

THIS WEEK IN BRIEF

Starting with intermittent hemodialysis failed noninferiority to continuous renal replacement therapy in ventilated or vasopressor-dependent kidney injury, and 90-day mortality was 63.3% vs 53.6% in a trial stopped early (ICRAKI). An earlier vasopressin trigger (VASSPR) and isoflurane sedation (SAVE-ICU) were neutral on mortality.

Intraoperative dobutamine in septic source-control surgery cut 7-day kidney injury by about 12 percentage points. Oxygen targets after arrest, phenobarbital for withdrawal and antifungal timing in candidemia showed no outcome differences.

Strategic priorities. ECMO: Bagshaw (rank 6), ADQI and ELSO statements on CRRT during ECMO. Ventilation: Sella (rank 4) on weaning modes and SAVE-ICU (rank 3) in ventilated hypoxemic patients; sepsis and hemodynamics: VASSPR (rank 2) and the dobutamine trial (rank 5). Cardiogenic shock and temporary MCS: no new trial or original research; a three-part narrative series on shock systems of care (US Cardiology Review) and an Impella weaning protocol review (J Cardiothorac Vasc Anesth) were reviewed and not briefed.

1.30

hazard ratio for 90-day death with intermittent hemodialysis first, in a trial stopped early (Gaudry, ICRAKI)

0.98

adjusted odds ratio for 28-day death with an earlier vasopressin trigger in septic shock (Peltan, VASSPR)

NNT 8

to prevent one postoperative AKI with intraoperative dobutamine in septic shock (perioperative dobutamine trial)

AT A GLANCE

#	Study	Design	Result in one line	Signal
1	Gaudry: ICRAKI, IHD vs CRRT first Gaudry et al, N Engl J Med 2026	Open-label noninferiority RCT, stopped early, 554 adults	Noninferiority not shown for MAKE90; 90-day mortality 63.3% vs 53.6%, HR 1.30	Change practice
2	Peltan: VASSPR vasopressin Peltan et al, JAMA 2026	Cluster-crossover RCT, 13 US hospitals, 3,959 adults	28-day mortality 31.8% vs 33.0%; adjusted OR 0.98 (95% CI 0.87 to 1.06)	Confirms practice
3	Jerath: SAVE-ICU inhaled sedation Jerath et al, JAMA 2026	Pragmatic RCT, 14 Canadian ICUs, 780 adults	Hospital mortality 42.5% vs 43.8%; RR 0.98 (95% CI 0.84 to 1.14)	Confirms practice
4	Sella: advanced weaning modes Sella et al, Crit Care 2026 (in press)	Network meta-analysis, 23 RCTs, 3,755 adults	Severe asynchrony RR 0.38 with NAVA; mortality signal from 97 patients	Watch
5	Dobutamine in source control Chinese Perioperative Septic Shock Investigators, JAMA 2026	Open-label RCT, 39 Chinese hospitals, 584 adults	7-day AKI 22.8% vs 34.7%; adjusted RR 0.64 (95% CI 0.49 to 0.83)	Consider locally
6	Bagshaw: CRRT during ECMO Bagshaw et al, Blood Purif 2026 (accepted)	Consensus statement, 12 statements, ADQI XXXVI	Integrated or separate circuits both defensible; nine shared quality indicators	Consider locally
7	Bradley: phenobarbital vs diazepam Bradley et al, JAMA Intern Med 2026	Target trial emulation, 754 US hospitals, 24,643 adults	Length of stay difference -0.21 days (95% CI -0.42 to 0.00); ventilation 3.1% vs 2.7%	Confirms practice
8	Khan: oxygen targets after arrest Khan et al, Acad Emerg Med 2026	Meta-analysis, 11 RCTs, 4,136 adults	Mortality RR 0.96 (95% CI 0.88 to 1.06); hypoxemic episodes RR 1.65	Confirms practice
9	Wozniak: antifungal timing Wozniak et al, Crit Care 2026 (in press)	Pooled cohort, 158 centres, 272 adults	28-day mortality, weighted HR 1.23 (95% CI 0.82 to 1.83)	Consider locally
10	Blok: PROFLUID fluid therapy Blok et al, JAMA 2026	Prospective cohort, 206 ICUs in 41 countries, 2,454 adults	2.8 L per day; maintenance 31.9% and creep 30.9% vs resuscitation 16.0%	Consider locally

Signals: **CHANGE PRACTICE** **CONSIDER LOCALLY** **CONFIRMS PRACTICE** **WATCH** Click a title to jump to its card · [This week on SharePoint](#)

The studies

1. ICRAKI: intermittent hemodialysis first was not noninferior to CRRT, and more patients died

CHANGE PRACTICE Gaudry et al, N Engl J Med 2026 · Open-label noninferiority RCT, stopped early, 554 adults · Certainty: **Moderate** · [PDF](#) · [Briefing](#)

Bottom line. In ventilated or catecholamine-dependent adults with acute kidney injury (AKI) and an indication for renal replacement therapy (RRT), starting with intermittent hemodialysis (IHD) failed to show noninferiority to continuous RRT (CRRT) for major adverse kidney events by day 90 (MAKE90): 78.1% vs 71.6%, adjusted risk difference 6.28 percentage points (95% CI -1.22 to 13.79) against a 7.5 point margin. Kaplan-Meier 90-day mortality was 63.3% vs 53.6%, HR 1.30 (95% CI 1.04 to 1.63), in a trial stopped at 554 of 1000 planned patients.

Population: Adults with AKI, an RRT indication, and invasive ventilation or catecholamines; mean SOFA 12 · **Intervention:** IHD as the initial modality, held through day 3 · **Comparison:** CRRT (hemodialysis, hemofiltration or hemodiafiltration) · **Outcome:** MAKE90: death, RRT dependence, or creatinine more than 25% above baseline

RESULTS

- Death by day 90: 164/260 (63.1%) vs 147/275 (53.5%), an absolute increase of 9.6 points with IHD first (NNH about 10, from crude counts). Day 28 mortality 53.6% vs 44.8%.
- RRT dependence at day 90 2.1% vs 2.3%; RRT cessation by day 28 41.2% vs 52.7% (subdistribution HR 0.77, 95% CI 0.61 to 0.97). Hypotension 68.8% vs 66.5%.
- Fragility (unadjusted, Fisher exact, two-sided alpha 0.05): reverse fragility index 3 for the primary outcome, so three more IHD events would make the crude comparison significant; fragility index 3 for crude day-90 death.

CAVEATS

- Stopped at 55% of planned enrolment after descriptive 28-day mortality looks without prespecified stopping rules, which tends to inflate effect size; the authors judge the direction more robust than the magnitude.
- Mortality was a secondary outcome. Hypotension rates were similar, so the mechanism is unexplained; the catecholamine escalation signal on IHD days is post hoc.
- Open label; 19 randomized patients were excluded from analysis; more chronic kidney disease and emergency surgery in the IHD arm, although a post hoc adjusted analysis agreed. Delivered IHD dose was slightly below target, and prolonged intermittent therapy was not tested.

How it fits. KDIGO 2012 weakly favoured CRRT for unstable patients, and earlier trials and the Cochrane review found no mortality difference; the one earlier trial with a mortality difference (Mehta 2001) favoured IHD. ICRAKI enrolled only patients with a documented indication, as defined by the timing trials. Critical Care Reviews (Mac Sweeney) judges that it removes reassurance that initial IHD is close enough to CRRT, while warning of exaggeration from early stopping. The accompanying NEJM editorial (Palevsky) could not be read.

2. VASSPR: an earlier vasopressin trigger did not change septic shock mortality

CONFIRMS PRACTICE Peltan et al, JAMA 2026 · Cluster-crossover RCT, 13 US hospitals, 3,959 adults · Certainty: **Moderate** · [PDF](#) · [Briefing](#)

Bottom line. A hospital policy recommending vasopressin at 0.1 rather than 0.4 µg/kg/min norepinephrine equivalent increased and accelerated vasopressin use without changing 28-day mortality: 628/1,975 (31.8%) vs 655/1,984 (33.0%), adjusted marginal OR 0.98 (95% CI 0.87 to 1.06), adjusted risk difference -0.4 percentage points (95% CI -2.7 to 1.3). Kidney replacement therapy (KRT)-free days and 90-day mortality were also unchanged.

Population: All adults with septic shock on a vasopressor at 13 Intermountain hospitals · **Intervention:** Recommend vasopressin 0.03 units/min at 0.1 µg/kg/min norepinephrine equivalent · **Comparison:** Recommend it at 0.4 µg/kg/min, and not below that ·

Outcome: 28-day all-cause mortality

RESULTS

- Among patients reaching 0.07 µg/kg/min, vasopressin use was 68.0% vs 42.7%, started at a median 0.14 vs 0.34 µg/kg/min and 0.8 hours sooner. Strict adherence 45.1% vs 65.6%.

- 90-day mortality 37.9% vs 38.4%; new KRT 8.1% vs 8.3%. New or persistent cardiogenic shock 7.4% vs 6.3% (adjusted OR 1.19, 95% CI 1.01 to 1.42; NNH about 91), one of 17 safety outcomes without multiplicity adjustment.
- Reverse fragility index (unadjusted, Fisher exact, alpha 0.05): 34 fewer deaths under the lower threshold would make the crude difference significant. The trial's own analysis is a cluster-adjusted model.

CAVEATS

- The trial tests a recommendation as clinicians used it; higher-threshold recipients started at a median 0.34 µg/kg/min, compressing the contrast, and the time difference was under an hour.
- Observed intracluster correlation (0.021) was seven times the assumed value and one hospital enrolled 1,429 patients, so power may have been lower than planned; a small benefit is not excluded.
- Open label, one integrated US health system, and slightly more stress-dose corticosteroid use under the lower threshold.

How it fits. International guidelines suggest adding vasopressin as norepinephrine doses escalate, without a set trigger. VASST was neutral, and its less severe subgroup and observational studies (including OVISS and target trial emulations) favoured early use. In the accompanying JAMA editorial, Pirracchio and Seymour accept the neutral answer and argue that a single norepinephrine threshold is the wrong frame, calling for dynamic, personalized strategies tested in SMART or reinforcement learning designs; both coauthored OVISS.

3. SAVE-ICU: isoflurane-based sedation did not lower mortality in hypoxemic respiratory failure

CONFIRMS PRACTICE Jerath et al, JAMA 2026 · Pragmatic RCT, 14 Canadian ICUs, 780 adults · Certainty: **Moderate** · [PDF](#) · [Briefing](#)

Bottom line. In ventilated adults with acute hypoxemic respiratory failure (AHRF), an isoflurane-based inhaled sedation strategy did not reduce hospital mortality compared with usual intravenous sedation: 161/379 (42.5%) vs 171/390 (43.8%), RR 0.98 (95% CI 0.84 to 1.14), absolute difference -1.37 percentage points (95% CI -8.37 to 5.64). Ventilator-free days did not differ, and secondary outcomes leaned against isoflurane.

Population: Ventilated adults with AHRF (PaO₂:FIO₂ below 300 mm Hg, or COVID-19), sedated under 72 hours • **Intervention:** Isoflurane prioritized as sole sedative, intravenous adjuncts allowed • **Comparison:** Usual intravenous sedation, analgesia first • **Outcome:** All-cause hospital mortality

RESULTS

- Rescue hypoxemia therapies 63.9% vs 55.0%, difference 8.89% (95% CI 1.95% to 15.83%; NNH about 11). Delirium- and coma-free days median 2 vs 4, driven by longer coma.
- Adverse events 9.1% vs 4.3% (NNH about 21). All 5 serious adverse events occurred with inhaled sedation, including 2 unrecognized intracranial pathologies with raised intracranial pressure and 1 propofol infusion syndrome.
- Reverse fragility index (unadjusted, Fisher exact, alpha 0.048): 22 fewer deaths in the inhaled arm would be needed for a significant difference.

CAVEATS

- Open label, with intravenous co-sedation on about half of intervention days (5.2% to 100% across sites), so the trial compares strategies and cannot isolate a drug effect.
- End-tidal agent concentrations, daily doses and full RASS data were not reported; deep sedation (RASS -4 to -5) affected 55.5% to 90.5% of patients on any given day.
- The 10% target effect was optimistic, and harm up to about 5.6 percentage points remains within the confidence interval. Secondary outcomes were not adjusted for multiplicity.

How it fits. SESAR (sevoflurane in ARDS) found fewer ventilator-free days and higher mortality; SAVE-ICU does not reproduce that harm in a less COVID-heavy population (26% vs 55% COVID-19). In the accompanying JAMA editorial, Jabaudon, the SESAR lead author, writes that missing agent concentrations, co-sedation and deep sedation prevent separating drug effect from oversedation, and that inhaled sedation is not yet a first-line replacement for intravenous regimens; he discloses ties to Sedana Medical. In an Editor's Note, McEvoy and Seymour value the pragmatic design, size and community enrolment, while noting limited RASS recording.

4. Advanced weaning modes: NAVA and PAV reduce asynchrony, with outcome gains resting on few patients

WATCH Sella et al, Crit Care 2026 (in press) • Network meta-analysis, 23 RCTs, 3,755 adults • Certainty: **Low** • [PDF](#) • [Briefing](#)

Bottom line. Against pressure support ventilation (PSV), neurally adjusted ventilatory assist (NAVA) and proportional assist ventilation (PAV) reduced severe asynchrony (RR 0.38, 95% CI 0.16 to 0.89, and RR 0.06, 95% CI 0.00 to 0.97). NAVA was associated with higher weaning success (RR 1.13, 95% CI 1.00 to 1.48, low certainty) and lower hospital mortality (RR 0.59, 95% CI 0.40 to 0.86), from a node of 252 patients with no 28-day mortality signal. Adaptive support ventilation (ASV) and SmartCare/PS showed no outcome benefit.

Population: Adults in the weaning phase of invasive ventilation • **Intervention:** NAVA, PAV or PAV+, ASV or IntelliVent-ASV, SmartCare/PS • **Comparison:** PSV • **Outcome:** Weaning success (spontaneous breathing trial or extubation success)

RESULTS

- With NAVA, ventilation duration MD -4.95 days (95% CI -9.32 to -0.59) and 28-day ventilator-free days MD 4.35 (95% CI 0.52 to 8.18). PAV weaning success RR 1.12 (95% CI 1.00 to 1.25), moderate certainty.
- No significant differences in reintubation, ICU mortality or 28-day mortality; the reintubation and ICU mortality networks have no NAVA arm.
- Absolute event counts are not given in the main text, so no NNT can be derived.

CAVEATS

- Star-shaped network around PSV, so mode-versus-mode rankings are indirect. Weaning success pools breathing trial success with extubation success at 48 hours and 7 days.
- Hospital mortality was one of 11 outcomes with no multiplicity adjustment described; small-study effects could not be tested. No trial was blinded.
- Internal inconsistencies: the NAVA confidence interval differs between abstract and results, and the abstract labels an RR as an MD.

How it fits. Earlier pairwise reviews disagreed, and earlier network analyses either excluded NAVA or omitted asynchrony. In the ventilator-free day network, which includes the recent PAV (Bosma 2025) and closed-loop (Sinnige 2026) trials, PAV and ASV had larger arms than NAVA and showed no effect. No accompanying editorial or external commentary was found.

5. Intraoperative dobutamine during source-control surgery reduced postoperative AKI in septic shock

CONSIDER LOCALLY Chinese Perioperative Septic Shock Investigators, JAMA 2026 • Open-label RCT, 39 Chinese hospitals, 584 adults • Certainty: **Moderate** • [PDF](#) • [Briefing](#)

Bottom line. Adding dobutamine 5 mcg/kg/min to norepinephrine during surgery reduced new or worsening AKI within 7 days from 102/294 (34.7%) to 66/290 (22.8%), adjusted RR 0.64 (95% CI 0.49 to 0.83), risk difference - 11.94 percentage points (95% CI -19.21 to -4.66), NNT about 8. Mortality and KRT did not differ significantly, and tachycardia was more frequent.

Population: Adults with Sepsis-3 septic shock needing source-control surgery of over 1 hour • **Intervention:** Dobutamine 5 mcg/kg/min plus norepinephrine to MAP 65 mm Hg, until the end of surgery • **Comparison:** Norepinephrine alone • **Outcome:** New or worsening KDIGO AKI within 7 days

RESULTS

- 28-day mortality 16.2% vs 20.4% (RR 0.75, 95% CI 0.55 to 1.04); KRT within 7 days 9.0% vs 10.9%. Stage 2 and 3 AKI were lower in post hoc analyses.
- Tachycardia 41.0% vs 29.9% (RR 1.42, 95% CI 1.16 to 1.74; NNH about 9); atrial fibrillation 2.8% vs 2.4%. Cardiac index rose 0.72 L/min/m² more in the monitored subset.
- Fragility index (Fisher exact, alpha 0.05, reported counts): 13; turning 13 non-events into AKI in the dobutamine arm would remove significance.

CAVEATS

- Open label, so anesthesiologists could alter fluids or vasopressors; creatinine drove most diagnoses, which partly mitigates this.
- The control AKI rate (34.7%) fell well short of the assumed 48%, so the observed effect exceeds the hypothesized 25% relative reduction.
- Patients were not selected by cardiac function. Chinese tertiary centres, median weight 60 kg, mainly abdominal sources; medical septic shock was excluded.

How it fits. Surviving Sepsis Campaign guidance suggests dobutamine for cardiac dysfunction with persistent hypoperfusion on very low-certainty evidence, and observational data had linked it to worse kidney outcomes. Prior trials were very small or tested other comparisons (CATS, against epinephrine). No linked JAMA editorial was found; Critical Care Reviews judges the renal signal credible and mortality and dialysis benefit unproven, pending independent confirmation.

6. ADQI and ELSO statements on CRRT during ECMO set protocols, training and quality indicators

CONSIDER LOCALLY Bagshaw et al, Blood Purif 2026 (accepted) · Consensus statement, 12 statements, ADQI XXXVI · Certainty: **Very low** · [PDF](#) · [Briefing](#)

Bottom line. This joint Acute Disease Quality Initiative (ADQI) and Extracorporeal Life Support Organization (ELSO) work group issued 12 statements on CRRT during extracorporeal membrane oxygenation (ECMO). Its firmest positions are organizational: written dual-therapy protocols, interprofessional training and quality measurement. Circuit configuration and anticoagulation are left to patient, device and institutional factors, because comparative evidence is one 80-patient pilot trial and case series.

Population: Neonates, children and adults on venovenous or venoarterial ECMO needing CRRT · **Scope:** Institutional standards, circuit configuration, anticoagulation, performance indicators · **Evidence:** Expert opinion, one pilot RCT, case series and cohorts

RESULTS

- E-CRRT pilot (80 patients, separate vs integrated circuits): median circuit life 72 vs 71 hours, higher access pressures with integration, no difference in adverse events or 28-day mortality; 10 crossovers and no confidence intervals reported.
- Proposed benchmarks: effective treatment time of at least 20 hours per day, downtime under 10%, and circuit lifespan of 60 to 72 hours. Figures show air embolism risk when a dialysis catheter tip sits near a drainage cannula.

CAVEATS

- No search strategy, evidence grading, voting thresholds or agreement levels reported; the literature synthesis was done by two authors.
- Reporting errors: Table 3 cites references absent from the list, and the bleeding definition gives 2 g/L where 2 g/dL is almost certainly intended.
- Pediatric-heavy panel; two authors disclose ties to the maker of the CRRT platform used in the pilot trial. Impella and other temporary MCS are outside its scope.

How it fits. Neither KDIGO nor ELSO previously had comprehensive guidance on combining the two therapies, and the forthcoming KDIGO AKI update will include an ECMO section. AKI occurs in 40 to 80% of ECMO patients, and RRT on ECMO is associated with a 3 to 4-fold higher risk of death, possibly reflecting illness severity. No external commentary was found.

7. Phenobarbital vs diazepam for alcohol withdrawal: no meaningful difference in stay or ventilation

CONFIRMS PRACTICE Bradley et al, JAMA Intern Med 2026 · Target trial emulation, 754 US hospitals, 24,643 adults · Certainty: **Low** · [PDF](#) · [Briefing](#)

Bottom line. Among adults admitted with alcohol withdrawal syndrome (AWS), starting phenobarbital instead of diazepam on the admission day gave a marginal length of stay of 4.1 vs 4.3 days (difference -0.21 days, 95% CI -0.42 to 0.00) and an invasive ventilation risk of 3.1% vs 2.7% (risk difference 0.4%, 95% CI -0.7% to 1.4%). Delirium, ICU transfer, mortality and cost were similar.

Population: Adults with present-on-admission AWS in the Premier database, 2022 to 2024 · **Intervention:** Phenobarbital started on the admission day · **Comparison:** Diazepam started on the admission day · **Outcomes:** Hospital length of stay; invasive ventilation

RESULTS

- Self-directed discharge 9.5% vs 12.6% (risk difference -3.1%, 95% CI -4.9% to -1.3%; NNT about 32), the only secondary outcome that differed.
- Monotherapy subgroup: length of stay 3.8 vs 4.2 days (difference -0.46, 95% CI -0.75 to -0.17). No effect modification by liver disease, and negative control outcomes were null.

CAVEATS

- Observational, with a sicker phenobarbital group (initial ICU care 21.9% vs 9.8%; ventilated on the admission day 2.9% vs 0.7%) and no CIWA scores.
- Dose, loading and route were unknown; about two thirds also received another benzodiazepine on day one, and about half later received midazolam or lorazepam.
- Seizures (12 events) and deaths were too rare to compare, and outcomes rest on administrative codes.

How it fits. Pathway studies showing shorter stays with phenobarbital mostly compared it with lorazepam; this is a large direct comparison with a long-acting benzodiazepine, and no randomized trial in severe hospitalized AWS exists. The accompanying editorial by Dempsey and Anderson, available only in part, describes rapid adoption of phenobarbital on surprisingly limited evidence, with few comparisons against long-acting benzodiazepines.

8. Conservative oxygen after cardiac arrest: no survival or neurological benefit, and more hypoxemia

CONFIRMS PRACTICE Khan et al, Acad Emerg Med 2026 · Meta-analysis, 11 RCTs, 4,136 adults · Certainty: **Moderate** · [PDF](#) · [Briefing](#)

Bottom line. Across 11 trials including LOGICAL, restrictive oxygen targets after cardiac arrest did not reduce all-cause mortality (1,033/2,052 vs 1,016/2,025; RR 0.96, 95% CI 0.88 to 1.06; moderate certainty) or unfavourable neurological outcome (RR 0.96, 95% CI 0.88 to 1.04; low certainty). Hypoxemic episodes were more frequent: 549/1,464 vs 339/1,420, RR 1.65 (95% CI 1.41 to 1.92), high certainty.

Population: Adults resuscitated from cardiac arrest receiving invasive ventilation · **Intervention:** Conservative or restrictive oxygen targets · **Comparison:** Higher or usual-care oxygen · **Outcomes:** All-cause mortality; unfavourable neurological outcome

RESULTS

- Hypoxemic episodes in 37.5% vs 23.9% of patients from pooled crude counts (NNH about 7).
- Strict hypothermia subgroup mortality RR 0.77 (95% CI 0.62 to 0.96) vs normothermia RR 1.00 (95% CI 0.92 to 1.09), interaction $P = .02$; trial sequential analysis did not confirm the benefit.
- Ventilator-free days to day 28 MD 2.14 (95% CI 0.14 to 4.14), from 2 trials; ventilation duration and ICU stay unchanged.

CAVEATS

- Pools prehospital trials of 17 to 61 patients with large ICU oxygen saturation target trials, and control arms in the largest trials avoided severe hyperoxemia.
- The hypothermia subgroup tracks trial era and size, and the trials in each temperature stratum are not named.
- Table 1 rows for EXACT and the HOT-ICU substudy appear transposed; any effect on pooled data is unknown.

How it fits. Guidelines recommend titrating after the first blood gas following return of spontaneous circulation, avoiding both hypoxemia (SpO₂ below 90%) and severe hyperoxemia, and BOX and EXACT found no benefit from lower targets. This update roughly doubles the randomized sample of earlier neutral meta-analyses. The authors reject reading the result as evidence that severe hyperoxemia is safe. No external commentary on this meta-analysis was found.

9. Candidemia in the ICU: early adequate antifungal therapy was not associated with survival

CONSIDER LOCALLY Wozniak et al, Crit Care 2026 (in press) · Pooled cohort, 158 centres, 272 adults · Certainty: **Very low** · [PDF](#) · [Briefing](#)

Bottom line. Among ICU patients with hospital-acquired candidemia who survived 48 hours after the index culture, an active, adequately dosed antifungal within 2 days was not associated with 28-day mortality: crude 40.9% vs 37.0%, inverse probability weighted HR 1.23 (95% CI 0.82 to 1.83). Severity (SOFA, HR 1.13 per point) and unachieved source control (HR 2.11, 95% CI 1.09 to 4.09) were associated with death.

Population: Adults with ICU hospital-acquired *Candida* bloodstream infection · **Exposure:** Active, adequately dosed antifungal within 2 days of the culture · **Comparison:** Later, inadequate or no therapy · **Outcome:** 28-day in-hospital mortality

RESULTS

- Treated patients were sicker: SOFA 9 vs 8, hypotension 52.0% vs 36.2%. Frailty models gave HR 1.27 and 1.29, both with intervals crossing 1.
- Subgroups were imprecise: hypotension HR 1.58 (95% CI 0.89 to 2.81); *C. glabrata* HR 0.44 (95% CI 0.15 to 1.29). A 1-day window also showed no association.

CAVEATS

- Confounding by indication: colonization, prior antifungals, risk scores and rapid diagnostics were unavailable.
- Only 105 deaths, and the interval does not exclude a modest benefit. The 48-hour landmark removed 18 early deaths, the patients in whom timing could matter most.
- The comparator mixes day-3 treatment with no treatment, and EUROBACT-1 data are 15 years old.

How it fits. The case for early therapy rests on older retrospective cohorts, many outside the ICU, while several ICU series found no clear benefit; guidelines favour rapid treatment when candidemia is suspected. Only a randomized trial of empiric versus deferred therapy could resolve the confounding. No external commentary was found.

10. PProFLUID: most fluid in ventilated patients is maintenance and drug-carrier volume

CONSIDER LOCALLY Blok et al, JAMA 2026 · Prospective cohort, 206 ICUs in 41 countries, 2,454 adults · Certainty: **Moderate** · [PDF](#) · [Briefing](#)

Bottom line. In invasively ventilated adults, median input over the first 3 days was 2.8 L per study day (1.8 mL/kg/h), below the 3 mL/kg/h restrictive threshold, with balance near neutral by day 2 or 3. Maintenance or replacement fluid (31.9%) and creep fluid used to carry drugs and keep lines open (30.9%) supplied almost two thirds of volume, and resuscitation 16.0%. Case-mix-adjusted volume ranged from 2.1 to 3.9 L per day between ICUs.

Population: Adults ventilated within 3 days of ICU admission for at least 24 hours · **Exposure:** Usual-care fluid therapy, all sources recorded · **Comparison:** None (descriptive) · **Outcomes:** Volume, balance, indication and type of fluid

RESULTS

- Severity changed volume little: 2.7 L per day in the mildest SOFA tertile vs 2.9 L in the most severe. Cardiogenic shock (73 patients) received 1.4 mL/kg/h.
- Balanced crystalloids made up 48.9% of intravenous fluid and 0.9% saline 27.0%; the site share of balanced solutions ranged from 20.3% to 96.7%.
- ICU mortality was 32.3%; no associations between fluid dose and outcomes were reported.

CAVEATS

- Descriptive: it cannot show that maintenance, creep or liberal site practice causes harm.

- Prehospital, emergency department and pre-intubation fluids were not recorded, which likely lowers the resuscitation share.
- A median of 10 patients per ICU, few North American patients (116), and participating units may have a special interest in fluids.

How it fits. FACTT, CLASSIC and CLOVERS established that restrictive strategies are at least as safe as liberal ones, and earlier international studies described resuscitation fluids. A 2018 single-centre study (Van Regenmortel) showed maintenance and creep fluids outweigh resuscitation, and PROFLUID extends this across six continents. No accompanying editorial or external commentary was found.

Pattern of the week. Three large pragmatic trials this week tested choices ICU teams make every day: which dialysis modality to start, when to add vasopressin and which sedative to run. Two (VASSPR and SAVE-ICU) were neutral on mortality, with confidence intervals that exclude large effects, and one (ICRAKI) was stopped early for higher mortality with an option long regarded as interchangeable. PROFLUID adds that much of what ventilated patients receive is the volume around the active therapy: maintenance fluid and drug carriers.

Issue 775: 96 items catalogued; 10 ranked articles briefed, all from the full-text articles, plus 17 editorial and commentary summaries. Not summarized: Martin-Loeches, Sepsis without borders (J Intensive Med), full text blocked by a publisher bot check. Prepared with AI assistance.

References

1. Gaudry S, Boubaya M, Louis G, Chaïbi K, de Montmollin E, Bohé J, et al; ICRAKI Trial Group. Intermittent or continuous renal-replacement therapy in acute kidney injury. *N Engl J Med*. 2026. doi:10.1056/NEJMoa2608397
2. Peltan ID, Groat D, Jacobs JR, Tillman EH, Klippel C, Brintz BJ, et al. Effect of vasopressin initiation threshold on septic shock mortality: the VASSPR cluster crossover randomized strategy trial. *JAMA*. 2026. doi:10.1001/jama.2026.21333
3. Jerath A, Slessarev M, Martin C, D'Aragon F, Carrier FM, Senaratne J, et al; SAVE-ICU Investigators and the Canadian Critical Care Trials Group. Isoflurane-based inhaled sedation in mechanically ventilated adults with acute hypoxemic respiratory failure: the SAVE-ICU randomized clinical trial. *JAMA*. 2026. doi:10.1001/jama.2026.18471
4. Sella N, De Cassai A, Bassi M, Congedi S, Dissegna P, Edoni F, et al. Advanced assisted ventilation modes for weaning from invasive mechanical ventilation in adult patients: a systematic review and network meta-analysis of randomized controlled trials. *Crit Care*. 2026. doi:10.1186/s13054-026-06387-x
5. Chinese Perioperative Septic Shock Investigators for the Chinese Peri-Operative Organ Protection Group. Intraoperative dobutamine plus norepinephrine to prevent postoperative acute kidney injury in septic shock: a randomized clinical trial. *JAMA*. 2026. doi:10.1001/jama.2026.21322
6. Bagshaw SM, Antonini MV, Lepage-Farrell A, McMullan DM, Mottes T, Gist KM, et al. Best practices in performing CRRT during ECMO: workgroup statements from the joint Acute Disease Quality Initiative (ADQI) and Extracorporeal Life Support Organization (ELSO) consensus conference on ECMO, AKI, fluid management and CRRT. *Blood Purif*. 2026. doi:10.1159/bpu/abpag023
7. Bradley T, Feeney M, Law AC, Peterkin AF, Fantasia KL, Walkey AJ, et al. Comparative effectiveness of phenobarbital vs diazepam for alcohol withdrawal syndrome. *JAMA Intern Med*. 2026. doi:10.1001/jamainternmed.2026.4939
8. Khan MM, Saboor A, Aqil M, Jan R, Hanif R, Muiz A, et al. Conservative versus higher oxygen targets post-cardiac arrest: a systematic review, meta-analysis, and trial sequential analysis. *Acad Emerg Med*. 2026;33(10):e70422. doi:10.1111/acem.70422
9. Wozniak H, Tabah A, Bassetti M, Laupland K, Paiva JA, Ruckly S, et al. Early adequate empiric antifungal therapy and 28-day mortality in ICU patients with candidemia: a pooled patient-level analysis of EUROBACT-1 and EUROBACT-2 cohorts. *Crit Care*. 2026. doi:10.1186/s13054-026-06373-3
10. Blok SG, de Grooth HJ, Pisani L, Barbas C, Chew M, Dubin A, et al; PROFLUID Investigators. Fluid therapy in mechanically ventilated critically ill adult patients. *JAMA*. 2026. doi:10.1001/jama.2026.21291