

Dear Editor,

We wish to submit for publication a letter, “More research is needed to quantify risks, benefits and cost-effectiveness of universal mupirocin usage”. This is in response to Hentem *et al* “Prevention of Surgical Site Infections: Decontamination With Mupirocin Based on Preoperative Screening for *Staphylococcus aureus* Carriers or Universal Decontamination?” Clin Infect Dis. (2015) doi: 10.1093/cid/civ990, published ahead of print 9th December 2016.

We write as authors of the study referenced in the editorial commentary [1] in which we concluded that there would be a significantly greater increase in the prevalence of mupirocin-resistant MRSA after 5 years of universal use of mupirocin compared with targeted mupirocin treatment [2]. While we welcome its publication, we have identified a number of limitations with the model which we believe should be highlighted to your readers.

Yours sincerely,

Sarah R. Deeny

Modelling and Economics Unit, Centre for Infectious Disease Surveillance and Control,
Public Health England and Health Protection Research Unit in Modelling Methodology,
London, UK

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More research is needed to quantify risks, benefits and cost-effectiveness of universal mupirocin usage.

Sarah R. Deeny^{1*}

Colin J. Worby²

Olga Tosas Auguet³,

Ben S. Cooper^{3,4},

Jonathan Edgeworth^{5,6}

Barry Cookson⁷

Julie V. Robotham¹

1. Modelling and Economics Unit, Centre for Infectious Disease Surveillance and Control, Public Health England and Health Protection Research Unit in Modelling Methodology, London, UK

2. Center for Communicable Disease Dynamics, Harvard School of Public Health, Boston, MA, USA

3. Centre for Tropical Medicine and Global Health, Nuffield Department of Clinical Medicine, University of Oxford, Oxford, UK

4. Mahidol-Oxford Tropical Medicine Research Unit, Bangkok, Thailand

5. Centre for Clinical Infection and Diagnostics Research, Department of Infectious Diseases, King's College London, London, UK

6. Guy's and St Thomas' NHS Foundation Trust, London, UK

7. Division of Infection and Immunity, University College London, London, UK

*Corresponding author

TO THE EDITOR— We read with interest Hetem *et al* [1], in which the authors use a simple deterministic mathematical model to simulate the dynamics of mupirocin resistance (MupR) in a single surgical ward. They compare the impact of universal mupirocin usage to screening and targeted mupirocin treatment for *Staphylococcus aureus* decontamination prior to surgery. They conclude that “universal decolonization seems associated with an equally low risk of MupR in *S. aureus*” and recommend universal mupirocin use.

Their model has usefully highlighted the importance of understanding the long-term impact of universal mupirocin usage. We have previously modelled the impact of mupirocin treatment of methicillin-resistant *S. aureus* (MRSA) but did not explicitly consider the impact on methicillin-sensitive *S. aureus* (MSSA) [2]. We showed that MupR MRSA transmitted less well than mupirocin sensitive MRSA in the absence of mupirocin usage. We suggested this reduced ability to transmit, and the fact that MupR is found only in some strain types [3], are the reasons why there has not been greater expansion of MupR clones following mupirocin usage in some settings [2]. In our simulations, we found that universal, rather than targeted usage of mupirocin, could lead to approximately twice the increase in the long-term prevalence of MupR MRSA after 5 years; 21.3% (95% CI 20.9%–21.7%) compared to 9.1% (95% CI 8.7%–9.6%) [2]. When the full uncertainty of all parameters were accounted for through sensitivity analysis, MupR prevalence increased in 50%–75% of simulations with universal usage, but only ~10% of simulations with ‘screen and treat’ usage [2]. The interplay between fitness, MupR and usage, and transmissibility of MSSA strains is unknown and, given our findings, would need to be assessed before considering widespread adoption of a universal mupirocin policy.

There are two key limitations of Hentem *et al*’s model. Firstly, it did not account for patient re-admissions, instead assuming a fixed prevalence of mupirocin resistance on admission. This prevented the simulation of onward transmission from readmitted patients colonised on a previous admission, and its impact on the long term prevalence of MupR, an important dynamic in the transmission of antibiotic resistance in *S. aureus* [4]. Secondly, the model assumes that mupirocin treated patients, who are not current *S. aureus* carriers, are not at increased risk of acquiring MupR strains through transmission of MupR *S. aureus*, also a limitation with our own model [2]. Available evidence neither supports nor contradicts this assumption, highlighting the need for further research to estimate key epidemiological parameters.

These two limitations mean that the model may substantially underestimate the impact of universal mupirocin use on MupR. We are therefore concerned that the model, though useful in helping to think about resistance, may not represent a reliable and robust basis to inform policy.

Without screening, an outbreak of MupR *Staphylococcus spp.* could go largely undetected until a MupR infection occurred. Left undetected, such outbreaks can spread widely and prove difficult to control [4].

We would thus argue for prudent usage of mupirocin, where possible targeting use to known MRSA or MSSA carriers. Where there is clear evidence of patient benefit (as in pre-operative surgical patients) we accept that there may be a case for universal use if targeted use is not

possible, but more research is needed to quantify risks, benefits and cost-effectiveness of different policies.

Conflicts of interest

The authors have no conflicts of interest to declare.

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