Rotavirus vaccine efficacy in African and Asian countries

The report by George Armah and colleagues (Aug 21, p 606)[1] on the efficacy of a pentavalent rotavirus vaccine in sub-Saharan Africa is encouraging news for the control of rotavirus gastroenteritis in African children. Interestingly, the same vaccine is about 50% less efficacious than reported in some developed countries.[2] Although the absolute proportion of severe diarrhoeal disease prevented is still much higher in the African setting, the relative poor performance of enteric vaccines in these populations deserves further mechanistic study.

Two issues deserve consideration in assessing this vaccine in low-income, high-burden countries. First, although use of the endpoint of severe diarrhoea across sites provides standardisation, differences in care-seeking behaviour and out-of-pocket payment for paediatric health-care services in some settings could compromise case ascertainment.

Second, rotavirus infection is a systemic illness with diarrhoea as the predominant manifestation. There are many reports of extraintestinal manifestations of rotavirus infection in children,[2] the occurrence of rotaviraemia and antigenaemia in the absence of diarrhoea,[3] and complications such as gram-negative bacterial sepsis with significant morbidity and mortality, often after the acute episode of gastroenteritis.[4] Clearly, the effect of disease can persist after the acute diarrhoea, as shown in Malawi[5] where clinical disease was not more severe in HIV-infected children than in non-HIV-infected children, but where significantly more HIV-infected children died several weeks after acute rotavirus gastroenteritis.

These observations suggest that, to fully determine its true public health effect, the rotavirus vaccine should be assessed against all-cause morbidity and mortality and not just diarrhoea in settings with a high prevalence of comorbid conditions.

I declare that I have no conflicts of interest.

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The design of the studies by George Armah and colleagues[1] and K Zaman and colleagues[2] on the efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in African and Asian countries neglects a crucial factor: breastfeeding.

The authors write that breastfeeding was not restricted. However, in low-income settings, breastfeeding can be protective against severe rotavirus diarrhoea[3]—a finding confirmed in a high-income country.[4] With this in mind, we think that infants should have been stratified at randomisation by exclusive breastfeeding status. This, as well as the duration of exclusive and overall breastfeeding, could then have been taken into account in the analysis of results.

In our opinion, such data would make policy-making easier, because we would know the relative protection conferred by two interventions and the expected results in settings with different rates of breastfeeding. This omission is surprising, as is the Comment (which should have been assigned to experts with no link to vaccine producers),[5] suggesting that future trials might consider withholding breastmilk around the time of vaccine administration.

Finally, we would like to appeal to the international public health community that supports specific single-disease interventions to avoid making, and disseminating, calculations based on the assumption that once a specific proximal cause of death is prevented, or cured, the whole proportion of that cause-specific attributable mortality is avoided. Unfortunately, with the persistency of underlying risk factors and the timing of exposure, children will probably encounter other micro-organisms and will suffer from replacement mortality, so that the ultimate number of avoided deaths will be much less. This is not the case for measures to decrease the overall exposure and vulnerability of children, such as those on underlying determinants. The protection, promotion, and support of breastfeeding belongs to this group.

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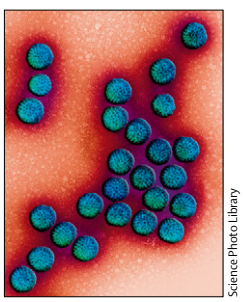

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