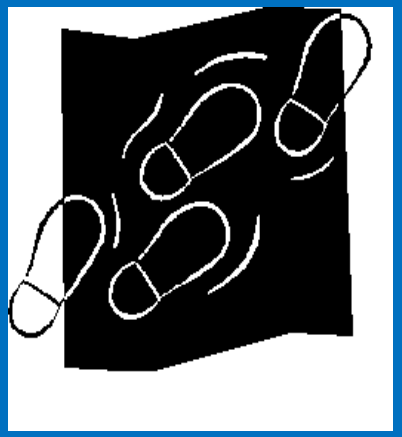
# Clinical Trials



April 2021

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Parkinson's and Movement Disorders
Center of Maryland
and
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# No Conflicts

- I have no financial interest with any entity producing marketing, re-selling, or distributing healthcare goods or services consumed by, or used on patients
- I will not be discussing the use of off-label products

# Clinical Research is Different than Clinical Practice

- **Practice**: interventions designed solely to enhance the well-being of a patient with a reasonable expectation of success

- **Research**: an activity designed to test an hypothesis, permit conclusions to be drawn and to contribute to generalizable knowledge

Belmont Report

# What Are Clinical Trials?

- Clinical trials are experiments on humans designed to evaluate the safety and efficacy of new treatments (drugs, medical devices, therapies).

# Clinical Trials

- Phases and Designs
- Key Personnel
- Informed Consent
- Inclusion/Exclusion Criteria
- How and why to participate in clinical trials

# Clinical Trial Phases

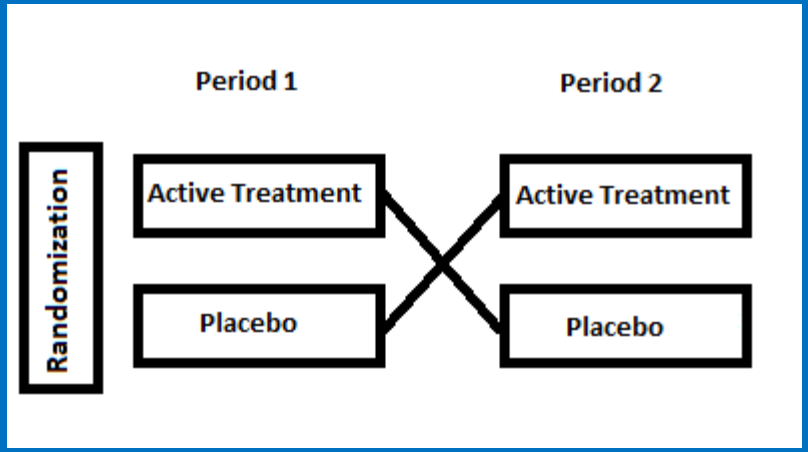
| Phase | Description | |
|---|---|---|
| 0 | Exploratory study involving limited hu | |
| 1 | Safety studies usually involvi volunteers and often | 1/3 |
| 2 | Studies in 1 ing preliminary data on eff evaluated. | 1/2 |
| 3 | er more info on safety and s, different patient populations and doses xplored in 100 – thousands of patients | 1/3 |
| | Studies performed <u>after</u> FDA approval in thousands of patients. Gather more info on safety, efficacy or optimal use. May be required by FDA. Real Life Experiences. | |

**Overall 94.5% of Trials Fail**

From: clinicaltrials.gov

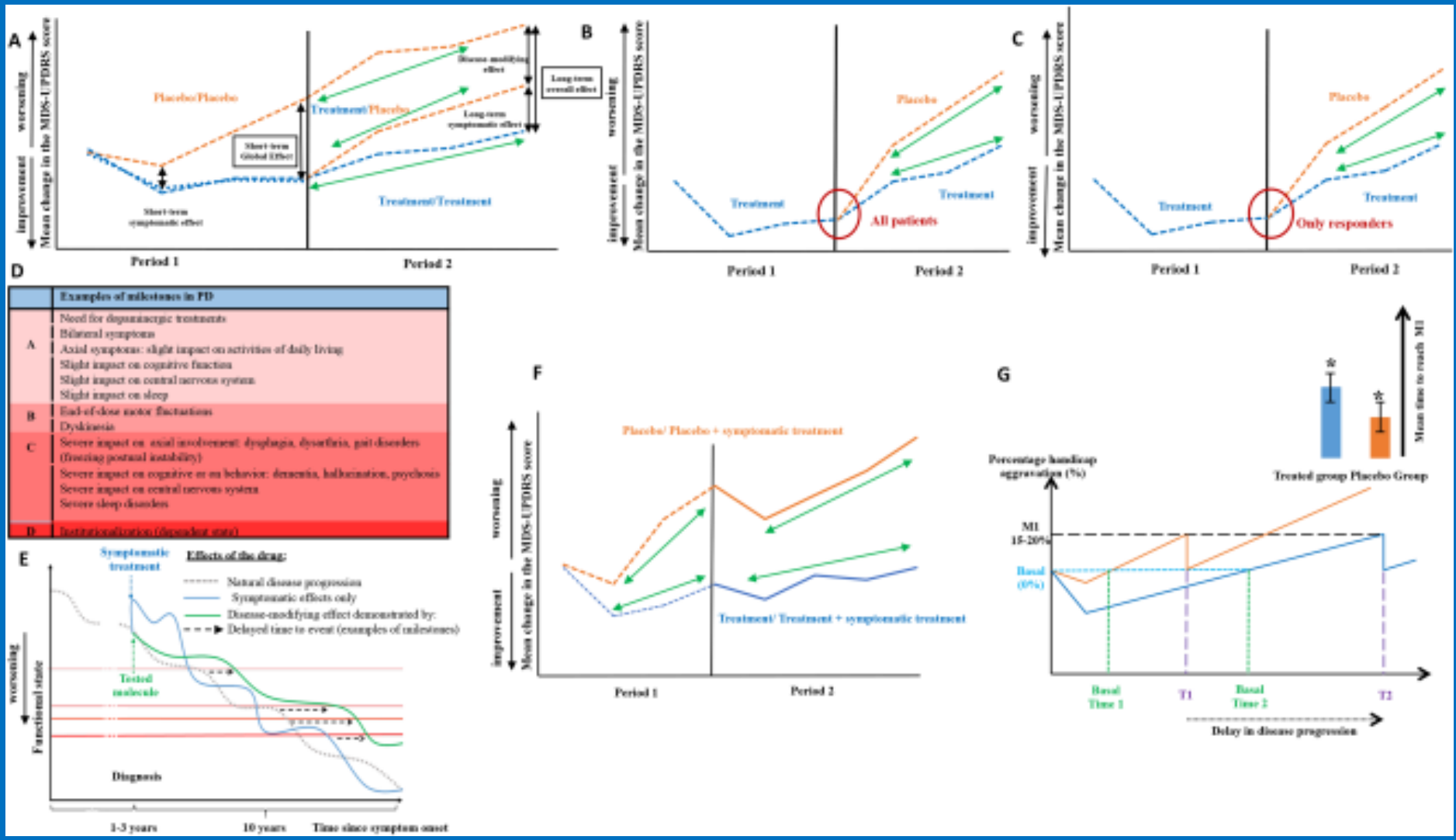
# Clinical Trial Designs

- **Trial Designs**
  - Parallel Group
  - Cross Over
  - Non-comparative (non-controlled)
- **Blinding**
  - Open Label
  - Single Blind
  - Double blind
- **Comparison**
  - Difference comparison
  - Non-Inferiority
  - Equivalence




http://www.pharmaschool.co/ukonline2.asp?id=37

# New perspectives on study designs for evaluating neuroprotection in Parkinson's disease




**Movement Disorders**
Volume 32, Issue 10, pages 1365-1370, 13 JUL 2017 DOI: 10.1002/mds.27055
http://onlinelibrary.wiley.com/doi/10.1002/mds.27055/full#mds27055-fig-0001

# Clinical Trials

- Phases and Types
- Key Personnel: roles
- Informed Consent
- Inclusion/Exclusion Criteria
- How and why to participate in clinical trials

Patient
Patient representative
Physician/Investigator
Study Coordinator
Sponsor
Study Monitor
IRB

# Key Personnel

- **Patient** – the patient has both rights and responsibilities
  - Know the risks of participation
  - Know what alternatives there are
  - Know that can withdraw without penalty
  - Make decision to enroll without feeling pressure from research staff
  - Know the name, credentials and contact info for study personnel
  - Know the purpose of the study
  - Know who will have access to your information
  - Know what procedures may be performed and what drugs/devices will be used
  - Follow direction of researchers
  - Provide accurate information about your medical conditions
  - Inform research staff of any adverse experiences
  - Informing staff and/or IRB if you feel your rights have been violated
- **Patient's representative**

# Key Personnel – You see

- **Physician/Investigator** – ensure that study is conducted according to the investigator agreement with the sponsor; protect the rights, safety and welfare of subjects in the study, control drugs and devices under investigation. The principal investigator (PI) is responsible for overseeing other study personnel.

- **Study Coordinator** - Research professional working under direction of PI, supporting, coordinating, managing and carrying out clinical research

# Key Personnel – You Don't See

- **Sponsor** – a person or pharmaceutical company who takes responsibility for and initiates a clinical investigation
- **Study Monitor** – person delegated by sponsor to oversee the conduct of the clinical trial
- **Institutional Review Board (IRB)** – any board or group designated by an institution to review, approve the initiation of and conduct periodic review of biomedical research involving humans. IRB personnel include physicians, researchers and community members. Roles:
  - Ensure study is ethical
  - Rights and welfare of subjects are protected
  - Ensures risks are minimized and reasonable
  - Reviews consent form

# Clinical Trials

- Phases and Types
- Key Personnel
- **Informed Consent**
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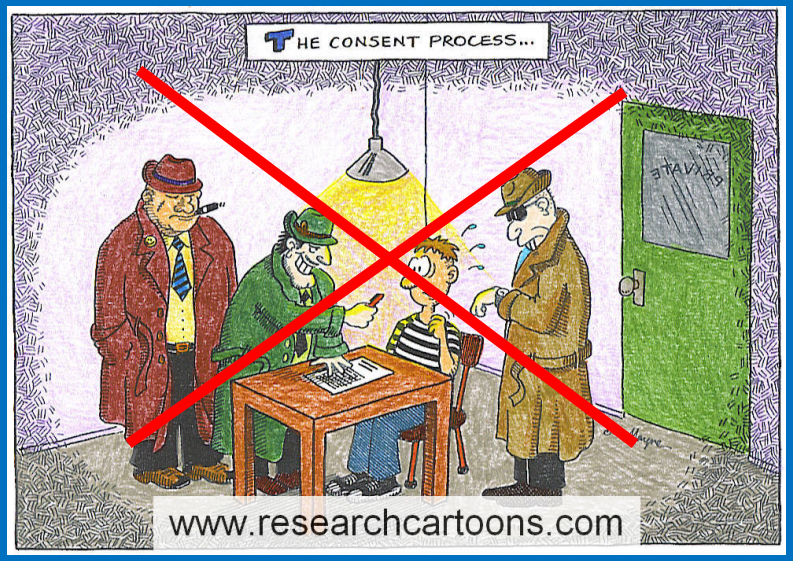


# Acute Arrest of Cerebral Circulation in Man

- 126 male inmates with schizophrenia
- Age: 17-31
- Blood pressure cuff inflated around their necks to 600 mm Hg
- Subjects developed syncope

Rossen et al 1943

# Tuskegee Syphilis Experiment

- Conducted by US Public Health Service (1932-1972)
- Studied natural progression of untreated syphilis in 600 impoverished rural African-American men in Alabama
- Subjects enticed into study with free health care, meals and free burial insurance
- None were informed they had disease
- None were treated with penicillin when it became a proven treatment in the 1940's
- 40 wives got disease, 19 children born with syphilis

# Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects

- Created by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1978)
- Developed in setting of Tuskegee Syphilis Study
- **Three Core Principles**
  - Respect for persons
  - Beneficence
  - Justice
- **Primary Areas of Application**
  - Informed Consent
  - Assessment of risks/benefits
  - Selection of subjects


Belmont Conference Center located in Elkridge, MD

# Basic Ethical Principles

- **Respect for Persons**
  - Individuals treated as autonomous agents
  - Persons with diminished autonomy are entitled to protection
  - Subjects enter research voluntarily and with adequate information
- **Beneficence** – Making efforts to secure a person's well-being; here an obligation
  - Do no harm
  - Maximize possible benefits, minimize possible harms
- **Justice**
  - Who receives benefits from research and who bears the burdens?

Belmont Report

# Informed Consent

**Subjects must be given the opportunity to choose what does and does not happen to them. Signing a consent form indicates the subject is giving informed consent.**


- **Information**
  - Research procedure
  - Purpose
  - Risks/benefits
  - Ability to ask questions and withdraw from study
- **Comprehension**
  - Adapt to subject's capacities
  - Obligation of researcher to ensure understanding
- **Voluntariness**
  - Must be free of coercion and undue influence

Belmont Report

# Clinical Trials

- Phases and Types
- Key Personnel
- Informed Consent
- **Inclusion/Exclusion Criteria**
- How and why to participate in clinical trials

# Inclusion/Exclusion Criteria

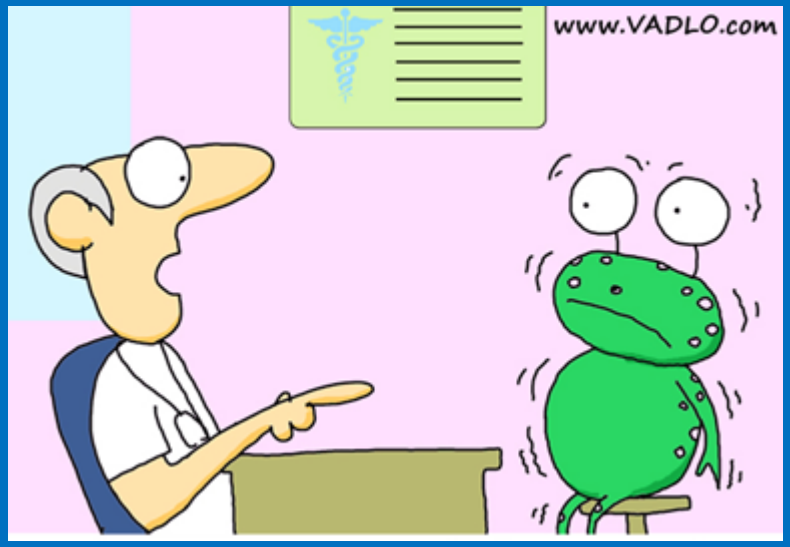
- Inclusion Criteria: factors which allow subjects to participate in a clinical trial.
- Exclusion Criteria: factors which disqualify subjects from participating in a clinical trial

# Example of Inclusion/Exclusion Criteria

- **Inclusion**
  - Signed Consent
  - Age 30-80
  - Dx of PD fulfilling UK Brain bank criteria
  - Stage I-III on Hoehn & Yahr scale
  - Patients experience motor fluctuations with 2 hours daily off time
  - Must be on stable carbidopa/levodopa and other meds
  - Must take > 4 doses/day, but total dose < 1600 mg l-dopa
  - Must have >25% difference in ON and OFF scores on UPDRS
  - Normal cognition with score > 24 on MMSE
- **Exclusion**
  - Dyskinesias severe enough to interfere with study procedures
  - Pregnant or lactating women
  - Know contraindication to l-dopa including h/o melanoma and narrow-angle glaucoma
  - Previous surgery for PD
  - Psychotic symptoms or suicidal ideation in prior 12 months
  - Cancer unless no evidence for disease > 3 years
  - Drug/ETOH abuse
  - Prohibitive medications
  - Symptomatic orthostatic hypotension
  - Any condition making patient unsuitable

# So who participates?

- People who are aware of the study
- People who are willing
- People who have PD (and little else)
- People who have time



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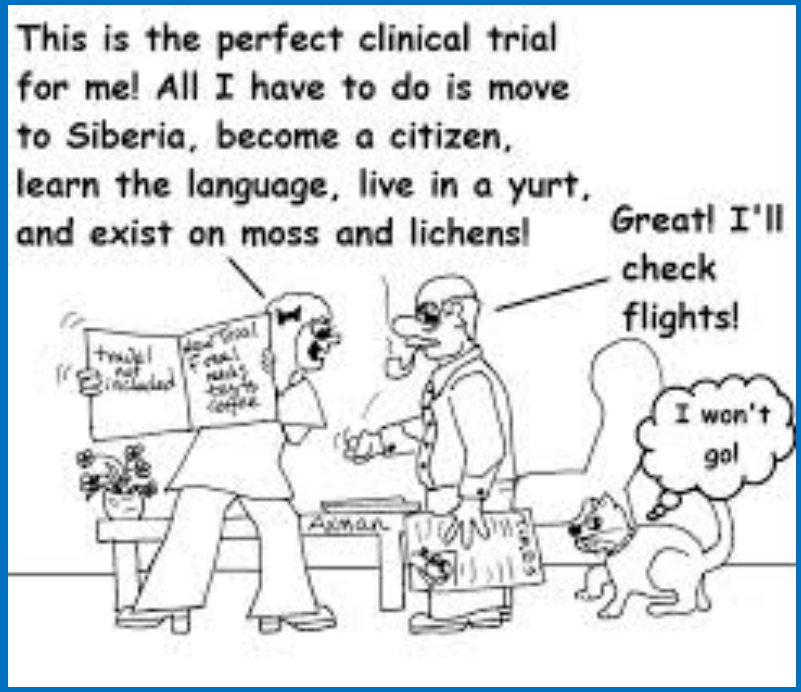
- **How and why to participate in clinical trials**

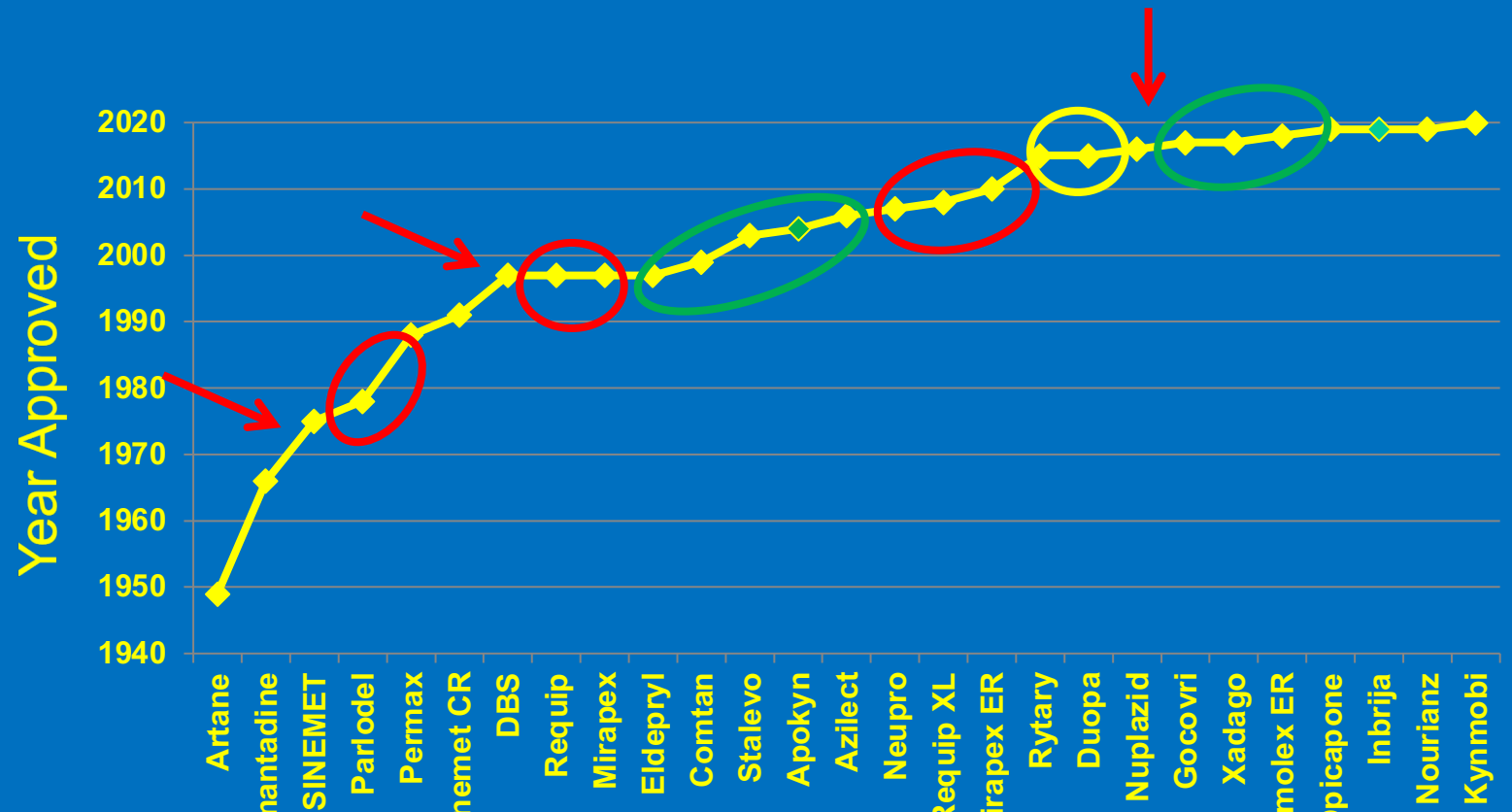


# Why Participate?

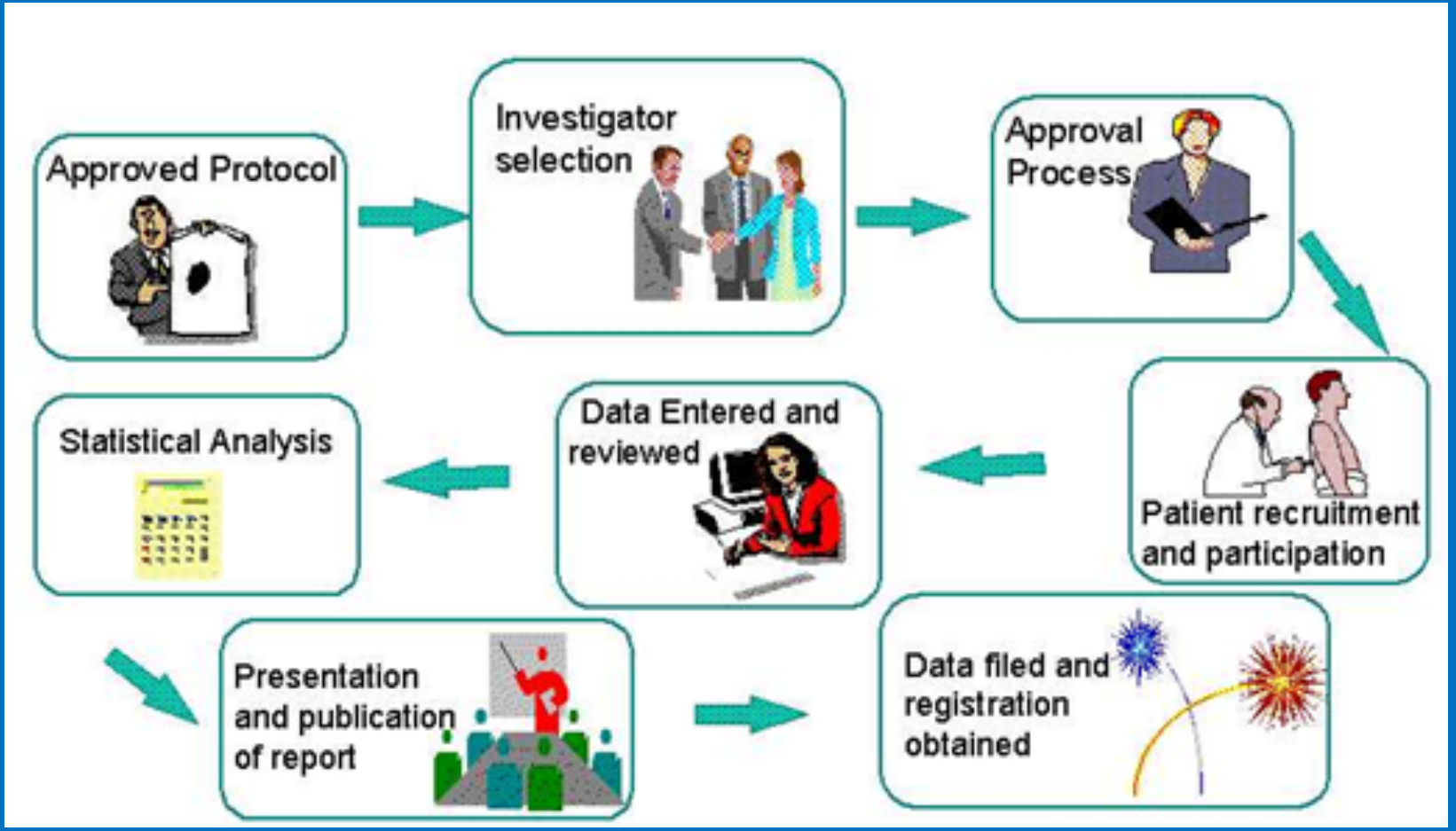
- **Contribute to scientific/medical knowledge: results can improve care or diagnosis of future patients**

- **Some trials may give subjects the possibility of receiving benefits.**
- **Monetary or other compensation should NOT be a reason to participate**
- **You get to spend more time with your doc**

# FDA Approvals in PD



# Getting New Medications Approved Takes Time




http://www.clinical-trials-info.com/tag/clinical-research-definition/

# How to Find Clinical Trials

- https://foxtrialfinder.michaeljfox.org/
- https://clinicaltrials.gov/ct2/search/index

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

# Conclusions

- Clinical tri[illegible]e the way to a[illegible]dvance tre[illegible]
- Pat[illegible] knowledge clini[illegible] consent to[illegible]
- Rese[illegible] respect t[illegible] and e[illegible]e treated appro[illegible]
- Most c[illegible] Baltim[illegible] Washin[illegible]ve clir[illegible] program[illegible]