Clinical Infection in Practice 21 (2024) 100342

Contents lists available at ScienceDirect

Clinical Infection in Practice

journal homepage: www.sciencedirect.com/journal/clinical-infection-in-practice

Case Reports and Series

Uncomplicated *Staphylococcus aureus* bacteraemia: Partial oral treatment is comparable to fully intravenous treatment – A single centre retrospective cohort study

Razan Saman [a,1,*], Hannah Mooney [a,1], Andrew Kirby [a,b], Fiona McGill [a]

[a] Leeds Teaching Hospitals Trust, St James's University Hospital, Beckett Street, Leeds, West Yorkshire LS9 7TFB, UK
[b] University of Leeds, Woodhouse Lane, Leeds LS2 9JT, UK

ARTICLE INFO

Keywords:
Staphylococcus aureus
Bacteraemia
Oral antibiotics
Intravenous

ABSTRACT

Background: *Staphylococcus aureus* bacteraemia (SAB) is a serious infection associated with high mortality. Current treatment often consists of 14 days of intravenous antibiotics. Significant variability in practice is seen, with some advocating an intravenous to oral antibiotic switch can be considered in uncomplicated SAB.
We aimed to describe current antimicrobial strategies used to manage uncomplicated SAB in our UK based hospital. We also assessed outcomes of patients with uncomplicated SAB in those treated with a intravenous to oral antibiotic switch within 14 days.
Methods: This was a single-centre, retrospective, cohort study between 2018 and 2020 of patients with SAB. Patients with complicated SAB were excluded. Outcomes measured were 90-day relapse, 30-day mortality and length of stay.
Results: We identified 237 patients with SAB, 103 of whom had uncomplicated bacteraemia and were included in the analysis. Of these, 38 (37 %) had an intravenous to oral antibiotic switch within 14 days. Oral antibiotics used included flucloxacillin (n = 32, 84 %), linezolid (n = 4, 11 %), co-trimoxazole (n = 1, 3 %), and doxycycline (n = 1, 3 %). 30-day mortality was lower in patients who received an intravenous to oral switch within 14 days compared to those who did not (16 % vs 37 % $p = 0.026$). In order to exclude patients who died early or had inadequate courses of antibiotics, we removed those who received less than 7 days antibiotics. On re-analysis there was no statistical difference in outcomes except for median length of stay (14 days vs 32 days $p < 0.0001$), which was shorter for the group receiving an oral switch.
Conclusions: There is clinical equipoise in whether patients in our centre receive an intravenous to oral switch for uncomplicated SAB. Treatment of uncomplicated SAB with an intravenous to oral switch within 14 days, demonstrated similar clinical outcomes to standard intravenous therapy with reduced length of stay.

Introduction

Staphylococcus aureus bacteraemia (SAB) is a serious infection, associated with a mortality, at one month, of 18 %–30 % (Bai et al., 2022; Kern, 2010). There is a high rate of complications, including metastatic infection, local extension and relapse (Kern, 2010).

SAB can be classified as complicated e.g. deep seated or metastatic infection or uncomplicated (Liu et al., 2011; Kaasch et al., 2015; Holland et al., 2014) with important differences regarding treatment and prognosis. The duration of treatment for uncomplicated SAB is widely accepted to be a minimum of 14 days from the first negative blood culture (Liu et al., 2011, Brown and Brown, 2021; Holland et al., 2014). However, the optimal route of antibiotics for SAB is unknown, and there has been a lack of agreement between guidelines (Liu et al., 2011; Brown and Brown, 2021).

There is significant variability in practice amongst infection specialists, with a proportion advocating that an intravenous to oral switch (IVOS) can be considered in uncomplicated SAB (Diallo et al., 2018).

The benefits of IVOS more generally include reducing the risk associated with intravenous access, a shorter length of stay and reduced cost and carbon footprint (Willekens et al., 2019; Kouijzer et al., 2021; Walpole et al., 2023). However, the safety of an IVOS in SAB has not

* Corresponding author at: Chelsea and Westminster Hospital, 369 Fulham Road, London SW10 9NH, UK.
E-mail addresses: razan.saman@nhs.net (R. Saman), hannah.mooney2@nh.net (H. Mooney), A.Kirby@leeds.ac.uk (A. Kirby), f.mcgill@nhs.net (F. McGill).
[1] Joint first authors

https://doi.org/10.1016/j.clinpr.2024.100342
Received 23 October 2023; Received in revised form 3 January 2024; Accepted 4 January 2024
Available online 9 January 2024

been proven, and current evidence regarding the route of antibiotics for SAB is limited to largely observational studies.

Several retrospective studies of both uncomplicated and complicated SAB have demonstrated a low rate of relapse associated with the use of oral antibiotics, and no increase in mortality (Kouijzer et al., 2021; Platts et al., 2022; Bupha-Intr et al., 2020; Gunter et al., 2022; Itoh et al., 2018; Jorgensen et al., 2019). One prospective cohort study comparing intravenous antibiotics with oral linezolid for low-risk SAB demonstrated no statistically significant difference between the groups in 90-day relapse and 30-day mortality (Willekens et al., 2019).

Interventional studies are required to evaluate the use of oral antibiotics for SAB. An ongoing randomised controlled trial is investigating a switch to oral antibiotics after 5–7 days of IV therapy for SAB (Kaasch et al., 2015). Meanwhile a platform trial is underway investigating several aspects of antibiotic management of SAB including early oral switch (Tong et al., 2022).

At our institution the management of uncomplicated SAB appeared to be Inconsistent with regards to the choice, duration and route of antibiotics. The aim of this study was to describe current management of uncomplicated SAB and to compare the outcomes of patients receiving a full course of intravenous therapy to those who received an oral switch.

Methods

This retrospective observational study included cases of SAB identified via a search of the laboratory information management system between November 2018 and February 2020 at a tertiary hospital, Leeds Teaching Hospitals NHS Trust, in the United Kingdom. Adult patients with SAB deemed to be uncomplicated at time of diagnosis were included. Patients were deemed to have uncomplicated SAB if they did not meet the criteria for complicated SAB (see Fig. 1). Clinical data for each patient was manually retrieved via the electronic patient record system, and prescribing data was collected via the electronic prescribing system Medchart (CSC). The study was conducted with approval from the Hospitals Caldicott guardian and informed consent was not required from the patients.

Outcome parameters were 90-day relapse, defined as a new episode of SAB within three months of completing treatment for an episode of SAB; 30-day mortality, 90-day mortality and length of stay.

Continuous variables were described as means for normally distributed data and medians for skewed data, and categorical variables as absolute count and relative percentage. Fisher's exact test were used to analyze categorical data, including death during admission, 30-day mortality and 90-day relapse. Mann-Whitney U was used for continuous data, including the length of stay outcome. Statistically significance was identified at the 5 % level (P value < 0.05) and data was analyzed with GraphPad, PRISM (version 10).

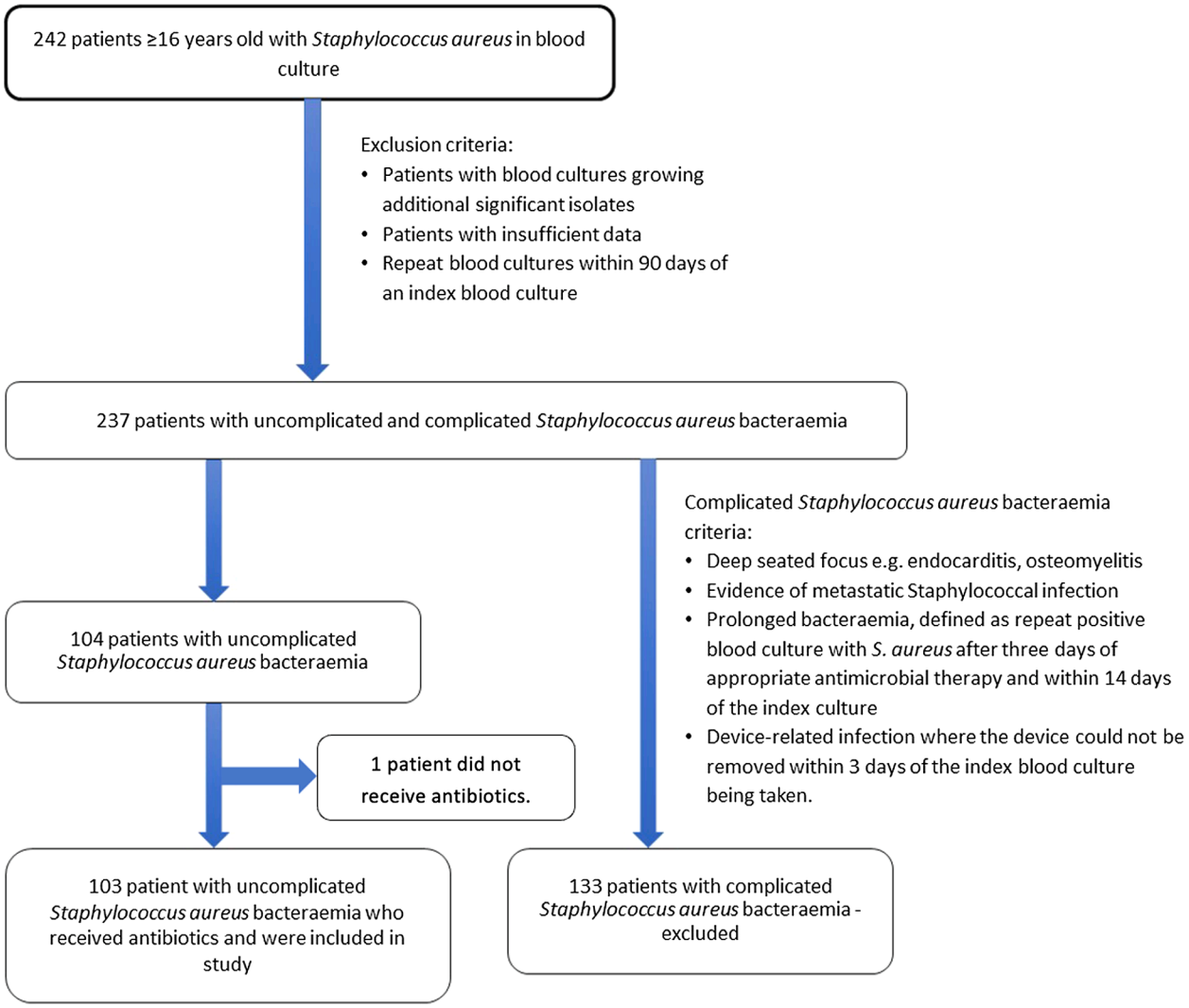

Fig. 1. Study flowchart.

Results

A total of 242 episodes of SAB were identified, of which, 103 (43 %) were uncomplicated, received antibiotics and were included in the analysis (Fig. 1). Baseline characteristics are shown in Table 1. Median age was 68 (IQR, 52–81 years) ranging from 20 to 96 years old and males made up 57.3 % (n = 59) of cases. A total of 56 cases (54.4 %) were community acquired; defined as SAB in patients in whom one or more positive blood culture was obtained within the first 2 days of admission. The source was not confirmed in 37 (35.9 %) cases, only 21.1 % (n = 8) of which received an IVOS. The most common confirmed source of bacteraemia was intravascular catheters (19 cases, 18.4 %).

Of 104 patients with uncomplicated SAB, 103 received antibiotics. The most commonly prescribed initial antibiotic prior to confirmation of SAB was piperacillin-tazobactam (29 patients, 28 %). For methicillin-susceptible SAB, the most commonly prescribed intravenous targeted antibiotic was flucloxacillin (69/98 patients, 70 %). For methicillin-resistant SAB, the most commonly prescribed targeted intravenous antibiotic was teicoplanin (4/5 patients, 80 %).

A switch from IV to oral antibiotics took place for 38/103 (37 %) patients with the majority of patients 71/103 (69 %) having 14 or more days of antibiotics. The oral antibiotics used in our study for patients with uncomplicated SAB, who received IVOS, were flucloxacillin (n = 32/38, 84 %), linezolid (n = 4/38, 11 %), trimethoprim-sulfamethoxazole (n = 1/38, 3 %) and doxycycline (n = 1/38, 3 %). The minimum duration of oral antibiotics received was 1 day with a median duration across IVOS cases of 7 days.

Outcome characteristics

For the 103patients with uncomplicated SAB, 30-day mortality was significantly higher in the IV antibiotic group compared to the IVOS group (37 % vs 16 %, p = 0.023) determined using the Fisher's exact test (Table 2). To determine whether there were significant differences in comorbidities or severity of illness between the two groups, the Charlson comorbidity index (CCMI), maximum CRP level within 72 h of blood culture being taken, maximum National Early Warning Score (NEWS) the day blood culture was taken and presence of fever day blood culture was taken were compared between the two groups. There were no significant differences in any of these measures respectively (mean CCMI 5 vs 5, p = 0.843, median CRP 164 vs 147, p = 0.296, median NEWS score 4 vs 3p = 0.386, 62 % vs 69 %, p = 0.516).

There was a group of patients 32/103 (31 %) who did not complete 14 days of antibiotics. Of these 21 (66 %) died before the 14 days with the majority of these deaths (16/21; 76 %) occurring in the first 7 days of antibiotic therapy. When excluding those who received less than 7 days of antibiotics (n = 18 patients), 30-day mortality was similar between the IV and IVOS group (17 % vs 16 %, p = 0.879) and there was no statistically significant difference in death during admission and 90-day relapse (Fig. 2.). For patients receiving at least 7 days of antibiotics the length of stay was significantly shorter in the IVOS group, with median of 14 days compared with 32 days for the IV group (p < 0.0001).

Table 1
Characteristics and treatment duration of patients with uncomplicated SAB.

	Total, n = 103	Complete IV*, n = 65	IVOS**, n = 38
Male sex, n (%)	59 (57.3)	33 (50.8)	26 (68.4)
Median age, years (IQR)	68 (52–81)	69 (55–82.5)	66 (47–76)
Acquisition, n (%)			
Community	56 (54.4)	35 (53.8)	21 (55.3)
Nosocomial	47 (45.6)	30 (46.2)	17 (44.7)
Source of infection, n (%)			
Unknown	37 (35.9)	29 (44.6)	8 (21.1)
Catheter-related bloodstream infection	19 (18.4)	12 (18.5)	7 (18.4)
Skin and soft-tissue infection	14 (13.6)	8 (12.3)	6 (15.8)
Peripheral cannula infection	12 (11.7)	6 (9.2)	6 (15.8)
Parotitis	3 (2,9)	0 (0)	3 (7.9)
Pneumonia	9 (8.7)	6 (9.2)	3 (7.9)
Other[1]	9 (8.7)	4 (6.2)	5 (13.2)
MRSA, n (%)	5 (4.9)	2 (3.1)	3 (7.9)
Charlson comorbidity index ≥3, n (%)	85 (82.5)	57 (87.7)	28 (73.7)
Mean Charlson comorbidity index (SD)	5 (2.89)	5.1 (2.67)	4.9 (3.28)
Presence of fever at 72 hr, n (%)	20 (19.4)	13 (20.0)	7 (18.4)
NEWS ≥ 3, n (%)	33 (32.0)	24 (36.9)	9 (23.7)
Median duration of antibiotics, days (IQR)			
Total	15 (11–17)	14 (6–17)	15 (13.75–17)
IV		14 (6–17)	8 (4.75–10)
PO		0	7 (5–9.25)

* Patient group who received complete course of IV antibiotic therapy.
** Patient group who received an IV to oral switch of their antibiotic therapy.
[1] Other sources of uncomplicated Staph aureus bacteraemia included submandibular sialadenitis = 1, parotitis = 3, superficial thrombophlebitis = 1, urinary = 3, groin abscess drained = 1, facial abscess = 1, periorbital cellulitis = 1, infected rectal stump = 1, contaminant = 1.

Discussion

In this study, relapse rates for patients who underwent intravenous to oral switch were equivalent to patients managed with intravenous antibiotics alone. When excluding patients who received fewer than seven days antibiotics, 30-day mortality was equivalent between the two groups. This is consistent with several other studies which have demonstrated equivalent or better outcomes in patients who have undergone an intravenous to oral switch for uncomplicated SAB (Platts et al., 2022; Itoh et al., 2018; Jorgensen et al., 2019; Willekens et al., 2019; Bupha-Intr et al., 2020). There was no significant statistical difference in comorbidity or severity of illness between the two groups.

In terms of notable differences in our cohort compared to previous studies, firstly our cohort includes a higher proportion of community-acquired cases (Platts et al., 2022; Liu et al., 2019). Secondly, the source of bacteraemia was not identified in a large proportion of our cohort, whereas the most frequent source in several other studies was intravascular catheters (Platts et al., 2022; Itoh et al., 2018; Jorgensen et al., 2019; Willekens et al., 2019). A possible concern could be an undiagnosed deep source of infection, and that may explain why patients with unknown source were less likely to receive an IV to oral switch. There seems to be no unifying regimen used for oral switch when looking at other studies of IVOS, but one study, similar to ours, showed a beta-lactam was the most commonly used antibiotic (Platts et al., 2022). Oral beta-lactams have not historically been recommended for SAB due to limited data and low bioavailability; the absolute bioavailability of oral flucloxacillin is 54.4 ± 18.8 % (Gath et al., 1995) compared to almost 100 % with oral linezolid or trimethoprim-sulfamethoxazole. However, with our IVOS being 84 % flucloxacillin and demonstrating outcomes are no worse, we believe this is a future avenue to consider and will be assessed in the early oral switch domain of the SNAP trial (Tong et al., 2022). The duration of total therapy for uncomplicated SAB patients was a median 15-day course, on par with that reported in other studies of low-risk SAB (Willekens et al., 2019; Bupha-Intr et al., 2020) and is associated with a shorter length of stay in hospital. Of note and for

Table 2
Outcomes of 103 patients with uncomplicated SAB.

	IV (n = 65)	IVOS (n = 38)	P-value
Death during admission	25 (38 %)	7 (18 %)	0.047
30-day mortality	24 (37 %)	6 (16 %)	0.026
90-day relapse	1 (2 %)	1 (3 %)	>0.999
Median length of stay, days (IQR)	22 (14–39)	14 (8.75–26.25)	0.073

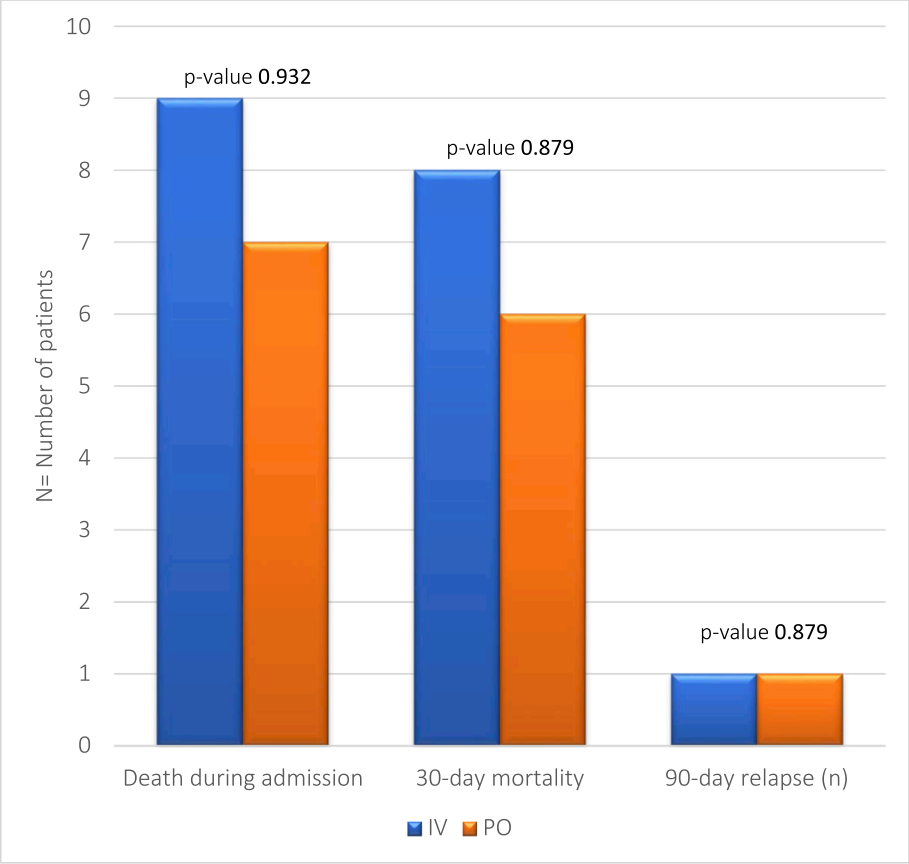

Fig. 2. Outcome of 85 patients with uncomplicated SAB who received ≥7 days antibiotics.

further research, the IVOS patient group received a median of 8 days IV antibiotics, potentially supporting a switch at 7–8 days of IV.

This study has a number of limitations, given the design is an observational, retrospective, single-centre study. It was not controlled therefore the intravenous to oral switch, the timing of the switch, antibiotic choice and total duration of switch was at the discretion of the treating physician. We only analyzed uncomplicated SAB. Given the increasing body of evidence for using oral antibiotics in complex deep-seated infections, further studies are required to investigate the role of oral antibiotics in these infections when associated with SAB, which was notably excluded in the OVIVA trial (Bejon et al., 2019). We plan for further work looking at antibiotic management and outcomes in the cohort of complicated infections. Furthermore, our cohort included very few cases of MRSA (five, 4.8 %) and so the results are most applicable to bacteraemia with methicillin-susceptible *Staphylococcus aureus*.

The strength of this study is that it is a pragmatically designed real-life depiction of patients with uncomplicated SAB and their management pathway. We included SAB with unknown source, an important and significant portion of patients that has been historically removed from analyses of similar studies (Chong et al., 2013). A further strength is that this study looked at oral switch to any class of antibiotic and did not limit analysis to one specific oral antibiotic class.

Conclusion

Our study adds to a limited pool of evidence in support of early oral switch. This study suggests that treating uncomplicated SAB with an IV to oral switch was comparable to continued IV therapy with lower associated 30-day mortality. More work is required in the form of randomized controlled trials to address this question and which antibiotics and duration are suited for early oral switch.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Razan Saman: Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Methodology. **Hannah Mooney:** Formal analysis, Data curation, Writing – original draft, Writing – review & editing, Methodology. **Andrew Kirby:** Writing – review & editing. **Fiona McGill:** Conceptualization, Supervision, Writing – review & editing, Methodology.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

Andrew Kirby is supported by the National Institute for Health and Care Research (NIHR) Leeds Biomedical Research Centre. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the department of Health and Social Care.

References

Bai, A.D., Lo, C.K.L., Komorowski, A.S., Suresh, M., Guo, K., Garg, A., Tandon, P., Senecal, J., Del Corpo, O., Stefanova, I., Fogarty, C., Butler-Laporte, G., McDonald, E. G., Cheng, M.P., Morris, A.M., Loeb, M., Lee, T.C., 2022. *Staphylococcus aureus*

bacteraemia mortality: a systematic review and meta-analysis. Clin Microbiol Infect. 28 (8), 1076–1084. https://doi.org/10.1016/j.cmi.2022.03.015. Epub 2022 Mar 23 PMID: 35339678.

Bejon, P.A., Li, H.K., Rombach, I., Walker, S., Scarborough, M., 2019. The OVIVA trial. Lancet Infect. Dis. 19 (10), 1058. https://doi.org/10.1016/S1473-3099(19)30482-7. PMID: 31559961; PMCID: PMC7613513.

Brown, N.M., Brown, E.M., Guideline Development Group, 2021. Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA): updated guidelines from the UK. J. Antimicrob. Chemother. 76 (6), 1377–1378. https://doi.org/10.1093/jac/dkab036. PMID: 33582806.

Bupha-Intr, O., Blackmore, T., Bloomfield, M., 2020. Efficacy of early oral switch with β-lactams for low-risk *Staphylococcus aureus* bacteremia. Antimicrob Agents Chemother. 64 (7), e02345–e10419. https://doi.org/10.1128/AAC.02345-19. PMID: 32015029; PMCID: PMC7318028.

Chong, Y.P., Moon, S.M., Bang, K.-M., Park, H.J., Park, S.-Y., Kim, M.-N., Park, K.-H., Kim, S.-H., Lee, S.-O., Choi, S.-H., Jeong, J.-Y., Woo, J.H., Kim, Y.S., 2013. Treatment duration for uncomplicated *Staphylococcus aureus* bacteremia to prevent relapse: analysis of a prospective observational cohort study. Antimicrob. Agents Chemother. 57 (3), 1150–1156.

Diallo, K., Thilly, N., Luc, A., Beraud, G., Ergonul, Ö., Giannella, M., Kofteridis, D., Kostyanev, T., Paño-Pardo, J.R., Retamar, P., Kern, W., Pulcini, C., ESGAP, ESGBIS, 2018. Management of bloodstream infections by infection specialists: an international ESCMID cross-sectional survey. Int. J. Antimicrob. Agents 51 (5), 794–798. https://doi.org/10.1016/j.ijantimicag.2017.12.010. Epub 2018 Jan 5. PMID: 29309899.

Gath, J., Charles, B., Sampson, J., Smithurst, B., 1995. Pharmacokinetics and bioavailability of flucloxacillin in elderly hospitalized patients. J. Clin. Pharmacol. 35 (1), 31–36. https://doi.org/10.1002/j.1552-4604.1995.tb04742.x. PMID: 7751411.

Gunter, S.G., Wingler, M.J.B., Cretella, D.A., Wagner, J.L., Barber, K.E., Stover, K.R., 2022. Intravenous versus oral step-down for the treatment of *Staphylococcus aureus* bacteremia in a pediatric population. Pharmacy (Basel) 10 (1), 16. https://doi.org/10.3390/pharmacy10010016. PMID: 35076616; PMCID: PMC8788527.

Holland, T.L., Arnold, C., Fowler Jr., V.G., 2014 Oct 1. Clinical management of *Staphylococcus aureus* bacteremia: a review. J. Am. Med. Assoc. 312 (13), 1330–1341. https://doi.org/10.1001/jama.2014.9743. PMID: 25268440; PMCID: PMC4263314.

Itoh, N., Hadano, Y., Saito, S., Myokai, M., Nakamura, Y., Kurai, H., 2018. Intravenous to oral switch therapy in cancer patients with catheter-related bloodstream infection due to methicillin-sensitive Staphylococcus aureus: a single-center retrospective observational study. PLoS One 13 (11), e0207413. https://doi.org/10.1371/journal.pone.0207413. PMID: 30496212; PMCID: PMC6264473.

Jorgensen, S.C.J., Lagnf, A.M., Bhatia, S., Shamim, M.D., Rybak, M.J., 2019. Sequential intravenous-to-oral outpatient antibiotic therapy for MRSA bacteraemia: one step closer. J. Antimicrob. Chemother. 74 (2), 489–498. https://doi.org/10.1093/jac/dky452. PMID: 30418557.

Kaasch, A.J., Fätkenheuer, G., Prinz-Langenohl, R., Paulus, U., Hellmich, M., Weiß, V., Jung, N., Rieg, S., Kern, W.V., Seifert, H., 2015. Early oral switch therapy in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): study protocol for a randomized controlled trial. Trials 16 (1).

Kern, W.V., 2010. Management of *Staphylococcus aureus* bacteremia and endocarditis: progresses and challenges. Curr. Opin. Infect. Dis. 23 (4), 346–358. https://doi.org/10.1097/QCO.0b013e32833bcc8a. PMID: 20592532.

Kouijzer, I.J.E., van Leerdam, E.J., Gompelman, M., Tuinte, R.A.M., Aarntzen, E.H.J.G., Berrevoets, M.A.H., Maat, I., Bleeker-Rovers, C.P., van Crevel, R., Ten Oever, J., 2021. Intravenous to oral switch in complicated *Staphylococcus aureus* bacteremia without endovascular infection: a retrospective single-center cohort study. Clin. Infect. Dis. 73 (5), 895–898. https://doi.org/10.1093/cid/ciab156. PMID: 33606007; PMCID: PMC8423458.

Liu, C., Bayer, A., Cosgrove, S.E., Daum, R.S., Fridkin, S.K., Gorwitz, R.J., Kaplan, S.L., Karchmer, A.W., Levine, D.P., Murray, B.E., Rybak, J.M., Talan, D.A., Chambers, H. F., Infectious Diseases Society of America, 2011. 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. 52 (3), e18–e55. https://doi.org/10.1093/cid/ciq146. Epub 2011 Jan 4. Erratum in: Clin. Infect. Dis. 2011 Aug 1;53(3):319. PMID: 21208910.

Liu, C., Strnad, L., Beekmann, S.E., Polgreen, P.M., Chambers, H.F., 2019. Clinical practice variation among adult infectious disease physicians in the management of *Staphylococcus aureus* bacteremia. Clin. Infect. Dis. 69 (3), 530–533. https://doi.org/10.1093/cid/ciy1144. PMID: 30601989; PMCID: PMC7962895.

Platts, S., Payne, B.A.I., Price, D.A., Pareja-Cebrian, L., Schwab, U., 2022. Oral step-down for *Staphylococcus aureus* bacteraemia: an opportunity for antimicrobial stewardship? Clin. Infect. Pract. 16, 100202 https://doi.org/10.1016/j.clinpr.2022.100202. PMID: 36394002; PMCID: PMC7613828.

Tong, S.Y.C., Mora, J., Bowen, A.C., Cheng, M.P., Daneman, N., Goodman, A.L., Heriot, G.S., Lee, T.C., Lewis, R.J., Lye, D.C., Mahar, R.K., Marsh, J., McGlothlin, A., McQuilten, Z., Morpeth, S.C., Paterson, D.L., Price, D.J., Roberts, J.A., Robinson, J. O., van Hal, S.J., Walls, G., Webb, S.A., Whiteway, L., Yahav, D., Davis, J.S., Staphylococcus aureus Network Adaptive Platform (SNAP) Study Group, 2022. The *Staphylococcus aureus* network adaptive platform trial protocol: new tools for an old foe. Clin. Infect. Dis. 75 (11), 2027–2034. https://doi.org/10.1093/cid/ciac476. Erratum in: Clin. Infect. Dis. 2023 Apr 17;76(8):1532-1533. PMID: 35717634; PMCID: PMC9710697.

Walpole, S.C., Eii, M.N., Lyons, T., Aldridge, C., 2023. Improving antimicrobial use to protect the environment: what is the role of infection specialists? Antibiotics (Basel) 12 (4), 640. https://doi.org/10.3390/antibiotics12040640. PMID: 37107002; PMCID: PMC10134973.

Willekens, R., Puig-Asensio, M., Ruiz-Camps, I., Larrosa, M.N., González-López, J.J., Rodríguez-Pardo, D., Fernández-Hidalgo, N., Pigrau, C., Almirante, B., 2019. Early oral switch to linezolid for low-risk patients with *Staphylococcus aureus* bloodstream infections: a propensity-matched cohort study. Clin. Infect. Dis. 69 (3), 381–387. https://doi.org/10.1093/cid/ciy916. PMID: 30351401.