## Hierarchy of processed evidence

"Processing" evidence

Primary Studies → Summaries → Guidelines

RCTs
Cohort studies
Case control studies

Meta-analyses

Validation

RCTs
Meta-analyses

## Practice Guidelines

Methods of development

Informal: Systematic assessment of expert opinion.

Evidence-based: Structured review of published and unpublished literature, expert assessment of data, consensus development, identification of "gray zones."

## Practice Guidelines

Limitations

- Database limitations
  - Confounding
  - Bias
  - Generalizability
- Failure to recognize risk aversion
  - Physician
  - Patient
- Lack of specificity

## Practice Guidelines

Utility

- Achieve consistency after consensus
- Stimulate reconsideration of clinical strategies

## Key Point:

**Guidelines are only as good as the data and the process.**

## In conclusion:

- *Investigational tools*
  - Case control studies
  - Cohort studies
  - Randomized control trials
  - Meta-analyses
- *US trends in information acquisition, management and use.*
  - Embedded information retrieval
  - Dependency on meta-analyses
  - Use of "administrative" data bases
    - Billing data
    - Demographic registration data
    - Test result data

## In conclusion (continued):

- *US checks and balances*
  - Role of academic medical centers
  - Role of professional societies
  - Role of government agencies
    - National Institutes of Health
    - Agency for Health Care Research and Quality

## In conclusion (continued):

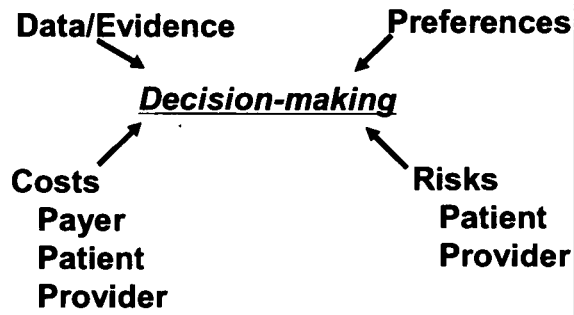
- *Lessons for our Japanese colleagues*
  - Build for future utilities in electronic records
  - Maintain checks and balances
  - Retain diversity/variability

## Where are we?

## Evidenced-based medical care is old and new...

## Managing the wealth of data is the challenge

## Information integration in practice




## Assessing Information For Use In Clinical Practice:

### "Evidence-based medicine" for patient care

John D. Goodson, M.D.
Associate Professor of Medicine

Thank you

Questions?

## Ajay K. Singh, M.D.

Dr. Singh is Clinical Director, Renal Division, and Director, Dialysis Services, Brigham and Women's Hospital.

He is also Medical Director of KidNE Renal Disease Management.

He is also Director of the Brigham/Faulkner dialysis unit at the Faulkner Hospital.

Dr. Singh is Associate Professor of Medicine, Harvard Medical School.

Dr. Singh directs postgraduate CME courses sponsored by Harvard Medical School in both nephrology and internal medicine.

In addition, to his roles in medical education, Dr. Singh's interests lie in the diagnosis and management of lupus nephritis and chronic kidney disease.

He has several clinical research studies currently underway in these areas. He runs a busy chronic kidney disease clinic at the Brigham and attends on the inpatient consultative and dialysis services.

# Organizing a Successful Clinical Trial

Ajay K. Singh, MB., MRCP (UK), MBA
Brigham and Women's Hospital
Harvard Medical School

Disclosures: Grants-NIH, NKF, Ortho Biotech, Watson, Amgen, Roche. Speakers Bureau-Ortho Biotech, Abbott, Pfizer, Watson. Consultant: Ortho Biotech, Amgen

## Classifications of Research Studies: Three Main Types

Observational Studies:
- Groups are studied & contrasts made between groups
- The observed data collected are analyzed

Analytic Studies:
- Also called Experimental
- Study the impact of a certain therapy
- Ultimately the investigator controls factor being studied

Clinical Trial:
- Considered the "true" experimental study
- "Gold Standard" of clinical research
- Often a prospective study that compares the effect and value of an intervention against a control in human subjects

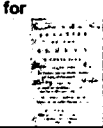
## The Purpose of a clinical trial

- *The major objective of a comparative trial is to provide a precise and valid treatment comparison.*
- *The trial design can contribute to this objective by:*
  - *preventing bias*
  - *ensuring an efficient comparison*
  - *possessing sufficient simplicity so as to encourage participation and minimize errors.*

Kalish and Begg, 1985

## Historical Context First "Clinical Trials"

- Clinical Trials have a long history – even if not acknowledged as *Clinical trials*
- Formal record of clinical trials dates back to the time of the *"Trialists":*
  - Dr. Van Helmont's proposal for a therapeutic trial of bloodletting for fevers [1628]
  - Dr. Lind's, a ship surgeon, trial of oranges & limes for scurvy [1747]



## Historical Context First "Clinical Trials"

Alexander Fleming
Winner of the Nobel Prize in Physiology or Medi 1945

Historical Highlights of Drug Trials
- 1909: Paul Ehrlich - Arsphenamine
- 1928: Alexander Fleming - Penicillin
- 1935: Gerhard Domagk - Sulfonamide
- 1944: Schatz/Bugie/Waksman – Streptomycin
- By 1950, the British Medical Res. Council developed a systematic methodology for studying & evaluating therapeutic interventions

## Phases of Clinical Trials

| Phase | Participants | | Research questions |
|---|---|---|---|
| | Number | Characteristics | |
| I | 20-80 | Usually young, healthy, male volunteers | Tolerability<br>Pharmacokinetics<br>Pharmacodynamics |
| II | 100-300 | Patients rather than volunteers | Effectiveness<br>Dosage, Safety |
| III | 1,000<br>-3,000 | Approximate real-life patient population | Compare to placebo, current treatments<br>Effects of compound on targets, side-effects |

## Phases of Clinical Trials (cont.)

| Phase | Research questions |
|---|---|
| IIIb | Marketing – cost/value<br>Compares with market leader<br>Further data on safety and efficacy |
| IV | New formulations<br>Identify best patients<br>Safety assessment |

Hall, John "The Drug Development Process"

http //clinicaltrials gov/ct/gui/info/whatis;jsessionid= FBB62CC45DC724E2251E4920PB6084CC#phases

Gudant

## Core Components of Clinical Trials

- Involve human subjects
- Move forward in time
- Most have a comparison CONTROL group
- Must have method to measure intervention
- Focus on unknowns: effect of medication
- Must be done before medication is part of standard of care
- Conducted early in the development of therapies

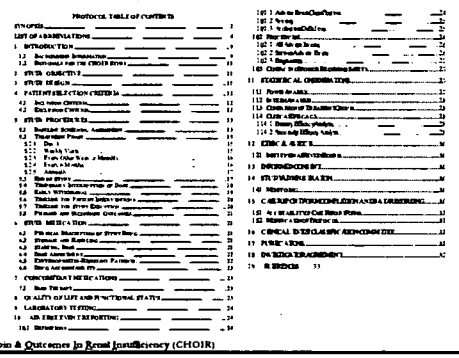
## *WHAT IS THE QUESTION?*

Each clinical trial must have a primary question

The primary question, as well as any secondary or subsidiary questions, should be carefully selected, clearly defined and stated in advance

A study protocol is the starting point

## CASE EXAMPLE: CHOIR



Correction of Hemoglobin & Outcomes in Renal Insufficiency (CHOIR)

## CASE EXAMPLE: CHOIR

PROTOCOL TABLE OF CONTENTS



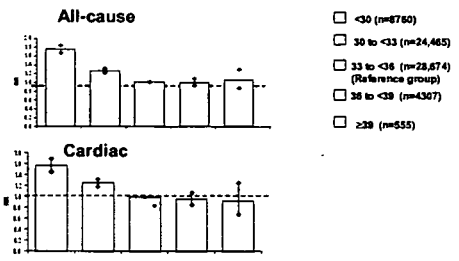
## *In patients with impaired kidney function, does higher hemoglobin lead to improved outcomes (CVD)*

*Treatment group:*
Erythropoietin therapy Q-weekly to target Hb 13.5 g/dl

vs

*Control group:*
Erythropoietin therapy Q-weekly to target Hb 11.3 g/dl

## Lower Hb Levels Associated With Higher Mortality Risk in ESRD Patients




Reproduced with permission from Collins AJ et al. *J Am Soc Nephrol.* 2001;12:2465-2473.

## Effects of Partial Correction of Anemia on Left Ventricular Size

| Study | N | Duration (mo) | Mean HCT Pre-EPO (%) | Mean HCT Post-EPO (%) | % Reduction in LVM |
|---|---|---|---|---|---|
| London '89 | 11 | 6 | 20.4 | 31.8 | 17 |
| Macdougall '90 | 9 | 12 | 19.8 | 32.6 | 29 |
| Silberberg '90 | 22 | ≥6 | 18.9 | 34.2 | 15 |
| Cannella '91 | 9 | 6 | 17.7 | 29.4 | 32 |
| Colan '91 | 10 | 6 | 21.0 | 30.0 | 35 |
| Low-Friedrich '91 | 25 | ≥4 | 23.7 | 30.9 | 11 |
| Pascual '91 | 15 | 12 | 19.7 | 32.2 | 34 |
| Goldberg '92 | 15 | 7 | 22.9 | 32.7 | 35 |
| Martinez-Vea '92 | 9 | 24 | 20.8 | 32.3 | 25 |
| Zehnder '92 | 12 | ≥12 | 25.8 | 34.2 | 30 |
| Carletti '93 | 10 | ≥6 | 21.0 | 31.0 | 2 |

HCT = [illegible]; LVM = left ventricular mass

## Randomized Controlled Trials of High- vs Low-dose EPO, High vs Low Hb Target

| | US Normal Hct Study | Scandinavian Normal Hct Study | ECAP | LVH study |
|---|---|---|---|---|
| Patient type (N) | Dialysis with CAD or CHF (N = 1233) | HD, PD, CKD Excluded heart disease (N = 416) | Stage 3–4 CKD (N = 241) | HD with no CAD or LV dilation (N = 596) |
| Low target | 30% | 9–12 g/dL | 11–12 g/dL | 9.5–11.5 g/dL |
| High target | 42% | 13.5–16 g/dL | 13–15 g/dL | 13.5–14.5 g/dL |
| 1° end point | Death + MI | 6-min walking test | Delay in CKD progression | LVVI |
| Result | High arm worse | High arm insignificantly worse | CVD events 25% vs 18% (high vs low) | No difference |
| Comment | Terminated early due to high arm losing | Unable to measure 1° outcome | Terminated early due to PRCA | 96 weeks of treatment |

ECAP = Effect of Early Correction of Anaemia on the Progression of Chronic Kidney Disease; CAD = coronary artery disease; HD, hemodialysis; PD = peritoneal dialysis; LV = left ventricular; MI = myocardial infarction; PRCA = pure red cell aplasia.

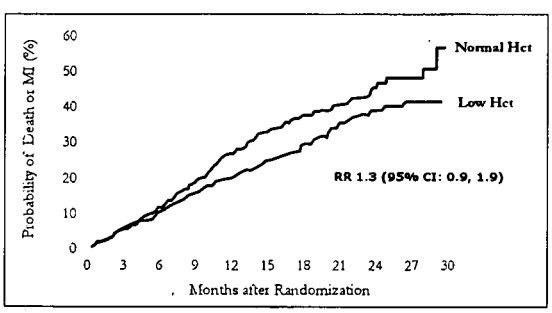
Besarab A et al. *N Engl J Med* 1998;339:584-590.
Furuland H et al. *Nephrol Dial Transplant* 2003;18:353-361.
Rossert J et al. *Am J Kidney Dis.* 2006;47:738-750.
Parfrey PS et al. *J Am Soc Nephrol.* 2005;16:2180-2189.

## Results of Normal Hematocrit Study

| | Low Hct | Normal Hct |
|---|---|---|
| n | 618 | 615 |
| Hct | 30 | 42 |
| Epoetin dose | 160 | 460 |
| Total deaths | 150 | 183 |
| Non-fatal MI | 14 | 19 |
| RR | | 1.3 (0.9-1.9) |

Besarab et al. N Engl J Med 339:584-590, 1998

## Composite Endpoint Analysis




Besarab et al. N Engl J Med., 339:584-590, 1998.

## CHOIR Hypothesis

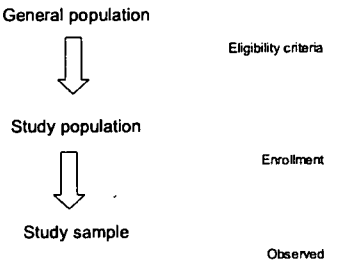
- Compared outcomes of CKD patients randomly assigned to treatment groups that differed only in targeted hemoglobin levels
  - 11.3 vs 13.5 g/dL
- Tested primary hypothesis that the level of anemia correction with once weekly dosing of epoietin-alfa in patients with chronic kidney disease decreases mortality and cardiovascular morbidity

## Define the Study Population

- **Definition: "is the subset of the Population with the condition or characteristics of interest defined by the eligibility criteria"**
- **Should be defined in advance, starting unambiguous inclusion (eligibility) criteria.**
- **These criteria will impact on the study design, ability to generalize and participant recruitment.**

## Study Population

Subset of the general population determined by the eligibility criteria




## CHOIR Study Population

Inclusion Criteria

- •Hb < 11 g/dl
- •Age ≥ 18
- •Steady-state GFR ≥ 15 ml/min and ≤ 50 ml/min

## CHOIR Study Population

Exclusion Criteria

- •Uncontrolled hypertension
- •Iron overload (TSAT) >70% or ferritin >1000 ng/mL
- •Unstable angina pectoris or angina at rest
- •Refractory iron deficiency anemia (TSAT is < 20% despite appropriate IV iron repletion)
- •Currently receiving rHuEPO or having received it within 3 months of study entry.

## Possible Clinical Trial Designs

- **Randomized/blinded trial**
- **Randomized/double blinded trial**
- **Non-randomized concurrent controlled trial**
- **Placebo trial**
- **Historical controlled trial**
- **Crossover Trial**
- **Withdrawal trial**

## Non-randomized Trials May Be Appropriate

- **Early studies of new and untried therapies**
- **Uncontrolled early phase studies where the standard is relatively ineffective**
- **Investigations which cannot be done within the current climate of controversy (no "clinical equipoise")**
- **Truly dramatic response**

## Advantages of Randomized Control Clinical Trial

1. Randomization "tends" to produce comparable groups
2. Randomization produces valid statistical tests

| CHOIR Selected Baseline Characteristics | Group A Hb 13.5 g/dL | Group B Hb 11.3 g/dL |
|---|---|---|
| Age | 66.0 (14.3) | 66.3 (13.5) |
| Gender (male) % | 43.8 | 45.9 |
| Race (Black) % | 28.6 | 29.3 |
| Ethnicity (Hispanic) % | 12.5 | 13.5 |
| Smoking % | 47.5 | 44.6 |
| BMI | 30.4 (7.7) | 30.4 (7.5) |
| Mean Arterial Pressure | 93.3 (12.1) | 92.5 (12.0) |

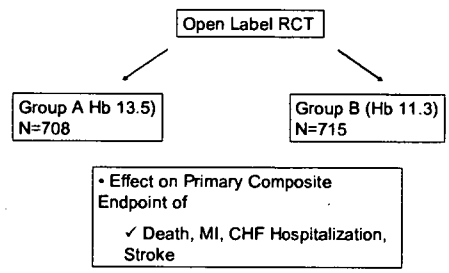
## Disadvantages of Randomized Control Clinical Trial

1. Generalizable Results?
   - Participants studied may not represent general study population.
2. Recruitment
   - Hard
3. Acceptability of Randomization Process
   - Some physicians will refuse
   - Some participants will refuse
4. Administrative Complexity

## Simplified

- Randomized: Schemes used to assign participant to one group
  - Ex: Every 3 gets higher dose
- Nonrandomized: All with Hep. C = cases; others = controls
- Blinded: Participants do not know if in experimental or control group
- Double Blinded: Participants AND staff do not know group assignment
- Open Label: Participants AND staff *know* group assignment
- Placebo: Inactive pill w/ no therapeutic value

## CASE EXAMPLE: CHOIR




## Endpoint Considerations

- Define endpoints
  - Use established definitions wherever possible
  - Frequently guided by regulatory authorities and by sample size considerations
- Use independent adjudication if possible
  - EXAMPLE: CHOIR study -- Duke CEC used.
    - Committee of 3 to 5 members
    - Charter for functioning of committee
    - Membership should be diverse (cardiologist, nephrologist etc)

## CASE EXAMPLE: CHOIR

### Endpoints

Primary Endpoint: Composite endpoint of
- Death,
- Myocardial infarction
- Stroke
- CHF hospitalization (excluding RRT)

Secondary Endpoints

All cause mortality, CHF hospitalization, Myocardial infarction, Stroke, Renal replacement therapy, Cardiovascular hospitalizations, All cause hospitalizations, Change from baseline in hemoglobin / hematocrit, Epo dose, iron stores, Development of incident CHF (determined using NHANES I criteria), Change from baseline in Glomerular filtration rate, Health related quality of life and functional status

**Myocardial infarction**
2 of the following
- •Chest pain for ≥ 15 minutes
- •Abnormal cardiac enzymes
- •New EKG findings suggestive of MI

**Stroke**
- A new neurologic deficit of sudden onset that is not reversible within 24 hours and which is not due to a readily identifiable non vascular cause (i.e brain tumor, trauma)

**CHF Hospitalization**
- Unplanned CHF presentation requiring admission during which patient received IV therapy with inotropes, diuretics or vasodilators. (Hospitalization involving renal replacement therapy excluded)

**CASE EXAMPLE: CHOIR**

## Clinical Endpoints Committee

- Events triggered off the case report form
- Sites queried for source documents
- Source documents reviewed by committee to see if a priori definitions of the outcomes were met and entered into the clinical database as an event

## Other Elements in Clinical Trial Protocol

- **Sample size & power calculations**
- **Ethical issues**
- **Recruitment**

**CASE EXAMPLE: CHOIR**



## Statistical Plan

- Need to have one
- Definition: "statistical analysis plan (SAP) contains definitions of analysis populations, derived variables and statistical methods for the analysis of efficacy and safety".
- Components:
  - Details on randomization and blinding
  - Discussion on early termination of study
  - Sample size determination
  - Discussion of planned analyses
    - Primary and secondary endpoints
    - Definition of visit windows
    - Definition of baseline values
    - Methods of analyses

**CASE EXAMPLE: CHOIR SAP**

- Definitions
  - Primary and secondary endpoints
    - ***A composite event*** consists of all cause mortality, myocardial infarction, stroke, or hospitalization for congestive heart failure not including those hospitalization during which RRT occurs.
    - ***A composite event occurred during the study*** is defined as the event that occurred between the day of the first dose of study medication administered and up to 30 days after the last dose of the study medication. The composite events occurred during the study will be included in the efficacy analyses.
  - Definition of visit windows
    - subjects do not always adhere to the protocol visit schedule, develop rules to assign actual visits to protocol visits.
  - Definition of baseline values
    - "The Baseline assessment on a variable for a subject is the last observed value of that variable obtained for that subject on or prior to Day 1. Specifically for hemoglobin, hematocrit, blood pressure, and heart rate values, the Baseline value will be the value on Study Day 1. If any of these values at Day 1 is missing, the missing value will be imputed using the corresponding value collected at the Screening visit."

## Statistical Power

- Statistical power computations provide a basis for deciding if statistical tests are sufficiently powerful to detect effects if they are actually there (in the population).
- Suppose you test a null hypothesis
- Ho: x=y
- Power is the Probablility of rejecting the null hypothesis, ie x is not equal to y
- Power depends on:
  - Alpha (significance level)
  - Effect size
  - Sample size

## Study Participant Recruitment

- **Identify eligible participants**
- **Explain study**
- **Provide informed consent**
- **Reassess eligibility**
- **Assign to one group**

**Participants should be told:**

- **May have side effects (adverse effects)**
- **Time commitment**
- **Benefits & risks**
- **May withdraw at any time**
- **Enrollment 100% voluntary**

**CASE EXAMPLE: CHOIR**

## Recruitment

- 130 sites in the US
- Investigator and Coordinator meetings
- Newsletter
- Monitor visits
- Site visits by PI
- Regular phone calls with groups of sites
- Policy regarding site attrition

## Ethics of Clinical Trials: Protection of Participants

**3 ethical principles guide clinical research:**

- **Respect for Persons: Treatment of person as autonomous**
- **Beneficence: Issue re: potential conflict between good of society vs. individual**
- **Justice: Treatment of all fairly & all equally share benefits & risks**

## Ethical Norms of Clinical Trials

**Sound study designs take into account:**

- **Randomization or sharing of risks**
- **Proper use of placebo**
- **Processes to monitor safety of rx/tx**
- **Competent investigators**
- **Informed consent**
- **Equitable selection of participants**
- **Compensation for study related injuries**

## Ethical Issues: Protection of Human Subjects

- **Rely on integrity of investigator but outside groups also have oversight**
- **Participants' rights protected by Institutional Review Boards [IRBs]**
  - **An IRB is defined as: "any board, committee or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of biomedical research involving human subjects"**

## Human Subjects' Protection

IRB responsible for such tasks:

- Review research to ensure that potential benefits outweigh risks
- Develop and issue written procedures
- Review research for risk/benefit analysis & proper protection of subjects
- Issue written notice of approval/disapproval to the Investigator
- Review and respond to proposed protocol changes submitted by the Investigator

## Human Subjects' Protection

### IRB Responsibilities (continued):

- Review reports of deaths, and serious and unexpected adverse events received from the Investigator
- Conduct periodic continuing review of the study, study risks, selection of subjects, privacy of subjects, confidentiality of data, and the consent process

## Development of Ethical Guidelines

| | |
|---|---|
| 1803 | Percival's Medical Ethics |
| 1900 | The Directive on Human Experimentation |
| 1947 | Nuremberg Code |
| 1964, 1975, 1983, 1989, 1996, 2000 | Declaration of Helsinki |
| 1979 | Belmont Report |
| 1982, 1993, 2002 | International Ethical Guidelines for Biomedical Research Involving Human Subjects |

http://www.patientcenters.com/trials/news/ethics_of.html, Emanuel, Ezekiel, et al "What Makes Clinical Research Ethical?" Talbot, David and Joan Perou "Ethical Issues"

## Historical Context: Nuremberg Code, 1947 – Key Points

- Voluntary informed consent
- Experiment must be for the good of society, & results not obtainable by other means
- Experiment should be based upon prior animal studies
- Physical & mental suffering & injury should be avoided
- No expectation that death/disabling injury will occur from the experiment
- Risk vs. benefit
- Protect subjects against injury, disability, or death
- Only scientifically qualified persons to be involved
- Subject can terminate her/his involvement

## Informed Consent: A Part of Human Subject Protection

**Objectives of Informed Consent**

To Ensure:

- Voluntariness
- Comprehension
- Information

To Demonstrate That:

- Person freely gave consent to participate
- Consent given by a competent person
- Person has been given all information
- Person knows this is research – not treatment

## Components of Informed Consent

- Must Include the Following Information:
- Why research being done?
- What researchers want to accomplish
- What will be done and for how long
- Risks & benefits of trial
- Other treatments available
- Can withdraw from trial whenever desire
- Compensation for unexpected injuries

## Vulnerable Populations

Groups thought not to have autonomy to give informed consent:
- children
- mentally impaired, individuals with dementia
- Prisoners

OR

Who may be unduly influenced to participate:
- students
- subordinates
- pregnant women (actually, the fetuses)
- patients (care-giver vs. researcher)

## Vulnerable Populations

To safe guard these groups, special requirements such as:

- Only parent can consent for minor
- Consents must be in subject's native language.
- Prisoners: only some types of research allowed

## Inclusion in Clinical Trials

- NIH Revitalization Act of 1993: Guidelines that require inclusion of women* & minorities in clinical studies
- New guidelines stipulate that:
  - Women & minorities are to be included in all human subject research
  - They are to be included in Phase III trials to allow sufficient power to note differences
  - Cost cannot be a barrier
  - Outreach activities must take place to include & follow these groups

* Historically women were excluded because of reproductive age (ages 18-45) and fear of harm to potential unborn child

## Issues in Clinical Trials: Use of Placebo Trials

On international realm, 1999 "Declaration of Helsinki" revised to address use of placebos:

- Placebos not ethical in virtually all studies that involve diseases with PROVEN tx
- Remain ethical in trials where no proven tx
- Revisions due to controversy over use of placebos in attempting to find easy/cheap way to reduce HIV perinatal transmission
  - 1998 study in Ivory Coast, Uganda, & Thailand: HIV+ pregnant women given either placebo or shorter course of AZT

## Participation in Clinical Trials

Why Some Participate:
- Give back to society
- Exhausted all other txs
- Health care services
- Payment & incentives
- Support
- Others??

Why Some Do Not?
- Mistrust of studies
- Do not want to be "guinea pig"
- Do not meet criteria
- Cannot give up time for study visits
- Barriers: lang., distance

## Taking Part in Research Studies: Questions to Ask

- What is study about?
- What are the goals? Are they achievable?
- What will be the impact?
- Study sponsor?
- Input into protocols?
- What happens after study is over?
- How results will be disseminated?

## The Impact of Studies

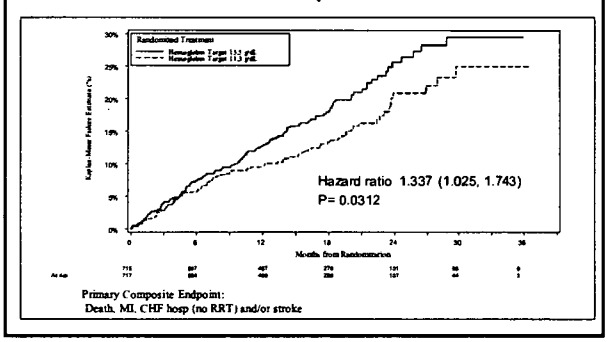
- Some clinical trials have been critical to patient health & provision of health care
- For instance:
  - Cardiovascular trials for ACS
  - Hypertension trials
  - 1st trial of AZT
  - Various cancer treatments
  - ACE/ARB trials in kidney disease

## The Impact of Studies

Other clinical trials have not been as successful for a variety of reasons:

- Medications did not work as in laboratory
- Loss to Follow-Up of too many patients
- Harmful substance
- Unethical & poorly conducted study (Ex: Tuskegee Study & recent Gene Replacement Study)

**CHOIR: Kaplan-Meier Plot of the Time to the Primary Composite Event between Randomization and Termination: ITT Population**




## CHOIR Summary

- Targeting Hb to 13.5 g/dL associated with an increased risk of composite event of death, myocardial infarction, CHF hospitalization, and stroke
- Primary end point was explained by a higher rate of death and CHF hospitalization
- **Increased risk with targeting Hb to 13.5 g/dL and achieving 13 g/dL**

## Summary

- Clinical Trials have a long history
- Different phases of clinical trials
- Clinical trials often yield important results that affect health and well being
- For success: Must follow guidelines & protocol
- Must ensure well-being of participant

International Symposium
for the Innovation of EBM Education

# A Multi-Disciplinary Grass Roots Activity in EBM Education in Tokyo
## –from the experience of EBM-Tokyo and pES club

Eishu NANGO, MD
Department of General Medicine
Tokyo-kita Social Insurance Hospital

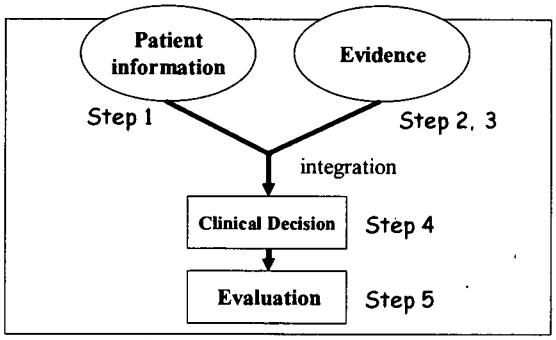


# Self-introduction

- 1973 born in Tokyo
- 1998 graduated from Medical School
- 1999 met EBM
- 2001 started EBM Journal Club
- 2002 attended as primary care physician
  started EBM education
- specialty: primary care, EBM, medical education



# EBM : Evidence-Based Medicine





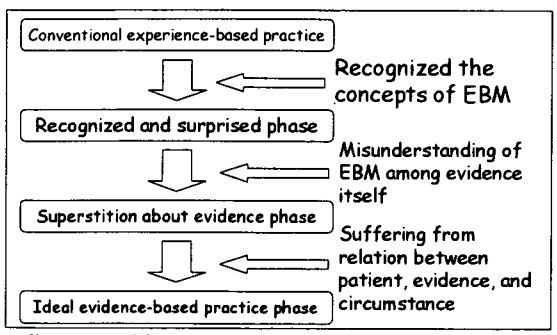

# Merits of EBM practice

True endpoint:
➢providing high-quality care to patients

Surrogate endpoints:
➢appraising articles critically
➢searching technique
➢communication skill with patients and co-workers

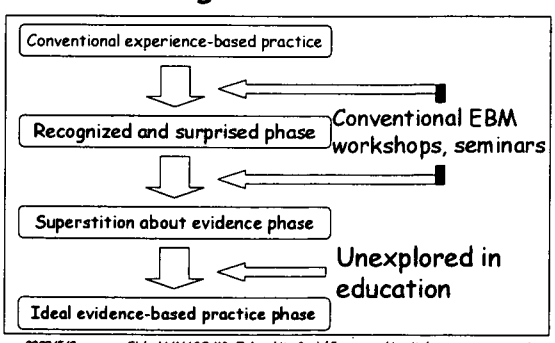


# Maturity process of EBM practice






# Positioning of EBM education



## Current condition of EBM education in undergraduate school

- In undergraduate education, EBM is not taught as a tool for clinical decision but is taught only clinical epidemiology in a part of public health or internal medicine.
- Technical terms of EBM, such as OR, RR, NNT, sensitivity and specificity, likelihood ratio, p-value and 95% CI, are not taught with carrying a meaning at clinical situation.



## Current condition of EBM education for health care providers

- In the EBM lectures provided from drug companies, researches introduce evidence with a lot of bias and let audience to misunderstand them.
- There are less EBM workshops which introduce the concept of EBM and share methods of lifelong learning.
- There are less colleague who study together continually.



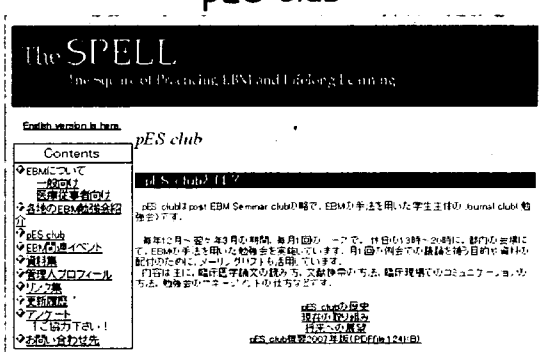
## The value of spreading EBM

- Recognize the need of critically appraising medical information
- Recognize the need of multi-disciplinary team practice
- Master how to do lifelong learning with busy work

⇨ pES club and EBM-Tokyo



## pES club



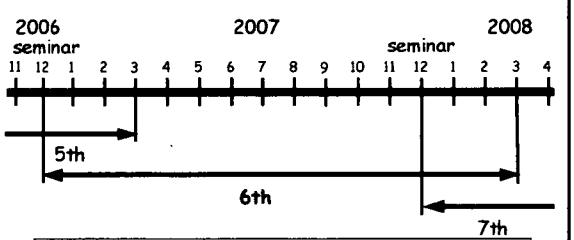



## pES club

- "post EBM Seminar club"
- EBM study group for healthcare students since 2002
- Monthly meeting, yearly camp, 15 months
- SGD（Small Group Discussion）style
- Medical, dental, pharmaceutical, nursing students
- Many different kind of lecturers who practice EBM in clinical setting



## Program for the year of pES club




- Learning the basic knowledge and skills for practicing the five steps of EBM in a year

## First semester (Jan to May)

- Learn critically appraised medical articles and statistical knowledge
- Study design
  - Therapy and Prevention (RCT, SR)
  - Diagnosis (cross sectional study)
  - Prognosis and Etiology (Cohort study)
  - Harm (Case-control study)



## Second semester (Jun to Dec)

- Train each step specifically
  - Step1 : type of question, PICO
  - Step2 : PubMed and other data source
  - Step3 : Critically appraise
  - Step4 : communication, application
- The camp : Training the Tutors Days (TTD)
- EBM practice session



## Third semester (Jan to Mar)

- Overlap with next first semester
- Learn by teaching new members
  - The skills of critically appraise
  - The skills of managing group works
  - The skills of presentation
- Know as much about own growth



## From EBM education to human education

- Many Japanese students cannot use right Japanese
- Not mature as a member of society and afraid of becoming to medical provider
- Plan as lecturers learn themselves
  - How to write e-mail and medical certification
  - propriety
  - Logical speaking
  - presentation



## The numbers of pES members

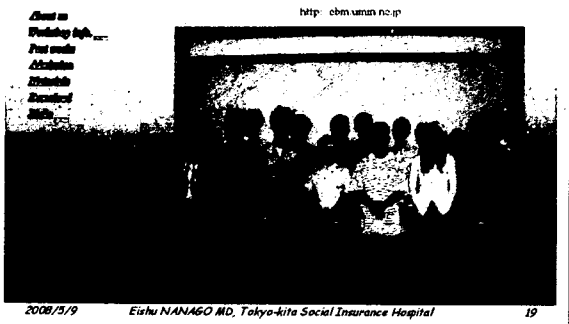
| | med | dent | pharm | nursing | total |
|---|---|---|---|---|---|
| #1 (year of 2002) | 10 | | | | 10 |
| #2 (year of 2003) | 9(2) | 5 | | | 14(2) |
| #3 (year of 2004) | 3(1) | 7(4) | 5 | | 15(5) |
| #4 (year of 2005) | 3 | 5(1) | | 2 | 10(1) |
| #5 (year of 2006) | 7(1) | 5(2) | 5 | 3(1) | 20(4) |
| #6 (year of 2007) | 10(4) | 4 | 3 | 3(3) | 20(7) |
| total | 34 | 19 | 13 | 4 | 70 |

※ ( ) continuator

## EBM-Tokyo

EBM-Tokyo

*Welcome to*
*EBM-Tokyo homepage*





## EBM-Tokyo

- To spread the concept of EBM and improve members' skill, it started in March 2002.
- Activities
  - Produce EBM workshop twice a year
  - Join workshops as tutor or lecturer
  - Dispatch tutors to various study groups
- The members are medical providers, healthcare students and others as volunteers

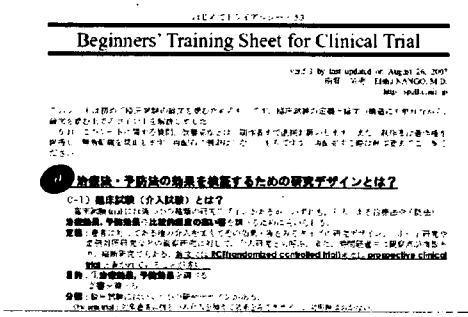


## Workshop

- Twice a year
- Beginners' course and Experts' course
  - Beginners' : learn about critically appraise
  - Experts' : learn specific theme in depth
- Small group style (with 8-10 members)
- Two expert tutors support discussion on each group
- Find new colleague to learn EBM



## Beginners' Training Sheet Serise


Beginners' Training Sheet for Clinical Trial



## Remaining problem on Grass Roots Activity in EBM education

- Colleague
  - Reading articles by several is significant
  - Workshop needs many staffs
- Time
- Motivation
  - compensation
- Sense to catch appropriate topics



## Thank you very much

# Development of problem solving skills in Japanese residency program

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倉敷中央病院

# Contents

- Background
- Japanese reform of medical education
- Core competency of residency program
  - Japan vs US
- Problem solving skill development of the program guideline.

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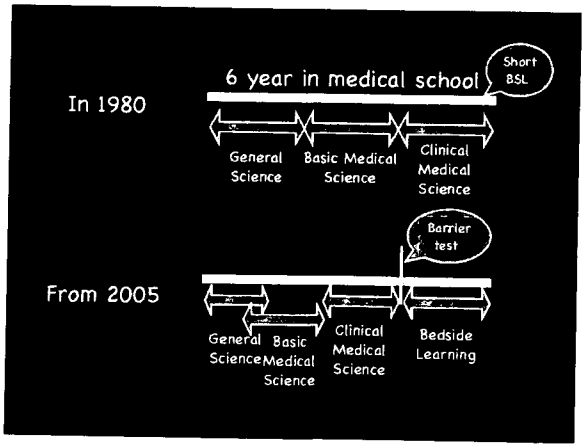
# Background

- National examination at the graduation of medical schools is no longer regarded as a guarantee of lifelong competency as a physician.
- Knowledge gained at a medical school become outdated soon after graduation.
- The goal of continuing medical education is to achieve and keep clinical competency of physician in his or her chosen specialties
- Development of Clinical problem solving skills is the most important competency for their professional life

# Japanese reform of medical eduction

Classroom to Bedside
Knowledge to Skill
Contents & Structure to Competency & Outcome

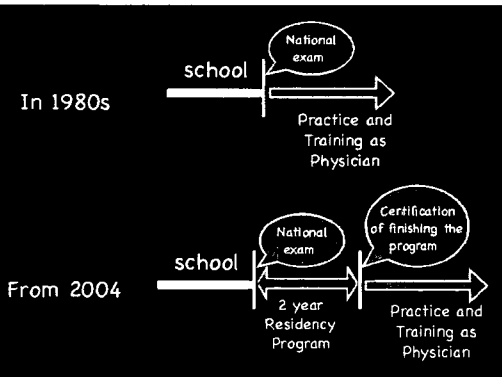
# Undergraduate Medical Education



## Reform of Under-graduate Education

- Students spend more time at the bedside of patients than before.
  - Less than 1 year -> Nearly 2 years.
- Clinical skill assessment of the students has become a key part of medical education.
  - Objective structured clinical examination (OSCE) and Computer based Test before bedside learning
- Problem-based learning was introduced.

## Residency Program




## Reform of Residency Training Program

- In 2004, two-year residency program is obligated after passing of the national license examination.
  - Japanese Ministry of Health, Labor and Welfare (MHLW) set the guideline for the residency program.
  - After 2006, a certificate of the residency program is required to become a Japanese health insurance manager.

## Training and Continuing Education of Medical Specialty in Japan

- In Japan, the credible accreditation of medical specialty had been lacking.
  - Most of the specialties were accredited by each Japanese society of medical specialties based on the length of training and membership.
  - In Japan there was no independent accreditation organization with governmental support, such as JCAHO in US.

## Accreditation of Residency Program

- Quite recently, Japan Council for Evaluation of Postgraduate Clinical Training (JCEP) has been established.
- JCEP is a non-profit organization that evaluates teaching hospitals and their residency programs in Japan
- The evaluation is focused on the structure and contents of the hospitals.
- Structure & Content to Competency & Outcome

## Contents or Competencies

- Determining the structure and contents of training duration is not enough for curricular development.
- Japanese health care consumers are highly demanding physicians with high competency.

## Contents or Competencies

Personal view of Developing the training program

## Traditional concept of training.

- Traditional requirements of residency training were a fixed period of time of the training, structural educational contents and actual experience with patients.
- The curricular development was focused on determining the length of the training period and the number of treated patients during the period.
- There was little attention to the actual needed time and patient volumes for acquisition of the physician competency as a specialist for each trainee. And the outcome of the training assessed after the end of training as a qualifying examination

## Competency based Training

- The competences of the specialty should be defined clearly.
- The assessment of acquired competences of trainees is available during the training.
  - These trainees with prior learning can save the training time and the trainees without specific experience might become a competent specialist after adding the specific short training

## Shifting Paradigms

| | Structure-based (time-based) | Competency-based |
|---|---|---|
| Driving force for curriculum | Content-knowledge acquisition | Outcome-knowledge application |
| Driving force for process | Teacher | Learner |
| Path of learning | Hierarchical teacher -> student | Non-hierarchical teacher <-> student |
| Typical assessment tool | Single subjective measure | Multiple objective measures |
| Program completion | Fixed time | Variable time |

Carraccio C et al: Acad Med 2002, 77: 361-367

## Key component of Competency based training

- Identification of specific competencies. Pre-defined skills and knowledge as core competencies.
  - Surveillance is necessary. Core-competencies (standard) should be set.
- Instruction and Training program aimed at a learner achieving competency.
  - Efficient local training program should be developed.
- Certification based on the correct assessment of competencies achieved off-the-job and on-the-job.
  - Assessment tool should be provided.