Planning infection control interventions using modelling and analysis of patients transfers

Ben Cooper
Nuffield Department of Medicine
University of Oxford
no disclosures
past  present  future
Mathematical modellers of the spread of infection can get carried away by the elegance of their formulae, and politicians are easily impressed by their double differential equations, which caused millions of animals to be needlessly killed during the 2001 foot and mouth disease outbreak.

Hugh Pennington
09-11-01
This is next
Take Penicillin Now
Death to America
Death to Israel
Allah is great
Table 1. Estimates of cumulative total smallpox cases after 365 days with no intervention

<table>
<thead>
<tr>
<th>No. initially infected(^a)</th>
<th>No. infected per infectious person(^b)</th>
<th>Cumulative total no. of smallpox cases, days postrelease(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30 days</td>
</tr>
<tr>
<td>10</td>
<td>1.5</td>
<td>31</td>
</tr>
<tr>
<td>10</td>
<td>3.0</td>
<td>64</td>
</tr>
<tr>
<td>1,000</td>
<td>1.5</td>
<td>3,094</td>
</tr>
<tr>
<td>1,000</td>
<td>3.0</td>
<td>6,387</td>
</tr>
</tbody>
</table>

Meltzer et al, EID 2001
Smallpox vaccination timeline

- Modellers speak to experts who tell them most transmission occurs before rash
- Modellers build models which predict mass vaccination necessary to control deliberate smallpox release
- Modellers present findings in White House and publish in Science, PNAS, NEJM
- Government order smallpox vaccination for military personnel and voluntary vaccination for frontline medical staff.
- 38,885 voluntary vaccinations during 2003 resulted in three deaths, two permanent disabilities, and 10 life-threatening illnesses

2002

2003
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2002

- New models show that outbreaks could readily be controlled by contact tracing and case isolation alone (findings confirmed by other groups). Findings published in Am J Epidemiol (and not presented in White House)
- Fitting models to data shows that almost all transmission occurred after rash develops (contradicting earlier model assumption)

2003

Other modellers speak to other experts and decide to speak to the data
Smallpox transmission and control: Spatial dynamics in Great Britain. (Riley & Ferguson PNAS 2006)
Poxy Models & Rash Decisions. (Cooper, PNAS 2006)
Data & image courtesy of John Edmunds & John Read
Monitoring the spread of meticillin-resistant Staphylococcus aureus in The Netherlands from a reference laboratory perspective

T. Donker a,b, T. Bosch c, R.J.F. Yoma c, A.P.J. Haenen a, W.M. van Ballegooijen a, M.E.O.C. Heck d, L.M. Schauls e, J. Wallinga f, H. Grundmann a,b

a University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands
b National Institute for Public Health and the Environment (RIVM), Bilthoven, The Netherlands
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T. Donker \textsuperscript{a,b,c,1}, T. Bosch \textsuperscript{b}, R.J.F. Yoma \textsuperscript{b}, A.P.J. Haenen \textsuperscript{b}, W.M. van Ballegooijen \textsuperscript{b}, M.E.O.C. Heck \textsuperscript{1}, L.M. Schouls \textsuperscript{1}, J. Wallinga \textsuperscript{c}, H. Grundmann \textsuperscript{a,b}

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A

B

C

Weeks since January 1, 2008

Odds ratio for belonging to a cluster

Contact with farm animals
Admitted from hospital abroad
Adopted child abroad
Regular visits to hospital abroad
Known MRSA carrier
Admission from hospital with known MRSA problem
Shared room with MRSA carrier
Community-acquired (finding <48h after risk admission)
Lacking obvious risk factors

Contact tracing
HCW unprotected contact with MRSA carrier*
Identifying the effect of patient sharing on between-hospital genetic differentiation of methicillin-resistant *Staphylococcus aureus*

Hao-Han Chang¹, Janine Dorset²,³, Jibbe Donker⁴, Colin J. Worthy⁴, Edward J. Fell⁴, William P. Hanage³, Stephen D. Bentley⁵, Susan S. Huang⁴ and Marc Lipsitch⁷

![Graph showing the effect of patient sharing on between-hospital genetic differentiation of methicillin-resistant Staphylococcus aureus](image-url)
Patient Referral Patterns and the Spread of Hospital-Acquired Infections through National Health Care Networks

Tjibbe Donker¹,²*, Jacco Wallinga¹,³, Hajo Grundmann¹,²

*Corresponding author.
Patient Referral Patterns and the Spread of Hospital-Acquired Infections through National Health Care Networks

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2010
The relative importance of large problems far away versus small problems closer to home: insights into limiting the spread of antimicrobial resistance in England
The relative importance of large problems far away versus small problems closer to home: insights into limiting the spread of antimicrobial resistance in England

TIK Donker1,2,7, St. Katherine L. Henderson1, Jodee L. Hopkins4, Andrew R. Dodgson6, Stephanie Thomas6, Dominik W. Cook2,5, Tim E. A. Peacock2,7, Alan P. Johnson1,4, Neil Woodford4,6, A. Scott Walker6,7 and Julie V. Robotham1,7

Fig. 3 The geographical distribution of carbapenemase-producing Enterobacteriaceae isolates per resistance mechanism, calculated as the number of confirmed isolates per 100,000 hospital admissions (a–c) based on Hospital Episode Statistics data for 2013–2014. Clear differences can be discerned between mechanisms, with high prevalence of KPC and high OXA-48-like prevalence in different parts of the North-West. d The geographical distribution of the majority carbapenemase (colour) reflects both single hospital outbreaks as well as multi-institutional outbreaks, such as in the Manchester and Lancashire referral regions.
Inference and control of the nosocomial transmission of MRSA.

(Pei et al, eLife 2018)
Inference and control of the nosocomial transmission of MRSA.
(Pei et al, eLife 2018)
iv. Models to choose interventions

Effectiveness of interventions:
- Screening
- Eradication therapy
- Isolation

Transmission parameters

Health Economic parameters:
- Cost of interventions
- QALY loss due to MRSA
- Attributable mortality
- Additional length of stay

Transmission model
(individual-based, microsimulation model)

MRSA deaths, infections, admissions, ...

Assessment of effectiveness and cost effectiveness of interventions

Economic parameters:
- Cost of interventions
- QALY loss due to MRSA
- Attributable mortality
- Additional length of stay

Robotham et al., BMJ 2011
To estimate rates of colonization and duration of carriage, we modeled colonization and carriage dynamics... state r to state s, was modelled by the linear equation:

\[ \lambda C_f \sum_0 \lambda_0 \cos \#t_8 \lambda_8 \lambda_8 \sum_2 00 \lambda_{8t} \sum_4 \lambda_0 \text{log} \lambda_c \sum_2 (C_c \lambda_c \lambda_r v) \]

where \( \lambda \) is a set of covariates.
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Hugh Pennington
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But the work of B.S. Cooper and his colleagues is simple, biologically plausible, and persuasive. In an article in the Proceedings of the National Academy of Sciences of the USA, ‘Methicillin-Resistant Staphyloccocus aureus in Hospitals and the Community: Stealth Dynamics and Control Catastrophes’, they show that carriers are the problem. Many infected patients are repeatedly admitted to hospital. So the control of single hospital outbreaks is an incomplete victory.
Conclusions

Bad models kill. Good models save lives. Or help us think.

Future models accounting for referral networks are can help inform policies when infection control decisions can be made at a national or regional level.

For MDR Gram negatives a better understanding of dynamics and natural history in the community and hospital settings is needed.
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