Key issues in the persistence of poliomyelitis in Nigeria: a case-control study

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Summary

Background The completion of poliomyelitis eradication is a global emergency for public health. In 2012, more than 50% of the world's cases occurred in Nigeria following an unanticipated surge in incidence. We aimed to quantitatively analyse the key factors sustaining transmission of poliomyelitis in Nigeria and to calculate clinical efficacy estimates for the oral poliovirus vaccines (OPV) currently in use.

Methods We used acute flaccid paralysis (AFP) surveillance data from Nigeria collected between January, 2001, and December, 2012, to estimate the clinical efficacies of all four OPVs in use and combined this with vaccination coverage to estimate the effect of the introduction of monovalent and bivalent OPV on vaccine-induced serotype-specific population immunity. Vaccine efficacy was determined using a case-control study with CIs based on bootstrap resampling. Vaccine efficacy was also estimated separately for north and south Nigeria, by age of the children, and by year. Detailed 60-day follow-up data were collected from children with confirmed poliomyelitis and were used to assess correlates of vaccine status. We also quantitatively assessed the epidemiology of poliomyelitis and programme performance and considered the reasons for the high vaccine refusal rate along with risk factors for a given local government area reporting a case.

Findings Against serotype 1, both monovalent OPV (median 32·1%, 95% CI 26·1–38·1) and bivalent OPV (29·5%, 20·1–38·4) had higher clinical efficacy than trivalent OPV (19·4%, 16·1–22·8). Corresponding data for serotype 3 were 43·2% (23·1–61·1) and 23·8% (5·3–44·9) compared with 18·0% (14·1–22·1). Combined with increases in coverage, this factor has boosted population immunity in children younger than age 36 months to a record high (64–69% against serotypes 1 and 3). Vaccine efficacy in northern states was estimated to be significantly lower than in southern states ($p \leq 0·05$). The proportion of cases refusing vaccination decreased from 37–72% in 2008 to 21–51% in 2012 for routine and supplementary immunisation, and most caregivers cited ignorance of either vaccine importance or availability as the main reason for missing routine vaccinations (32·1% and 29·6% of cases, respectively). Multiple regression analyses highlighted associations between the age of the mother, availability of OPV at health facilities, and the primary source of health information and the probability of receiving OPV (all $p<0·05$).

Interpretation Although high refusal rates, low OPV campaign awareness, and heterogeneous population immunity continued to support poliomyelitis transmission in Nigeria at the end of 2012, overall population immunity had improved due to new OPV formulations and improvements in programme delivery.

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Introduction

In May, 2012, after more than 20 years of mass vaccination campaigns, the 65th World Health Assembly declared that the completion of poliomyelitis eradication was a "programmatic emergency for global public health".[1] Substantial financial and political pledges to poliomyelitis eradication have recently reintensified efforts, and prevalence of poliomyelitis is at a historical low, although transmission in Afghanistan, Pakistan, and Nigeria remains persistent. Globally, case numbers have fallen (1651 cases in 2008 *vs* 223 in 2012), and India, once one of the most entrenched reservoirs, is now free of indigenous poliovirus transmission.[2] However, in Nigeria, poliomyelitis cases doubled between 2011 and 2012, with sustained transmission of all three serotypes in 2012 (103 and 19 cases due to serotypes 1 and 3 wild poliovirus and eight due to circulating vaccine-derived poliovirus type 2 [cVDPV2]).[2,3] In 2012, Nigeria was the global epicentre of poliovirus outbreaks, astonishing those who commended its success during 2010 when case numbers fell by 95%.[4]

The 2011 Nigeria Emergency Action Plan has been refined to further involve key political and traditional leaders, and hundreds of volunteer community mobilisers have been charged with reaching every child in Nigeria to administer the vaccines to combat the recent setbacks.[5] The 2012 plan built on lessons learnt in previous years, aiming to integrate almost real-time feedback from teams on the ground with the highest level of governance to ensure chronically missed children are protected and supplies reach the most vulnerable children.[6] Additionally, in November, 2009, the Advisory Committee on Poliomyelitis Eradication recommended the introduction of bivalent oral poliovirus vaccine (bOPV) to supplementary immunisation activities in areas with sustained transmission of wild-type poliovirus

serotypes 1 and 3, but the efficacy of bOPV in Nigeria has not yet been assessed.[7] Such an assessment is especially important during this period of rapid increase in demand and manufacture of the vaccine and when discussions are underway regarding its potential use during routine immunisation in place of trivalent vaccine (tOPV).[8]

In this Article we explain why Nigeria has been experiencing continued high caseloads despite achieving record successes in vaccine coverage and political and community engagement by identifying the key factors driving poliovirus transmission.

Methods

Study design and procedures

We used acute flaccid paralysis (AFP) surveillance data from Nigeria collected between January, 2001, and December, 2012, to estimate the clinical efficacies of all four oral poliovirus vaccines (OPVs) using a case-control study. This was combined with vaccination coverage to estimate the effect of the introduction of monovalent OPV (mOPV) and bOPV on vaccine-induced serotype-specific population immunity.

To assess efficacy, children aged under 15 years with confirmed poliomyelitis (due to wild-type 1 or 3 poliovirus or cVDPV2) were matched with up to five randomly selected control children with non-poliomyelitis AFP chosen from the AFP surveillance database produced by the government of Nigeria (appendix). Cases were matched to controls by state and by date (within 1 month) and age at onset of paralysis (within 6 months). These criteria were chosen to maximise the number of matches while controlling for differential exposure to poliovirus. Vaccine efficacy was also estimated separately for north and south Nigeria, by age of the children, and by year.

See Online for appendix

To investigate vaccine-induced population immunity, we estimated the proportion of children younger than 36 months who were protected against each poliovirus serotype, on the basis of the reported vaccination history of children with non-poliomyelitis AFP and our estimates of vaccine efficacy. These children were assumed to be representative of the underlying population. Detailed 60-day follow-up data were collected from children with confirmed poliomyelitis and were used to assess correlates of vaccine status.

Finally, we quantitatively assessed the epidemiology of poliomyelitis and programme performance and considered the reasons for the high vaccine refusal rate along with risk factors for a given local government area (LGA) reporting a case.

Institutional ethics approval was not sought because this is a retrospective study using anonymised national surveillance data detailing the use of standard vaccines licensed by the National Regulatory Authority of the Government of Nigeria.

Statistical analysis

We assumed that all vaccines were received through supplementary immunisation activities, because the database does not distinguish between routine vaccinations or supplementary immunisation activities. We used bootstrap resampling methods to minimise the effect of outliers and bias introduced by the matching process. Vaccine efficacy was estimated by conditional logistic regression for 1000 randomly matched sets, producing a distribution of estimates for each vaccine type. 95% CIs (2·5th and 97·5th percentiles of bootstrapped estimates) around the median estimate represent the uncertainty introduced by the matching criteria. Sensitivity of the vaccine efficacy estimates to the matching criteria was examined and the analysis was repeated under the assumption that the first three doses received were through routine immunisation (ie, tOPV) and the remainder via supplementary immunisation activities. The prevalence of non-poliomyelitis enteroviruses by region was examined and compared by the Fisher's exact test.

The probability of vaccine-induced immunity in each child was estimated on the basis of the number of doses of each OPV type received and a randomly sampled value for the efficacy of each OPV using the range of estimates from the case-control study and accounting for covariance of the estimates. The mean of this quantity for children with non-poliomyelitis AFP was calculated and weighted by age to match the age distribution of the population.

	Type 1			Type 2	Type 3		
	tOPV	mOPV1	bOPV	tOPV	tOPV	mOPV3	bOPV
All states							
No routine coverage	19·4% (16·1 to 22·8)	32·1%* (26·1 to 38·1)	29·5%* (20·1 to 38·4)	48·5% (43·1 to 53·1)	18·0% (14·1 to 22·1)	43·2%* (23·1 to 61·1)	23·8% (5·3 to 44·9)
100% routine coverage	21·1% (18·2 to 24·0)	36·0%* (24·7 to 47·0)	24·2% (12·1 to 37·4)	22·0% (19·5 to 25·3)	17·6% (13·8 to 21·4)	40·4% (–0·2 to 66·0)	25·1% (3·7 to 54·1)
Northern states	19·2% (15·8 to 22·7)	28·8%* (21·9 to 35·6)	29·9%* (20·4 to 38·9)	48·9% (43·4 to 53·2)	17·7% (13·5 to 21·9)	40·9% (16·7 to 63·0)	24·0% (5·3 to 45·4)
Southern states	35·6%† (21·1 to 56·9)	52·5%† (40·4 to 65·2)	NA	NA	40·9% (3·9 to 68·3)	58·2% (20·4 to 85·1)	NA

Data are median values from the distribution of vaccine efficacy estimates with 95% CIs (2·5th and 97·5th percentile intervals) derived from conditional logistic regression on 1000 matched sets. Controls were matched to cases by date of onset (within 1 month), age at onset (within 6 months), and state. Estimates for vaccine efficacy in north and south Nigeria use the assumption of no routine coverage. mOPV=monovalent oral poliovirus vaccine. bOPV=bivalent oral poliovirus vaccine. tOPV=trivalent oral poliovirus vaccine. NA=not applicable. *p<0·05 compared with tOPV estimate. †p≤0·05 compared with northern states estimate.

***Table 1*: Estimated efficacy of one dose of trivalent oral poliovirus vaccine, serotype 1 or 3 monovalent oral poliovirus vaccine, and bivalent oral poliovirus vaccine**