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Trial of Mobile Stroke Units

TO THE EDITOR: Grotta et al. (Sept. 9 issue)¹ report that the deployment of mobile stroke units (MSUs) in urban regions resulted in better outcomes than standard emergency medical services (EMS) transport for patients with acute ischemic stroke who were eligible for tissue plasminogen activator (t-PA). We are uncertain whether these results can be generalized to other (e.g., rural) regions, as discussed in the accompanying editorial.² Travel times for the MSU to reach a patient with a suspected stroke should be taken into account, so we wonder what would be the appropriate catchment area for a MSU to be cost-effective? The lack of a difference in time from 911 alert to EMS or MSU arrival seems to indicate that MSUs were stationed at every EMS base station. Although this approach might be effective in a densely populated area, the appropriate locations of MSU base stations could be studied in less populated areas. Modeling studies that include region-specific characteristics could support such analyses to estimate the cost-effectiveness of MSU implementation in a specific region.^{3,4}

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No potential conflict of interest relevant to this letter was reported.

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4. Maas WJ, Lahr MMH, Buskens E, van der Zee D-J, Uyttenboogaart M. Pathway design for acute stroke care in the era of endovascular thrombectomy: a critical overview of optimization effort. *Stroke* 2020;51:3452-60.

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TO THE EDITOR: Grotta et al. report better disability outcomes at 90 days in patients with acute ischemic stroke who were treated in MSUs than in patients who received standard care by EMS. The percentage of patients with a final diagnosis

of “stroke reversed by t-PA” was approximately twice as high in the MSU group as in the EMS group (Table S5 in the Supplementary Appendix, available with the full text of the article at [NEJM.org](https://www.nejm.org)). Previous work has suggested that the inter-rater reliability for differentiating stroke from symptoms that mimic stroke is only fair.¹ A sensitivity analysis that included only patients with a final diagnosis of “definite stroke” could be reported to determine whether the risk difference for favorable outcomes is maintained. This analysis would also be informative regarding the presence or absence of subjective adjudication in the context of the nonrandomized design of their trial.

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No potential conflict of interest relevant to this letter was reported.

1. Liberman AL, Rostanski SK, Ruff IM, Meyer AND, Maas MB, Prabhakaran S. Inter-rater agreement for the diagnosis of stroke versus stroke mimic. *Neurologist* 2018;23:118-21.

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THE AUTHORS REPLY: In response to Maas et al: similar times from 911 alert to arrival of the MSU or EMS on the scene were achieved with the use of a single MSU in each city in our trial. After the 911 alert, the MSU was dispatched from a centrally located hospital or fire station base; the nearest available EMS unit to the scene was dispatched simultaneously. Our trial did not include rural regions, so we agree that our results cannot be generalized to nonurban settings. The Houston MSU has a dispatch catchment radius of 8 miles from its base, but that radius can be extended to 12.4 miles (interquartile range, 9.7 to 15.2) with the use of a “rendezvous” model, in which the MSU meets an EMS squad transporting a patient with stroke from outside the usual MSU catchment area while EMS is en route to the stroke center.¹ In a comparison of cost savings from improved outcomes with operational costs from the Saarland MSU database that covers a relatively rural region,² cost efficiency (ratio ≥ 1) occurred with a range of more than 10 miles and was

highest at 27 to 41 miles and with a population density of more than 202 persons per square mile.

In response to Garg: our trial used more rigorous classification methods than the trial by Liberman et al.³ Adjudications were performed solely by expert vascular neurologists and were based on access to the entire medical record and imaging, not fictional written vignettes.

Data from a National Institute of Neurological Disorders and Stroke (NINDS) study of t-PA⁴ support the accuracy of the diagnostic classifications used in our trial. The incidence of symptom resolution by 24 hours among patients who received in-hospital t-PA in our trial (12.8%) was similar to that among patients who received in-hospital t-PA in the NINDS study (10.6%). This compares with the 17.7% incidence of 24-hour symptom resolution with a faster start of thrombolytic treatment in the prehospital t-PA group in our trial.

We performed the requested sensitivity analysis for outcomes only in patients with a final diagnosis of definite stroke in the MSU group (420 patients) and the EMS group (311 patients); the mean score on the utility-weighted modified Rankin scale (range, 0 to 1, with higher scores indicating better outcomes) at 90 days was 0.67 in the MSU group and 0.60 in the EMS group (95% confidence interval [CI] for difference, 0.02 to 0.13), and the adjusted odds ratio of a

score on the modified Rankin scale of 0 or 1 (range, 0 to 6, with higher scores indicating more disability) was 2.46 (95% CI, 1.69 to 3.59), driven by more scores of 0 in the MSU group. These findings reinforce the evidence of outcome benefit from MSU care in the populations that we included in the trial.

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Since publication of their article, the authors report no further potential conflict of interest.

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Inadequate Support

TO THE EDITOR: The patient described by Pichan et al. (Sept. 2 issue)¹ smoked one pack of cigarettes daily and had a 60-pack-year history of smoking tobacco. This history may have contributed to the development of scurvy. In cross-sectional studies, smokers have been shown to have lower serum levels of ascorbic acid than nonsmokers.^{2,3} Their metabolic turnover of ascorbic acid is reported to be twice as high as that of nonsmokers, possibly the result of increased catabolism or increased circulation of products that oxidize ascorbic acid.⁴ Smokers are estimated to require approximately 50% more ascorbic acid per day than nonsmokers. Since smokers are at risk for low levels of vitamin C, they should be

encouraged to increase vitamin C consumption when cessation of smoking is not within reach.

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No potential conflict of interest relevant to this letter was reported.

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