GOOD EVIDENCE MATTERS

GEMs of the Week

SPOTLIGHT

Does Your Patient Have Liver Cirrhosis and Upper GI Bleed? Let's Talk About Prophylactic Antibiotics!

Cardiac Arrest in the Field

IV or IO for Vascular Access?

To DNR or Not to DNR

The Effect of Shared Decision-Making on Code Status Choice

The End of Sepsis?

The Intervention Turning the Tide on Maternal Infection

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Does Your Patient Have Liver Cirrhosis and Upper GI Bleed? Let's Talk About Prophylactic Antibiotics!

Effectiveness of Prophylactic Antibacterial Drugs for Patients with Liver Cirrhosis and Upper Gastrointestinal Bleeding: A Systematic Review and Meta-Analysis

Wang Z, Hu HS, Zhao LM, Li Y, Liu XD. Effectiveness of prophylactic antibacterial drugs for patients with liver cirrhosis and upper gastrointestinal bleeding: a systematic review and meta-analysis. *Front Pharmacol*. 2024;15:1324848. Published 2024 Mar 14. doi:10.3389/fphar.2024.1324848

KEY TAKEAWAY: Prophylactic antibiotics reduce infection risk, mortality, occurrence of rebleeding, and length of hospital stay in patients with liver cirrhosis and gastrointestinal (GI) bleeding.

STUDY DESIGN: Systematic review and meta-analysis of 17 randomized controlled trials (RCTs) and eight cohort studies (N=13,670)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Prophylactic antibiotics are sometimes given to patients with cirrhosis and GI bleed based on a variety of independent studies, to reduce the overall high mortality of variceal GI bleeding in cirrhosis patients. There are limited comprehensive research of various antibiotics and their prophylactic effects, particularly for patients with cirrhosis. This meta-analysis aims to assess the effect of prophylactic antibiotics on mortality and infection rates as well as rebleeding and length of hospital stay in patients with cirrhosis and GI bleed.

PATIENTS: Patients diagnosed with cirrhosis and upper GI bleeding

INTERVENTION: Prophylactic administration of antibacterial drugs

CONTROL: No administration of prophylactic drugs (standard of care) or placebo

PRIMARY OUTCOME: Infection rate and mortality rate
Secondary Outcome: Rebleeding rate, length of hospital stay

METHODS (BRIEF DESCRIPTION):

- Studies from US, China, Taiwan, UK, Spain, Australia, and Korea studying patients with both cirrhosis and GI bleed were included in the review.
- Patients received primarily cephalosporins or quinolones, with a few studies using penicillins, aminoglycosides, and other classes. Dose and protocol varied widely among studies.
- Control groups varied and included either standard of care or placebo.
- Meta-analysis was conducted and the 17 RCTs were pooled to assess incidence of death, infection, rebleeding, and length of stay. Cohort study data was also used in some antibiotic outcome measures.
- Primary outcomes measured were infection and mortality rate calculated from the pooled meta-analysis data.
- Secondary outcomes measured were rebleeding and length of hospital stay calculated from the pooled meta-analysis data.

INTERVENTION (# IN THE GROUP): Not available

COMPARISON (# IN THE GROUP): Not available

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- Antibiotic prophylaxis reduced patient mortality compared to placebo or standard of care (16 studies, n=1,706; relative risk [RR] 0.66; 95% CI, 0.51–0.83; I^2=25%).
- Antibiotic prophylaxis decreased the risk of infection compared to placebo or standard of care (17 studies, n=1,755; RR 0.41; 95% CI, 0.35–0.49; I^2=10%).
  - Prophylactic use of antibiotics reduced infection rates when pooled by drug class (RCT and cohort data):
    - Quinolones (3 studies, n=330; RR 0.26; 95% CI, 0.17–0.40; I^2=0%)
    - Quinolones or penicillin (1 study, n=102; RR 0.35; 95% CI, 0.2–0.62; I^2=not applicable)
    - Cephalosporins (12 studies, n=1,913; RR 0.43; 95% CI, 0.33–0.55; I^2=39%)
    - Cephalosporins or quinolones (5 studies, n=1,118; RR 0.49; 95% CI, 0.38–0.61; I^2=0%).
  - No significant difference was found when pooling all other antibiotic classes (2 studies, n=237; RR 0.76; 95% CI, 0.54–1.1; I^2=0%).

Secondary Outcome –

- Antibiotic prophylaxis decreased the risk of rebleeding compared to placebo or standard of care

(11 studies, n=1,757; RR 0.42; 95% CI, 0.31–0.56; I^2=44%).

- Antibiotic prophylaxis decreased the length of hospital stay compared to placebo or standard of care (5 studies, n=544; mean difference [MD] –5.3 days; 95% CI, –7.5 to –3.0; I^2=78%).

LIMITATIONS:

- Causes of patient mortality were not discussed. Thus, we cannot determine if mortality was due to bacterial infections or disease in general. It is also not possible to assess whether antibiotics directly decrease mortality or if antibiotics decrease infection rates which indirectly affect mortality rate.
- Follow-up time is not specified and could have been too short to capture 30-day mortality in these patients
- Antibiotic protocols varied widely including dose, route, and duration of administration, so determining a single best regimen is not possible from this study.
- Only a few of the included RCTs provided stratification by Child-Pugh classification of liver disease; differential antibiotic effects among different stages of cirrhosis are possible and would not be detected in this meta-analysis.
- This meta-analysis excluded cohort studies due to high heterogeneity and differential characteristics of patient cohorts, but the cohort studies included far larger sample sizes than the RCTs. Further large RCTs are needed to clarify these initial results.

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Cardiac Arrest in the Field: IV or IO for Vascular Access?

Intraosseous or Intravenous Vascular Access for Out-of-Hospital Cardiac Arrest

Vallentin MF, Granfeldt A, Klitgaard TL, et al. Intraosseous or Intravenous Vascular Access for Out-of-Hospital Cardiac Arrest. *N Engl J Med*. 2025;392(4):349-360. doi:10.1056/NEJMoa2407616

KEY TAKEAWAY: In patients who experience a non-traumatic out-of-hospital cardiac arrest, there is no evidence of superiority between the vascular access methods of intraosseous (IO) vs intravenous (IV) when it comes to achieving return of spontaneous circulation.

STUDY DESIGN: Multicenter, nonblinded, parallel group, randomized controlled trial (RCT)

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Prompt vascular access, alongside cardiopulmonary resuscitation (CPR), is crucial in cardiac arrest patients to allow for the administration of advanced cardiac life support (ACLS) medications, which aid in achieving a return of spontaneous circulation (ROSC). This study aimed to determine whether there is superiority between IV or IO access in obtaining sustained ROSC, as there is little data on this topic.

PATIENTS: Adults with non-traumatic out-of-hospital cardiac arrest

INTERVENTION: IO access

CONTROL: IV access

PRIMARY OUTCOME: Sustained return of spontaneous circulation

Secondary Outcome: Survival at 30 days, survival at 30 days with favorable neurologic outcomes, quality of life at 30 days, survival at 90 days, survival at 90 days with favorable neurologic outcomes, quality of life at 90 days

METHODS (BRIEF DESCRIPTION):

- The study was performed in conjunction with emergency medical services (EMS) agencies throughout all regions of Denmark.
- Patients who were ≥18 years old and had out-of-hospital cardiac arrests were included in the study.
- The mean age was 69±15 years old and 70% of patients were men.
- 77% of patients initially presented in a non-shockable rhythm.
- Patients who were suspected of having cardiac arrest due to trauma, had vascular access prior to randomization, or who were previously in the trial were excluded.
- Patients were randomized 1:1 to IV or IO access via a sealed envelope that was opened while en route by the responding physician.
  - Patients assigned to the IV group would attempt to have IV access established first.
  - Patients assigned to the IO group would attempt to have IO access established first.
    - Of the 731 patients assigned IO, 361 underwent humeral vascular access while 370 underwent tibial vascular access.
  - In the event the first method of vascular access failed, patients would receive the alternative option, thus changing groups.
- The primary outcome was sustained return of spontaneous circulation, defined as a palpable pulse that was maintained without chest compression for 20 minutes.
- Secondary outcomes were measured using the following:
  - Survival at 30 and 90 days
  - Survival at 30 and 90 days with favorable neurologic outcomes was measured using a modified Rankin scale with a range of 0–3, with higher scores reflecting more disability.
  - Quality of life at 30 and 90 days was measured using the EuroQol Group 5-Dimension 5-Level (EQ-5D-5L) questionnaire. Scores range from 0–100, with higher scores reflecting a better quality of life.

INTERVENTION (# IN THE GROUP): 731

COMPARISON (# IN THE GROUP): 748

FOLLOW-UP PERIOD: 90 days, but long-term outcomes at one year ongoing

RESULTS:

Primary Outcome –

- IO access resulted in sustained return of spontaneous circulation in 221 patients (30%) compared to 214 patients (29%) in the IV access group (risk ratio [RR] 1.1; 95% CI, 0.90–1.2; risk difference [RD] 1.6; 95% CI, –3.0 to –6.3).

Secondary Outcome –

- IO resulted in 85 patients (12%) being alive at 30 days compared to 75 patients (10%) in the IV group (RR 1.2; 95% CI, 0.87–1.6; RD was not statistically different between the groups).
- IO resulted in 67 patients (9%) being alive at 30 days with favorable neurologic outcomes compared to 59 patients (8%) in the IV group (RR 1.2; 95% CI, 0.83–1.6; RD was not statistically different between the groups).
- IO resulted in a mean score of 78±19 on the EQ-5D-5L at 30-day survival compared to 74±20 in the IV group (RD was not statistically different between the groups).

LIMITATIONS:

- This study was more optimized for the outcome of sustained ROSC, but it did not strongly analyze long-term outcomes.
- Treating physicians were not blinded to patients' assignments.
- Because of the emergency setting, some patients did not have any vascular access attempt, and some crossed over to their unassigned group due to failure to establish access via their original group's method.
- Establishment of vascular access within two tries was more successful in the intraosseous group compared to the intravenous group.

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To DNR or Not to DNR: The Effect of Shared Decision-Making on Code Status Choice

A Randomized Trial of Shared Decision-Making in Code Status Discussions

Becker C, Gross S, Beck K, et al. A Randomized Trial of Shared Decision-Making in Code Status Discussions. *NEJM Evid*. 2025;4(5):EVIDoa2400422. doi:10.1056/EVIDoa2400422

KEY TAKEAWAY: Using shared decision-making, a checklist, and a decision aid in code status discussions with hospitalized patients increases preference for do not resuscitate (DNR) over full-code status.

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Code status is one of the primary ways patients can assert their autonomy in the event of a cardiac arrest. However, patients often misunderstand the outcomes of cardiopulmonary resuscitation, leading to code status decisions that may not reflect their true preferences or prognosis. Code status discussions are frequently inadequate, lacking clarity and individualized information. The effect of shared decision-making on patients' code status choices has not previously been studied.

PATIENTS: Adults admitted to an inpatient medical service

INTERVENTION: Shared decision-making approach and use of decision aid in code status discussion

CONTROL: Usual care

PRIMARY OUTCOME: Frequency of choosing DNR code status

Secondary Outcome: Level of decisional uncertainty

METHODS (BRIEF DESCRIPTION):

- Study was conducted at six teaching hospitals in Switzerland from 2019–2023.
- Resident physicians were randomized to receive training in shared decision-making or general communication training.
- Hospitalized patients (mean age 68 years old) cared for by residents in the intervention group had code status discussions using a shared decision-making checklist with a decision aid.
- Patients cared for by residents in the control group received their usual care.
- Patients with cognitive impairment, severe mental health issues, or severe hearing impairment were excluded. Patients with poor expected outcomes following resuscitation, using a validated tool, were also excluded.
- Decisional uncertainty was measured within 24 hours following the code status discussion using the Decisional Conflict Score. Scores range from 0–100, with lower scores indicating less conflict.
- Patient charts were reviewed 30 days after discharge to assess additional secondary outcomes.

INTERVENTION (# IN THE GROUP): 1,370

COMPARISON (# IN THE GROUP): 1,293

FOLLOW-UP PERIOD: One day

RESULTS:

Primary Outcome –

- More patients in the shared decision-making group chose DNR code status than the control group (50% vs 37%, respectively; adjusted risk ratio [aRR] 1.4; 95% CI, 1.3–1.5; NNT=8).

Secondary Outcome –

- Shared decision-making decreased decisional uncertainty compared to control (adjusted difference −7.1; 95% CI, −9.4 to −4.7).

LIMITATIONS:

- Residents were randomized but they likely work in teams, so knowledge of shared decision-making may have been shared between colleagues in the intervention and control groups.
- Patients and residents were not blinded to the intervention, which could introduce bias in how discussions were conducted or how outcomes were reported.
- The study did not assess clinical outcomes, so there is no direct correlation between DNR preference and hospitalizations or in-hospital arrests.
- Patients with cognitive impairment, severe mental illness, or language barriers were excluded, which may limit the relevance of findings to more vulnerable or diverse populations.
- The study did not analyze the actual content of code status conversations, so it's unclear which elements of the intervention were most effective.

- The study ran from 2019–2023, before and during the COVID pandemic. Patients' baseline awareness and understanding of resuscitation may have changed during the pandemic.

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The End of Sepsis? The Intervention Turning the Tide on Maternal Infection

A Multicomponent Intervention to Improve Maternal Infection Outcomes

Lissauer D, Gadama L, Waitt C, et al. A Multicomponent Intervention to Improve Maternal Infection Outcomes. *N Engl J Med*. 2026;394(17):1685-1695. doi:10.1056/NEJMoa2512698

KEY TAKEAWAY: The Active Prevention and Treatment of Maternal Sepsis Intervention (APT-Sepsis), a three-tier complex prevention program, reduces the combined outcome of maternal death and severe infection compared to standard care in pregnancy and recently pregnant women in resource limited settings such as Malawi and Uganda.

STUDY DESIGN: Two arm, parallel, open-label, cluster-randomized controlled clinical trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Maternal infections are the third leading cause of maternal death in low-resource settings, contributing heavily to peripartum morbidity. While basic infection controls exist, comprehensive, facility-wide approaches lack sufficient study. Furthermore, real-world guideline implementation faces critical barriers including staff shortages and turnover, technological and material gaps, high financial costs, and healthcare worker protocol fatigue.

PATIENTS: Pregnant and recently pregnant women

INTERVENTION: Multicomponent sepsis bundle (APT-Sepsis)

CONTROL: Standard care

PRIMARY OUTCOME: Infection-related maternal deaths, near-misses, severe illness

Secondary Outcome: Neonatal deaths, stillbirths, process outcomes for adoption of program behaviors

METHODS (BRIEF DESCRIPTION):

- The authors conducted a two arm, parallel, open-label, cluster-randomized trial assessing a multicomponent intervention in Malawi and Uganda.
- The two-level inclusion criteria were set at both patient and facility levels:
  - At the patient level, eligible participants included pregnant women, recent postpartum women, those seeking prenatal care, in labor or delivery, or presenting with pregnancy-related complications.
  - Eligible facilities were geographically diverse hospitals in Malawi or Uganda, capable of cesarean sections, blood transfusions, hosting at least 1,600 births annually, and meeting basic requirements such as electricity and water.
- Individual patient consent was waived as the intervention targeted healthcare providers; formal participation agreements were instead established at the national and institutional levels.
- Baseline facility measures were similar between groups, with a 26% vs 22% cesarean rate and 2.5% vs 2.6% neonatal death rate in the intervention and control groups respectively. Critical equipment such as oxygen and blood-pressure devices was functional less than 10% of the year.
- Facilities were randomized using a minimization algorithm, balancing groups by country, weekly live births, and baseline event rates.
- The trial's three phases included a six-month baseline (190,500 live births), a three-month implementation transition (data excluded from effectiveness analysis), and a 12-month intervention phase (240, 894 live births).
- Intervention hospitals implemented the APT-Sepsis bundle to improve hand hygiene, optimize antiseptic and antibiotic use, and utilize the Fluids, Antibiotics, Source control, Transfer, Monitoring (FAST-M) treatment bundle, an evidence-based framework for maternal sepsis management in resource-limited settings, for early detection.
- Control hospitals were provided with standard WHO and national guidelines.
- The primary outcome was a composite of maternal death, near-miss, or severe infection, determined via facility records, with a blinded committee resolving any conflicting classifications.
- Secondary outcomes included neonatal deaths, stillbirths, and process outcomes measuring provider behaviors.

INTERVENTION (# IN THE GROUP):

- Facilities: 30

- Live births: 124,298

COMPARISON (# IN THE GROUP):

- Facilities: 29
- Live births: 116,596

FOLLOW-UP PERIOD: 42 days

RESULTS:

Primary Outcome –

- The APT-Sepsis intervention reduced the primary composite outcome compared to standard of care (1.4% vs 1.9%, respectively; risk ratio [RR] 0.68; 95% CI, 0.55–0.83; NNT=200), an effect that was consistent across countries and facilities.
- The effect was driven primarily by a reduction in severe infection-related illness. Component-specific relative risks were:
  - Severe infection-related illness (RR 0.68; 95% CI, 0.55–0.84)
  - Maternal near-miss events (RR 0.82; 95% CI, 0.44–1.5)
  - Maternal death (RR 1.2; 95% CI, 0.51–2.9)

Secondary Outcome –

- Neonatal mortality rates were not statistically significant between the groups.
- The APT-Sepsis Intervention improved several key process outcomes compared to standard of care, including:
  - Adherence to hand hygiene (33% vs 15%, respectively; mean difference [MD] 14; 95% CI, 10–19)
  - Appropriate antibiotic prophylaxis (74% vs 58%, respectively; MD 15; 95% CI, 4.0–26)
  - Complete vital signs on admission (48% vs 15%, respectively; MD 32; 95% CI, 25–40) and for suspected sepsis (60% vs 34%, respectively; MD 28; 95% CI, 16–40)
  - IV fluids administered within one hour for suspected sepsis (33% vs 22%, respectively; MD 13; 95% CI, 4.8–22)

LIMITATIONS:

- Evaluators' knowledge of facility assignments may have influenced outcome classification.
- The multicomponent design made it difficult to isolate the most effective individual actions.
- Lack of microbiological data prevented confirmation of specific pathogens.
- Requiring patients to return for follow-up care may have resulted in underreporting of post-discharge events.
- Scaling to other regions would require significant adaptation to local health systems and customs.

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