

# REFERENCES

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# INDEX

*Listed below are, in their alphabetical order, all of the terms in sections I – 1. 2, I – 2. 2, I – 3. 2, II – 2-4, III – 2-4, and III – 2-4. Associated with each term is specification of the section(s) in which the term appears.*

Abnormal I – 1. 2    Abstract I – 2. 2    Accuracy I – 2. 2, II – 4    Acquired I – 1. 2    Acute I – 1. 2    Adjusted rate I – 1. 2    Adjustment II – 4    Administrative II – 3    Admissibility II – 3, II – 4    Aetiology I – 1. 2    Age group II – 4    Agent I – 1. 2    Alternative hypothesis I – 3. 2    Analysis I – 2. 2, 3. 2    Analysis of covariance I – 3. 2    Analysis of data II – 4    Analysis of variance I – 3. 2    Analytical I – 2. 2    Analytic epidemiology II – 2    Anamnesis I – 1. 2    Ancillary study II – 4    Anomaly I – 1. 2    Antagonism II – 3    Applied I – 2. 2    Applied research I – 2. 2    Assessment I – 1. 2    Association II – 3, 4    Assumption I – 2. 2, 3. 2, II – 4    Asymptotic I – 3. 2    At risk I – 1. 2    Attributable I – 1. 2    Attributable risk II – 4

Base II – 4    Baseline II – 4    Base population II – 4    Basic research I – 2. 2    Bayesian I – 3. 2    Bayes' rule/theorem I – 3. 2    Bernoulli distribution I – 3. 2    Bias I – 3. 2, II – 4    Biased base II – 4    Biased documentation II – 4    Biased result II – 4    Biased sampling II – 4    Biased selection II – 4    Biased study II – 4    Binomial distribution/model I – 3. 2    Biometry I – 3. 2    Biostatistics I – 3. 2    Blinding III – 4    Blocking III – 4

Candidate I – 1. 2    Care I – 1. 2    Case I – 1. 2, II – 4    Case-base study II – 4    Case-control study II – 4    Case-fatality rate I – 1. 2    Case finding I – 1. 2    Case-referent study II – 4    Case series II – 4    Catchment area I – 1. 2    Catchment population I – 1. 2, II – 4    Category I – 2. 2, II – 3    Causal contrast II – 3, 4    Causal criteria/considerations II – 4    Causal determinant II – 3    Causal inference II – 4    Causality I – 2. 2    Causal rate-ratio II – 3    Causal versus descriptive research II – 3    Causation II – 3    Cause I – 1. 2    Cause-probability score II – 4    CEA III – 2    Centile II – 4    Central limit theorem I – 3. 2    Ceteris paribus I – 1. 2    Characteristic II – 3    Characterizer II – 3    Chi-squared distribution/model/test I – 3. 2    Chronic I – 1. 2    CI II – 4    Class II – 3    Client I – 1. 2    Clinical I – 1. 2    Clinical diagnosis I – 1. 2

Clinical epidemiology I – 1. 2 Clinical etiognosis I – 1. 2 Clinical medicine I – 1. 2 Clinical prognosis I – 1. 2 Clinical research/study III – 2 Clinical trial III – 4 Clinician I – 1. 2 Closed population II – 4 Cochrane collaboration III – 4 Coding II – 4 Cohort II – 4 Cohort fallacy II – 4 Cohort study II – 4 Cohort time II – 4 Collinearity I – 3. 2 Combinatorial I – 3. 2 Community diagnosis I – 1. 2 Community etiognosis I – 1. 2 Community health I – 1. 2 Community medicine I – 1. 2 Community prognosis I – 1. 2 Community trial II – 4 Comorbidity I – 1. 2 Comparability II – 4 Comparative parameter II – 3 Comparison group/population II – 4 Competing cause I – 1. 2 Complete randomization III – 4 Compliance I – 1. 2, III – 4 Complication I – 1. 2 Concept I – 2. 2 Conception I – 2. 2 Conclusion I – 2. 2, II – 4 Confidence interval I – 3. 2, II – 4, III – 4 Confounder-adjustment II – 4 Confounder score II – 4 Confounding II – 4 Confounding bias II – 4 Confounding by indication III – 4 Congenital I – 1. 2 Consent III – 4 Contamination III – 4 Continuous variate I – 3. 2 Contra-indication I – 1. 2 Contributing cause I – 1. 2 Control II – 4, III – 4 Control group II – 4 Control of confounding II – 4 Correct diagnosis/etiognosis/prognosis I – 1. 2 Correlation coefficient I – 3. 2 Corroboration I – 2. 2 Cost II – 4 Cost-effectiveness analysis III – 2 Course I – 1. 2 Covariance I – 3. 2 Covariate I – 3. 2 Cox regression III – 2 Credibility II – 3 Cross-sectional II – 3 Cross-validation II – 4 Crude rate I – 1. 2 Cumulative incidence I – 1. 2 Curative I – 1. 2 Cure I – 1. 2

Data I – 2. 2, II – 4 Data analysis II – 4 Data Safety and Monitoring Board III – 4 Datum I – 2. 2 Death rate I – 1. 2 Decile II – 4 Deduction I – 2. 2 Defect I – 1. 2 Definition I – 2. 2 Dependent parameter II – 2 Dependent variate I – 3. 2 Derivative study I – 2. 2 Descriptive epidemiology II – 2 Descriptive statistic I – 3. 2, II – 4 Design I – 2. 2, II – 4 Design matrix II – 4 Design versus analysis II – 2 Determinant I – 1. 2, 2. 2 Determinism I – 2. 2 Deviance statistic/test I – 3. 2 Diagnosed I – 1. 2 Diagnosing I – 1. 2 Diagnosis I – 1. 2 Diagnostic I – 1. 2 Diagnosticating I – 1. 2 Diagnostic probability function III – 3 Diagnostic profile I – 1. 2 Diagnostic study III – 4 Diagnostic test's properties III – 3 Dichotomous II – 3 Dimension I – 2. 2 Directionality II – 4 Direct standardization I – 1. 2 Discovery I – 2. 2 Discrete variate I – 3. 2 Disease I – 1. 2 Disorder I – 1. 2 Distribution I – 3. 2 Distribution function I – 3. 2 Distribution matrix II – 4 Doctor I – 1. 2 Documentation bias II – 4 Domain II – 3 Dose-response I – 1. 2 Double blinding III – 4 DPF III – 3 Dummy variate II – 4 Dynamic cohort II – 4 Dynamic population II – 4

Early detection/diagnosis I – 1. 2 EBM I – 1. 2 Effect I – 1. 2, 3. 2, II – 3 Effectiveness I – 1. 2, III – 2 Effectiveness research III – 2 Effect measure II – 3 Effect modification II – 3 Efficacy I – 1. 2, III – 2 Efficiency II – 4 Efficient I – 3. 2 Eligibility II – 4 Empirical I – 2. 2, II – 4 Empiricism I – 2. 2 Endemic I – 1. 2 Endpoint III – 4 EPF III – 3 Epidemic I – 1. 2 Epidemiologic II – 2 Epidemiological II – 2 Epidemiological research

II – 2 Epidemiologist I – 1. 2, II – 2 Epidemiologist vis-à-vis statistician II – 2 Epidemiology I – 1. 2, II – 2 Epistemic/epistemological/epistemology I – 2. 2 Equipoise III – 4 Error I – 3. 2 Estimate I – 3. 2 Estimation I – 1. 2, II – 3 Estimator I – 3. 2 Ethics III – 4 Etiogenesis I – 1. 2 Etiogenetic/etiologic time II – 3 Etiogenetic fraction I – 1. 2 Etiogenetic/etiologic study II – 4 Etiognosing I – 1. 2 Etiognosis I – 1. 2 Etiognosticating I – 1. 2 Etiognostic probability function III – 3 Etiognostic study III – 4 Etiologic fraction I – 1. 2 Etiologic proportion I – 1. 2 Etiologic study II – 4 Etiology I – 1. 2 Evaluation I – 1. 2 Evidence I – 2. 2, II – 4 Evidence-Based Medicine I – 1. 2 Exact P-value/test I – 3. 2 Expectation I – 3. 2 Experiment I – 2. 2 Expert I – 1. 2, II – 4, III – 4 Expert system I – 1. 2 Explanandum I – 2. 2 Explanans I – 2. 2 Explanation I – 2. 2 Explanatory I – 2. 2 Explanatory trial III – 3 Exposure I – 1. 2, II – 3 External validity II – 4

Fact I – 2. 2 Factoid I – 2. 2 Factor I – 1. 2 Factorial design I – 2. 2 False negative I – 1. 2 False positive I – 1. 2 Fatality I – 1. 2 Fatality rate I – 1. 2 F-distribution/test I – 3. 2 Finding I – 1. 2, 2. 2, II – 4 Fisher's exact test I – 3. 2 Fixed cohort II – 4 Fractile II – 4 Frequentism/frequentist I – 3. 2 F-test I – 3. 2 Function I – 3. 2

Gaussian distribution/model/test I – 3. 2 General I – 2. 2 General linear model I – 3. 2 Generalizability II – 4 Generalization I – 2. 2 Generalized linear model I – 3. 2 General population II – 4 Genetics vis-à-vis epidemiology II – 2 Genus I – 2. 2 GLM I – 3. 2 Gnosis I – 1. 2 Gnostic expert paneling III – 4 Gnostic probability function III – 3 Good diagnosis/etiognosis/ prognosis I – 1. 2 Goodness of fit III – 4 GPF III – 3 Group II – 4

Hawthorne effect III – 4 Hazard I – 1. 2, III – 2 Hazard ratio III – 2 Health I – 1. 2 Healthcare I – 1. 2 Health-related quality of life III – 2 Health service I – 1. 2 Health services research II – 2 Healthy worker effect II – 4 Hermeneutics I – 2. 2 Hierarchy of evidence II – 4, Hill's considerations for causal inference II – 4 History I – 1. 2 Homoscedasticity I – 3. 2 HR III – 2 HRQL III – 2 Hygiene I – 1. 2 Hypergeometric distribution/model/test I – 3. 2 Hypothesis I – 2. 2, 3. 2, II – 2 Hypothesis testing I – 3. 2, II – 2

Iatrogenesis I – 1. 2 Idiosyncrasy I – 1. 2 Illness I – 1. 2 Impairment I – 1. 2 Incidence I – 1. 2 Incidence rate I – 1. 2 Independence II – 2 Independent parameter II – 2 Independent variate I – 3. 2 Index category II – 3 Indication I – 1. 2, III – 2 Indicator I – 1. 2, II – 3, III – 2 Indicator variate II – 2, 4 Indirect standardization I – 1. 2 Induction I – 2. 2 Induction period I – 1. 2 Inference I – 2. 2, 3. 2 Inferential statistic I – 3. 2, II – 4 Information I – 2. 2, 3. 2 Informativeness II – 4 Informed consent III – 4 Injury I – 1. 2 Institutional Review Board III – 4 Instrumental I – 2. 2 Insufficient cause II – 3 Intention to treat III – 4 Interaction I – 3. 2 Intercept I – 3. 2 Internal validity II – 4 Interpretation I – 2. 2 Interval estimate I – 3. 2, II – 4 Interval

scale I – 2. 2 Intervention I – 1. 2, III – 3 Intervention-prognostic study III – 4 Intervention-prognostic study III – 4 Intervention study III – 4 Intervention time II – 3 Investigation I – 1. 2 IRB III – 4

Kaplan-Meier-Greenwood statistics III – 4 Knowledge I – 2. 2 Knowledge-based medicine I – 1. 2

Latency period I – 1. 2, II – 3 Latent I – 1. 2 Law I – 2. 2 Lemma I – 2. 2 Level of test I – 3. 2 Likelihood III – 4 Likelihood function I – 3. 2 Likelihood ratio III – 3 Linear I – 3. 2 Lingua franca I – 2. 2 Link III – 3 Logic I – 2. 2 Logistic model I – 3. 2 Logistic regression I – 3. 2 Logit I – 3. 2 Longitudinal II – 3

Main effect I – 3. 2 Management I – 1. 2 Mantel-Haenszel estimate II – 4 Mantel-Haenszel test statistic II – 4 Matching II – 4 Matrix II – 4 Maximum likelihood I – 3. 2 Mean bias I – 3. 2 Mean square error I – 3. 2 Measurement I – 1. 2, 2. 2 Median bias I – 3. 2 Medicine I – 1. 2 Meta-analysis II – 4 Meta-epidemiological clinical research III – 2 Methodology II – 4 M-H II – 4 Mid-P I – 3. 2 Misclassification I – 2. 2 ML I – 3. 2 Model I – 3. 2 Morbidity I – 1. 2 Mortality I – 1. 2 Mortality rate I – 1. 2 Multicollinearity I – 3. 2 Multiple comparison problems I – 3. 2, II – 4 Multiple regression I – 3. 2 Multivariate regression I – 3. 2

Natural course I – 1. 2 Natural experiment I – 2. 2 Natural history I – 1. 2, 2. 2 Natural quasi-experiment I – 2. 2 Natural science I – 2. 2 Necessary cause II – 3 Negative I – 1.2, 2. 2 Negative confounding II – 4 Negative study II – 4 Nested case-control study II – 4 Nominalism I – 2. 2 Nominal scale I – 2. 2 Non-central hypergeometric distribution I – 3. 2 Non-experimental I – 2. 2 Normal I – 1. 2 Normal distribution I – 3. 2 Nosocomial I – 1. 2 Nosology I – 1. 2 Noumenon I – 2. 2 Noxiousness I – 1. 2 Nuisance parameter I – 3. 2 Null distribution II – 4 Null hypothesis I – 3. 2, II – 2 Null P-value I – 3. 2 Null value II – 4

Objective I – 2. 2 Objective of study II – 3 Object of study II – 3 Observation I – 2. 2 Observational I – 2. 2 Occam's/Ocham's razor I – 2. 2 Occurrence I – 1. 2 Occurrence relation II – 3 Odds I – 3. 2 Odds ratio II – 4 Omnibus null hypothesis I – 3. 2 Ontal/ontic/ontological I – 2. 2 Ontology I – 2. 2 Open population II – 4 Operationalization II – 4 OR II – 4 Ordinal scale I – 2. 2 Original study I – 2. 2 Outcome I – 1. 2, II – 3 Outcome-probability score II – 4 Outcomes research III – 2 Overdiagnosis I – 1. 2 Overmatching II – 4 Overparametrization/overfitting III – 3 Overt I – 1. 2

Palliation/palliative I – 1. 2 Parameter I – 1. 2, 3. 2 Parsimony I – 2. 2 Pathogenesis I – 1. 2 Pathognomonic I – 1. 2 Patient I – 1. 2 Pattern recognition I – 1. 2 Percentile II – 4 Person-characteristic II – 3 Person-moment

II-4 Person-time II-3 Person-years II-3 Phenomenon I-2.2 Physical examination I-1.2 Physician I-1.2 Placebo III-3 Plausibility II-3 Point estimate I-3.2, II-4 Point source I-1.2 Poisson distribution I-3.2 Polytomous II-3 Population II-3 Population-based II-4 Population-time II-3, 4 Positive I-1.2 Positive confounding II-4 Positive (negative) predictive value I-1.2 Positive study II-4 Posterior I-3.2 Post-test informativeness/probability III-3 Power I-3.2, II-4 PPF III-3 Practice I-1.2 Pragmatic trial III-3 Precision I-2.2, II-4 Preclinical I-1.2 Prediction/predictive I-1.2 Prescription I-1.2 Presumption I-2.2 Pre-test informativeness/probability III-3 Prevalence I-1.2 Prevalence rate I-1.2 Prevention of confounding II-4 Prevention/preventive I-1.2, II-2 Preventive medicine I-1.2 Primary base II-4 Primary diagnosis I-1.2 Primary objectives II-3 Principle I-2.2 Principle of parsimony I-2.2 Prior I-3.2 Probability I-3.2 Probability density I-3.2 Probability sample/sampling I-3.2 Professionalism I-1.2 Profile I-1.2 Prognosing I-1.2 Prognosis I-1.2 Prognostic probability function III-3 Prognostic study III-4 Proof I-2.2 Propensity score II-4 Prophylaxis/prophylactic I-1.2 Proportional hazards model III-2 Proposition I-2.2 Prospective II-3, 4 Protocol II-4 Public health I-1.2 Publication bias II-4 Pure I-2.2 P-value I-3.2 P-value function I-3.2

QALY III-2 Quality-adjusted life year III-2 Quality of study methodology II-4 Quality of study object(s) II-3 Quantitative research II-2 Quartile II-4 Quasi-experiment I-2.2 Quasi-rate II-4 Quasi-scientific medicine I-1.2 Quintile II-4

Randomization III-4 Randomized controlled trial III-4 Randomized trial III-4 Random sample I-3.2 Random variable/ivariate I-3.2 Rare-disease assumption II-4 Rate I-1.2 Rate ratio II-3 Rationalism I-2.2 Ratio scale I-2.2 RCT III-4 RCTism III-4 Realism I-2.2 Realization I-3.2 Received knowledge I-2.2 Receiver operating characteristic curve III-3 Reduction III-4 Reference category II-3 Referent II-3 Regressand I-3.2 Regression analysis II-4 Regression coefficient I-3.2 Regression toward the mean III-4 Regressor I-3.2 Rehabilitation/rehabilitative I-1.2 Relative risk II-4 Relevance II-3 Replication I-2.2, III-4 Replication distribution II-4, Representative sample II-4 Reproducibility I-2.2, II-4 Research I-2.2 Research design II-2 Residual confounding II-4 Restricted randomization III-4 Result I-1.2, 2.2, II-4 Retrospective II-3, 4 Risk I-1.2 Risk factor/indicator II-3 ROC curve III-3 RR II-3, 4 Rule-in diagnosis I-1.2 Rule-out diagnosis I-1.2

Safety I-1.2 Salubrious I-1.2 Salutary I-1.2 Sample I-3.2 Sample distribution I-3.2 Sample size II-4 Sample size determination I-3.2, II-4, III-4 Sample distribution I-3.2 Sampling I-3.2 Sampling distribution I-3.2 Scalar I-3.2 Scale I-2.2 Science I-2.2 Scientific community

II – 4 Scientific medicine I – 1. 2, Scientific time II – 3 Screening I – 1. 2  
 SD I – 3. 2 SE I – 3. 2 Secondary base II – 4 Secondary diagnosis I – 1. 2  
 Secondary objectives II – 3 Selection bias II – 4 Sensitivity I – 1. 2 Sequela  
 I – 1. 2 Serendipitous I – 2. 2 Shrinkage III – 4 Sickness I – 1. 2 Sign I –  
 1. 2 Significance I – 3. 2 Simple random sampling II – 4 Simple regression  
 I – 3. 2 Simplicity I – 2. 2 Size of study II – 4 Slope I – 3. 2 Soma I – 1. 2  
 Source population II – 4 Specificity I – 1. 2 Specific rate I – 1. 2 Standard  
 deviation I – 3. 2 Standard error I – 3. 2 Standard-Gaussian distribution I –  
 3. 2 Standard population II – 4 Standardized rate I – 1. 2, II – 4 Statistic  
 I – 3. 2 Statistical significance I – 3. 2, II – 4 Statistics I – 3. 2 Status I –  
 1. 2 Stochastic II – 4 Stratified random sampling II – 4 Study I – 1. 2, 2. 2  
 Study base II – 4 Study design II – 2 Study group II – 4 Study population  
 II – 4 Study time II – 4 Subacute I – 1. 2 Subdomain II – 3 Sufficient  
 cause II – 3 Superpopulation II – 3 Surgery I – 1. 2 Survey II – 2 Survival  
 analysis III – 4 Survival rate I – 1. 2 Susceptibility I – 1. 2 Syllogism I – 2. 2  
 Symptom I – 1. 2 Symptomatology I – 1. 2 Syndrome I – 1. 2 Synthesis I –  
 2. 2 Systematic error II – 4 Systematic review III – 4

$T_0$  II – 4 Target population II – 4 Taxonomy I – 2. 2 Technology assessment  
 III – 2 Tertile II – 4 Test I – 1. 2, 2. 2, 3. 2 Testability II – 3 Test-based  
 confidence interval II – 4 Test statistic I – 3. 2 Theorem I – 2. 2 Theoretical  
 I – 2. 2 Theory I – 2. 2, II – 2 Theory of clinical medicine III – 2 Theory  
 of epidemiology II – 2 Therapeutic/therapy I – 1. 2 Thesis I – 2. 2 Thought  
 experiment I – 2. 2 Time II – 3 Translational research III – 2 Treatment I –  
 1. 2 Trichotomous II – 3 Trochoc fallacy II – 4 Truth I – 2. 2 t- test I – 3. 2  
 Type I error I – 3. 2, II – 4 Type II error I – 3. 2, II – 4

Underlying cause I – 1. 2 Uniform 0-1 distribution I – 3. 2 Universal I – 2. 2

Validation II – 4 Validity II – 4 Variable/variante I – 3. 2, II – 3 Variance I –  
 3. 2 Vector I – 3. 2

Wald statistic I – 3. 2

# HIERARCHY OF CONCEPTS

What follows is my suggestion for the sequence in which concepts might best (most logically) be introduced (and justified) – for their most ready apprehension by the students – in an *introductory course* on epidemiological research (cf. Introduction in this book).

The sequence (and coverage) I here suggest is predicated on two *premises*:

1. Each student is preparing – or considering preparation – for a career in ‘epidemiological’ research – the actual meaning of ‘epidemiological’ possibly being that of ‘meta-epidemiological clinical.’
2. Each student is suitably prepared for the course: (S)he has studied the here-relevant statistics (sect. I – 3), or (s)he is taking a course on those concepts parallel with this one; and (s)he has a sufficient level of proficiency in English (the lingua franca of modern science and, hence, the language of this course).

The point of departure in this course naturally is to be the concept of *epidemiology*, with the understanding that this is the segment of medicine that concerns morbidity in the community/population an epidemiologist is caring for, morbidity in its components specific to particular illnesses, these illness-specific morbidities in terms of rates of the occurrence of the respective illnesses. Grasping the full burden of this statement requires possession of a number of concepts other than that of epidemiology, from the concept of medicine to those of *rate*, starting from rate per se and then introducing the duality constituted by rates of incidence and those of prevalence. This will naturally lead to the concepts of adjustment and standardization of rates.

Where a clinician’s concern is to prevent a case of an illness from occurring in an individual, an epidemiologist’s corresponding concern is to reduce *morbidity* from the illness, by community-level preventive measures. While all of community medicine is *preventive medicine*, there now is considerable confusion among academic epidemiologists about the scope of preventive medicine, as viewed from the vantage of epidemiology. The course should develop a tenable concept of preventive medicine, in part because this term remains in use as a synonym for ‘epidemiology’ and ‘community medicine’ (along with ‘social medicine’).

The conception of epidemiology as community-level preventive medicine is made more concrete by coming to appreciate the principal *modalities* of preventive care in community medicine: education, regulation, and service. More to the same effect is delineation of what, in generic terms, tends to be involved in each of these three. A point of particular note that thus arises is that an epidemiologist's health-education pertaining to prevention of a particular illness is mass education of the individuals in the community, about self-care, with the content the same as in the corresponding aggregate of education/teaching/counseling in clinical preventive care. The mass education needs to involve the distinction-making that is inherent in the preventive care by clinicians. Individuals in the population need to be guided to the appropriate source (website) for guidance as to risk assessment, etc.

Such understanding of the nature of the practice of community medicine implies the nature of its *knowledge-base*: The proximal aim of the practice typically is removal of health hazards, behavioral and environmental (micro- and macro-environmental); only exceptionally is it invocation of an intervention (a vaccination, most notably, for constitutional change). The knowledge-base thus is about health hazards – their health effects – first and foremost; and to a minor extent it is about the effects of preventive interventions.

The knowledge-base of community-level preventive medicine in respect to health hazards is about causal origin – etiology, *etiogenesis* – of illness. The students need to achieve a secure grasp of the concept of etiogenesis of illness, this *pari passu* with the concept of pathogenesis. They need to learn that at issue in this is one of the two fundamental types of cause-effect relation that are of concern in medicine; and they need to learn to distinguish it, securely, from the other one, which mainly has to do with intended effects of interventions, preventive and other.

The topic of the knowledge-base of epidemiology (its practice) leads to the concept of science and that of *research* in it, original and derivative, including the concept of evidence as the product of a piece of research, a study. The students get to understand that epidemiological research does not constitute a science; and that scientific knowledge is not the direct product of epidemiological research. They also get to appreciate that some epidemiological studies (on rates) are not pieces of research but, instead, matters of particularistic fact-finding.

Now the students are ready to be introduced to the concept of *etiologic/etiogenetic study*. In this, the natural beginning is the intuitive understanding that of central importance in this is a *case series* of the illness – successively identified cases documented in respect to the risk factor at issue.

It is good to think about this case series first on the counterfactual premise that causation – here etiogenesis – is a phenomenon (instead of being a nomenon). If this were the case, attention would focus on the cases preceded by the risk factor in its index category; and note would be taken of the proportion of these cases such that the antecedent actually was etiogenetic to the case. Structurally, the essence of the study would be such a restricted case series together with the documentation in it of the etiogenetic proportion for the factor at issue, proportion specific to cases occurring in association with the factor, the index category of the risk factor.

The challenge that arises from etiogenesis actually being but a noumenon is the need to provide for the case series being a manifestation (phenomenal) of the etiogenesis at issue, in terms of the etiogenetic proportion of interest (cf. above). This means that the case series is to serve documentation of rates of the outcome's occurrence in a defined study base – index and reference rates in it – conditionally on extraneous determinants of the outcome's rate of occurrence. This implies the *essence (structural) of an etiogenetic study*, including the measure of the etiogenetic proportion that it involves (as an implication of the rate ratio).

This essence of the study, in turn, implies the generic *process* to produce it, starting from the commitment to a particular source population, whether defined directly or as the catchment population of the way in which the initial (pre-reduction) case series is derived. A bit more specifically, the initial commitment is to a source population-time, to a source base, that is; and the final phase of the process now generally is the fitting of a logistic probability function to the data (now in the form of realizations for statistical variates).

While this essence, structural and procedural, of an etiogenetic study is dictated by logic, it is necessary for the students to also learn about two related concepts: that of '*cohort study*,' as this was adopted as a matter of misguided use of intervention-prognostic experiments as paradigmatic for non-experimental etiogenetic studies [9]; and that of '*case-control study*,' as this misguidedly was adopted as the solution to the feasibility problems in 'cohort studies' on rare illnesses [9]. Critical in this is the exposition of the respective fallacies, and how the correction of these leads to the singular essence of etiogenetic studies.

The common involvement of *logistic regression* in the etiogenetic study and also in the '*case-control study*,' and the common use of *Cox regression* in the '*cohort study*,' calls for addressing the concepts of – and in – these two types of regression, at this point in this course.

Now the students are ready to learn, concretely, *the duality in causality-oriented, directly practice-serving studies* in medicine, that constituted by the etiogenetic/etiognostic study on one side and the intervention-prognostic study on the other side [9]. The students learn that not only is the logic-dictated etiogenetic/etiognostic study not patterned after the intervention-prognostic study; it serves as a paradigm for an important aspect of RCTs, to transform the RCT from a study addressing a 'hazard ratio' (single-valued) to one producing a prognostic (intervention-prognostic) probability function (empirical) – with the involvement of logistic, rather than Cox, regression.

Once the students have a secure understanding of the essence of *the* etiogenetic study, they are ready – and they need – to learn about the principal use of this study – about *testing of etiogenetic hypotheses*. They need to learn the difference between the statistical and scientific conceptions of hypothesis and, especially, the difference between frequentist-statistical hypothesis-testing and the scientific matter of testing etiogenetic hypotheses. Important in this is, among other things, getting to understand that scientific testing ends with the evidence (original or derivative) it produces, leaving inference – the final stage in the production of scientific knowledge – to the relevant scientific community to engage in.

This use of the evidence from an etiogenetic study leads to consideration of the quality of it, the degree to which the result of the study is free from *bias*. The concepts of the three fundamental types of potential bias in an etiogenetic study need to be introduced. Given that this triad is not generally well-understood, learning it should not be impeded by the distraction of cataloguing subtypes of these.

Meant by ‘the result’ that may be biased in an etiogenetic hypothesis-testing study is, principally at least, the *empirical value* – single – it produces, or produced, for the rate ratio pertaining to the causal contrast at issue. This value – a ‘statistic’ – is the product, ultimately, of a statistical procedure, involving logistic regression, stratification, or both (in stratification by a confounder score). These procedures need to be introduced. And it is important to underscore that the rate-ratio’s thus-obtained empirical value is not a ‘point estimate’ of the RR.

Coupled with the result of an etiogenetic hypothesis-testing study commonly is a measure of its imprecision. The students need to learn what replication-distributional properties an interval measure of this is supposed to have, the principal ways in which it is obtained, and – very importantly – that ‘interval estimate’ and ‘confidence interval’ are misnomers for this measure.

Also commonly coupled with the result of these studies is a *null P-value*. As with an interval measure of imprecision, the students need to learn what distributional properties the null P-value is supposed to have, and what are the principal ways of deriving this statistic from the data. The teacher may very well criticize the term and concept of ‘testing statistical significance,’ but (s)he must not make the error of questioning the role of hypothesis-testing in statistical science.

From testing etiogenetic hypotheses the teaching naturally moves to studies for *quantification* of an etiogenetic effect. For orientation to this, the students already are quite well prepared to receive the point that these studies do not produce estimates (point or interval) but only evidence for estimation (inferential, by members of the relevant scientific community).

As estimation, different from hypothesis-testing, is quantification, it presupposes *specificity* about that which is the object of the quantification. At issue here is specificity in respect to the contrasted etiogenetic histories, for one. But in addition, distinctions need to be made among subdomains of the overall domain of the study, based on potential modifiers of the RR’s magnitude. This leads the teacher to address the expressions of these specificities in the log-linear model for the incidence density of the illness, in the domain of the study, the model that implies for  $\log(\text{RR})$  as a function of those particulars. At issue in this is specifics of the study’s object design, bearing on its methods design (of the particulars within the study’s a-priori essence, structural and procedural).

For the students to be able to rise above all of these particulars (even if only introductory) of research on the etiogenesis of illness, it is good, I think, of the teacher to delineate (the broadest particulars of) what characterizes a good etiognostic study – as to its implications for the advancement of the knowledge-base of community-level preventive medicine. For, this has bearing on the students’ decisions about whether this line of research indeed will be what their future careers will be about.

As one notable alternative to epidemiological – generally etiogenetic – research in the students’ career plans is meta-epidemiological clinical research, it is good, I think, of the teacher to introduce the students to the essence of research for *clinical diagnosis* – genuine essence, with a central role, again, for logistic regression. This, it needs to become clear, is in sharp contrast to what now is being taught, and practiced, by ‘clinical epidemiologists’ [16].

The other alternative to consider is *garnering the existing tacit knowledge* of diagnostic and prognostic experts of clinical medicine in the form of probability functions for codification in expert systems, to guide clinical practices in the interest of both quality-assurance and cost-containment in the framework of quasi-scientific medicine.

In closing, I note that a student with a solid, maximally logical orientation to epidemiological and meta-epidemiological clinical research may not have a more successful career than the one who is taught to appreciate ‘cohort studies’ and ‘case-control studies,’ and diagnostic tests’ ‘sensitivity’ and ‘specificity,’ etc. (S)he may not end up with more publications, but (s)he most assuredly will make more *contributions* to the advancement of the knowledge-base of medicine. (Yes, there is ‘epidemiological’ research with purposes other than those noted above, but they do not belong in an introductory course on ‘epidemiological’ research.)