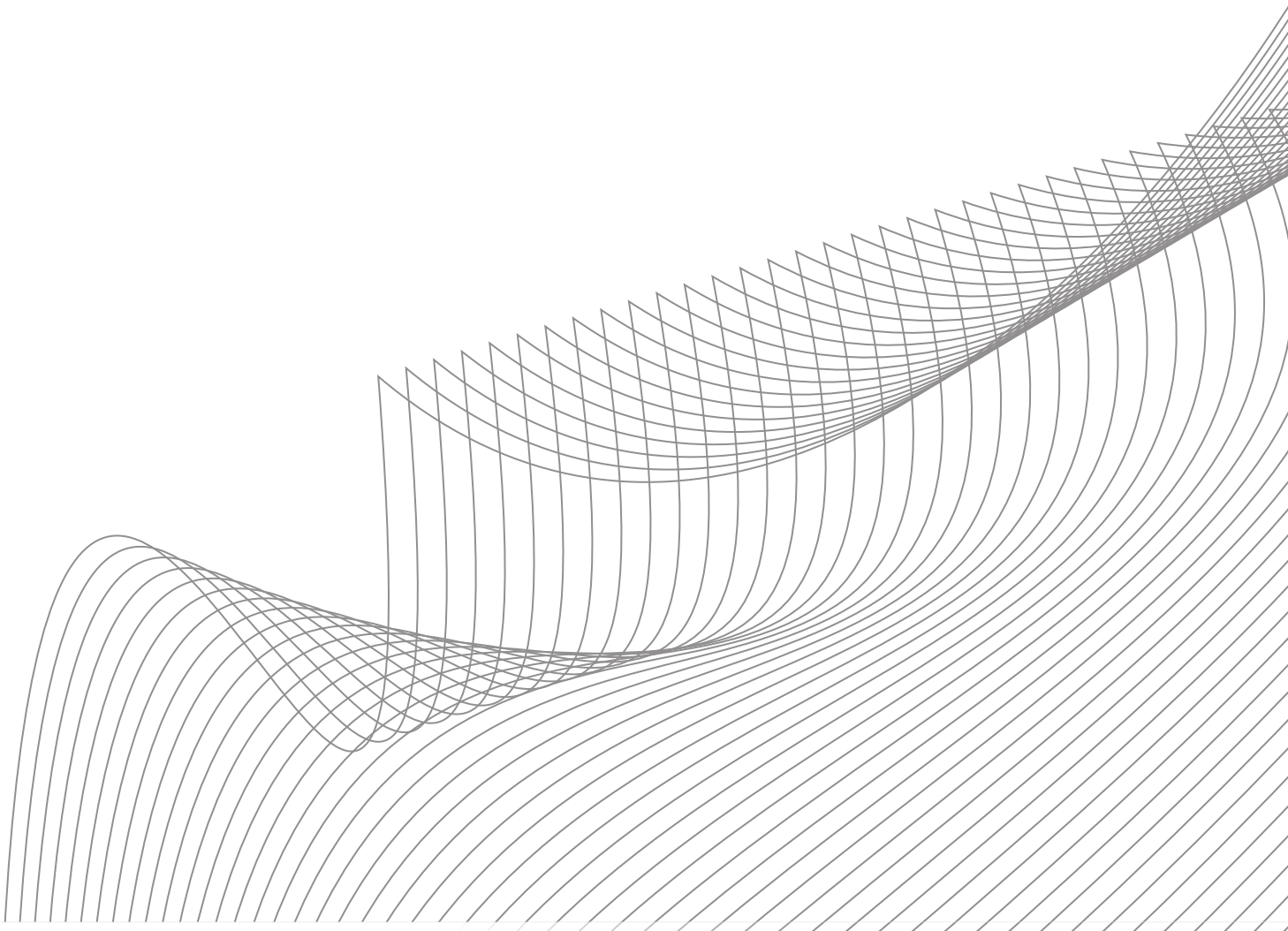
Australian Government
Department of Health and Aged Care

2023 · Volume 47

Communicable Diseases Intelligence

The utility of empirical mupirocin for eradication of methicillin-resistant *Staphylococcus aureus* colonisation in Far North Queensland, Australia

Isabel Guthridge, Stuart Campbell, Simon Smith, Josh Hanson



https://doi.org/10.33321/cdi.2023.47.9
Electronic publication date: 28/02/2023
http://health.gov.au/cdi

Communicable Diseases Intelligence
ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

Communicable Diseases Network Australia
Communicable Diseases Intelligence contributes to the work of the Communicable Diseases Network Australia.
http://www.health.gov.au/cdna

Communicable Diseases Intelligence (CDI) is a peer-reviewed scientific journal published by the Office of Health Protection, Department of Health and Aged Care. The journal aims to disseminate information on the epidemiology, surveillance, prevention and control of communicable diseases of relevance to Australia.

Website
http://www.health.gov.au/cdi

Contacts
CDI is produced by the Office of Health Protection, Australian Government Department of Health and Aged Care, GPO Box 9848, (MDP 6) CANBERRA ACT 2601

Email:
cdi.editor@health.gov.au

Submit an Article
You are invited to submit your next communicable disease related article to the Communicable Diseases Intelligence (CDI) for consideration. More information regarding CDI can be found at: http://health.gov.au/cdi.

Further enquiries should be directed to:

cdi.editor@health.gov.au.

Surveillance summary

The utility of empirical mupirocin for eradication of methicillin-resistant *Staphylococcus* aureus colonisation in Far North Queensland, Australia

Isabel Guthridge, Stuart Campbell, Simon Smith, Josh Hanson

Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are common in Far North Queensland (FNQ) and their incidence is increasing. Decolonisation regimens that include topical mupirocin are recommended in Australian guidelines to reduce recurrent infection. Mupirocin resistance was identified in 3,932/15,851 (24.8%) methicillin-sensitive *Staphylococcus aureus* (MSSA) isolates and in 533/5,134 (10.4%) MRSA isolates from FNQ between 1997 and 2016. Factors associated with mupirocin resistance in multivariate analysis were an MSSA isolate, age < 40 years, rural residence and female gender. These data support the use of mupirocin in MRSA decolonisation in FNQ, although addressing the underlying social determinants of health that drive the incidence of *S. aureus* infections remain a priority for local healthcare provision.

Keywords: Mupirocin; Staphylococcus aureus; MRSA; decolonisation; Tropical Australia

Background and methods

Recurrent staphylococcal skin infections (SSI) are common in Far North Queensland (FNQ), and the proportion caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is increasing.[1,2] This is a challenging therapeutic problem, particularly in rural and remote areas where the social determinants of health contribute to higher rates of staphylococcal colonisation and infection.[3–5] Decolonisation regimens that include nasal mupirocin are recommended to eradicate *S. aureus* carriage[6,7] and may reduce recurrent infections.[8]

This study examined mupirocin resistance in *S. aureus* isolates in FNQ to determine the utility of mupirocin in local empirical staphylococcal decolonisation regimens. There was a focus on rural and remote areas where there are high rates of MRSA infection and limited access to timely microbiology testing. Far North Queensland, an area of around 380,000 km^2 in tropical north-eastern Australia, extends from Tully in the south to the Torres Strait Islands in the north; 65% of the population of 280,000 people live in the urban Cairns region.[9] Approximately 17% of the FNQ population identify as Aboriginal and/or Torres Strait Islander Australians.[9]

We interrogated the Queensland Health electronic laboratory database (AUSLAB) for *S. aureus* isolates from both inpatient and outpatient clinical specimens in FNQ between 1 January 1997 and 31 December 2016. Patient demographics and the isolates' antibiograms were recorded. Isolates were deemed urban if they were collected in Cairns, and rural if not. Repeat isolates collected within < 12 months from the same patient were excluded, as were isolates from non-FNQ residents. Isolates were defined as MRSA if there was *in vitro* resistance to oxacillin or cefoxitin. Mupirocin resistance testing was performed using the Vitek2 system (bioMérieux, France) with 2 mg/L used as the resistance breakpoint. Further testing to distinguish between low-level and high-level mupirocin resistance was not performed. Statistical

Table 1: Characteristics of mupirocin sensitive and resistant *S. aureus* isolates in Far North Queensland, Australia, 1 January 1997 – 31 December 2016

Category	Mupirocin sensitive	Mupirocin resistant	*p* value[a]
All isolates	16,520 (78.7%)	4,465 (21.3%)	
MSSA[b]	11,919 (75.2%)	3,932 (24.8%)	
MRSA[c]	4,601 (89.6%)	533 (10.4%)	
Median age (interquartile range)	36 (17–56)	25 (9–44)	<0.001
< 40 years old	9,008 (54.5%)	3,091 (69.2%)	<0.001
Female gender	7,016 (42.7%)	2,029 (45.7%)	<0.001
First Nations Australian	6,654 (42.7%)	1,795 (43.2%)	0.6
Remote isolate	10,410 (63.0%)	3,082 (69.0%)	<0.001

a Groups were compared using the chi squared test.

b MSSA: methicillin-sensitive *Staphylococcus aureus*.

c MRSA: methicillin-resistant *Staphylococcus aureus*.

analysis was performed with statistical software (Stata version 14.2, USA). Groups were compared using the chi-squared test and multivariate logistic regression analysis, as appropriate, whilst trends over time were determined using an extension of the Wilcoxon rank-sum test. The study was approved by the FNQ Human Research Ethics Committee (HREC/16/QCH/112–1085).

Results and discussion

There were 46,304 *S. aureus* isolates found in AUSLAB from clinical specimens in FNQ for the study period. Of these isolates, 20,985 had mupirocin susceptibility testing performed during the study period;[i] mupirocin resistance was present in 4,465 (21.3%). Mupirocin resistance was identified in 3,932/15,851 methicillin-sensitive *Staphylococcus aureus* (MSSA) isolates (24.8%) and in 533/5,134 MRSA isolates (10.4%) (Table 1). There was no change in the proportion of isolates with mupirocin resistance during the study period (p for trend = 0.50). In multivariate analysis, mupirocin resistance was more likely in MSSA isolates, in people < 40 years of age, in people from rural locations, and in females (Table 2). Aboriginal and/or Torres Strait Islander ethnicity was not associated with mupirocin resistance.

The rate of mupirocin resistance in FNQ is higher than the global rates of 7.6% and 13.8% reported in MSSA and MRSA respectively.[10] It is also much higher than the rate of 1.2% (MSSA) and 0.8% (MRSA) described in Australian national data for 2016, although the higher rates in FNQ are partly explained by the fact that the national series only reports high-level resistance.[11] The distinction between high- and low-level resistance is important, because although high-level mupirocin resistance predicts failure of decolonisation regimens containing mupirocin, the impact of low-level mupirocin resistance is less clear.[12] Unfortunately, the retrospective nature of this FNQ study and the limited capacity of local laboratories precluded the determination of high- and low-level resistance.

Despite this limitation, these data do have implications for local clinical management. As mupirocin resistance rates in FNQ MRSA isolates are relatively low, our study suggests that topical mupirocin remains suitable for empirical use

i Please see Appendix A, Table A.1 for a comparison of characteristics of isolates undergoing testing for mupirocin resistance versus those that were not tested.

Table 2: Multivariate logistic regression analysis of predictors of mupirocin resistance in *S. aureus* isolates, Far North Queensland, Australia, 1 January 1997 – 31 December 2016

	Odds ratio	95% confidence interval	*p* value[a]
Age < 40 years	1.94	1.80–2.08	< 0.001
Rural location	1.25	1.16–1.34	< 0.001
Female gender	1.11	1.04–1.19	0.002
MSSA isolate[b]	2.85	2.59–3.14	< 0.001

a Variables were assessed using multivariate logistic regression analysis.

b MSSA: methicillin-sensitive *Staphylococcus aureus*.

in MRSA decolonisation regimens, although it cannot be unequivocally recommended for MSSA decolonisation.

The increased rates of mupirocin resistance observed in young people in FNQ may reflect higher rates of recent mupirocin exposure, a primary driver of resistance.[13] Topical mupirocin was previously used extensively in FNQ for impetigo, which occurs more commonly in children, but has been superseded by oral trimethoprim/sulphamethoxazole or intramuscular benzylpenicillin.[14–16] It might be anticipated, therefore, that mupirocin resistance will fall in young people in the future.

Rural location was also an independent predictor of mupirocin resistance. Australian data have demonstrated state to state variation, with Queensland reporting high-level mupirocin resistance rates of 3.1% (MRSA) and 3.5% (MSSA) compared with the Australian average of 0.8% (MRSA) and 1.2% (MSSA).[11] Although this FNQ study presents more granular data than prior reports, it is unable to characterise the spatial epidemiology of mupirocin resistance in more detail (e.g., specific communities). Mupirocin resistance was more common in women, possibly due to asymmetric gender roles in child rearing and higher rates of mupirocin resistance in younger people.[17] Gender variation in overall rates of *S. aureus* infection has previously been described[18] although this was not apparent in a prior FNQ study.[1]

Our study has limitations. Mupirocin testing was not performed on 55% of isolates; the reasons for this varied over the study timeframe.[ii] Isolates were more commonly collected in rural areas despite most FNQ residents having an urban address. Similarly, 49.8% of isolates were collected from Aboriginal and/or Torres Strait Islander Australians, who represent only 17% of the FNQ population. This is likely due to the disproportionate burden of skin infections borne by Indigenous Australians living in rural areas; regional variation in specimen collection practices, or the use of alternative pathology providers, may also contribute to this finding. The study also lacks concomitant clinical data.

Interventions that reduce the burden of recurrent *S. aureus* infections are necessary, as these infections are common, debilitating, and potentially life-threatening. The efficacy of topical mupirocin has been compared to other regimens, primarily in elective surgery cohorts. In one study, topical mupirocin achieved clearance rates similar to neomycin and superior to octenidine, although no reduction in infection was seen.[19]

ii Of the four public laboratories in FNQ, only a single site (Cairns Hospital) has access to automated testing (Vitek 2). Manual methods for determining mupirocin resistance are not routine at these peripheral sites. As not all clinical specimens are referred to Cairns, many isolates did not have any mupirocin testing performed. Please see Appendix A, Table A.1 for a comparison of characteristics of isolates that did—or did not—have mupirocin resistance testing.

In another, nasal iodine was marginally superior to mupirocin in preventing *S. aureus* infection.[20]

In conclusion, our data support the empirical use of mupirocin in MRSA—but not MSSA—decolonisation in FNQ. Its role in other infections requires further evaluation. However, ultimately, a concerted public health effort addressing the underlying socioeconomic disadvantage that drives the acquisition and spread of S. *aureus* infections is likely to have a greater health impact than the optimisation of different eradication regimens.

Acknowledgements

The research was funded under the Australian National Health and Medical Research Council grant numbers 1046812, 1098337, and 1131932 (The HOT NORTH initiative).

Author details

Dr Isabel Guthridge[1,*]
Dr Stuart Campbell[1,*]
Dr Simon Smith[1]
Dr Josh Hanson[1,2]

1. Division of Medicine, Cairns Hospital, Cairns, Australia.

2. Kirby Institute, University of New South Wales, Sydney, Australia.

*Dr Guthridge and Dr Campbell contributed equally to this article.

Corresponding author

Dr Stuart Campbell

Department of Medicine, Cairns and Hinterland Hospital and Health Service, Queensland, Australia

Email: stuartc345@gmail.com.

References

1. Guthridge I, Smith S, Horne P, Hanson J. Increasing prevalence of methicillin-resistant *Staphylococcus aureus* in remote Australian communities: implications for patients and clinicians. *Pathology*. 2019;51(4):428–31. doi: https://doi.org/10.1016/j.pathol.2018.11.015.

2. Harch SAJ, MacMorran E, Tong SYC, Holt DC, Wilson J, Athan E et al. High burden of complicated skin and soft tissue infections in the Indigenous population of Central Australia due to dominant Panton Valentine leucocidin clones ST93-MRSA and CC121-MSSA. *BMC Infect Dis*. 2017;17(1):405. doi: https://doi.org/10.1186/s12879-017-2460-3.

3. von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of *Staphylococcus aureus* bacteremia. *N Engl J Med*. 2001;344(1):11–6. doi: https://doi.org/10.1056/NEJM200101043440102.

4. Toshkova K, Annemüller C, Akineden O, Lämmler C. The significance of nasal carriage of *Staphylococcus aureus* as risk factor for human skin infections. *FEMS Microbiol Lett*. 2001;202(1):17–24. doi: https://doi.org/10.1111/j.1574-6968.2001.tb10774.x.

5. Turnidge JD. High burden of staphylococcal disease in indigenous communities. *J Infect Dis*. 2009;199(10):1416–8. doi: https://doi.org/10.1086/598219.

6. Therapeutic Guidelines. Recurrent staphylococcal skin infection. [Internet.] Melbourne: Therapeutic Guidelines Ltd.; April 2019. [Accessed on 12 March 2022.] Available from: https://tgldcdp.tg.org.au/viewTopic?topicfile=staphylococcal-skin-infection&guidelineName=Antibiotic#toc_d1e47.

7. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis*. 2011;52(3):18–55. doi: https://doi.org/10.1093/cid/ciq146.

8. Huang SS, Singh R, McKinnell JA, Park S, Gombosev A, Eells SJ et al. Decolonization to reduce postdischarge infection risk among MRSA carriers. *N Engl J Med*. 2019;380(7):638–50. doi: https://doi.org/10.1056/NEJMoa1716771.

9. Australian Bureau of Statistics (ABS). Community Profiles. [Internet.] Canberra: ABS; 2017. [Accessed on 22 March 2022.] Available from: https://www.abs.gov.au/websitedbs/D3310114.nsf/Home/2016CensusCommunityProfiles.

10. Dadashi M, Hajikhani B, Darban-Sarokhalil D, van Belkum A, Goudarzi M. Mupirocin resistance in *Staphylococcus aureus*: a systematic review and meta-analysis. *J Glob Antimicrob Resist*. 2020;20:238–47. doi: https://doi.org/10.1016/j.jgar.2019.07.032.

11. Coombs GW, Daley DA, Lee YT, Pang S for the Australian Group on Antimicrobial Resistance. Australian Group on Antimicrobial Resistance (AGAR) Australian *Staphylococcus aureus* Sepsis Outcome Programme (ASSOP) Annual Report 2016. *Commun Dis Intell (2018)*. 2018;42. PII: :S2209-6051(18)00021-0.

12. Patel JB, Gorwitz RJ, Jernigan JA. Mupirocin resistance. *Clin Infect Dis*. 2009;49(6):935–41. doi: https://doi.org/10.1086/605495.

13. Upton A, Lang S, Heffernan H. Mupirocin and *Staphylococcus aureus*: a recent paradigm of emerging antibiotic resistance. *J Antimicrob Chemother*. 2003;51(3):613–7. doi: https://doi.org/10.1093/jac/dkg127.

14. Bowen AC, Tong SYC, Chatfield MD, Carapetis JR. The microbiology of impetigo in Indigenous children: associations between *Streptococcus pyogenes*, *Staphylococcus aureus*, scabies, and nasal carriage. *BMC Infect Dis*. 2014;14:727. doi: https://doi.org/10.1186/s12879-014-0727-5.

15. Ray GT, Suaya JA, Baxter R. Incidence, microbiology, and patient characteristics of skin and soft-tissue infections in a U.S. population: a retrospective population-based study. *BMC Infect Dis*. 2013;13:252. doi: https://doi.org/10.1186/1471-2334-13-252.

16. Bowen AC, Tong SYC, Andrews RM, O'Meara IM, McDonald MI, Chatfield MD et al. Short-course oral co-trimoxazole versus intramuscular benzathine benzylpenicillin for impetigo in a highly endemic region: an open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2014;384(9960):2132–40. doi: https://doi.org/10.1016/S0140-6736(14)60841-2.

17. Muir N, Bohr Y. Contemporary practice of traditional Aboriginal child rearing: a review. *First Peoples Child & Family Review*. 2020;9(1):66–79.

18. Tong SYC, Bishop EJ, Lilliebridge RA, Cheng AC, Spasova-Penkova Z, Holt DC et al. Community-associated strains of methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* in Indigenous northern Australia: epidemiology and outcomes. *J Infect Dis*. 2009;199(10):1461–70. doi: https://doi.org/10.1086/598218.

19. Allport J, Choudhury R, Bruce-Wootton P, Reed M, Tate D, Malviya A. Efficacy of mupirocin, neomycin and octenidine for nasal *Staphylococcus aureus* decolonisation: a retrospective cohort study. *Antimicrob Resist Infect Control*. 2022;11(1):5. doi: https://doi.org/10.1186/s13756-021-01043-1.

20. Phillips M, Rosenberg A, Shopsin B, Cuff G, Skeete F, Foti A et al. Preventing surgical site infections: a randomized, open-label trial of nasal mupirocin ointment and nasal povidone-iodine solution. *Infect Control Hosp Epidemiol*. 2014;35(7):826–32. doi: https://doi.org/10.1086/676872.

Appendix A: Supplementary material

Table A.1: Comparison of mupirocin testing across major variables

Variable	Not tested N = 25,319	Tested N = 20,985	*p* value[a]
MSSA[b]	20,951 (83%)	15,851 (76%)	< 0.0001
MRSA[c]	4,368 (17%)	5,134 (24%)	< 0.0001
Median age (interquartile range)	35 (16–56)	33 (15–53)	0.0001
< 40 years old	14,114 (56%)	12,099 (58%)	< 0.0001
Female gender	11,250 (45%)	9,045 (43%)	0.004
Indigenous Australian	9,325 (58%)	8,449 (43%)	< 0.0001
Remote isolate	18,588 (73%)	13,492 (64%)	< 0.0001

a Groups compared using the Chi-squared test.

b Methicillin-sensitive *S. aureus*.

c Methicillin-resistant *S. aureus*.