efficacy.[9] Taken together, the quality of evidence for treating postmenopausal osteoporosis might not be good enough to be extrapolated to female nursing home residents. How many fractures could have been prevented by giving risedronate to this group of patients is unknown. Further study is needed. Therefore, randomized, controlled trials considered to be the golden evidence might be bronze and should be used cautiously to measure quality of care in nursing homes, such as for the treatment of postmenopausal osteoporosis. Unintended consequences could be avoided.[10]

Huai Yong Cheng, MD, MPH
Columbia University Medical Center
New York, NY

ACKNOWLEDGMENTS

Financial Disclosure: None

Author Contributions: Huai Yong Cheng was responsible for all aspects of producing this letter.

Sponsor's Role: None.

REFERENCES

1. Rosen CJ. Postmenopausal osteoporosis. N Engl J Med 2005;353:595–603.
2. Wallace RB. Bone health in nursing home residents. JAMA 2000;284:1018–1019.
3. Jachna CM, Shireman TI, Whittle J et al. Differing patterns of antiresorptive pharmacotherapy in nursing facility residents and community dwellers. J Am Geriatr Soc 2005;53:1275–1281.
4. Colón-Emeric CS, Lyles KW. Antiresorptive pharmacotherapy in older women: Where the evidence-based medicine rubber meets the geriatric road. J Am Geriatr Soc 2005;53:1425–1426.
5. Greenspan SL, Schneider DL, McClung MR et al. Alendronate improves bone mineral density in elderly women with osteoporosis residing in long-term care facilities. A randomized, double-blind, placebo-controlled trial. Ann Intern Med 2002;136:742–746.
6. Cranney A, Waldegger L, Zytaruk N et al. Risedronate for the prevention and treatment of postmenopausal osteoporosis. Cochrane Database Syst Rev 2003;(4):CD004523.
7. Altman DG. Poor-quality medical research-what can journals do? JAMA 2002;287:2765–2767.
8. Altman DG. The scandal of poor medical research. BMJ 1994;308:283–284.
9. Moher D, Pham B, Jones A et al. Does quality of reports of randomized trials affect estimates of intervention efficacy reported in meta-analyses? Lancet 1998;352:609–613.
10. AGS Ethics Committee. Measuring quality of care for nursing home residents-considering unintended consequences. Ann Long Term Care 2005;13:40–41.

THE ACCURACY OF THE MINI-COG IN SCREENING LOW-EDUCATED ELDERLY FOR DEMENTIA

To the Editor: We have read with profound interest the stimulating article by Borson et al.[1] comparing the accuracy of the Mini-Mental State Examination (MMSE) with that of the Mini-Cog in a population of multiethnic elderly. We would like to make some comments about three of their results.

1. "The Mini-Cog was not affected by levels of education." Level of education is probably one of the most important variables influencing performance on cognitive tests, and very low levels of formal schooling may be the main factor explaining the variation in results of cognitive tests between people of different ethnic groups,[2,3] but the detection of dementia using cognitive tests is progressively more difficult the lower the educational level of the subject. The Clock Drawing Test (CDT), for example, although supposedly resistant to educational and cultural heterogeneity, was evaluated in a group with a high proportion of illiterate subjects, and its performance (63% sensitivity, 59% specificity) would not recommend it as a screen in that population, whereas in the group with 5 to 8 years of schooling, its accuracy was good.[4] Onestudy,[2] when applying the CDT in a multiethnic population, also found considerably worse performance in those with less than 6 years education. It is also important to point out that this effect of schooling is much more pronounced in the less-educated populations, and that educational effect is minor when comparison is made between subjects with relatively high educational levels.[3] This may be the case with the sample of Borson et al.,[1] in which the average years of education were 11.5, 10.4, and 8.5 for normal individuals, those with mild cognitive impairment, and those with dementia, respectively. It would seem that the levels of schooling implied by these means are uniformly too high to draw any conclusion about the effect of education on the Mini-Cog.

2. "In the semiliterate and illiterate group, the Mini-Cog accurately detected cognitive impairment in 92%, with 27% false positives." These results are surprisingly good for those who manage a large population of illiterate adults. In the same group in which the CDT was tested (a sample in which 76% of the individuals had less than 5 years schooling and 25% were illiterate) a post hoc analysis was made of the Mini-Cog, and it did not perform as well; sensitivity was 77% and specificity 48%.[5] Limitations due to the post hoc methodology and eventual misclassifications in the sample cannot entirely account for this discrepancy.

The number of years of formal schooling may not reflect writing and reading abilities perfectly. The authors used an informant-based classification of levels of literacy (illiterate, semiliterate, literate) that we do not know how to correlate with actual years of schooling or whether it is more accurate than the latter in revealing previous writing and reading abilities. Because they do not state the number of years of education of the individuals in each informant-based category, it is not possible to make this comparison directly. The most plausible explanation for their results is that the levels of schooling of the semiliterate and illiterate subjects in their sample were high.

3. "The MMSE performed poorly in the semiliterate and illiterate group, with 64% false-positive results." MMSE score is strongly related to education, and to overcome this problem, there have been suggestions of cutoff point adjustments.[6,7] For example, onestudy[8] proposed a cutoff of 13 for those with less than 1 year of schooling and 18 for those with less than 5 years of schooling;[9] another study suggested 19 of 20 for illiterate and a third study.[10] 18 of 19. The cutoff point used in the Borson study[1] (23/24) may have been too high and therefore have contributed to its worse performance vis-à-vis the Mini-Cog in the low educational-level subgroup.

For those who work in developing countries, where mean levels of education of the population are low, the challenge of diagnosing dementia is enormous, and the development of simple and effective screening tests for this population is a priority, but even in developed countries,

where low education is less of a problem, there is still a need to improve dementia detection in the underprivileged segments of the population.

In conclusion, the Mini-Cog has definite advantages over the MMSE, at least when applied to the better-educated patient groups, but we are not convinced of its worth in older people with low levels of education.

Roberto Alves Lourenço, MD, MSc, PhD
Internal Medicine Department
Medical Sciences School
Sergio Telles Ribeiro Filho, MD
Open University for Studies on the Elderly
Rio de Janeiro State University
Rio de Janeiro, Brazil

ACKNOWLEDGMENTS

Financial Disclosure: The authors state that they have no financial disclosures or conflict of interests to report on any aspect of the items reported here.

Author Contributions: Roberto Alves Lourenço and Sergio Telles Ribeiro Filho: preparation of the letter.

Sponsor's Role: There are no sponsors.

REFERENCES

1. Borson S, Scanlan JM, Watanabe J et al. Simplifying detection of cognitive impairment: Comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. J Am Geriatr Soc 2005;53:871–874.
2. Storey JE, Rowland JT, Basic D et al. Accuracy of the Clock Drawing Test for detecting dementia in a multicultural sample of elderly Australian patients. Int Psychogeriatr 2002;14:259–271.
3. Ostrosky-Solis F, Ardila A, Rosselli M et al. Neuropsychological test performance in illiterate subjects. Arch Clin Neuropsychol 1998;13:645–660.
4. Lourenço RA, Ribeiro Filho ST, Moreira IFH et al. The Clock-Drawing Test: Utility in elderly with low education level. J Am Geriatr Soc 2004;52:S58.
5. Lourenço RA, Ribeiro Filho ST, Scanlan JM. A post hoc study of the Mini-Cog in a group of low education elderly. J Am Geriatr Soc 2005;53:S145–S146.
6. Crum RM, Anthony JC, Bassett SS et al. Population-based norms for the Mini-Mental State Examination by age and educational level. JAMA 1993;269: 2386–2391.
7. Parker C, Philp I. Screening for cognitive impairment among older people in black and minority ethnic groups. Age Ageing 2004;33:447–452.
8. Bertolucci PH, Brucki SM, Campacci SR et al. The Mini-Mental State Examination in a general population: Impact of educational status. Arq Neuropsiquiatr 1994;52:1–7.
9. Almeida OP. Mini-Mental State Examination and the diagnosis of dementia in Brazil. Arq Neuropsiquiatr 1998;56:605–612.
10. Lourenço RA, Veras RP, Ribeiro Filho ST. Mini-Mental State Examination in an elderly population: Validity in a primary health care setting. J Am Geriatr Soc 2004;52:S82.

RESPONSE TO DRS. LOURENÇO AND RIBEIRO FILHO

To the Editor: Lourenço and Ribeiro Filho's[1] remarks reinforce the important and well-known point that cognitive screening tools do not necessarily perform the same way in different populations. The sample they describe is strongly skewed toward very low levels of education, the group for which cognitive screening tools are generally weakest at distinguishing between individuals with and without dementia. Indeed, they find that a post hoc approximation of the Mini-Cog (3-item recall from the Mini-Mental State Examination (MMSE) and a different clock drawing and scoring method) performed less well in their sample than we reported.[2] It is possible that sample and population differences could account for a good portion of this discrepancy, because a much higher proportion of (76%) of their sample had less than 5 years of education, and 25% were illiterate, compared with 17% semi- and nonliterate subjects in our sample. In our hands, the Mini-Cog performed less well in that subgroup (mean years of education 1.6) than it did in the group as a whole but not as poorly as it did in Lourenço et al.'s studies, and the smaller effect of low literacy was largely eliminated in analyses of the whole sample.

Nevertheless, we are puzzled by some of Lourenço et al.'s results. Bias in cognitive screens from low educational level increases sensitivity at the cost of specificity, resulting in good detection of true-positives but undesirable proportions of false-positives. Lourenço et al.[1] found surprisingly low sensitivity (77%) and specificity (48%) for their post hoc Mini-Cog approximation.[3] It is not obvious why sensitivity should be so low. Lourenço et al. show similarly low sensitivity for the MMSE[4] and for clock drawing by itself,[3] both of which are known to produce excessive false-positives in very poorly educated persons. In contrast to their results, the sensitivity of the Mini-Cog, MMSE, and clock drawing were all above 90% in our semi- and nonliterate subgroup.[2] Consistent with our results, a study of poorly educated older Greeks found greater than 90% sensitivity and poor specificity for the MMSE and Cambridge Cognitive Examination (CAMCOG).[4] Lourenço et al.'s poor sensitivity for all screens therefore appears to differ markedly from predictions and from results of other studies of cognitive screening in poorly educated populations. This raises the possibility that methods of classifying subjects as demented or not might have influenced their results.

Their method[4] placed cognitive tests at the center of the diagnostic approach, posing the dilemma of circular reasoning. Moreover, *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria require evidence of cognitive decline and functional disability due to cognitive impairment if a dementia diagnosis is to be assigned. The approach we have taken in samples of mixed educational and cultural background was designed to avoid the problem of educational and cultural confounding by using detailed informant-based histories of cognitive and functional change and blinding raters to results of cognitive tests in making initial cognitive classifications. Informant data were lacking for most subjects in the Brazilian study,[3] which implies that cognitive history was not available. Instead, they relied on the CAMCOG, Revised, an excellent battery of neuropsychological screens and tests but one that was developed on better-educated persons in the United Kingdom and is strongly affected by education and literacy.[5] They do not describe how, or whether, the geriatricians responsible for assigning dementia diagnoses in this research protected their judgments from the influence of potentially confounded cognitive test scores.

Finally, we would emphasize the purpose for which the Mini-Cog was developed. The principal objective was to facilitate cognitive screening in primary care medical practices and other settings in which cognitive assessment expertise is usually minimal. Our goal was to construct a practical approach that would not require modification to

address the majority of older adults in first-world countries, and we believe that we have succeeded. In our data set, we find that the Mini-Cog functions significantly better than the MMSE with standard cutpoints in subjects with low education and literacy. It was not designed to function optimally in populations broadly characterized by extremely low levels of education or literacy. In such settings, informant-based screening or individualized function-based screening might do better than any cognitive screen that relies on standard neuropsychological paradigms. To our knowledge, the jury is still out, and much remains to be done.

Soo Borson, MD
James M. Scanlan, PhD
Department of Psychiatry and Behavioral Sciences
University of Washington
Seattle, WA

ACKNOWLEDGMENTS

Financial Disclosures: Dr. Borson discloses previous research support from Pfizer and Janssen, neither of which supported the work referred to in this letter. Dr. Borson also discloses advisory board and speakers' bureau roles with Pfizer, Novartis, Forest, and Janssen Pharmaceutica. These roles present no conflict in this work. Dr. Scanlan has nothing to disclose.

Author Contributions: Dr. Borson drafted this letter of response, which was revised with Dr. Scanlan before submission.

Sponsor's Role: Dr. Borson was Principal Investigator of the study on which results in the original submission and this response letter were based. She was responsible for the overall design, methods, subject recruitment, data verification, and preparation of results. Dr. Scanlan collaborated on analytic design and conducted all pertinent data analyses.

REFERENCES

1. Lourenço RA, Ribeiro Filho ST. The accuracy of the Mini-Cog in screening poorly educated older people for dementia. J Am Geriatr Soc 2006;54: 376–377.
2. Borson S, Scanlan JM, Watanabe J et al. Simplifying detection of cognitive impairment: Comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. J Am Geriatr Soc 2005;53:871–874.
3. Lourenço RA, Ribeiro Filho ST, Scanlan JM. A posthoc study of the Mini-Cog in a group of low-education elderly. J Am Geriatr Soc 2005;53:S145–S146.
4. Lourenço RA, Veras RP, Ribeiro Filho ST. Mini-Mental State Examination in an elderly population: Validity in a primary healthcare setting. J Am Geriatr Soc 2004;52:S82.
5. Fountoulakis KN, Tsolaki M, Mohs RC et al. Epidemiological dementia index: A screening instrument for Alzheimer's disease and other types of dementia suitable for use in populations with low education level. Dement Geriatr Cogn Disord 1998;9:329–338.

CARBOCISTEINE REDUCES FREQUENCY OF COMMON COLDS AND EXACERBATIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

To the Editor: Various kind of viruses, including rhinovirus and influenza virus, have been reported to cause chronic obstructive pulmonary disease (COPD) exacerbations.[1] Mucolytic drugs prevent acute exacerbations of chronic obstructive bronchitis.[2] Mucolytic drugs, including carbocisteine, have various effects, such as the reduction of elastic modules of mucus and improvement of mucociliary transport.[3] Therefore, it is conceivable that mucolytic drugs may modulate the function of airway epithelial cells, including the expression of intercellular adhesion molecule-1, a receptor for major rhinoviruses that are the most commonly implicated pathogens of common colds,[4] although the effects of carbocisteine have not been studied on the prevention of the common cold in patients with COPD.

In the present study, a prospective, randomized, double-blind, controlled trial was performed to examine the effects of carbocisteine on the frequency of common colds and exacerbations in patients with COPD. Patients diagnosed with COPD[5] were enrolled and treated with sustained-release theophylline, inhaled oxitropium bromide, inhaled β_2-agonist, or a combination of these but did not receive inhaled or oral corticosteroids. One hundred fifty-six patients were randomly assigned to receive carbocisteine therapy (1,500 mg/d, 78 patients, carbocisteine group) or placebo therapy with tablets of lactose (1,500 mg/d, 78 patients, control group) until the end of the study, between October 2001 and June 2005 at the Tohoku University Hospital, Sendai, Japan. Ten symptoms of upper respiratory tract infections were recorded in each patient, and common cold was defined as a total symptom score of greater than 5, as described previously.[6] A COPD exacerbation was defined as an acute and sustained worsening of COPD symptoms requiring changes to regular treatment, as previously described.[7] The primary endpoints of this study were to compare the rate and number of common colds and exacerbations of the carbocisteine group and the control group. The rate and number of common colds and acute exacerbations of COPD were observed for 12 months. It was estimated that 50 patients per group needed to be enrolled on the basis of experimental-treatment group to confer a power of 80% for a two-sided 0.05 level by sample size analysis.[8] Actual accrual was 78 eligible patients in each group. The sample sizes for the two groups were thought to be sufficient to demonstrate the primary endpoints in the present study. Significance was accepted at $P < .05$. The Tohoku University Ethics Committee approved the study, and written informed consent was obtained from all patients.

None of the patients in either group died or had any apparent adverse effects from carbocisteine therapy during the study period. None of the 156 patients with COPD were lost to follow-up, and all were analyzable. Age, sex, smoking history, stage of COPD, and lung function test were matched between the two groups (Table 1). The mean number $\pm$ standard deviation of common colds for 12 months was significantly lower in the carbocysteine group (1.69 ± 0.18 per person) than in the control group (3.14 ± 0.35 per person; $P < .001$, Student t test) (Table 1). The use of carbocisteine was closely associated with a lower frequency of development of common colds more than twice per year in patients with COPD (relative risk = 0.4, 95% confidence interval (CI) = 0.2–0.8, $P = .009$). The number of exacerbations for 12 months was also significantly lower in the carbocisteine group than in the control group ($P < .001$, Student t test) (Table 1). One hundred eight COPD exacerbations related to 245 common colds (44%) occurred in the control group and 42 exacerbations related