

Minding your P's and Q's

ABSTRACT REASONING

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Some of the methodologic reasoning that goes into producing the life tables found in morbidity/mortality abstracts may go unnoticed. This issue of the *Journal* furnishes the opportunity to look at the "abstract reasoning" that went into two such abstracts.

The first is a mortality study of long-term survival following anticoagulant-treatment of myocardial infarction. The second is a morbidity study of the risk of colorectal cancer following rectosigmoid adenoma.

The mortality abstract is a 20-year follow-up study of 1416 patients enrolled between 1963 and 1966 in England, Scotland, and Wales. It is a uniserial, unizonal, multisectional¹ prospective clinical trial, with follow-up 94% complete to 20 years. The mean age of the study group at entry was 58.4 years, and only 16% survived to the end of follow-up. The abstract is submitted by Dr. Richard Singer, the acknowledged dean of mortality abstraction among medical directors, and this year's recipient of the John Elder Award for journalistic excellence and insurance medicine writing.

The second abstract (colorectal cancer morbidity) is a study of 1618 subjects assembled at St. Mark's Hospital, London, during a rolling-entry period of 1957 to 1980. They were followed an average of 13.9 years (minimum follow-up being 2 years, with 334 subjects followed more than 20 years). Follow-up to one of the five study end-points (death, cancer, 86th birthday, colonoscopy, or end-of-study [May, 1988]) appears to have been 100% complete. Thus, this study represents a unizonal, multiserial, multisectional, retroactive¹ (historical prospective) study with 22,462 person-years of follow-up. This is the first abstract for the two authors, Drs. Fran Watson and Susan Sokoloski, who attended their first Advanced Mortality Methodology Workshop at the Academy meeting only this October. They distinguished themselves there as students of mortality methodology, and now hold the record for speed of conversion of a Workshop article to a *Journal* abstract.

Twenty-year follow-up of anticoagulant treated MI

In 1966, the Medical Research Council in Britain conducted a comparative trial of the efficacy of high-dose

versus low-dose 28-day anticoagulation in 1427 hospitalized patients with acute MI. No significant survival difference between the two groups was found at 28 days. Twenty years later, through medical record linkage between the participating medical centers and the National Health Service and Social Security Office, 1330 of these original patients were traced, and both arms of the original study were combined to create a cohort of sorts. This cohort (MI patients subjected to an anticoagulation protocol during their 28 day acute hospital stay) was followed in historical prospective fashion to death or to 20-23 years of follow-up.

The source article for Singer's abstract contained a cumulative mortality curve (Q) (article's Figure 2) which plotted annual data points in semi-logarithmic fashion (log Q versus time, in years). In displaying the data in his Table 345M1-1, Singer divided first year mortality into two intervals, acute (hospital inpatient) mortality during the first four weeks, and mortality experienced during the remainder of the first year (four weeks to one year). He then showed subsequent follow-up by five year durations. For expected mortality, Singer utilized the Q' plot in the same Figure 2 of the source article. These annual Q' points were based on 1971 life tables for England and Wales.

As Singer discusses in his abstract, it appears that these 1971 population life tables were used to calculate the first year q' for the cohort (all ages and both sexes combined) and then advanced year to year as if the cohort were aging a full year for each elapsed year of study duration. This approach to estimating expected mortality would underestimate the true comparative mortality, observed to expected, with a more exaggerated effect at the higher durations due to compounding of any error. (The negative EDR at duration 15-20 years, as explained by Singer, is probably attributable to this handling).

Lacking a 1971 England/Wales life table to examine, it is not clear whether the authors used the "mean q'," or the "q' for the mean age" of the study participants, for their first-year q'. But if one experiments with a 1969-71 U.S. Life Table, one finds the author's first year q' to be very close to q' for mean age 59. Further using this US Life Table — and making the assumption that the authors *did* advance q' by a full year for each duration

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— one obtains results identical to the study's expected q' at five years, and is within a few percent at subsequent quinquennial durations.

It is possible that the England/Wales 1971 table differs in some material respect from the US 1969-71 tables over the age ranges in question, such that authors may not in fact have mistakenly equated " q' for the mean age" with "mean q' ." (Reasons why it would generally be incorrect to do so have been discussed previously in the "Guidelines"²). Assuming the authors were *not* mistaken in their estimation of first year q' , they still could have improved upon their method of q' progression in one of two alternative ways. They could have chosen a different rate of increase for q' — six to eight percent per year, for instance — or (assuming the age and sex roster for survivors was available year by year) they could have derived exact q' for successive durations from an annual recalculation of the mean q' .

Going a step further, one wonders if a contemporaneous Group Life table might not have been more accurate still, since the degree of selection applied to study subjects was significant. (Reasons for exclusion from study included prior stroke, valvular heart disease, anemia, severe hypertension, and other factors). Use of Group Life tables for deriving first year mean q' , together with an appropriate advancement of mean q' by duration, would likely have produced late duration EDRs more consistent with those found in Singer's table 345M1-2. Singer has yet again given readers a thoughtful abstract to ponder.

Diseases of the Colon and Semi-Colon: *NEJM* 1992;326:658

Watson and Sokoloski have provided a clear and informative abstract on colorectal cancer risk following polypectomy for symptomatic rectosigmoid adenomas (supplying useful data on colons, with sparing use of colons in their data). The Sokoloski/Watson style — with its simple lines and clear tables — is refreshingly crisp and spare, especially to those of us who still burden readers with complex-compound overpunctuated sentences; like this one.

The source-article spared the abstractors the task of deriving their own expected morbidity rates since it directly provided comparative morbidity in SIR form. (SIRs — Standardized Incidence Ratios — are morbidity ratios that have already been calculated by the authors.) Moreover, the expected morbidity rates (in this case, for cancer) used by the authors were quite precise — matching for age, sex, and calendar-year. Watson and Sok-

oloski's Tables 156M1-1,2, and 3 present the key findings stratified in several informative ways.

Their study subjects consisted of a group of referred symptomatic individuals (rectal bleeding being the most common symptom) who underwent rigid-scope polypectomy for rectosigmoid adenoma. Hence, it is not a screening study. Moreover, the authors were interested in conducting a natural history study uninfluenced by colonoscopy or colonoscopic findings, and thus they excluded colonoscopic interventions. In addition, to exclude co-existent (synchronous) colorectal cancer, any cancers diagnosed within two years of study entry were also excluded in order to be counting incident cases, and not a mixture of incident and prevalent cases. This exclusion differs from the truncation of early-years exposure seen in last issue's abstract on pancreatic cancer (25(3):354-5) in that only those subjects with synchronous malignancy (25 patients) were excluded. (In the pancreatic cancer abstract, the first two years worth of exposure on *all* study subjects was excluded.) The authors of this adenoma study for some reason (perhaps National Health Service guidelines rationalizing cancer care services for patients over the age of 85) terminated follow-up at attainment of 86 years of age, introducing a right-truncation of exposure of an unknown (although presumably small) degree. Other exclusions are cited in the abstract.

Of interest in connection with the Watson-Sokoloski abstract is the recent report³ of the Practice Parameters Committee of the American College of Gastroenterology. The Sokoloski-Watson source-article had concluded that colonoscopy was unlikely to be cost-effective in the care or FU of low-risk adenoma patients. The ACG seems to make the opposite recommendation, namely that post-polypectomy colonoscopy should be routine, although they do discuss individualizing the decision for polyps <0.5 cm in diameter.

Prostatic Cancer and PSA

The P's and Q's in the last issue of the *Journal* carried a discussion of prostatic cancer and PSA. Readers may be interested in two articles published in the *Annals of Internal Medicine*, subsequent to the last *Journal* — a review article by Kramer et al on "Prostate Cancer Screening: What we Know and What we Need to Know," and an accompanying editorial, "Using PSA to Diagnose Prostate Cancer: Sailing in Uncharted Waters."⁴

The former poses the introductory question "is cure possible in those for whom it is necessary, and is cure

necessary in those for whom it is possible?" It points out that while PSA may have some value in combination with other prostate evaluation methods, no PSA assay is approved by the FDA for screening or diagnosis (yet). It discusses the confounding potential of selection bias, lead-time bias, and length bias, and suggests five criteria which should be satisfied before any test can be considered useful or effective in the mass screening of asymptomatic screenees:

1. The disease should represent a substantial burden to public health and have a prevalent asymptomatic, nonmetastatic phase. (This is true for prostate cancer).
2. The asymptomatic nonmetastatic phase should be recognizable (This is also generally true for prostatic cancer).
3. The screening test should have "reasonable" values for sensitivity, specificity, and predictive value, have low risk and low cost, and be acceptable to screener and screenee. (Possibly true for prostate cancer, but sensitivity, specificity, and positive predictive value are largely unknown in the *screening* setting. False negative rates are especially hard to know since the gold standard — prostate biopsy — is generally not performed on PSA-negative screenees when the value of stand-alone PSA results is being assessed).
4. Curative potential should be substantially better in early, compared to late, stages of disease (While often assumed true for prostatic cancer, the authors point out that this has not been proven or established).
5. Treatment of screen-detected patients should improve outcome as measured by cause-specific mortality (not reported to date for prostate cancer.)

The authors note that except for nonmelanous skin cancer, prostate cancer has less impact on average years of life lost per person dying of the disease than any other malignancy. Other useful and interesting information is to be found in this article.

Pancreatic Cancer

The last issue of the *Journal* also carried an abstract on pancreatic cancer incidence after chronic pancreatitis.

The *New England Journal of Medicine* (1993;329:1502-3) has since carried a letter to the editor and a reply from the author of the source-article. They discussed the issue of selection bias and the possible confounding factor of counting prevalent vs. incident cases. The author produced data showing consistently elevated morbidity ratios whether incident cases or prevalent cases of chronic pancreatitis were being included in their longitudinal risk study.

Fecal Occult Blood Testing

Finally, two issues ago in this *Journal*, there appeared an abstract on fecal occult blood screening for colorectal cancer. Readers may be interested in reading both the subsequent letters to the editor in the *New England Journal of Medicine* (1993; 329:1351-4) in response to the source-article, and the replies (2) of the authors.

Triennial Course and the 1991 Compend

Dr. Richard Braun will be the primary instructor for the Mortality Methodology workshops that will be given in February in Phoenix in connection with the Board's Triennial Course. Medico-actuarial subjects to be covered include life table methodology and uses of conditional probability. Dr. Braun is a member of the Academy's Morbidity Mortality Committee, and also chairs the Liaison Committee for Morbidity/Mortality (liaising with the SOA and HOLUA/IHOU). His mortality abstract on AIDS (a composite abstract from eight source articles) will soon be appearing in the *1991 Compend*. A more complete description of the *Compend* — what it contains and what its value might be to readers — can be found in the pre-publication notice on page 408 in this issue.

References

1. Feinstein AR. *Clinical Epidemiology: The Architecture of Clinical Research*. Philadelphia, Saunders, 1985:22-228.
2. Singer RB, Kita MW. Guidelines for evaluation of follow-up articles and preparation of mortality abstracts. *JIM* 1991;23(1):25-26.
3. Bond JH, et al. Polyp guidelines: Diagnosis, treatment, and surveillance for patients with nonfamilial colorectal polyps. *Ann Intern Med* 1993;119:836-843.
4. *Ann Intern Med* 1993;119:914-923 and 948-949.