

# Polio Modeling and Data Analysis Report

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*Nigeria*

## **EMOD Polio Team, Global Good**

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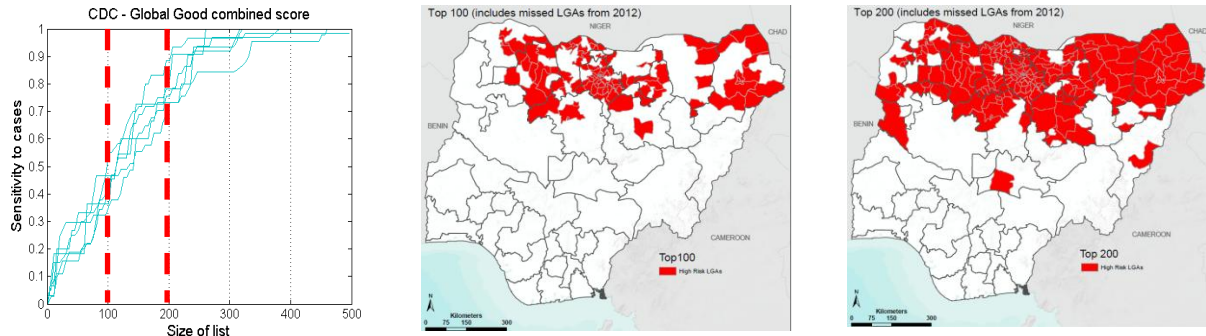
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### **Summary**

- We review the predictive power of the CDC/Global Good very-high-risk and high-risk lists, since their creation in April 2012, and show their sensitivities to be better than previous estimates.
- We evaluate the concordance of independent monitoring (IM) with lot-quality assessment sampling (LQAS). We show that IM is biased and highly discordant with LQAS, but we find indications that IM may have recently begun to improve.
- In the context of recent efforts to improve SIA quality, we quantify the gains in SIA coverage achieved by poor-performing LGAs in northern Nigeria over the past 3 years using LQAS data. In 2010, these LGAs were achieving 27% to 55% SIA coverage; they are now achieving 54% to 70%.
- We suggest a modification to the LQAS lot selection strategy which would reduce the uncertainty of SIA coverage estimates, and would be more effective at detecting poor-performing LGAs.
- We evaluate immunity trends using non-polio AFP samples dose history, and compare them with force of infection and invasion threshold estimates. While all northern states have seen an increase of immunity in average since 2010, however, in some states the immunity for worst performing LGAs have dropped this year and more attentions are needed to focus on those LGAs.
- A preliminary analysis of historical poliovirus genetic sequences suggests novel causal links between cases, and outlines how phylogenetic analysis may provide information about the dynamics of polio transmission across large geographical distances.

### **Performance of CDC-Global Good combined High Risk LGA List**

During the first quarter of 2012, we collaborated with the CDC and WHO to combine in-country expertise, the CDC model, and our vulnerability scores into a single, optimal risk score. The CDC utilized a logit model (GEE) to account for repeated measures over time and predict cases based on previous WPV case presence, as well as campaign measurements such as 0-dose fraction, and percent of missed children; our model focused on estimating past immunity based on dose histories from non-polio AFP samples and campaign history. The two risk scores were linearly combined to maximize the predictive power, based on historical case data. From the combined score, a very-high-risk (VHR) list and a high-risk (HR) list were created, including 100 and 200 LGAs respectively (see **Figure 1**).



**Figure 1.** (A) Proportion of the polio cases occurring in areas identified as high-risk using the CDC/Global Good combined risk score. Each turquoise line represents the sensitivity of the CDC/GG combined risk score methodology. Multiple lines represent the historical validations over a 6-month period in the last 3 years. Sensitivity naturally increases with list size. (B-C) Location of top 100 and top 200 LGAs (from the CDC/GG/WHO presentation to NPHCDA on April 23, 2012).

Based on the line list of cases as of September 7, 2012, 60 WPV and 3 type 2 VDPV cases were identified in Nigeria in 2012. In **Table 1**, we present the detected fraction of new cases since the very-high and high-risk lists were created. The performance of the list is in accordance with previous historical validations (as shown in **Figure 1A**), with 66% of cases coming from LGAs in the top 100 list and over 91% of cases coming from LGAs in the top 200 list.

List	WPV (1+3)	VDPV2	Unpredicted areas
Nigeria VHR (Top 100)	40/60 (66.7%)	3/3 (100%)	Ikara, Kaduna (3) Batsari, Katsina (3) Mashi, Katsina (3) Mariga, Niger (2) Sandamu, Katsina (2) Birnin Kudu, Jigawa Buij, Jigawa Kuban, Kaduna Gassol, Taraba Makarfi, Kaduna Wamakko, Sokoto Karasuwa, Yobe
Nigeria HR (Top 200)	55/60 (91.6%)	3/3 (100%)	Mariga, Niger (2) Birnin Kudu, Jigawa Buji, Jigawa Gassol, Taraba

**Table 1.** Fraction of polio cases predicted by the high-risk list after the March data drop (as of September 7, 2012), and infected areas which were not predicted by the very-high-risk and high-risk lists.

## Concordance between IM and LQAS

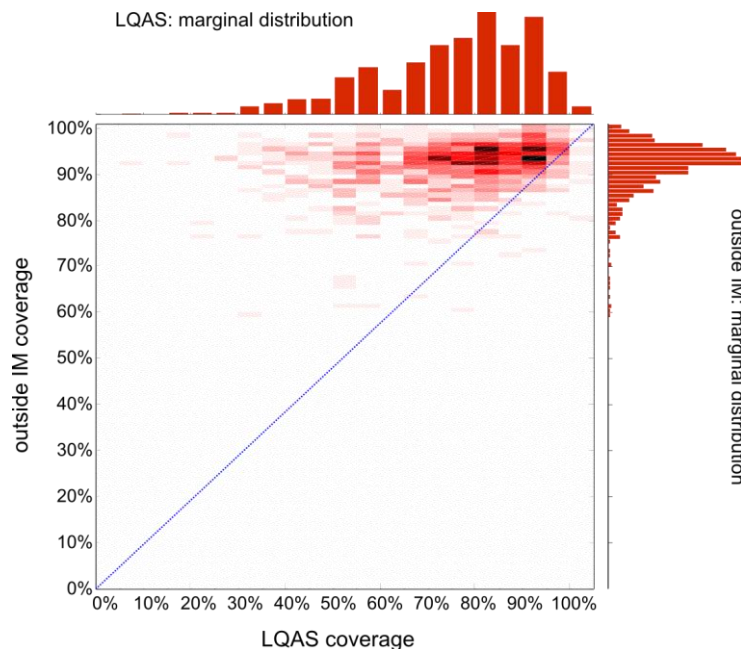
### Overview

Independent monitoring (IM) was designed to be an indicator of the quality of vaccination campaigns, and to help identify poor performing areas. However, in many districts, polio cases continued to be detected even when independent monitoring indicates that vaccination campaigns are of high quality. In order to study this discordance, Nigeria began to collect lot-quality assessment sampling (LQAS) in November 2009.

In this section, we analyze the concordance between independent monitoring and lot-quality assessment sampling, and we find the two to be strongly discordant throughout the northern states. We also study this concordance over time and find that IM may have recently begun to improve; the next campaigns should allow us to be more conclusive on this topic. However, even if the recent improvements are sustained, independent monitoring remains highly discordant with LQAS and should not be used to determine where to collect LQAS.

### Results

In order to measure the concordance between IM and LQAS, we matched 865 of the 894 LQAS lots collected in Nigeria, since November 2009, with the corresponding out-of-house IM result (from the same LGA). In Error! Reference source not found.2, we plot the number of times a given LQAS-IM coverage pairs appears in the data set. The marginal distribution of IM and LQAS coverage values are shown to the right and above the graph respectively.



**Figure 2** – Two-dimensional histogram of IM-LQAS coverage pairs, collected between 2010 and 2012. The frequency of observations is presented on a color scale: the more frequent a specific IM-LQAS pair,

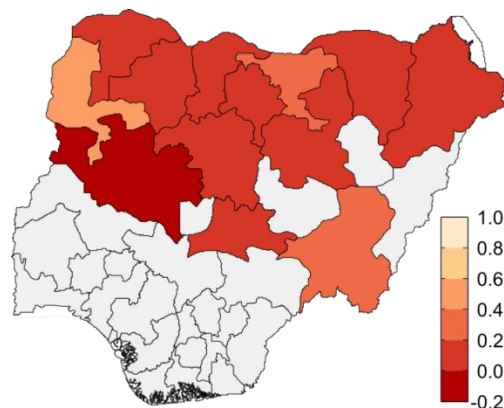
the darker the shade of red. The histograms of the LQAS and IM coverage data are shown in the margins.. If IM was an unbiased indicator of coverage, it would lie along the diagonal (blue) line.

IM coverage is strongly biased upwards compared to LQAS. 87% of the matched LQAS lots had lower coverage than the corresponding out-of-house IM coverage. If IM was unbiased, this fraction would be 50%. IM thus systematically underestimates the fraction of missed children during vaccination campaigns.

Little information is gained about coverage from IM results. For example, if out-of-house IM reports coverage above 90%, there is a 48% chance that LQAS will report a covered fraction below 80%, and a 15% chance that LQAS will report a covered fraction below 60%. Thus, good coverage reports through IM provide little to no assurance that the underlying SIA quality was actually sufficient.

The degree of concordance between IM and LQAS can be measured using correlation coefficients. For example, across the 865 matched IM-LQAS lots, the Pearson correlation coefficient is 23% and the Spearman rank correlation coefficient is 20%. IM thus capture only 23% of the LQAS variance.

As shown in Error! Reference source not found.3, this discordance between IM and LQAS is not restricted to a few states, but is equally pervasive throughout the North; Kebbi and Jigawa states are marginally better, but Niger state is worse.

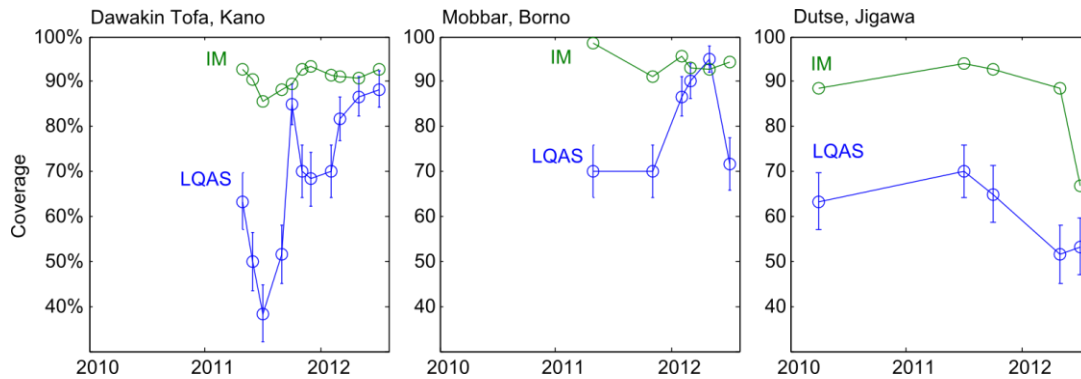


**Figure 3** - Concordance of outside independent monitoring with lot-quality assessment in Northern Nigeria. Pearson correlation is used as a measure of concordance: perfect concordance has a coefficient of 1, no concordance has a coefficient of 0, and negative coefficients correspond to anti-concordance. Only the states with sufficient data are presented. Poor IM-LQAS performance is seen approximately across all northern states.

Trends in coverage, as asserted by LQAS, will not necessarily be detectable by IM. As shown in Error! Reference source not found.5, IM failed to detect the three most statistically coverage increase trends uncovered by LQAS.

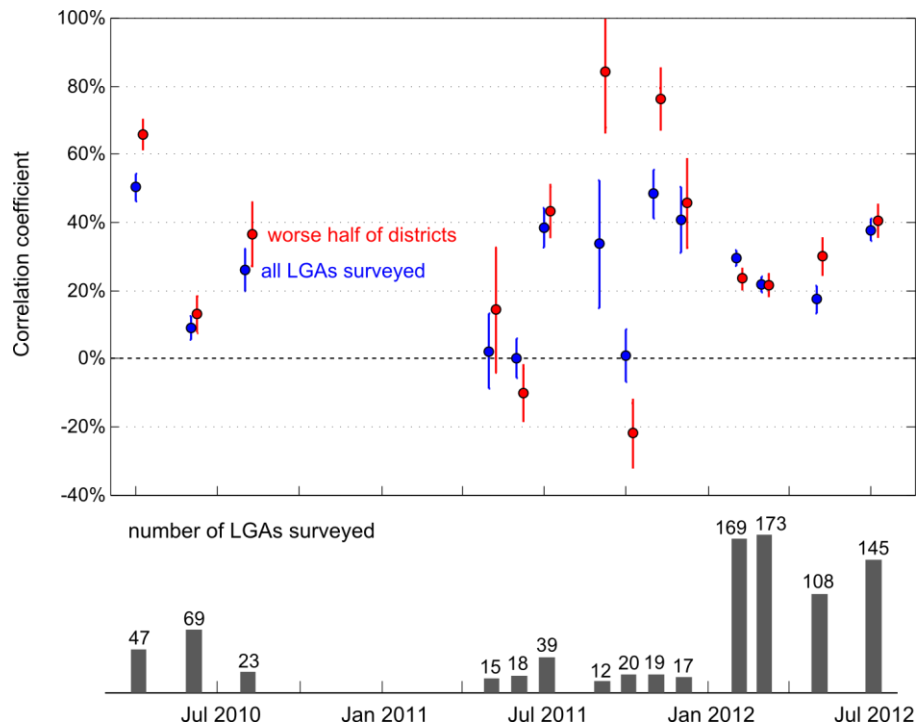
Tracking the concordance between IM and LQAS over time can be useful to assess the impact of recent efforts to improve the reliability of IM. In **Figure 4**, we show the evolution of the IM-LQAS correlation, per SIA, since 2010. Blue circles represent the Pearson correlation coefficient between the LQAS lots

collected during a specific SIA and the corresponding out-of-house IM coverage. The error bars are the standard deviation of the correlation coefficient distribution when alternate LQAS coverage are calculated by sampling a beta distribution parameterized using the number of missed children for each LQAS lots. Red circles are similarly calculated except that the analysis is restrained to the worse half of the districts, as determined from LQAS data.



**Figure 5** - Strongest, most statistically certain, trends in LQAS data are inconsistent with the (outside) IM data from the same LGAs.

As shown in **Figure** , no clear trend can be detected prior to the 2012 scale up of LQAS. Since February 2012, the correlation between IM and LQAS has been stable, although there is indication that the correlation in the worse performing districts has been improving since the March campaign. We can confirm the robustness of these findings by monitoring the IM-LQAS correlation in future campaigns.



**Figure 4** - Evolution of the concordance between (outside) IM and LQAS; for Nigeria since November 2009. Concordance is measured using the Pearson correlation coefficient. Blue circles represent the IM-LQAS correlation averaging over all LGAs surveyed, while the red circles is this correlation for worse 50% of the districts surveyed (as asserted by LQAS). No clear trend can be detected prior to the 2012 scale up of LQAS. Since March, correlation between IM and LQAS appears stable between when averaging across all LGAs, but the worse performing districts show a clear upward trend in concordance.

## Tracking SIA quality and LQAS lot selection strategy

### Overview

As an accurate, albeit not very precise measure of vaccination coverage, lot-quality assessment samples can be used to evaluate other measures of coverage (e.g., independent monitoring or non-polio AFP), to track the quality of vaccination campaigns, and to estimate population immunity.

By tracking the vaccination coverage achieved, we can evaluate the impact that programmatic changes (e.g., intensification of the microplanning process, use of GPS/GIS in some states, the change in team composition, or the staff surge) may have on the quality of vaccination campaigns. Additionally, by summing the individual impact of campaigns over time, it is possible to estimate population immunity and evaluate the risk of ongoing transmission.

Our analysis of LQAS data from northern Nigeria shows that quality is increasing in multiple states. However, we found that the current lot-selection strategy for LQAS could be made more effective at detecting poor-performing districts if lots were collected both in LGAs categorized as very high-risk (within the top 100 CDC/GG list) and in all the other LGAs.

## Methods

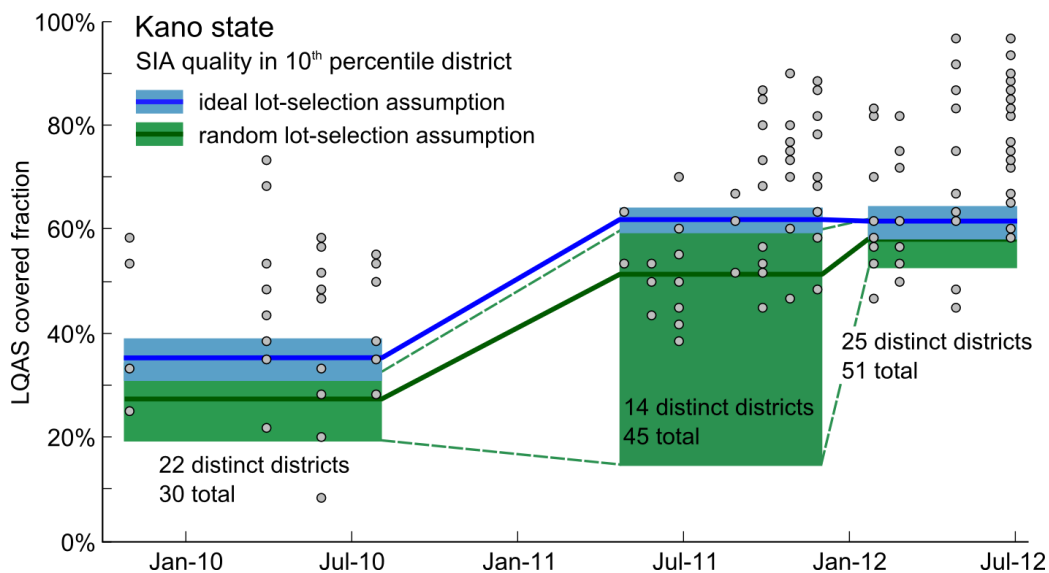
Tracking quality is more effective at state level than at district level because more lots are available for analysis; in the 10 northern states, the median number of times an LGA has been measured using LQAS is 2, while the median number of lots a state has received is 65. Furthermore, inferences can be made about the distribution of lots at the state level which allow us to estimate what SIA coverage poor, median, and good performing districts are achieving without focusing on any specific LGA.

Poor-performing districts with a history of WPV transmission, which have not attained vaccination coverage (SIA quality) sufficiently high to interrupt transmission, pose the greatest risk to eradication. While the exact number of poor-performing districts which would prevent eradication is situation specific, we tentatively estimate this threshold fraction to be the 10% worst performing LGAs, and focus on what the 10<sup>th</sup> percentile districts are achieving.

The set of distinct LGAs measured from a state can be taken as samples from a finite set. Multiple LQAS lots from the same LGA are combined to reduce the uncertainty of the coverage estimate. From this set of measurements, a coverage for each LGA is generated by sampling a beta distribution parameterized from the total number of missed children and the total number of children sampled in that LGA. The resulting list of coverage, one coverage value per LGA, is ordered and the 10<sup>th</sup> percentile coverage and its 90% confidence interval are calculated using the hypergeometric probability distribution function. This process is repeated to average over the uncertainty of the LQAS coverage estimates.

Historically, the LGAs where LQAS is conducted have been chosen based on the high-risk list so as to focus on poor performers. However, this is not a guarantee that all poor performers will be found since the list has limited predictive power. In order to put bounds on the effect of this selection strategy, we calculate the 10<sup>th</sup> percentile coverage first while assuming that the lot-selection strategy has been ideal, i.e., the LGAs measured were the worst performing (the high-risk list had perfect predictive power). Then, for comparison, we assume that the lot-selection strategy was equivalent to random selection of LGAs (the high-risk list had zero predictive skill). The currently used lot-selection strategy is somewhere between these two bounds.

In **Figure 6**, these two scenarios are compared in estimating what SIA coverage poor performers in Kano state have achieved in the last 3 years. The ideal lot-selection estimates coverage are about 10% larger than the random lot-selection estimates. The most important difference however is the greater uncertainty under random lot-selection assumption, in late 2011. This uncertainty can be significantly reduced by increasing the number of distinct districts measured, even without increasing the total number of lots collected, as seen for the 2012 period.



**Figure 6** - Tracking SIA quality using LQAS under different lot selection strategies. The blue line represents what SIA coverage 10<sup>th</sup> percentile performers would be achieving if the selection of lots was ideal, whereas the green line represents what they would be achieving if the selection of lots was random. The green and blue rectangles represent the 90% confidence interval around the estimated value. Note that the blue rectangles are overlaid above part of the green rectangles; the green dashed lines show where the 90% confidence interval end. The number of distinct districts and total number of lots used in each time interval is indicated on the figure.

## Results

In Table 2, we evaluate the SIA quality achieved by poor-performers in northern states in two periods, using the method presented above and the random lot-selection assumption. This shows that, over the last 2 years, these states have significantly improved what their poor-performing districts are achieving in terms of coverage. For example, the 10<sup>th</sup> percentile district in Kano used to cover approximately 27% of children during SIAs, while they are now covering approximately 58%. However, in many cases, there is significant uncertainty as to what the poor-performers are achieving due to the limited number of distinct districts which have been measured in those states. The precision achieved in estimates of coverage during the most recent period is due to the aggregation of 14 months of data. Bi-annual or quarterly estimates of SIA coverage would be less precise.

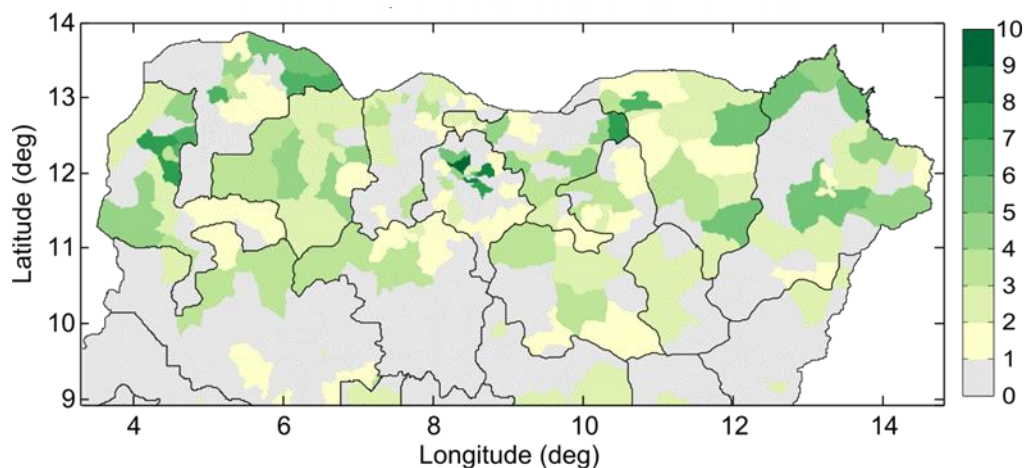
State	(rank /#LGA)	Nov 2009 – Aug 2010	May 2011 – Jul 2012
Kano	(5 <sup>th</sup> /44)	27% (19 - 34)	58% (53 - 61)
Borno	(3 <sup>rd</sup> /27)	48% (13 - 56)	67% (57 - 71)
Zamfara	(2 <sup>nd</sup> /14)	49% (38 - 55)	68% (61 - 71)
Yobe	(2 <sup>nd</sup> /17)	34% (24 - 41)	65% (58 - 69)
Jigawa	(3 <sup>rd</sup> /27)	26% (3 - 54)	54% (43 - 59)
Kebbi	(3 <sup>rd</sup> /21)		68% (60 - 74)
Bauchi	(3 <sup>rd</sup> /20)	50% (7 - 66)	70% (65 - 73)
Katsina	(4 <sup>th</sup> /34)	49% (19 - 62)	63% (54 - 69)



Kaduna	(3 <sup>rd</sup> /23)	44% (8 - 54)	70% (15 - 77)
Sokoto	(3 <sup>rd</sup> /23)	55% (10 - 66)	61% (14 - 69)

**Table 2** – Evolution of SIA quality in poor performing (10<sup>th</sup> percentile) districts of select northern states, over the last 3 years. Because there is a finite number of LGAs, the 10<sup>th</sup> percentile district must actually be a specific N<sup>th</sup> worst performer. For example, the 5<sup>th</sup> worst performer in Kano is equivalent to the 10<sup>th</sup> percentile performer, while in Zamfara, because there are only 14 LGAs, the 2<sup>nd</sup> worst is closest to the a 10<sup>th</sup> percentile performer.

Intrinsically, the sample size of 60 limits what coverage improvements can be detected through repeated measurements of the same LGA. In fact, of the 67 LGAs which have been measured with LQAS more than twice since November 2009, only 3 LGAs have shown a statistically significant trend in coverage. Most information about SIA quality is gained by the first LQAS lot conducted in a given LGA; additional lots provide less information. Extending the number of districts measured, by conducting LQAS in both poor-performing and well-performing districts would improve the amount of information which can be gained from analyzing LQAS data.



**Figure 7** - Distribution of LQAS lots collected since November 2009 in northern Nigeria. Number of lots collected is shown by a green color scale. Numerous districts have been measured often while others remain unsurveyed.

The high-risk list shows significant skill in predicting where cases will happen next and is thus a helpful tool in determining where to conduct LQAS. The downside of using only this list to select which LGAs to survey is that it leaves multiple LGAs unmeasured, as shown in **Figure 7**. Furthermore, an overly focal LQAS lot-selection strategy can lead to significant uncertainty in estimating coverage (see Figure 6, late 2011 period).

When using the top 200 very high-risk list to select where to collect LQAS, it is also preferable to treat all LGAs in the list equally and not to prioritize those with higher risk scores. Overall, all LGAs within this list have approximately equivalent risk of reporting cases. The low-risk LGAs which fall outside of this list should also be sampled, since they could become infected as well.

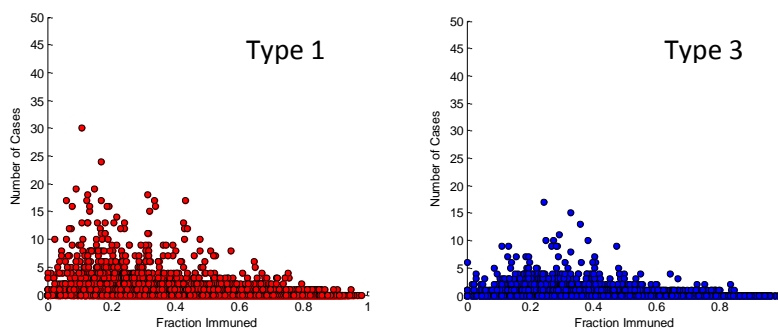
### Our LQAS lot-selection suggestions

1. Select the number of lots (N) to be collected in a given state so that it is proportional to twice its population in very-high risk districts (top 100) added to the population in all other LGAs. This will naturally focus on high-risk states while also providing lots in apparently low-risk areas.
2. If enough lots can be collected, all LGAs in northern states should be measured at least once every 6 months.
3. If not enough lots are available to conduct recommendation #2, then the following lot-selection strategy can be used:  
If a state has X LGAs within the very high-risk list (top 100) out of a total of Z LGAs, then the N lots to be collected should be separated as such between the two categories of LGAs:  
$$\frac{2X}{X+Z} N$$
 lots randomly distributed among the very high-risk list (top 100)  
$$\frac{Z-X}{Z+X} N$$
 lots randomly distributed among the LGAs outside of the very high-risk list
4. Once the number of lots per category has been determined, lots should be randomly selected within that category with a probability proportional to the population of the districts in the list.

### Invasion Threshold and Immunity Trends from NP-AFP samples

In epidemic models, invasion threshold, or force of infection defines the virus transmissibility, as well as the minimum immunity (herd immunity) required to protect the area. The question remains for estimating the appropriate herd immunity in the country, so that all high-risk LGAs were below the herd immunity so we won't miss them, but in the meanwhile, we are not selecting a R0 that is too high and too many LGAs were included.

In the GG outbreak vulnerability model, we calculated the invasion threshold using a data-driven approach, by observing the past outbreaks inside LGAs/districts as well as their immunity. Between Jan 2003 and Jul 2012, we calculated the immunity of each LGA each year based on non-polio AFP samples, and find the maximum unprotected immunity for infected LGAs with persistent transmission, defined as LGA having more than 2 annual polio cases. **Figure 8** shows the full scatter plot between annual type 1 WPV cases versus annual immunity level between 2003 and 2011. If we assume no transmission will persist above this threshold, this immunity then becomes the minimum protected immunity (aka. herd immunity) based on evidences from the past 8 years.



**Figure 8.** Relationship between type 1 (red) and type 3 (blue) immunity and number of cases annually for all LGAs in Nigeria. The plot contains data between Jan 2003 and Jul 2012. Invasion threshold, defined as maximum immunity having 2 or more cases, is around 80% for both cases.

In **Figures 9-11**, the immunity and number of cases over time was presented for northern states. For immunity, to distinguish protected/unprotected LGAs, we use red color to represent a district having 2 or more annual cases, and grey otherwise.

During 2003-2006 most states have seen a sharp decrease of immunity which results in a large number of cases. Since then, the improvement of the vaccine campaigns lead to an overall increase of immunity, especially after 2009. This year most states show a continuous increase of immunity, complimenting the recent efforts of the Program. However, in the meanwhile, it is noticeable that looking at the distribution of LGA immunity inside states, in some states the lowest immunity that the LGA has was lower than the previous years, and the distribution is wider compared to previous years. Besides, the overall immunity level for most LGAs is still below the global invasion threshold, making them still vulnerable to infection. We have listed a number of LGAs with significant immunity drops over the past year (>1%) and highlighted LGAs with significant immunity drops (>10%) in **Table 3**. Continuous efforts should be put on improving the vaccination campaign and coverage for low-immunity areas. Current or future monitoring data could be used as quality metric with a much faster turnaround, for example, LQAS results, dose history from LQAS samples.

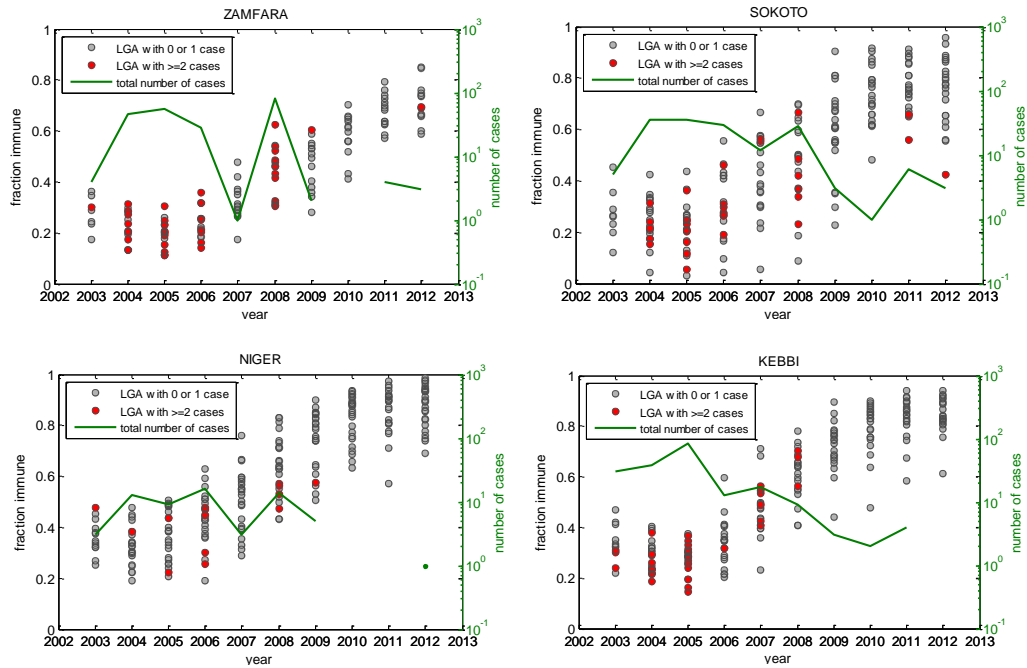
It is possible that the invasion threshold is different for different states, but under the current data, we are unable to evaluate and calculate the exact threshold by state, given the inadequate number of high immunity LGAs, for example, in Zamfara or Kano as shown in the figures below. In this case, it is safer to assume the global invasion threshold for those states to make sure we don't miss high-risk areas, even if the actual threshold might be lower.

State	LGA
Bauchi	Alkaleri, Damban, <b>Itas/Gad</b> , Tafawa-B
Borno	<b>Askira/u</b> , Gubio, Kukawa, Maiduguri, <b>Monguno</b> , Ngala
Jigawa	Gwaram
Kaduna	Birnin Gwari, Chikun, Giwa, Kaduna North, Sabon Gari
Kano	Albasu, Bagwai, Dala, Gabasawa, Garko, Minjibir, <b>Rimin Gado</b> , Takai
Katsina	<b>Dan Musa</b> , Malumfashi, Mani, Rimi, Safana
Kebbi	Birnin Kebbi, Fakai
Sokoto	Gwadabaw, Kware, Rebah, Shagari, <b>Sokoto North</b> , Sokoto South, Wamakko, Yabo
Yobe	<b>Damaturu</b> , Fune, Karasuwa

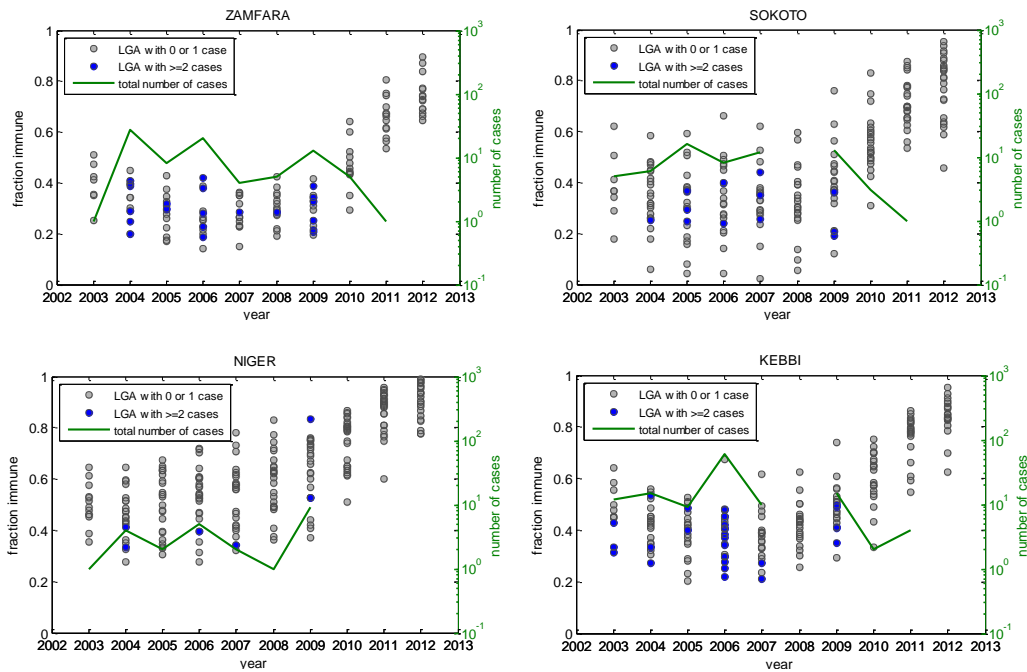
Zamfara	Bukkuyum, Gusau, Zurmi
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**Table 3.** VHR/HR LGAs with recent immunity drops ( $\geq 1\%$ ) for type 1 or type 3. LGA in red indicates significant immunity drops over the past year ( $>10\%$ ).

### Type 1

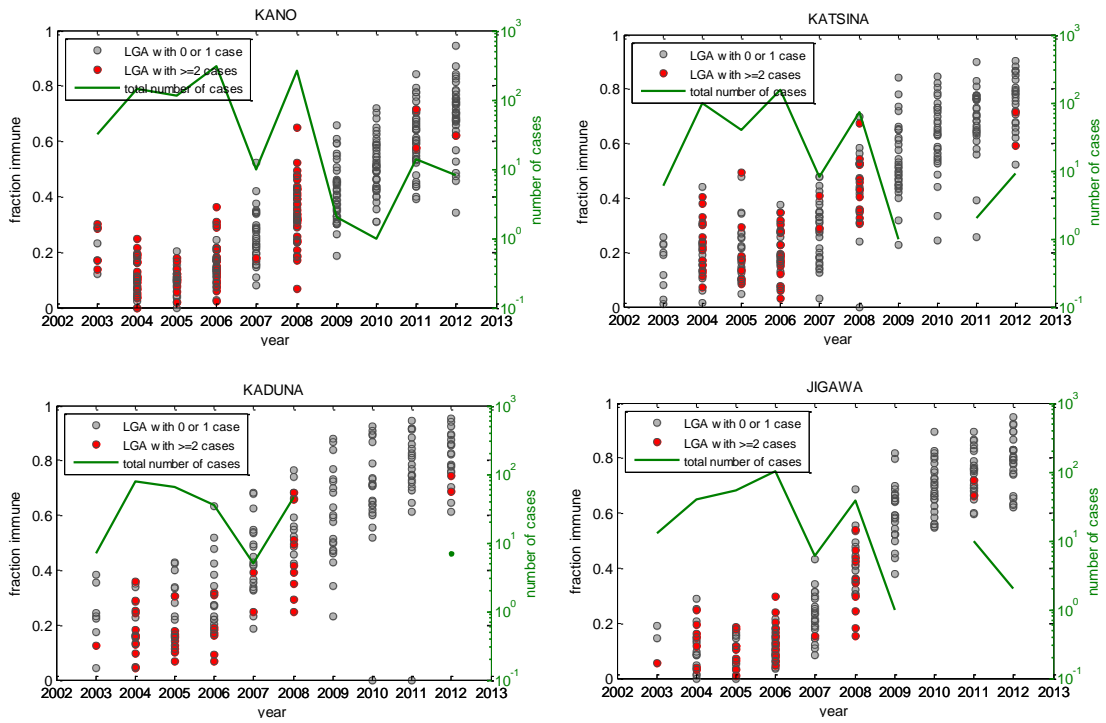


### Type 3

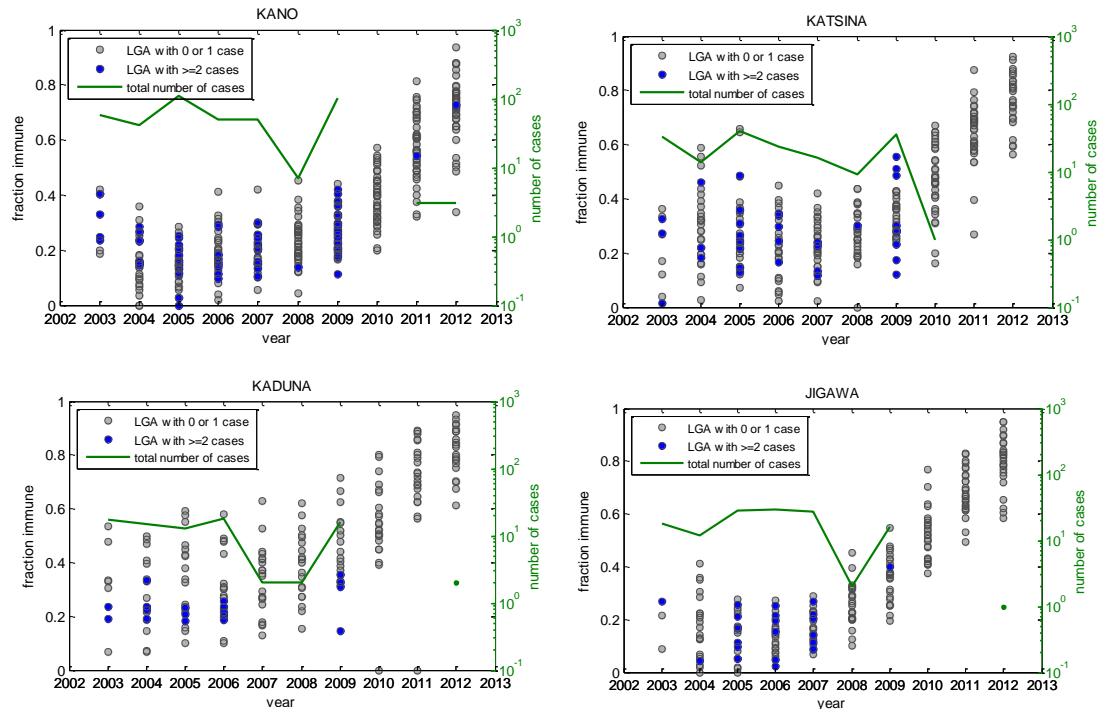


**Figure 9.** Type 1 and Type 3 Immunity changes over time for all LGAs in the state, as well as number of type 1 WPV cases in the state, Northwest (NW) Region

### Type 1

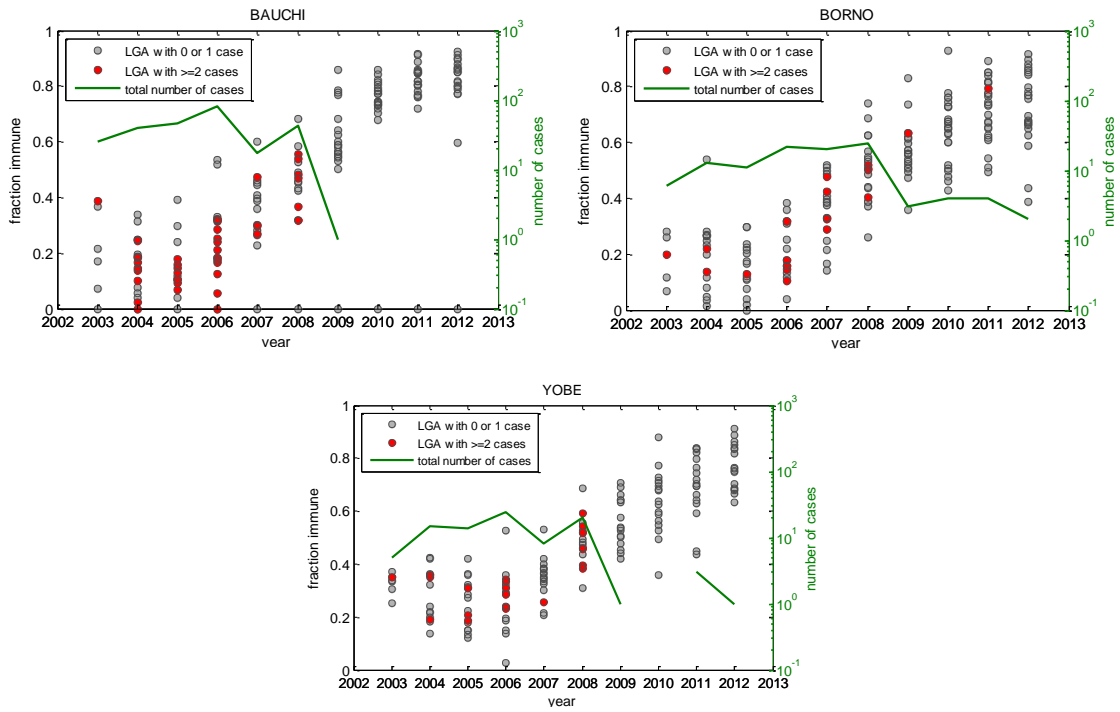


### Type 3

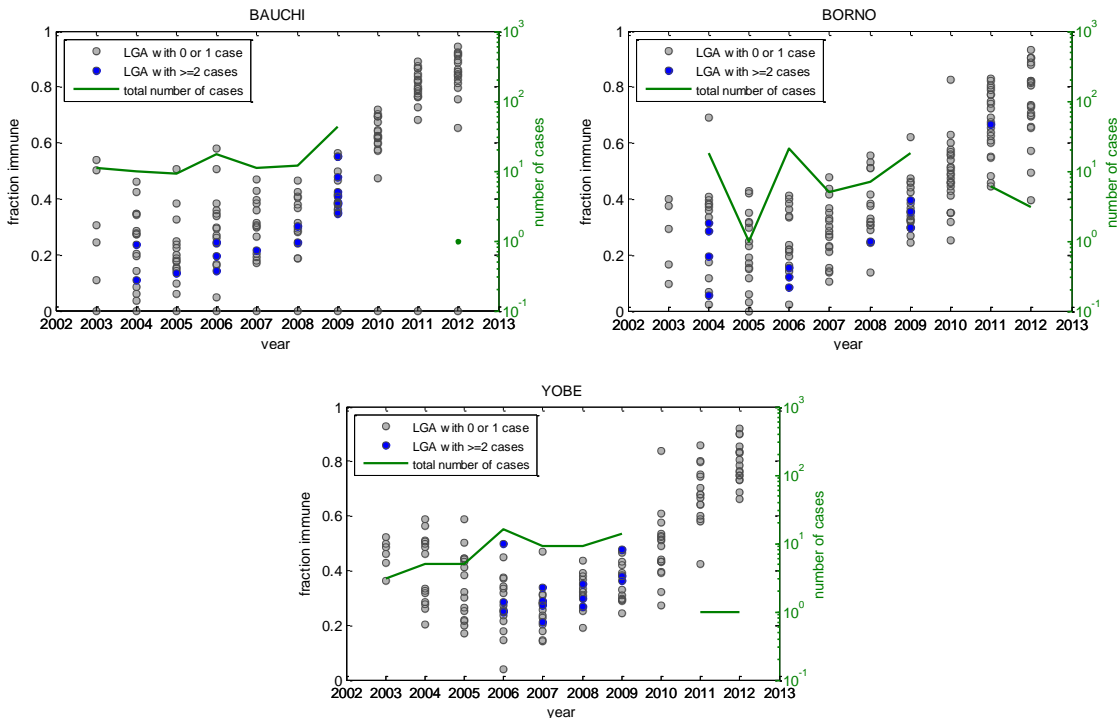


**Figure 10.** Type 1 and Type 3 Immunity changes over time for all LGAs in the state, as well as number of type 1 WPV cases in the state, North Central (NC) Region

### Type 1



### Type 3



**Figure 11.** Type 1 and Type 3 Immunity changes over time for all LGAs in the state, as well as number of type 1 WPV cases in the state, North East (NE) Region

## Identify spatial clusters and transmission pathways from poliovirus genetic sequences

To improve the accuracy of our risk analysis, it is necessary to identify the transmission pathways that enable polio circulation. By analyzing historical poliovirus sequences, we are working to reconstruct historical patterns of transmission. Observed cases provide information about where and when virus is circulating, and the phylogenetic analysis of the sequences provides evidence for hidden causal links between cases. We are working to identify epidemiologically-relevant population clusters and to identify the most frequent and recent transmission paths. Our goal is to eventually incorporate the results of our analysis into our models to better account for the role geographical mixing plays in determining overall outbreak risk.

Our planned next steps are:

1. Identify historically well-mixed population clusters at the subnational scale.
2. Reconstruct historical transmission events and identify transmission pathways between geographic areas at the sub-national and local, epidemiologically-defined scales.
3. Estimate effective reproduction numbers and variations of the force of infection within and between well-mixed populations.
4. Construct a migration model that separates transmission dynamics from local disease dynamics. We will correlate the inferred local mixing and transmission structure with existing information about transportation networks and local poliovirus incidence and prevalence

While our methodologies are still being developed, our results will derive from correlating genetic similarities between cases with information about demographics, immunity, vaccination history, disease dynamics, and poliovirus mutation dynamics. The information we obtain about spatial structure is being used to improve models of importation and corresponding outbreak risk due to coupling between regions. It may also be useful for future SIA planning by enabling more precise estimation of where cases are likely to appear next given current cases. Estimates of the effective reproduction number may also provide information about population immunity and may be useful for assessing surveillance quality.

### Preliminary Results

Currently we are analyzing the relationships among cases of wild types 1 and 3 and cVDPV type 2 from Nigeria that occurred between the start of 2003 and March 1, 2012. Progress is being made on points 1, 2, and 3 above. Below are examples demonstrating the information available from the sequenced cases.

### Summary

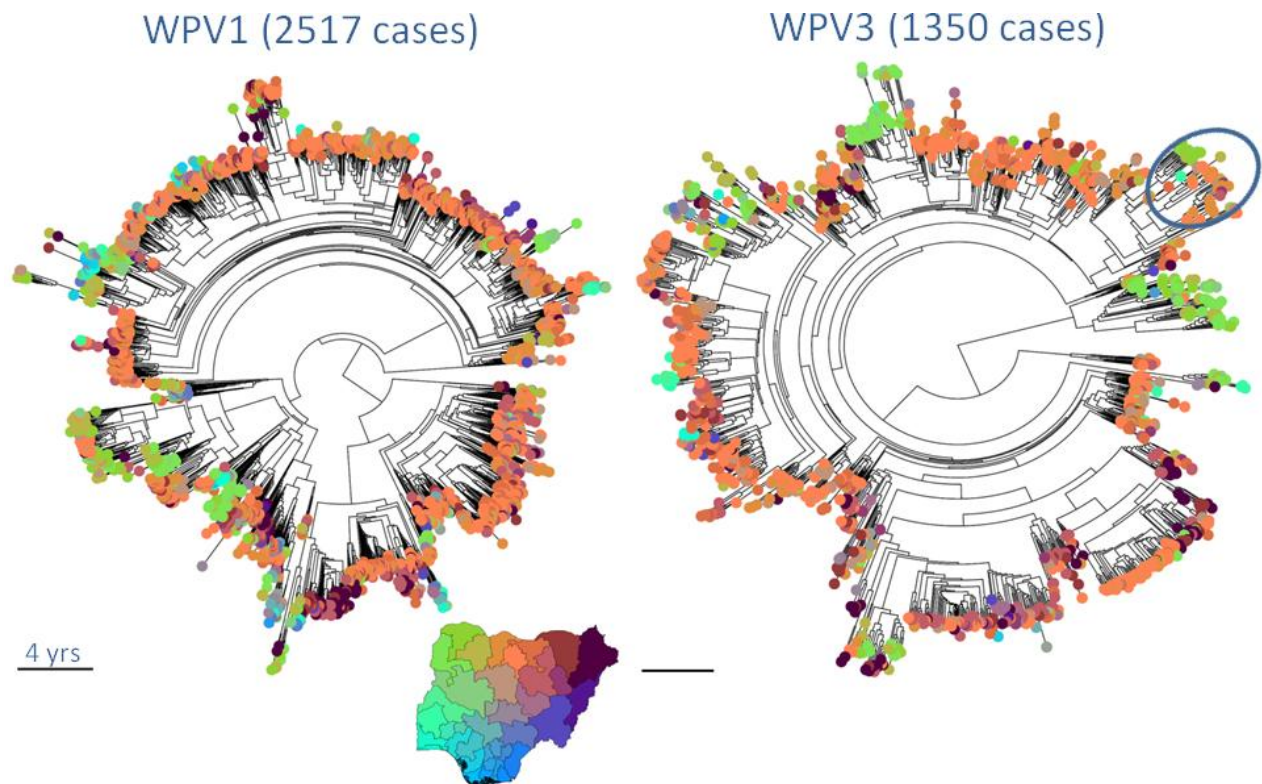
The genetic relationships define clusters of cases. The largest clusters group cases over multiple years and correspond to different regions of the country. Cases that are linked within a cluster indicate persistent endemic circulation in a region and links between clusters indicate times and potential routes of transmission. On shorter timescales, cases linked over a year or less are indicative of individual transmission events between LGAs. By reconstructing probable transmission events and correlating them with estimates of population immunity and vaccination coverage, we aim to derive a finer understanding of local transmission and historical campaign successes and failures, and that information



will be useful for optimizing future success. Additionally, the detailed historical record provides a high-resolution reference for calibrating our detailed, individual-based polio model.

### Hierarchical Cluster Analysis

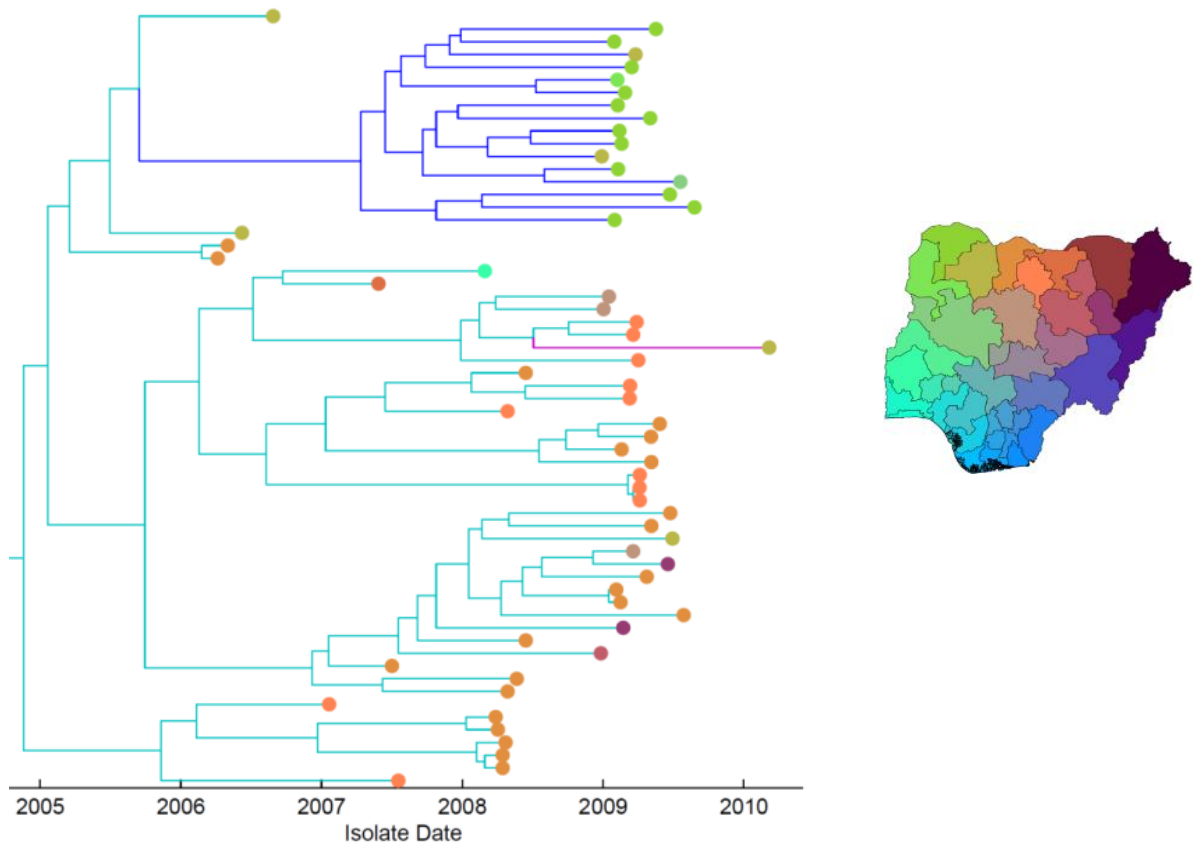
**Figure 12** shows the inferred phylogenetic tree for the 2517 cases of WPV1 and 1350 cases of WPV3 that we have isolates for from January 2003 through March 1, 2012. Genetic similarity among cases is indicated by the length of the paths through the branches that connect them: cases with more similar viral sequences have shorter paths. Branch lengths are inferred from the number of nucleotide mutations between cases and the known mutation rate the using a standard Bayesian model for the coalescent process. One can see that spatial location correlates with genetic similarity.



**Figure 12.** Phylogenetic tree showing the relationships among wild-type cases in Nigeria. Leaves (dots) indicate individual paralytic polio cases and are colored by state. Branch lengths indicated estimated time between nodes (branch intersections). The coalescent times of internal nodes—the times of common ancestors between cases—are inferred times of unobserved viral ancestors through which observed cases are linked. The circled subset of the WPV3 tree is shown in Figure 12.

The genetic relationships become more informative when we zoom in to a finer resolution. **Figure 13** shows the circled section of the WPV3 tree from Figure 1. Branches of the tree are clustered to highlight ancestral relationships: each cluster contains cases with common ancestry approximately 4 years deep at most. This sub tree shows two archetypal types of structures. In the Northwest, there is an outbreak of cases in early 2009 arises from an estimated importation date (time to earliest ancestor) near the start of 2007. Also shown is the genetic lineage of an endemic sub strain of WPV3 virus in Kano and Katsina from which cases are observed over a multi-year period. In addition, we see an example of a

likely transmission pathway. The outbreak in the Northwest has its two nearest links to Zamfara in early 2006, which are in turn most closely linked to cases in Kano. Note that the timing of the cases is consistent with at least 3 years of silent transmission from Kano, through Zamfara, and into Kebbi and Sokoto (which likely reintroduced infection to Zamfara leading to its cases in 2009). We also see an orphan case in Zamfara in 2010 that is most closely related to infection in Kano. Multiple examples of long periods of silent transmission may indicate surveillance limitations in Kano prior to 2009.

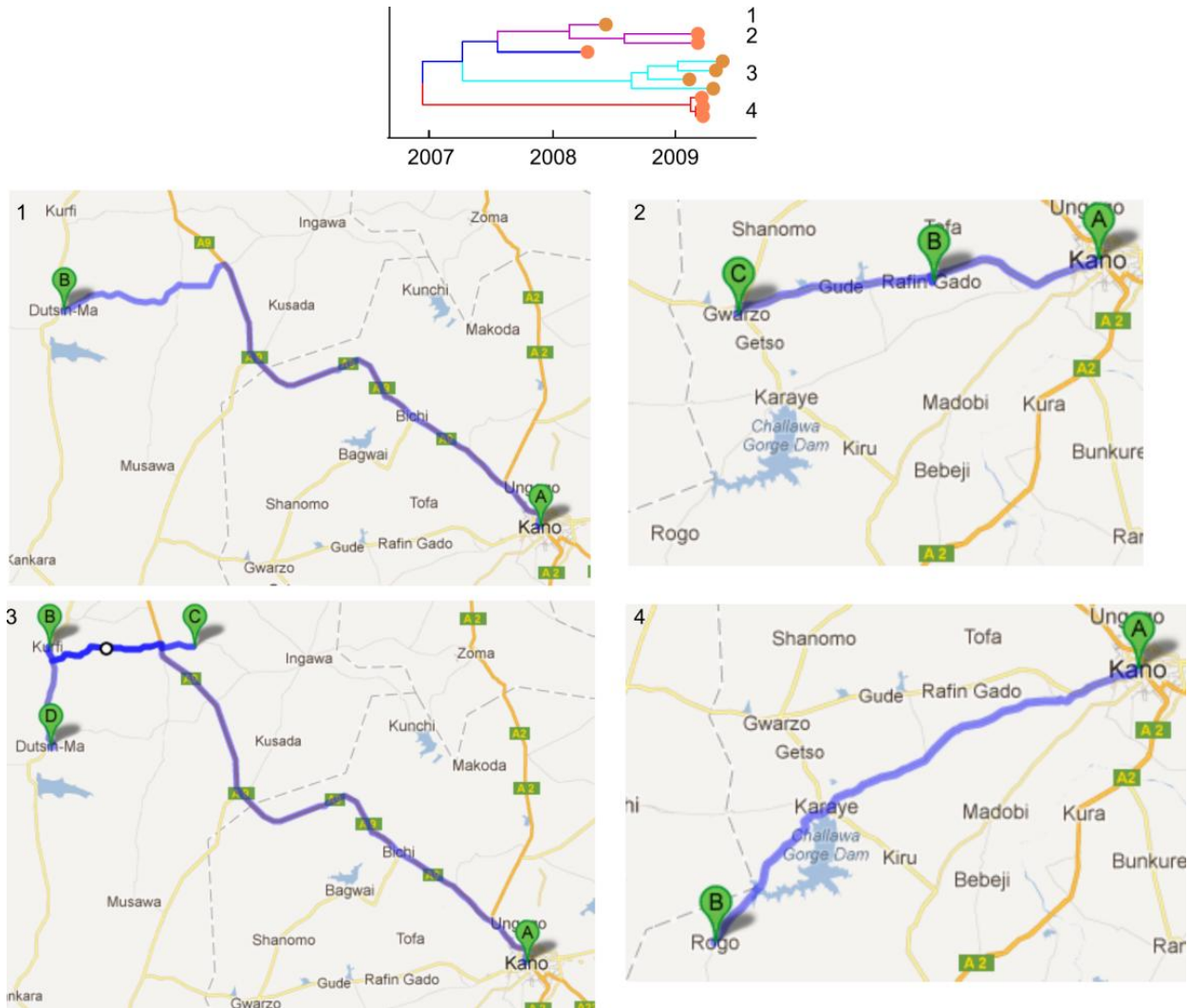


**Figure 13.** WPV3 sub tree showing an outbreak in the Northwest, endemic infection in Kano and Katsina, and a late orphan case in Zamfara. We observe transmission within and between well-mixed subnational populations (mixing pools) over multiple years. Tip colors represent the geolocation of cases by state, and colors on the lineages represent the clustering of cases.

### Identifying historical transmission events at the LGA level

In **Figure 14**, we focus on the purple cluster in **Figure 12**. Out of the 1350 sequenced cases of AFP due to WPV3, the 11 cases shown below are more closely linked to each other than they are to any others, as is determined by the similarities of their genetic compositions. Combined with the timing and location of the cases, we can infer probable transmission events. Over the three year period shown, a sub-strain of WPV3 circulated in Kano. In 2008—2009, this circulating virus sourced cases in Kano and nearby LGAs. The earliest case in this subtree occurs in mid-2008 in Fagge, Kano. Because Kano city is the largest population center in the region, it is likely that this earliest case is representative of the source population. From Kano, there are likely four transmission events represented by this data. In 2008 and again in 2009, infection propagates outward toward Dutsin-Ma and neighboring towns (panels 1 and 3).

In addition, in 2009, there are two distinct and approximately simultaneous transmissions toward Gwarzo and Rogo (panels 2 and 4). Without the phylogenetic relationships, the simultaneity and geographic nearness may suggest one larger outbreak spanning Gwarzo and Rogo, but the depth of the common ancestor between the Gwarzo and Rogo cases is evidence for separate transmissions sourced from a larger common pool.



**Figure 14.** A subset of the cluster in Figure 2, clustered at a depth of 1 year. This example indicates that there was a sub-strain of WPV3 circulating in Kano city over a roughly three year period that sourced four outbreaks along three different transportation routes. Tip colors represent the geolocation of cases by state, and colors on the lineages represent the clustering of cases.

## Appendix

### Immunity and Coverage Estimates from AFP database

The non-polio AFP records in the database were used as random samples to assess population immunity. We used all non-polio AFP samples from 2 years before to time of interest. The length was chosen to balance the need between having enough samples and reflecting recent immunity changes. Average immunity coverage is calculated for all non-polio records during this period.

Population immunity was estimated based on approximate number of doses of tOPV, or mOPV for a non-polio AFP sample, and per-dose seroconversion rates. Since the database only records the total number of SIA doses, we divide the remaining number into the approximate number of doses for each type by looking at different types of SIA campaigns performed from date of birth to date of onset. Per-dose polio seroconversion rates were calculated for mOPV and tOPV, from [1].

Past year routine immunization coverage was found through the recorded routine doses in non-polio samples. The SIA exposure rate is the average SIA coverage ratio over a certain period, calculating the fraction between SIA dose history in non-polio samples and the actual number of campaigns performed in the district. The coverage for a district is calculated by a weighted average for all AFP cases which overlap with the period we are interested in.

### Reference

[1] Jenkins HE, *et al.* (2010) Implications of a circulating vaccine-derived poliovirus in Nigeria. *New England Journal of Medicine* 362(25):2360-2369.