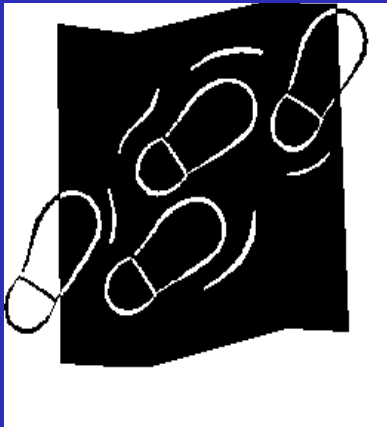


Clinical Trials



March 23, 2019
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Parkinson's and Movement Disorders
Center of Maryland
and
Johns Hopkins University



PARKINSON FOUNDATION
OF THE NATIONAL CAPITAL AREA
A COMMUNITY OF EDUCATION AND SUPPORT

Conflicts of Interest

- I receive payment for conducting clinical trials from Enterin Pharmaceuticals and Key Touch Medical.
- 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 or services or will point out any off-label uses

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

What Are Clinical Trials?

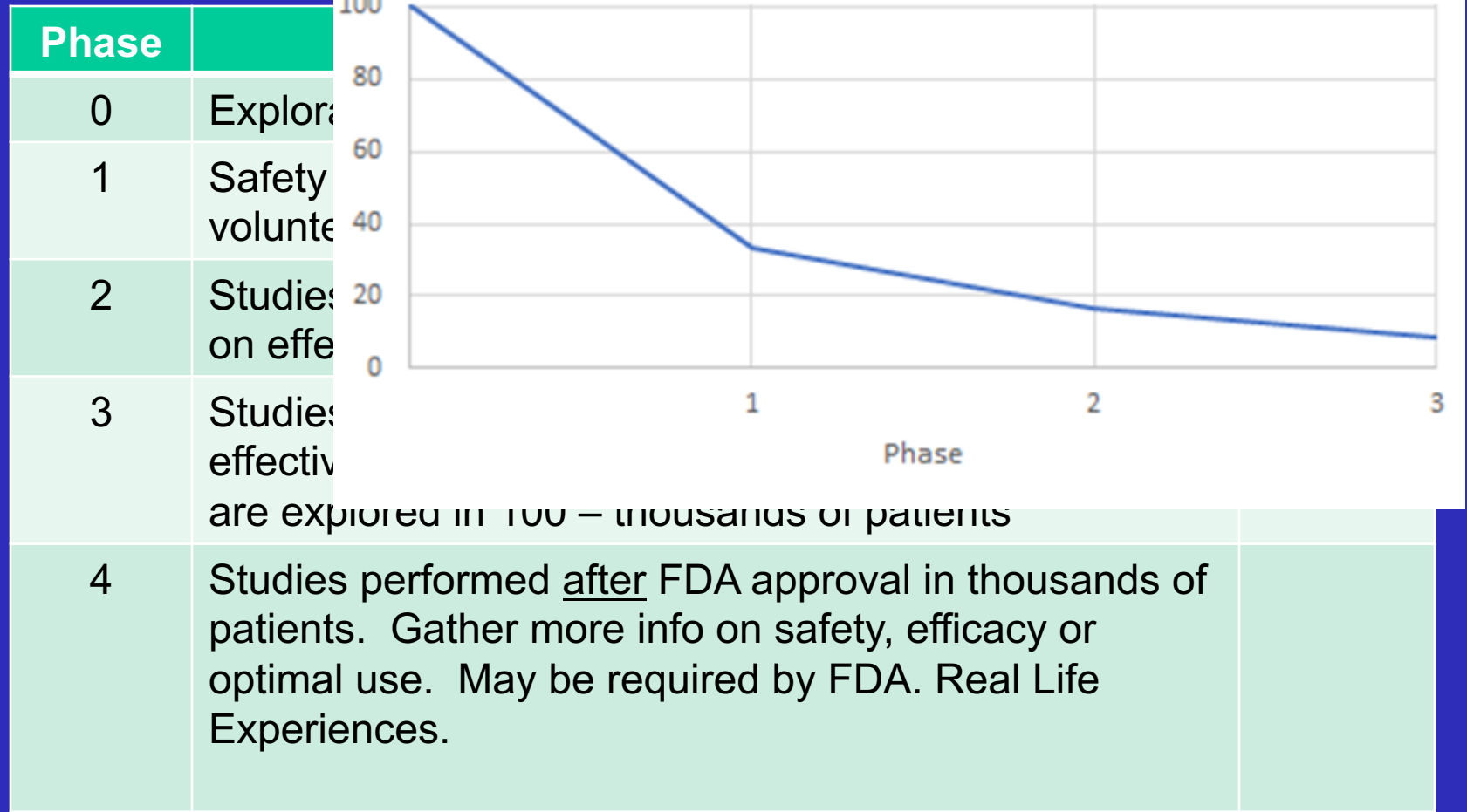
- Clinical trials are experiments on humans designed to evaluate the safety and efficacy of new treatments (drugs, medical devices, therapies).



Clinical Trials

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

Clinical Trial Phases

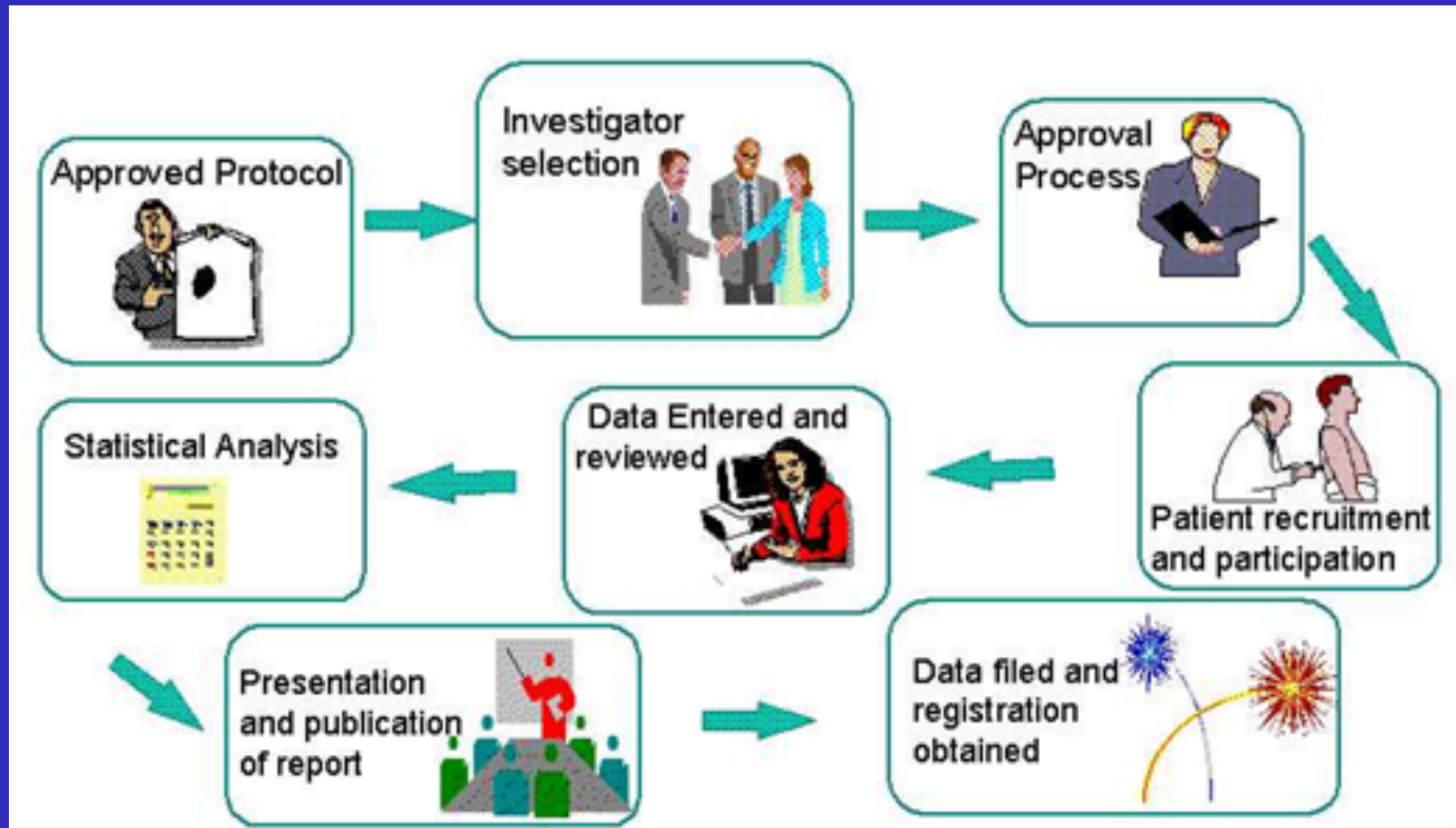


Economics of New Drugs

- Clinical trials of new drugs cost about \$19 million per drug (range \$2-347 million)
- Average total cost per drug: \$1.395 billion*

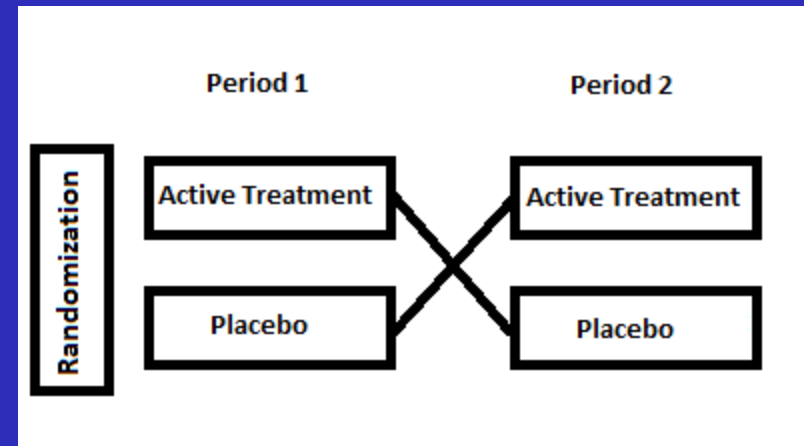


Getting New Medications Approved Takes Time



Clinical Trial Designs

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



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

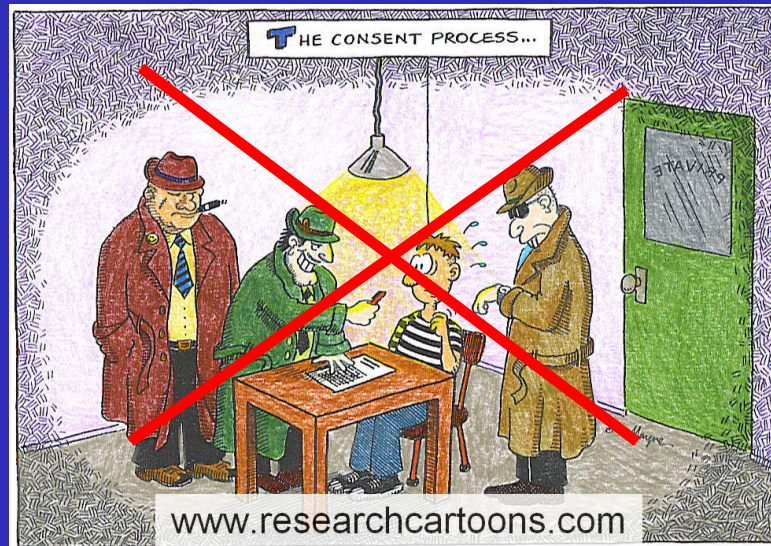


Key Personnel – You Don't See

- **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**
- Inclusion/Exclusion Criteria
- How and why to participate in clinical trials



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



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?

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

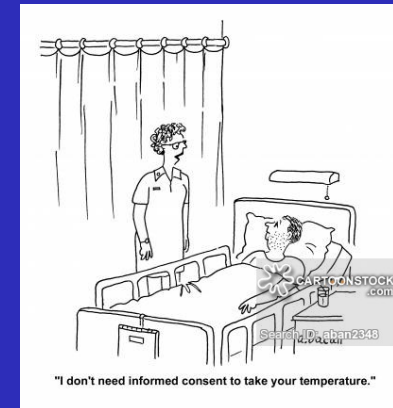
- Research procedure
- Purpose
- Risks/benefits
- Ability to ask questions and withdraw from study

– Comprehension

- Adapt to subject's capacities
- Obligation of researcher to ensure understanding

– Voluntariness

- Must be free of coercion and undue influence



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
- Known 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



Clinical Trials

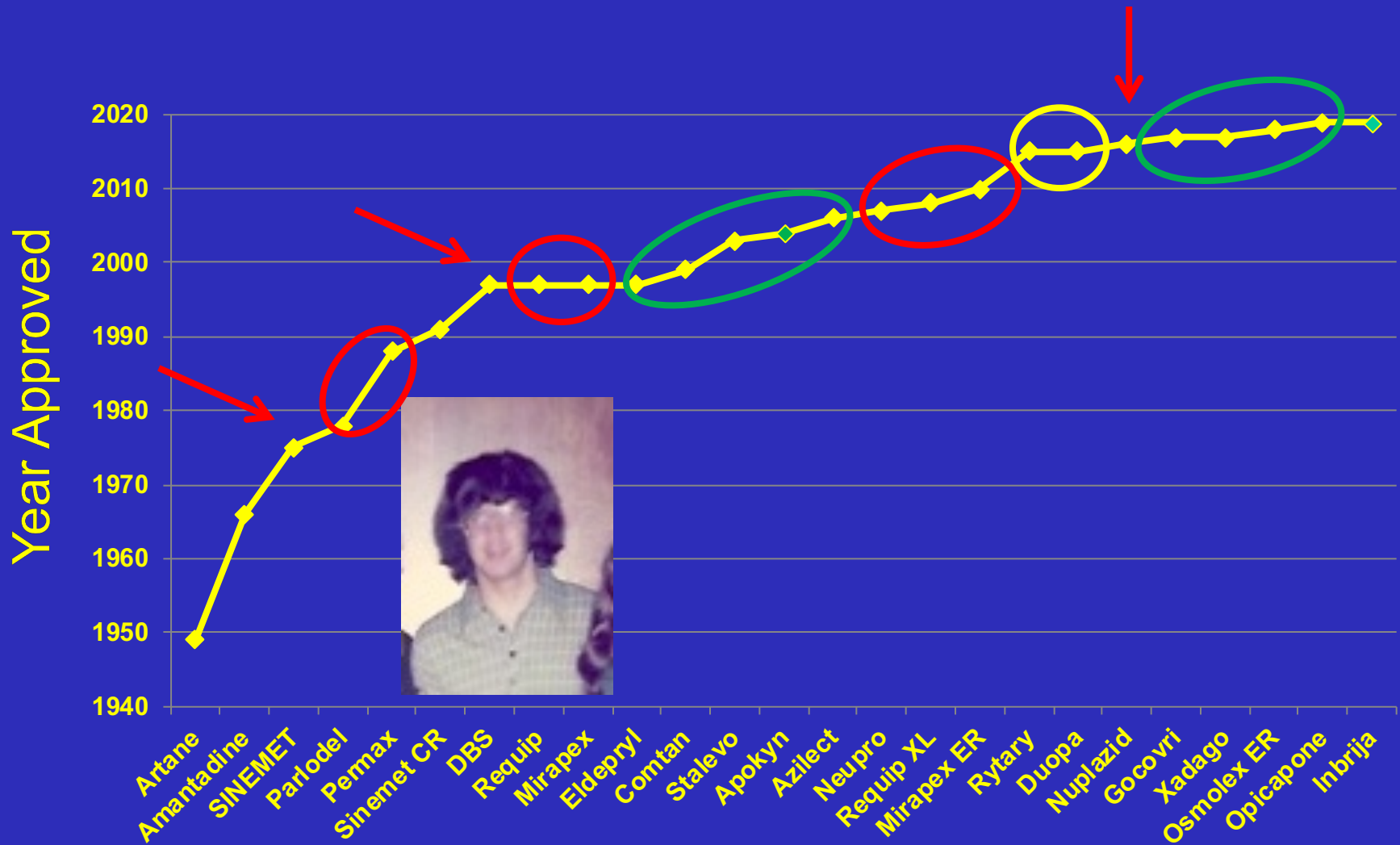
- Phases and Types
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Why Participate?

- 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



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 trials are the way to advance treatments
- Patients must be knowledgeable about clinical trials and consent to participate
- Researchers must respect the patients and ensure they are treated appropriately
- Most centers in the Baltimore/ Washington area have clinical trial programs

