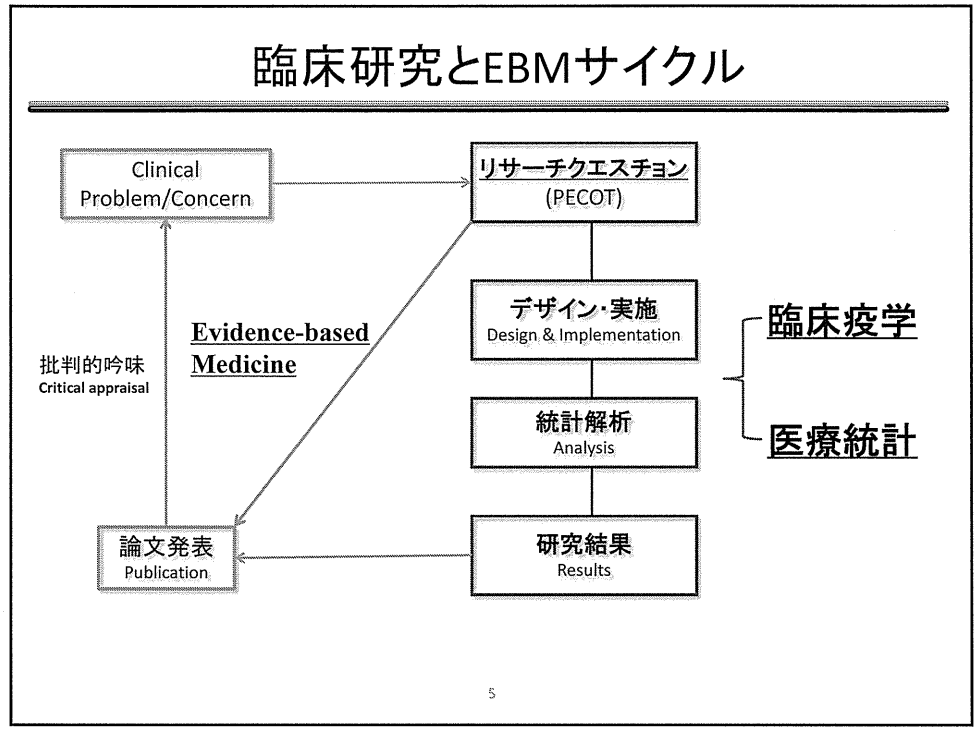
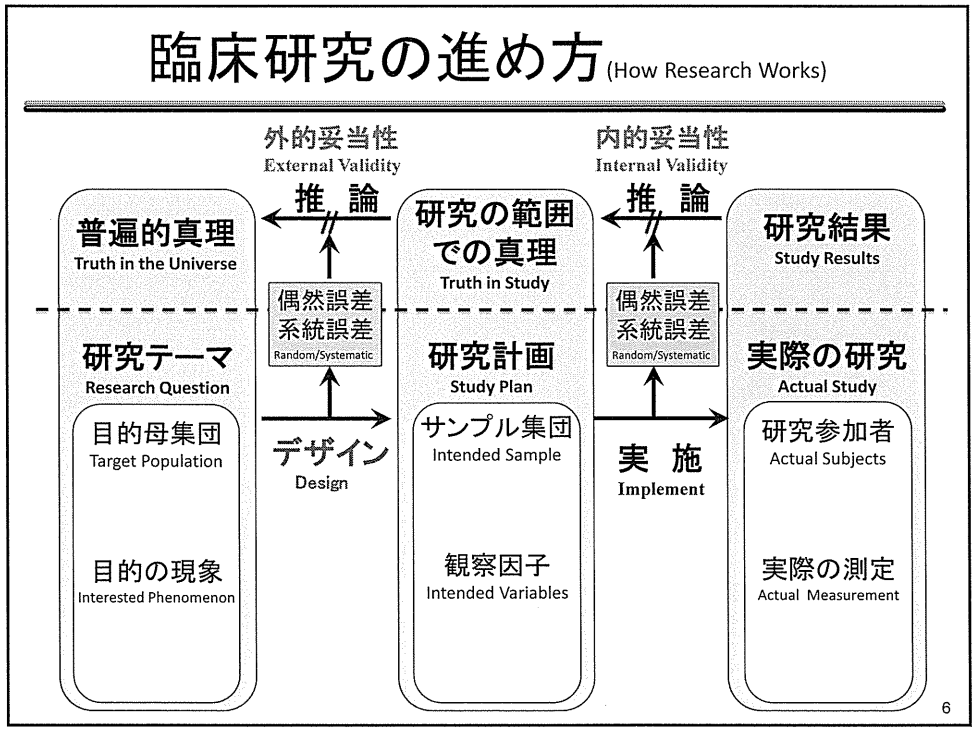
浦山先生


臨床研究とEBMサイクル
Clinical
Problem/Concern
リサーチクエスチョン
(PECOT)
デザイン・実施
Design & Implementation
統計解析
Analysis
研究結果
Results
論文発表
Publication
Evidence-based
Medicine
批判的吟味
Critical appraisal
臨床疫学
医療統計
5


臨床研究の進め方 (How Research Works)
外的妥当性
External Validity
内的妥当性
Internal Validity
推 論
推 論
普遍的真理
Truth in the Universe
研究の範囲
での真理
Truth in Study
研究結果
Study Results
偶然誤差
系統誤差
Random/Systematic
偶然誤差
系統誤差
Random/Systematic
研究テーマ
Research Question
研究計画
Study Plan
実際の研究
Actual Study
目的母集団
Target Population
サンプル集団
Intended Sample
研究参加者
Actual Subjects
デザイン
Design
実 施
Implement
目的の現象
Interested Phenomenon
観察因子
Intended Variables
実際の測定
Actual Measurement
6

研究計画書の構造

表 1-1 研究プロトコールのアウトライン

構成要素	目的
研究テーマ	どういうテーマを研究しようとしているか？
研究の意義(背景)	なぜその研究テーマが重要か？
研究デザイン	どのように研究を実施するか？
研究期間	
研究のタイプ	
対象者	どのような研究対象者をどのように獲得するか？
選択基準	
サンプリング方法	
観察因子(変数)	どのような因子(変数)を測定するか？
予測因子	
交絡因子	
アウトカム	
統計学的事項	研究の規模はどれくらいで，データをどのように解析するか？
仮説	
サンプルサイズの推定	
解析方法	

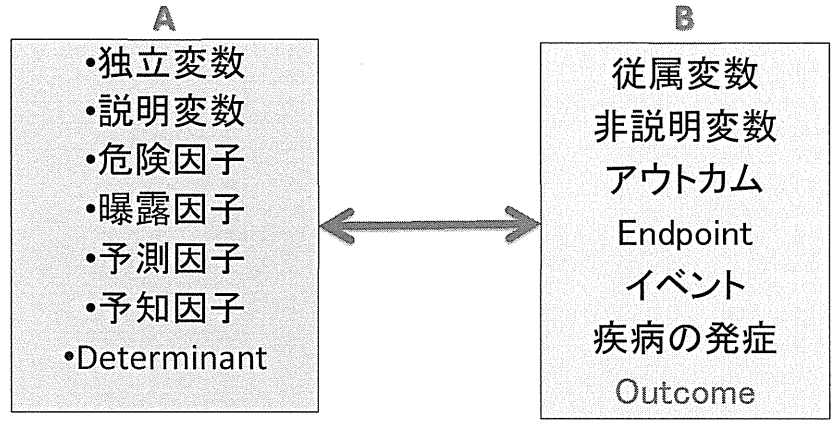
7

Hulley et al., *Designing Clinical Research*, 2007.

研究テーマのタイプ

カテゴリー	説明
頻 度 Frequency	ある疾患の罹患率や発症率 Prevalence/Incidence
病 因 Pathogenesis	ある疾患の原因や危険因子 cause/risk factor
診 断 Diagnosis	ある診断法の診断能 Diagnostic Performance
予 後 Prognosis	ある疾患の平均生存期間など Survival, etc
治療・予防 Treatment Prevention	ある治療法の治療効果や予防効果 Therapeutic/preventive effect
害 Harm	ある治療法による副作用や不利益な影響 negative effects of treatment

リサーチクエスチョン



Aがない患者に比べて、Aがある患者は、Bの発生率が高い、または低いか？

疑問の定式化 (*formulate a question*)

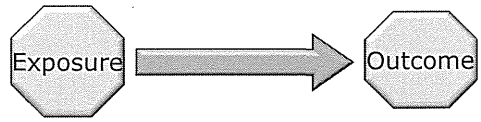
PECOT

臨床的な疑問を解決可能な形であげる

research question

	要素	ヒント	吟味
P	対象一母集団 (Population)	目的とする母集団 intended pop. 研究可能なサンプル集団 study population	代表性？Representativeness?
I (E)	曝露/介入 (Intervention/ Exposure)	薬物療法、カウンセリング 検査、スクリーニング 環境因子への曝露など Therapy, screening, env. exposures, etc.	ランダム割り付け？ ベースラインの調整 交絡因子の測定 コンプライアンス Randomization, adjustment, confounding, compliance, etc.
C	比較対象 (Control)	標準治療、プラシーボ Standard treatment, placebo Non-diseased, non-exposed	
O	アウトカム (Outcome)	死亡、無病生存、検査値・症状の改善、診断、疾患の発症 Mortality, survival, onset of disease, response to therapy, etc.	測定方法は客観的か ブラインド化？ Objective measurement methods, blinding
T	観察期間 (Time)	アウトカムを評価するのに適切な観察期間 appropriate observation period to evaluate outcome	フォローアップ率 Follow-up rate

研究デザインの種類
EPIDEMIOLOGICAL STUDY DESIGN OPTIONS



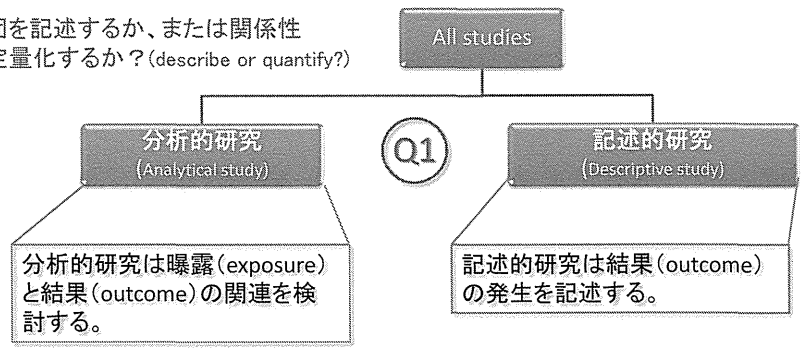
研究をデザインする目的はなにか?

- ✓ 系統的に研究課題に答えを導くため (systematic)
- ✓ バイアスやエラーをできる限り取り除き (controlling error)
- ✓ 他者においても再現できる方法を作る (reproducible)

11

研究デザインの種類 (1)

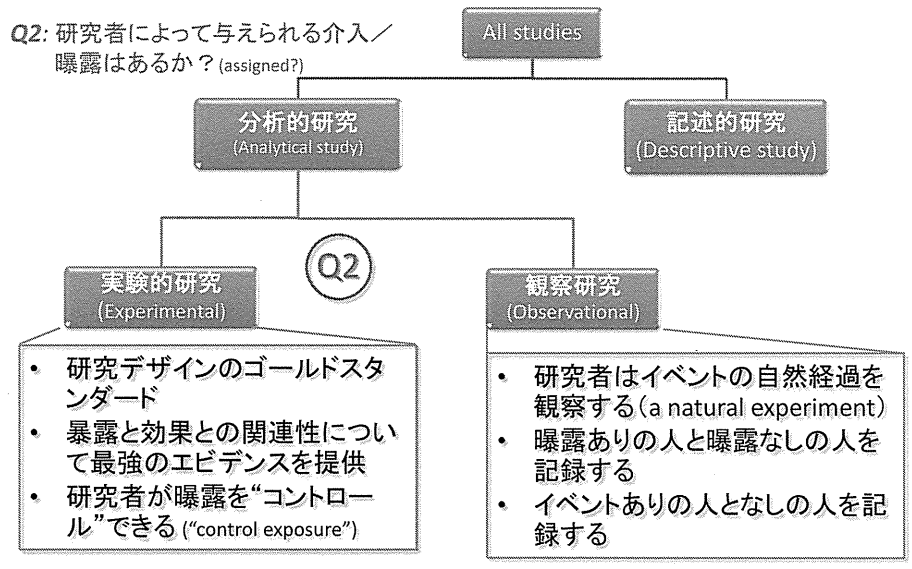
Q1: 集団を記述するか、または関係性を定量化するか?(describe or quantify?)



12

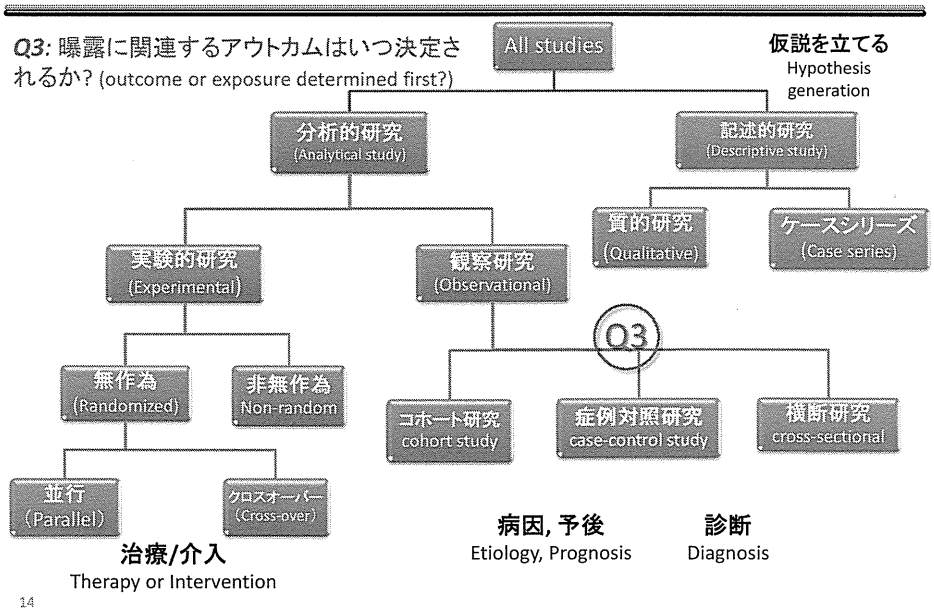
浦山先生

研究デザインの種類 (2)



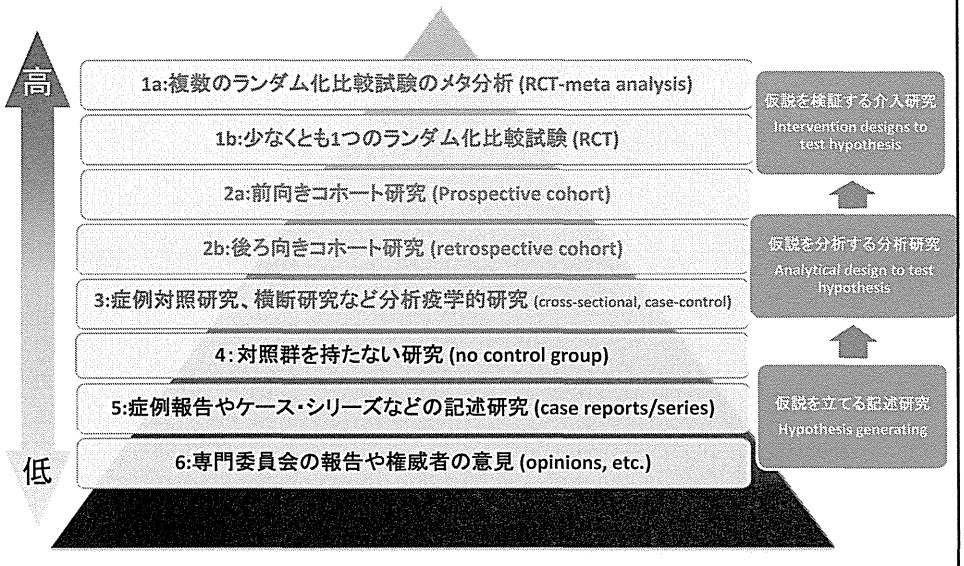
13

研究デザインの種類 (3)



14

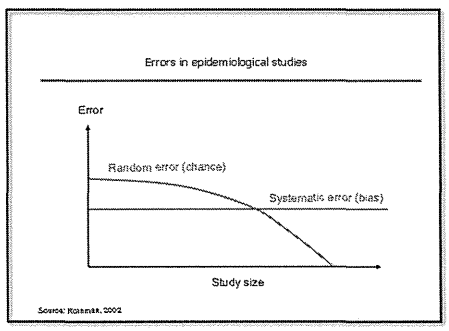
エビデンス・レベル
Evidence Level



**Oxford University, Centre for EBM*

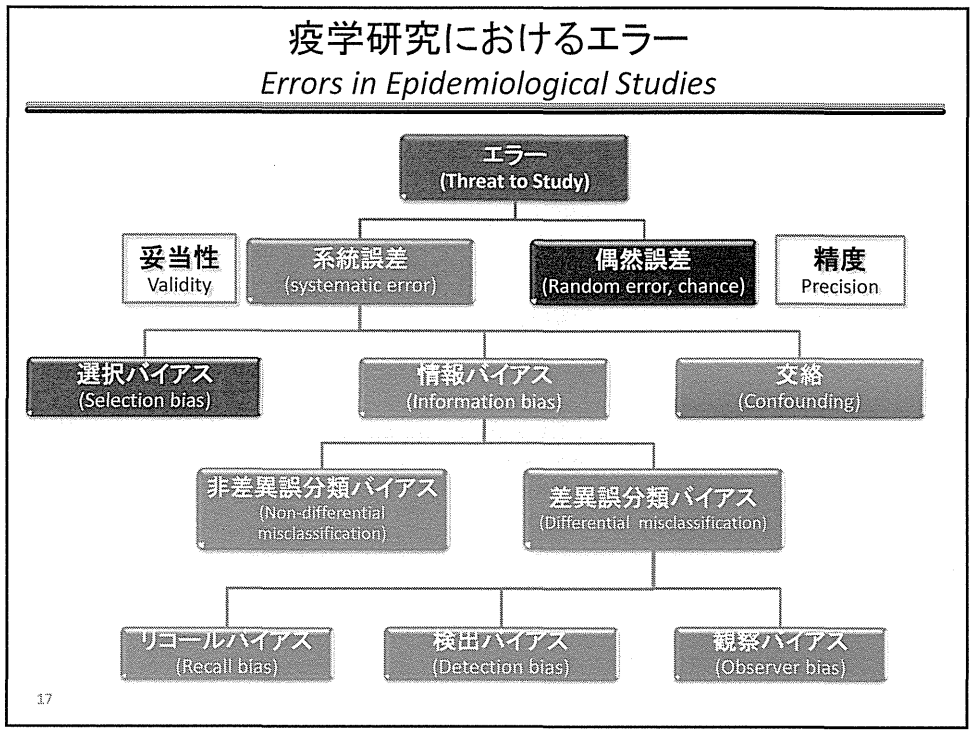
疫学研究におけるエラー
ERRORS in EPIDEMIOLOGICAL STUDIES

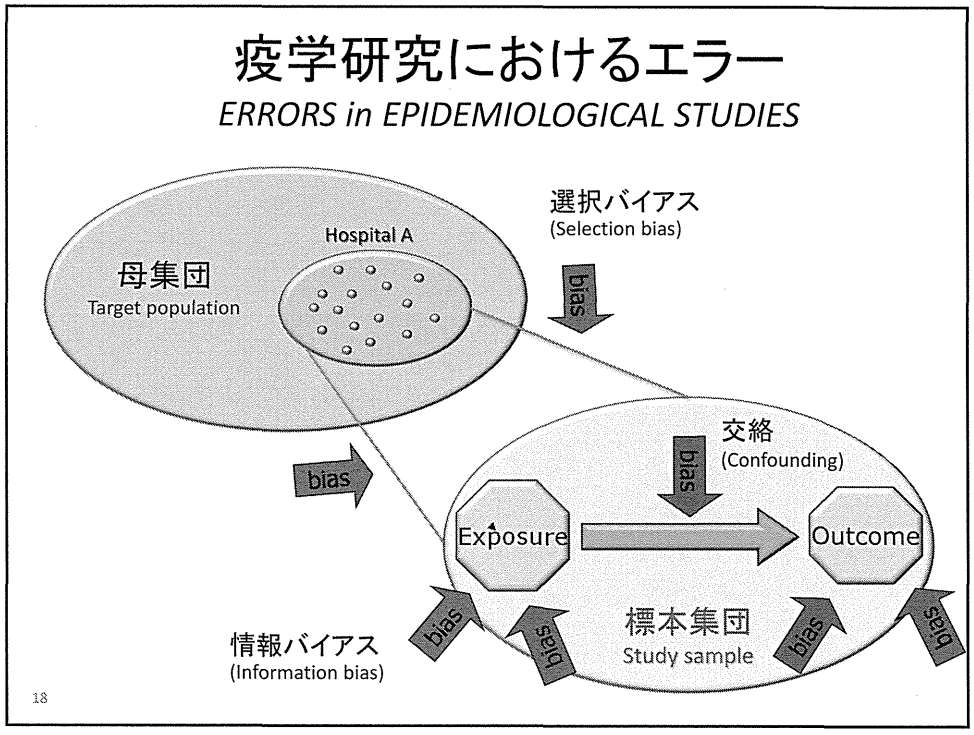
- 系統誤差, systematic error（妥当性 validity、正確性 accuracy）
  - バイアス (bias)：データ収集、分析、解釈、出版、またはデータのレビューなどにおいて、真実とは系統的に異なる結論を導き出すこと (Last J. *A dictionary of epidemiology*, 2001)
  - 交絡 (confounding)：疾患と曝露の間に存在する第三因子の存在を考慮にいれていない誤った関連
- 偶然誤差, random error（偶然 chance、精度 precision）
  - 標本のばらつきのために真値の周辺に結果がばらつくこと (sampling variation)



16

浦山先生

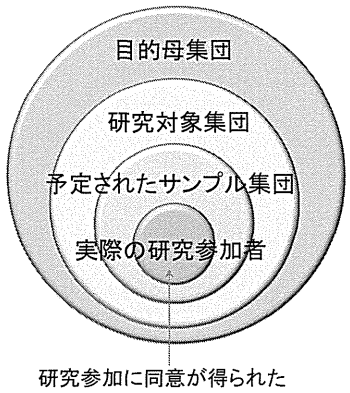

疫学研究におけるエラー
Errors in Epidemiological Studies
エラー
(Threat to Study)
妥当性
Validity
系統誤差
(systematic error)
偶然誤差
(Random error, chance)
精度
Precision
選択バイアス
(Selection bias)
情報バイアス
(Information bias)
交絡
(Confounding)
非差異誤分類バイアス
(Non-differential misclassification)
差異誤分類バイアス
(Differential misclassification)
リコールバイアス
(Recall bias)
検出バイアス
(Detection bias)
観察バイアス
(Observer bias)
17


疫学研究におけるエラー
ERRORS in EPIDEMIOLOGICAL STUDIES
母集団
Target population
Hospital A
選択バイアス
(Selection bias)
bias
bias
交絡
(Confounding)
bias
Exposure
Outcome
情報バイアス
(Information bias)
bias
bias
標本集団
Study sample
bias
bias
18

浦山先生

'PECOT'のPを定義する

小児白血病患者のうつ病リスクに関する研究



- 広いレベルで、どのような集団に研究結果を一般化したいか？（例：日本中すべての小児白血病患者）
- **包含基準包／組み入れ基準**
（研究の実現可能性を考慮）：

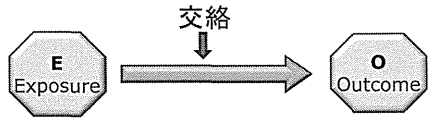
特性	例
地理的特性	東京の5つの病院において
属性	年齢6～15歳
臨床的特性	化学療法Aを受けている
時間的特性	2005年～2013年に診断された

- **除外基準**（除外すべき特殊な小集団は？）：

特徴	理由
これまでの情緒面の問題	高リスクグループ
ダウン症候群	特殊なサブグループ

19

'PECOT' の 'E-C-O' を定義する



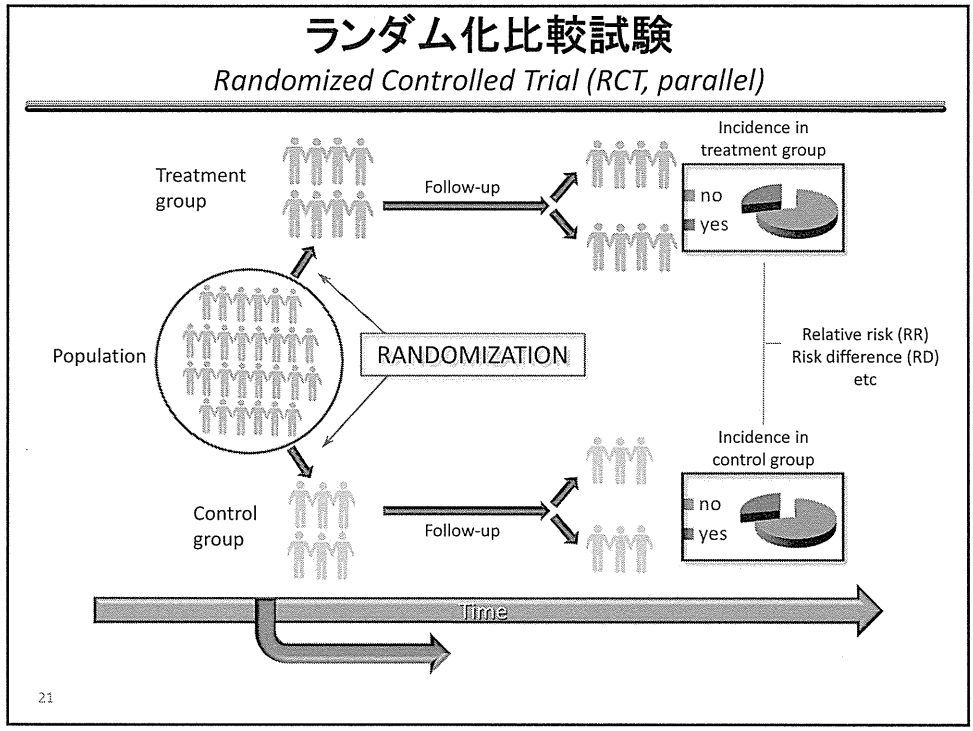
- 年齢、性別、人種
- 社会経済的地位
- 血糖値
- LDL, HLD
- HbA1c
- 食事
- 運動
- ストレス
- 喫煙

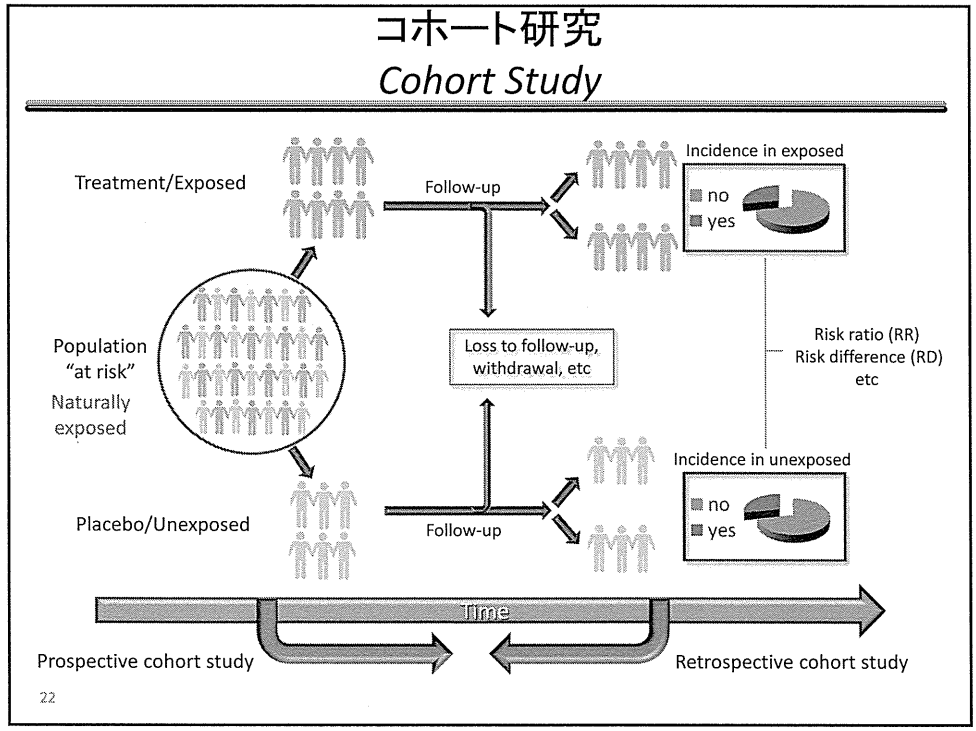
- 癌
- 心筋梗塞
- 死亡
- 肥満
- メタボリックシンドローム
- 自己免疫疾患
- 痛み、ストレス、疲労感
- 症状（e.g. 関節のこわばり）
- 生活の質 (QOL)

各々、妥当性、精密さに関しては長所・短所あり、それぞれの観察者、被験者、測定器がもつ潜在的なエラーがある。

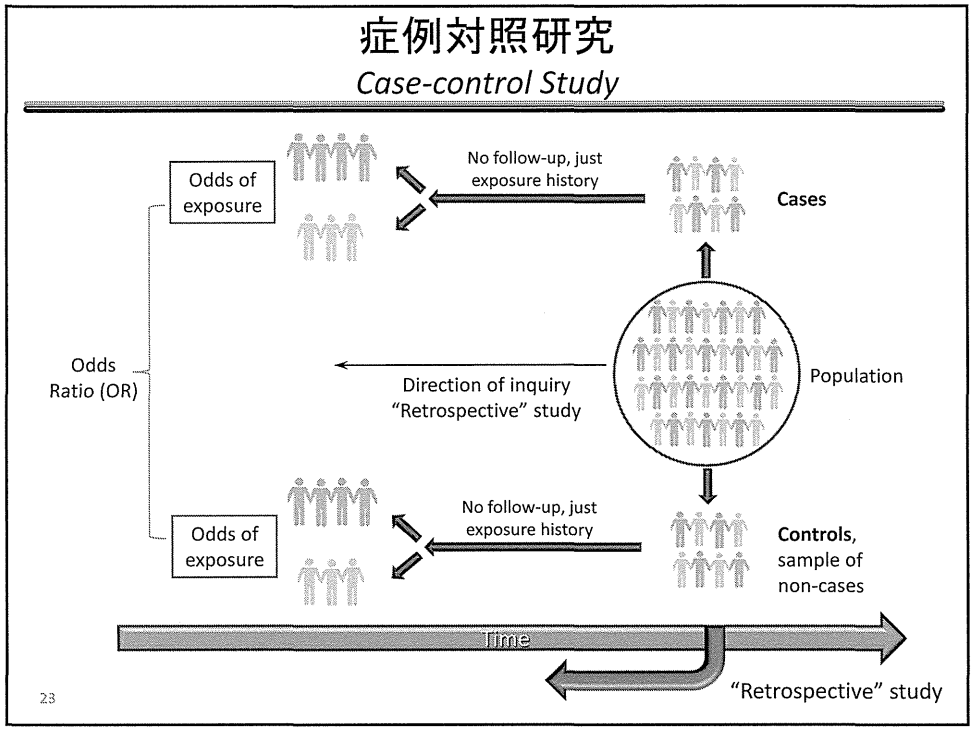
20

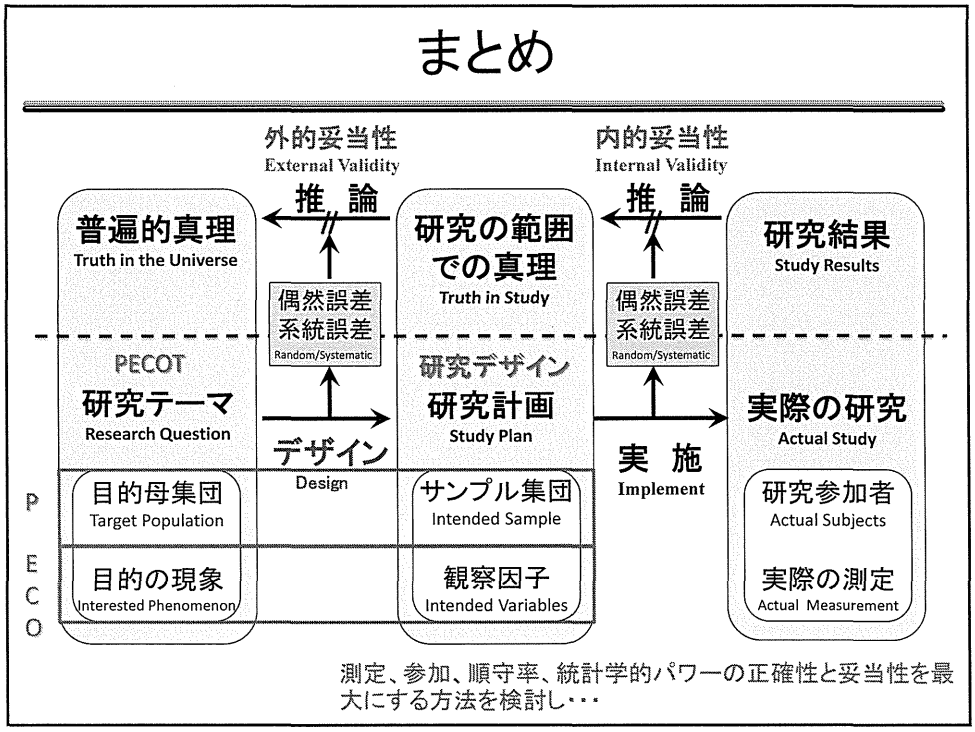
浦山先生


ランダム化比較試験
Randomized Controlled Trial (RCT, parallel)
Treatment group
Follow-up
Incidence in treatment group
no
yes
Population
RANDOMIZATION
Relative risk (RR)
Risk difference (RD)
etc
Incidence in control group
Control group
Follow-up
no
yes
Time
21

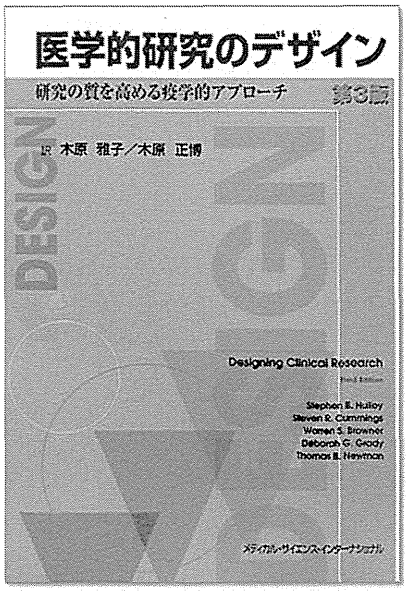

コホート研究
Cohort Study
Treatment/Exposed
Follow-up
Incidence in exposed
no
yes
Population "at risk"
Naturally exposed
Loss to follow-up, withdrawal, etc
Risk ratio (RR)
Risk difference (RD)
etc
Placebo/Unexposed
Follow-up
Incidence in unexposed
no
yes
Time
Prospective cohort study
Retrospective cohort study
22

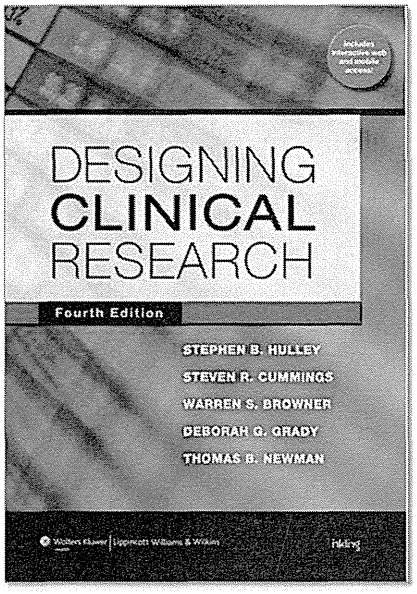
浦山先生


症例対照研究
Case-control Study
Odds of exposure
No follow-up, just exposure history
Cases
Odds Ratio (OR)
Direction of inquiry
"Retrospective" study
Population
Odds of exposure
No follow-up, just exposure history
Controls, sample of non-cases
Time
"Retrospective" study
23


まとめ
外的妥当性
External Validity
内的妥当性
Internal Validity
推 論
推 論
普遍的真理
Truth in the Universe
研究の範囲での真理
Truth in Study
研究結果
Study Results
偶然誤差
系統誤差
Random/Systematic
偶然誤差
系統誤差
Random/Systematic
PECOT
研究テーマ
Research Question
研究デザイン
研究計画
Study Plan
実際の研究
Actual Study
デザイン
Design
実 施
Implement
P
E
C
O
目的母集団
Target Population
サンプル集団
Intended Sample
研究参加者
Actual Subjects
目的の現象
Interested Phenomenon
観察因子
Intended Variables
実際の測定
Actual Measurement
測定、参加、順守率、統計学的パワーの正確性と妥当性を最大にする方法を検討し・・・

浦山先生


医学的研究のデザイン
研究の質を高める疫学的アプローチ
第3版
木原 雅子／木原 正博
DESIGN
Designing Clinical Research
Stephen B. Hulley
Steven R. Cummings
Warren S. Browner
Deborah G. Grady
Thomas B. Newman
メディカル・サイエンス・インターナショナル


DESIGNING
CLINICAL
RESEARCH
Fourth Edition
STEPHEN B. HULLEY
STEVEN R. CUMMINGS
WARREN S. BROWNER
DEBORAH G. GRADY
THOMAS B. NEWMAN

25

The ABC's of Publication and Presentation

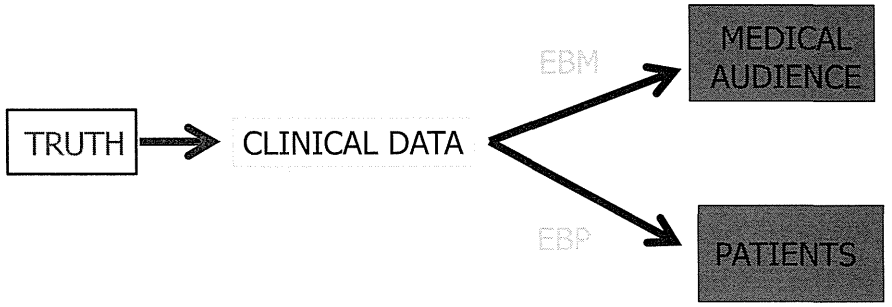
Gautam A. Deshpande, MD
Senior Researcher, St. Luke's Life Science Institute
Asst Clinical Professor of Medicine, Univ of Hawaii
12/23/2013

1

What's At Stake?

これは何で大事ですか？

Our main job as biomedical professionals is to make science applicable and understandable to our audience FOR THE BETTERMENT OF HUMANKIND.



2

Objectives

- To review HOW to put together an excellent manuscript in English that *maximizes your chances of publication.*

- To review HOW to prepare for a presentation in English.

3

A Brief Word About Language

Bilingual Community

Japanese	English
The language of patient care…	*The language of professionals…*

4

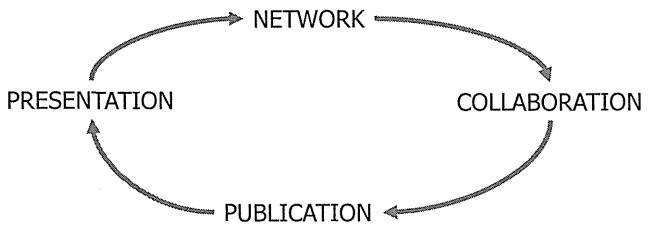
Why Should I Do Research in English? *Publications*

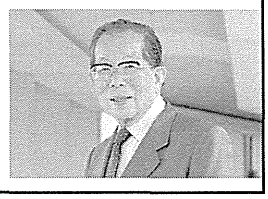
- The majority of *cited* research is done in English.
- English maximizes your chances to have a lasting effect on the medical community at large.
- English opens up your avenues for publication and increases your chances of publication and maximization of IMPACT FACTOR.

5

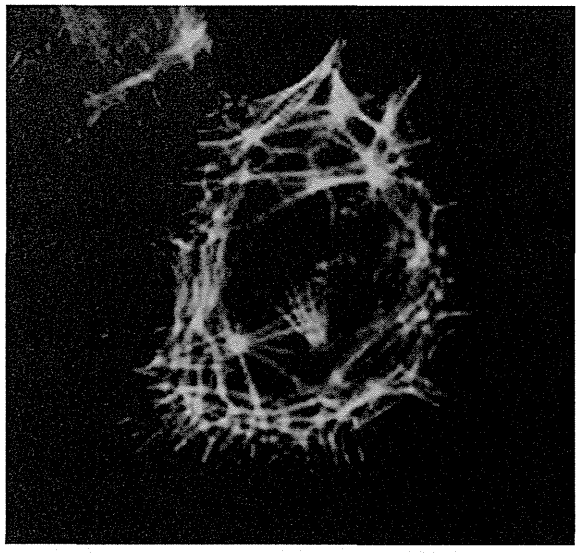
Why Should I Do Research in English? *Presentations*

- The majority of *international presentations* are done in English.
- English maximizes your chances for collaborations and growing networks.





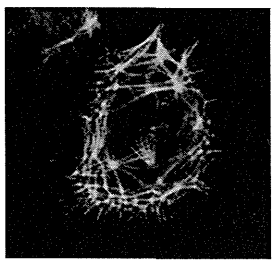
Manuscript Preparation



7

Manuscript Preparation: Understand the Format

- Formats change *drastically* based on...
  - ...the type of manuscript
    - Case review
    - Systematic Literature Review
    - Meta-analysis
    - RCT
  - ...and the publishing journal



8

Manuscript Preparation: Understand the Format

- During literature, look at the formats of the majority of your *most important papers*.*
  - ABSTRACT
    - LENGTH: *Write towards the goal length.*
    - FORMAT: *Narrative versus statistics.*
  - MANUSCRIPT
    - ORGANIZATION
    - SUBHEADERS, TABLES, FIGURES
      - Ex. research algorithms in methods section

* *Most importantly BE CONSISTENT!*

9

Manuscript Preparation: Starting the Manuscript

- OUTLINE! OUTLINE!! OUTLINE!!!
  - INTRO
    - BACKGROUND
      - X # of sentences [each sentence should have a clear goal]
      - ADD CITATIONS TO OUTLINE!
        - » 1-2 citations for each data-driven sentence. Avoid multiple citations for one sentence and avoid repeating citations.
    - PURPOSE
      - 1 SENTENCE FOR HYPOTHESIS
      - 1 SENTENCE FOR EACH GOAL OF STUDY
  - METHODS
  - RESULTS
    - 1 PARAGRAPH FOR EACH RESULT: Result 1, 2, 3, 4....
  - DISCUSSION
    - 1 PARAGRAPH FOR DISCUSSION OF EACH RESULT: Result 1, 2, 3, 4....

Manuscript Preparation: Starting the Manuscript

- OUTLINE! OUTLINE!! OUTLINE!!!
  - DISCUSSION
    - State the major results of the study
      - 1 PARAGRAPH FOR DISCUSSION OF EACH RESULT
      - Explain the meaning of each results

      ] 1, 2, 3....
    - Relate your findings to those of similar studies or projects
    - State the (clinical) relevance of the results
    - Acknowledge the limitations
    - Make suggestions for further research
    - Give the "Take-Home Message" in the form of a conclusion.

Manuscript Preparation: Using Language

- Know the *topic-specific phrasing and use**
  - These tend to be recurrent in the literature, so read as much as you can!
  - Keep a database of phrases as you do a lit search
  - Common phrases/usage do not need citation

* *Most importantly BE CONSISTENT!*

12

Manuscript Preparation: Understand the Language

metabolic syndrome

The metabolic syndrome?

The metabolic *S*yndrome?

The *M*etabolic Syndrome?

Metabolic Syndrome?

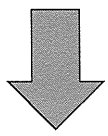
MS ?

...multiple sclerosis?

13

Manuscript Preparation: Understand the Language

- Know the *topic-specific phrasing and use*
  - These tend to be recurrent in the literature
  - Keep a database of these as you do a lit search
  - Common phrases/usage do not need citation



Be aware of plagiarism!

14

Manuscript Preparation: Using the Language

- Be able to *clearly explain the complex*
  - statistical methodology
  - embryonic development
  - discordant results

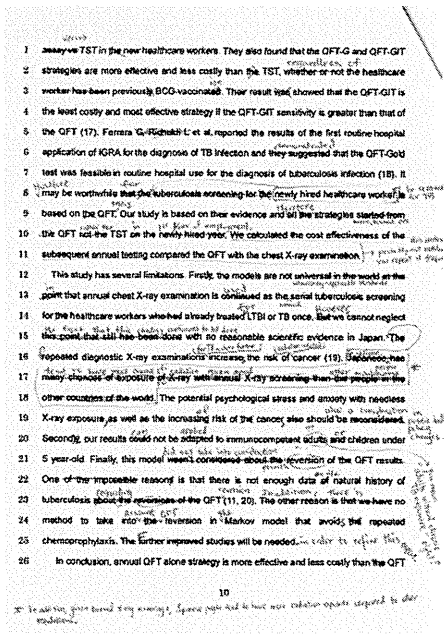
15

Try to Avoid...

- ...run-on sentences
  - If your sentence is >3 lines, its too long!!!
- *..."On the other hand..."*
  - Do not use conversational phrasing
- ...non-standard reference formats
- ...hiding design or sample limitations...
- ~~exaggerations~~

Editing Your Work

17



1 assay vs TST in the new healthcare workers. They also found that the QFT-G and QFT-GIT
2 strategies are more effective and less costly than the TST, whether or not the healthcare
3 worker has been previously BCG-vaccinated. Their result was showed that the QFT-GIT is
4 the least costly and most effective strategy if the QFT-GIT sensitivity is greater than that of
5 the QFT (17). Ferrara G, Richeldi L, et al. reported the results of the first routine hospital
6 application of IGRA for the diagnose of TB infection and they suggested that the QFT-Gold
7 test was feasible in routine hospital use for the diagnosis of tuberculosis infection (18). It
8 may be worthwhile that the tuberculosis screening for the newly hired healthcare workers is
9 based on the QFT. Our study is based on their evidence and all the strategies started from
10 the QFT not the TST on the newly hired year. We calculated the cost effectiveness of the
11 subsequent annual testing compared the QFT with the chest X-ray examination.
12 This study has several limitations. Firstly, the models are not universal in the world as the
13 point that annual chest X-ray examination is continued as the serial tuberculosis screening
14 for the healthcare workers who had already treated LTBI or TB once. But we cannot neglect
15 this point that still has been done with no reasonable scientific evidence in Japan. The
16 repeated diagnostic X-ray examinations increase the risk of cancer (19). Therefore, the
17 many chances of exposure of X-ray with annual X-ray screening than the people in the
18 other countries of the world. The potential psychological stress and anxiety with needless
19 X-ray exposure as well as the increasing risk of the cancer also should be reconsidered.
20 Secondly, our results could not be adapted to immunocompetent adults and children under
21 5 year-old. Finally, this model wasn't considered about the reversion of the QFT results.
22 One of the impossible reasons is that there is not enough data of natural history of
23 tuberculosis about the reversions of the QFT (11, 20). The other reason is that we have no
24 method to take into the reversion in Markov model that avoids the repeated
25 chemoprophylaxis. The further improved studies will be needed.
26 In conclusion, annual QFT alone strategy is more effective and less costly than the QFT

10

-*Cross-reference* your work with the literature

-Do *pre-edit* prior to submitting your work to a professional editing company

-Be clear with your expectations for editors: do you want *comments or corrections*? ("Both" is only feasible in the final drafts!)

18