Protective efficacy of a monovalent oral type 1 poliovirus vaccine: a case-control study

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Summary

Background **A high-potency monovalent oral type 1 poliovirus vaccine (mOPV1) was developed in 2005 to tackle persistent poliovirus transmission in the last remaining infected countries. Our aim was to assess the efficacy of this vaccine in India.**

Methods **We estimated the efficacy of mOPV1 used in supplementary immunisation activities from 2076 matched case-control pairs of confirmed cases of poliomyelitis caused by type 1 wild poliovirus and cases of non-polio acute flaccid paralysis in India. The effect of the introduction of mOPV1 on population immunity was calculated on the basis of estimates of vaccination coverage from data for non-polio acute flaccid paralysis.**

Findings **In areas of persistent poliovirus transmission in Uttar Pradesh, the protective efficacy of mOPV1 was estimated to be 30% (95% CI 19–41) per dose against type 1 paralytic disease, compared with 11% (7–14) for the trivalent oral vaccine. 76–82% of children aged 0–23 months were estimated to be protected by vaccination against type 1 poliovirus at the end of 2006, compared with 59% at the end of 2004, before the introduction of mOPV1.**

Interpretation **Under conditions where the efficacy of live-attenuated oral poliovirus vaccines is compromised by a high prevalence of diarrhoea and other infections, a dose of high-potency mOPV1 is almost three times more effective against type 1 poliomyelitis disease than is trivalent vaccine. Achieving high coverage with this new vaccine in areas of persistent poliovirus transmission should substantially improve the probability of rapidly eliminating transmission of the disease.**

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Introduction

By early 2004, the transmission of indigenous wild poliovirus had been interrupted in all but six countries of the world as a result of a concerted international eradication effort.[1] In four of these countries—Nigeria, Niger, Pakistan, and Afghanistan—sustained transmission was the result of a failure to immunise a sufficiently high proportion of children against poliomyelitis.[2] However, In India and Egypt, poliovirus transmission persisted despite immunisation coverage with four doses of the trivalent oral poliovirus vaccine of more than 90% among children aged less than 5 years.[3,4]

In recognition of the grave threat that persistent transmission in India and Egypt posed to the Global Polio Eradication Initiative, the programme's international oversight body urgently reviewed a range of options in October, 2004, to enhance the effectiveness of vaccination in these areas. By that time, transmission of wild type 2 poliovirus had been interrupted worldwide and type 3 poliovirus had been eliminated in Egypt and all but one state of India. Consequently, the Advisory Committee on Polio Eradication recommended the rapid development, licensing, and introduction of a new monovalent oral type 1 poliovirus vaccine (mOPV1).[1] This new vaccine possesses five times the potency of licensed monovalent vaccines used in the early 1960s (1×10^6 median cell culture infective doses [$CCID_{50}$] *vs* 200 000 $CCID_{50}$ per dose).[5] Through an extraordinary public-private development effort this new mOPV1 was licensed by April, 2005, in India and Egypt and used in mass polio immunisation campaigns in India (April, 2005) and Egypt (June, 2005).[6,7]

The efficacy of mOPV1 has major implications for international public health. The Global Polio Eradication Initiative has invested US$5 billion in eradication over a 20-year period and a key role is now proposed for monovalent vaccines in the strategic approach to interrupting the transmission of remaining indigenous wild poliovirus and managing the risks of re-emergent transmission of poliovirus after global certification of eradication.[8,9]

Especially important to the programme is the effectiveness of the monovalent vaccine under field conditions of poor sanitation and high population density, where a high prevalence of diarrhoeal disease and other infections have been shown to interfere with the efficacy of trivalent oral poliovirus vaccine as well as to favour the transmission of wild poliovirus.[10–12] In Egypt, no indigenous strain of wild poliovirus has been detected since the introduction of mOPV1.[6] In India, however, a polio outbreak in 2006 allowed us to study the efficacy of this new vaccine under field conditions. Our aim was to determine the protective efficacy of mOPV1 in India and explore the consequent implications of mOPV1 for global polio eradication and post-eradication risk management.

Methods

Patients and procedures

Since the introduction of mOPV1 use in India in 2005, vaccination efforts have focused on the northern states of

Uttar Pradesh—where over 80% of all type 1 cases of poliomyelitis in India in 2006 occurred—and Bihar. Frequent rounds of vaccination with mOPV1 have been interspersed with use of trivalent vaccine to maintain immunity to type 3 poliovirus. In the few districts with continued reporting of type 3 poliomyelitis, monovalent vaccine against type 3 (mOPV3) has also been used in up to two immunisation rounds.

We extracted data for cases of type 1 poliomyelitis and control individuals from the database of the National Polio Surveillance Project, which detects and investigates cases of acute flaccid paralysis in children aged less than 15 years in India. The National Polio Surveillance Project is an active surveillance system that receives reports from over 10 000 health-care institutions and 15 000 health-care practitioners.[13] All cases of acute flaccid paralysis undergo standard clinical, epidemiological, and laboratory investigations, including the collection of two stool samples to test for wild poliovirus. Data were extracted for patients in whom paralysis developed between January 1, 1997, and December 31, 2006. Laboratory confirmation of suspected cases of poliomyelitis was not routinely done before this time. Cases of acute flaccid paralysis without information on vaccine doses received or that did not have two adequate stool samples and had residual paralysis compatible with poliomyelitis were excluded from the analysis.

Institutional ethics approval was not sought since this is not a prospective intervention study. The paper reports an analysis of a National Surveillance database recording use of standard vaccines licensed by the National Regulatory Authority of the Government of India for use in India. The database is anonymised and free of personally identifiable information.

A case of type 1 poliomyelitis was defined as any case of acute flaccid paralysis with virological confirmation of type 1 wild poliovirus. Virological confirmation was done by the national laboratory network supported by the National Polio Surveillance Project. We estimated the sensitivity of laboratory testing for type 1 poliovirus from the consistency in results across the two stool samples collected from each case of acute flaccid paralysis.[14] The tests are assumed to be 100% specific since virus is grown in culture and all positive samples are sequenced in the VP1 region of the viral genome to allow differentiation of genotype and to identify any identical sequences that would indicate potential cross-contamination of samples.

Cases of acute flaccid paralysis from which wild poliovirus was not isolated from stool samples were defined as non-polio acute flaccid paralysis and could have been caused by a wide range of conditions including Guillain-Barré syndrome, trauma, and infection with other enteroviruses.[15] Control individuals were selected from these cases of non-polio acute flaccid paralysis and were matched to each case of poliomyelitis by district, age of onset of paralysis (to within 1 month), and date of onset of paralysis (to within 3 months). Matching criteria were chosen to reduce differences in exposure to wild poliovirus between cases and controls to a minimum, and are consistent with criteria used previously to estimate the efficacy of the trivalent vaccine.[10] We estimated the probability that a case of non-polio acute flaccid paralysis was actually infected with type 1 poliovirus (ie, the risk of misclassification) from the sensitivity and specificity of laboratory testing and the prevalence of type 1 poliovirus among all reported cases of acute flaccid paralysis.[14]

The number of doses of oral poliovirus vaccine reported by the parent to have been received by each case and control was extracted from the case investigation data. Individuals who recorded dose information were masked to the polio status of the child, which only became available after virological testing of the stool samples. These data do not differentiate between doses of oral poliovirus vaccine received through routine immunisation services, which use only trivalent vaccine, and supplementary immunisation activities, which use trivalent or monovalent vaccine. We therefore estimated the efficacy of mOPV1 under the assumptions of either 0% or 100% coverage by routine services. In the first case, we assumed that none of the total reported doses of vaccine were received through routine services. In the second case, the first three doses reported by cases and controls were assumed to have been trivalent vaccine received through routine services. The number of doses of monovalent and trivalent vaccine received by each case and control through supplementary immunisation activities was determined from their exposure to activities with different vaccine types based on their district of residence, date of birth, and date of onset of paralysis. For example, a child born on November 22, 2004, in Moradabad district in Uttar Pradesh, with date of onset of paralysis of November 12, 2005, would have been exposed to seven rounds of supplementary immunisation, four of which were with mOPV1 and the rest with trivalent vaccine. To estimate the number of doses of oral poliovirus vaccine of a particular type received by a child with acute flaccid paralysis, we multiplied the number of doses reported to have been received by the child by the fraction of supplementary immunisation activities that used vaccine of that type.

Statistical analysis

Vaccine efficacy was calculated by comparing the number of doses received by cases with that of matched controls by use of conditional logistic regression.[16] The odds of infection with paralytic poliovirus in India shows a log-linear relationship with the number of doses of trivalent vaccine received.[10] This finding is consistent with the mechanism of action of oral poliovirus vaccine, which shows an all-or-nothing response to vaccination in terms of protection against paralytic disease, with a probability of protection per dose that is independent of the number

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of earlier doses.[17,18] We therefore estimated the log-odds of a paralytic infection with type 1 poliovirus as a linear function of the number of doses of vaccine of different types:

$$\ln(\text{odds}) = \beta_m x_m + \beta_t x_t + E$$

where $(1-e^{\beta_m})$ is the per-dose protective efficacy of mOPV1 against type 1 paralytic poliovirus, $(1-e^{\beta_t})$is the per-dose protective efficacy of the trivalent vaccine against type 1 poliovirus, and x_m and x_t are the number of doses of mOPV1 and trivalent vaccine received, respectively. Each matched case-control pair has a particular level of exposure to wild poliovirus, E, which is unknown and can be eliminated from the analysis by maximising the conditional likelihood.[16] We estimated vaccine efficacy separately for the states of Uttar Pradesh and Bihar, and for the rest of India, by including an interaction term, since the efficacy of trivalent vaccine in these two northern states has been shown to be lower than in the rest of India.[10] We also examined the possibility of interference between mOPV1 and doses of trivalent vaccine by testing for an interaction.

To examine the hypothesis of a constant efficacy per dose for mOPV1, we also treated the estimated number of doses received as a categorical variable, and this unconstrained model was compared with the model with a constant per dose efficacy by use of the likelihood ratio statistic. Potential differences in mOPV1 efficacy by age were also examined by the inclusion of an interaction term for the age at onset of paralysis by 6-month age-groups. We tested the robustness of the process used to assign the vaccine type of each reported dose by examining the estimated efficacy of oral poliovirus vaccine irrespective of vaccine type before and after the introduction of monovalent vaccine in 2005.

The overall effectiveness of mOPV1 in Uttar Pradesh was assessed by calculating the proportion of children who were protected by vaccination against type 1 paralytic poliovirus, by 3-month age-groups, in the last quarter of 2004 (ie, just before the introduction of mOPV1) and the last quarter of 2006. This was estimated from the number doses of mOPV1 and trivalent vaccine received by children with non-polio acute flaccid paralysis, who are assumed to have the same level of vaccine coverage as other children from the same age-group and location, and the estimated efficacy for each of these vaccines (see webappendix for further details). A comparison was made with the estimated proportion of children protected in the last quarter of 2004 in the rest of India, where wild poliovirus transmission had been interrupted for the previous 2 years and continued immunisation had maintained the reproductive number below one, the threshold for persistence.[10] Immunity among 0–23-month-old children in the rest of India at this time is therefore indicative of exposure to vaccine virus alone, not wild poliovirus. The implications of mOPV1 for post-eradication risk management were assessed by calculating the number of doses of mOPV1 or of trivalent vaccine required to achieve a level of protection comparable with that which interrupted wild poliovirus transmission and maintained polio-free status in the rest of India.

All statistical analyses were implemented with the statistical programming language R.

	Cases of poliomyelitis	Matched cases of poliomyelitis
Age (years)		
<1	1820 (37%)	851 (41%)
1–2	2471 (50%)	1051 (51%)
3–4	458 (9%)	141 (7%)
5+	217 (4%)	33 (2%)
Location		
Uttar Pradesh	2973 (60%)	1499 (72%)
Bihar	439 (9%)	204 (10%)
Rest of India	1554 (31%)	373 (18%)
Period		
1997–2001	2540 (51%)	816 (39%)
2002–2006	2426 (49%)	1260 (61%)
Exposed to mOPV1, assuming		
(a) no routine tOPV	534 (11%)	451 (22%)
(b) first three doses routine tOPV	479 (10%)	405 (20%)
Total	4966 (100%)	2076 (100%)

Data are n (%). mOPV1=monovalent oral type 1 poliovirus vaccine. tOPV=trivalent oral poliovirus vaccine.

Table 1: **Characteristics of matched cases of type 1 poliomyelitis and all reported cases of type 1 poliomyelitis, 1997–2006**

Role of the funding source

The funding source had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data. NCG had final responsibility to submit for publication.

See Online for webappendix

	Vaccine	Location	Vaccine efficacy
	Trivalent	Rest of India	23% (17–29)
		Bihar	19% (8–29)
		Uttar Pradesh	11% (7–14)
No routine tOPV	Monovalent	Rest of India	36% (0–72)
		Bihar	18% (0–43)
		Uttar Pradesh	30% (19–39)*
First three doses routine tOPV	Monovalent	Rest of India	42% (0–71)
		Bihar	19% (0–47)
		Uttar Pradesh	31% (20–41)†

Data are efficacy (95% CI). tOPV=trivalent oral poliovirus vaccine. *Significantly better than trivalent vaccine in Uttar Pradesh, p=0·0007. †Significantly better than trivalent vaccine in Uttar Pradesh, p=0·0004.

Table 2: **Estimated per dose protective efficacy of mOPV1 and trivalent vaccine against paralysis by type 1 poliovirus in India**

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Articles

Results

122 173 cases of acute flaccid paralysis were identified. Of these, 2580 did not have two adequate stool samples and had residual paralysis compatible with poliomyelitis and were thus excluded from the analysis; a further 5773 cases did not report the number of vaccine doses received and were also excluded. 4966 cases of type 1 poliomyelitis had complete dose information for the entire study period; of these, 2076 were matched with suitable controls (table 1). The age distribution of matched cases was much the same as that for all reported cases of poliomyelitis. There was a greater probability of finding a matched control in Uttar Pradesh in recent years because there were more reported cases of non-polio acute flaccid paralysis in this region compared with other parts of India; in 2006, 388 (86%) cases of type 1 poliomyelitis reported from Uttar Pradesh were matched with a control. Between 438 and 460 matched controls were exposed to at least one supplementary immunisation activity with mOPV1, depending on the assumed routine coverage with trivalent vaccine.

See Online for webfigures 1 and 2

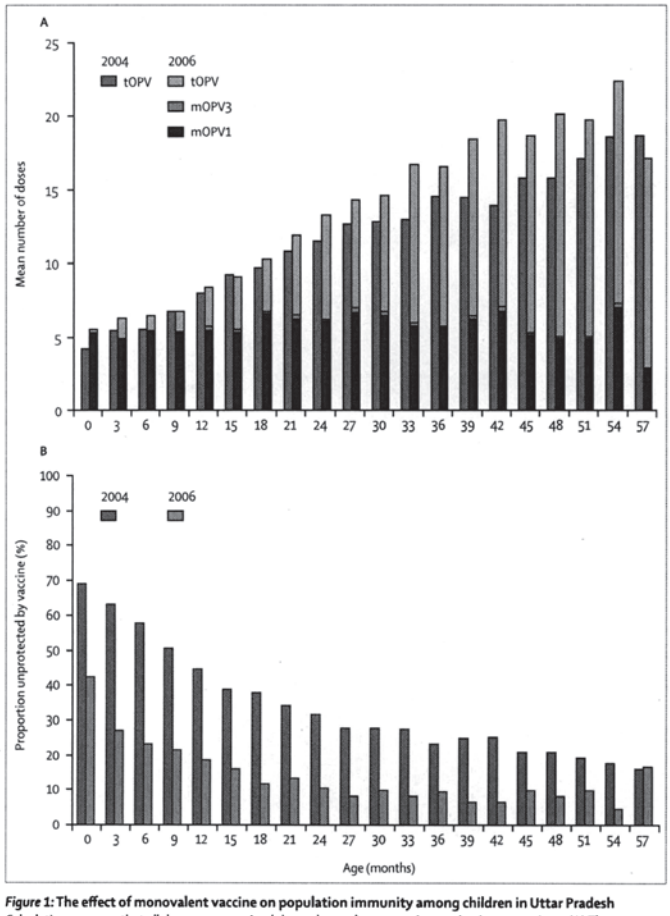

Figure 1: **The effect of monovalent vaccine on population immunity among children in Uttar Pradesh**
Calculations assume that all doses were received through supplementary immunisation campaigns. (A) The mean number of doses of each type of oral poliovirus vaccine received by children in Uttar Pradesh by 3-month age-groups, comparing the last quarter of 2004 with 2006. (B) The proportion of children in Uttar Pradesh who remained unprotected by oral vaccine against type 1 paralytic poliovirus in the last quarter of 2004 and 2006, based on the estimated coverage and efficacy of monovalent and trivalent vaccines. mOPV1=monovalent oral type 1 poliovirus vaccine. mOPV3=monovalent oral type 3 poliovirus vaccine. tOPV=trivalent oral poliovirus vaccine.

We estimate that the protective efficacy of mOPV1 in Uttar Pradesh is 30% (95% CI 19–39) per dose under the assumption of no routine coverage with trivalent vaccine and 31% (20–41) under the assumption of 100% coverage of routine programmes with up to three doses of trivalent vaccine (table 2). Both efficacy estimates are significantly higher than that for trivalent vaccine against type 1 poliovirus in Uttar Pradesh, which we estimated to be 11% per dose, irrespective of the assumption about routine coverage ($p=0\cdot0007$ and $0\cdot0004$ for each assumption). The estimate of mOPV1 efficacy is largely independent of the assumption about routine coverage with trivalent vaccine. Therefore, our (conservative) point estimate of mOPV1 efficacy is 30% per dose, with a CI of 19–41%, which spans the intervals for our two estimates. In Bihar and the rest of India, there were insufficient cases of poliomyelitis in 2006 to allow us to estimate mOPV1 efficacy precisely (table 2). As expected, there was no significant interaction between doses of mOPV1 and of trivalent vaccine in protecting against paralytic type 1 poliovirus, since supplementary immunisation activities occured at least 4 weeks apart to avoid interference between vaccine virus doses ($p=0\cdot54$ and $p=0\cdot21$ for each assumption).

The estimated odds of infection with paralytic poliovirus was found to fall exponentially with increasing number of doses of mOPV1 or trivalent vaccine, consistent with the assumption of a constant vaccine efficacy per dose (webfigure 1). Furthermore, the model with a constant probability of providing protection per dose did not give a significantly worse fit than the unconstrained model with differing efficacy by number of vaccine doses previously received (likelihood ratio test $p=0\cdot9$). The estimated efficacy of mOPV1 was not dependent on age at onset of paralysis.

We estimated that the sensitivity of testing for type 1 poliovirus from cases of acute flaccid paralysis with two stool samples was 97%, which is consistent with previous estimates.[10,19] The prevalence of type 1 poliovirus among all cases of acute flaccid paralysis was estimated to be 4·7% and the probability of misclassifying a child paralysed by type 1 poliovirus as a non-polio acute flaccid paralysis control to be 0·0017.

Figure 1 shows the effect of mOPV1 on the proportion of children protected by vaccination against type 1 paralytic poliovirus for Uttar Pradesh, assuming 0% routine coverage with trivalent vaccine. Similar results were found when we assumed that there was 100% routine coverage with trivalent vaccine (webfigure 2). The number of doses of oral poliovirus vaccine received by children aged 0–23 months, as estimated from data

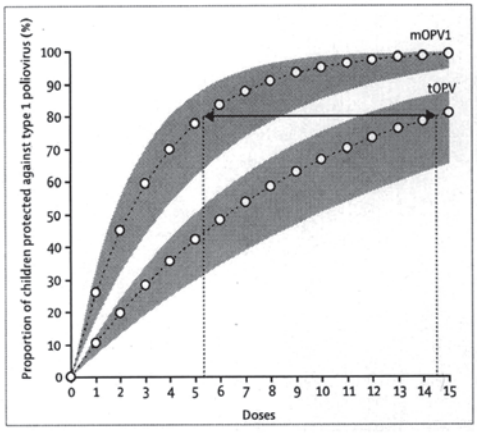

Figure 2: **Proportion of children protected against type 1 paralytic poliovirus**
Based on vaccine efficacy estimates for Uttar Pradesh. The shaded areas represent 95% CI for the per dose efficacy estimates. mOPV1=monovalent oral type 1 poliovirus vaccine. tOPV=trivalent oral poliovirus vaccine.

for cases of non-polio acute flaccid paralysis, shows a marginal improvement, from an average of seven doses in the last quarter of 2004 to eight doses for the same period in 2006 (figure 1). However, there was a substantial improvement in population immunity between the two periods, since in 2006 about half of the doses received in this age-group were mOPV1 (45–69%, depending on assumed coverage of routine services; figure 1 and webfigure 2). Consequently, in the last quarter of 2004, 59% of children aged 0–23 months in Uttar Pradesh were protected against type 1 poliovirus, compared with 76–82% of children in this age-group in the last quarter of 2006. This finding is comparable with an estimated 81% of children aged 0–23 months protected against type 1 poliovirus in the rest of India (excluding Bihar) during the last quarter of 2004.

The overall protective efficacy of vaccine given to children in Uttar Pradesh, irrespective of the inferred vaccine type, was estimated to be 25% (95% CI 17–31) per dose in 2006, compared with 9% (5–14) in the 5 years preceding the distribution of monovalent vaccine ($p=0\cdot0002$). This increase in overall vaccine efficacy following the introduction of mOPV1 supports the notion that this vaccine has greater efficacy than does trivalent vaccine, irrespective of the process used to classify the type of vaccine for each reported dose.

The greater efficacy of mOPV1 leads to much more rapid protection of children than with trivalent vaccine in Uttar Pradesh (figure 2). Each child would need to receive about five doses of mOPV1 to achieve an estimated 78% (range 61–87) level of vaccine-generated immunity, which is comparable with that needed to interrupt wild poliovirus transmission in the rest of India. By contrast, 14 doses of trivalent vaccine would be needed to reach such a level of protection.

Discussion

Our results show that, in the state of Uttar Pradesh, the monovalent vaccine is about three times more likely to result in a protective immune response against type 1 paralytic poliomyelitis than is the trivalent vaccine, irrespective of the assumption about routine immunisation. This increased efficacy is probably caused by the absence of interference between the three Sabin vaccine strains.[20] Even balanced formulations of trivalent poliovirus vaccines tend to result in preferential infection and seroconversion to type 2 virus, especially in developing countries, most likely explaining the global eradication of wild type 2 poliovirus in 1999.

The relative efficacy of mOPV1 is somewhat better than expected from seroconversion studies after vaccine administration, in which a relative rate of seroconversion per dose of 2–2·5 was found.[5] However, an estimated per dose efficacy of 30% is substantially lower than an overall seroconversion rate of 72% (range 53–89) observed in four small studies from developing countries,[5] which is probably the result of the higher prevalence of diarrhoea and other infections in Uttar Pradesh. Such infections can severely compromise the efficacy of live-attenuated oral poliovirus vaccine, as has been shown for the trivalent vaccine.[11,12] Vaccine quality is unlikely to be a problem, since temperature-sensitive vaccine vial monitors have been used in India since 1998, and routine testing of samples of vaccine vials from the field have found consistently high vaccine potency (>10^6 $CCID_{50}$ per dose). We were unable to generate precise estimates of the efficacy of mOPV1 outside Uttar Pradesh; nevertheless, efficacy is probably higher in the rest of India because of the lower prevalence of diarrhoea and other infections.

Although the estimated per dose efficacy of mOPV1 is below that observed in other studies, its efficacy was three times greater than that of the trivalent vaccine in the same setting, which has important implications for interrupting the remaining chains of wild poliovirus transmission in India as well as managing post-eradication risks. Most importantly, our estimate that 76–82% of children aged 0–23 months were protected by vaccine against type 1 paralytic poliovirus in Uttar Pradesh in the last quarter of 2006 due to the use of mOPV1 in over half the supplementary immunisation activities compares favourably with the estimated 81% achieved in the rest of India (excluding Bihar) at the end of 2004 when endemic transmission of type 1 wild poliovirus had been stopped for 2 years and the reproductive number maintained below the threshold for persistence.[19] In both cases, actual population immunity will be somewhat higher than these estimates of primary vaccine-derived immunity, due to natural exposure to wild poliovirus, secondary vaccine virus transmission, and the presence of maternal antibodies that protect children in the first few months of life.

Although a proportion of the children who seroconvert after immunisation with oral poliovirus vaccine can still

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become infected with poliovirus, the observation of a herd effect sufficient to interrupt transmission in the rest of India is consistent with studies that show that the duration and titre of viral excretion in children who become infected after immunisation are substantially reduced compared with unimmunised children.[21–23] In Uttar Pradesh, the proportion of children that need to be protected to interrupt transmission could be higher than in the rest of India, since higher population densities and poorer sanitation probably result in a greater transmission potential of wild poliovirus.

The higher per dose efficacy of mOPV1 compared with trivalent vaccine would facilitate a much more rapid increase in population immunity during an outbreak response in the post-eradication era. In the setting of Uttar Pradesh, five doses of mOPV1 would be needed to protect about 80% of children against type 1 poliomyelitis (figure 2). A comparable level of protection with trivalent vaccine would require 14 doses. This lends support to the idea of the stockpiling monovalent vaccines for managing the risks associated with polioviruses in the post-eradication era, as proposed by the Advisory Committee on Polio Eradication.[6]

Several factors could affect the precision of our estimate of the field efficacy of mOPV1. The number of doses of vaccine of different types recorded for each case of acute flaccid paralysis relies on accurate reporting of doses received and correct classification of the vaccine dose administered. Any misreporting that might have occurred is unlikely to have affected our estimate of vaccine efficacy, since more detailed follow-up of a subset of cases of poliomyelitis in 2005 found no tendency towards under-reporting or over-reporting of doses. Misclassification of vaccine doses received by individuals with acute flaccid paralysis will lead to an underestimate of the true mOPV1 efficacy, since trivalent doses could erroneously be recorded as mOPV1. Although such a misclassification could have some effect on our estimate of mOPV1 efficacy, the proportion of children missed by each supplementary immunisation activity is small (<5%) and exposure to different types of such activities is strongly correlated with the number of doses reported by individuals with acute flaccid paralysis, suggesting misclassification—and misreporting—is limited (webfigure 3). That mOPV1 is more effective than trivalent vaccine is lent strong support by the increased estimated efficacy of oral poliovirus vaccine in 2006, irrespective of vaccine type, compared with the 5 years before its introduction. Before the introduction of mOPV1, estimated vaccine efficacy based on data gathered since 1997 did not change over time.[10]

See Online for webfigure 3

Children with non-polio acute flaccid paralysis are a suitable control group for the analysis since they come from the same communities as reported cases of poliomyelitis. The estimate of vaccine efficacy would be biased if these children were in fact paralysed due to infection with type 1 poliovirus. However, the estimated probability of misclassification is very low; indeed, just three cases of type 1 poliomyelitis would be expected to be misclassified as controls over the entire period of the analysis and less than one during 2005–06, when mOPV1 was in use. Although just under half the cases of type 1 poliomyelitis could be matched, the tendency to select recent cases from Uttar Pradesh in the analysis of efficacy does not introduce bias, since the analysis is stratified by location and there has been no temporal change in the efficacy of the trivalent vaccine.[10] Furthermore, the estimate of mOPV1 efficacy is largely based on matched case-controls from the outbreak in 2006 centred on Uttar Pradesh, when 86% of cases were matched with controls. Indeed the estimated efficacy of mOPV1 remains at 30% per dose (range 19–41) when based on these cases alone.

Further studies are required to refine our understanding of the field efficacy of mOPV1, and also monovalent vaccine against type 3 poliovirus, and their role in interrupting the final chains of wild poliovirus transmission worldwide and managing post-eradication risks. Seroconversion studies after administration of trivalent vaccine and mOPV1 should be completed in India and elsewhere to assess the relative immunogenicity of these vaccines in different settings. However, most important to the elimination of poliovirus from the four remaining endemic areas in the world is achieving and sustaining high coverage with oral poliovirus vaccine of the appropriate type in all geographical areas and among all population subgroups. The 2006 outbreak of type 1 poliomyelitis in India, despite the introduction of a substantially more efficacious vaccine since mid-2005, serves as stark evidence of the need for high coverage with multiple doses of vaccine as early as possible in life in these areas. Achieving such coverage will require sustained dialogue with local communities and strong political commitment. If these conditions can be met, the prospects are now very good for the elimination of wild poliovirus transmission worldwide.

Contributors

NCG and RBA conceived the analysis and wrote the final manuscript. NCG applied the analysis, JW coordinated surveillance of acute flaccid paralysis, SD supported the analysis, SB supervised data collection, JMD did the laboratory testing of cases, and DLH and RWS contributed to the concept and review of the paper. All authors reviewed the analysis and contributed to the writing of the paper.

Conflict of interest statement

We declare that we have no conflict of interest.

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