Practical Psychiatric Epidemiology

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Here is a short review of *Practical Psychiatric Epidemiology*, Prince, M., Stewart, R., Ford, T., and Hotopf, M. (Eds.) (Oxford, 2003).

There is already a **review** in *The Bristish Journal of Psychiatry* (2005, 186: 268). Hereafter, I would like to quote some of the main ideas of this nice textbook on research and methodological aspects of psychiatric epidemiology. Although this textbook is mostly dedicated to students in epidemiology or psychiatry (which I am not, of course), it contains a huge amount of useful references and advices to whom may be concerned with the analysis of comparative studies in the biomedical domain. The growing interest in genetic-related studies and the now available statistical methods to deal with large-scale surveys or Quality of Life studies allow for a deeper understanding and takings of mental health problems. These emerging issues in psychiatric epidemiology offer a new research area open to inter-disciplinary collaboration.

Basically, psychiatric epidemiology is concerned with the study of prognosis and treatment of psychiatric disorders. Contrary to more 'classical' **epidemiology**, study on mental health related pathology does not always involve biological events or signals, thus emphasizing the need to build questionnaire or dedicated interview that might lead to some useable manifest variables. With this in mind, some of this work has more to do with usual psychometrics (i.e. the science of the measurement of mental phenomena). Generally speaking, work related to health care aims at answering three kind of question:

- *What is going on?* Only history taking, examination and diagnosis allow the practician to deal with such a question.
- *Why?* Answer to this question may be provided by aetiological research based on transversal or longitudinal studies.
- *What do we do about it?* Answer to this question relies on intervention studies, including RCTs, but is obviously associated with some ethical problems.

These topics are treated at length in Section 2 of the textbook, which we will resume in a few paragraphs on. Further, quoting Eaton (1986) cited on page 5,

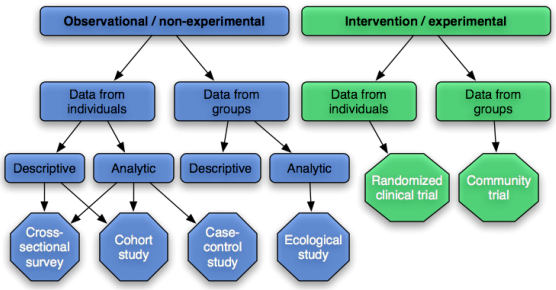
> "Epidemiology is a branch of medicine, and thus the assumptions of the medical model of disease are implicit. The most important assumption is that the disease under study actually exists... In psychiatry this assumption is assuredly more tenuous than in other areas of medicine, because psychiatric diseases tend to be defined by failure to locate a physical cause... "

This is just to say that psychiatric epidemiology has to be distinguished from classical epidemiological in the way data can be collected and inference may be drawn. Indeed,

it is not very easy to design a study where we deliberately manipulate risk factors, nor when we decide to continue a study that would affect someone's welfare. Thus, studies are mainly of observational nature per se, and there we run into problems related to confounding or mediating effects that are often not easily solvable.

Section 1 is mainly devoted to the history of psychatric epidemiology and the new tools developed so far. Most of these statistical apparatus grow on measurement theory which put emphasis on validity and reliability of the measurement of mental processes. Such topics are dealt at length by G. Dunn in his textbook *Statistics in Psychiatry* (See next section). Additionally, case-control and cohort studies have provided much more interesting results than cross-sectional surveys developed in the eighteen century. These kind of study design are discussed in the next section, but see below. Cross-cultural issues are discussed in a separate chapter: V. Patel mainly points to the comparability of psychiatric disorders measurement in different countries whose social and cultural setting may interfere with a direct and clear-cut interpretation of the results.

Section 2 reviews the basic experimental design used to assess or uncover significant marker of mental disorders. As shown in the next figure, this includes: cross-sectional, case-control and cohort or longitudinal studies, randomized clinical trials, and post-hoc or meta-analysis. In short, the design and analysis of a study aims at maximizing the precision and validity of its findings. Avoiding bias or confounding effect is thus the primary goal of any epidemiologist, especially because most of the studies under consideration are observational per se. Strict control over experimental factors or exposure, like in an RCT, are thus generally lacking.



Here are the main advantages and drawbacks of each design:

- *Ecological studies*: possible 'ecological fallacy' effect.
- *Cross-sectional surveys*: no direct evidence of causality, representative sampling frame, response rate, not applicable to rare disorders.
- *Case-control study*: mainly retrospective, subjects defined by outcome, can handle multiple exposures, odds-ratio approximately equal to relative risk in a cohort study for rare disorders (prevalence $< 10\%$), prone to several form of bias (selection, information, i.e. observer and recall).

- *Cohort study*: longitudinal (prospective) design or historical cohort or population cohort, subjects designed by their exposure, not well-suited for rare disorders, can handle multiple outcomes/exposures, no information bias.
- *Intervention study*: allocating exposure to subjects and comparing the outcome of interest in different random groups, no information bias provided trials are double-blind.

I also reproduce Table 5.1 (page 87) as it summarizes much of the characteristics of each study design.

	Cross-sectional survey	Case-control	Cohort	Ecological	Clinical trial
Subject selection	Defined population	Caseness	Exposure	Aggregated data	Caseness
Source of bias	Selection, Non-response, Information (Recall and observer)	Selection, Information (Recall and observer)	Information (observer only), Loss to follow up (selection)	Selection of population, Ecological fallacy	Selection, Information (reduced by blinding)
Probability of confounding	Medium	Medium	Low	High	Very low if randomized
Resources	Quick and cheap	Relatively quick and cheap	Lengthy and expensive	Relatively quick and cheap	Relatively expensive
Applications	Planning services, Mapping secular and geographical trends, Identifying correlates	Rare outcomes, Single outcomes, Multiple exposures	Rare exposure, Single exposures, Multiple outcomes	Rare outcomes, Rare exposures, Multiple exposures, Population exposures such as air pollution	Efficacy of new interventions, Effectiveness of new interventions, Hypothesis testing, Mechanisms
Measures of effect	Prevalence	Odds ratio	Relative risk	Correlation/ regression coefficient	Relative risk/odds ratio/difference between means

Probably the most well-known designs are the Case-control and Cohort design study. Case-control studies are most appropriate when the disorder under study is (i) rare, (ii) takes a long time to develop after the exposure (sometimes referred to as the latent period), and (iii) where the exposure is common. Cohort studies are more appropriate when the disorder is (i) common, (ii) it does not take long to develop, and (iii) the exposure is rare. They both come with their own drawbacks and interpreting the results gathered through such approaches often involves a careful inspection of the hypothetical causal pathways.

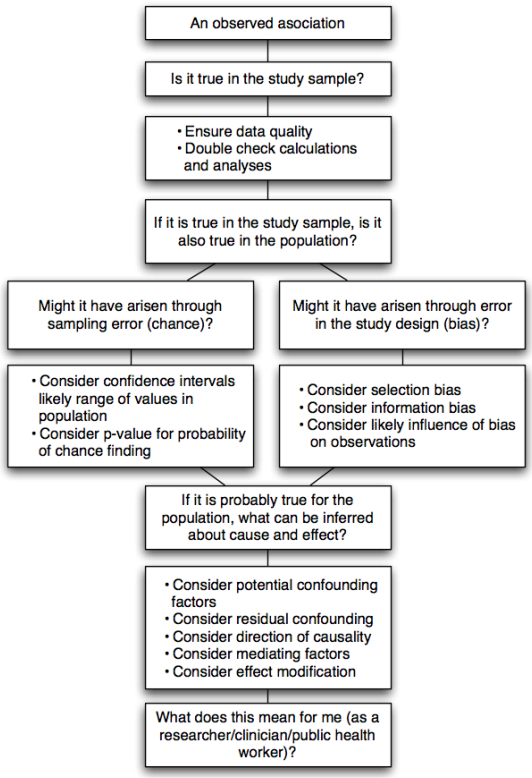
In either case, we need to ensure the proper recording of the data, as well as appropriate statistical analysis. While the former may be facilitate with dedicated software[a], care must be taken when analyzing data gathered through complex sampling frame, like stratified sampling with unequal sampling weights or cluster sampling. Such designs call for specialized software like SAS or Stata, though SPSS now has some survey design capabilities (since version 15). S.J. Pocock gives a nice overview of clinical trials and how to manage them: **When to stop a clinical trial** (pdf).

Section 3 puts emphasis on the reading of data, in particular on the relevance of causality in the interpretation of a significant association between symptoms, biological or genetical markers, and disturbed behavior or mental trouble. This is probably the most interesting aspect of such studies, and obvisouly the harder one... Many software are available for study comparison, also known as meta-analysis (e.g. **Revman**), but read the chapter **Software for meta-analysis and publications bias** (pdf) of *Publication Bias in Meta-Analysis: Prevention, Assessment and Adjustments*, H. Rothstein, A.J. Sutton, and M. Borenstein (Eds.), Wiley 2005. There is also this interesting article, **Meta-analysis of Observational Studies in Epidemiology** and **Investigating and dealing with publication and other biases in meta-analysis**, written by J.A.C. Sterne and coll. Both are available on-line.

The fundamental question when interpreting research findings is to consider what observations 'mean' and what can be inferred from them. The **CONSORT statement** also provides useful guidelines for reporting results gained through RCTs. The diagram below illustrates the checking process that every critical reviewer may follow in order to ensure that a correct inference can be done based on the observed results.

Robert Stewart offers in Chapter 13 an extensive discussion around causal pathways and how inferential aspects shall be handled. The table reproduced in the next page (right panel) summarizes the approach promulgated by Hill (1965) which includes 9 different criteria related to causation effect. His original article was indeed entitled **'The environment and disease: association or causation?'** (pdf).

[a] **EpiInfo** is a free package that can handle many of the usual statistical routines. It also includes a data editor which allows for double data entry comparison. Further, it can handle map files (ArcView compatible) and get data stroed in a SQL database.



Criterion	Description	Limitations
1. Strength	A strong effect size for an association	This reduces the chance of minor unmeasured confounding, but assumes that major confounding factors have been accounted for. Weak associations may also be causal.
2. Consistency	Repeated observations of an association in different populations/circumstances	This assumes that all necessary causal factors are evenly distributed between populations. If a risk factor-outcome association were present only in men, would this imply non-causality?
3. Specificity	A risk factor leads to a single outcome	There is no reason why a risk factor should be associated with a single disorder (e.g. multiple disorders associated with alcohol misuse).
4. Temporality	The cause should precede the effect	A study should ideally demonstrate this. However the fact that one event follows another does not rule out the opposite direction of causation on other circumstances. For example, depression may cause physical ill-health but the opposite may also occur.
5. Biological gradient	A 'dose-response' relationship	This assumes that the 'ceiling' of risk has not been reached. A single life-event may be sufficient to cause depression with no influence of further events. Of little use for cross-sectional associations since a 'dose-response' pattern of association would be predicted with either direction of causation.
6. Plausibility	That the hypothesis is biologically plausible	Frequently a highky subjective judgement, given the volume of the biological literature. There are many historical examples of important findings rejected on the ground of implausibility at the time (e.g. Darwin's theory of the Origin of Species).
7. Coherence	That the interpretation does not conflict with the known biology of the disease	This depends heavily on the quality of the anciliary information. It also is not entirely consistent with the principle of hypothesis refutation.
8. Experimental evidence	Evidence from interventional research	Interventional research may not be ethical and/or feasible for many cause effect investigations. The intervention may not be discrete enough to infer causation.
9. Analogy	Similar associations in other fields	A highly subjective judgement.

Hill, 1965

Causation, or causality interpretation, are by far the most difficult aspects of epidemiological research. Cohort and cross-sectional studies might both lead to confoundig effects for example. Another set of criteria has been proposed by H.B. Asher (*Causal Modeling*, Sage, 1976), as cited by S. Menard (*Longitudinal Research*, Sage University Paper 76, 1991):

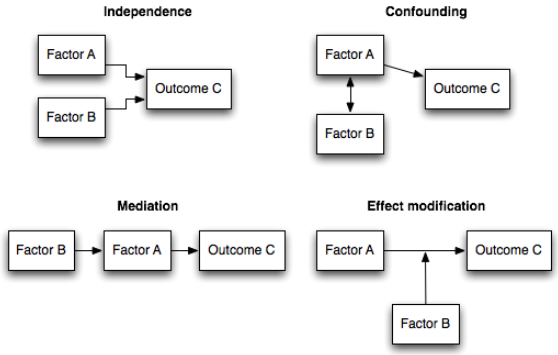
1. The phenomena or variables in question must covary, as indicated for example by differences between experimental and control groups or by nonzero correlation between the two variables.

2. The relationship must not be attributable to any other variable or set of variables, i.e., it must not be spurious, but must persist even when other variables are controlled, as indicated for example by successful randomization in an experimental design (no difference between experimental and control groups prior to treatment) or by a nonzero partial correlation between two variables with other variable held constant.

3. The supposed cause must precede or be simultnaeous with the supposed effect in time, as indicated by the change in the cause occuring no later than the associated change in the effect.

While the first two criteria can easily be checked using a cross-sectional or time-ordered cross-sectional study, the latter can only be assessed with longitudinal data, except for

biological or genetic characteristics for which temporal order can be assume without longitudinal data. Of course, the situation becomes more complex in case of a non-recursive causal relationship. To catch up some of the most useful concepts, here is a brief illustration of the main cause-effect relationships one may encounter in an observational study:



The interested reader could also refer to Chapter 2 of Rothman's *Modern Epidemiology*[b] (1998, Lippincott Williams & Wilkins, 2nd Edition).

Finally, **Section 4** covers additional topics, not usually found in more classical textbooks, such as genetic epidemiology, health economics or qualitative research.

Additional links

Here are some useful links about actual survey or health related information systems, as well as various links related to medical statistics.

- **The European Health Survey System**
- **OCDE Santé**
- **Medical algorithms**
- **Publications Bias**
- **CONSORT, Transparent Reporting of Trials**

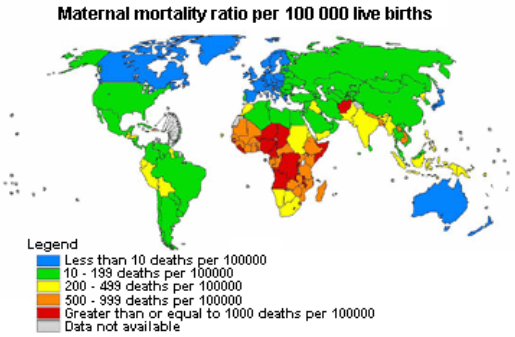
Finally, I have compiled some of the most relevant bibliography entries (to my opinion, of course) in the following BibTeX file: **PEP.html** (**PEP.bib**).

Remark

When I am looking for some large-scale (aggregated or not) dataset, I usually search the **Eurostat** database which contains data collected for the European Commission. In

[b] Now in its 3rd Edition (2008)!

the case of biomedical data, a useful resources is the **World Health Organization**. For instance, the **Global Health Atlas** includes standardized data and statistics for infectious diseases at country, regional, and global levels. The figure below is taken from their homepage.



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