

## □ Confounding by Indication – Simple Definition:

Confounding by indication is a type of bias that occurs in observational studies when the reason (indication) for prescribing a treatment is related to the outcome being studied.

In other words: patients receive a treatment because they are at higher risk or more severely ill — and that underlying risk (not the treatment itself) influences the outcome.

□ Classic Example: Suppose you're studying whether patients who receive anticoagulants have a higher risk of stroke.

You find that anticoagulant users have more strokes. You might wrongly conclude that anticoagulants cause strokes. But in reality, those patients were prescribed anticoagulants because they already had a higher risk of stroke (e.g., atrial fibrillation).

So the increased stroke rate reflects the underlying condition, not the harmfulness of the drug.

□ Why It Matters in Research: Randomized controlled trials (RCTs) avoid this bias by randomizing treatment.

Observational studies (e.g., cohort, case-control) are vulnerable unless adjustments (like propensity score matching or instrumental variable analysis) are made.

△ Key Point: Confounding by indication is not just any confounding — it specifically refers to confounding caused by the clinical reasoning behind the decision to treat.

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