Meatal cleaning: discrepancies in need of explanation

We read the Article by Oyebola Fasugba and colleagues[1] with interest. The study investigated the efficacy of using chlorhexidine versus normal saline for meatal cleaning before urinary catheter insertion to reduce the incidence of catheter-associated asymptomatic bacteriuria and urinary tract infection. Regrettably, the authors do not discuss the striking discrepancy between the unadjusted and adjusted incidence rate ratios (IRRs) for both outcomes. For catheter-associated asymptomatic bacteriuria they found 1·00 case per 100 catheter days in the control period versus 0·68 cases per 100 catheter days in the intervention period, which we calculated to be an unadjusted IRR of 32%, but the reported reduction (Poisson regression) is 74%. For catheter-associated urinary tract infection they found 0·45 cases per 100 catheter days versus 0·17 cases per 100 catheter days, resulting in an unadjusted IRR of 62% (our calculation). However, the paper reports an adjusted decrease of 94%. It is unusual for adjusted and unadjusted IRRs to differ so substantially. We are curious to hear what explanations the authors have for these discrepancies.

We declare no competing interests.

*Johannes C van der Wouden, Ivo Smeele
j.vanderwouden@amsterdamumc.nl

Amsterdam UMC, Vrije Universiteit, Amsterdam Public Health Research Institute, Amsterdam 1081 HV, Netherlands (JCvdW); and Dutch College of General Practitioners, Utrecht, Netherlands (IS)

1 Fasugba O, Cheng AC, Gregory V, et al. Chlorhexidine for meatal cleaning in reducing catheter-associated urinary tract infections: a multicentre stepped-wedge randomised controlled trial. *Lancet Infect Dis* 2019; **19:** 611–19.

Authors' reply

We thank Johannes C van der Wouden and Ivo Smeele for their interest in our study. The differences in the reported estimates of effect can be explained by the statistical methods used in the analysis.

The primary analysis that was specified in our study protocol was based on aggregated weekly rates of catheter-associated asymptomatic bacteriuria and catheter-associated urinary tract infection (UTI).[1] This is analogous to performing piecemeal interrupted time-series analyses using Poisson regression on multiple time series, with the intervention effect estimated by the step at the time of crossover. In this statistical model, calendar time was included as a covariate and hospital and intervention as fixed effects. As noted in figures 2 and 3 of the Article, an increasing pre-intervention trend might have exaggerated the impact of the intervention.[1]

We noted a baseline imbalance in age at one participating site, and the method used does not easily permit adjustment for individual risk factors. We therefore performed two sensitivity analyses, first excluding the site where the age imbalance was evident, and second using individual patient data adjusting for age and sex. The latter is analogous to an adjusted before-and-after analysis on multiple series. We further note that this analysis used a logistic regression, in which the estimate of effect is expressed as an odds ratio.

On reflection, a sensitivity analysis that would have been more similar to our primary analysis would have included time as well as age and sex in a logistic regression. However, when we reanalyse our data with this approach, the odds ratio associated with the intervention is 0·37 (95% CI 0·25–0·54) for catheter-associated asymptomatic bacteriuria and 0·10 (95% CI 0·03–0·38) for catheter-associated UTI. This suggests a 63% reduction in the odds of catheter-associated asymptomatic bacteriuria and a 90% reduction in the odds of catheter-associated UTI with the use of chlorhexidine.

The valid question that is being asked is how the counterfactual analysis should be defined in stepped-wedge studies; that is, what would have happened without the intervention being implemented? Although we felt duty-bound to report the primary prespecified analysis, we also performed secondary sensitivity analyses in the interests of transparency. We feel comfortable in concluding that chlorhexidine is associated with a substantial reduction in hospital-acquired UTI. Furthermore, a cost-effectiveness analysis, which accounts for uncertainty around effect sizes, found the intervention to be cost-effective.[2]

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*Allen C Cheng, *Brett G Mitchell, Oyebola Fasugba, Nicholas Graves, Jane Koerner, Peter Collignon
brett.mitchell@newcastle.edu.au

School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia (ACC); Infectious Prevention and Healthcare Epidemiology Unit, Alfred Hospital, Melbourne, VIC, Australia (ACC); Faculty of Arts, Nursing and Theology, Avondale College of Higher Education, Wahroonga, NSW 2258, Australia (BGM); School of Nursing and Midwifery, University of Newcastle, Newcastle, NSW, Australia (BGM); Nursing Research Institute, Australian Catholic University & St Vincent's Health Australia Sydney, NSW, Australia (OF); Lifestyle Research Centre, Avondale College of Higher Education, Cooranbong, NSW, Australia; Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, QLD, Australia (NG); University of Canberra, Canberra, ACT, Australia (JK); Medical School, Australian National University, Acton, ACT, Australia (PC); and Australian Capital Territory Pathology, Canberra Hospital and Health Services, Garran, ACT, Australia (PC)

1 Fasugba O, Cheng AC, Gregory V, et al. Chlorhexidine for meatal cleaning in reducing catheter-associated urinary tract infections: a multicentre stepped-wedge randomised controlled trial. *Lancet Infect Dis* 2019; **19:** 611–19.

2 Mitchell BG, Fasugba O, Cheng AC, et al. Chlorhexidine versus saline in reducing the risk of catheter associated urinary tract infection: a cost-effectiveness analysis. *Int J Nurs Stud* 2019; **97:** 1–6.