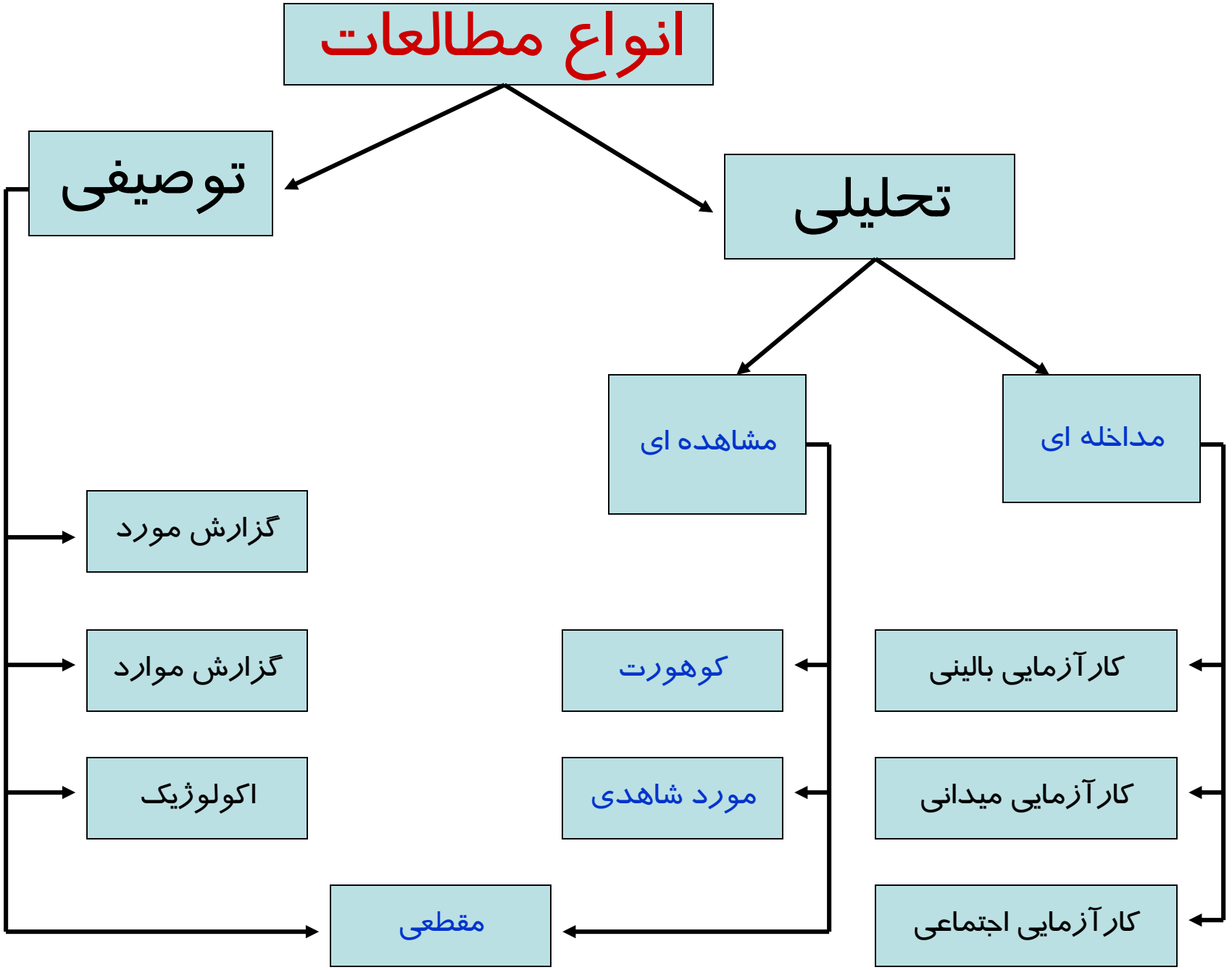

بسم الله الرحمن الرحيم

روش تحقیق

Dr.Yousef Alimohamadi
Epidemiologist

مطالعه

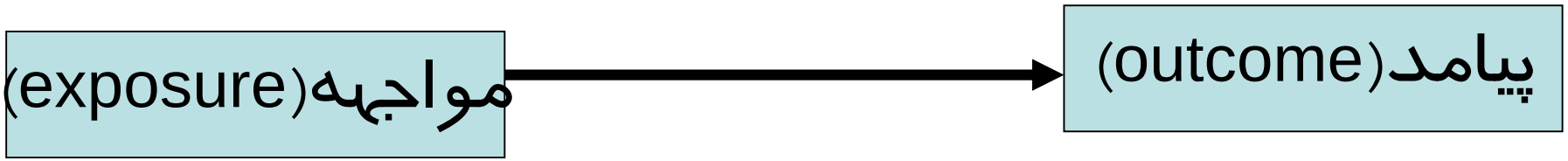
type of study


انواع مطالعات
توصیفی
تحلیلی
مشاهده ای
مداخله ای
گزارش مورد
گزارش موارد
اکولوژیک
کوهورت
مورد شاهدی
مقطعی
کارآزمایی بالینی
کارآزمایی میدانی
کارآزمایی اجتماعی

مطالعات مداخله ای

- اسامی مختلف:

مطالعات مداخله ای=تجربی=Interventional=Experimental



- توجه به مسائل اخلاقی در این نوع پژوهش مهم است

مطالعه تجربي روي انسان

در بيماري‌هائي كه در حيوانات قابل توليد نيستند و با كارآزمائيهاي حيواني بي‌ضرر بودن آنها ثابت شده است به كار مي‌رود

قاطعانه ترين رويكرد به مشكلات علمی است

ملاحظات اخلاقی و مالی از موانع اصلی انجام آن است

انواع مطالعات مداخله ای :

الف) كارآزمائي‌هاي تصادفي شده

ب)كارآزمائي‌هاي غيرتصادفي

كارآزمائي شاهددار تصادفي شده (Randomized Controlled Trials **RCT**)

مراحل انجام:

1- طراحي دستورالعمل اجرا

2- انتخاب جمعيت مرجع و جمعيت مورد آزمايش

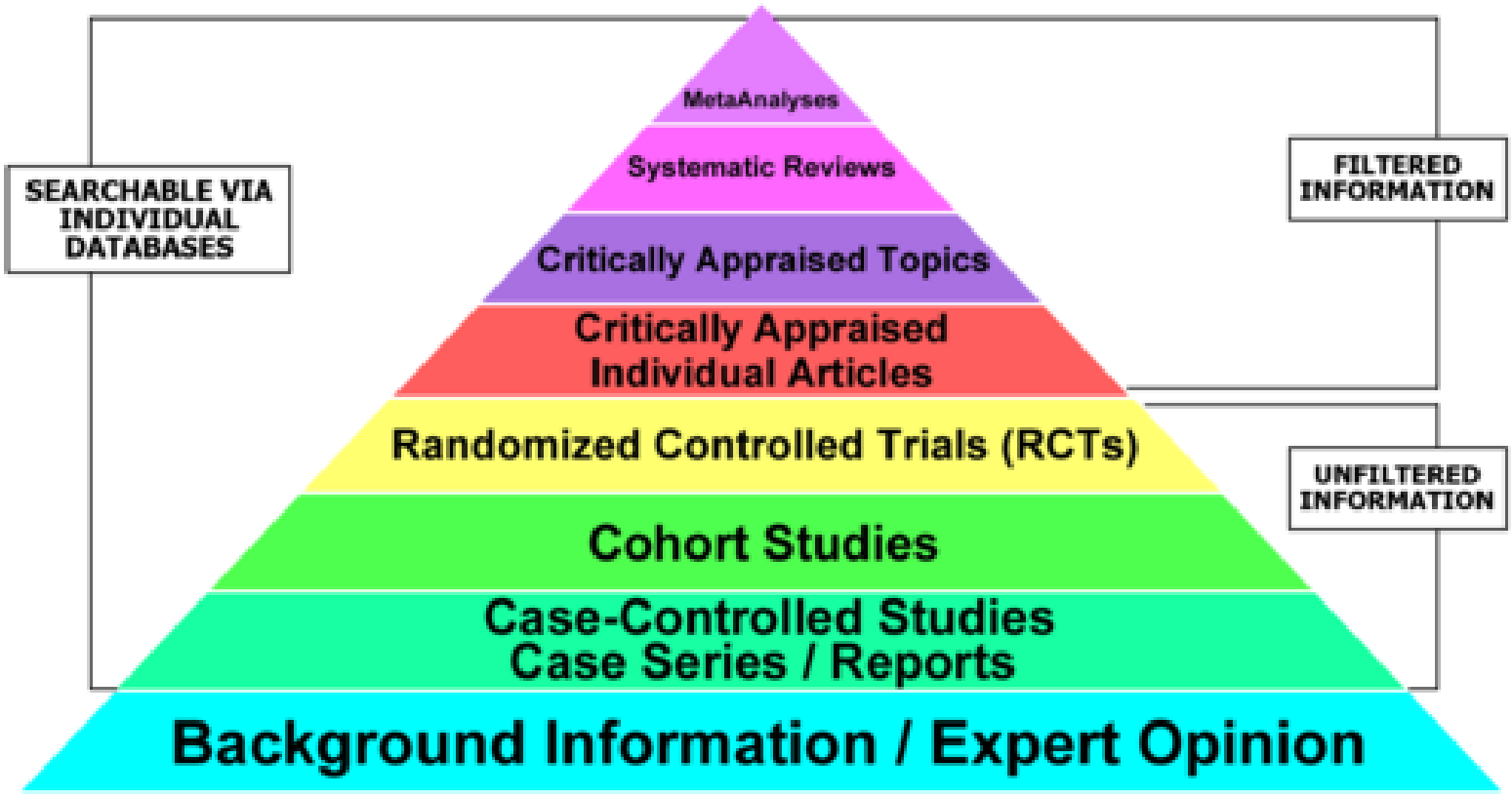
3- تصادفي كردن

4- دستكاري يا مداخله

5- پيگيري

6- بررسي پيامد

Level of evidence



تعریف کارآزمایی بالینی

کارآزمایی بالینی مطالعه ای است آینده نگر که برای مقایسه اثرات و ارزش یک مداخله (یا مداخله ها) در برابر شاهد در نمونه های انسانی انجام می شود.

هدف کارآزمایی بالینی

- ارزیابی کارایی (efficacy) و اثربخشی (effectiveness) یک مداخله یا داروی جدید

- کمک به روشن شدن نقش داروها یا مداخله های جدید در عملکرد بالینی

طبقه بندی انواع کارآزمایی

- کارآزمایی بالینی (clinical trial):

  برروی بیماران انجام میشود.

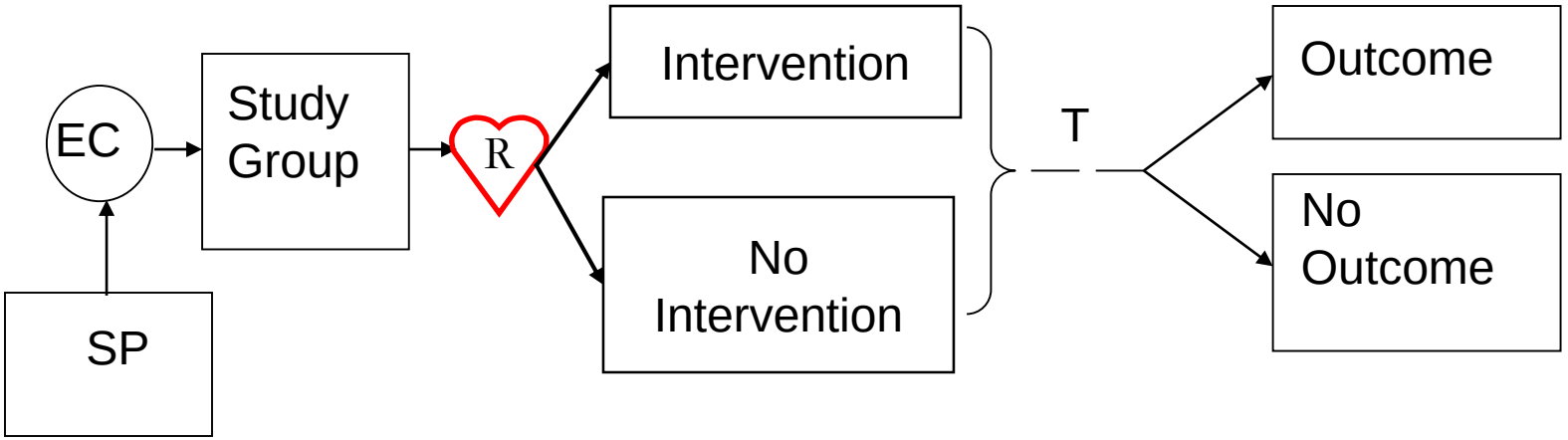
- کارآزمایی میدانی (field trial) یا کارآزمایی پیشگیری:

به منظور جلوگیری از ایجاد یا گسترش یک بیماری یا پیامد سلامتی انجام میشود.(بر افراد سالم انجام می شود)

- کارآزمایی جامعه (community trial):

بر روی دو یا چند جامعه انجام می شود و واحد درمانی آن به جای فرد، "جامعه" است.

طرح کلی کارآزمایی بالینی



SP = Study Population
EC = Eligibility Criteria
R = Randomize intervention
T = Elapsed time

PHASES OF CLINICAL TRIALS

- Phase Zero trials- Pre-human animal and laboratory testing
- Phase I trials
- Phase II trials
- Phase III trials
- Phase IV trials

Phase 0: Preclinical

- Pre-clinical (*in vitro)* animal studies
- Looking for dose-response

- Phase 0 trials serves as a good tool for clinical researchers in testing the safety and efficacy of drugs **at micro level** before the onset of phase I trial

- By design, phase 0 trials threaten lower risks to human subject than traditional phase I trials. As such, fewer preclinical supporting data are required prior to conducting a phase 0 trial.

Phase I

- **Patients:** 20 to 100 healthy volunteers or people with the disease/condition.
- **Length of Study:** Several months
- **Purpose:** Safety and dosage
- **Percentage of Drugs that Move to the next Phase:** 70%

- Phase I trials are the first stage of testing in human subjects.
- This phase is designed to assess the safety, tolerability,pharmacokinetic,
  and pharmacodynamics of a drug.
- Dose escalating (intolerable side effects-MTD)
- Single ascending dose, multiple ascending dose, food effect – cross over studies.

Phase II

- **Patients:** Up to several hundred people with the disease/condition.
- **Length of Study:** Several months to 2 years
- **Purpose:** Efficacy and side effects
- **Percentage of Drugs that Move to the Next Phase:** 33%

- After dose finding, the next goal is to evaluate whether the drug has any biological activity or effect.
- On larger groups of volunteers and patients (100-300) and are designed to assess how well the drug works.
- When the development process for a new drug fails, this usually occurs during Phase II trials when the drug is discovered not to work as planned, or to have toxic effects.

- Phase II studies are sometimes divided into Phase IIA and Phase IIB.
  - Phase IIA is specifically designed to assess dosing requirements (how much drug should be given).
  - Phase IIB is specifically designed to study efficacy (how well the drug works at the prescribed dose(s)).

Phase III

- **Patients:** 300 to 3,000 volunteers who have the disease or condition
- **Length of Study:** 1 to 4 years
- **Purpose:** Efficacy and monitoring of adverse reactions
- **Percentage of Drugs that Move to the Next Phase:** 25-30%

- The most expensive, time-consuming and difficult trials to design and run.
- Sometimes called the "pre-marketing phase".
- It is typically expected that there be at least two successful Phase III trials, demonstrating a drug's safety and efficacy, in order to obtain approval from the appropriate regulatory agencies such as **FDA**.

Phase IV

- **Patients:** Several thousand volunteers who have the disease/condition
- **Purpose:** More about the side effects and safety of the drug

- Often called Post Marketing Surveillance Trials.
- After registration, used in routine conditions.
- Rare side-effects.
- Study design (Observational studies).
- Cost-effectiveness analysis in different conditions.

Clinical Trial Steps

- Study population definition (Eligibility criteria)
- Design
- Sample size
- Control group
- Random allocation
- Blindness
- Intervention
- Outcome assessment
- Complications
- Compliance
- Data management
- Analysis
- Report

Types of Trial Designs(Cont.)

- Comparison Structure:
  - Parallel,
  - Crossover and
  - Group Allocation Designs
- Extensions of the Parallel Design:
  - Factorial and
  - Large, Simple Designs
- Testing for Hypotheses Other than Superiority:
  - Equivalency and
  - Non-Inferiority Designs
- Adaptive Designs

Single Arm Trials

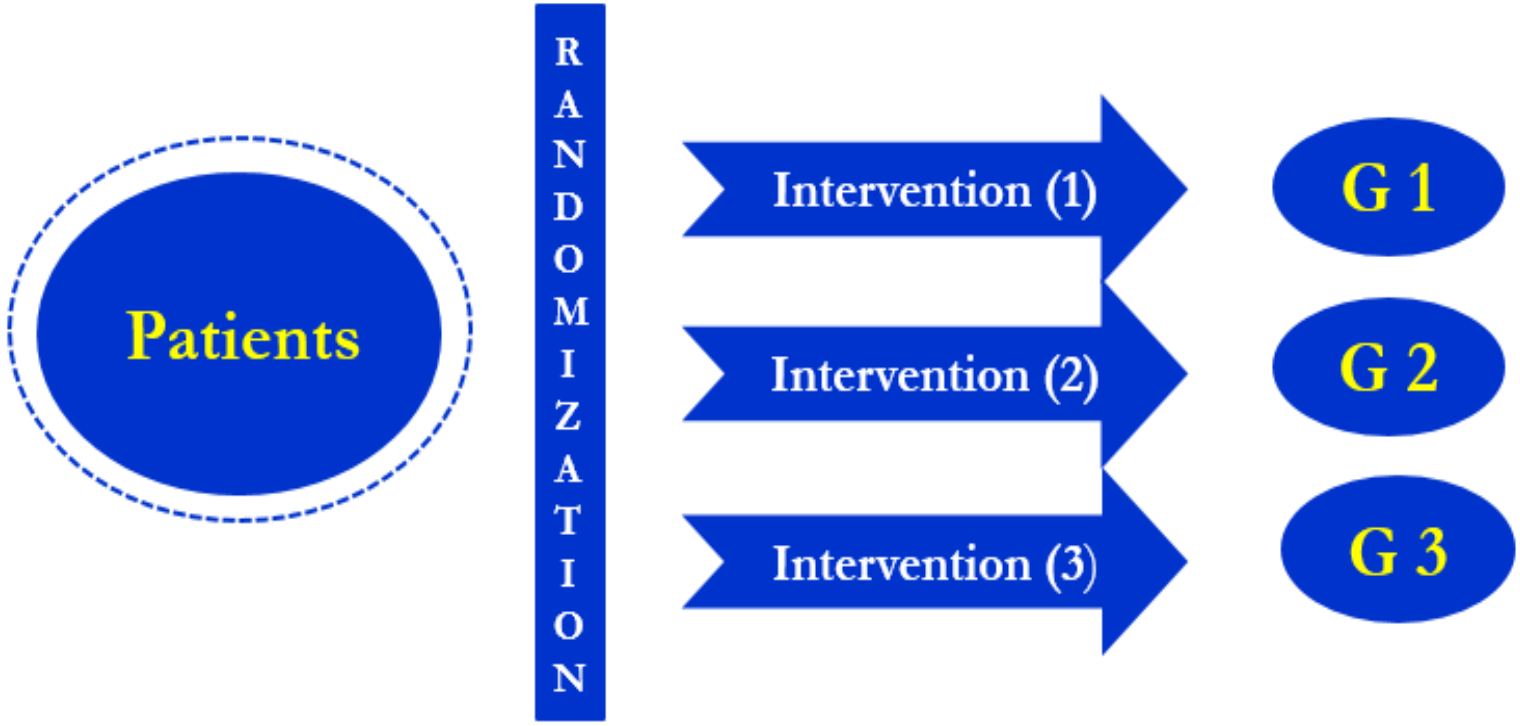
- Mostly in phase II clinical trials

Single Arm Trials (Cont.)

- Advantages:
  - All resources, i.e. subjects and financial costs, are concentrated on one group
  - Specify how many subjects should respond to the new treatment in order to justify further investigation
  - Useful for serious diseases such as cancers
- Disadvantages:
  - By not conducting a randomized comparison, we are left with all the difficulties of interpretation the results

Parallel Group Designs

"Gold-Standard" of Clinical Research.



Parallel Group Design(Cont.)

- There are as many groups as study treatments under comparison.
- Each person is randomly assigned to one treatment group.
- All treatment groups are treated and evaluated simultaneously.

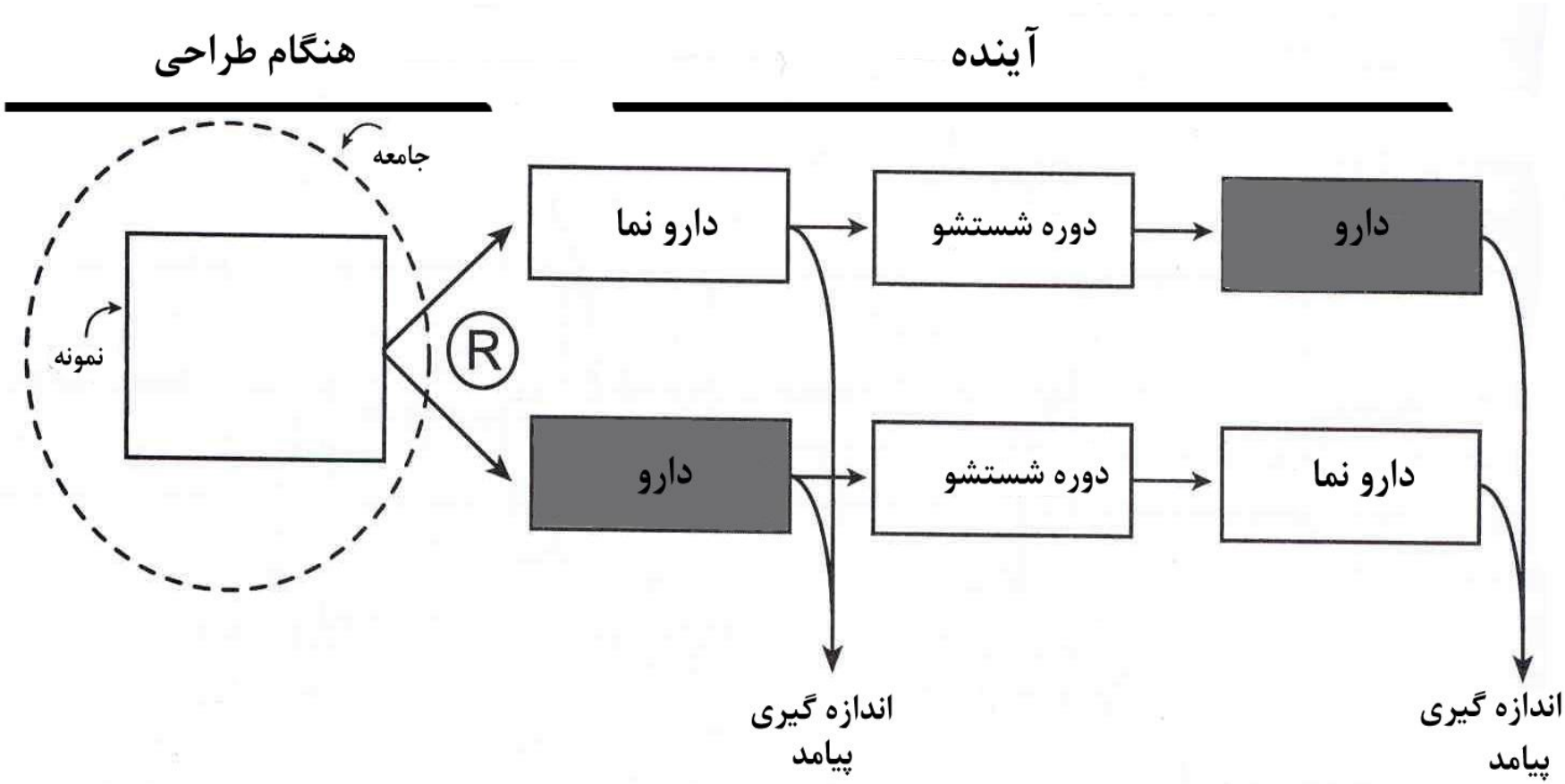
Parallel Group Design(Cont.)

- Advantages:
  - The duration of the study is shorter
  - It is applicable to acute conditions
  - The statistical analysis requires fewer assumptions
  - It is simpler and makes bias-free comparisons easier to obtain.

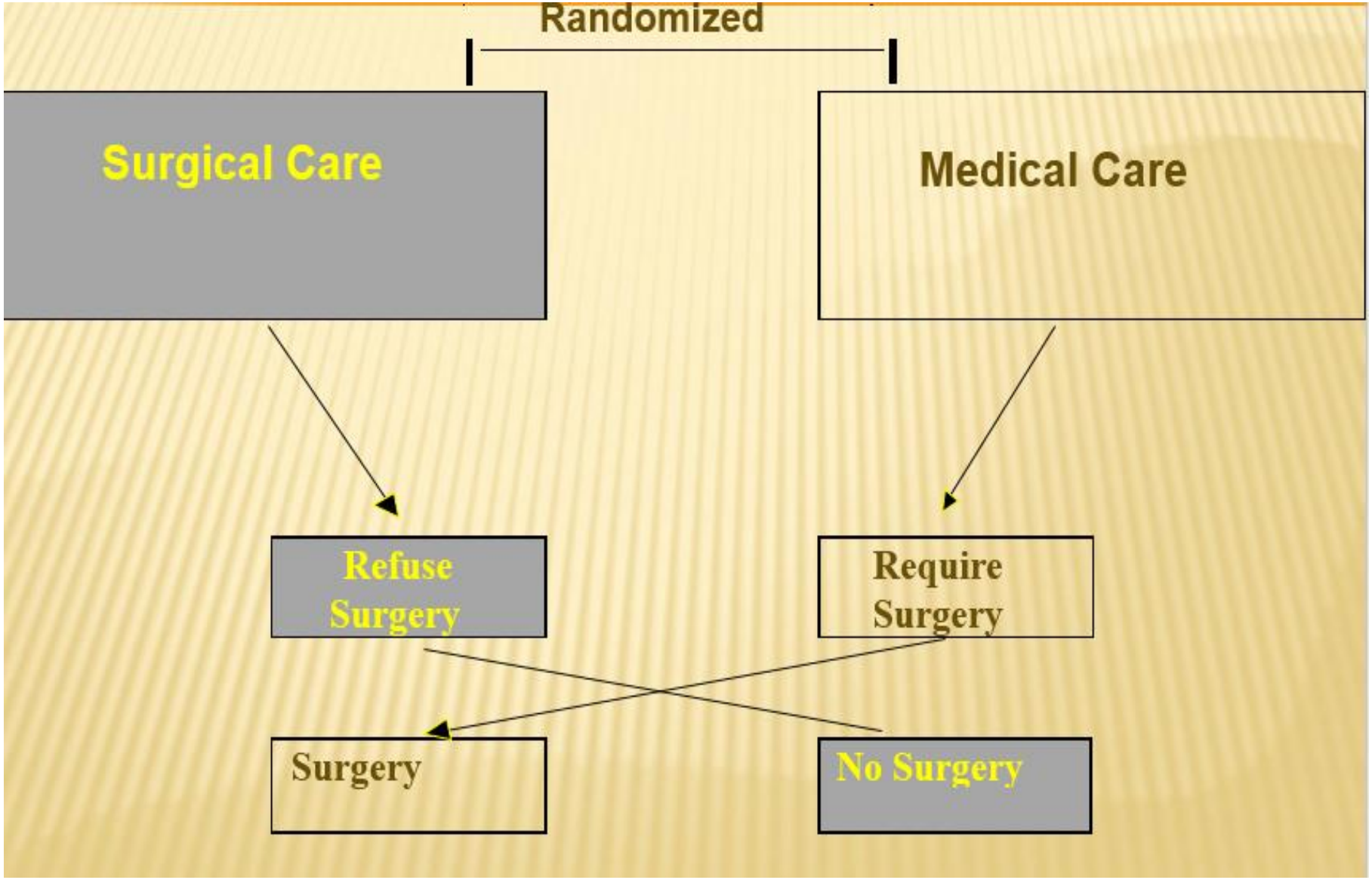
Parallel Group Design(Cont.)

- Disadvantages:
  - It requires a larger sample size.
  - In some few situations, it cannot be applied.

طراحی متقاطع:CROSS-OVER DESIGN



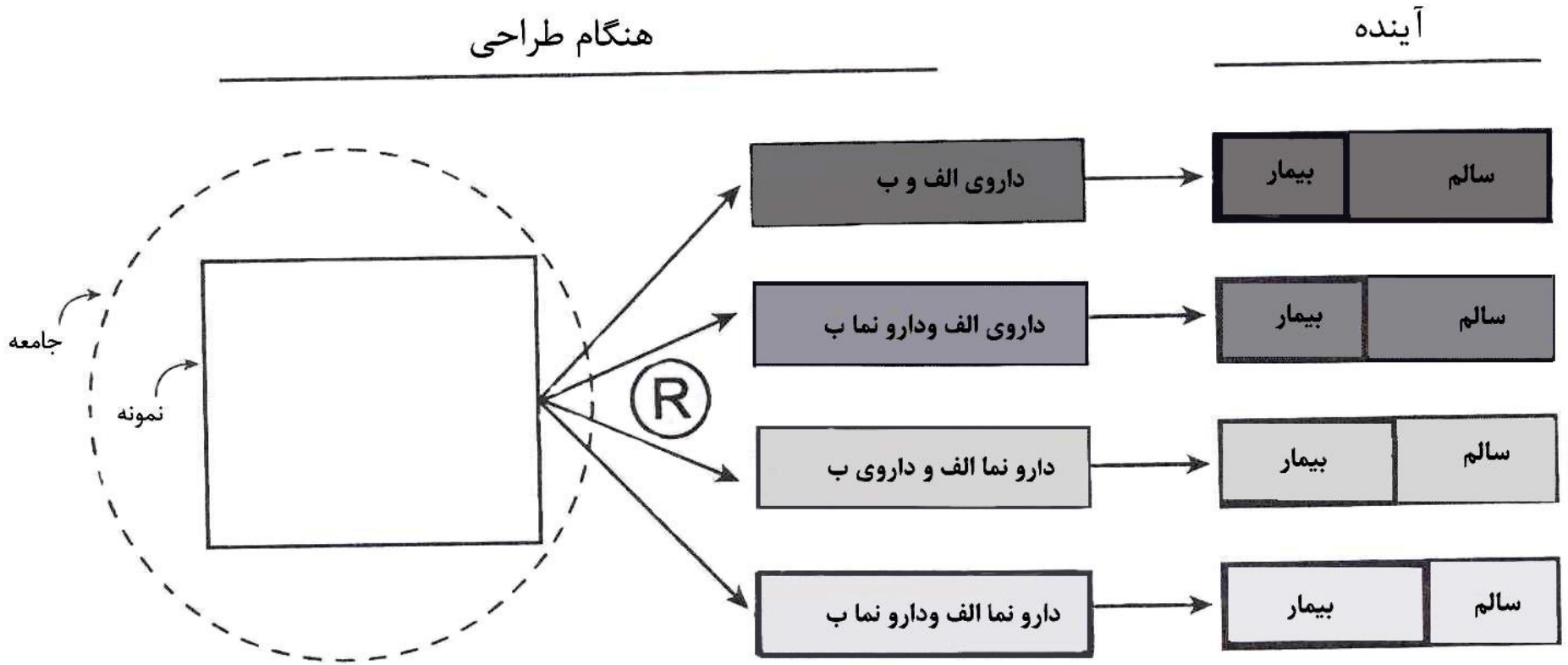
DESIGN OF A **UNPLANNED** CROSSOVER TRIAL



- Advantages:
  - It removes the interpatient variability from the comparison between treatments.
  - It provides the best unbiased estimates for the differences between treatments.
  - It decreases number of patients needed.

- Disadvantages:
  - Treatment can’t have permanent effects or cures.
  - It increases the duration of the study.
  - Its analysis is not straightforward. Researchers should consider the paired design, period and carry over effects.
  - Dropouts more significant.

طراحی فاکتوریل: FACTORIAL DESIGN



2×2 Factorial Trial Design

		A		
		Yes	No	Total
B	Yes	n_{AB}	n_{BO}	N_B
	No	n_{AO}	n_{OO}	$N_{B'}$
	Total	N_A	$N_{A'}$	N

Factorial trial designs are useful in two circumstances:

1) When two or more treatments do not interact, factorial designs can test the main effects of each using smaller sample sizes and greater precision than separate parallel groups designs.
2) When it is essential to study treatment interactions, factorial designs are the only way to do so.