

Heat-Stable Oral Rotavirus Vaccine

TO THE EDITOR: Isanaka and colleagues (March 23 issue)¹ tested a heat-stable rotavirus vaccine in Niger and report an efficacy of 66.7% against severe rotavirus gastroenteritis in the per-protocol population. The purpose of rotavirus vaccination is ultimately to reduce the incidence of diarrhea and diarrhea-related death. However, the rate of severe gastroenteritis due to any cause was not significantly lower among the vaccinated infants than among those who received placebo (difference in rate, 1.97 cases per 100 person-years; 95% confidence interval [CI], -1.28 to 5.22). The lack of efficacy against severe gastroenteritis has not been highlighted in the discussion although this information is crucial for decision makers. The intention-to-treat analysis more closely reflects efficacy in real-world conditions. Everyone who received the first dose of vaccine was included in the intention-to-treat analysis; 86% of them went on to receive all three doses per the protocol and were included in the per-protocol analysis. In the intention-to-treat analysis, there was a significantly higher rate of gastroenteritis due to any cause in the vaccine group than in the placebo group (difference in rate, -6.59 cases per 100 person-years; 95% CI, -11.89 to -1.29 [negative difference values favor the placebo group]). Again, there was no benefit of the vaccine against severe gastroenteritis. This vaccine could aggravate the problem it is meant to solve in resource-poor countries.

Jaspreet Kaur, M.B., B.S.
Jacob Puliyeel, M.D.

St. Stephen's Hospital
Delhi, India
puliyeel@gmail.com

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

1. Isanaka S, Guindo O, Langendorf C, et al. Efficacy of a low-cost, heat-stable oral rotavirus vaccine in Niger. *N Engl J Med* 2017;376:1121-30.

DOI: 10.1056/NEJMc1705793

THE AUTHORS REPLY: Kaur and Puliyeel highlight the importance of rotavirus vaccination, but we disagree that the purpose of rotavirus vaccination is to reduce the incidence of all-cause diarrhea and diarrhea-related death. Rotavirus vaccination is intended to reduce the incidence of diarrhea and diarrhea-related death caused by rotavirus. However, because rotavirus is known to be the single largest contributor to diarrhea morbidity in some geographic settings,¹ it is not surprising that large-scale vaccination can have an important effect on the overall burden of diarrhea. Experience from contexts in which rotavirus vaccination has been provided at large scale suggests a positive effect on the incidence of hospitalization, clinic visits, and diarrhea-related death.²

Sheila Isanaka, Sc.D.

Harvard T.H. Chan School of Public Health
Boston, MA

Ali Djibo, M.D.

University of Niamey
Niamey, Niger

Rebecca F. Grais, Ph.D.

Epicentre
Paris, France
rebecca.grais@epicentre.msf.org

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

1. Kotloff KL, Nataro JB, Blackwelder WC, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. *Lancet* 2013;382:209-22.

2. Burnett E, Jonesteller CL, Tate JE, Yen C, Parashar UD. Global impact of rotavirus vaccination on childhood hospitalizations and mortality from diarrhea. *J Infect Dis* 2017 April 18 (Epub ahead of print).

DOI: 10.1056/NEJMc1705793

Sickle Cell Disease

TO THE EDITOR: The review of sickle cell disease by Piel et al. (April 20 issue)¹ is timely and highlights the need to address the lack of research

about this disease in sub-Saharan Africa. The authors rightly state that in the past two decades, childhood mortality has been reduced in sub-