

#s in EVERYDAY LIFE OUTLINE

Class 3: Medical and Health Studies

Ricki Lewis (RALEWIS@NYCAP.RR.COM)

The slides for this presentation are unavailable. We provide herewith

- A detailed summary of the material presented.
- A preliminary class outline.
- A factsheet on clinical trials that was provided as a class handout.

Further details can be obtained directly from the presenter.

DETAILED SUMMARY

The session instructor examined sources of science news and feature stories. Slides summarized concepts and liberally used cartoons, illustrations, and photographs. This session consisted of many examples loosely organized into three sections.

Anatomy of a medical journal: In order to get a flavor for the way that medical journals use and present statistics, we examined a recent issue of *The New England Journal of Medicine* (2/28/08). This is important because the media often report information from such journals. The eight articles in this issue dealt with

- “The vanishing nonforensic autopsy
- Vasopressin + norepinephrine in septic shock to raise blood pressure
- “Severe anemia in Malawiain children”
- Lupus-genome-wide association (GWA) studies
- Osteoporosis drugs

- Once-a-year fracture prevention
- CT to diagnose appendicitis
- Inheritance of cystic fibrosis

They illustrated such concepts as the value of negative evidence; the importance of context, bias, and invalid assumptions; confusing correlation with causation; odds ratio to evaluate cancer risk; sample size requirements; and cost/benefit analysis in utilizing an expensive medical scanning technology. Some examples did not fit a specific category but were still intriguing, such as the effect on incidence of cystic fibrosis before and after prenatal screening (enabling women to terminate affected pregnancies) became common.

The drug approval process: A short bridging discussion considered the steps of the drug approval process in the US, from basic research, to preclinical (animal) studies, to clinical trial design. We talked about how health studies enter the news, and how the media misuse terms such as “proof” and “theory.” A handout (attached) listed commonly used terms, and covered incidence and prevalence; risk; association, correlation, and causation (“do firefighters cause fires?”); the importance of determining the underlying mechanism (smoking and lung cancer); and future additions to the drug approval process (biomarkers and pharmacogenomics).

Sources of distortion: We used news releases (mostly from www.eurekalert.org) to illustrate and categorize statistical errors and misinterpretations. The examples dealt with such topics as

- Do artificial sweeteners promote or prevent weight gain?
- Does watching World Cup soccer provoke cardiac events?
- Low card diet and heart disease.
- Post-marketing surveillance.
- Antidepressants and suicidality.

They illustrated inappropriate extrapolations; errors of omission and study drop-outs; test duration and sample size limitations (the reason why many blockbuster drugs show adverse effects only *after* they have been marketed); meta-analyses; confounding factors; and flawed surrogate markers.

The session concluded with take-home messages in evaluating health studies in the news. Students should be on the lookout for the underlying logic; missing or irrelevant information; confounding factors; lack of controls; and whether researchers or reporters have an agenda or conflict.

For further information, contact Ricki Lewis (ralewis@nycap.rr.com)

PRELIMINARY CLASS OUTLINE

I. Introduction: Statistics in genetics (my work)

- cystic fibrosis carrier case (genetic counseling)
- clinical trials of drugs for Huntington disease
- general reporting guidelines
- From Mendel's laws to linkage to association studies
- Genetic tests: absolute vs relative risk (breast cancer complexity)
- Gene expression profiling and disease risk (JNCI)

II. Clinical trial design for observational studies:

- Case-control
- Cohort
- Cross sectional

The STROBE statement (PLoS Medicine, Oct. 2007 = "Strengthening the Reporting of Observational Studies in Epidemiology Statement" (handout)

Example: testing the hypothesis that people who work with insects don't get bug bites (me)

III. 10 Sources of Distortion

1. The "carbs are good for you one week, carbs are bad for you next week" phenomenon - on the nature of science behind medicine ("Do We Really Know What Makes Us Healthy?" by Gary Taubes, New York Times magazine, Sept 16, 2007)

example: EurekAlert! News releases:

Feb 8: "Study confirms that low-calorie sweeteners are helpful in weight control"

Feb 10: "Artificial sweeteners linked to weight gain."

Failure to understand how science is done: no such thing as scientific or clinical "proof"; difference between theory and hypothesis. Only evidence and interpretation count.

2. Correlation + cause: Is an association due to chance or an evidence-supported explanation or mechanism?

- Digit ratio: index to ring finger length ratio ("2D:4D")
- "Cardiovascular events during World Cup Soccer" (NEJM, 1/31/09)
- "Low carbohydrate diet score and the risk of coronary heart disease in women" (NEJM 11/9/06)
- Race and prescribing practices
- Association studies

3. "time-to-event" omissions (kidney cancer)
4. small sample size
 - Importance of post-marketing surveillance "Improving detection of adverse effects of marketed drugs" JAMA 7/18/07 (Celebrex, Avandia)
 - Runner's high - endorphins on PET scans of 10 runners
5. participants do not have the same disease subtype
 - "Effects of a low-glycemic load vs low-fat diet in obese young adults," JAMA 5/16/07
 - cancer, ALS
6. untested extrapolations of study results (gender, age)
 - "In Their Prime, and Dying of Cancer" Science, Aug 31, 2007
7. inappropriate comparisons - apples + oranges
 - cancer drug study (Annals of Oncology)
 - meta analyses ("Meta-analysis: the effect of dietary counseling for weight loss" Annals of Internal Medicine 7/3/07)
8. unwillingness to give up popular ideas - the diet dilemma
 - "Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women," JAMA 3/7/07. (or "Why I can't find low-carb Ben and Jerry's anymore")
9. confounding factors - anti-depressants and suicidality (Ricki's articles)
10. Oops! When assumptions are wrong. The telling tale of Vytorin ("What's cholesterol got to do with it?" by Gary Taubes, *The New York Times*, 1/27/08)

CLINICAL TRIAL FACTSHEET

Arm: Any of the treatment groups in a randomized trial. Most randomized trials have two "arms," but some have three "arms," or even more.

Randomized Trial: Participants assigned by chance to an arm.

Baseline: Information at the start of a study to which deviations are compared.

Endpoints: Outcomes of trials; must be set before trial.

1. **Primary** The main outcome, such as survival, recurrence, improvement.
2. **Composite endpoints** >1 outcome measure, such as hospitalization and mortality.
3. **Surrogate** A measure of effect of a certain treatment that correlates with a true endpoint, but may not be related to the true endpoint. A biomarker.

Control Group: The standard to which experimental observations are compared.

Placebo: An inactive substance used to assess the tested treatment's effectiveness.

Open-Label Trial: Investigators and participants know which drug or vaccine is given.

Single-Blind Study: Investigator or participant unaware of treatment.

Double-Blind Study: Neither participants nor investigators know which participants are receiving the experimental drug and which are receiving a placebo (or another therapy).

Inclusion/Exclusion Criteria: Factors used to determine whether a person may enter a clinical trial. Usually based on age, gender, type and stage of a disease.

needed to treat: How many patients must get treatment to help one?

Odds ratio: The ratio of the odds of an event occurring in one group to the odds of it occurring in another group. (That is, "1" = both groups same.)

Prospective: A trial that begins and goes forward in time.

Retrospective: A trial that relies on recall of past events.

Sample size # of individuals in control or experimental group. >30 unless pilot study.

Time to event analysis Who gets better or dies sooner.

Prevention Trials: Test ways to prevent disease or its recurrence.

Treatment Trials: Test new treatments or treatment combinations.

Meta analysis Pooling of data from more than one study.