

ROTAVIRUS VACCINE (Comment)**How cost effective are the new rotavirus vaccines ?**

Both of the newly licensed rotavirus vaccines are, at present, quite expensive. This presents something of a challenge because, as the monograph says, the vaccines are going to be of most value in communities where diarrhoea remains a common cause of serious illness and even death in early infancy – and these are the communities that will be least able to afford a vaccine without external help.

An independently conducted economic analysis by the US Centres for Disease Control in 2006 looked at the case for making the new rotavirus vaccine available to all young babies in the United States. It concluded that a national programme might well result in 255,000 fewer physician visits, 137,000 fewer emergency department visits, 44,000 fewer hospital admissions, and 13 fewer deaths to children under five in the country each year. Even so, from a health care perspective, this meant that vaccination only stood a chance of paying for itself if the cost of RotaTeq[®] and its administration could be kept below \$12 per dose, and would lead to a net *increase* in health care expenditure if the cost of giving each dose was as much as \$38. From a rather wider society-based perspective the relevant costs were said to be somewhere between \$52 and \$89 per dose respectively. This has done nothing to deter the American Academy of Pediatrics from recommending a policy of universal vaccination even though the American vaccine is currently being sold for \$55 per vial. They have clearly, and not unreasonably, concluded that this is something that the country can well afford even though it is not a policy that can be recommended purely on cost-benefit grounds. A study in the Netherlands has argued that use could be cost-effective, but one from Hong Kong has suggested that a course only becomes clearly cost-effective if it costs less than \$40. Not atypically, the first study (Goossens *et al.*, 2008) had been funded by the manufacturer, and the second study (Ho *et al.*, 2008) had not.

These estimates are, of course, based on what it currently costs to treat a typical case of infectious childhood gastroenteritis or diarrhoea. Many children are currently hospitalised who could be treated on an outpatient basis, and even more are rehydrated intravenously even though we have known, for more than twenty years, that oral rehydration is nearly always simpler and safer, and also less distressing to all concerned. Children's doctors in many other countries remain equally wedded to unnecessarily complex ways of managing gastroenteritis. Recent surveys have found that intravenous rehydration is still the strategy being adopted for more than four fifths of all hospitalised children in Canada and Australia even when dehydration is quite mild (< 5%). Half the paediatric units in the UK also currently adopt much the same approach (Messahel and Hussain, 2008).

It also has to be acknowledged that most of the studies of vaccine efficacy to date have been done in countries where rotavirus gastroenteritis is least of a health hazard. The early studies on Rotateq were undertaken in Europe and North America, but 99% of the 440,000 childhood deaths caused by this virus every year occur in the poorest parts of the world. The World Health Organisation estimates that there are only 15,000 deaths a year in South America each year and only 200 in Europe (WHO, 2007). It will be difficult to do studies of efficacy in the poorest parts of the world, but even in Latin America (where at least one high quality study of Rotarix has been funded by GlaxoSmithKline), efficacy was not as high as in the European trial.

Rotarix reduced rotavirus-associated hospital admissions by 96% in the recent European trial, but it only reduced the incidence of serious diarrhoea by 83% in the first year, and by 79% in the second year of life, in the recent study in Latin America (Linhares *et al.*, 2008) possibly, in part, because it is not as effective against some of the strains currently prevalent in these countries. There is also some concern that widespread use of the current vaccine might also, in time, lead to the selective spread of relatively resistant viral strains (Gurgel *et al.*, 2008). Which of the two vaccines is going to be most effective is also still unknown. Rotarix, a monovalent vaccine, aims to mimic natural immunity by introducing homologous and broadly reactive heterotypic immunity against other human rotavirus strains. RotaTeq, a pentavalent bovine-human reassortant vaccine, on the other hand, has been designed to elicit serotype-specific responses to the most commonly circulating human serotypes.

So, while in other less affluent health care settings the balance of advantage may be very different, the 'opportunity cost' of adopting a policy of universal vaccination (i.e. the value of what will have to be left undone if such limited money as is available is spent on this) will still need careful assessment. Which vaccine works best will also only become clearer over time. In the countries that could most easily afford universal prophylaxis (Tate *et al.* 2009; Forster *et al.* 2009) one consideration will be whether a parental perception that the vaccine programme is becoming too 'burdensome' may result in some children failing to receive the vaccines they need to protect them from other even more serious infections. The fact that co-administration does not seem to affect the efficacy of other well established vaccines is reassuring (Dennehy *et al.* 2008). A policy of prevention clearly has most to offer in those countries where access to treatment, if the baby *does* become seriously ill, is limited or nonexistent, but these are the very countries that are least able to afford these new vaccines at the present time (Chokshi and Kesselheim, 2008).

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