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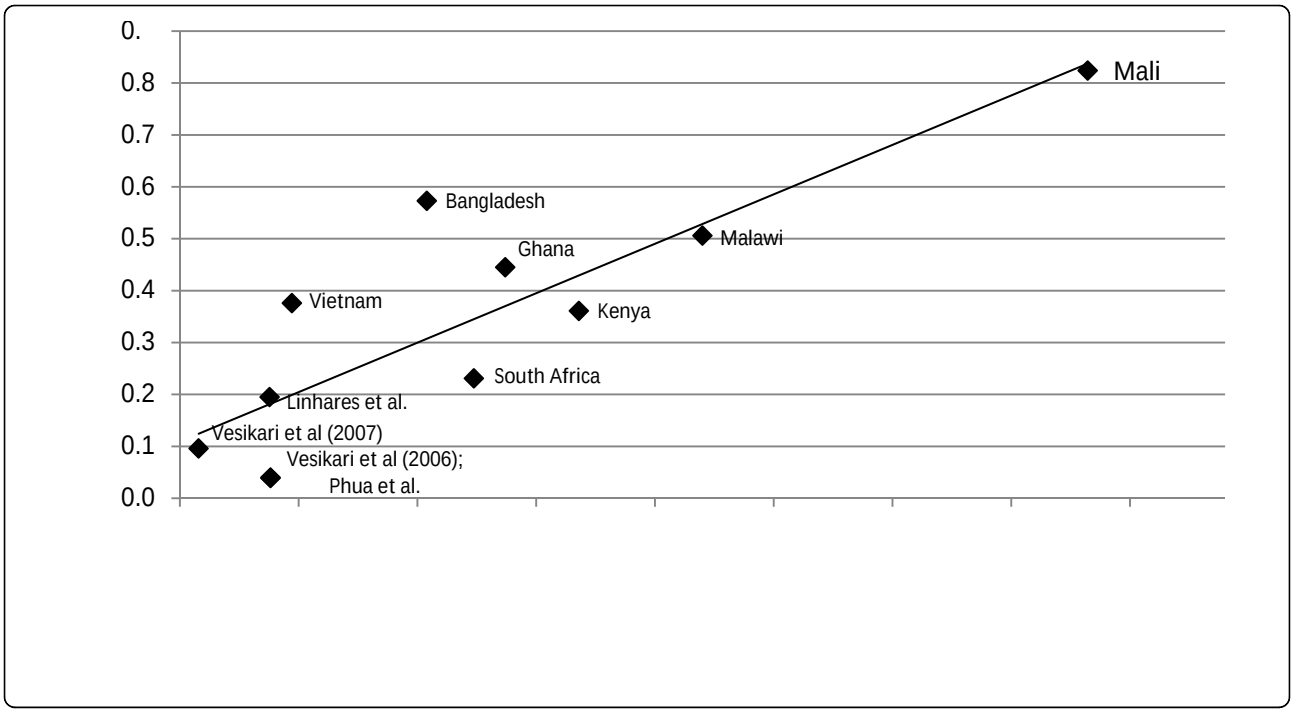
in o r final re ie . Since this re ie [5-8], 4 st dies ha e been p blished pro iding additional data for Asia and s b-Saharan Africa, here pre io s data ere not a ailable.

We screened the ne l p blished st dies according to o r original incl sion and e cl sion criteria and abstracted ke ariables according to the CHERG adapted GRADE techniq e (Grading of Recommendations Assessment, De elopment and Adaptation) [10] for each of the follo ing st d o tcomes: rota ir s hospitali ations, all diarrhea hospitali ations, incidence of rota ir s infections, and incidence of se ere all-ca se diarrhea infections (Additional File 1) [9]. For this anal sis e e cl ded st dies that incl ded children ho recei ed less than the recommended accine dose. Man of the pi otal st dies led to m ltiple p blications; e abstracted data from all p blications (Addi-

o tcome of efficac against se ere rota ir s gastroenteri-

to capt re an additional effect the accine ma ha e ith regard to pop lation le el herd imm nit ; st dies to date ha e not been designed to capt re this and th s a possible effect is impossible to q antif .

There are n mero s h potheses as to h the protecti e efficac of the accine aries b region and st d pop lation ith markedl lo er protecti e efficac rates in pop lations ith high infant mortalit . Some reasons ma incl de ariation in host response d e to passi e imm nit ia breastfeeding or nderl - ing n tritional differences; differences in rates of se ere disease; and ariation in endemic disease ers s seasonal peaks. It is also possible that bacteria and other ir ses ma remain important ca ses of se ere morbidit in lo -income settings as compared to children in high-income settings here impro ements in ater and sanitation ha e irt all eliminated these pathogens from the comm nit setting. Co-infection ith more than one potential pathogen in these settings is common and it is possible that the rota ir s fo nd b




imm ne response to the accine [20]. There is also limited e idence to s ggest that s bstantial ariation in strains incl ded in the accine and s bseq ent circ - lating stains in the comm nit ma ca se lo er effecti eness in the comm nit , q antif ing the effect of this ariation across settings is diffic lt [21]. Unfort natel , the appropriate st dies ha e not been done to determine hich, if an , of these h potheses e plains the obser ed differences. Additional descripti e etiolog st dies are needed to more f ll nderstand the role of ario s pathogens; incl ding differences in rota ir s strains in ca sing se ere

disease in de eloping co ntries and the relati e pathogenicit , i.e. the likelihood of indi id al pathogens to ca se disease. Understanding h protecti e efficac aries b pop lation is critical to impro e pon the c rrentl a ailable accine or to enhance the indi id al effect of the accine ithin different pop lations.

Despite the red ced effect si e obser ed in lo - income pop lations, the rota ir s accine ma still red ce rota ir s mortalit b 50%, an important benefit for some of the orld's most lnerable children. Rota ir s accine can be deli ered on the ro tine imm ni ation sched le pro iding an opport nit to pre ent morbidit and mortalit in areas here care seeking beha iors for diarrhea are not ideal. Pre enting diarrhea mortalit needs a m lti-prong approach. We ha e n mero s pre enti e and treatment tools, incl ding rota ir s accine and oral reh dration and inc for management of illness. Co ntries and international organi ations need to prioriti e control of diarrheal mortalit as part of a comprehensi e child s r i al strateg .

## Conclusions

There is strong e idence s ggesting that rota ir s accine decreases rota ir s specific mortalit and th s all diarrhea mortalit in all regions of the orld. Tho gh the effect si e appears to be greater among children li - ing in de eloped co ntries as compared to lo -income co ntries, the increased risk of diarrhea mortalit is greater in de eloping co ntries therefore increasing the j stification for the contin ed promotion of this important child s r i al tool.

## Additional material

Additional File 1: is an excel file and contains details of all of the studies that were abstracted, including issues related to study design and quality of data as it relates to the question of interest.

Additional File 2: is an excel file and provides a summarizes the quality assessment of rotavirus vaccine trials.

Acknowledgements

BMC Public Health

Authors' contributions

Competing interests

: 13 A 2011

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