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in our final review. Since this review [5-8], 4 studies have been published providing additional data for Asia and sub-Saharan Africa, where previous data were not available.

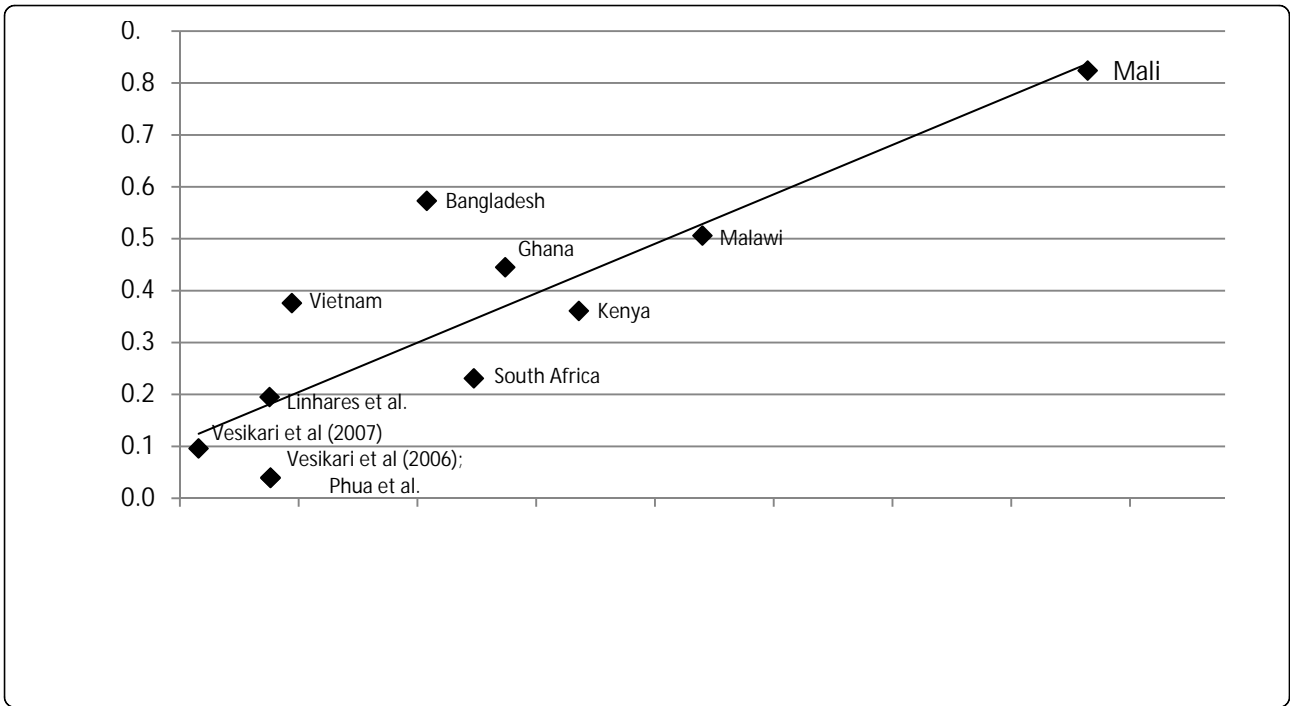
We screened the newly published studies according to our original inclusion and exclusion criteria and abstracted key variables according to the CHERG adapted GRADE technique (Grading of Recommendations Assessment, Development and Adaptation) [10] for each of the following study outcomes: rotavirus hospitalizations, all diarrhea hospitalizations, incidence of rotavirus infections, and incidence of severe acute diarrhea infections (Additional File 1) [9]. For this analysis we excluded studies that included children who received less than the recommended vaccine dose. Many of the pivotal studies led to multiple publications; we abstracted data from all publications (Addi-

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to capture an additional effect the vaccine may have with regard to population level herd immunity; studies to date have not been designed to capture this and thus a possible effect is impossible to quantify.

There are numerous hypotheses as to why the protective efficacy of the vaccine varies by region and study population with markedly lower protective efficacy rates in populations with high infant mortality. Some reasons may include variation in host response due to passive immunity via breastfeeding or underlying nutritional differences; differences in rates of severe disease; and variation in endemic disease versus seasonal peaks. It is also possible that bacteria and other

viruses may remain important causes of severe morbidity in low-income settings as compared to children in high-income settings where improvements in water and sanitation have virtually eliminated these pathogens from the community setting. Co-infection with more than one potential pathogen in these settings is common and it is possible that the rotavirus found b



immune response to the vaccine [20]. There is also limited evidence to suggest that substantial variation in strains included in the vaccine and subsequent circulating strains in the community may alter effectiveness in the community, quantifying the effect of this variation across settings is difficult [21].

Unfortunately, the appropriate studies have not been done to determine which, if any, of these hypotheses explains the observed differences. Additional descriptive etiologic studies are needed to more fully understand the role of various pathogens; including differences in rotavirus strains in various settings.

F... et al. A...
JAMA 301(21)
A... Clin
Infect Dis 49(3)
BMC Biol 8
E...
24... J Infect Dis
201(3)

