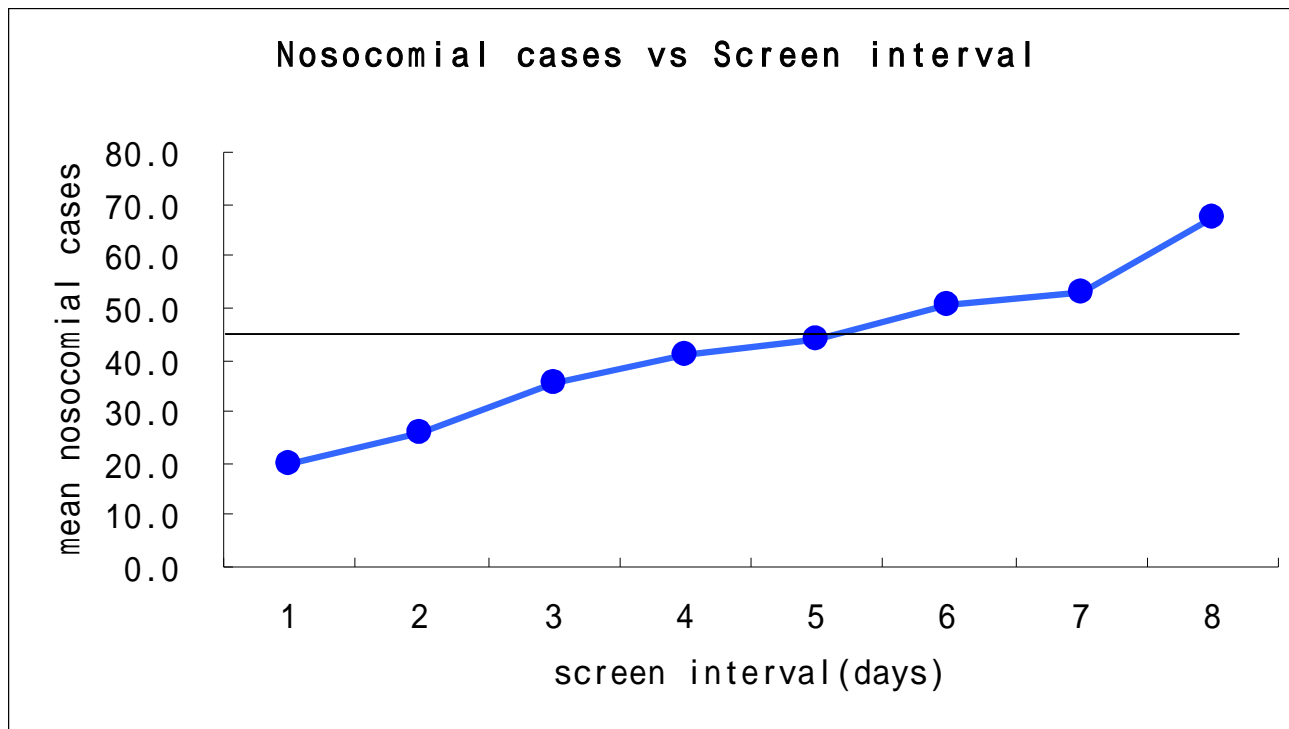
- What if the test response time is other than 1 or 3 days?
- Test duration is set between 0.5 to 6 days.
- Model runs 50 replications for each setting and the mean is used for analysis.



Total admissions: 1334; mean of external cases: 45

What-if analysis: screening interval (interim results)

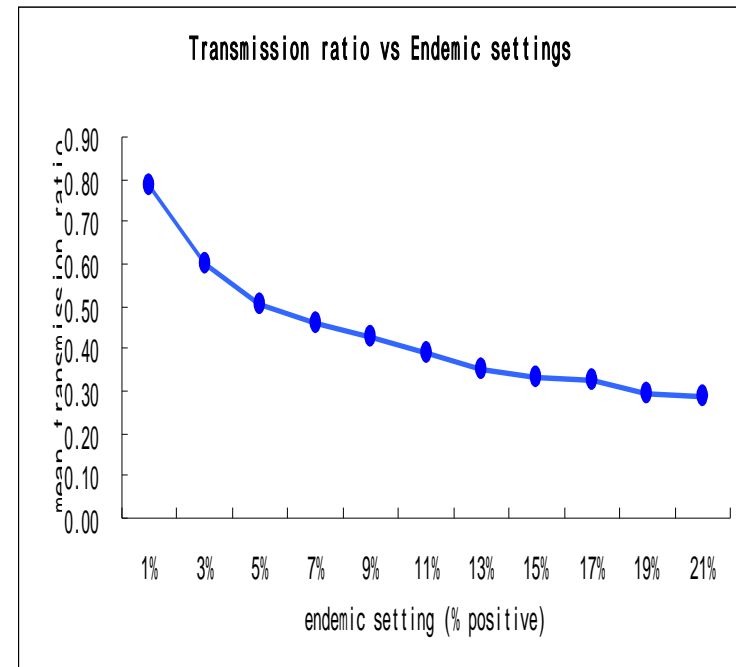
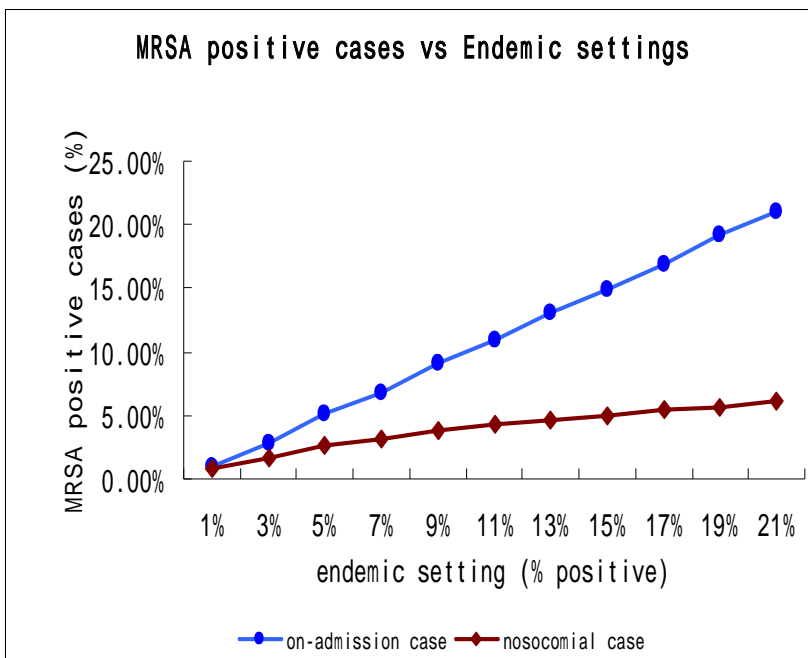
- ▣ What if the screening interval is other than 4 days?
- ▣ Screening interval is set between 1 and 8 days.



Total admissions: 1334; mean of external cases: 45

What-if analysis: endemic setting (interim results)

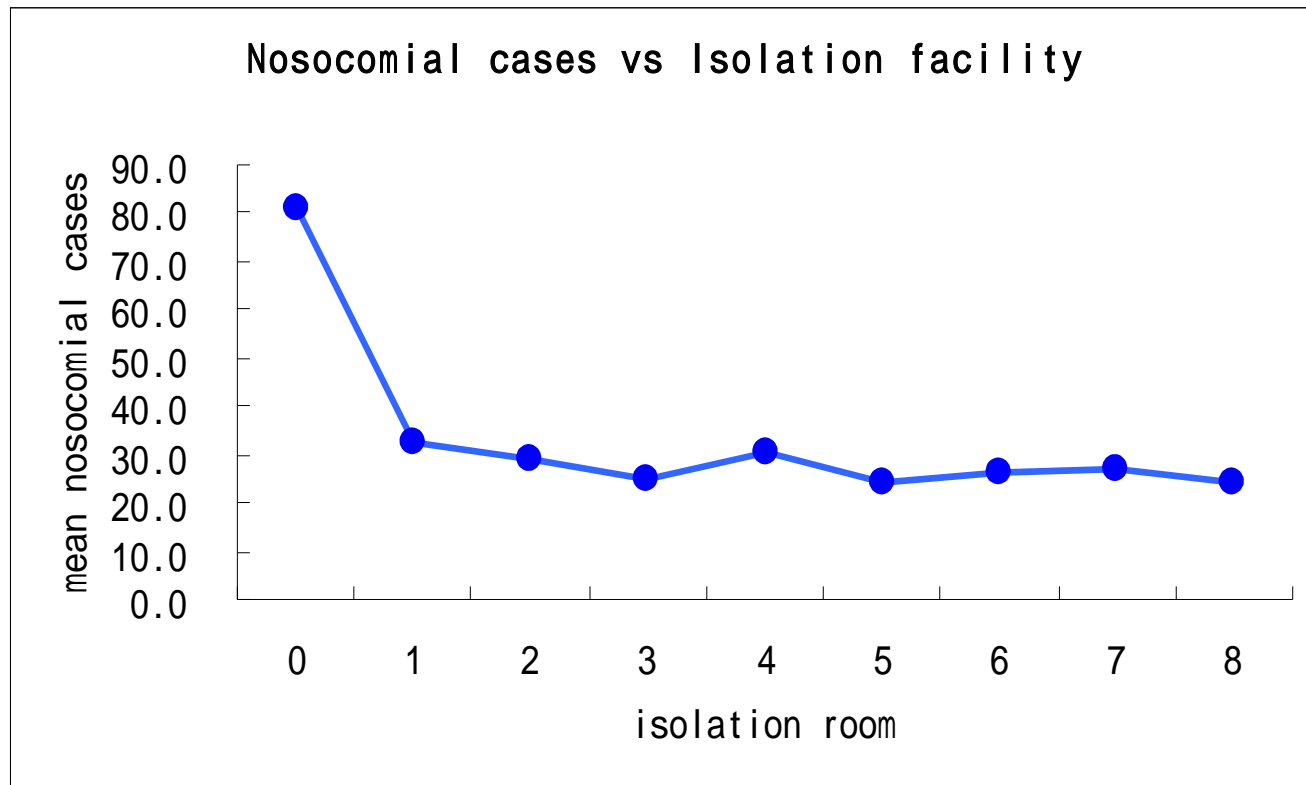
- What if the endemic setting is other than 3.4%?
- Endemic setting is set between 1% and 21%.



Total admissions: 1334; mean of external cases varies (13 – 280)

What-if analysis: isolation facility (interim results)

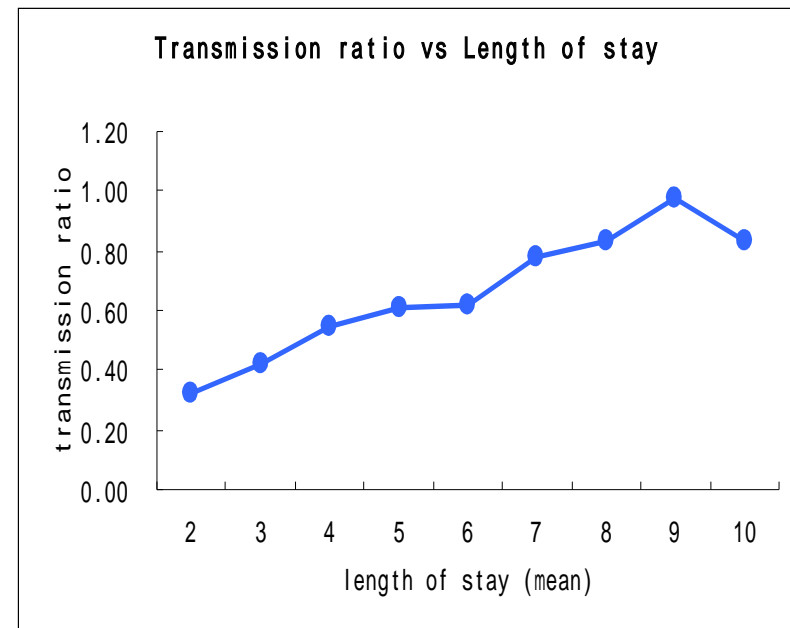
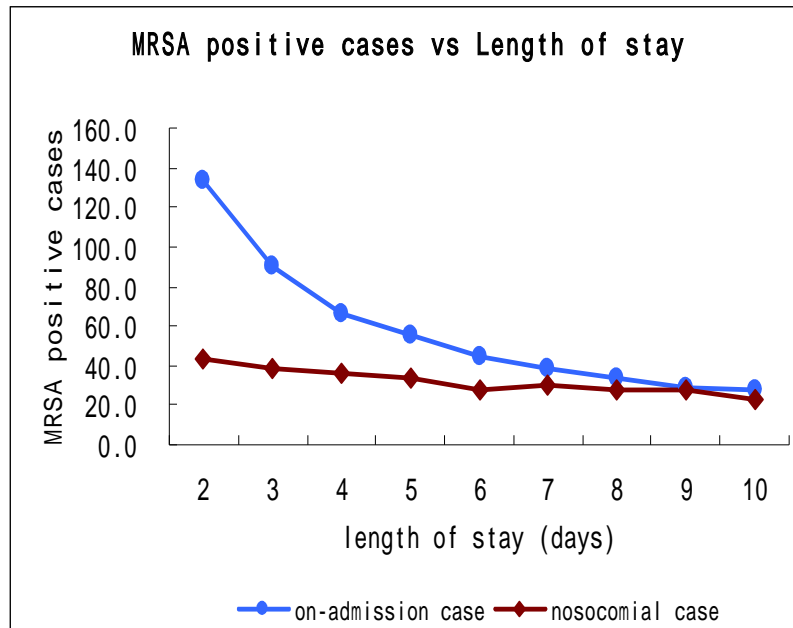
- Number of isolation room is set between 0 and 8 with default endemic setting (3.4%)



Total admissions: 1334;
mean of external cases: 45

What-if analysis: length of stay (1) (interim results)

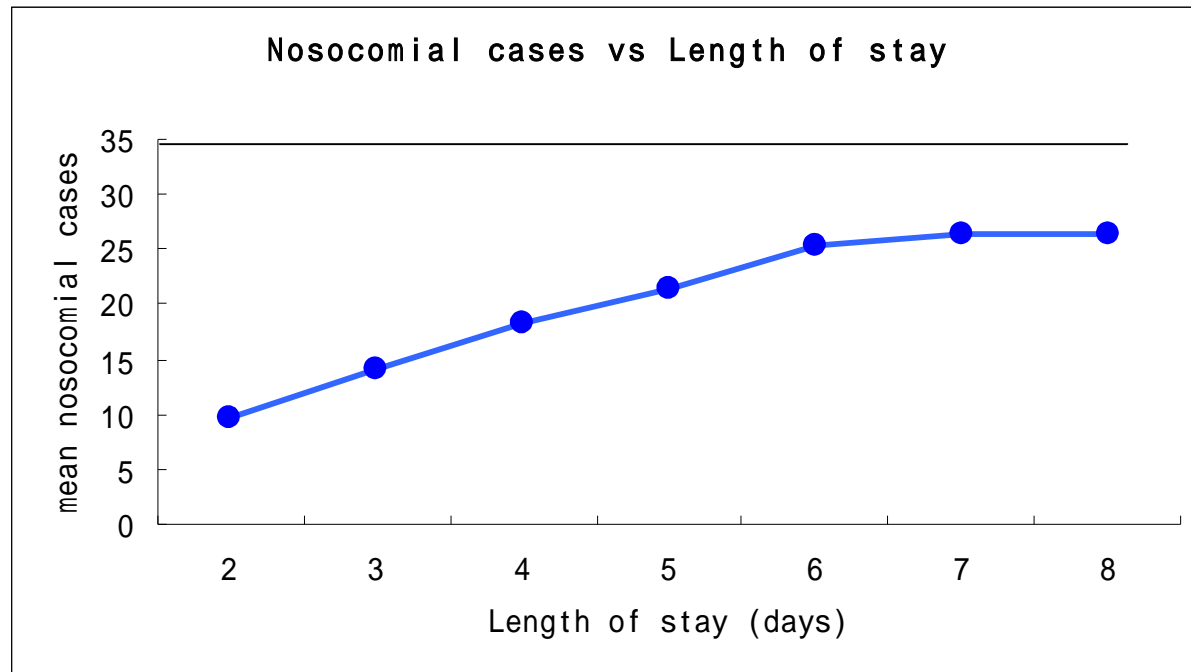
- What if the mean length of stay is other than 5.87 days?
- Mean length of stay is set between 2 and 10 days.
- Occupancy kept constant (admission rate varies)



Total admissions varies (3916 - 783); mean of external cases varies (133 - 27)

What-if analysis: length of stay (2) (interim results)

- What if the mean length of stay is other than 5.87 days?
- Mean length of stay is set between 2 and 8 days.
- Admission rate kept constant (occupancy varies)



Total admissions: 1031; mean of external cases: 35

Further investigations

- Effect of isolation wards being used intermittently or exclusively for other purposes (eg C. Difficile);
- Effect on choice of test of reduced transmission rate – eg hand washing etc.
- Test sensitivity of results to “estimated” parameters.

Benefits of modelling

- ⌘ Assumptions are well specified.
- ⌘ Policy changes can be tested in the model.

Caution

- ⌘ Model is as good as the assumptions and data used.

THE END

