Clinical Epidemiology for the uninitiated

'Clinical epidemiologist have one foot in clinical care and the other in clinical practice research. As clinical epidemiologists we apply a wide array of scientific principles, strategies and tactics to answer questions about health and health care'

Clinical Epidemiology How to do Clinical Practice Research

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Defining the question – the hardest bit

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Box 1

FINER criteria for a good research question

F	Feasible	• Adequate number of subjects • Adequate technical expertise • Affordable in time and money • Manageable in scope
I	Interesting	• Getting the answer intrigues investigator, peers and community
N	Novel	• Confirms, refutes or extends previous findings
E	Ethical	• Amenable to a study that institutional review board will approve
R	Relevant	• To scientific knowledge • To clinical and health policy • To future research

Deciding which question to ask

- Which question is most important to the patient's well being?
  (Have you taken into account the patient's perspective?)
- Which question is most feasible to answer in the time you have available
- Which question are you most likely to encounter repeatedly in your practice?
- Which question is most interesting to you?

Further reading:: Richardson W, Wilson M, Nishikawa J, & Hayward RS, The well-built clinical question: a key to evidence-based decisions [editorial]. ACP J Club 1995, 123, A12-3.

7 types of research questions

1. How common is the problem	Prevalence	**PO**
2. Is early detection worthwhile	Screening	**PICO**
3. Is the diagnostic test accurate	Diagnosis	**PICO**
4. What will happen if we do nothing	Prognosis	**PO**
5. Does this intervention help	**Treatment**	**PICO**
6. What are the common harms of an intervention	**Treatment**	**PICO**
7. What are the rare harms of an intervention	**Treatment**	**PICO**

Skills for clinical epidemiology

This booklet is designed as a tool to highlight and assess the skills you will require to undertake a particular research study. In planning a research study we need to decide on the skills we currently have expertise in, those which we can work on to improve, and the ones that we will require outside help for.

For each skill required within a given methodology you should give yourself a current appropriate score:

Skills Level	Score
No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
Could undertake the skill but would require considerable help	3
Could undertake the skill requiring input only for the most difficult tasks	4
Can teach the skill	5

For example:
For analysis of observational data you may decide you need skills in using SPSS database software. If you have never heard of SPSS or never used it you would score one. If you have downloaded SPSS and played around with it, could open the database and do simple descriptive analyses then you would score two. If you could open SPSS and input your own data and codes and analyse this data score three. If you can do all of the last task and perform difficult statistical tests like regression then score four, and if you could demonstrate to your colleagues how to do all of the tasks then score yourself five.

There is no right or wrong answer, the main idea of the scoring system is to consider the skills required for a given methodology, the skills you already have to hand, the ones you will want to improve and seek extra training for (actions that need to be identified), or the skills for which you decide you need outside help from an expert. Of note, it is impossible to score 5 on every skill required for each research method: this is why most successful epidemiological projects involve a team with mixed skills.

The Methods discussed in this work book include:

- **Systematic reviews**
- **Cohort/observational studies**
- **Surveys/questionnaires**
- **RCTs**
- **Diagnosis**
- **Generic skills**

Before embarking on any clinical research study a key requirement is Good Clinical Practice (GCP) training. GCP is the ethical and practical standard to which all clinical research is conducted and can be taken as an online course, which requires updating. In addition, to goes without saying that ethics and data protection are a fundamental part of all research based in healthcare.

Systematic reviews

A systematic review asks a clearly focused clinical question, aims to assess all of the relevant evidence to answer the specific question whilst assessing the quality of the evidence, and undertakes a synthesis of the results. A systematic review may or may not include a meta-analysis. For therapy reviews the type of evidence included is usually from randomised trials. Reviews can also be undertaken for diagnostic and prognostic questions as well as for comparative effectiveness, which might include a network meta-analysis.

Skill Required	Current Score	Action Required
Question formulation		
Protocol development		
Literature search published studies		
Literature search unpublished studies		
Development of inclusion criteria		
Data abstraction		
Quality assessment (GRADE)		
Data analysis		
Use of Revman		
Use of Stata for optional analysis		
Pooling of data		
Interpretation of meta-analyses		
Interpretation of heterogeneity		
Forest plots		
Subgroup analyses		
Sensitivity analyses		
Implications for practice		
Writing of Review		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
Could undertake the skill but would require considerable help	3
Could undertake the skill requiring input only for the most difficult tasks	4
Can teach the skill	5

Cohort/Observational Studies

Observational studies observe the effect of a risk factor, test or treatment without influencing what happens. A cohort is any group who are linked in some way and followed over time and observed to see what happens. A cohort or observational study examines what happens to a group exposed to a particular variable, compared with a group not exposed. In case-control studies researchers use existing records to identify people with a certain problem (cases) and a similar group without the problem (controls) and make comparisons between them in order to identify differences in exposures between cases and controls.

Skill Required	Current Score	Action Required
Question formulation		
Literature reviewing		
Ethics		
Protocol development		
Recruitment		
Sample size		
Questionnaire design		
Measurement choice		
Measurement instrument knowledge		
Matching		
Database knowledge		
Access database or other		
Analyses		
• Dealing with confounding		
• Univariate analyses		
• Multivariate analyses		
• Time to event analyses		
• Survival analyses		
Cleaning and checking data		
Dealing with missing data		
Confounding		
Presentation of results		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
Could undertake the skill but would require considerable help	3
Could undertake the skill requiring input only for the most difficult tasks	4
Can teach the skill	5

Surveys/questionnaires and cross sectional studies

Questionnaire surveys are a cheap and quick research tool used by many medical researchers to investigate various aspects of health and disease. **Cross-sectional studies** examine the relationship between disease and other variables of interest as they exist in a defined population at a single point in time, or over a short period of time.

Skill Required	Current Score	Action Required
Question formulation		
Survey planning and design		
Form and response set e.g. direction of response		
Single item questions		
Batteries of questions		
Scales		
• Weighting item scores		
• Attitude measurement scales		
• Likert scale		
• Visual analogue		
• Scale values		
Questions		
• Ordering		
• Wording		
• Leading questions		
• Response choices		
• Open ended questions		
• Closed questions		
Response rates		
Survey piloting		
Missing data		
Imputation		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
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Can teach the skill	5

Randomized controlled trials

Randomized controlled trials (RCTs) require specific skills that are normally part of the function of a clinical trials unit and are therefore normally beyond the remit of an individual researcher. However each RCT requires an individual to be the principal investigator, who needs a working knowledge of the skills outlined.

Skill Required	Current Score	Action Required
Question formulation		
Ethics/ trial registration		
Protocol		
• Sample size		
• Recruitment		
• Participant selection		
• Inclusion exclusion criteria		
• Patient entry forms		
• Randomization		
• Information sheets		
• Consent forms		
• Patient flow diagram		
Protocol adherence		
Different designs (factorial, crossover)		
Audit trail/ trial documentation		
Systems for distributing interventions		
Emergency code breaking		
Follow up procedures		
Event monitoring and reporting		
Event adjudication		
Primary analyses		
• Secondary analyses		
• Composite outcomes		
• Surrogate outcomes		
• Subgroup analyses		
• Missing data		
• Significance testing		
CONSORT reporting		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
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Diagnostic studies

A diagnostic test is any kind of medical test performed to aid in the diagnosis or detection of disease, injury or any other medical condition. A diagnostic study aims to compare a new test (index test) with a reference standard) gold standard and compares the accuracy of the new approach.

Skill Required	Current Score	Action Required
Question formulation		
Collaboration		
Ethics		
Protocol development		
• Clinical setting		
• Recruitment strategy		
• Choosing the right population		
• Sample size calculation		
• Eligibility criteria		
• Developing proforma		
• Equipment procurement		
• Measurement criteria		
Test interpretation		
Database construction		
Gold standard		
Analyses		
• Univariate		
• Multivariate		
• Test accuracy		
• Data cleaning checking		
• Combining diagnostic tests		
• Measuring test impact		
Randomized controlled trials of diagnostic tests		
Systematic reviews of diagnostic tests		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
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Qualitative studies

Qualitative Research is used to gain an understanding of underlying reasons, opinions, and motivations in a variety of health care problems and situations.

Skill Required	Current Score	Action Required
Question formulation		
Sampling		
Data collection		
• Focus groups		
• In-depth interviews		
• Semi-structured interviews		
• Observation		
Action Research		
Field Notes/audio collection		
Interviews		
• Structured		
• Semi-structured		
• Unstructured		
Transcription		
Content analysis		
Computerized data analysis (NVivo/ATLAS)		
Categorisation		
Coding		
Thematic Analysis		
Ethnography		
Grounded Theory		
Phenomenology		
Descriptive/interpretative		
Generic skills		
• Group skills		
• Facilitating		
• Moderating		
• Listening/observing		
Presenting research findings		
Other ( )		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
Could undertake the skill but would require considerable help	3
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Generic Research Skills

Skill Required	Current Score	Action Required
Communication Skills		
Presentation Skills		
Writing		
• Abstract		
• Background		
• Methods		
• Discussions		
• Reviews		
• Grants		
Collaboration		
Literature searching		
Question formulation		
Project Planning		
Ethics submission		
Research and Governance		
Grant funding		
Presenting data		
• Tables		
• Figures		
Analyzing data		
• Excel		
• SPSS		
• STATA		
• R		
Systematic reviews		
Data management		
Access database		
Teaching		
Study designs		
Quality assessment tools (e.g STARD. QORUM)		

No idea of the skill	1
Heard of the skill and would be able to undertake basics	2
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Basic Statistical competencies:

Sampling theory:
- Population vs. sample
- Frequency distributions, variables and types of data, bias and variation.

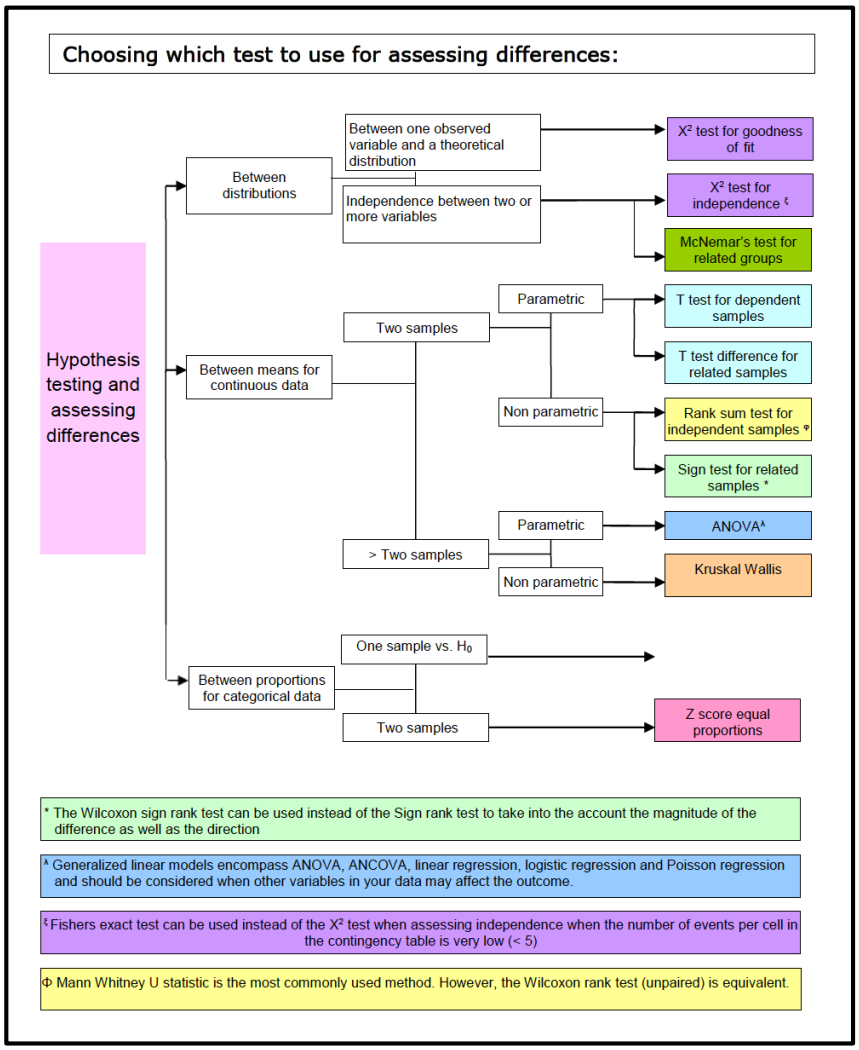
Normal distribution:
- Estimation including mean, standard deviation and normal range, standard error and confidence intervals;
- Inability of the normal distribution to describe all continuous data.

Two-sample analyses:
- Hypothesis testing and confidence intervals for unpaired and paired normal data;
- Chi-squared for proportions,
- Link between estimation and hypothesis testing.

Dichotomous data:
- Binomial distribution
- Sampling distribution of proportions including large sample approximations
- Confidence intervals and hypothesis testing.

Relating two variables:
- Parametric and non-parametric measures of correlation.

Overview of clinical and epidemiological research:
- Clinical vs. statistical significance,
- Iterative loop of research,
- Fundamental equation of error.



Topics preparatory to critical appraisal
Types of observational study; intervention studies including randomized and cross-over trials; introduction to meta-analysis.

Graphical methods:
For clinical and biological data including histograms and scatterplots, survival curves, forest plots etc.

2 x 2 tables:
Odds ratios and relative risks and their CIs and interpretation

Other situations:
Lognormal distribution, Poisson distribution, use of t-tables for smaller samples.

Nonparametric statistics: summary measures for non-normal data, introduction to nonparametric hypothesis tests.

Estimation and hypothesis testing:
In observational studies and trials using normally distributed data, dichotomous data, survival data, linear regression; concepts of adjustment and matching for covariates.

Global Competencies for EBM:

The core competencies for Evidence-Based Medicine include:

Principles and Basic Practices of Evidence Based Medicine

- Describe and apply to a clinical case the basic principles of EBM.
- Describe how EBM, clinical experience and individual patient issues interact.
- Describe the limitations of EBM.
- Describe the interaction of EBM and health care policies.

Question formulation

- Describe how to formulate an answerable, searchable question.
- Identify the type of clinical question (e.g. treatment, prognosis, aetiology).
- Describe where and how to look for information to answer different types of clinical questions at the point of care (when answers are needed quickly).
- Describe where and how to look for answers to different types of clinical questions when clinical decisions can wait.

Critical Appraisal

- How to read a scientific paper - what are the component parts of a basic scientific paper
- Assess the primary literature - how to retrieve primary studies and how to design studies of effectiveness for basic sciences.
- Distinguish relevant from irrelevant evidence.
- Define and apply criteria to medical information to determine relevance when answering clinical questions.
- Describe a hierarchical approach to levels of evidence specific to types of conclusions.
- Identify the most valid study design for studies of therapy, prognosis, and diagnosis.
- Determine methodological quality of evidence, assessing the following types of studies for validity (identify important threats to validity and identify critical flaws in study design):
    - a therapeutic study
    - a prognosis study
    - a diagnostic study
    - a clinical prediction guide study
    - a practice guideline
    - a systematic or meta-analysis review
    - a health economics study
    - a case-control study.

Determining the clinical significance of results.

- Clinically interpret the results of an RCT, including concepts of RRR vs. ARR, how to determine NNT, p values, confidence intervals, risk/benefit analysis, and balancing NNT and NNH.
- Calculate and interpret pre-test and post-test probabilities, (sensitivity, specificity, PPV, NPV, likelihood ratios), test/treatment thresholds.
- Describe and distinguish between statistical and clinical significance.
- Describe criteria for what makes a good screening test and apply the criteria to screening tests.

Implementing Evidence for patient care

- Communicate evidence to patients, describing how values can introduce appropriate and inappropriate biases into patient-physician communications.
- Integrate evidence into common clinical presentations
- Use the information in relation to patient care, health promotion, giving advice and information to patients, and research and education
- Understand and have experience of the principles and methods of improvement, including audit
- Access information sources and use the information in relation to patient care, health promotion, giving advice and information to patients, and research and education.