Conducting the Clinical Trials; Why and How

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의학 (Medicine)

- 인간을 질병으로부터 구하고 건강법을 모색하는 학문
- "Wikipedia" the science and art of healing. It compasses a range of health care practices evolved to maintain and restore health by the prevention and treatment of illness.

Declaration of Helsinki

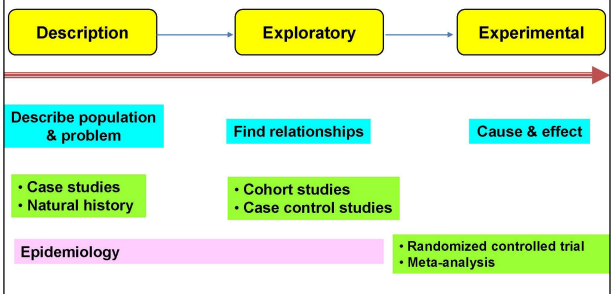
2. It is the **duty of the physician to promote and safeguard the health of the people**. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
4. **Medical progress is based on research** which ultimately must rest in part on experimentation involving human subjects.
6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. **Even the best proven prophylactic, diagnostic, and therapeutic methods must continuously be challenged through research** for their effectiveness, efficiency, accessibility and quality.

World Medical Association, 1964

Growing prevalence of chronic disease

- As the population grows and ages, its health care needs continue to expand
- Chronic disease and diseases of the elderly are becoming increasingly prevalent
- Health care cost is quickly rising

Continuum of clinical research



** From Portney & Gross*

Clinical trial

A prospective study comparing the effect and value of intervention(s) against control in human subjects

Research designs

	No	Yes
Intervention	Observational	Experimental
Data collected forward	Retrospective	Prospective
>1 Observations	Cross-sectional	Longitudinal

Why we need clinical trials?

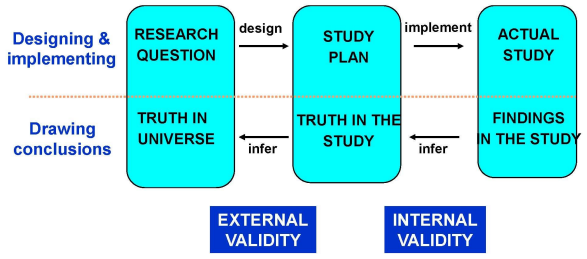
- For patients
  - Clinical trials are mandatory for the development of better medicines.
  - Access to new medicines.
  - Better quality of care
- Financial advantages
- Infrastructure for efficient drug development

What new medicines have done?

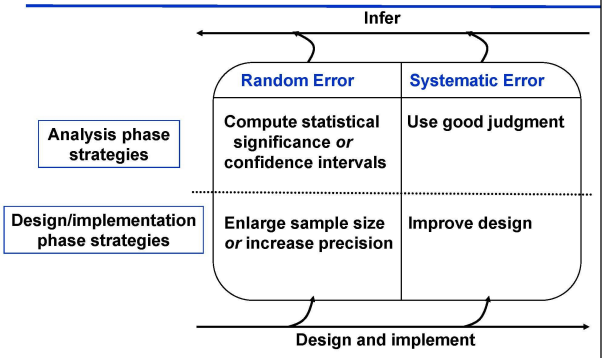
- Extending life
- Preventing the need for care
  - Hospital, emergency, long-term care
- Improving health & quality of life
- Controlling health care costs
- Strengthening the economy

PhRMA 2006

Physiology of Research; Design & implementation



Research Errors



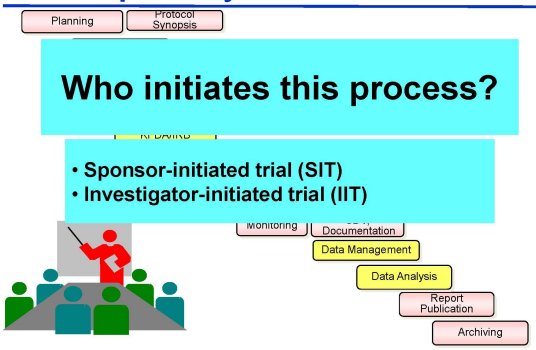
Anatomy of Research

- Research question — objectives
- Significance — background
- Design
- Subjects — eligibility, recruitment
- Variables — predictor, outcome
- Statistical issues

Good research question; FINER

- Feasible
  - Adequate number of subjects & technical expertise
    Affordable in time and money, manageable in scope
- Interesting
- Novel
  - Confirm, refute, or extends previous findings, provide new findings
- Ethical
- Relevant
  - To scientific knowledge, clinical & health policy, and future research directions

Critical pathway in clinical trials



Endpoint

- The criterion by which patient benefit is measured.
- Primary endpoint; The main result that is measured at the end of a study to see if a given treatment worked (e.g., overall survival). It should be decided before the study begins.

Ideal "Endpoint"

1. Easy to diagnose or observe
2. Free of measurement or ascertainment errors
3. Observed independent of treatment assignment
4. Clinically relevant
5. Chosen before the start of data collection

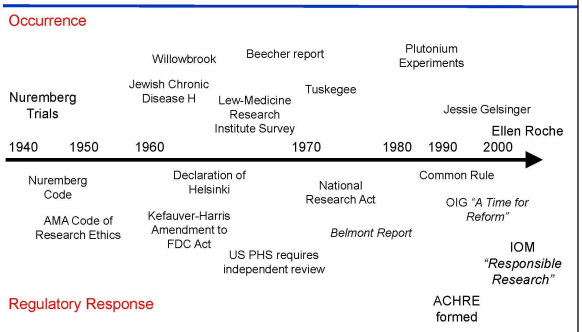
Surrogate Endpoints

- Be a correlate of the true clinical outcome
- Fully capture the net effect of treatment on the clinical outcome

Surrogate endpoints: Examples

Disease	True endpoint	Surrogate endpoint
Cancer	Survival	PFS, response rate
Diabetes mellitus	Survival	Blood glucose level
Glaucoma	Loss of vision	Intraocular pressure
Mental illness	Mental status	Psychological test score

Evolution of human subjects protection in clinical studies



Subject Protection Reform

- "No matter how much we improve our system of checks and balances, the primary responsibility for full and thoughtful disclosure, enrollment without coercion, monitoring of the conduct of a trial, reporting of adverse events, and confidentiality must remain with the local primary investigator. This approach provides the essential basis for trust."

Slater EE, NEJM, 2002;346:402-4

Professional integrity in clinical research

"The presence of an intelligent, informed, conscientious, compassionate, and responsible investigator."

Henry Beecher