***Staphylococcus aureus* bacteraemia**

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Dear Editor—

In the 15 December 2019 issue of *Clinical Infectious Diseases*, Inagaki et al report on 30-day readmission after *Staphylococcus aureus* bacteraemia (SAB) in a retrospective population-based analysis capturing half of US hospitalisations in 2014 [1]; the overall 30-day readmission rate was 22%, in-hospital death occurred in 13% and MRSA bacteraemia was associated with readmission for bacteraemia recurrence, increased mortality and longer hospitalisation. Due to the depth of data derived from the Nationwide Readmissions Database (NRD) used in this study, information regarding clinical management is not available and this warrants further discussion. Re-admission, relapse and mortality in SAB are affected by duration of IV anti-Staphylococcal antibiotic, bedside Infectious Diseases consultation and adequacy of source control [2-5], none of which are accounted for by Inagaki and colleagues.

We conducted a retrospective observational study of all patients with SAB (n= 83) over a 3-year period (August 2015 - July 2018) at our busy District General Hospital in London, UK (table 1). Our cohort has similarities to the US cohort in Inagaki et al: ours is the second most deprived local authority in England [6], HIV prevalence is high 1% [7], and the median Charlson co-morbidity score was 2. However, there are also important differences; all our patients have public health care, our rate of MRSA bacteraemia was 4.8% vs 48% in the US cohort, and 19% of our cohort were people who inject drugs (PWID) compared with 10-11% in the US cohort.

Despite a 10-fold lower rate of MRSA bacteraemia the overall in-hospital mortality in our patient cohort was 14.5%, comparable to the US study. 3-month re-admission and *S. aureus* infection relapse rates were also similar; 36.1% and 15.7% respectively. This suggests that factors other than methicillin-resistance are major drivers of mortality and re-admission rates in SAB 48/55 of our complicated SAB cases had data available on duration of IV anti-Staphylococcal therapy (IVAST). Mean duration of IVAST was significantly shorter in the 9/48 cases who relapsed (13.6 days (SD 9.9), vs 28.4 days (SD 18.2); p=0.023), confirming that inadequate duration of IVAST is a significant risk factor for relapsed *S. aureus* infection. Only 33 patients in our cohort (39.8%) had bedside Infection specialist reviews, however trends towards lower mortality (6% vs 20%, NS), decreased length of stay (median 31 days vs 35.5 days, NS) and lower 3-month readmission rate (33.3% vs 38.0%, NS) were seen in this group. Lack of bedside Infection specialist reviews likely influenced the high relapse rates and low compliance with optimal IV durations we observed. Although Inagaki and colleagues comment on longer hospitalisation in patients with MRSA bacteraemia no figures for median length

of hospital stay (LOS) were provided; in our cohort the overall median LOS was 32 days (IQR 16-52.5).

Our study was not designed to assess cost, however the average cost of an overnight stay in our hospital is £300, whereas nurse delivery of OD Ceftriaxone in the community is more than 10x cheaper (£25). Eight (9.6%) patients in our cohort were switched to ceftriaxone prior to completion of standard IV flucloxacillin therapy to facilitate outpatient antibiotic therapy (OPAT). Median length of IV flucloxacillin in this group was 12 days (IQR 7-16) and 7/8 had complicated SAB. For those who switched to ceftriaxone early to facilitate OPAT the median LOS was 13 days (IQR 9-17). There were no deaths or relapsed infections in this group, however 1 patient developed *C. difficile* infection.

In conclusion, we agree with Inagaki et al that SAB carries significant costs in terms of mortality, length of hospital stay and re-admission but would like to emphasize that choice of anti-Staphylococcal agent, duration of intravenous therapy, and bedside Infectious Diseases review are all key factors impacting on clinical outcome in SAB; none of which can be adequately accounted for in large scale registry-based studies. Administration of an appropriate duration of IVAST is particularly key in preventing relapsed *S. aureus* infection. This can be difficult to achieve due to social factors such as drug dependence, particularly in non-teaching urban hospital settings such as ours. National and international guidance on the management of SAB is needed and strategies to safely facilitate early discharge including administration of flucloxacillin using 24-hour infusion devices, use of long-acting lipoglycopeptides, or use of once-daily cephalosporins warrant further research.

All authors have no potential conflicts to disclose.

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Table 1. Clinical features, management and outcomes in Staphylococcus aureus bacteraemia cases treated at our centre between August 2015 - July 2018 (n = 83)

CLINICAL AND BACTERIOLOGIC FACTORS	
Age, median years (IQR)	56 (45-74)
Male, n (%)	53 (63.9)
Patient risk factors	
IVDU, n (%)	16 (19.2)
Central IV catheter, n (%)	4 (4.8)
Other prosthetic device, n (%)*	21 (25.3)
Penicillin allergy, n (%)**	15 (18.1)
CHARLSTON index, median (IQR)	2 (0-3)
Acquisition, n (%)	
Community-acquired	57 (68.7)
Hospital-acquired	19 (22.9)
Healthcare-associated	7 (8.4)
Antibiotic resistance, n (%)	
MSSA	79 (95.2)
MRSA	4 (4.8)
PVL, n/tested (%)	11/80 (13.8)
Complicated, n (%)	70 (84.3)
Deep focus of infection, n (%)	
Skin/soft tissue (abscess/cellulitis)	36 (43.4)
Lungs (septic emboli/PVL pneumonia)	13 (15.7)
Endocarditis	16 (19.3)
Bone/Joint (OM, septic arthritis, discitis)	26 (31.3)
Brain (septic emboli/abscess)	6 (7.2)
Genitourinary (prostate/bladder abscess)	4 (4.8)
Duration of bacteraemia, n (%)	
1 day	58 (69.9)
2-4 days	19 (22.9)
5 or more days	6 (7.2)
MANAGEMENT	
Echocardiography performed, n (%)	66 (79.5)
Repeat BC 48-72 hours after start of IV anti-Staphylococcal therapy, n (%)	52 (62.7)
Intravenous anti-Staphylococcal antibiotic, n (%)	
Flucloxacillin	54 (65.1)
Glycopeptide	27 (32.5)
Neither of the above	2 (2.4)
Antibiotics for complicated SAB ǂ (n = 55)	
Duration of IV anti-Staphylococcal antibiotics, median days (IQR)	28 (12-34)
Appropriate duration IV received, n (%)	29 (52.7)
Total duration of anti-Staphylococcal antibiotics, median (IQR)	34 (28-44)
Antibiotics for uncomplicated SAB ǂ (N = 11)	
Duration of IV anti-Staphylococcal antibiotics, median days (IQR)	14 (7-18)
Appropriate duration IV received, n (%)	8 (72.7)
Total duration of anti-Staphylococcal antibiotics, median (IQR)	28 (14-31)
Source control, n (%)	
Therapeutic surgical procedure	15 (18.1)

Radiologically guided therapeutic aspiration	8 (9.6)
Infection team bedside review, n (%)	33 (39.8)
OPAT, n (%)	16 (19.2)
OUTCOMES	
Intensive care	
ITU review, n (%)	39 (47.0)
ITU admission, n (%)	21 (25.3)
Length of ITU stay, median days (IQR)	8 (4-27.5)
Outcomes	
Length of hospital stay, median days (IQR)	32 (16-52.5)
In-hospital mortality	12 (14.5)
30-day mortality	8 (9.6)
Relapse of Staph aureus infection	13 (15.7)
Re-admission within 3 months	30 (36.1)

IVDU: intravenous drug user, MSSA: Methicillin-sensitive Staph aureus; MRSA: Methicillin-resistant Staph aureus; PVL: Panton-Valentine Leukocydin; OM: osteomyelitis; BC: blood culture; OPAT: out-patient antibiotic therapy; SAB: Staphylococcus aureus bacteraemia; ITU: intensive treatment unit, IQR: inter-quartile range

*4 orthopaedic devices, 5 intra-cardiac devices, 1 PEG tube, 1 portex drain

**3 4 severe ('severe rash' or anaphylaxis)

***25 received Teicoplanin and 2 received vancomycin. 4 had MRSA bacteraemia, 6 had PVL positive MSSA bacteraemia, and 12 had a documented penicillin allergy.

Ł excluding those who died, were transferred elsewhere or self-discharged during IV therapy