Editors' Note: Submissions to WriteClick this week raise and refute methodologic concerns. Drs. Young and Shapiro challenge Meador and colleagues' use of disease prevalence alone as a marker of disease burden in their study, "Disparities in NIH funding for epilepsy research." Based on their own analysis of NIH funding of neurologic disorders comparing disability-adjusted life year and economic burden, the WriteClick submitters conclude that, while epilepsy compares favorably, headache disorders are relatively underfunded. The authors respond by explaining the rationale behind their methodology and calling for greater transparency in the process of NIH funding allocation to avoid disparities of any kind. In reference to the editorial written by Drs. Marquardt and Barnett on the CREST trial, Drs. Demaerschalk, Howard, and Brott counter that despite the grouping of symptomatic and asymptomatic patients together, their statistical methodology makes it possible to draw conclusions about each cohort separately.

Megan Alcauskas, MD, and Robert C. Griggs, MD

DISPARITIES IN NIH FUNDING FOR EPILEPSY RESEARCH

William B. Young, Philadelphia; Robert E. Shapiro, Burlington, VT: We read with interest the report of Meador et al.¹ regarding NIH funding. They have done a service to the field of neurology by raising the issue of disparities in NIH research allocations.

The stated core mission of the NINDS is to "... reduce the burden of neurologic disease ..."² However, the Institute has no formal policy for consideration of disease burden in prioritizing resource allocations, allowing competing priorities to dominate such as proposal quality, feasibility, need to counter emerging public health threats, desire to capitalize on unique research breakthrough opportunities, need to maintain existing research infrastructure, and possibly the efforts of well-resourced advocacy and political influences. Disease burden is now an afterthought.

A lack of consensus exists as to the most appropriate measures of disease burden to employ in policy making. One metric is the cumulative

annual economic impact of a disease in a population. Another example is the disability-adjusted life year (DALY) that the WHO has adopted for its Global Burden of Disease survey.³ While the DALY has some limitations, it also has the virtue of combining the prevalence, age-sensitive mortality (years of life lost due to premature death), and weighted morbidity (years of life lost due to disability) attributed to a disease in a given population into a single metric.

Meador and colleagues' reliance on disease prevalence alone is misguided. Ingrown toenails do not deserve more funding than cancer because they are more prevalent. Another limitation of the analyses of Meador et al. includes their choice of only a few neurologic disorders as comparators, and their exclusion of migraine and headache disorders from their study on the grounds that these disorders were absent from the 2010 NIH RCDC RePORT. However, they were listed.⁴

We have expanded Meador and colleagues' table to include migraine and headache disorders and have also calculated the 2010 NIH funding levels of all included disorders relative to epilepsy for DALYs, and economic costs where these data are available (see table).

In this limited analysis of 8 neurologic disease categories, it is apparent that NIH research allocations for epilepsy compare favorably relative to 2 broad measures of disease burden: DALYs and economic costs. Conversely, migraine and headache disorders are grossly underfunded by all measures.

We strongly agree with the conclusions of Meador et al. that "there should be a direct link between the impact of disease on the US population and relative funding for research by the government," and that the reason for funding disparities across diseases should be transparent. We urge NIH to fund further studies directed toward improving measures of disease burden and to adopt, without delay, a formal policy that is considerate of disease burden in funding prioritization.

Table NIH funding adjusted for prevalence and impact

	Migraine	Headache	Epilepsy	MS	Parkinson	Stroke	Alzheimer	ALS
2010 NIH funding (\$ in millions) ⁴	\$15	\$19	\$161	\$151	\$172	\$391	\$529	\$59
NIH funding relative to epilepsy	0.09	0.12	1.00	0.94	1.07	2.43	3.29	0.37
Prevalence per 1,000 population ^{5,6}	121	470	7.1	0.9	9.5 for > age 65	10	67 for > age 65	0.04
No US persons in 2005 (in millions)	35.461	138.9	2.098	0.266	0.349	2.956	2.459	0.012
NIH funding relative to epilepsy adjusted for relative prevalence	0.006	0.002	1.00	7.40	6.42	1.72	2.80	61.08
2004 DALYs (in thousands) ⁷	151	N/A	48	36	80	418	413	N/A
NIH funding per DALY	\$99	N/A	\$3,354	\$4,194	\$2,150	\$935	\$1,281	N/A
NIH funding relative to epilepsy adjusted for relative DALYs	0.03	N/A	1.00	1.25	0.64	0.28	0.38	N/A
Annual US economic costs (\$ in billions) ^{8,9}	N/A	\$31	\$12.5	\$6.8	\$6	\$62.7	\$172	N/A
NIH funding relative to epilepsy adjusted for relative economic costs	N/A	0.05	1.00	1.72	2.23	0.48	0.24	N/A

Author Response: Kimford J. Meador, Atlanta; Jacqueline French, New York; David W. Loring, Atlanta; Page B. Pennell, Boston: We apologize for the absence of migraines and headaches in our publication. The NIH RePORT site was updated after we accessed it for the manuscript, so we do not know if migraines and headaches were subsequently added. Note that migraines and headaches are only listed for 2010 with an estimate for 2011, while the 6 diseases in our report date back to 2007.

The approach in our study was to use data from the NIH RePORT site and match it to prevalence rates from an article by an NIH employee. This has the advantage of using data derived from the NIH rather than disparate sources. We specifically chose comparisons across 6 neurologic disorders (i.e., epilepsy, stroke, Alzheimer disease, Parkinson disease, multiple sclerosis, and amyotrophic lateral sclerosis) that have considerably greater morbidity/mortality than many other prevalent medical conditions with relatively little impact, such as the example that Young and Shapiro cited of “ingrown toenails.” Thus, we believe that prevalence comparisons in our article are clinically meaningful.

As the authors note, a “lack of consensus exists as to the most appropriate measures of disease burden to employ in policy making.” The conceptual and technical basis of the DALY has been criticized as being flawed, and thus, allocating resources based on the DALY is questionable.¹⁰

Young and Shapiro give 2 references for their derivation of economic data. One reference is an article about NIH funding for headaches, and the other reference is for a link to a PDF, which has a link to an Alzheimer

site (alz.org). Thus, it is unclear to us how the economic data are derived for the other neurologic disorders.

We appreciate that Drs. Young and Shapiro are advocating for patients with headache, similar to our advocacy for epilepsy patients. That disparities in funding exist is clear, but it is uncertain why they exist. Although we previously suggested several possibilities in our publication, there needs to be greater transparency in the process in order to assess the appropriateness of the funding distributions. Our health care policy including research funding should be transparent in how expenditures are determined. The effects of these expenditures should be monitored, and funding adjusted in order to achieve maximum benefits.

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CAROTID STENOSIS: TO REVASCULARIZE, OR NOT TO REVASCULARIZE: THAT IS THE QUESTION

Bart M. Demaerschalk, Scottsdale, AZ; George Howard, Birmingham, AL; Thomas G. Brott, Jacksonville, FL: In their editorial, Drs. Marquardt and Barnett¹ contend that because the CREST trial² grouped symptomatic and asymptomatic patients together, the trial denied information about the benefit of endarterectomy (CEA) and stenting (CAS) in these separate conditions. We respectfully disagree.

In CREST,² a prespecified aim was estimation of modification of the treatment effect by symptomatic status assessed through inclusion of the interaction term in the proportional hazards model as a single variable. By that method, there was no evidence of a

differential effect for patients with symptomatic or with asymptomatic carotid stenosis for any of the primary or secondary outcomes.² For example, Drs. Marquardt and Barnett may take issue with the inclusion of periprocedural myocardial infarction as a component of the primary outcome in CREST. However, we found no evidence of treatment effect by symptomatic status for stroke and death. Furthermore, after the periprocedural period the incidences of ipsilateral stroke with CAS and CEA were similarly low (2% and 2.4%, respectively; $p=0.85$).

Our conclusions differ substantially from those of Drs. Marquardt and Barnett. Both endarterectomy and stenting have an important role to play in the management of carotid stenosis. Clinicians and their patients now have 2 safe and effective options³ for revascularization of the carotid artery.

Editor's Note: The authors of the article were offered the opportunity to respond but declined.

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CORRECTION

Determinants of survival in progressive multifocal leukoencephalopathy

In the article “Determinants of survival in progressive multifocal leukoencephalopathy” by A. Marzocchi et al. (*Neurology*[®] 2009;73:1551–1558), there is an error in the labeling of the y-axis in figures 3 and 4. The y-axis should read “Cumulative probability of survival categorized by the presence of IRIS” in figure 3 and “Cumulative probability of survival categorized by CD4 count at baseline” in figure 4.

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William B. Young, Kimford J. Meador, Robert E. Shapiro, et al.

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