Effectiveness of Oral Polio Vaccination Against Paralytic Poliomyelitis: A Matched Case-Control Study in Somalia

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Background. After the last case of type 1 wild poliovirus (WPV1) was reported in 2007, Somalia experienced another outbreak of WPV1 (189 cases) in 2013.

Methods. We conducted a retrospective, matched case-control study to evaluate the vaccine effectiveness (VE) of oral polio vaccine (OPV). We retrieved information from the Somalia Surveillance Database. A case was defined as any case of acute flaccid paralysis (AFP) with virological confirmation of WPV1. We selected two groups of controls for each case: non-polio AFP cases (“NPAFP controls”) matched to WPV1 cases by age, date of onset of paralysis and region; and asymptomatic “neighborhood controls,” matched by age. Using conditional logistic regression, we estimated the VE of OPV as (1–odds ratio) ×100.

Result. We matched 99 WPV cases with 99 NPAFP controls and 134 WPV1 cases with 268 neighborhood controls. Using NPAFP controls, the overall VE was 70% (95% confidence interval [CI], 37–86), 59% (2–83) among 1–3 dose recipients, 77% (95% CI, 46–91) among ≥4 dose recipients. In neighborhood controls, the overall VE was 95% (95% CI, 84–98), 92% (72–98) among 1–3 dose recipients, and 97% (89–99) among ≥4 dose recipients. When the analysis was limited to cases and controls ≤24 months old, the overall VE in NPAFP and neighborhood controls was 95% (95% CI, 65–99) and 97% (95% CI, 76–100), respectively.

Conclusions. Among individuals who were fully vaccinated with OPV, vaccination was effective at preventing WPV1 in Somalia.

Keywords. Vaccine effectiveness; oral polio vaccine; Somalia.

The Global Polio Eradication Initiative (GPEI) implemented milestones for polio eradication and expanded programmatic support in 2012. During this year, the World Health Assembly declared ending polio a “programmatic emergency for global public health,” and 2012 ended with the fewest polio cases in the fewest countries since the program was established in 1988 [1]. However, this progress was slowed by the importation of WPV1 and subsequent outbreaks in previous polio-free countries in Horn of Africa and Middle East regions in 2013 [2, 3]. Unless these new outbreaks are immediately controlled, the World Health Assembly-endorsed milestone of stopping all polio transmission globally by the end of 2014 will be in jeopardy [1]. Somalia, a country in the Horn of Africa, was one of the countries affected by the 2013 polio resurgence. In spite of government collapse and civil strife since 1991, Somalia successfully interrupted transmission of indigenous polio in 2002 using a network of local staff and volunteers trained and supported by GPEI partners. However, in 2005, the country was reinfected by WPV1 that originated from Nigeria, causing an outbreak that lasted until March 2007 and ultimately included 228 cases of paralytic polio. From 2008 onward, Somalia experienced a decline in the polio population immunity caused, in large part, by a ban on supplemental immunization activities (SIAs) by
local militia groups. This ban, in the context of an already weak routine immunization (RI) program and a worsening humanitarian crisis led to the accumulation of an estimated 1 million children under 5 years of age susceptible to WPV by end of 2012; the largest concentration of unimmunized children in the world (this number reduced to half-million in 2013). This undervaccinated population facilitated the emergence of circulating vaccine-derived poliovirus (cVDPV) from 2008 to 2013.

The success of the initiative to stop all polio transmission globally by the end of 2014 depends on reaching every child with an effective oral poliovirus vaccine (OPV) that will induce high levels of immunity to WPV. Previous published studies have shown a wide range of OPV vaccine effectiveness in different settings and countries [4]. To estimate the vaccine effectiveness (VE) of OPV against WPV1 in the Somalia context, we conducted a retrospective matched case-control study.

METHODS

Study Location
Somalia borders Kenya, Ethiopia, and Djibouti and is divided into 3 geopolitical and administrative zones (northeast [Puntland], northwest [Somaliland], and south-central zone) and 19 regions. The civil war in Somalia that started in 1991 forced millions of Somalis to flee their homes for internally displaced people (IDP) camps inside Somalia and refugee camps in neighboring Kenya, Ethiopia, and Yemen (Figure 1). The rapid population movement hampered service delivery, increased spread of WPV1, and made vaccination of children in Somalia difficult.

Since the Expanded Programme on Immunization (EPI) started in 1979 in Somalia, the vaccine coverage rate has been extremely low in the country [6]. Through a network of health facilities, Somalia implements the traditional 6 antigens of EPI vaccines, including trivalent OPV (tOPV) given at a birth, 6 weeks, 10 weeks, and 14 weeks following birth. All OPV doses received through RI were tOPV. In addition, from 1998, Somalia has been conducting yearly supplementary immunization activities (SIAs) in all zones. From 2008 until the confirmation of the outbreak, except during 1 round in July 2008, Somalia had used tOPV in all SIAs, aimed to interrupt transmission of cVDPV2 (Table 3). In 2013, bivalent OPV was used extensively after the outbreak was confirmed in Somalia.

Study Design and Data Collection
We used a retrospective matched case-control study design to assess the vaccine effectiveness (VE) of OPV during the outbreak of WPV in Somalia from 9 May to 31 December 2013. We retrieved information from the Somalia Surveillance Database, which is operated and maintained by the WHO Somalia office. Case-investigation forms of AFP cases, contact forms, and laboratory results are entered into Information for Action...
System, a system for data entry, storage, and analysis based on EpiData software.

**Cases**

A case of AFP was defined as acute flaccid paralysis in a child aged <15 years or any paralytic illness in a person of any age when polio is suspected. A “hot case” was defined as AFP in an unimmunized or underimmunized child <5 years of age with the following signs: fever at onset of paralysis, asymmetric paralysis, and rapid progression of paralysis (within 3 days). All AFP cases were investigated by polio officers, and 2 stool specimens were collected from each AFP case following the AFP surveillance guidelines [7]. For each AFP case, 1 stool sample was collected from each of 3 neighborhood contacts. An AFP contact is defined as anyone of similar age to the AFP case and residing in the same household or neighborhood. Stool samples collected from AFP cases and contacts in Somalia were sent to the Regional Polio Laboratory in Nairobi (KEMRI) for virus isolation, typing, and intra-typic differentiation following standard testing procedures [8]. WPV strains isolated by KEMRI polio lab were sent to the Centers for Disease Control and Prevention (Atlanta, Georgia) or the National Institute for Communicable Diseases (Johannesburg, South Africa) for sequencing.

A WPV1 case was defined as any AFP case in which WPV1 was isolated from the stool specimen of the AFP case or any of the contacts. Cases of AFP from which neither a WPV nor a VDPV was isolated from stool samples were defined as nonpolio AFP (NPAFP).

**Controls**

We selected 2 different control groups. “NPAFP controls”: for each case, we selected 1 nonpolio AFP control matched to each case of WPV by age (within ±6 month), date of onset of paralysis (within ±3 months), and region. We did not match by sex because of the reduction in the number of matched pairs. “Neighborhood controls”: For each case, we selected 2 of the neighborhood contacts who were asymptomatic living in the same household or neighborhood of the WPV case, and matched by age (within ±24 months). The 2 different control groups (NPAFP and Neighborhood) allows for the estimation of VE under to potentially different sources of confounding. Both are matched on age, geography, and time, though to differing degrees.

**Vaccination Status**

Vaccination status of the AFP cases and contacts were recorded in the case investigation form (CIF) along with other clinical and demographic details. Vaccination was ascertained by parental/guardian recall or by vaccination card, where available. The CIF captured information on the number of OPV received through SIAs, RI, and date of the last OPV dose. The source of vaccination information (recall vs card) and type of OPV were not indicated in the CIF. The total number of OPV doses (overall) was defined as the sum of OPV doses received from SIAs and RI.

**Analysis**

Cases and matched controls were compared on age, sex, clinical characteristics, and vaccination status using Wald \( \chi^2 \) test from conditional logistic models. The conditional logistic regression was used to calculate the odds ratio and 95% confidence intervals of OPV vaccination among cases and matched controls. We

![Table 1. Summary of cases and controls included in each analysis, Somalia, 2013](https://academic.oup.com/jid/article-abstract/210/suppl_1/S187/2194400/1)
calculated VE as \((1-\text{OR} \times 100)\) [9]. We calculated overall VE as any dose vs no doses. We also calculated VE from models fitting OPV doses as a continuous variable and as an ordinal variable (unvaccinated, 1 to 3 doses and ≥4 doses recipients). To assess the impact of potential of measurement error due to recall, we estimated overall VE among children <24 months; and to assess the impact of potential misclassification of case status we estimated VE among cases confirmed by their own stool sample and their matching controls. Data analysis was performed using SAS version 9.3 (SAS Institute Inc, Cary) analyzing each control group separately. Statistical significance was defined as \(P<.05\). All tests were 2-sided.

Institutional review board approval was not required for this study as it was considered part of public health emergency response by CDC, and the data were extracted from the Somalia Surveillance Database without personal identifiers.

### RESULTS

#### Characteristics of Cases and Controls

Of the 189 confirmed WPV1 cases reported in 2013, we matched 99 WPV1 cases with 99 NPAFP controls and 132 WPV1 cases with 264 neighborhood controls. There were no significant differences between the matched WPV1 cases (99) and the unmatched WPV1 cases (90) in relation to age, sex, and region. There was a significant difference in vaccination status: WPV1 cases included in the case-NPAFP matched analysis were more likely to be unvaccinated than those not included (64% vs 49%, \(P=.036\)). There was no difference in the proportion of stool adequacy (2 specimens collected ≥24 hours apart and within 14 days after paralysis onset) among the WPV1 cases (89%) and NPAFP controls (88%) included in the study. There was no association between sex and WPV1 in the univariate analyses of NPAFP controls; but there was a borderline association between sex and WPV1 in the neighborhood controls. Adding a variable for sex in the regression models had no appreciable impact on the estimates; therefore, the variable was not included in the models.

#### Analysis Using NPAFP Controls

The clinical, vaccination, and demographic characteristics of cases and NPAFP controls are shown in Table 1. The clinical presentation of WPV1 cases and matched controls were similar. The cases and controls were similar in most respects; however, statistically significant differences between cases and controls were observed by the total doses of OPV received and “hot case” (Table 1). Sixty-four percent of the cases were unvaccinated vs 42% among matched controls.

The overall VE was 70% (95% CI, 37–86); VE increased by number of doses received: 59% (95% CI, 2–83) among 1- to 3-dose recipients, 77% (95% CI, 46–91) among ≥4-dose recipients, with unvaccinated children as the reference point (Table 2), though there was no significant difference between 1–3 and ≥4-doses (\(P=.18\)).

The overall VE was 95% (95% CI, 65–99) when the analysis was limited to cases and controls ≤24 months of age, (55 pairs of cases and controls), the age group in which parents will have a shorter recall period.

When we limited the analysis to WPV cases that were only confirmed by the AFP cases and excluded cases confirmed by contacts (76 pairs of cases and controls), the overall VE was 77% (95% CI, 40–91).

#### Analysis Using Neighborhood Controls

The cases and neighborhood controls were similar in most aspects, but different with respect to the total number of OPV doses received and age (Table 1). The median number of overall OPV doses was 0 among WPV1 cases and 3 among neighborhood controls.

The overall VE was 95% (95% CI, 84–98); VE increased by number of doses received: 92% (95% CI, 72–98) among 1- to
3-dose recipients, 97% (95% CI, 89–99) among ≥4-dose recipients, with unvaccinated children as the reference point (Table 2). There was a significant difference between 1–3 and ≥4 doses (P = .02).

The overall VE was 97% (95% CI, 76–100), when the analysis was limited to cases and controls ≤24 months of age (45 pairs of cases and controls).

The overall VE reduced to 92% (95% CI, 65–98) when we matched age to within 6 months instead of 24 months (77 pairs of cases and controls). However, the overall VE increased to 98% (95% CI, 82–99) when we excluded the neighborhood controls that had positive WPV1 stool samples (81 pairs of cases and controls).

DISCUSSION

After 6 years of being polio free, Somalia experienced a large and widespread WPV1 outbreak during 2013. Our findings from a matched case-control study suggest that OPV was highly effective in preventing WPV1 among vaccinated individuals. The estimated VE for 1 or more doses of OPV was 70% when WPV cases were matched with NPAFP controls and 95% when WPV1 cases were matched with healthy neighborhood controls. The estimated increase in VE for each additional dose was 18% in the NPAFP matched analysis and 37% in the neighborhood matched analysis.

Our study’s VE estimates are comparable with other VE estimates in endemic and outbreak countries that used the same methodology and similar sample size. A case-control study in Pakistan found OPV VE to be 74% [10] and in a similar study in Gambia, VE of ≥3 doses of trivalent oral polio vaccine was 72% [11]. Other studies have also reported a higher VE for OPV similar to the result in the neighborhood match in our study [12, 13]. Conversely, recent studies from countries where transmission of indigenous WPV has never been interrupted (at the time of the study) showed OPV VE estimates to be low for all types of OPV compared to our study [14–16]. In those studies, the low VE in those countries was believed to be related to higher prevalence of diarrhea and enterovirus, poor sanitation, and high population density; however, VE estimates against WPV1 were higher for the bivalent oral polio vaccine (bOPV) and monovalent OPV (mOPV) compared to the less immunogenic tOPV [14–16].

Without knowing vaccine type—a variable that would have to be imputed, because these data are not collected as part of routine surveillance—we could not calculate the VE estimates for each type of OPV used in Somalia in 2013. But we believe that the main contributing factor to the high OPV VE in our study was the fast and frequent use of bOPV in Somalia.

Apart from the first SIAs that were conducted within 5 days of confirmation of the index case using tOPV, the rest of the 8 SIAs and 1 Child Health Days conducted in Banadir region (the epicenter of the outbreak) used bOPV (Table 3). All age-group SIAs that were conducted within 5 days of confirmation of the index case using tOPV, the rest of the 8 SIAs and 1 Child Health Days conducted in Banadir region (the epicenter of the outbreak) used bOPV (Table 3). All age-group SIAs targeting children <10 years of age using bOPV were conducted 3 times in Banadir, twice in South Central Zone, and once in the Northern zones. SIAs targeting children <10 years of age using bOPV were conducted 4 times.
in Banadir, 3 times in SCZ, and twice in the Northern zones. Moreover, bOPV was used to vaccinate 50 000–85 000 children <10 years of age every week at transit and cross-border points.

In our results, the unexpected difference in the overall VE by control groups, 70% vs 95%, could be explained by differences in the control group selection process. Although the first group of controls were individuals with acute flaccid paralysis similar in clinical presentation to the confirmed cases, the second group of controls were healthy individuals. Parents of controls with acute flaccid paralysis, who, at the time of the interview did not yet know if their child’s paralysis was polio or another illness, would have been subject to the same biases as parents of polio cases, particularly with respect to the number of vaccine doses reported [14]. Second, there was difference in the matching by age for the nonpolio AFP controls we matched within 6 months, whereas for the neighborhood controls the matching for age was within 24 months. Neighborhood controls were, on average, older, had more opportunities to receive vaccine, and may have been more likely to have been alive before the ban on polio SIAs. This explanation is supported by the similarity of the overall VE in the two control groups when we limited the analysis to ≤24 months (95% vs 97%). Third, neighborhood controls may have been better matched with respect to certain virus exposure factors. Because of the small sample size, in the NPAFP-control analysis, we matched the nonpolio AFP controls by region, making it difficult to control for confounding factors such as socioeconomic status, sanitation, and whether the village is accessible or there is a ban on SIAs. Each of the control groups has its strengths and weaknesses in estimating the OPV VE in Somalia.

Our study has several limitations inherent to retrospective case-control studies [17]. First, although all the WPV1 cases were laboratory confirmed, approximately 25% of the WPV1 cases included in our analysis were confirmed by isolation of WPV1 from healthy contacts rather than the AFP case; thereby creating the chance of misclassifying a nonpolio AFP case as a confirmed case based on a positive contact. Second, it is possible that some of the NPAFP cases included in our study as controls were actually WPV cases but misclassified on the basis of stool specimens negative for WPV. This could occur because excretion is intermittent, delayed collection of samples, mishandling of specimens, or false-negative result [8]. Misclassification of NPAFP controls could reduce the calculated VE. Third, we lacked complete clinical information on contacts. Fourth, data collected did not include the type of OPV; therefore, VE estimates for each OPV formulation could not be determined. Fifth, the vaccination status of cases and controls was based on parental/guardian recall. We tried to minimize recall bias by assessing the VE for children ≤24 months of age, giving a shorter recall period, because we found difference in the overall VE and VE for children ≤24 months [11].

As of early 2014, data indicate that WPV1 transmission might have been interrupted in Banadir, since no new case of WPV1 has been detected there for more than 5 months in the presence of good surveillance indicators. Several factors, including multiple expanded age-group SIAs, revision of microplans, introduction of independent monitoring of SIAs, active participation of all stakeholders, and relative peace and stability in Banadir, might have contributed to the possible interruption of transmission of WPV1 there. Despite these gains made so far, the program is faced with tough and unpredictable challenges in protecting the children of Somalia from WPV1. A possible but very real threat is the potential movement of large populations resulting from either renewed fighting or famine. This, in addition to the refugees, traders, and nomadic pastoralists frequently crossing the porous borders with neighboring countries make it possible for WPV1 to spread easily through the Horn of Africa. Previously, the frequent movements of these mobile populations facilitated the spread of poliovirus inside Somalia and into neighboring countries. Similar to the 2005–2007 WPV1 outbreaks, the 2013 outbreak spread to Kenya and Ethiopia. The cross-border transmission of WPV1 necessitates a regional approach and synchronization of all response activities and surveillance.

In conclusion, the analysis confirms the effectiveness of OPV against WPV1 in a setting such as Somalia. To consolidate and sustain the gains achieved so far, the national, religious, and clan leaders, in collaboration with the GPEI, should work closely to reach the half-million inaccessible, unvaccinated children in Somalia with the necessary vaccines.

Notes
Acknowledgments. We would like to thank Dr Ghulam Popal, WHO Representative for Somalia, and Mr Sikander Khan, UNICEF Somalia Representative, for their tremendous support and dedication to the polio eradication activities in Somalia. We would also like to thank all the field staff, the regional staff, and the headquarters staff of WHO and UNICEF. Finally, we would like to thank Dr Gregory L. Armstrong for reviewing our manuscript and giving us insightful comments and suggestions and Dr Kathleen Wannemuehler, CDC Atlanta, for reviewing our manuscript and providing feedback on the methodology and the statistical analyses.

Disclaimers. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, World Health Organization, or United Nations Children’s Fund.

Financial support. This work was supported by the Centers for Disease Control and Prevention and the World Health Organization.

Supplement sponsorship. This article is part of a supplement entitled “The Final Phase of Polio Eradication and Endgame Strategies for the Post-Eradication Era,” which was sponsored by the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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