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Early Ultrasound and Time to Antibiotic Therapy in Emergency Department Patients With Suspected Infection: A Propensity-Weighted Analysis of 15,660 Encounters

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Abstract

Study Objective:

To determine whether early ultrasound is associated with more timely antibiotic administration among hospitalized emergency department (ED) patients with suspected infection.

Methods

We performed a retrospective cohort study using MIMIC-IV-ED linked with hospital, microbiology, medication, radiology, and intensive care datasets. Adult ED encounters resulting in hospital admission were eligible. Suspected infection was defined using a Sepsis-3–inspired operational definition requiring both systemic antibiotic administration within 24 hours of ED arrival and microbiological culture sampling within ± 24 hours of ED arrival. Early ultrasound was defined as an ultrasound examination documented within 2 hours of ED arrival. The primary outcome was antibiotic administration within 6 hours. Overlap-weighted propensity-score analyses were performed.

Results

Among 425,087 ED encounters screened, 201,695 resulted in hospital admission. A total of 18,144 encounters met the suspected-infection definition, and 15,660 had complete covariate data. Early ultrasound occurred in 791 encounters (5.1%). Early ultrasound was associated with higher odds of antibiotic administration within 6 hours (OR 1.46, 95% CI 1.13–1.87; p = 0.003), shorter time to first antibiotic administration (− 0.27 h, 95% CI − 0.44 to − 0.11; p = 0.001), and earlier antibiotic administration in weighted Cox analysis (HR 1.12, 95% CI 1.04–1.20; p = 0.002). No significant association was observed with hospital mortality (OR 1.04, 95% CI 0.75–1.46; p = 0.804). No significant associations were observed for ICU admission or vasopressor use.

Conclusions

Early ultrasound was associated with improved timeliness of antibiotic administration but not with lower mortality or ICU utilization, suggesting that ultrasound may function primarily as a diagnostic process accelerator within ED infection care pathways.

Introduction

Timely antimicrobial therapy remains a fundamental component of emergency care for patients with suspected infection [1]. Early recognition and treatment are central principles of contemporary sepsis management, and international guidelines consistently emphasize prompt initiation of appropriate antimicrobial therapy, particularly among patients with sepsis and septic shock [2]. Delayed antibiotic

administration has been associated with adverse outcomes in multiple observational studies, although the magnitude of benefit associated with increasingly aggressive treatment targets remains a subject of ongoing debate [3, 4]. Importantly, delays in treatment are often multifactorial and may arise not only from logistical barriers but also from uncertainty regarding the presence, source, or severity of infection [5].

Diagnostic uncertainty is a common challenge in the emergency department (ED), where patients frequently present with nonspecific symptoms, incomplete clinical information, and competing diagnostic possibilities [6]. Clinicians must often make therapeutic decisions before definitive diagnostic confirmation is available, balancing the risks of delayed treatment against concerns regarding unnecessary antimicrobial exposure [7]. Consequently, diagnostic tools capable of rapidly narrowing the differential diagnosis and increasing clinician confidence may have important effects on time-sensitive treatment decisions. Although substantial attention has been devoted to antimicrobial stewardship, comparatively less attention has been paid to the role of diagnostic acceleration in facilitating timely therapy [7].

Ultrasound has become increasingly integrated into emergency medicine practice because it provides rapid bedside information without radiation exposure or transportation delays [8]. Point-of-care and radiology-performed ultrasound examinations can assist in identifying pulmonary, biliary, urinary, abdominal, soft-tissue, and cardiovascular sources of infection while simultaneously excluding alternative diagnoses. In patients with suspected sepsis, focused cardiac and hemodynamic ultrasound may also contribute to risk stratification and guide early resuscitative decisions [9]. Previous investigations have demonstrated the diagnostic utility of ultrasound across a wide range of infectious conditions, including pneumonia, acute cholecystitis, pyelonephritis, and undifferentiated shock [10–12]. As a result, ultrasound has become a routine component of emergency department evaluation in many institutions.

Despite widespread adoption, relatively little evidence exists regarding whether early ultrasound influences clinically relevant process-of-care outcomes. Most published studies have focused on diagnostic accuracy, agreement with reference standards, procedural guidance, or clinical decision-making [10–12]. Whether ultrasound translates into more timely delivery of definitive therapies, such as antimicrobial treatment, remains less well understood. From a systems perspective, this question may be particularly important because ultrasound is uniquely positioned to accelerate diagnostic clarification during the earliest stages of patient evaluation.

Therefore, we evaluated whether early ultrasound was associated with more timely antibiotic administration among hospitalized ED patients meeting an operational suspected-infection definition adapted from the Sepsis-3 framework. We hypothesized that ultrasound performed early during ED evaluation would be associated with earlier antibiotic administration and shorter time to treatment.

Methods

Study Design and Data Source

We performed a retrospective observational cohort study using the Medical Information Mart for Intensive Care Emergency Department (MIMIC-IV-ED) database linked with MIMIC-IV hospital datasets [13]. MIMIC-IV contains de-identified data on emergency department encounters, hospital admissions, medication administration, microbiology testing, radiology reports, and intensive care unit (ICU) admissions from a tertiary-care academic medical center. The study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and to the REporting of studies Conducted using Observational Routinely-collected Data (RECORD) recommendations for observational studies using routinely collected health data [14, 15].

Study Population

Adult ED encounters resulting in hospital admission were eligible for inclusion. To identify encounters in which clinicians actively suspected infection during the ED evaluation, suspected infection was defined using an operational definition adapted from the Sepsis-3 framework, requiring both administration of at least one systemic antibiotic within 24 hours of ED arrival and microbiological culture sampling within ± 24 hours of ED arrival [16]. Encounters lacking complete information required for propensity-score estimation were excluded from the primary complete-case analysis. Patterns of missingness are summarized in Supplementary Table S5.

Exposure Definition

The exposure of interest was early ultrasound, defined as an ultrasound examination documented within 2 hours of ED arrival. Ultrasound examinations were identified through radiology reports using predefined ultrasound-related search terms. The first documented ultrasound examination was used to determine exposure timing. Sensitivity analyses evaluated alternative exposure windows of 1 hour and 6 hours after ED arrival.

Outcomes

The primary outcome was administration of systemic antibiotics within 6 hours of ED arrival. Secondary outcomes included antibiotic administration within 3 hours, time from ED arrival to first antibiotic administration, vasopressor administration within 6 hours, ICU admission within 6, 12, and 24 hours, any ICU admission, hospital length of stay, and hospital mortality.

Statistical Analysis

Continuous variables are reported as mean (standard deviation) or median (interquartile range), as appropriate, whereas categorical variables are presented as counts and percentages. Baseline

characteristics were compared descriptively between patients undergoing early ultrasound and those not receiving early ultrasound.

To reduce confounding arising from non-random ultrasound utilization, propensity scores were estimated using multivariable logistic regression. Covariates included demographic characteristics (age, sex, and race), arrival characteristics, triage acuity, presenting vital signs (heart rate, respiratory rate, systolic and diastolic blood pressure, oxygen saturation, and temperature), shock-triage status, and ED length of stay. These variables were selected a priori based on clinical plausibility and their potential association with both ultrasound utilization and study outcomes.

Propensity-score overlap weighting was applied to create a weighted pseudo-population emphasizing patients with the greatest probability of receiving either treatment strategy. Covariate balance before and after weighting was assessed using standardized mean differences (SMDs), with an absolute SMD < 0.10 considered indicative of adequate balance.

The primary outcome, antibiotic administration within 6 hours of ED arrival, was evaluated using overlap-weighted logistic regression and reported as odds ratios (ORs) with 95% confidence intervals (CIs). Secondary binary outcomes, including antibiotic administration within 3 hours, vasopressor administration within 6 hours, ICU admission, and hospital mortality, were analyzed using the same approach.

Continuous outcomes, including time to first antibiotic administration and hospital length of stay, were analyzed using overlap-weighted linear regression models and reported as mean differences with corresponding 95% confidence intervals.

Because antibiotic administration is inherently a time-dependent process, a secondary time-to-event analysis was performed using an overlap-weighted Cox proportional hazards model. Hazard ratios (HRs) greater than 1 indicate earlier antibiotic administration among patients undergoing early ultrasound. Time zero was defined as ED arrival.

Pre-specified sensitivity analyses evaluated alternative exposure definitions based on ultrasound performed within 1 hour and within 6 hours of ED arrival. In addition, subgroup analyses were conducted according to shock-triage status to explore whether associations differed according to baseline physiologic instability.

All statistical analyses were performed using R version 4.6.0 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided p-value < 0.05 was considered statistically significant.

Results

Cohort Derivation and Baseline Characteristics

Among 425,087 ED encounters screened, 201,695 resulted in hospital admission. A total of 18,144 encounters met the Sepsis-3–inspired suspected-infection definition, and 15,660 had complete covariate data available for propensity-score estimation. Early ultrasound within 2 hours was performed in 791 encounters (5.1%), whereas 14,869 encounters did not receive early ultrasound. The cohort derivation is shown in Fig. 1.

Baseline differences between groups were modest before adjustment. The largest imbalances were observed for ED length of stay, diastolic blood pressure, respiratory rate, and arrival transport. After overlap weighting, covariate balance was excellent, with all weighted standardized mean differences approximately zero (Table 1 and Figure S1). Covariate balance, effective sample size, and overlap-weight distribution are reported in Supplementary Tables S1–S3 and Supplementary Figures S1–S3. Cohort flow counts and missingness patterns are summarized in Supplementary Tables S4 and S5.

Table 1

Baseline characteristics according to early ultrasound status *Values are n (%) or median (interquartile range). Early ultrasound was defined as ultrasound within 2 hours of emergency department arrival. SMD denotes standardized mean difference; BP, blood pressure; ED, emergency department.*

Characteristic	Early ultrasound (n = 791)	No early ultrasound (n = 14,869)	SMD before	SMD after
Male sex	410 (51.8)	7,757 (52.2)	-0.003	0.000
Acuity, median (IQR)	2 (2–3)	2 (2–3)	-0.034	0.000
Temperature, median (IQR)	98.4 (97.8–99.3)	98.4 (97.8–99.5)	-0.005	0.000
Heart rate, median (IQR)	91 (79–108)	93 (80–108)	-0.011	0.000
Respiratory rate, median (IQR)	18 (16–20)	18 (16–20)	-0.146	0.000
Oxygen saturation, median (IQR)	98 (97–100)	98 (96–100)	0.054	0.000
Systolic BP, median (IQR)	126 (109–142)	127 (111–144)	-0.070	0.000
Diastolic BP, median (IQR)	70 (58–81)	71 (61–82)	-0.172	0.000
Shock-triage positive	484 (61.2)	9,421 (63.4)	-0.022	0.000
ED length of stay, median (IQR), h	5.3 (3.9–7.1)	5.9 (4.2-8.0)	-0.232	0.000
Arrival by ambulance	353 (44.6)	7,590 (51.0)	-0.064	0.000

Primary and Secondary Outcomes

Early ultrasound was associated with higher odds of antibiotic administration within 6 hours of ED arrival (OR 1.46, 95% CI 1.13–1.87; p = 0.003). No significant association was observed for antibiotic administration within 3 hours (OR 1.06, 95% CI 0.91–1.22; p = 0.457). Outcome estimates are summarized in Fig. 2. Detailed estimates for binary outcomes are reported in Table 2. Crude outcome rates are reported in Supplementary Table S6.

Table 2

Association between early ultrasound and binary outcomes *Odds ratios compare ultrasound within 2 hours of emergency department arrival with no early ultrasound and are estimated using overlap-weighted logistic regression. ICU denotes intensive care unit.*

Outcome	Odds ratio (95% CI)	P value
Antibiotics ≤ 6 h	1.46 (1.13–1.87)	0.003
Antibiotics ≤ 3 h	1.06 (0.91–1.22)	0.457
Vasopressors ≤ 6 h	0.79 (0.54–1.16)	0.231
ICU admission ≤ 6 h	0.96 (0.79–1.16)	0.678
ICU admission ≤ 12 h	0.99 (0.84–1.16)	0.868
ICU admission ≤ 24 h	0.98 (0.84–1.15)	0.844
Any ICU admission	1.09 (0.94–1.27)	0.252
Hospital mortality	1.04 (0.75–1.46)	0.804

Patients receiving early ultrasound received antibiotics earlier, with a mean difference of − 0.27 hours (95% CI − 0.44 to − 0.11; p = 0.001), corresponding to approximately 16 minutes earlier treatment. In the overlap-weighted Cox analysis, early ultrasound was similarly associated with earlier antibiotic administration within 12 hours (HR 1.12, 95% CI 1.04–1.20; p = 0.002). The cumulative distribution of antibiotic administration times is shown in Fig. 3. Continuous outcomes and time-to-event analyses are summarized in Table 3.

Table 3

Time-to-care and continuous outcomes *Mean differences compare early ultrasound with no early ultrasound. Negative values indicate shorter time among patients receiving early ultrasound. The Cox model estimate is a hazard ratio; values greater than 1 indicate earlier antibiotic administration. ICU denotes intensive care unit.*

Outcome	Estimate (95% CI)	P value
Time to first antibiotic	-0.27 (-0.44 to -0.11)	0.001
Time to first vasopressor	0.57 (-0.47 to 1.62)	0.283
Time to ICU admission	19.81 (-5.87 to 45.49)	0.130
Hospital length of stay	1.19 (0.43 to 1.95)	0.002
Time to first antibiotic within 12 h (Cox model)	1.12 (1.04–1.20)	0.002

Early ultrasound was not significantly associated with vasopressor administration within 6 hours (OR 0.79, 95% CI 0.54–1.16; p = 0.231), ICU admission within 6 hours (OR 0.96, 95% CI 0.79–1.16; p = 0.678), ICU admission within 12 hours (OR 0.99, 95% CI 0.84–1.16; p = 0.868), ICU admission within 24 hours (OR 0.98, 95% CI 0.84–1.15; p = 0.844), any ICU admission (OR 1.09, 95% CI 0.94–1.27; p = 0.252), or hospital mortality (OR 1.04, 95% CI 0.75–1.46; p = 0.804). Hospital length of stay was longer among patients receiving early ultrasound (mean difference 1.19 days, 95% CI 0.43 to 1.95; p = 0.002).

Sensitivity and Subgroup Analyses

Sensitivity analyses using alternative ultrasound exposure windows were broadly consistent with the primary analysis. When early ultrasound was defined as ultrasound within 1 hour, it was associated with antibiotic administration within 3 hours (OR 1.37, 95% CI 1.07–1.76; p = 0.012) and shorter time to first antibiotic administration (mean difference − 0.44 hours, 95% CI − 0.71 to − 0.18; p = 0.001). When early ultrasound was defined as ultrasound within 6 hours, it remained associated with antibiotic administration within 6 hours (OR 1.16, 95% CI 1.01–1.33; p = 0.035), although the magnitude of association was attenuated. Sensitivity analyses using alternative exposure windows are reported in Supplementary Tables S7–S10 and Supplementary Figure S4.

In exploratory subgroup analyses, early ultrasound was associated with antibiotic administration within 6 hours among shock-triage–positive patients (OR 1.52, 95% CI 1.05–2.20; p = 0.026). Among shock-triage–negative patients, the corresponding association did not reach statistical significance (OR 1.36, 95% CI 0.96–1.93; p = 0.084). Shock-triage subgroup results are reported in Supplementary Table S11 and Supplementary Figure S5. The exploratory spline analysis of ultrasound timing and antibiotic administration is shown in Supplementary Figure S6.

Discussion

In this large propensity-weighted cohort of hospitalized ED patients meeting an operational suspected-infection definition adapted from the Sepsis-3 framework, early ultrasound was associated with improved timeliness of antibiotic administration. Ultrasound performed within 2 hours of ED arrival was associated with higher odds of antibiotic administration within 6 hours, shorter time to first antibiotic administration, and earlier antibiotic delivery in weighted time-to-event analysis. However, these process improvements were not accompanied by lower hospital mortality, reduced vasopressor use, or lower ICU utilization.

These findings should be interpreted in the context of the broader sepsis literature, in which antibiotic timing remains clinically important but complex. Prior observational studies have shown that delays in antimicrobial therapy may be associated with worse outcomes, particularly among patients with septic shock or high illness severity [17–19]. At the same time, more recent guideline discussions and evidence syntheses emphasize that rigid time targets may not apply uniformly across all patients with suspected infection, because the probability of infection, severity of illness, and risk of unnecessary antibiotic exposure vary substantially [20–22]. Our results are consistent with this more nuanced framework: early ultrasound was associated with improved treatment timeliness, but the absolute reduction in time to antibiotics was modest and did not translate into a measurable mortality difference. Specifically, early ultrasound was associated with administration of antibiotics approximately 16 minutes earlier, suggesting that its principal effect may be on workflow efficiency rather than on major downstream clinical outcomes. We could not fully account for secular trends in ED sepsis care, ultrasound utilization, and antibiotic timing across the study period. Improvements in institutional sepsis workflows over time may have contributed to earlier antibiotic administration independently of ultrasound use.

Several mechanisms may explain the observed association. Diagnostic uncertainty is a major driver of treatment delay in ED patients with possible infection [23]. Ultrasound may reduce this uncertainty by rapidly identifying potential infectious sources, supporting or excluding competing diagnoses, and increasing clinician confidence in initiating antimicrobial treatment [24]. This mechanism is biologically and operationally plausible. Lung ultrasound has been shown to improve diagnostic confidence in community-acquired pneumonia, and point-of-care ultrasound improves diagnostic accuracy for abscess in skin and soft-tissue infection. Similarly, ultrasound is increasingly used in patients with dyspnea, hypotension, and undifferentiated shock, where it may clarify cardiopulmonary or hemodynamic diagnoses during early evaluation [10, 12, 25–28]. A prospective controlled study of bedside POCUS during ward emergencies found that protocolized POCUS was associated with improved immediate diagnostic adequacy and shorter time to initial treatment, supporting the concept that ultrasound can influence clinical workflow beyond diagnostic accuracy alone [28]. In addition, a systematic review of POCUS in dyspnea, nontraumatic hypotension, and shock concluded that POCUS improves diagnostic accuracy in acute respiratory and circulatory deterioration, although evidence for downstream outcome improvement remains heterogeneous [29]. Thus, ultrasound may influence antibiotic timing not by acting as a therapy, but by accelerating the diagnostic pathway that precedes treatment.

Importantly, the absence of a hospital mortality association should not be interpreted as evidence that ultrasound lacks clinical value. Mortality in patients with suspected infection is influenced by many downstream factors, including baseline severity, antimicrobial appropriateness, pathogen susceptibility, source control, organ dysfunction, and subsequent inpatient management [30]. A diagnostic intervention that advances antibiotic administration by approximately 16 minutes may improve a process-of-care metric without being expected to independently change mortality in a broad hospitalized suspected-infection cohort. This interpretation is also consistent with randomized and systematic evidence from emergency ultrasound studies in hypotension and shock, where ultrasound may improve diagnostic accuracy or management processes without consistently demonstrating downstream outcome benefits [12, 27, 28].

The longer hospital length of stay observed among patients receiving early ultrasound should not be interpreted as evidence of harm. It may reflect residual confounding by diagnostic complexity, greater clinical concern, additional downstream testing, or identification of conditions requiring longer inpatient management. Nevertheless, it also raises the possibility that earlier or more intensive diagnostic evaluation may increase downstream resource use without necessarily improving mortality [31].

The subgroup findings further support a process-based interpretation. The association between early ultrasound and antibiotic administration within 6 hours appeared stronger among shock-triage–positive patients than among shock-triage–negative patients. This suggests that ultrasound may be most useful when diagnostic uncertainty coexists with physiologic instability, a setting in which rapid source identification and treatment decisions are particularly time-sensitive [27]. However, these subgroup analyses were exploratory and should be interpreted cautiously.

Taken together, our findings position early ultrasound as a potential diagnostic process accelerator within ED infection care pathways [24]. Rather than suggesting that ultrasound directly improves survival, the results support a more modest and clinically plausible role: early ultrasound may help clinicians reach actionable diagnostic conclusions faster, thereby improving the timeliness of antimicrobial therapy. Prospective studies should evaluate whether structured early-ultrasound pathways can improve source identification, antibiotic appropriateness, time to source control, and patient-centered outcomes in higher-risk ED populations.

Limitations

Several limitations should be acknowledged. First, the retrospective observational design precludes causal inference, and residual confounding remains possible despite extensive propensity-score adjustment and excellent post-weighting covariate balance. Clinicians may preferentially perform ultrasound in patients with unmeasured characteristics that influence both diagnostic pathways and treatment decisions. Early ultrasound may also be a marker of more efficient clinical teams, lower ED crowding, greater clinician expertise, or more streamlined diagnostic workflows rather than a direct cause of earlier antibiotic administration. Because measures of ED crowding, staffing intensity, clinician-

level expertise, and team-level efficiency were not available, residual organizational confounding cannot be excluded.

Second, exposure misclassification is possible. Because ultrasound exposure was identified through radiology documentation, undocumented bedside point-of-care ultrasound (POCUS) examinations performed by emergency physicians were likely not fully captured. Some patients classified as unexposed may therefore have received ultrasound evaluation, resulting in exposure misclassification and contamination of the control group. This bias would be expected to attenuate differences between groups and may partly explain the modest effect size observed.

Third, the effect of early ultrasound likely varies according to the suspected infectious source and examination type. Because ultrasound was analyzed as a broad diagnostic process rather than a syndrome-specific or protocolized point-of-care ultrasound intervention, we could not determine whether the observed association was driven by pulmonary, biliary, urinary, soft-tissue, or intra-abdominal presentations. Similarly, we could not distinguish whether potential benefits were attributable to specific ultrasound applications or to the broader diagnostic workflow in which ultrasound was incorporated.

Fourth, the operational suspected-infection definition was adapted from the Sepsis-3 framework and was designed to identify encounters in which clinicians actively suspected infection. Although this approach has face validity and is widely used in observational research, it does not represent a formally adjudicated diagnosis of infection or sepsis and may have resulted in inclusion of some patients ultimately found to have noninfectious conditions.

Fifth, medication administration timestamps were used as surrogates for treatment timing and may not perfectly reflect the exact time at which antibiotics were administered. Similarly, the timing of documented ultrasound examinations may not fully correspond to the timing of image acquisition or clinical interpretation.

Sixth, complete-case analysis was used for propensity-score estimation, introducing the possibility of selection bias if missingness was not completely random. Finally, this study was conducted within a single academic healthcare system, and patterns of ultrasound utilization, antimicrobial prescribing, and emergency department workflow may differ across institutions, potentially limiting generalizability.

Despite these limitations, the large sample size, detailed time-stamped clinical data, rigorous propensity-score methodology, and consistency of findings across multiple analytical approaches strengthen confidence in the overall conclusions.

Conclusions

Among hospitalized ED patients meeting an operational suspected-infection definition adapted from the Sepsis-3 framework, early ultrasound was associated with more timely antibiotic administration, including higher odds of receiving antibiotics within 6 hours and shorter time to treatment. However,

these improvements in care processes were not accompanied by lower hospital mortality or reduced ICU utilization. These findings suggest that ultrasound may function primarily as a diagnostic process accelerator within emergency care pathways and support prospective evaluation of structured early-ultrasound strategies to improve diagnostic efficiency and treatment delivery in patients with suspected infection.

Declarations

Funding

The authors received no specific funding for this work.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this study.

Ethics Approval and Consent to Participate

This study used the publicly available, de-identified MIMIC-IV and MIMIC-IV-ED databases. Access to the databases requires completion of human-subjects research training and execution of a data-use agreement. Because the data are fully de-identified, the requirement for informed consent was waived by the database governance framework.

Data Availability

The data used in this study are available from PhysioNet to credentialed users who complete the required training and data-use agreement for access to MIMIC-IV and MIMIC-IV-ED.

Code Availability

The statistical code used for cohort construction and analysis is available from the corresponding author upon reasonable request.

Author Contributions

DO conceived the study, designed the analysis, performed the statistical analysis, interpreted the data, and drafted the manuscript. CCDG, FC, and SV contributed to data interpretation and critically revised the manuscript for important intellectual content. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Prior Presentation

This work has not been previously presented.

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Use of Artificial Intelligence Tools

The authors used ChatGPT (OpenAI, San Francisco, CA, USA) to assist with English-language editing, improvement of manuscript readability, and refinement of the study flow diagram (Figure 1). The authors reviewed, verified, and approved all manuscript content, analyses, interpretations, figures, and conclusions. No artificial intelligence tool was used for data extraction, statistical analysis, result generation, or scientific decision-making.

References

1. Leung LY, Huang HL, Hung KK, Leung CY, Lam CC, Lo RS, Yeung CY, Tsoi PJ, Lai M, Brabrand M, Walline JH, Graham CA (2024) Door-to-antibiotic time and mortality in patients with sepsis: Systematic review and meta-analysis. Eur J Intern Med 129:48–61 Epub 2024 Jul 20. PMID: 39034174
2. Prescott HC, Antonelli M, Alhazzani W, Møller MH, Alshamsi F, Azevedo LCP, Belley-Cote E, De Waele J, Derde L, Dionne JC, Evans L, Gershengorn HB, Hodgson CL, Honarmand K, Kesecioglu J, McIntyre L, Mer M, Nunnally ME, Oczkowski SJW, Rochwerg B, Akinola OO, Akuamoah-Boateng KA, Alberto L, Angus DC, Arabi YM, Azoulay E, Cecconi M, Convocar PF, De Pascale G, Doi K, Du B, Egi M, Elie-Turenne MC, Ferrer R, Fox-Robichaud A, French C, Freund Y, Gong MN, Hale CP, Hammond NE, Hashmi M, Heunks L, Iwashyna TJ, Jacob ST, Klompas M, Kwizera A, Leeies M, Lejnieks JD, Levy MM, Machado FR, Maia MO, Masur H, Maves RC, McGloughlin S, McPeake J, Mohr NM, Myatra SN, Ostermann M, Peake SL, Pletz MW, Roberts JA, Rosa RG, Sawyer RG, Schorr CA, Simpson SQ, Weng L, Wiersinga WJ, Rhodes A, Coopersmith CM (2026) Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2026. Crit Care Med 54(4):725–812. 10.1097/CCM.0000000000007075. Epub 2026 Mar 23. PMID: 41869847
3. Tang F, Yuan H, Li X, Qiao L (2024) Effect of delayed antibiotic use on mortality outcomes in patients with sepsis or septic shock: A systematic review and meta-analysis. Int Immunopharmacol. ;129:111616. 10.1016/j.intimp.2024.111616. Epub 2024 Feb 3. PMID: 38310764
4. Im Y, Kang D, Ko RE, Lee YJ, Lim SY, Park S, Na SJ, Chung CR, Park MH, Oh DK, Lim CM, Suh GY (2022) Korean Sepsis Alliance (KSA) investigators. Time-to-antibiotics and clinical outcomes in patients with sepsis and septic shock: a prospective nationwide multicenter cohort study. Crit Care 26(1):19. 10.1186/s13054-021-03883-0. PMID: 35027073; PMCID: PMC8756674
5. Draeger L, Fleischmann-Struzek C, Gehrke-Beck S, Heintze C, Thomas-Rueddel DO, Schmidt K (2025) Barriers and facilitators to optimal sepsis care - a systematized review of healthcare professionals' perspectives. BMC Health Serv Res 25(1):591. 10.1186/s12913-025-12777-8. PMID: 40275226; PMCID: PMC12020105

6. Meier N, Pedersen KZ, Andresen LC, Andersen O (2024) Patients with Non-Specific Complaints in Emergency Departments: A Growing Patient Safety Concern in an Aging Population with Multimorbidity. Healthc (Basel) 12(20):2014. 10.3390/healthcare12202014. PMID: 39451428; PMCID: PMC11506877
7. Klompas M, Lapão LV, Taylor SP (2025) Antibiotics for suspected sepsis: who and when? Intensive Care Med 51(6):1142–1144. 10.1007/s00134-025-07940-y. Epub 2025 May 19. PMID: 40387882
8. Belisle Haley C, McKelvy D, Mackenzie DC (2022) Growth and globalization of point-of-care ultrasound publications in emergency medicine. J Clin Ultrasound. ;50(4):515–520. 10.1002/jcu.23169. Epub 2022 Mar 7. PMID: 35253236
9. Díaz-Gómez JL, Mayo PH, Koenig SJ (2021) Point-of-Care Ultrasonography. N Engl J Med. ;385(17):1593–1602. 10.1056/NEJMra1916062. PMID: 34670045
10. Orso D, Guglielmo N, Copetti R (2018) Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. Eur J Emerg Med. ;25(5):312–321. doi: 10.1097/MEJ.0000000000000517. PMID: 29189351
11. Dupriez F, Niset A, Couvreur C, Marissiaux L, Gendebien F, Peyskens L, Germeau B, Fasseaux A, Rodrigues de Castro B, Penaloza A, Vanpee D, Bobbia X (2024) Evaluation of point-of-care ultrasound use in the diagnostic approach for right upper quadrant abdominal pain management in the emergency department: a prospective study. Intern Emerg Med 19(3):803–811. 10.1007/s11739-023-03480-9. Epub 2023 Dec 2. PMID: 38041765
12. Basmaji J, Tang JE, Arntfield R, Desai K, Ball IM, Fiorini K, Slessarev M, Honarmand K, Jones P, Lau V, Lewis K, Orozco N, Meade M, Park B, Prager R, Rochwerg B, Thabane L, Wong MYS, Guyatt G (2025) The diagnostic accuracy of point-of-care ultrasound in shock: a systematic review and meta-analysis. Can J Anaesth 72(7):1118–1129 English. 10.1007/s12630-025-02997-1
13. Johnson AEW, Bulgarelli L, Shen L, Gayles A, Shammout A, Horng S, Pollard TJ, Hao S, Moody B, Gow B, Lehman LH, Celi LA, Mark RG (2023) MIMIC-IV, a freely accessible electronic health record dataset. Sci Data. ;10(1):1. doi: 10.1038/s41597-022-01899-x. Erratum in: Sci Data. 2023;10(1):31. 10.1038/s41597-023-01945-2. Erratum in: Sci Data. 2023;10(1):219. doi: 10.1038/s41597-023-02136-9. PMID: 36596836; PMCID: PMC9810617
14. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative (2008). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. ;61(4):344-9. doi: 10.1016/j.jclinepi.2007.11.008. PMID: 18313558
15. Benchimol EI, Smeeth L, Guttmann A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langan SM, RECORD Working Committee (2015) The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement. PLoS Med 12(10):e1001885. 10.1371/journal.pmed.1001885. PMID: 26440803; PMCID: PMC4595218
16. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, Rubenfeld G, Kahn JM, Shankar-Hari M, Singer M, Deutschman CS, Escobar GJ, Angus DC (2016) Assessment of Clinical

Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. ;315(8):762 – 74. doi: 10.1001/jama.2016.0288. Erratum in: JAMA. 2016 May 24–31;315(20):2237. 10.1001/jama.2016.5850. PMID: 26903335; PMCID: PMC5433435

17. Rüddel H, Thomas-Rüddel DO, Reinhart K, Bach F, Gerlach H, Lindner M, Marshall JC, Simon P, Weiss M, Bloos F, Schwarzkopf D, MEDUSA study group (2022) Adverse effects of delayed antimicrobial treatment and surgical source control in adults with sepsis: results of a planned secondary analysis of a cluster-randomized controlled trial. Crit Care 26(1):51. 10.1186/s13054-022-03901-9. PMID: 35227308; PMCID: PMC8883454
18. Liu VX, Fielding-Singh V, Greene JD, Baker JM, Iwashyna TJ, Bhattacharya J, Escobar GJ (2017) The Timing of Early Antibiotics and Hospital Mortality in Sepsis. Am J Respir Crit Care Med 196(7):856–863. 10.1164/rccm.201609-1848OC. PMID: 28345952; PMCID: PMC5649973
19. Venkatesh B, Schlapbach L, Mason D, Wilks K, Seaton R, Lister P, Irwin A, Lane P, Redpath L, Gibbons K, Ergetu E, Rice M (2021) Impact of 1-hour and 3-hour sepsis time bundles on patient outcomes and antimicrobial use: A before and after cohort study. Lancet Reg Health West Pac 18:100305. 10.1016/j.lanwpc.2021.100305. PMID: 35024649; PMCID: PMC8654968
20. Gildea A, Mulvihill C, McFarlane E, Gray A, Singer M (2024) guideline committee. Recognition, diagnosis, and early management of suspected sepsis: summary of updated NICE guidance. BMJ. ;385:q1173. 10.1136/bmj.q1173. PMID: 38889923
21. Sterling SA, Miller WR, Pryor J, Puskarich MA, Jones AE (2015) The Impact of Timing of Antibiotics on Outcomes in Severe Sepsis and Septic Shock: A Systematic Review and Meta-Analysis. Crit Care Med 43(9):1907–1915. 10.1097/CCM.0000000000001142. PMID: 26121073; PMCID: PMC4597314
22. Rothrock SG, Cassidy DD, Barneck M, Schinkel M, Guetschow B, Myburgh C, Nguyen L, Earwood R, Nanayakkara PWB, Nannan Panday RS, Briscoe JG (2020) Outcome of Immediate Versus Early Antibiotics in Severe Sepsis and Septic Shock: A Systematic Review and Meta-analysis. Ann Emerg Med 76(4):427–441 Epub 2020 Jun 25. PMID: 32593430
23. Kutz A, Florin J, Hausfater P, Amin D, Amin A, Haubitz S, Conca A, Reutlinger B, Canavaggio P, Sauvin G, Bernard M, Huber A, Mueller B, Schuetz P (2016) TRIAGE Study group. Predictors for Delayed Emergency Department Care in Medical Patients with Acute Infections - An International Prospective Observational Study. PLoS ONE 11(5):e0155363. 10.1371/journal.pone.0155363. PMID: 27171476; PMCID: PMC4865227
24. Díez-Vidal A, Martínez-Martín P, González-Muñoz B, Tung-Chen Y (2024) Point-of-care Ultrasound in Infectious Diseases: Current Insights and Future Perspectives. Clin Infect Dis. ;79(2):420–429. 10.1093/cid/ciae285. PMID: 38769593
25. Javaudin F, Marjanovic N, de Carvalho H, Gaborit B, Le Bastard Q, Boucher E, Haroche D, Montassier E, Le Conte P (2021) Contribution of lung ultrasound in diagnosis of community-acquired pneumonia in the emergency department: a prospective multicentre study. BMJ Open 11(9):e046849. 10.1136/bmjopen-2020-046849. PMID: 34561254; PMCID: PMC8475146

26. Barbic D, Chenkin J, Cho DD, Jelic T, Scheuermeyer FX (2017) In patients presenting to the emergency department with skin and soft tissue infections what is the diagnostic accuracy of point-of-care ultrasonography for the diagnosis of abscess compared to the current standard of care? A systematic review and meta-analysis. BMJ Open. ;7(1):e013688. doi: 10.1136/bmjopen-2016-013688. Erratum in: BMJ Open. 2017;7(9):e013688corr1. 10.1136/bmjopen-2016-013688corr1. PMID: 28073795; PMCID: PMC5253602
27. Atkinson PR, Milne J, Diegelmann L, Lamprecht H, Stander M, Lussier D, Pham C, Henneberry R, Fraser JM, Howlett MK, Mekwan J, Ramrattan B, Middleton J, van Hoving DJ, Peach M, Taylor L, Dahn T, Hurley S, MacSween K, Richardson LR, Stoica G, Hunter S, Olszynski PA, Lewis DA (2018) Does Point-of-Care Ultrasonography Improve Clinical Outcomes in Emergency Department Patients With Undifferentiated Hypotension? An International Randomized Controlled Trial From the SHoC-ED Investigators. Ann Emerg Med 72(4):478–489. 10.1016/j.annemergmed.2018.04.002. Epub 2018 Jun 2. PMID: 29866583
28. Zieleskiewicz L, Lopez A, Hraiech S, Baumstarck K, Pastene B, Di Bisceglie M, Coiffard B, Duclos G, Boussuges A, Bobbia X, Einav S, Papazian L, Leone M (2021) Bedside POCUS during ward emergencies is associated with improved diagnosis and outcome: an observational, prospective, controlled study. Crit Care 25(1):34. 10.1186/s13054-021-03466-z. PMID: 33482873; PMCID: PMC7825196
29. Kok B, Wolthuis D, Bosch F, van der Hoeven H, Blans M (2022) POCUS in dyspnea, nontraumatic hypotension, and shock; a systematic review of existing evidence. Eur J Intern Med 106:9–38 Epub 2022 Aug 1. PMID: 35927185
30. Qin C, Ma D, Pang L, Hu M, Lin S, Zhou Z, Xu X, Ji C (2025) Prognostic factors of sepsis: a systematic review and meta-analysis. BMC Infect Dis 25(1):1670. 10.1186/s12879-025-12094-9. PMID: 41316021; PMCID: PMC12661681
31. Cid-Serra X, Royse A, Canty D, Johnson DF, Maier AB, Fazio T, El-Ansary D, Royse CF (2021) Effect of a Multiorgan Focused Clinical Ultrasonography on Length of Stay in Patients Admitted With a Cardiopulmonary Diagnosis: A Randomized Clinical Trial. JAMA Netw Open. ;4(12):e2138228. doi: 10.1001/jamanetworkopen.2021.38228. Erratum in: JAMA Netw Open. 2022;5(4):e2211248. 10.1001/jamanetworkopen.2022.11248. PMID: 34932107; PMCID: PMC8693211

Figures

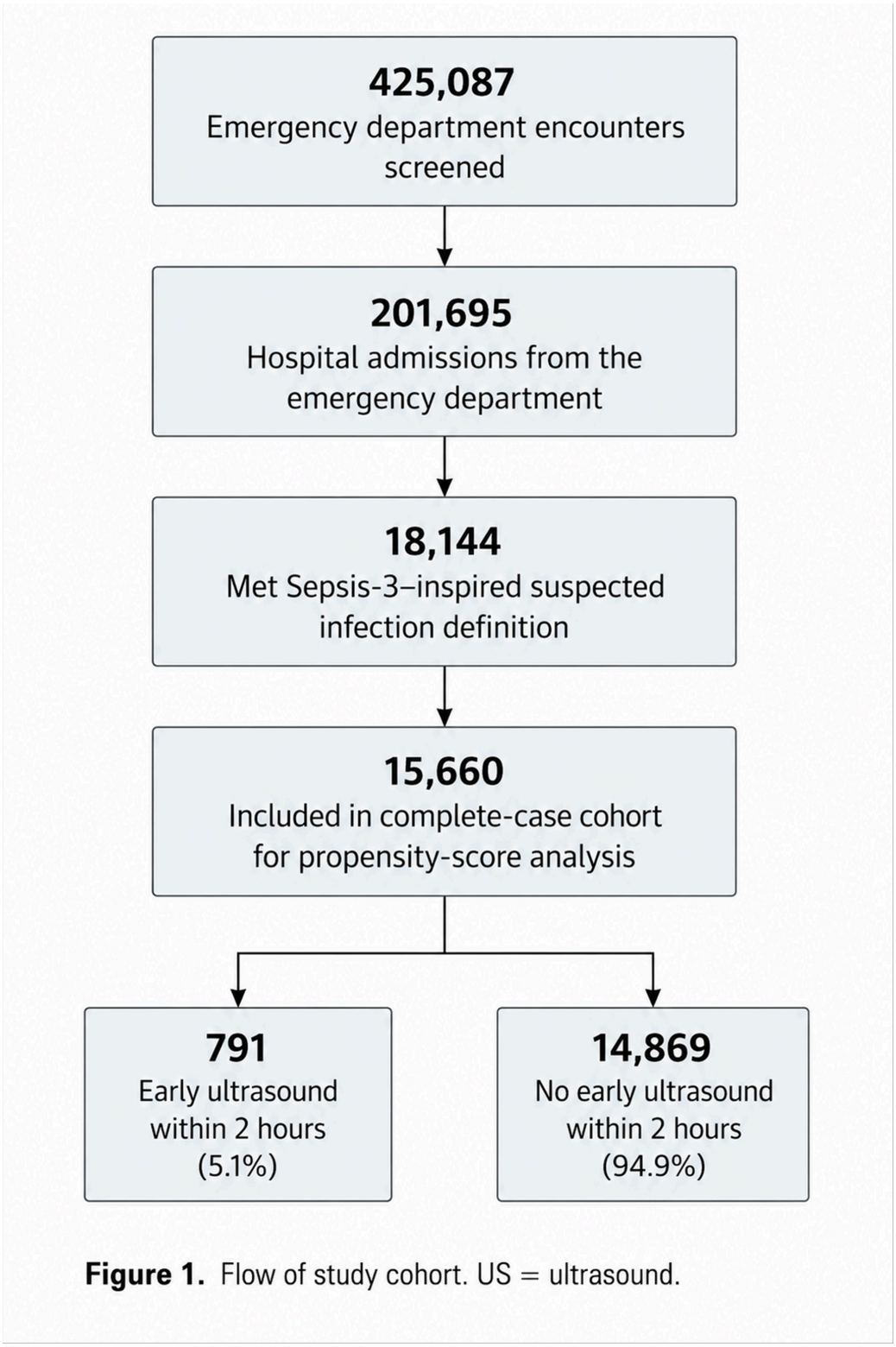


Figure 1

Study flow diagram. Flow diagram illustrating cohort derivation. Among 425,087 emergency department encounters screened, 201,695 resulted in hospital admission. A total of 18,144 encounters met the Sepsis-3–inspired suspected-infection definition. After restriction to encounters with complete covariate data for propensity-score estimation, the final analytic cohort included 15,660 encounters, of whom 791 underwent ultrasound within 2 hours of emergency department arrival and 14,869 did not.

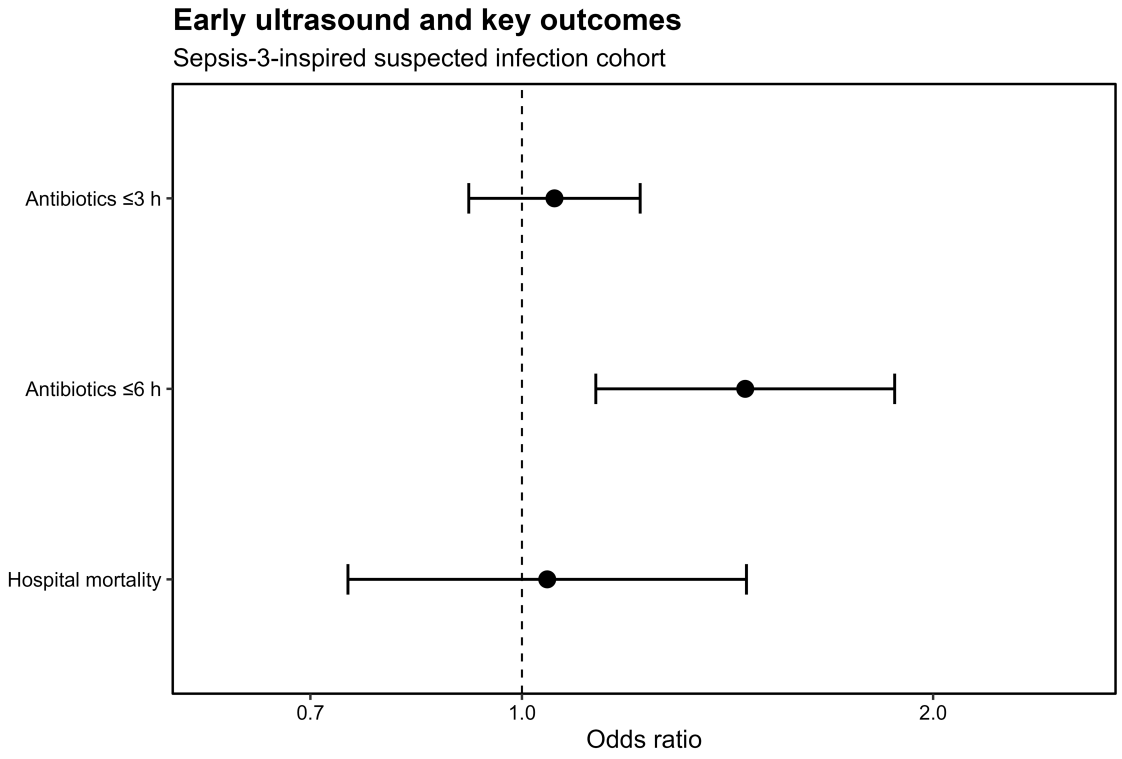


Figure 2

Association between early ultrasound and study outcomes. Forest plot showing overlap-weighted effect estimates for the association between ultrasound performed within 2 hours of ED arrival and clinical outcomes. Early ultrasound was associated with higher odds of antibiotic administration within 6 hours (OR 1.46, 95% CI 1.13–1.87) and earlier antibiotic administration in the weighted Cox model (HR 1.12, 95% CI 1.04–1.20). No significant associations were observed for hospital mortality (OR 1.04, 95% CI 0.75–1.46), ICU admission (OR 1.09, 95% CI 0.94–1.27), or vasopressor administration within 6 hours (OR 0.79, 95% CI 0.54–1.16). Negative mean differences indicate shorter times among patients receiving early ultrasound.

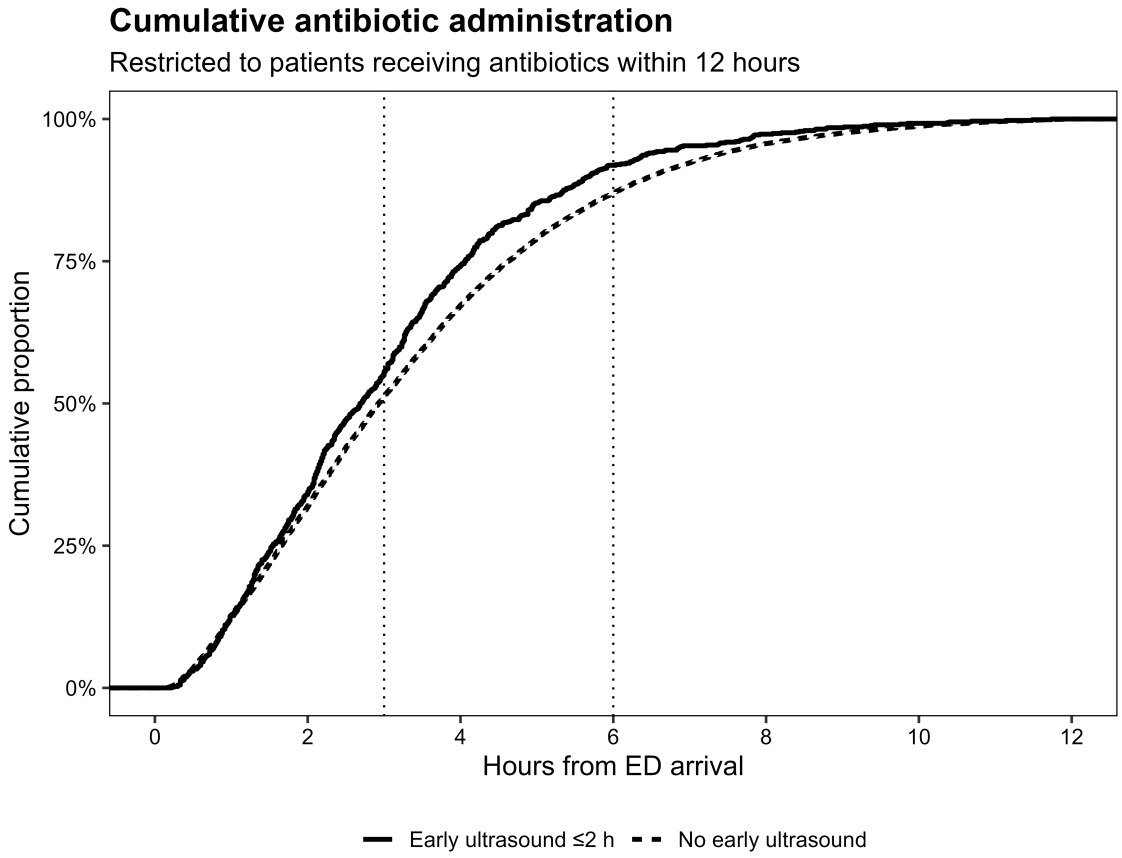


Figure 3

Time to antibiotic administration according to early ultrasound status. Empirical cumulative distribution function (ECDF) curves showing time from ED arrival to first antibiotic administration among patients receiving early ultrasound and those not receiving early ultrasound. Early ultrasound was associated with a shorter time to first antibiotic administration (mean difference −0.27 hours, 95% CI −0.44 to −0.11; p=0.001), corresponding to approximately 16 minutes earlier treatment.

Supplementary Files

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