Interpreting the results of small trials

The randomized controlled trial of preventive home nursing visits for frail elderly people reported by Dawn Dalby and colleagues[1] raised several key issues regarding the design, interpretation and reporting of trials testing the efficacy of interventions in the elderly population.

With the testing of complicated interventions and the chronic shortage of resources in this area, clinical trials may be conducted with inadequate numbers of patients to reliably demonstrate positive effects. Dalby and colleagues enrolled 142 patients, giving the trial a prestudy power of 50%. Inadequate sample size will likely result in findings that have high statistical variability (low precision). Consequently, the 95% confidence intervals around the point estimates of the primary outcome for the control and intervention groups will be imprecise and are likely to overlap and result in statistically insignificant results. As the number of patients in the trial increases, the 95% confidence intervals become more precise with less overlap (if there is a positive treatment effect) and the results may become statistically significant. For these reasons, the study by Dalby and colleagues does not demonstrate that nursing visits are ineffective. In fact, no firm conclusions can be drawn from its results.

The authors cited their lack of adequate power as a possible explanation for their lack of statistically significant results. From a methodological and theoretical perspective, Goodman and Berlin[2] have argued against the use of post hoc power to explain negative trials. Once a trial is completed, they argue, the use of confidence intervals, rather the post hoc power, is the proper way to interpret trials with results that do not reach statistical significance.

The danger inherent in conducting small, inadequately powered trials is that potentially effective interventions will be judged as ineffective simply because of the inability to detect statistically significant and clinically important benefits. Consequently, caution must be exercised when embarking on small trials and interpreting the results.

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References
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2. Goodman SN, Berlin JA. The use of predicted confidence intervals when planning experiments and the misuse of power when interpreting results. *Ann Intern Med* 1994;121:200-6.

Does the urea breath test tell us what we need to know?

The Feb. 8th issue of *CMAJ* had an interesting article by Carlo Fallone and colleagues concerning the urea breath test for *Helicobacter pylori* infection,[1] interesting not only for what the test will detect but for what tests it may push to the sidelines. There is certainly talk of the urea breath test lessening the need for gastroscopy, something that is welcomed as a means to cut costs and decrease patient discomfort and morbidity. But it does mean fewer chances to pick up premalignant lesions or early frank carcinoma. Protocols surrounding the urea test recommend scoping only when alarm signs appear, but clinical signs and symptoms are often the herald of higher stage disease. As a pathologist, all too often I see carcinoma cases from all parts of the GI tract presenting on the cutting table as advanced, node-positive disease.

It seems to me that at present we are not scanning, scoping or poking enough to detect the early, treatable malignancies. If our present diagnostic modalities are too expensive or risky for this more rigorous hunting, then surely more resources must be devoted to some sort of revolution in diagnostic imaging or direct visualization technology. Tasting and smelling for disease are no substitute for looking.

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Reference
1. Fallone CA, Veldhuyzen van Zanten SJO, Chiba N. The urea breath test for *Helicobacter pylori* infection: taking the wind out of the sails of endoscopy. *CMAJ* 2000;162(3):371-2.

[The authors respond:]

The point Julius Wroblewski has brought up is a good one. We would certainly like to detect lesions early, rather than at a point when they are no longer treatable. However, we