Short-course versus long-course antibiotic treatment in patients with uncomplicated gram-negative bacteremia: A systematic review and meta-analysis

Xiaoming Li MM¹,² | Chao Liu MD¹ | Zhi Mao MD² | Qinglin Li MD² | Shuang Qi MM¹,² | Feihu Zhou MD, PhD²

¹Medical School of Chinese PLA, Beijing, China
²Department of Critical Care Medicine, The First Medical Centre, Chinese PLA General Hospital, Beijing, China

Correspondence
Feihu Zhou, Critical Care Medicine, Chinese People’s Liberation Army General Hospital, 28 Fu-Xing Road, Beijing 100853, China. Email: feihuzhou301@126.com

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Abstract

What is known and objective: Gram-negative bacteremia remains a major health problem around the world. The optimal duration of antibiotic treatment has been poorly defined, and there are significant differences of opinion between clinicians. We conducted this systematic review and meta-analysis to compare the clinical outcomes of short-course and long-course treatments in patients with uncomplicated gram-negative bacteremia.

Methods: We searched public databases (PubMed, EMBASE and Cochrane Library) to identify eligible studies. The primary outcomes were all-cause mortality and the incidence of recurrent bacteremia through day 30. We used the Cochrane risk of bias assessment tool to evaluate the risk of bias for randomized controlled trials (RCTs) and the Newcastle-Ottawa Scale for non-RCTs.

Results and discussion: Six studies involving 2689 patients were included in the systematic review and meta-analysis. No significant difference was found between short-course and long-course antibiotic treatments in 30-day mortality (risk ratio [RR] 0.85; 95% confidence interval [CI] 0.65-1.13; \( P = 0.26 \)), 30-day recurrent bacteremia (RR 1.07; 95% CI 0.68-1.67; \( P = 0.78 \)), 90-day mortality (RR 0.84; 95% CI 0.57-1.24; \( P = 0.38 \)), 90-day recurrent bacteremia (RR 0.98; 95% CI 0.50-1.89; \( P = 0.94 \)), adverse events (RR 1.14; 95% CI 0.89-1.45; \( P = 0.30 \)), Clostridium difficile infection (RR 0.86; 95% CI 0.40-1.86; \( P = 0.71 \)) or resistance development (RR 1.19; 95% CI 0.66-2.14; \( P = 0.57 \)).

What is new and conclusion: Short-course was non-inferior to long-course antibiotic treatments for patients with uncomplicated gram-negative bacteremia. Considering the drug-related side effects and cost-effectiveness, a shorter duration of antibiotic treatment may be preferable for this particular population. However, additional high-quality RCTs are needed to further assess whether a shorter course
WHAT IS KNOWN AND OBJECTIVE

Although great progress has been made in medical science in the past few decades, bloodstream infections (BSI), particularly those due to gram-negative bacilli (GNB), remain a major health problem worldwide and are associated with high morbidity and mortality. More than 30% of hospital-acquired infections and approximately 45% of community-acquired infections are due to GNB, and gram-negative bacteremia increases the length of hospital stays and medical burdens. For patients with gram-negative bacteremia, the optimal duration of antibiotic treatment has been poorly defined and there is a significant difference of opinion between clinicians. In the absence of strong evidence on this issue, the duration of antibiotic treatment for patients with gram-negative bacteremia ranges from 7 to 14 days, which are based to some extent on clinical practice guidelines for catheter-related infections and expert opinion. Timely and adequate antibiotic treatment may improve the prognosis of patients with BSI; however, prolonged exposure to antibiotics may increase the incidence of adverse drug events, such as multidrug-resistant organisms and Clostridium difficile infections (CDI). Reducing the treatment duration is one way to reduce antibiotic consumption, which has become a major public health priority.

There are several systematic reviews and meta-analyses comparing the efficacy of short-course vs long-course antibiotic treatment for bacteremia, and no significant differences in terms of clinical outcomes have been identified. However, no reviews have focused on uncomplicated gram-negative bacteremia. A retrospective cohort study conducted by Nelson et al concluded that long-course antibiotic treatment may be superior to short-course. Two recently completed non-inferiority randomized controlled trials (RCTs) indicated that an antibiotic course of 7 days was non-inferior to a 14-day course in patients with uncomplicated gram-negative bacteremia. In order to examine the therapeutic equivalence between short-course and long-course antibiotic treatment for uncomplicated gram-negative bacteremia, we conducted this systematic review and meta-analysis.

METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA statement) guidelines to perform the meta-analysis.
2.3 | Data synthesis and analysis

The primary outcomes were the incidence of all-cause mortality and recurrent bacteremia within 30 days. The secondary outcomes included the incidence of all-cause mortality and recurrent bacteremia through day 90, CDI, resistance development and adverse events.

Clinical outcomes between the two groups were reported as risk ratios (RRs) and 95% confidence intervals (CIs). Statistical heterogeneity among the trials included in the meta-analysis was assessed and quantified using the $I^2$ statistic and chi-squared test, which estimates the percentage of total variation across studies due to heterogeneity rather than chance. When $I^2 < 50\%$ and $P > .10$ were considered to have no significant heterogeneity, we used the fixed-effect mode. Otherwise, the random-effects model was used as appropriate. We performed Egger's test to assess publication bias. To further ascertain which factors may have influenced clinical outcomes among the included studies, sensitivity and subgroup analyses were conducted within the particular groups: RCTs vs non-RCTs, special bacteremia vs non-special bacteremia and adults vs children.

If the two-sided $P$ value was $<.05$, the results were considered statistically significant. Except for Egger's test, which was conducted using STATA (version 14.0, Stata Corporation, College Station, TX), all other statistical analyses were performed using Review Manager (version 5.3, The Cochrane Collaboration, Oxford, UK).

3 | RESULTS

3.1 | Selection and characteristics of the studies

A total of 247 potentially relevant studies were identified by our search strategy, of which 124 duplicate publications were excluded. According to the inclusion and exclusion criteria, we excluded 112 studies by evaluating the titles and abstracts. After reading the full texts of the remaining eleven studies, only six studies containing a total of 2689 patients were included in the systematic review and meta-analysis. Two studies were excluded due to the unavailability of data. Three studies were excluded because patients were not clearly defined as having uncomplicated gram-negative bacteremia or $P$.010; Appendix S3).

The characteristics of the included studies are presented in Table 1 (RCT: 2; prospective: 1; retrospective: 3). The definition of short course and long course varied among the included studies, but ranged from 6 to 11 days for the short course and more than 10 days for the long course. The main causative pathogen was Escherichia coli, and the main source of bacteremia was the urinary tract. Five studies involved adults, while one involved children. Four studies included patients diagnosed with uncomplicated gram-negative bacteremia, whereas two studies only included patients with Enterobacteriaceae bacteremia or Pseudomonas aeruginosa in the bloodstream.

3.2 | Study quality and publication bias

Because blinding was not performed in one RCT study, we assessed performance bias and detection bias as unclear, while the other items were assessed as having low bias (Appendix S1). For non-RCTs, which were assessed by NOS, two scored 7 points, one 8 points and one 9 points (Appendix S2). Egger's test indicated that publication bias may exist ($P = .010$; Appendix S3).

3.3 | Primary outcomes

All studies reported 28- or 30-day all-cause mortality. There was no significant difference between the short-course and long-course groups (7.3% vs 6.3%, respectively). The pooled RR of 30-day all-cause mortality was 0.85 (95% CI 0.65.1.13; $P = .26$; Figure 2A). No heterogeneity was detected among the studies ($I^2 = 0\%$). Four studies reported the occurrence of recurrent bacteremia through day 30, and the pooled RR of 1.07 (95% CI 0.68.1.67; $P = .78$; Figure 3) indicated no significant difference between the two groups (4.2% vs 5.1%, respectively). No significant heterogeneity was detected among the studies ($I^2 = 23\%$).

We conducted subgroup analyses divided by study type, and neither the RCT subgroup nor the non-RCT subgroup showed statistically significant differences in 30-day all-cause mortality between short-course and long-course antibiotic treatments. The pooled RR was 0.83 (95% CI 0.44.1.55; $P = .56$) and 0.86 (95% CI 0.63.1.17; $P = .34$), respectively (Figure 2A). Subgroup analyses according to the type of bacteremia showed no statistically significant differences (specific bacteremia subgroup: RR 0.96; 95% CI 0.65.1.43; $P = .85$; non-specific bacteremia subgroup: RR 0.77; 95% CI 0.52.1.13; $P = .18$; Figure 2B). When we excluded the study on children, we also did not find a statistically significant
| Study          | Study type | Population | Definition of uncomplicated GNB                                                                 | Number (male) | Median age (IQR) | Definition of short-/long-course | Main pathogen (%) | Main source of bacteremia (%) |
|---------------|------------|------------|-------------------------------------------------------------------------------------------------|---------------|------------------|-------------------------------|------------------|-------------------------------|
| von Dach et al | RCT        | Uncomplicated GNB | Without complicated infections (eg, abscess, endocarditis)                                      | 169 (62)      | 78 (69-86)       | 7 d                           | Escherichia coli (73%) | Urinary tract (63%)            |
|               |            |            |                                                                                                 | 165 (71)      | 80 (67-85)       | 14 d                          | E coli (75%)      | Urinary tract (71%)            |
| Yahav et al   | RCT        | Uncomplicated GNB | Without other sources of infection, uncontrolled focus of infection, polymicrobial growth, specific pathogens (Brucella, Salmonella) | 306 (150)     | 71 (61.8-81)     | 7 d                           | E coli (60.8%)    | Urinary tract (69.3%)          |
|               |            |            |                                                                                                 | 298 (135)     | 71 (61-80)       | 14 d                          | E coli (65.1%)    | Urinary tract (66.8%)          |
| Sousa et al   | Prospective | Uncomplicated GNB | Without deep-seated infections such as not-drained intra-abdominal or pelvic abscesses           | 163 (78)      | 74 (26-94)       | 7-10 d                        | E coli (60%)      | Urinary tract (56%)            |
|               |            |            |                                                                                                 | 232 (137)     | 70 (18-105)      | >10 d                         | E coli (53%)      | Urinary tract (48%)            |
| Fabre et al   | Retrospective | P aeruginosa BSI | Without osteoarticular infections, endocarditis/endovascular infections or central nervous system infections | 72 (48)       | 61 (50-79)       | 7-11 d                        | P aeruginosa (100%) | Urinary tract (30.4%)          |
|               |            |            |                                                                                                 | 179 (111)     | 66 (52-76)       | >11 d                         | P aeruginosa (100%) | Urinary tract (30.3%)          |
| Chotiprasitsakul et al | Retrospective | Enterobacteriaceae Bacteremia | Without polymicrobial bacteremia                                                                  | 385 (194)     | 60 (49-69)       | 6-10 d                        | E coli (46%)      | Urinary tract (34.8%)          |
|               |            |            |                                                                                                 | 385 (211)     | 60 (49-70)       | 11-16 d                       | E coli (47.8%)    | Urinary tract (37.4%)          |
| Park et al    | Retrospective | Uncomplicated GNB | Without infective endocarditis, supplicative thrombophlebitis, CNS infection, osteomyelitis or deep-seated undrained abscesses | 170 (NA)      | 2.5 (0.6-11)     | 7-10 d                        | Klebsiella spp. (31.8%) | Central line (63.5%)         |
|               |            |            |                                                                                                 | 170 (NA)      | 2 (0.5-8)        | >10 d                         | Klebsiella spp. (28.2%) | Central line (61.1%)         |

Abbreviations: CNS, central nervous system; GNB, gram-negative bacteremia; NA, not available; IQR, interquartile range; P aeruginosa BSI, Pseudomonas aeruginosa bloodstream infections; RCT, randomized controlled trial.
FIGURE 2  Forest plot of comparison: long course vs short course. A, Subgroup analyses for 30-d mortality divided by study type (RCTs vs non-RCTs); (B) subgroup analyses for 30-d mortality divided by infecting organisms (specific bacteremia vs non-specific bacteremia); and (C) subgroup analyses for 30-d mortality divided patient’s age (adult group vs children group). RCT, randomized controlled trial [Colour figure can be viewed at wileyonlinelibrary.com]
difference between short-course and long-course antibiotic treatments (RR 0.86; 95% CI 0.64-1.14; \( P = .28 \); Figure 2C). No heterogeneity between studies was detected for the RCT subgroup, non-RCT subgroup, non-specific bacteremia subgroup or adult subgroup. The specific bacteremia subgroup showed mild heterogeneity (\( I^2 = 35\% \)).

### 3.4 | Secondary outcomes

Only two RCTs reported 90-day all-cause mortality and adverse events.\(^{12,13}\) No statistically significant difference was found in either 90-day all-cause mortality or adverse events, and the pooled RR was 0.84 (95% CI 0.57-1.24; \( P = .38; I^2 = 0\% \); Appendix S4a) and 1.14 (95% CI 0.89-1.45; \( P = .30; I^2 = 0\% \); Appendix S4b), respectively. The main adverse event in the study by Dach et al was CDI,\(^{13}\) while Yahav et al reported diarrhoea as the main adverse event.\(^{12}\) The data of 90-day recurrent bacteremia in three studies involving 1316 patients were available.\(^{12,13,23}\) The results failed to show that long-term treatment could reduce 90-day recurrent bacteremia compared with short-course treatment (RR 0.98; 95% CI 0.50-1.89; \( P = .94; I^2 = 0\% \); Appendix S4c). Four studies\(^{12,13,20,21}\) involving 2043 patients reported CDI and two studies\(^{12,21}\) involving 1374 patients reported resistance development. These results indicated that the duration of antibiotic treatment was not associated with CDI (RR 0.86; 95% CI 0.40-1.86; \( P = .71; I^2 = 0\% \); Appendix S4d) or resistance development (RR 1.19; 95% CI 0.66-2.14; \( P = .57; I^2 = 59\% \); Appendix S4e). Detailed results of the secondary analysis are presented in Table 2.
duration can increase adverse events and antibiotic resistance,
while inadequate antibiotic treatment may be associated with poor
clinical prognosis.\textsuperscript{5,29-31} A meta-analysis conducted by Havey et al,
including 24 RCTs, concluded that, in terms of a clinical cure, micro-
bio logic cure and survival among most patients with BSI, shorter-
duration therapy may be as effective as longer-duration therapy.\textsuperscript{5}
Another meta-analysis conducted by Tansari et al focusing on pa-
ients with bacteremia due to Enterobacteriaceae drew a similar con-
clusion that there was no significant difference in clinical outcomes
between the short-course and long-course antibiotic treatment
groups.\textsuperscript{10} Compared with complicated BSI, such as BSI complicated
by osteoarticular infections, central nervous system infections and
endocarditis, uncomplicated BSI may require a shorter duration of
antibiotic treatment and have a better prognosis. Moreover, for pa-
ients with uncomplicated gram-negative bacteremia, shortening the
antibiotic treatment duration may be more feasible and safer
than for complicated gram-negative bacteremia.

Among the included studies, the 30-day all-cause mortality rate ranged from 3.5% to 14.1% and from 2.5% to 10.1% in the short-course and long-course groups, respectively. Different in-
clusion and exclusion criteria among the studies may account for
these differences. The highest overall mortality rate was found in
a study conducted by Sousa et al, which included patients with im-
munosuppression. Moreover, a higher rate of inadequate empirical
antibiotic treatment, an independent risk factor for mortality,\textsuperscript{25}
exists in that study. In contrast, in an RCT conducted by Dach
et al, the 30-day all-cause mortality rate was 3.6% and 2.5% in the
short-course and long-course groups, respectively.\textsuperscript{13} Patients
with hemodynamic instability, immunosuppression and compli-
cated infections, which were associated with poor prognosis, were excluded.

Adverse events, recurrent bacteremia, CDI, and resistance de-
velopment must be taken into consideration when planning to adjust
the duration of antibiotic treatment. In our study, no significant dif-
ference was detected, which indicates that the safety and efficacy of
short-course and long-course antibiotic treatment were comparable.
Only two RCTs had available data on distal complications and sup-
purative complications, and both studies found no significant difference
between the short-course and long-course groups.\textsuperscript{12,13}

Although our study suggested that short course was non-inferior
to long-course antibiotic treatment, the results should be interpreted
with caution. Our study has several limitations. First, non-RCTs
were included in our meta-analysis, meaning the data were prone to
confounding factors. Second, inclusion and exclusion criteria were
significantly different among the studies. Four studies included pa-
nents with mixed GNB infection, while one study only included pa-
nents with \textit{P aeruginosa} infection and another study only included pa-
nents with Enterobacteriaceae infection. Moreover, one study of
children was also included in our meta-analysis. However, no signifi-
cant heterogeneity was detected in any of the analyses. Third, due to
the limited data, we did not perform further analysis of medical costs
and length of hospital stay. There is an underlying assumption that
the antibiotics used were equally appropriate across studies. Finally,
our study focused on uncomplicated gram-negative bacteremia;
consequently, the findings cannot be generalized to other types of
bacteremia, so additional high-quality studies are required.

5 WHAT IS NEW AND CONCLUSIONS

This systematic review and meta-analysis found that short-course
antibiotic treatment was not inferior to long-course antibiotic treat-
ment for patients with uncomplicated gram-negative bacteremia.
Considering the drug-related side effects and cost-effectiveness, a
shorter duration of antibiotic treatment may be preferable for this
particular population. However, additional high-quality RCTs are
needed to compare efficacy, resistance development, cost-effec-
tiveness, and safety between short- and long-course treatments, and
to further assess whether a shorter course of treatment is of greater
benefit to patients with uncomplicated gram-negative bacteremia.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interests.

AUTHORS’ CONTRIBUTIONS

Xiaoming Li: conceptualization; data curation; formal analysis; meth-
ology; writing – original draft. Chao Liu: conceptualization; data
curation; investigation; and formal analysis. Zhi Mao: data curation; in-
vestigation; and project administration. Qinglin Li: formal analysis and
software. Shuang Qi: methodology and software. Feihu Zhou: funding
acquisition; supervision; validation; writing – review and editing.

DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this
published article (and its Supporting Information Appendix files).

ORCID

Feihu Zhou https://orcid.org/0000-0001-6154-013X

REFERENCES

1. Goto M, Al-Hasan MN. Overall burden of bloodstream infec-
tion and nosocomial bloodstream infection in North America and
Europe. Clin Microbiol Infect. 2013;19(6):501-509.
2. Diekema DJ, Beekmann SE, Chapin KC, Morel KA, Munson E, Doern
GV. Epidemiology and outcome of nosocomial and community-on-
set bloodstream infection. J Clin Microbiol. 2003;41(8):3655-3660.
3. Peleg AY, Hooper DC. Hospital-acquired infections due to
gram-negative bacteria. N Engl J Med. 2010;362(19):1804-1813.
4. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines
for the diagnosis and management of intravascular catheter-re-
lated infection: 2009 update by the Infectious Diseases Society of
America. Clin Infect Dis. 2009;49(1):1-45.
5. Ibrahim EH, Sherman G, Ward S, Fraser VJ, Kollef MH. The influence
of inadequate antimicrobial treatment of bloodstream infections on
patient outcomes in the ICU setting. Chest. 2000;118(1):146-155.
6. Levy SB, Marshall B. Antibacterial resistance worldwide: causes,
challenges and responses. Nat Med. 2004;10(12 Suppl):S122-S129.
7. Tamma PD, Avdic E, Li DK, Dzintars K, Cosgrove SE. Association of adverse events with antibiotic use in hospitalized patients. JAMA Intern Med. 2017;177(9):1308-1315.

8. Wintenberger C, Guery B, Bonnet E, et al. Proposal for shorter antibiotic therapies. Med Mal Infect. 2017;47(2):92-141.

9. Havey TC, Fowler RA, Daneman N. Duration of antibiotic therapy for bacteremia: a systematic review and meta-analysis. Crit Care. 2011;15(6):R267.

10. Tansari GS, Andreatos N, Pilakos EE, Mylonakis E. A systematic review and meta-analysis of antibiotic treatment duration for bacteremia due to Enterobacteriaceae. Antimicrob Agents Chemother. 2019;63(5):e02495-18.

11. Nelson AN, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. Optimal duration of antimicrobial therapy for uncomplicated gram-negative bloodstream infections. Infection. 2017;45(5):613-620.

12. Yahav D, Franceschini E, Koppel F, et al. Seven versus 14 days of antibiotic therapy for uncomplicated gram-negative bacteremia: a noninferiority randomized controlled trial. Clin Infect Dis. 2019;69(7):1091-1098.

13. von Dach E, Albrich WC, Brunel AS, et al. Effect of C-reactive protein-guided antibiotic treatment duration, 7-day treatment, or 14-day treatment on 30-day clinical failure rate in patients with uncomplicated gram-negative bacteremia: a randomized clinical trial. JAMA. 2020;323(21):2160-2169.

14. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.

15. Wells G.The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Paper presented at: Symposium on Systematic Reviews: Beyond the Basics 2000.

16. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603-605.

17. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177-188.

18. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-560.

19. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(709):629-634.

20. Park SH, Milstone AM, Diener-West M, Nussenblatt V, Cosgrove SE, Tamma PD. Short versus prolonged courses of antibiotic therapy for children with uncomplicated gram-negative bacteraemia. J Antimicrob Chemother. 2014;69(3):779-785.

21. Chotiprasitsakul D, Han JH, Cosgrove SE, et al. Comparing the outcomes of adults with Enterobacteriaceae bacteremia receiving short-course versus prolonged-course antibiotic therapy in a multicenter, propensity score-matched cohort. Clin Infect Dis. 2018;66(2):172-177.

22. Fabre V, Amoah J, Cosgrove SE, Tamma PD. Antibiotic therapy for Pseudomonas aeruginosa bloodstream infections: how long is long enough? Clin Infect Dis. 2019;69(11):2011-2014.

23. Sousa A, Perez-Rodriguez MT, Suarez M, et al. Short- versus long-course therapy in gram-negative bacilli bloodstream infections. Eur J Clin Microbiol Infect Dis. 2019;38(5):851-857.

24. Erickson RM, Tuttle BJ, Spivak ES, Timbrook TT. Impact of an antimicrobial stewardship bundle for uncomplicated gram-negative bacteremia. Open Forum Infect Dis. 2019;6(12):ofz490.

25. Giannella M, Pascale R, Toschi A, et al. Treatment duration for Escherichia coli bloodstream infection and outcomes: retrospective single-centre study. Clin Microbiol Infect. 2018;24(10):1077-1083.

26. Hojat LS, Bessesen MT, Huang M, et al. Effectiveness of shorter versus longer durations of therapy for common inpatient infections associated with bacteremia: a multicenter, propensity-weighted cohort study. Clin Infect Dis. 2019;https://doi.org/10.1093/cid/ciz1197

27. Lee CC, Hsieh CC, Yang CY, et al. Short versus long duration antimicrobial treatment for community-onset bacteremia: a propensity score matching study. Int J Antimicrob Agents. 2019;54(2):176-183.

28. Canton R, Morosini Ml. Emergence and spread of antibiotic resistance following exposure to antibiotics. FEMS Microbiol Rev. 2011;35(5):977-991.

29. Alvarez-Lerma F. Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit. ICU-acquired pneumonia study group. Intensive Care Med. 1996;22(5):387-394.

30. Chong YP, Moon SM, Bang KM, et al. Treatment duration for uncomplicated Staphylococcus aureus bacteremia: how long is long enough? Clin Infect Dis. 2018;69(11):2011-2014.

31. Chen HC, Lin WL, Lin CC, et al. Outcome of inadequate empirical antibiotic therapy in emergency department patients with community-onset bloodstream infections. J Antimicrob Chemother. 2013;68(4):947-953.

Supporting Information
Additional supporting information may be found online in the Supporting Information section.

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