Quiz: What is my bias?

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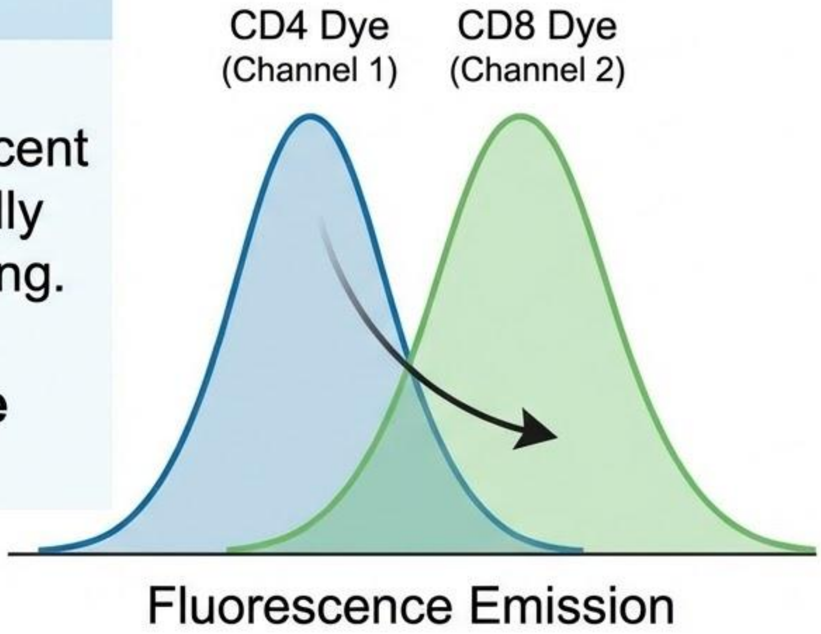
Flow Cytometry Scenario: Signal Spillover & Bias

Scenario:

A researcher measures CD4 and CD8 expression in T cells using two fluorescent dyes. The CD8 signal appears artificially high in samples with strong CD4 staining.

What type of bias is this, and can it be solved by randomization?



Solution: Measurement Bias & Mitigation.

Bias Type:

Measurement bias (systematic instrument artifact)

Does randomization solve it?

❌ No. The measurement system itself is biased.

Mitigation Strategies:

- Single-color controls
- Compensation matrices
- Spectral unmixing models

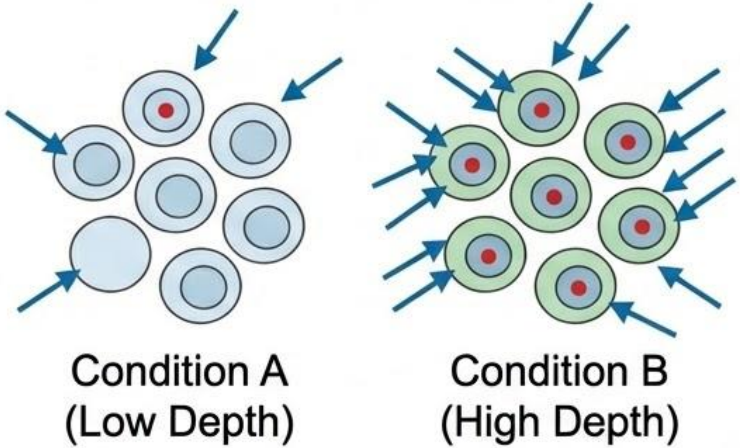
Single-cell RNA-seq: Dropout and Detection Bias

Context:

In Single-cell RNA sequencing, individual cells are sequenced. Many expressed genes are not detected due to low capture efficiency — producing excess zeros (“dropout”).

Scenario:

Gene X appears absent in 60% of cells in condition A but only 20% in condition B. However, condition A had lower sequencing depth.



Solution: Detection Bias & Mitigation.

Bias Type:

Measurement bias (detection bias due to technical sensitivity)

Does randomization solve it?

❌ No. Randomizing cell order does not fix detection inefficiency.

Mitigation Strategies:

- Depth normalization
- Imputation models
- Zero-inflated models
- Improved library prep.

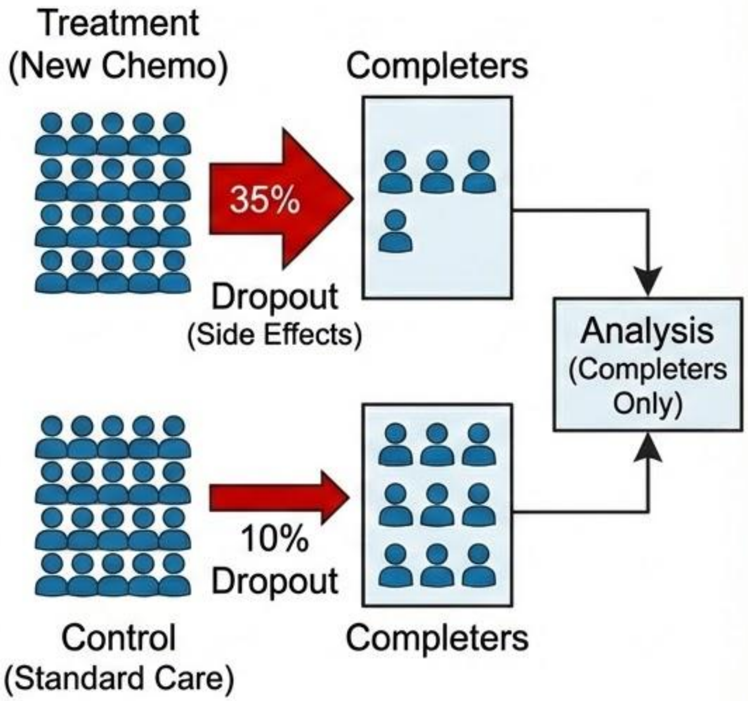
Clinical Trial Scenario: Attrition Bias

Context:

A randomized trial compares a new chemotherapy vs standard care. Patients with severe side effects are more likely to drop out.

Scenario:

Dropout rate is 35% in the treatment arm, 10% in control. Final analysis only includes completers.



What type of bias is this, and can it be solved by randomization?

Solution: Attrition Bias & Mitigation.

Bias Type:

Attrition bias (selection bias due to differential dropout post-randomization).

Does randomization solve it?

❌ No. Randomization balances baseline characteristics, but not post-randomization dropout, which is often related to the treatment itself.

Mitigation Strategies:

- Intention-to-Treat (ITT) analysis
- Imputation methods for missing data
- Sensitivity analysis
- Improved trial design to minimize dropout.

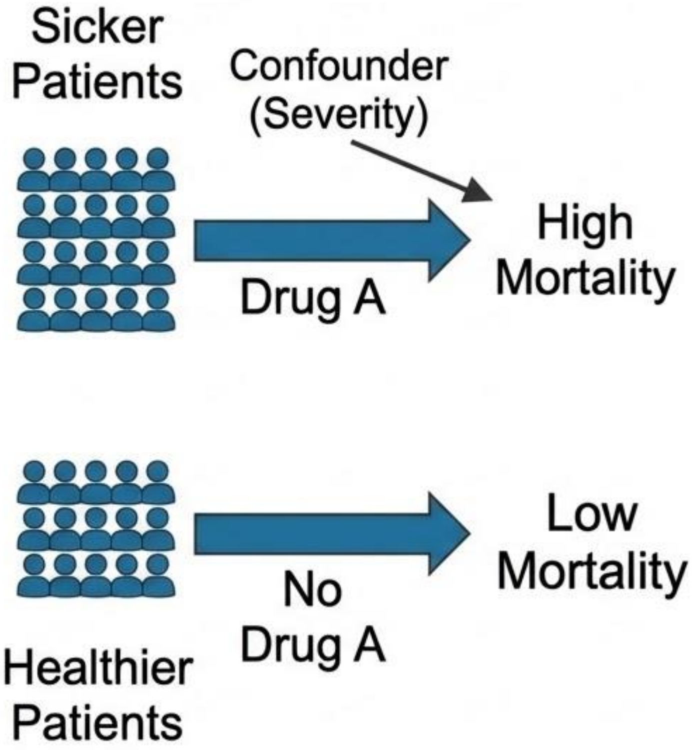
Problem: Confounding by Indication

Context:

In observational pharmacoepidemiology, sicker patients often receive stronger treatments.

Scenario:

Patients receiving Drug A have higher mortality than those not receiving it. Drug A is usually given only to the sickest patients.



Solution: Confounding by Indication & Mitigation

Bias Type:

Confounding by indication (confounding bias)

Does randomization solve it?

✅ Yes — in a randomized trial.
❌ No — in observational data unless adjusted.

Mitigation Strategies:

- Randomized controlled trial
- Propensity score matching
- Regression adjustment.

Problem: Immortal Time Bias

Context:

In survival analysis, “immortal time” refers to a period where outcome cannot occur by design.

Scenario:

A study claims patients receiving a transplant live longer. But patients must survive long enough to receive the transplant.

Solution: Immortal Time Bias & Mitigation

Bias Type:

Immortal time bias (time-dependent selection bias)

Does randomization solve it?

✓ Yes — if properly designed.
✗ No — in naive retrospective studies.

Mitigation Strategies:

- Time-dependent Cox models
- Proper risk set definition.

Problem: Collider Bias in Biomarker Studies

Context:

Researchers analyze only hospitalized COVID patients.

Scenario:

Among hospitalized patients, smokers appear less likely to die. But hospitalization is influenced by both smoking and severity.

Solution: Collider Bias & Mitigation

Bias Type:

Collider bias (selection bias via conditioning on a collider)

Does randomization solve it?

❌ No, not if conditioning on collider remains. Proper design avoids conditioning on post-exposure variables.

Mitigation Strategies:

- Avoid conditioning on common effects
- Causal diagrams (DAGs).

Problem: Misclassification Bias (Non-Differential)

Context:

Disease status determined via imperfect antibody test (90% sensitivity).

Scenario:

Some true positives are classified as negative equally across groups.

Solution: Misclassification Bias & Mitigation

Bias Type:

Measurement bias (non-differential misclassification)

Does randomization solve it?

❌ No.

Mitigation Strategies:

- Correct for sensitivity/specificity
- Bayesian measurement models.

Problem: Differential Misclassification

Context:

Side effects are self-reported.

Scenario:

Patients receiving the new drug are more carefully monitored, leading to higher reported side effects.

Solution: Differential Misclassification & Mitigation

Bias Type:

Detection bias (differential misclassification)

Does randomization solve it?

❌ Not automatically. Monitoring intensity must be equal.

Mitigation Strategies:

- Blinding
- Standardized outcome assessment.

Problem: Overadjustment Bias

Context:

Researcher adjusts for a mediator.

Scenario:

Study of obesity → diabetes adjusts for insulin resistance (which lies on causal path).

Solution: Overadjustment Bias & Mitigation

Bias Type:

Overadjustment bias

Does randomization solve it?

❌ Not if model incorrectly adjusts.

Mitigation Strategies:

- Use DAGs
- Adjust only for confounders.