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MAJOR ARTICLE

Achieving High Poliovirus Antibody Seroprevalence in Areas at Risk of Vaccine-Derived Poliovirus Transmission—Niger Experience

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Background. Outbreaks of vaccine-derived poliovirus type 2 (VDPV2) continue to expand across Africa. We conducted a serological survey of polio antibodies in high–polio risk areas of Niger to assess risk of poliovirus outbreaks.

Methods. Children between 1 and 5 years of age were enrolled from structures randomly selected using satellite imaging enumeration in Diffa Province, Niger, in July 2019. After obtaining informed consent, dried blood spot cards were collected. Neutralizing antibodies against 3 poliovirus serotypes were detected using microneutralization assay at the Centers for Disease Control and Prevention.

Results. We obtained analyzable data from 309/322 (95.9%) enrolled children. Seroprevalence of polio antibodies was 290/309 (93.9%), 272/309 (88.0%), and 254/309 (82.2%) for serotypes 1, 2, and 3, respectively. For serotypes 1 and 2, the seroprevalence did not significantly change with age ($P = .09$ and $P = .44$, respectively); for serotype 3, it increased with age (from 65% in 1–2-year-olds to 91.1% in 4–5-year olds; $P < .001$). We did not identify any risk factors for type 2 seronegativity.

Conclusions. With type 2 seroprevalence close to 90%, the risk of emergence of new cVDPV2 outbreaks in Niger is low; however, the risk of cVDPV2 importations from neighboring countries leading to local transmission persists. Niger should maintain its outbreak response readiness capacity and further strengthen its routine immunization.

Keywords. poliomyelitis; eradication; seroprevalence; vaccine-preventable diseases; immunizations.

Africa was certified wild poliovirus (WPV) free in October 2020 [1]. The last case of WPV in Africa was detected in 2016 in Nigeria. Globally, there were 140 cases of poliomyelitis caused by WPV in 2020, all detected in the last remaining endemic areas of Afghanistan and Pakistan [2].

In addition to WPVs, paralytic poliomyelitis can also result from the use of live oral poliovirus vaccines (OPVs), referred to as vaccine-derived polioviruses (VDPVs), which may in rare circumstances revert to neurovirulence following prolonged circulation in underimmunized populations [3–5]. When these revertant OPV strains circulate and the number of accumulated nucleotide substitutions in their viral capsid 1 protein exceeds 1% (serotypes 1 and 3) or 0.6% (serotype 2), they are called circulating vaccine-derived polioviruses (cVDPVs). cVDPV outbreaks continue to be detected in many African countries, with the vast majority being serotype 2 (cVDPV2) [2].

OPV vaccine is needed to achieve global poliovirus eradication; however, the risk of seeding cVDPV outbreaks with OPV's live Sabin viruses needs to be eliminated. The Global Polio Eradication Initiative (GPEI) launched a strategy of phased withdrawal of all vaccine poliovirus strains (Sabin stains) from OPV, starting with serotype 2. The first phase of this withdrawal was the switch from trivalent OPV (tOPV) containing all 3 poliovirus serotypes to bivalent OPV (bOPV) containing only serotypes 1 and 3 [6]. The switch was carried out in a globally synchronized manner in April 2016 with the hope that new cVDPV2 outbreaks would cease to occur in near future due to the removal of type 2 Sabin virus from OPV [7, 8]. Despite the global strategy to eliminate cVDPV2 cases and outbreaks, old cVDPV2 outbreaks proved difficult to control, and the majority of new ones either were seeded by monovalent OPV (mOPV2) vaccine used to respond to the existing cVDPV2 outbreaks in the country of emergence or were consistent with mOPV2 use by a neighboring country [9]. Instead of a predicted decreasing trend of paralytic cases caused by cVDPV2, there has been an expansion in geographic scope and in numbers of cVDPV2 cases (71 in 2018, 366 in 2019, and 732 in the first 11 months of 2020) [2].

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Niger has experienced several importations of cVDPV2. First, in 2018 a cVDPV2 outbreak from Nigeria spread to Southern Niger; second, in 2019 cVDPV2 from the same outbreak in Nigeria spread to Eastern Niger; and most recently, in 2020 cases were detected in Southwestern Niger, this time imported from countries in West Africa [10]. In total, Niger detected 20 paralytic cases and 11 nonparalytic healthy contacts infected by cVDPV2 since the switch from tOPV to bOPV [2].

As a response to these outbreaks, the government of Niger, supported by GPEI, carried out several national and subnational supplementary immunization campaigns with monovalent OPV type 2 (mOPV2) targeting children <5 years of age. In routine immunization, Niger introduced 1 full dose of intramuscular (0.5 mL) inactivated poliovirus vaccine (IPV) in 2015 and continues to administer bOPV in their immunization schedule. The estimated vaccination coverage with IPV as well as with the third bOPV dose was >80% from 2017 to 2019 [11].

Seroprevalence surveys of polio antibodies have been used as a tool to evaluate risk of poliovirus outbreaks, as well as to assess polio program performance and identify population immunity gaps. They have been routinely carried out in Nigeria, India, Pakistan, West Africa, Madagascar, and other areas and have led to changes in polio eradication strategies in these countries [12–22].

To better understand immunity in high–polio risk areas and populations and to assess risk of future outbreaks of VDPVs, we conducted a population-based seroprevalence survey of polio antibodies in an area of Niger that had experienced VDPV outbreaks in recent years. In our analysis, we focused primarily on type 2 seroprevalence because of the risk of cVDPV2 outbreaks either spreading to Niger from the neighboring countries or emerging in Niger as a result of mOPV2 use.

METHODS

This was a community-based, cross-sectional survey carried out in July 2019 in Diffa province in the southeastern part of Niger. Diffa is considered a high-risk province as it borders both Nigeria and Chad and hosts a large number of refugees and internally displaced persons fleeing Boko Haram terror in the Lake Chad Basin area [23]. The survey was conducted in 5 districts of Diffa—Bosso, Diffa, Goudoumaria, Maine Soroa, and N'guigmi—and included children 12–59 months of age.

Using ArcGIS software, a complete list of settlements was enumerated within the sampling frame in Diffa. Settlements were plotted onto a map over satellite imagery, and structures were manually digitized within the settlements. Structures were digitized without any inference as to their use (ie, residential vs nonresidential). Using a random number generator, the requisite number of structures was selected for inclusion in the study. One child aged 12–59 months and living in each selected structure was chosen at random.

Table 1. Demographic Indicators of Study Population

Indicator		n/N	%
Gender	Female	156/309	50.5
Age distribution	12–23 mo	60/308	19.5
	24–35 mo	80/308	26.0
	36–47 mo	89/308	28.9
	48–59 mo	79/308	25.7
Population group	Resident	275/309	89.0
	Refugee	19/309	6.2
	Internally displaced person	15/309	4.9
House type	Brick or concrete house	4/309	1.3
	Hut	117/309	37.9
	Tent	21/309	6.8
	Mud house	167/309	54.1
Type of toilet	Individual latrines	38/309	12.3
	Communal latrines	40/309	12.9
	Open air defecation	231/309	74.8
Water source	Running water	14/309	4.5
	Well water	226/309	73.1
	Village pump	56/309	18.1
	More than 1 source	13/309	4.2

A sample size of 334 children was calculated to be sufficient to detect, at the 95% confidence level, a seroprevalence point estimate with a precision of ~±5% assuming >80% seroprevalence and a proportion of nonconsenting parents <10%. Assuming that in ~2/3 of identified structures there will be at least 1 child in the targeted age group, 500 households were planned to be selected for inclusion in the study. GPS coordinates of the visited households were recorded.

A simple demographic questionnaire including poliovirus vaccination history was administered, and children's weight and height were recorded. Acute and chronic malnutrition were defined as weight for age z-score ≤2 and height for age z-score ≤2 SDs from the mean z-score, respectively. A vaccination card was requested, and documented vaccination history was recorded.

Table 2. Vaccination History as Recorded in Vaccination Card and Nutritional Status

Indicator	n/N	%
Vaccination history		
mOPV2 received in a campaign in 2019	309/309	100.0
Vaccination card available	80/309	25.9
3rd dose of OPV in routine immunization received	68/75	90.1
IPV received	60/71	84.5
1st dose of measles vaccine received	64/75	85.3
2nd dose of measles vaccine received	22/39	56.4
Nutritional status		
Chronic malnutrition (≤–2 z-score height for age)	122/301	40.5
Acute malnutrition (≤–2 z-score weight for height)	57/299	19.1
Severe chronic malnutrition (≤–3 z-score height for age)	60/301	19.9
Severe acute malnutrition (≤–3 z-score weight for height)	19/299	6.4

Abbreviations: IPV, inactivated poliovirus vaccine; mOPV2, monovalent oral poliovirus vaccine serotype 2; OPV, oral poliovirus vaccine.

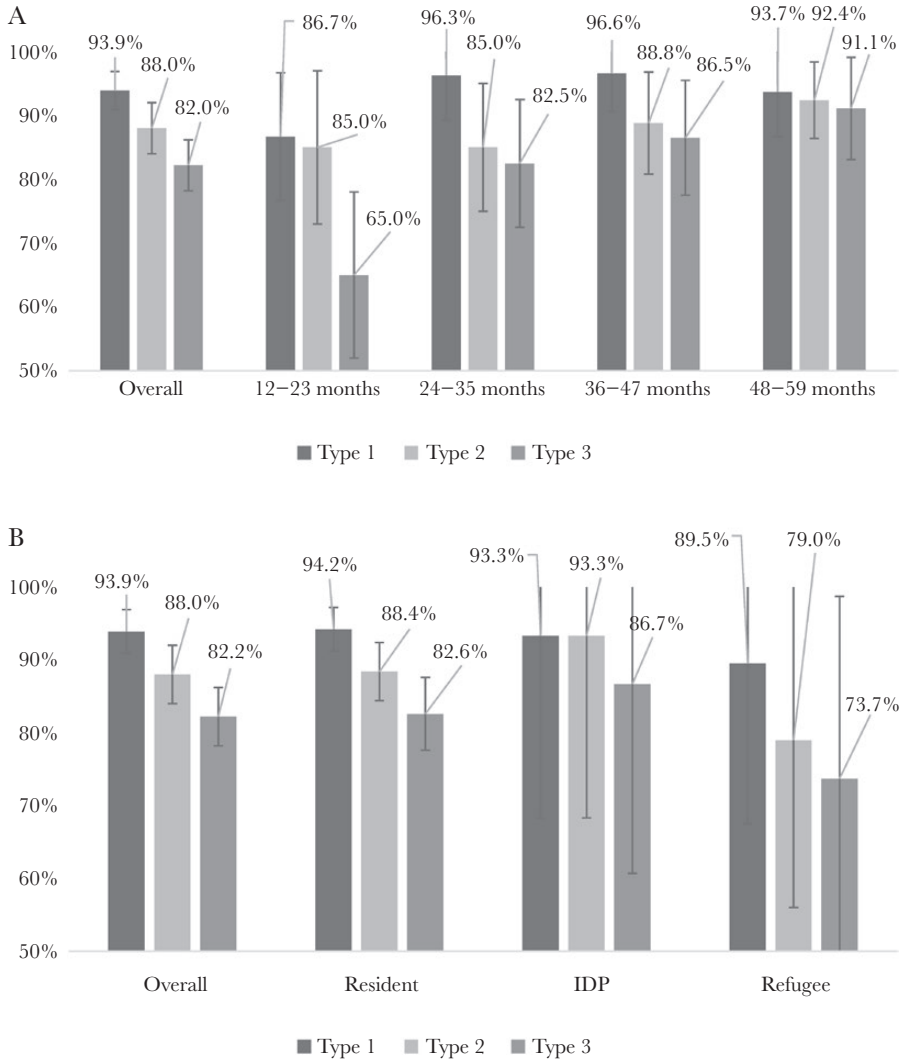

Figure 1. Seroprevalence of polio antibodies (95% confidence interval shown by error bars). A, Seroprevalence by age. B, Seroprevalence by residency status. Abbreviation: IDP, internally displaced people.

Trained phlebotomists generated dried blood spots (DBS) on Whatman 903-tm cards using the finger prick technique [24]. The DBS cards were shipped to the Centers for Disease Control and Prevention (CDC) in Atlanta and tested for the presence of poliovirus-neutralizing antibodies using standard neutralization assays [24]. Seropositivity was defined as reciprocal titers of poliovirus-neutralizing antibodies ≥8. The highest reported antibody titer was 1:1448. Titers were reported on a $\log_2$ scale.

Seroprevalence against all 3 poliovirus types was expressed as percentages with 95% confidence intervals. Seroprevalence was compared across the age groups using the chi-square test for trend. Seroprevalence was also associated with important risk factors using the chi-square test. *P* values <.05 were considered significant. Distribution of titers was presented using median for all 3 serotypes. Analysis of data was carried out using R, version 3.6.0 [25].

RESULTS

In total, 504 structures were visited, and 322 children enrolled; all caretakers consented to participate. In 3/322 (0.9%) children, the DBS was not collected due to refusal by the child, and 10/322 (3.2%) DBS did not have sufficient blood for analysis, resulting in 309/322 (95.9%) children included in the analysis.

The median age was 36 months, and 156/309 (50.5%) participants were female. The majority of children, 275/309 (89%), were residents of Diffa province, 19/309 (6.3%) were refugees, and 15/309 (4.9%) were internally displaced persons in our sample (Table 1).

A vaccination card was available for 80/309 (25.9%) children. The median number of doses of any type of OPV was reported to be 3, and 60/71 (84.5%) had a documented history of IPV. Chronic and acute malnutrition was observed in 122/301 (40.5%) and 57/299 (19.1%) children, respectively (Table 2).

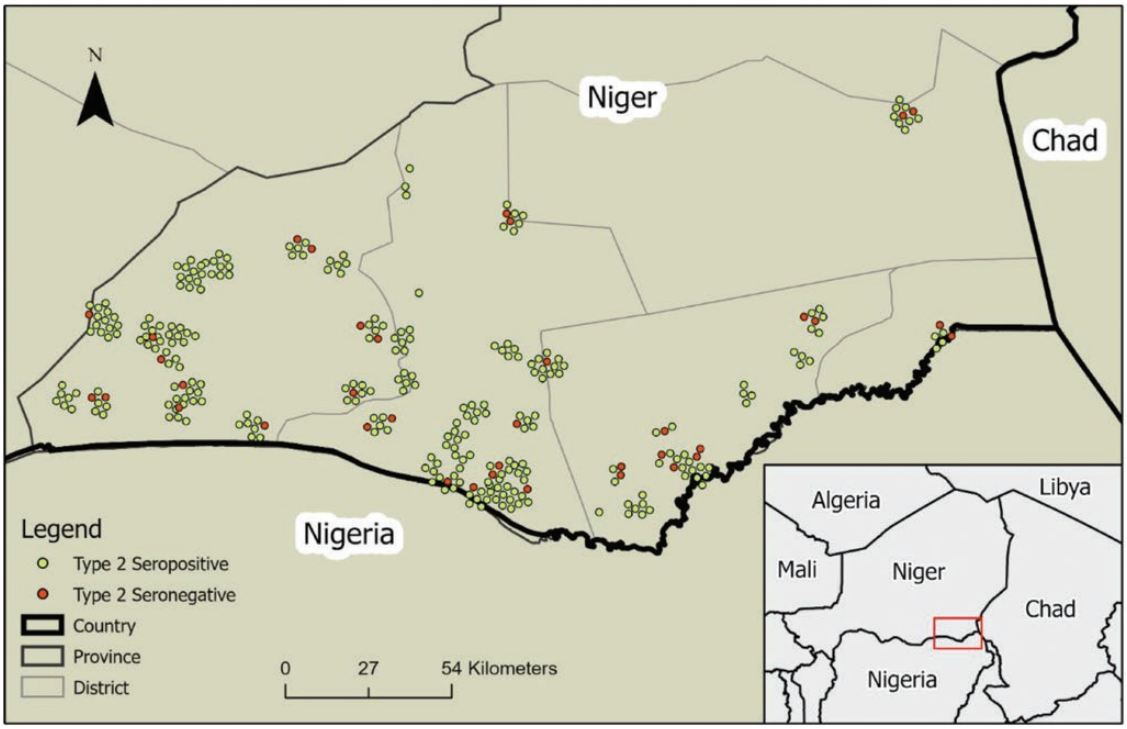

Figure 2. Geographic distribution of type 2 positive and negative study subjects (red dots: location of houses with type 2–seronegative children; green dots: location of houses with type 2–seropositive children).

Parents of all 309 children reported that their children received a dose of mOPV2 in the vaccination campaign that had been carried out in the weeks before the survey.

Seroprevalence of polio antibodies was 290/309 (93.9%), 272/309 (88.0%), and 254/309 (82.2%) for serotypes 1, 2, and 3, respectively. For serotypes 1 and 2, seroprevalence did not significantly change with age ($P = .09$ and $P = .44$, respectively); for serotype 3, seroprevalence increased with age (from 65% in 1–2-year-olds to 91.1% in 4–5-year-olds; $P < .001$). There were no significant differences found in seroprevalence between refugees, internally displaced people, or fixed residents (Figure 1A and B). Type 2–seronegative children were distributed throughout the study area. (Figure 2).

The median reciprocal titers of polio antibodies expressed on $\log_2$ scale were 8.51 (95% CI, 8.17–8.51), 6.83 (95% CI, 6.34–7.17), and 6.83 (95% CI, 6.51–6.83) for types 1, 2, and 3, respectively; the titers did not significantly change with age for any serotype (Figure 3).

We analyzed risk factors for type 2 seronegativity (Table 3); however, in the univariate analysis, we did not find any factors significantly associated with type 2 seroprevalence.

CONCLUSIONS

In the study area of the Diffa province, mOPV2 campaigns, immunity induced by OPV2 strains or possibly cVDPV2, and IPV in routine immunization were successful in raising type 2 antibody seroprevalence to nearly 90% in children 12–59 months old, regardless of residence status, location, or socioeconomic status. This is reassuring and suggests that in Diffa the campaign coverage with mOPV2 is high and the routine immunization program is functional in providing IPV-induced protection against poliovirus type 2. Seroprevalence for type 1 was 93%, and for type 3 it was 82%, surpassing the national coverage estimates of the third bOPV dose of around 80% [11].

We observed increasing seroprevalence for type 3 with age (from 65% in 12–23 months to 91.1% in 48–59 months). This may be explained by exposure to the higher number of bOPV mass vaccination rounds that have been carried out in Niger since 2016; between January 2016 and June 2019, 2 tOPV and 11 bOPV campaigns were conducted in the Diffa region. On the other hand, antibody titers show no significant change with age for any serotype.

We have not identified any risk factors significantly associated with seroprevalence, and we observed that seronegative children were spread in the study area without apparent clustering. This provides evidence that the vaccination activities did not miss any distinct populations in this area. Unlike a previous report from Pakistan that found an association between chronic malnutrition and lower seroprevalence, we did not observe malnutrition to be a risk factor [26].

Our study had some limitations. Long delay in laboratory testing of the DBS samples made it difficult to provide timely feedback to the polio program in Niger. Further, we did not collect

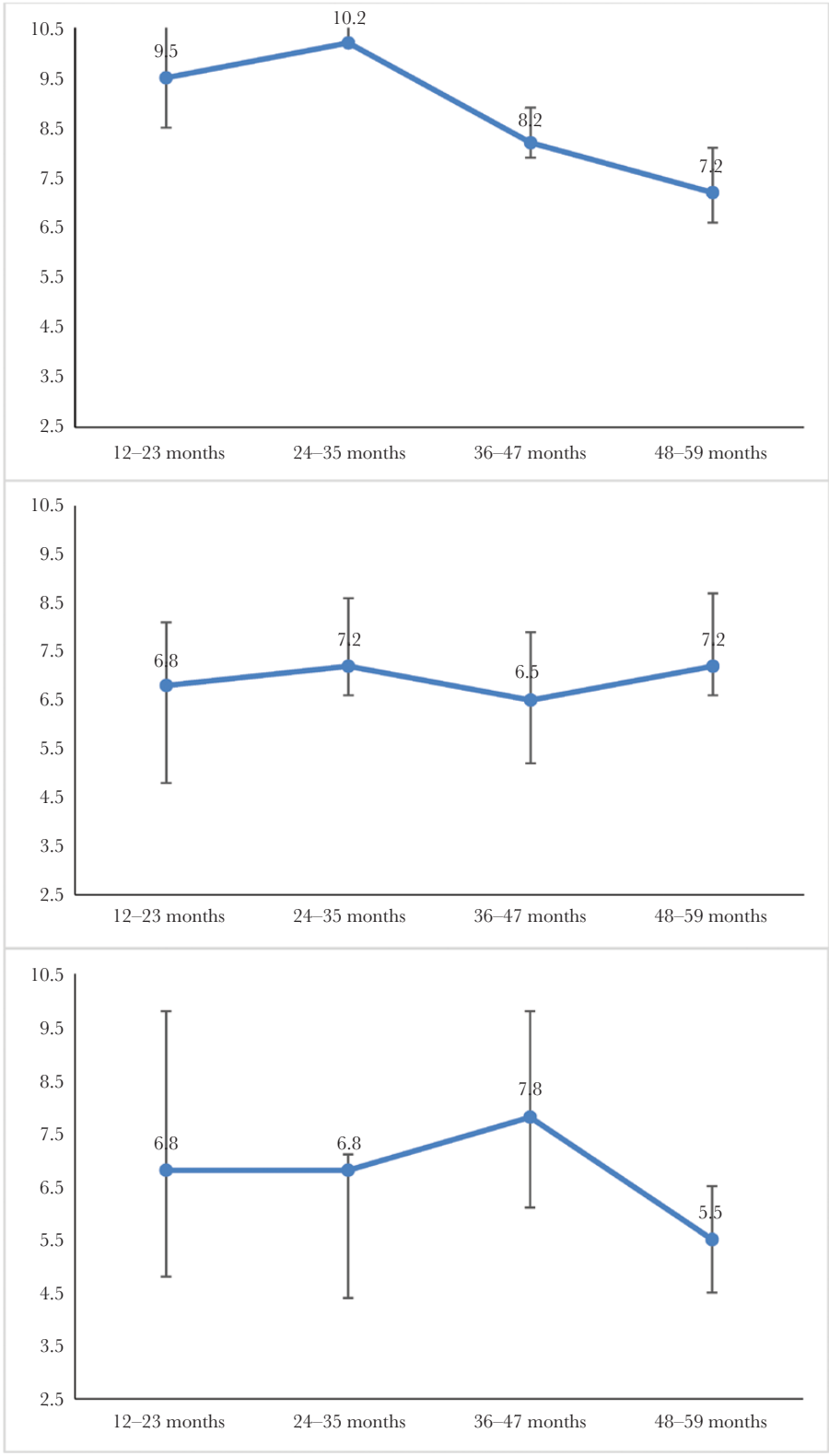

Figure 3. Median reciprocal titers of antipolio antibodies (log2 scale, 95% confidence intervals indicated by error bars). A, Serotype 1. B, Serotype 2. C, Serotype 3.

vaccination history by recall, and therefore we have vaccination history only from a subset of children whose parents kept vaccination cards (~25%); however, the vaccination history recorded in vaccination cards is similar to national coverage estimates. In reporting the total number of OPV doses received, we were unable to distinguish what type of OPV was administered. Further,

Table 3. Risk Factors for Type 2 Seronegativity (Univariate Analysis)

Factor	Type 2 Seroprevalence if Factor Present, %	Type 2 Seroprevalence if Factor Absent, %	*P* Value
Gender female	88.5	87.6	.41
Born after switch from tOPV to bOPV (April 2016)	86.5	91.0	.13
Age <2 y	85.0	88.8	.21
Being a refugee	79.0	88.7	.12
Documented history of IPV	91.4	90.9	.63
Chronic malnutrition	85.3	89.6	.26
Acute malnutrition	94.7	86.2	.08
Access to latrine (vs defecation in open)	89.3	85.9	.50
Water source (running water vs rest)	92.9	87.8	.57

Abbreviations: bOPV, bivalent oral poliovirus vaccine; IPV, inactivated poliovirus vaccine; OPV, oral poliovirus vaccine; tOPV, trivalent oral poliovirus vaccine.

waning of antibodies and exposure to cVDPV2 might have biased the relationship between vaccine intake and seroprevalence.

With type 2 seroprevalence close to 90%, the risk of emergence of new cVDPV2 outbreaks in Niger is low; however, the risk of cVDPV2 importations from neighboring countries leading to limited local transmission exists. In the past, Niger has been able to rapidly stop cVDPV2 outbreaks before they have chance to spread more widely with a series of high-quality vaccination campaigns. Therefore, Niger should maintain its polio outbreak response readiness capacity and further strengthen its routine immunization program.

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Patient consent. The patients' written consent was obtained, and the design of the work was approved by the Niger National Ethics Committee for Health Research and the Public Health Ethics Consultative Group at the World Health Organization.

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