

Session 1 (ASK): Solutions and facilitation notes

Foundations of Clinical Research · Level 1 · Neudata · Instructor copy. Do not share before the session.

These are **model** answers. Many other answers are acceptable: reward work that is specific, consistent and could be acted on. The course is online and the whole class works as one group: use the "what good looks like" boxes when you read the chat and when you type the class answer on the shared screen.

Quick quiz (segment 1.1): Rank the evidence (poll)

Answer (weakest to strongest): A (expert opinion), then B (registry cohort), then C (randomised trial, CLASSIC), then D (systematic review / meta-analysis of trials). Poll option 1: "A, B, C, D".

Source	Design	Real example
A	Expert opinion	None
B	Observational cohort	Similar to Paper 2: Hyun 2023, <i>Ann Intensive Care</i> . Positive cumulative fluid balance on ICU days 2–3 associated with higher 28-day mortality (day 2 cohort HR 2.13, 95% CI 1.48–3.06)
C	Randomised controlled trial	CLASSIC: Meyhoff et al., <i>N Engl J Med</i> 2022. 1,554 ICU adults with septic shock; 90-day mortality 42.3% restrictive vs 42.1% standard
D	Systematic review / meta-analysis	Pooled analyses of fluid-restriction trials

Discussion points (chat)

- What could make C weaker than B? Very small size, many losses to follow-up, poor allocation concealment, an outcome that does not matter to patients, or a population unlike ours.
- Why might B and C disagree? In a cohort, sicker patients receive more fluid, so fluid can look harmful even if it is not. This is **confounding by indication** (taught in Session 4). Randomisation removes this.
- The pyramid ranks **designs**, not individual papers. Quality must still be checked (Session 8).

Check your understanding (segment 1.1): types of research (chat)

Item	Answer
A Counting patients with septic shock who are fluid-positive on day 3 this year	Quantitative, primary
B Interviewing ICU nurses about why they hesitate to stop IV fluids	Qualitative, primary
C Re-analysing 3 years of ICU records for fluid balance and death	Quantitative, secondary (data already exist; still needs ethics review)

Item	Answer
D Survey of fluid prescribing + focus groups with doctors	Mixed methods, primary

Check your understanding (segment 1.2): spot the PICO in Paper 1's question (poll + chat)

"In adults with septic shock in the first 24 hours of vasopressors, does restricting non-resuscitative fluids, compared with usual care, reduce cumulative fluid balance at day 5?"

Poll answer: C, cumulative fluid balance, is the outcome. D (day 5) is the time point; A (septic shock) is part of the population; B is the intervention.

P	I	C	O	T
Adults with septic shock, in the first 24 hours of vasopressors	Restricting non-resuscitative fluids (maintenance fluids and fluids for drug dilution)	Usual care	Cumulative fluid balance (ml/kg)	Day 5

Common error: choosing "septic shock" as the outcome. It has already happened and defines who is eligible (P).

Exercise 1 (whole class): rescue the running example

Use the version the class chose in the poll. If the vote is split, work on A.

Version A: pilot trial (experimental, PICO)

P	Adults with septic shock in our ICU, within 24 h of starting vasopressors
I	Restrictive fluid protocol
C	Usual care
O	Cumulative fluid balance (ml/kg)
T	Day 5

In adults with septic shock in our ICU, does a restrictive fluid protocol, compared with usual care, reduce cumulative fluid balance at day 5?

Type: analytical, experimental (a pilot randomised trial, like Paper 1).

FINER: F green/amber (about 50 patients over 12–18 months) · I green · N amber to green (local setting, different protocol) · E amber (deferred or surrogate consent, Session 7) · R green.

H0: cumulative fluid balance at day 5 is the same in both groups. H1: it differs.

Version B: cohort (observational, PECO)

P	Adults with sepsis or septic shock admitted to our ICU
E	Positive cumulative fluid balance by day 3 (Exposure: we do not assign it)
C	Neutral or negative cumulative fluid balance by day 3
O	Death from any cause
T	By day 28

In adults with sepsis in our ICU, is a positive cumulative fluid balance by day 3, compared with a neutral or negative balance, associated with higher 28-day mortality?

Type: analytical, observational. This is Paper 2's question and the main question of the FLUID-ICU course study (Session 5).

FINER watch-points: F depends on patient numbers and on records of daily fluid balance; confounding by indication (sicker patients get more fluid) must be handled (Session 4).

H0: 28-day mortality is the same in patients with and without a positive fluid balance by day 3. H1: it differs.

Version C: descriptive (P + O)

P	Adults with septic shock admitted to our ICU over 6 months
O	Positive cumulative fluid balance
T	On ICU day 3

What proportion of adults with septic shock in our ICU have a positive cumulative fluid balance on day 3?

Type: descriptive. No hypothesis is needed: we **estimate** a proportion with its 95% CI.

FINER: F green (routine charts) · N amber (local data are new) · E green (usually low risk; still needs approval for records) · R green (shows whether the problem exists here).

What good looks like (Exercise 1)

- All boxes filled; the comparison is named, not "nothing".
- One primary outcome, **measurable**, with a **time point**.
- The sentence reads naturally and contains every PICO element.
- Common faults to correct: two outcomes in one question ("mortality and length of stay"); outcome without time; population too broad ("all patients"); intervention not defined ("better care").

Exercise 2 (individual): aim, objectives and hypothesis for the pilot

- *Aim:* To compare a restrictive fluid protocol with usual care in adults with septic shock in our ICU.

- **Objectives:** Primary: to compare cumulative fluid balance (ml/kg) at day 5 between groups. Secondary: to estimate the recruitment rate and protocol adherence (feasibility). (Optional third: to describe 28-day mortality and kidney injury needing dialysis in each group, exploratory.)
- **Hypothesis:** H0: cumulative fluid balance at day 5 is the same in both groups. H1: it differs.
- **Descriptive version C (no hypothesis):** To estimate the proportion of adults with septic shock in our ICU who have a positive cumulative fluid balance on day 3.

Vague-verb check (exit question 2): rewrite "To understand fluid balance in our ICU" as "To estimate the proportion of adults with septic shock in our ICU who have a positive cumulative fluid balance on day 3."

What good looks like

- H0 always states "no difference / no association".
- H1 is usually written as "differs" (in either direction), even when we expect benefit, because the intervention could also harm. One- vs two-sided tests are taught in Session 6.
- The hypothesis uses the **same** outcome and time point as the primary objective.
- Correct the misconception: data can **reject** H0 or **fail to reject** it; we never "prove H0". "No significant difference" is not "no difference" (Paper 1, n = 48, could not detect a mortality difference because it was not powered for it).

Exercise 3 (individual): Proposal builder 1, what good looks like

The trainer models Part 1 on screen for the pilot version (A) of the running example; each participant then writes Part 1 for their own question. Use this model as the quality benchmark, not as the answer. The references, problem statement and title are added next Saturday (Session 2).

PICO(T): P adults with septic shock within 24 h of starting vasopressors · I restrictive fluid protocol · C usual care · O cumulative fluid balance (ml/kg) · T at day 5.

Question: *In adults with septic shock in our ICU, does a restrictive fluid protocol, compared with usual care, reduce cumulative fluid balance at day 5?*

FINER: F green/amber (pilot of about 50 patients over 12–18 months) · I green · N amber to green (local setting, different protocol) · E amber (deferred or surrogate consent, Session 7) · R green.

Aim: To compare a restrictive fluid protocol with usual care in adults with septic shock in our ICU.

Objectives:

1. (Primary) To compare cumulative fluid balance (ml/kg) at day 5 between groups.
2. To estimate recruitment rate and protocol adherence (feasibility).
3. To describe 28-day mortality and kidney injury needing dialysis in each group (exploratory).

Hypothesis: H0: cumulative fluid balance at day 5 is the same in both groups. H1: it differs.

Feedback guide when reading drafts (not a grade)

Element	Good	Needs work
Topic	One focused problem from the participant's department	Three problems merged; "improve care in the ICU"

Element	Good	Needs work
Question	All PICO(T) elements; one primary outcome with time point	Two outcomes; no comparison; vague population
FINER	Each letter justified; red letters fixed	Ticked without thought
Aim/objectives	One aim; 2–3 measurable objectives; primary marked	"To understand...", "to study..."; more than 4 objectives
Hypothesis	Matches primary objective; H0 and H1; or correctly "descriptive"	Hypothesis about a different outcome

Exercise 4: Synonym list (homework)

Model for the running example: **P** septic shock · sepsis · vasopressor-dependent sepsis; **I** fluid restriction · restrictive fluid · conservative fluid · de-resuscitation; **O** mortality · death · survival.

Exit question: answers

1. **Feasible.** A mortality outcome needs well over a thousand patients (Novel is also amber because large trials already exist).
2. e.g. *"To estimate the proportion of adults with septic shock in our ICU who have a positive cumulative fluid balance on day 3."*

Extra practice (optional, at home): model answers

A. Scenarios: model PICO(T) answers

Scenario A: Ventilator-associated pneumonia (experimental). P adults on invasive mechanical ventilation for ≥ 48 h in the ICU · I twice-daily nurse checklist for head-of-bed elevation 30–45° · C usual care (no checklist) · O ventilator-associated pneumonia (stated definition) · T up to ICU day 28.

In adults ventilated for at least 48 hours in the ICU, does a twice-daily nurse checklist for head-of-bed elevation, compared with usual care, reduce the incidence of ventilator-associated pneumonia by ICU day 28? FINER watch-point: **F** (VAP definitions vary and VAP is not very common).

Scenario B: Pressure injuries (descriptive first). *What is the incidence of hospital-acquired pressure injuries (stage 2 or worse) among adults admitted to our medical ward over 6 months?* P adults admitted to the medical ward · O new pressure injury, stage 2 or worse · T during the admission, over 6 months. Descriptive: no hypothesis; estimate incidence with a 95% CI. Later analytical question: *does 2-hourly vs 4-hourly repositioning reduce new pressure injuries in at-risk adults?*

Scenario C: Delirium (experimental). P adults aged 65+ after hip-fracture surgery · I daily multicomponent non-drug delirium-prevention bundle · C usual care · O incident delirium (validated tool, e.g. 4AT or CAM) · T first 7 postoperative days. FINER watch-points: **E** (consent from patients who may become confused) and **F** (staff time).

Scenario D: Stroke door-to-needle time (observational, PECO). P adults with acute ischaemic stroke receiving thrombolysis in our emergency department · E pre-hospital ambulance alert · C no

pre-alert · O door-to-needle time (minutes) · T from arrival to start of thrombolysis. The outcome is continuous, so the hypothesis is about a difference in median or mean time.

Scenario E: Medication errors (experimental or before–after). P adults transferred from ICU to a general ward · I pharmacist-led medication reconciliation at transfer · C usual transfer process · O patients with at least one medication discrepancy · T within 48 hours of transfer. Watch-point: define "medication error"; one primary outcome only.

B. FINER: model answers

#	Main problem	Why
1	Feasible	Whole country, 10 years, mortality: far beyond any department's resources. (Large vitamin D trials already exist too, so Novel also fails.)
2	Ethical	Withholding antibiotics in septic shock causes harm; there is no equipoise. An ethics committee would refuse it.
3	Novel	The answer is already measured monthly. This is an audit question rather than a research question, so use the existing data.
4	Relevant (and Interesting)	No plausible mechanism and no impact on practice.

These are also on an extra slide ("More practice: which FINER letter fails?").

C. Hypotheses

a) Early mobilisation. H0: ICU length of stay is the **same** with early mobilisation and with usual care. H1: ICU length of stay **differs** between early mobilisation and usual care.

b) Proportion with positive fluid balance. No hypothesis needed. This is descriptive: we *estimate* a proportion with its 95% confidence interval.

Extra slides: research, audit or QI? (answers)

Project	Answer	Ethics route
Checking whether fluid balance is charted daily, against the unit protocol	Audit	Local/clinical-governance approval; usually no ethics committee
Testing a daily fluid-balance checklist in PDSA cycles	Quality improvement	Local approval; ethics review if it adds risk or goes beyond routine care
Randomising patients to restrictive or usual fluids	Research	Ethics committee approval + trial registration before the first patient
Interviewing nurses about why they hesitate to stop fluids	Research (qualitative)	Ethics committee approval (consent, confidentiality)

Project	Answer	Ethics route
Reviewing 3 years of ICU records to see if fluid balance is linked to mortality	Research (secondary data, observational)	Ethics committee approval or a formal waiver of consent

Key point: rules differ between institutions. When in doubt, ask the ethics committee **before** starting; journals ask for approval or a waiver at submission.