

## MEMORANDUM

To: Heinz Schneider  
From: Michael Stoto  
Re: Phenylephrine meta-analysis  
Date: January 27, 2007

I have reviewed the January 23 draft of the CHPH Phenylephrine Task Group's "Efficacy Meta-Analysis of Single-Dose 10 mg Phenylephrine vs. Placebo in Adults with Acute Nasal Congestion due to Common Cold" and am pleased to report that I find that the task group has addressed all of the issues raised in the December 20, 2006 conference call, and that in my judgment the analysis meets professional standards. As a result, I believe that the conclusions are justified.

There are, however, a number of aspects of the written report that I believe can be improved. They are the following:

- p. 6 In presenting the study objectives, it should be noted that (a) individual studies will be reanalyzed in a parallel fashion and (b) a pooled (individual-level) meta analysis will be performed.
- p. 12 The footnote to Table 2 is an important point to make, but it should be made in the conclusions section rather than here.
- p. 13 The discussion of logs and ratios is overly complicated and confusing. It is well known that the log transformation is appropriate for ratio measures, and that the results of analyses done in the log scale should be transformed back to the original scale for presentation. A geometric mean is indeed equivalent to the re-transformed mean of the logs, but this not actually being done in this analysis, so the term "geometric mean" should not be used.
- p. 14 The results of study #8, now discussed in the pooled analysis section, should be moved to the conclusions section of the paper.
- p. 15, l. 2 Add s to "statistical models"
- p. 15 I would have labeled the second model as #1 and visa versa since that way the three would be increasingly complex.
- p. 16 The second complete paragraph, beginning with "The results ...", is a result and should be moved to the results section.

- pp. 17 & 18    Tables 3 and 4 should present the estimated difference or summary difference and a 95% confidence interval, i.e. the information in Figures 1-8.
- Figures 1-8    Units should be given for the horizontal scale.

Comments on Phenylephrine Meta-analysis  
M. A. Stoto, December 17, 2006

1. Choice of studies
  - a. Why limit studies to before '76?
  - b. Did you search for other studies, before or after '76?
  - c. Complete references should be given for all studies
  - d. "Site" looks like it might be the company performing some of the trials
2. Non-included studies
  - a. Should list references and specific reason for exclusion
  - b. Were results qualitatively consistent with the included studies?
  - c. Was lack of individual-level data a reason for exclusion?
3. A priori choices
  - a. should be made clear, including reason, at the start
  - b. Rationale for excluding study #8 seems to depend on knowing that results would be significant without it
  - c. Was choice of  $\Delta$ NAR vs.  $\Delta \ln$ NAR a priori?
  - d. Model for individual study and M-A
  - e. 30 and 60 minute time points as most important output?
4. Time line
  - a. Note at the start that studies tested outcomes at different points
  - b. Were there results at other time points not reported here?
5. Data entry
  - a. Note more clearly that individual-level data were used.
6. Outcome measure
  - a.  $\ln$ -ratio NAR =  $\Delta \ln$ NAR, which seems like a reasonable measure if NAR is a ratio; why was transformation used instead?
  - b.  $\Delta \ln$ NAR might help with the departure from normality noted
7. Statistical model
  - a. make more clear that this is a **pooled** meta-analysis (MA-P)
  - b. List in text and tables as Model 1.a, 1.b, 2.a, 2.b, 3
8. Results
  - a. If  $\Delta$ NAR was chosen vs.  $\Delta \ln$ NAR a priori, it would be better to present it as such, with the alternative as a sensitivity analysis
  - b. Report effect sizes and 95% C.I., not P-values
  - c. Table 2 is hard to read since it does not make clear which studies has results at which levels and which didn't
  - d. Better to present Table 2 in tabular form (e.g. rows = time points, columns = study) with effect and 95% C.I. for each available effect estimate. Base on a priori choice of statistical model, then indicate differences where they appear
  - e. Table 2 (M-A results): Use same format as suggested above, with columns for Model 2 and Model 3
  - f. Note that time scale on graphs is not equally spaced
  - g. Show a forest plot for each key time point, with major analysis only

## Abbreviated Curriculum Vitae

**MICHAEL A. STOTO**

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Department of Health Systems Administration  
School of Nursing and Health Studies  
Georgetown University  
St. Mary's Hall, Room 235  
3700 Reservoir Road  
Washington DC 20057  
Telephone: (202) 687-3292  
E-mail: stotom@georgetown.edu

*Home address:*  
4404 Windom Pl. NW  
Washington, DC 20016  
Phone: (202) 244-4137  
E-mail: mstoto@rcn.net

### EDUCATION

Harvard University: Ph.D. in Statistics, 1979; A.M. in Statistics, 1977; recipient of National Science Foundation Graduate Fellowship.

Princeton University: A.B. in Statistics with High Honors, 1975.

### EMPLOYMENT

2006- Professor of Health Services Administration and Population Health, School of Nursing and Health Studies, Georgetown University  
2001-2006 Senior Statistical Scientist, RAND  
1998-2001 Professor and Chair, Department of Epidemiology and Biostatistics, School of Public Health and Health Services, George Washington University  
1997- Adjunct Professor of Biostatistics, Harvard University  
1983-1998 Senior Staff Officer, Institute of Medicine, National Academy of Sciences  
1979-1987 Assistant, then Associate Professor of Public Policy, J. F. Kennedy School of Government, Harvard University (on leave, 1983-1984)

### TEACHING EXPERIENCE

#### **Pardee RAND Graduate School**

2003- Research Synthesis and Meta-Analysis

#### **Harvard School of Public Health, Harvard University**

1997- Research Synthesis and Meta-Analysis for Public Health and Clinical Medicine

#### **George Washington School of Public Health and Health Services**

2000-2001 Research Synthesis and Meta-Analysis for Public Health and Clinical Medicine

### SELECTED PUBLICATIONS

1. Emerson JD, Stoto MA. Exploratory methods for choosing power transformations. *Journal of the American Statistical Association* 1982; 77: 103-108.
2. Hoaglin DC, Light RJ, Mosteller F, McPeck B, Stoto MA. *Data for decisions: Information strategies for policymakers*, Cambridge, MA: Abt Books, 1982.
3. Stoto MA. The accuracy of population projections. *Journal of the American Statistical Association* 1983; 78: 13-20.