

# Clinical Research Methods

## Observational and Interventional Study Designs

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June 30, 2010

# Disclosures

- Grant support from: National Institutes of Health (NEI,NINDS,NIA,NICHD), Michael J Fox Foundation, Medivation, Neurosearch and Pfizer
- Consultant to: United States Food and Drug Administration, National Institutes of Health (NINDS), Veteran's Administration (VA), Abbott, Biogen, Boehringer-Ingelheim, Ceregene, EMD Serono, Impax, Ipsen, Isis, Lilly, Lundbeck, Merz, Novartis, Orion, Otsuka, Schering-Plough (Merck), Sienna Biotech, Solvay, Synosia, Teva, UCB Pharma and Xenoport
- Legal consulting to Pfizer, Welding Rod Litigation Defendants

# Types of Studies

## Observational

case series – clinical observation

ecologic associations – existing data

cross sectional (prevalence) – existing/new data

case-control – new data

cohort – retrospective – existing/new data

prospective – new data

## Interventional

non-randomized trial

randomized, controlled trials

# Evidence of Causal Relationship

- Major:      Temporal  
              Biological Plausibility  
              Consistency  
              Alternative Explanations Explored
- Other:      Dose-response Relationship  
              Strength of Association  
              Cessation Effects

Gordis 1990

# RCT's – Why Bother?

- Randomization
- Blinding to treatment

Attempts to reduce bias and to improve the quality of evidence.

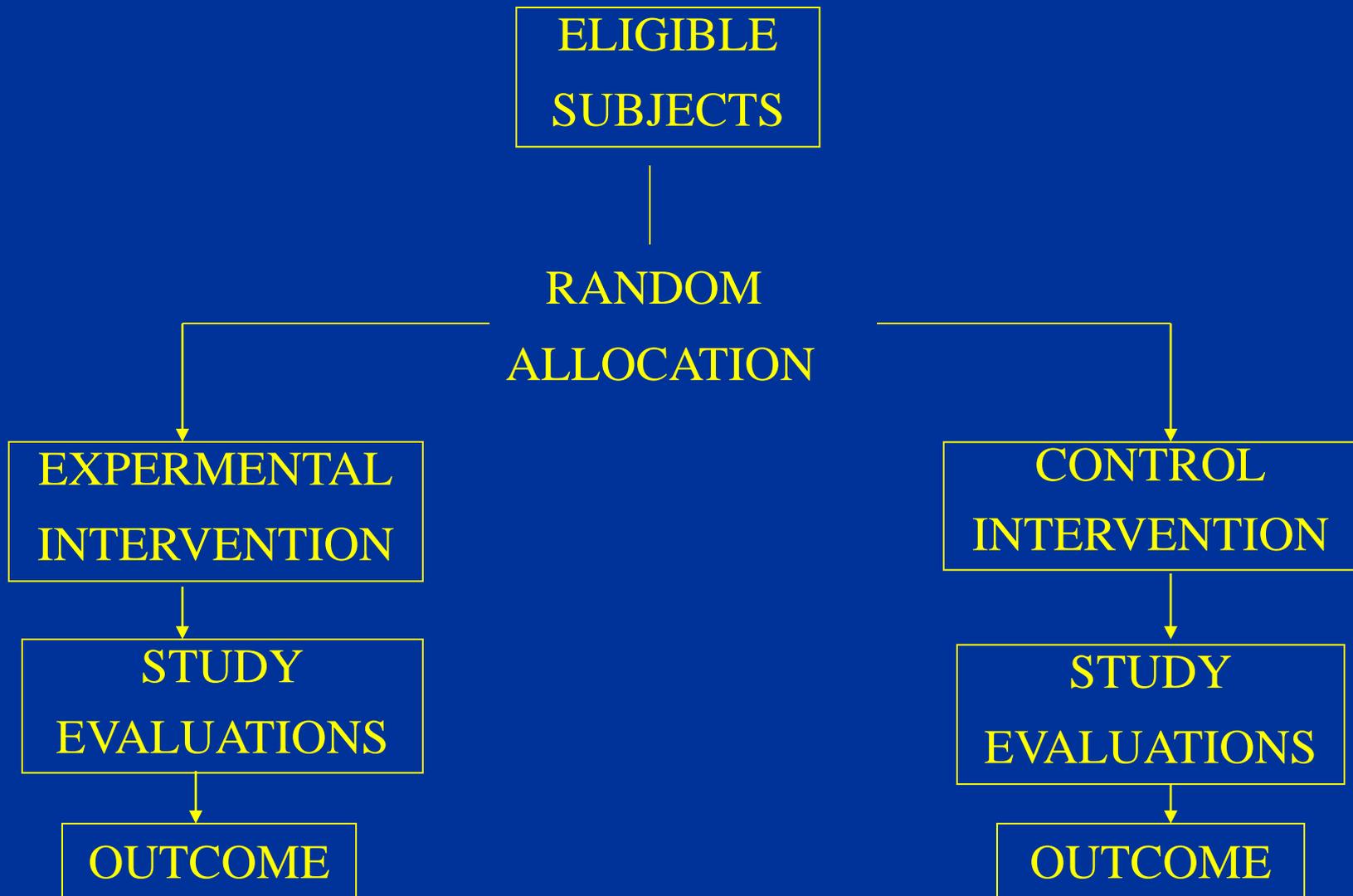
# RCT's – Bias Control

- Blinding or masking

# RCT's – Trial Designs

- Parallel group
  - Factorial designs
- Crossover
  - N-of-1

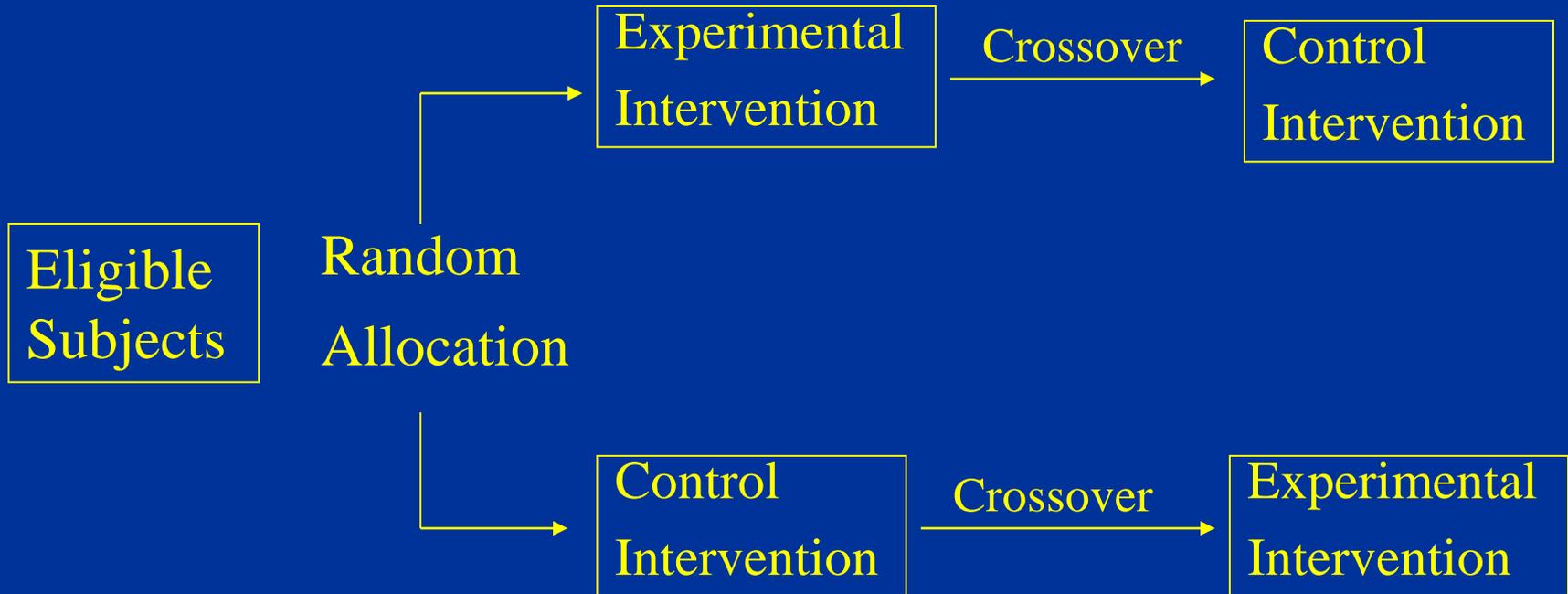
# Parallel Group Design

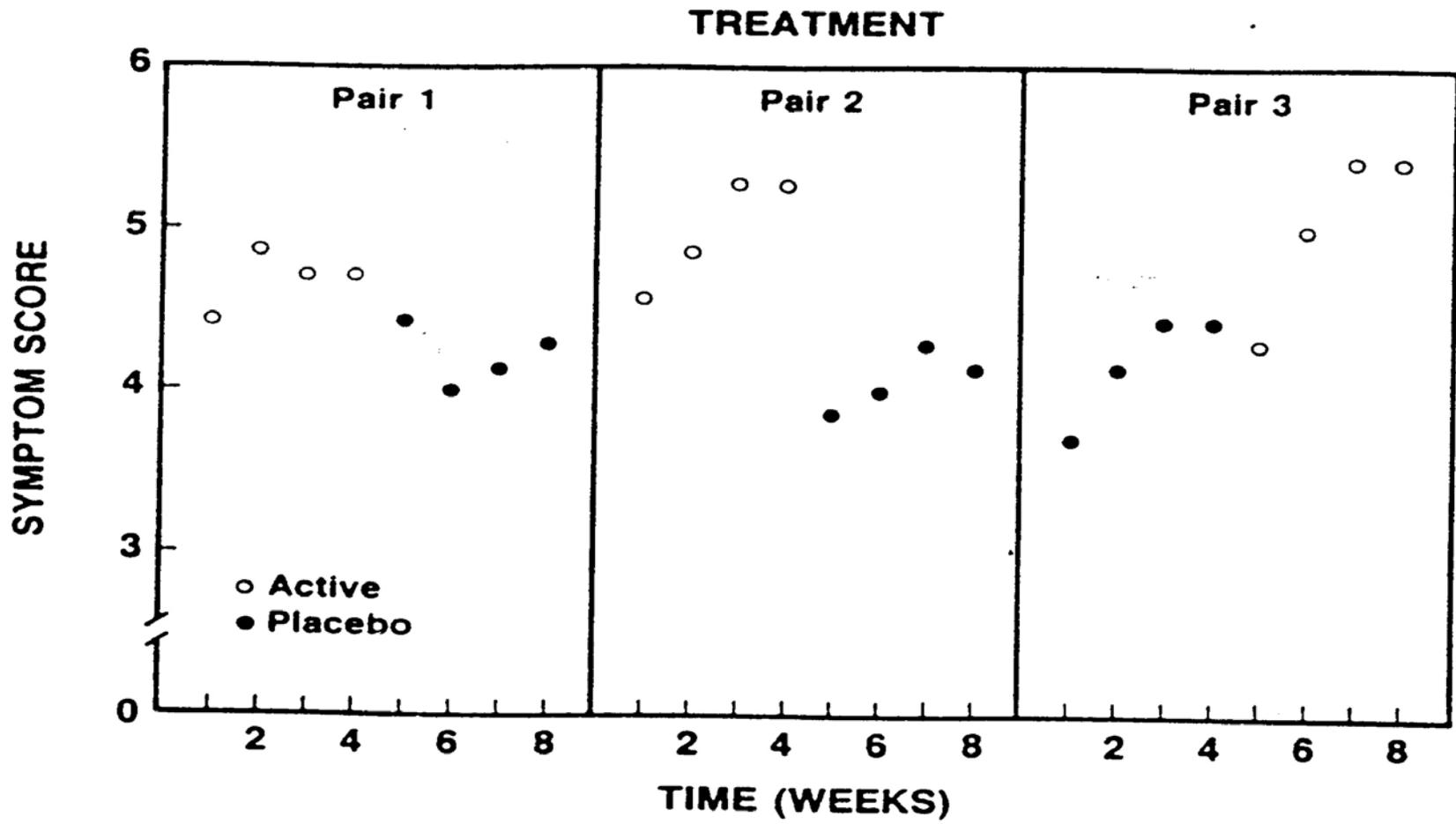


# 2 X 2 Factorial Design

		Intervention 1	
		Active	Control
Intervention 2	Active	A	B
	Control	C	D

# Crossover Design





# RCT's – Trial Designs

	PARALLEL GROUP	CROSSOVER
Sample Size	Bigger	Smaller
Lost to Follow-up	Manageable	Big Problem
Period Effects	Not Applicable	Big Problem
Short-Term Benefit	Good	Good
Slowing of Progression	Good	No Good
Episodic Disorders	OK	Ok, if frequent

## Observational

- Good power for rare events
- Entry criteria more generalizable
- Ethically permissible (exposures)
- Lower cost (sometimes)

## Interventional

- Best for causality (when feasible)
- Best evidence for treatment decisions
- Less confounding – although interactions still an issue

# Quality of Evidence Hierarchy

1. Trials
  - a. Randomized, double-blind, placebo controlled
  - b. Randomized, not blinded
  - c. Non-randomized
2. Cohort or Case Control
  - a. Hypothesis prespecified, confounders accounted for
  - b. Hypothesis not prespecified
3. Time Series Studies
4. Case Series Studies

Consider: Outcome definition, definition of risk factor,  
adequacy of sample size