Unit 5. Research Designs and Terminologies

Unit 5: Research Designs and Terminologies

Learning Goals

By the end of this unit, you will be able to:

- Differentiate **case reports** and **case series** and recognise their role in signal generation.
- Classify studies as **cross-sectional** or **longitudinal**, and choose appropriate measures.
- Plan and appraise **cohort** and **case–control** studies, including control of confounding.
- Understand the architecture of **clinical trials (RCTs)** and their variants.
- Conduct **literary research and reviews** with transparent, reproducible methods.
- Distinguish **preclinical methods**: **in-silico, in-vitro, in-situ, in-vivo**.
- Correctly use core **terminologies**: randomisation, matching, blinding, and bias.

---

1) Case Reports

What it is: A detailed description of an **individual patient** (or a few) highlighting unusual **presentation, diagnosis, management, outcome, or adverse event**.

Why it matters:

- Generates **hypotheses** and **early safety signals** (e.g., suspected herb–drug interaction).
- Teaches **diagnostic reasoning** and documentation quality.
- May describe **novel techniques** (e.g., a modification in *Nasya* administration for a specific anatomical variant).

Key elements (CARE guideline mindset):

- Clear timeline, baseline, differential diagnoses, intervention details (dose, route, *anupāna*), outcomes, follow-up, and informed consent for publication.
- Avoid **causal claims**; emphasise plausibility, not proof.

Strengths/limits: Quick, inexpensive, clinically rich / **no control group**, high risk of bias, cannot estimate frequency or effect size.

---

2) Case Series

What it is: A **descriptive** summary of several similar cases treated or observed in a defined period/place **without a comparator**.

Use:

- Early evaluation of **feasibility**, typical responses, adverse events, procedural refinements.
- Documentation of **service models** (e.g., whole-system Ayurvedic package for osteoarthritis over 12 months).

Cautions:

- Susceptible to **selection** and **publication** bias.
- Do not over-interpret; at best, provides **denominators** and suggests variables for future analytical studies.

PDF generated on 20 Apr 2026, 11:08 pm IST

3) Cross-Sectional and Longitudinal Studies

3.1 Cross-Sectional

Snapshot at one time; measures **prevalence** and associations.

- **Questions:** "How common is *Agni* impairment among OPD attendees?" "Is *Prakṛti* associated with BMI category?"
- **Measures:** Prevalence, mean/median, **prevalence ratio** or **odds ratio** for associations.
- **Strengths:** Fast, economical; useful for planning services.
- **Limits: Temporal ambiguity**—exposure and outcome measured together; cannot estimate incidence.

3.2 Longitudinal

Repeated observation over time; includes **cohort** studies, **panel** studies, and **repeated measures**.

- **Questions:** "What is the **incidence** of dyspepsia after dietary change?" "How do pain scores evolve after *Virechana* across 12 weeks?"
- **Measures:** Incidence rate/risk, **risk ratio (RR)**, **hazard ratio (HR)**; trajectories.
- **Strengths:** Temporal ordering supports causal inference; can assess **change**.
- **Limits:** Cost, **loss to follow-up**, changing exposure definitions.

---

4) Cohort Studies

Design logic: Enrol participants **free of outcome**, classify them by **exposure** (e.g., received *Basti* vs not), and **follow forward** to measure outcome occurrence. Can also be **retrospective** if reliable records exist.

Best for:

- Estimating **incidence** and **relative risk**.
- Studying **multiple outcomes** of one exposure (e.g., benefits and harms of a formulation).

Typical outputs:

- **Risk Ratio (RR)** = risk in exposed / risk in unexposed.
- **Hazard Ratio (HR)** from survival models when time-to-event is key.
- **Absolute Risk Difference** and **Number Needed to Treat/Harm (NNT/NNH)**.

Strengths: Clear temporality, direct computation of risks, multiple outcomes.
Limitations: Confounding by indication, large sample/time for rare outcomes, losses to follow-up.

Bias control:

- **Design:** restriction, **matching**, random sampling, careful exposure definition.
- **Analysis:** multivariable regression, **propensity scores**, inverse-probability weighting, sensitivity analyses.
- **Data quality:** validated outcomes, blinded adjudication when feasible.

---

5) Case–Control Studies

Design logic: Start with **cases** (have outcome) and select **controls** (do not). Look **back** to compare exposure histories.

Best for:

- **Rare outcomes** (e.g., herb-induced liver injury), **long latency** diseases, early signal testing.

Measure: Odds Ratio (OR) ≈ RR when outcome is rare.

- OR = (odds of exposure among cases) / (odds of exposure among controls).

Control selection:

- Should represent the **same source population** as cases.
- **Matching** (age, sex, clinic) can improve efficiency but avoid **overmatching** (don't match on variables in causal pathway).

Strengths: Efficient for rare outcomes, quicker, lower cost.
Limitations: Recall bias, **selection bias**, cannot directly estimate incidence; temporal sequence may be uncertain.

Good practices:

- Pre-define exposure windows; use records where possible to reduce recall bias.
- Use multiple control groups if justified; analyse matched data with appropriate models (e.g., conditional logistic regression).

---

6) Clinical Trials (Randomised Controlled Trials)

Essence: Investigators **assign interventions** by **randomisation** to compare outcomes.

6.1 Trial Taxonomy

- **Explanatory (efficacy) RCTs:** strict eligibility, fixed protocol, intensive follow-up; **high internal validity**.
- **Pragmatic (effectiveness) RCTs:** broad eligibility, flexible delivery in routine care; **high external validity**.
- **Cluster RCTs:** randomise clinics/wards/districts; adjust sample size for **intra-cluster correlation (ICC)**.
- **Stepped-wedge trials:** staggered rollout; all clusters eventually receive intervention.
- **Adaptive/platform trials:** modify arms or add/drop interventions based on interim data under pre-specified rules.

6.2 Core Architecture

- **Prospective registration**; pre-specified **primary outcome** and **analysis plan**.
- **Sample size** based on **MCID**, variance, alpha, and power.
- **Randomisation** (simple, block, stratified, minimisation) with **allocation concealment** (e.g., central randomisation, opaque sequentially numbered envelopes).
- **Blinding** of participants/personnel/outcome assessors where feasible.
- **Intention-to-treat (ITT)** analysis; sensitivity **per-protocol** analysis.
- **Data Safety Monitoring Board (DSMB)** for moderate-to-high-risk trials.
- **CONSORT**-aligned reporting of flow diagram, baseline, outcomes, harms.

6.3 Integrative/Ayurveda-Specific Notes

- **Describe whole-system care**: diagnostic framework (*doṣa, dūṣya, srotas, agni*), components (diet, lifestyle, *Pañcakarma*, formulations with botanical identity, dose, *anupāna*), and fidelity monitoring.
- Use **patient-important outcomes** (pain, function, quality of life) alongside validated **Ayurvedic constructs** (e.g., *Agni* scale), and monitor **herb–drug interactions**.

---

7) Literary Research and Reviews

Purpose: Synthesize **existing knowledge** or critically analyse **classical texts** and modern literature to answer a focused question.

7.1 Types

- **Narrative review:** broad overview; may be selective—useful for orientation but prone to bias.
- **Scoping review:** maps **what evidence exists**, concepts, and gaps; useful when questions are broad or heterogeneous.
- **Systematic review (with/without meta-analysis):** predefined protocol, **comprehensive search**, **risk-of-bias assessment**, and transparent synthesis.
- **Umbrella review:** review of systematic reviews.

7.2 Method (Systematic Mindset)

- Frame a **PICO/PEO** question; register a protocol where applicable.
- Search multiple sources (databases, theses, registries); document strategies.
- Use appropriate **risk-of-bias tools** (e.g., RoB 2 for RCTs, ROBINS-I for non-randomised, QUADAS-2 for diagnostic).
- If meta-analysis is possible, address **heterogeneity** (I^2), use **random/fixed effects** as justified, assess **publication bias** (funnel plots, Egger test).
- Grade certainty (e.g., **GRADE** framework) and present **summary of findings tables**.

7.3 Classical (Ayurveda) Literary Research

- Compare **manuscript variants**, commentaries (e.g., **Dalhaṇa**, **Cakrapāṇi**), and **paryāya (synonyms)** consistently.
- Trace **term evolution** (e.g., *Grahani*, *Pāṇḍu*) across *Saṃhitā* to later *Nighaṇṭu* literature; ensure accurate **botanical mapping** for dravyas.
- Maintain a **citation trail**; avoid selective quoting; document translation decisions.

---

8) Preclinical Methods

Method	Meaning	Typical Uses	Notes
In-silico	Computer-based modelling (QSAR, docking, ADMET, network pharmacology)	Prioritise leads, predict toxicity/interactions	Fast screening; needs experimental validation
In-vitro	Experiments in controlled environment outside a living organism (cell lines, organoids, enzyme assays)	Mechanisms, potency, preliminary toxicity	Standardise extract; ensure assay reproducibility
In-situ	Studies **within** natural tissue/site (e.g., tissue sections, localised measurements)	Localisation of molecules, receptor distribution	Preserves micro-environment; interpret with care
In-vivo	Experiments in **living organisms** (animal models)	Efficacy, safety, PK/PD, dose finding	Follow **3Rs** and **ARRIVE** reporting; justify species/model

Translational flow: in-silico → in-vitro → in-vivo → early clinical → trials → implementation. At each step, ensure **quality assurance** and **replicability** (materials, dose, processing).

---

9) Terminologies: Randomisation, Matching, Blinding, Bias

9.1 Randomisation

Definition: A process that uses **chance** to allocate participants to study arms, ensuring **comparable groups** on both measured and unmeasured factors.

Types:

- **Simple:** like repeated coin toss; risk of imbalance in small samples.
- **Block:** preserves balance within blocks (e.g., size 4/6); keep block size concealed.

- **Stratified:** separate randomisation lists within strata (e.g., site, severity).
- **Minimisation:** dynamic allocation balancing on multiple covariates.
- **Cluster randomisation:** units are clusters (clinics/schools).
- **Adaptive randomisation:** probabilities change using accruing data (pre-specified rules).

Allocation concealment vs blinding: concealment prevents **predicting** the next assignment **before** enrolment; blinding prevents **knowing** the assignment **after** allocation.

9.2 Matching

Definition: Selecting controls (or designing cohorts) so that groups are **similar** on potential confounders.

Types:

- **Individual matching:** one-to-one or many-to-one on variables like age, sex.
- **Frequency matching:** ensure similar **distribution** of a variable across groups.

Cautions:

- Avoid **overmatching** (matching on mediators or strong correlates of exposure that block causal pathways).
- Use **appropriate analysis** (e.g., conditional logistic regression for individually matched case–control studies).

9.3 Blinding (Masking)

Definition: Keeping participants, caregivers, outcome assessors, and/or analysts **unaware** of allocated intervention.

Levels:

- **Single-blind:** usually participant or assessor.
- **Double-blind:** participant **and** key trial personnel.
- **Triple-blind:** extends to data analysts/DSMB (with safeguards).

When blinding is difficult: use **objective outcomes**, **sham controls** where ethical, **central blinded assessment**, or **PROs** with validated instruments.

9.4 Bias

Definition: Systematic error that distorts the estimate away from the truth.

Major families:

- **Selection bias:** differences in who enters/retains in the study (e.g., volunteer bias, loss to follow-up).
- **Information (measurement) bias:** misclassification of exposure/outcome (recall bias, interviewer bias).
- **Confounding:** distortion by a third variable related to both exposure and outcome.

Mitigation:

- **Design:** randomisation, restriction, matching, standardised protocols, pilot testing, allocation concealment, blinding.
- **Analysis:** multivariable adjustment, propensity methods, instrumental variables, sensitivity analyses.
- **Reporting:** pre-registration, adherence to guidelines (CONSORT/STROBE/PRISMA), transparency about deviations.

Quick Selection Guide

Question	Prefer
Unusual clinical phenomenon?	**Case report/series** (signal)

Question	Prefer
How common at a point in time?	**Cross-sectional**
What is the incidence or prognosis?	**Cohort**
What caused a rare outcome?	**Case–control**
Does an intervention work?	**RCT** (pragmatic/explanatory/cluster as suited)
What does literature collectively show?	**Systematic review/meta-analysis**
Mechanism/toxicity before human use?	**Preclinical** (in-silico → in-vitro → in-vivo)

Take-Home Messages

- **Descriptive designs** (case report/series, cross-sectional) generate hypotheses; **analytical designs** (cohort, case–control, trials) test them.
- Choose designs by **question, feasibility, ethics, and risk of bias**, not by habit.
- In trials, **allocation concealment + blinding + ITT** protect validity.
- Literary research demands the same rigour as primary studies: **protocol, comprehensive search, risk-of-bias assessment, transparent synthesis**.
- Preclinical methods are complementary; always plan with **3Rs** and reporting standards.

Assessment

A. Multiple-Choice Questions (MCQs)

1. The most appropriate design to study **risk factors for a rare adverse hepatic event** after a proprietary formulation is:
   A) Cross-sectional
   B) Case–control
   C) Cohort
   D) Case series
   Answer: B
2. In a **cohort** study you can directly estimate:
   A) Incidence and risk ratio
   B) Odds ratio only
   C) Prevalence only
   D) Positive predictive value only
   Answer: A
3. **Allocation concealment** primarily prevents:
   A) Detection bias
   B) Selection bias at enrolment
   C) Recall bias
   D) Confounding
   Answer: B
4. When **individual randomisation may cause contamination** across participants, an appropriate design is:
   A) Case–control
   B) Cluster RCT
   C) Cross-sectional survey
   D) Case series
   Answer: B
5. **Overmatching** occurs when you match on:
   A) Age and sex
   B) A mediator on the causal pathway
   C) A confounder

D) A baseline risk factor unrelated to exposure
Answer: B

6. The **primary measure** in a standard case–control study is:
   A) Risk ratio
   B) Mean difference
   C) Odds ratio
   D) Hazard ratio
   Answer: C
7. **Pragmatic RCTs** are designed mainly to maximise:
   A) Internal validity only
   B) External validity and real-world applicability
   C) Blinding feasibility
   D) Surrogate outcomes
   Answer: B
8. A **scoping review** is most useful when:
   A) There are many homogeneous RCTs
   B) The question is broad and evidence is heterogeneous
   C) Meta-analysis is straightforward
   D) Only one case report exists
   Answer: B
9. **In-silico** methods are primarily used to:
   A) Validate outcomes clinically
   B) Model interactions and prioritise leads
   C) Estimate hazard ratios
   D) Replace all in-vivo work
   Answer: B
10. **Blinding** is least feasible in which trial?
    A) Capsule vs capsule
    B) Sham-controlled procedure
    C) Whole-system lifestyle + Panchakarma package vs usual care
    D) Placebo-controlled analgesic
    Answer: C

B. Short-Answer Questions (SAQs)

1. Differentiate with one example each: **case report** vs **case series** vs **cross-sectional**.
2. Define **risk ratio**, **odds ratio**, and **hazard ratio**; state which design typically uses each.
3. List **three strategies** to handle **confounding** in observational studies.
4. Explain **allocation concealment** and **intention-to-treat** with one line each.
5. Outline the **minimum steps** of a **systematic review** from question to conclusion.

C. Long-Answer Questions (LAQs)

1. You plan to evaluate a **whole-system Ayurvedic package** for knee osteoarthritis. Compare **pragmatic RCT**, **cluster RCT**, and **prospective cohort** in terms of validity, contamination, logistics, outcomes, and ethics. Conclude with a justified choice for a district-hospital network.
2. Design a **case–control study** to investigate **herb–drug interaction–related gastritis**. Define cases/controls, exposure window, matching plan, sample size concept, bias mitigation, and analysis outline.

D. Case Vignette (Applied Design Choice)

A teaching hospital pilots an **Abhyanga–Svedana** service for chronic low back pain. Administrators want: (i) immediate description of users and baseline pain; (ii) medium-term comparison of outcomes with usual care; (iii) a literature summary to guide policy.
Tasks:
a) Choose appropriate designs for (i), (ii), (iii).

b) List one key measure for each design.
c) Name one major bias to guard against in (ii) and one method to mitigate it.

End of Unit 5.