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Measles immunity among pregnant women aged 15–44 years in Namibia, 2008 and 2010[☆]



Cristina V. Cardemil^{a,*}, Anna Jonas^b, Anita Beukes^c, Raydel Anderson^d, Paul A. Rota^d, Bettina Bankamp^d, Howard E. Gary Jr^b, Souleymane Sawadogo^c, Sadhna V. Patel^c, Sikota Zeko^b, Clementine Muroua^b, Eseguel Gaeb^e, Kathleen Wannemuehler^a, Sue Gerber^c, James L. Goodson^a

^a Centers for Disease Control and Prevention, Global Immunization Division, 1600 Clifton Road, NE, Atlanta, GA 30333, USA

^b Ministry of Health and Social Services, Directorate of Special Programmes, Primary Health Directorate, and Family Health Division (Expanded Programme on Immunizations), Windhoek, Namibia

^c Centers for Disease Control and Prevention, Windhoek, Namibia

^d Centers for Disease Control and Prevention, Division of Viral Diseases, Atlanta, GA, USA

^e Namibia Institute of Pathology, Windhoek, Namibia

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SUMMARY

Background: Namibia experienced a large measles outbreak starting in 2009, with 38% of reported cases in adults, including women of reproductive age. Population immunity was assessed among pregnant women to determine whether immunization activities were needed in adults to achieve measles elimination in Namibia.

Methods: A total of 1708 and 2040 specimens sampled from Namibian pregnant women aged 15–44 years who were included in the 2008 and 2010 National HIV Sentinel Survey, respectively, were tested for measles immunoglobulin G antibody. The proportion of women seropositive overall and by 5-year age strata was determined, and factors associated with seropositivity were analyzed by logistic regression, including age, facility type, gravidity, HIV status, and urban/rural setting. Seropositivity in 2008 versus 2010 was compared.

Results: In both analysis years, measles seropositivity was lower in 15–19-year-olds (77%) and 20–24-year-olds (85–87%) and higher in 25–44-year-olds (90–94%) (2008, $p < 0.001$; 2010, $p < 0.001$). Overall measles seropositivity did not differ between 2008 (87%) and 2010 (87%) ($p = 0.7$). HIV status did not affect seropositivity.

Conclusions: Late in a large measles outbreak, 13% of pregnant women in Namibia, and almost one in four 15–19-year-old pregnant women, remained susceptible to measles. In Namibia, immunization campaigns with measles-containing vaccine should be considered for adults.

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1. Introduction

Globally, the number of reported measles cases decreased by 73% from 2000 to 2014.¹ In the World Health Organization (WHO) African Region, estimated measles deaths decreased during this period by 86%; nonetheless, outbreaks continued to occur in this

region and accounted for 73 914 cases and an estimated 48 000 deaths in 2014, representing 42% of the global measles mortality burden.¹

In the pre-vaccine era, measles was primarily an illness affecting children, and infection in young adults and during pregnancy was uncommon, estimated to occur in 6 per 100 000 pregnancies.^{2,3} However, as measles vaccine coverage increased in countries, the chance of measles virus exposure in childhood decreased substantially and the age at onset of disease shifted to include young adults and women of reproductive age.^{4–6} During 2009–2010, measles outbreaks in a number of African countries demonstrated this shift in measles epidemiology, characterized by cases occurring among older children and young adults.⁴

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* Corresponding author. Tel.: +1 404 639 8241; fax: +1 404 417 0962.
E-mail address: iyk8@cdc.gov (C.V. Cardemil).

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Namibia, a country in southwestern Africa, has an estimated population of 2.1 million.⁷ In 2014, Namibia had an HIV prevalence among adults aged 15–49 years of 16.0%, one of the highest in the world,⁸ and high compared with other countries in the Sub-Saharan Africa region.⁹ Routine measles vaccination at 9 months of age began in 1983, before independence from South Africa.¹⁰ WHO and United Nations Children's Fund estimates of coverage among 12–23-month-olds with the first dose of measles-containing vaccine in Namibia decreased from 76% in 1989 to 58% in 2001, ranged from 63% to 76% during 2002–2012, and increased to 83% in 2014.¹⁰ In addition to vaccination through routine immunization services, periodic measles supplementary immunization activities (SIAs) have been conducted every 3 years, starting in 1997, following the WHO-recommended strategy for measles mortality reduction, with reported administrative coverage of 90–104%.^{11,12}

From August 2, 2009 through February 2, 2011, a large measles outbreak occurred in Namibia, with 3256 laboratory-confirmed or epidemiologically linked cases.^{11,13} A distinguishing feature of this outbreak was that 38% of reported cases occurred among adults aged ≥ 15 years, including women of reproductive age. Measles cases in pregnant women in Namibia during this outbreak resulted in adverse maternal, fetal, and neonatal outcomes, including neonatal and maternal death.¹⁴ In response to the outbreak, outbreak response immunization (ORI) targeting children aged 6–59 months, regardless of previous measles vaccination, was conducted in seven districts in 2009–2010.¹³ ORI targeting all persons aged ≥ 6 months was implemented in February 2010 in Opuwo district, where the highest number of measles cases was reported during the outbreak,^{13,15} and ORI targeting persons aged 6 months to 35 years was conducted in three districts during May–June 2010.

To estimate measles population immunity in Namibian pregnant women before and late in the measles outbreak and to examine factors associated with seroprevalence (including HIV status), stored serum samples from the 2008 and 2010 national HIV surveys among pregnant women aged 15–44 years old were tested. It was reasoned that assessing the level of measles immunity in pregnant women in Namibia would provide substantial new knowledge towards understanding the level of susceptibility and the potential burden of disease in this population and would help guide immunization program activities needed in Namibia to achieve measles elimination.

2. Methods

2.1. National HIV Sentinel Survey

In 2008 and 2010, the Namibia Ministry of Health and Social Services (MoHSS) conducted a nationwide sentinel survey to estimate HIV prevalence in pregnant women aged 15–49 years. The survey was designed in accordance with the WHO standardized methodology for HIV prevalence surveys using convenient consecutive sampling of women attending antenatal clinic (ANC) service sites selected based on geographic representation from all regions and health districts, urban and rural clinics, areas with different population densities and sizes, and women of different socioeconomic status.^{16,17} All pregnant women aged 15–49 years were included in the survey if they attended an ANC for the first time during their current pregnancy, were not referred from another health facility, and agreed to a routine blood draw.

The 2008 survey enrolled 8174 women from all 34 districts, 35 main hospital sites, and 89 satellite health centers and clinics; 8024 (98.2%) enrollees had specimens collected during March 17 to July 31, 2008.¹⁷ The 2010 survey enrolled 7983 pregnant women from all 34 districts, 35 main hospitals, and 93 satellite health centers and clinics; 7888 (98.8%) enrollees had specimens

collected during March 22 to September 6, 2010.¹⁶ Most confirmed measles cases in the 2009–2011 outbreak occurred before the start of the 2010 survey (2519 of the 3256 confirmed cases, or 77%).¹³ In both surveys, unlinked, de-identified specimens were tested for HIV antibodies; all de-identified data fields were retained electronically (unique identification, district abbreviation and site number, facility type, date of ANC visit, woman's age, gravidity, town of residence, antiretroviral therapy participation, and counseling for prevention of maternal to child transmission). Specimens were stored at 4–8 °C at the Namibia Institute of Pathology (NIP) in Windhoek.

2.2. Laboratory testing

Laboratory testing to detect measles-specific immunoglobulin G (IgG) antibody was performed at the NIP in 2012, using an enzyme immunoassay (EIA) (Enzygnost, Siemens, Germany); the manufacturer's recommended standard operating procedures were followed. The manufacturer assigns specimens with corrected optical density (OD) values >0.2 as positive, specimens with values of 0.1–0.2 as equivocal, and specimens with values <0.1 as negative. However, these classifications are designed for testing individuals and not population studies.¹⁸ Using the quantitative evaluation recommended by the manufacturer, sample assays in the equivocal range resulted in titers ranging from 149 to 342 mIU/ml, which are higher than the accepted protective antibody concentration of 120 mIU/ml.^{19,20} As a result, specimens with OD ≥ 0.1 were considered to be positive, which is consistent with previous studies suggesting the antibody levels in the equivocal range are protective against measles.^{18,21,22} Positive, equivocal, and negative specimens are reported separately, but analyses were conducted using a combined grouping of positives and equivocals compared to negative specimens. Specimens that tested equivocal were retested as per the manufacturer's instructions, and if the result was confirmed, samples were classified as equivocal, otherwise as positive or negative.

To monitor the performance of the EIA assay, an in-house positive control for measles IgG was included on every EIA plate in addition to the controls supplied by the manufacturer. A 5% random sample of specimens was tested at the Centers for Disease Control and Prevention (CDC) in Atlanta, USA, for quality assurance; testing was found to be highly concordant with that at NIP (data not shown).

2.3. Sample size calculations

To estimate measles antibody seroprevalence within each 5-year age group with a desired precision of $\pm 5\%$, it was determined to be necessary to test 428 specimens in each age group, assuming a seroprevalence of 50%, probability of achieving the desired precision of 0.95, and 10% loss due to specimens not found or inadequate for testing. The number of specimens in the 45–49 years age stratum was too few to result in meaningful estimates and these samples were excluded. The number of specimens in the 40–44 years age stratum was fewer than the target, so all specimens were sampled. To control for the distribution of HIV-infected women within each age group, the target sample size was allocated to the HIV-positive and HIV-negative groups based on the observed distribution in the ANC sentinel survey.^{16,17}

2.4. Statistical analyses

A seroprevalence estimate and 95% confidence interval (CI) using the Wilson score method were calculated for each 5-year age group in each analysis year and within the following sub-populations: urban/rural setting, HIV status, gravidity, facility type (hospital, health center, or clinic), and health district. For each

analysis year, multiple logistic regression calculated the odds of seropositivity (positives and equivocal vs. negatives) while controlling for age group, urban/rural setting, HIV status, gravidity, and facility type. For the comparison of measles seroprevalence before and late in the outbreak in 2008 and 2010, the analysis was restricted to those birth cohorts present in both 2008 and 2010, and adjusted for the age they would have been in 2008, calculating an adjusted odds ratio (OR) for difference by year. All analyses included sampling weights, which were calculated based on the probability of selection of a specimen within each of the 12 age and HIV status strata from all specimens collected, and adjusted for non-response (i.e., specimens unavailable or inadequate for testing) in each of the strata by the propensity cell adjustment method. These weights were then scaled to the total sample size: (weight/sum of weights) × total sample. A large percentage of specimens were unavailable or inadequate for testing. However, demographic information was available for all women sampled, so multiple imputation was conducted using chained equations to impute seropositivity; the imputed results were compared with estimates based on available data. As the imputed estimates were not substantially different from the estimates based on the complete non-missing data, only the laboratory results from complete specimens tested are reported. The multiple imputations were done using the mice package in R statistical software version 3.1.2. Other data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Comparisons of seroprevalence among groups and between analysis years were calculated using the Mantel–Haenszel and Chi-square tests on the weighted data. This study received ethical approval from the CDC and the Namibia MoHSS.

3. Results

Of the 2638 specimens collected in 2008 that were selected for inclusion in the study, 1708 (64.7%) were tested (Table 1); 443 (16.8%) were unavailable, 437 (16.6%) had insufficient volume, one (0.04%) was hemolyzed and could not be used for laboratory testing, and 49 (1.9%) were missing the measles IgG laboratory result. Of the 2692 specimens collected in 2010 that were selected for inclusion in the study, 2040 (75.8%) were tested (Table 2); 389 (14%) were unavailable, 230 (8%) had insufficient volume, 29 (1%) were hemolyzed and could not be used for laboratory testing, and four (0.1%) were missing the measles IgG laboratory result. No substantial differences in the demographics of persons whose specimens were not tested and those of persons whose specimens were tested and included in the analysis was found, by age group, urban/rural setting, or gravidity (data not shown). A larger proportion of HIV-positive (74%) than HIV-negative (27%) specimens collected in 2008 were unavailable for testing; this was likely due to prior use of these specimens in antiretroviral resistance studies. Of the specimens collected in 2010 that were available for testing, no difference was observed in the proportion of HIV-positive (24%) and HIV-negative (24%) specimens.

Overall measles seroprevalence (positives and equivocal) was 87% (95% CI 86–89%) in 2008 and 87% (95% CI 85–88%) in 2010 (Tables 3 and 4). Measles antibody seroprevalence increased with increasing age group in both analysis years; in 2008, seroprevalence was 77% for 15–19-year-olds and 91–93% for ≥25-year-olds ($p < 0.001$), and in 2010, seroprevalence was 77% for 15–19-year-olds and 94% for 40–44-year-olds ($p < 0.001$). Seroprevalence differed by gravidity in 2008 ($p < 0.001$) and 2010 ($p < 0.001$). No

Table 1
Target and observed sample sizes by age group and HIV status, among pregnant women aged 15–44 years, from the 2008 HIV Sentinel Survey, Namibia

Age group, years	HIV status	Total specimens	Target sample size	% of total specimens sampled	Observed sample size	% not tested (target – observed/target)
15–19	Positive	77	25	32	4	84
	Negative	1428	457	32	332	27
20–24	Positive	339	68	20	17	75
	Negative	2085	414	20	306	26
25–29	Positive	445	115	26	35	70
	Negative	1428	367	26	271	26
30–34	Positive	327	132	40	40	70
	Negative	877	350	40	245	30
35–39	Positive	193	127	66	42	67
	Negative	548	335	61	254	24
40–44	Positive	44	44	100	9	80
	Negative	204	204	100	153	25
All ages	Both	7995	2638	33	1708	35

Table 2
Target and observed sample sizes by age group and HIV status, among pregnant women aged 15–44 years, from the 2010 HIV Sentinel Survey, Namibia

Age group, years	HIV status	Total specimens	Target sample size	% of total specimens sampled	Observed sample size	% not tested (target – observed/target)
15–19	Positive	86	32	37	24	25
	Negative	1264	450	36	335	26
20–24	Positive	282	60	21	46	23
	Negative	1994	422	21	321	24
25–29	Positive	410	110	27	81	26
	Negative	1398	372	27	283	24
30–34	Positive	373	145	39	110	24
	Negative	871	337	39	259	23
35–39	Positive	222	144	65	115	20
	Negative	523	338	65	252	25
40–44	Positive	71	71	100	53	25
	Negative	211	211	100	161	24
All ages	Both	7705	2692	35	2040	24

Table 3
Measles seroprevalence among pregnant women aged 15–44 years, overall and by age group, HIV status, gravidity, and setting, from the 2008 HIV Sentinel Survey, Namibia

	Unweighted total, N	Weighted % positive	95% CI ^a	Weighted % equivocal	95% CI ^a	Weighted % negative	95% CI ^a	Weighted % positive and equivocal ^b	95% CI ^a	p-Value ^c
Overall	1708	76	74–78	11	10–12	13	11–14	87	86–89	
Age group, years										<0.001
15–19	336	61	56–66	16	12–20	23	19–28	77	72–81	
20–24	323	74	70–78	13	10–16	13	10–16	87	84–90	
25–29	306	80	76–84	11	9–15	8	6–12	91	88–94	
30–34	285	86	81–90	6	4–10	8	5–12	92	88–95	
35–39	266	90	84–94	3	1–7	7	4–12	93	88–96	
40–44	162	89	78–95	2	0–10	9	4–20	91	80–96	
HIV status										0.855
Positive	147	78	71–84	10	6–16	12	8–19	88	81–92	
Negative	1561	76	74–78	11	10–13	13	11–14	87	86–89	
Gravidity										<0.001
1	509	66	63–70	15	12–18	19	16–22	81	78–84	
2	349	80	76–84	10	8–13	10	7–13	90	87–93	
3	264	76	71–81	12	9–17	11	8–16	89	84–92	
4+	519	88	84–91	5	3–7	7	5–10	93	90–95	
Setting										0.509
Rural	758	77	74–80	11	9–13	12	10–15	88	85–90	
Urban	950	76	73–79	11	9–13	13	11–16	87	84–89	

CI, confidence interval.

^a Wilson score method.^b Equivocals treated as positive.^c Chi-square comparing negatives vs. the sum of positives and equivocals.**Table 4**
Measles seroprevalence among pregnant women aged 15–44 years, overall and by age group, facility type, HIV status, gravidity, and setting, from the 2010 HIV Sentinel Survey, Namibia

	Unweighted total, N	Weighted % positive	95% CI ^a	Weighted % equivocal	95% CI ^a	Weighted % negative	95% CI ^a	Weighted % positive and equivocal ^b	95% CI ^a	p-Value ^c
Overall	2041	74	72–76	13	12–15	13	12–15	87	85–88	
Age group, years										<0.001
15–19	358	56	51–62	21	17–26	23	18–27	77	73–81	
20–24	368	71	68–75	13	11–16	16	13–19	85	81–87	
25–29	364	77	73–81	13	10–16	10	8–13	90	87–92	
30–34	369	80	75–84	11	8–15	9	6–12	91	88–94	
35–39	367	88	82–91	6	3–10	6	4–11	93	89–96	
40–44	215	91	82–95	4	1–11	6	2–13	94	87–98	
Facility										0.362
Hospital	232	74	68–79	14	10–18	13	9–17	87	83–91	
Health center	301	72	67–77	12	9–17	16	12–20	84	80–88	
Clinic	1508	74	72–76	13	12–15	13	11–14	87	86–89	
HIV status										0.478
Positive	430	76	71–80	12	9–16	12	9–16	88	84–91	
Negative	1611	73	71–75	13	12–15	13	12–15	87	85–88	
Gravidity										<0.001
1	566	66	62–69	15	13–18	19	17–23	81	77–83	
2	396	75	71–79	13	10–16	12	9–15	88	85–91	
3	349	75	70–79	15	12–20	10	7–14	90	87–93	
4+	730	82	79–86	10	7–12	8	6–11	92	89–94	
Setting										0.060
Rural	1130	72	70–75	13	12–16	14	12–17	86	86–90	
Urban	911	76	73–78	13	11–15	12	10–14	88	83–88	

CI, confidence interval.

^a Wilson score method.^b Equivocals treated as positive.^c Chi-square comparing negatives vs. the sum of positives and equivocals.

significant differences were observed in measles seroprevalence by facility type, HIV status, or urban/rural residence in 2008 and 2010. When stratified by age group, no significant differences were observed in measles seroprevalence by HIV status (Table 5) or by gravidity (data not shown). A comparison of measles seroprevalence in 2008 versus 2010 found no significant difference between years (OR 1.04, $p = 0.711$).

Table 6 shows the results from the multivariable models for 2008 and 2010, calculating the odds of measles seropositivity while adjusting for age group, HIV status, facility type, gravidity, and urban/rural setting. In 2008 and 2010, women 20 years of age and older had higher odds of seropositivity compared with women 15–19 years of age (2008, $p = 0.002$; 2010, $p = 0.010$).

Table 5

Measles seroprevalence among pregnant women aged 15–44 years, by age and HIV status, from the 2008 and 2010 HIV sentinel surveys, Namibia

Age group, years	HIV status	2008			2010		
		Unweighted total, N	Weighted % positive and equivocal (95% CI ^a)	Mantel–Haenszel p-Value	Unweighted total, N	Weighted % positive and equivocal (95% CI ^a)	Mantel–Haenszel p-Value
15–19	Negative	332	77 (73–82)	0.279	334	78 (73–82)	
	Positive	4	25 (5–70)		24	67 (46–82)	
20–24	Negative	306	87 (84–90)		322	85 (82–88)	
	Positive	17	88 (72–96)		46	83 (71–90)	
25–29	Negative	271	92 (88–94)		283	90 (87–93)	
	Positive	35	91 (80–97)		81	89 (82–94)	
30–34	Negative	245	93 (88–96)		259	91 (86–94)	
	Positive	40	88 (72–95)		110	92 (85–96)	
35–39	Negative	254	93 (88–96)		252	93 (88–96)	
	Positive	42	90 (71–97)		115	94 (85–98)	
40–44	Negative	153	90 (79–96)		161	96 (87–99)	
	Positive	9	100 (44–100)		54	91 (70–98)	
					0.370		

CI, confidence interval.

^a Wilson score method.**Table 6**Logistic regression calculating the odds of measles seropositivity among pregnant women aged 15–44 years from the 2008 and 2010 HIV sentinel surveys, Namibia^a

	2008			2010		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Age group, years			0.002			0.010
15–19	Ref.			Ref.		
20–24	1.80	1.23–2.63	0.002	1.38	0.96–1.98	0.079
25–29	2.77	1.67–4.59	<0.001	2.09	1.31–3.35	0.002
30–34	2.76	1.43–5.32	0.002	2.92	1.30–4.05	0.004
35–39	3.02	1.36–6.73	0.007	3.21	1.54–6.70	0.002
40–44	2.12	0.72–6.28	0.172	3.72	1.22–11.35	0.021
Facility ^b						0.456
Hospital				Ref.		
Health center				0.80	0.48–1.32	0.373
Clinic				0.99	0.65–1.52	0.974
HIV status			0.307			0.286
Positive	Ref.			Ref.		
Negative	1.34	0.76–2.36	0.307	1.22	0.85–1.74	0.286
Gravidity			0.063			0.258
1	Ref.					
2	1.64	1.10–2.46	0.016	1.39	0.96–2.00	0.080
3	1.11	0.67–1.84	0.680	1.42	0.89–2.27	0.142
4+	1.62	0.89–2.94	0.114	1.48	0.88–2.49	0.139
Setting			0.387			0.067
Rural	Ref.			Ref.		
Urban	0.88	0.66–1.18	0.387	1.28	0.98–1.68	0.067

OR, odds ratio; CI, confidence interval.

^a Seropositive included both seropositive and equivocal.^b Data for facility type were not available in 2008.

Table 7 shows the results for measles seroprevalence by health district; in 2008, seroprevalence ranged from 57% to 98%, and in 2010, seroprevalence ranged from 69% to 98%.

4. Discussion

This is the first study of measles antibody seroprevalence in Namibia. Because 13% of pregnant women and almost one in four 15–19-year-old pregnant women remained measles-susceptible late in the outbreak in 2010, this study highlights a population of women and their offspring at risk of measles and its complications. As these women age and new birth cohorts are added to the population, if SIAs do not target these young adults, overall population measles susceptibility might increase from current levels. Conducting periodic seroprevalence surveys in areas at high risk of outbreaks could be valuable for identifying geographic areas and sub-populations with low measles immunity. An indication of

results from these surveys, along with vaccination coverage data and case-based surveillance data, provide evidence for guiding age-specific vaccine introduction strategies as well as determining target age groups for SIAs. The findings of this study, together with other data sources such as surveillance data, should help guide ORI and SIA planning, including expanding target age groups beyond children when indicated, to reach the ≥93–95% population immunity needed to prevent measles outbreaks.²³ Theoretical disease modeling suggests achieving ≤6% to 8% measles susceptibility in all age groups will likely prevent measles outbreaks. However, heterogeneity of susceptibility exists, and higher levels of measles susceptibility may occur in infants and preschool aged children; in these settings, it may be necessary to achieve a relatively lower level of measles susceptibility in age groups known to have the highest contact and virus transmission rates, particularly school-aged children and young adults.²⁴

The occurrence of large measles outbreaks might have a significant boosting effect on overall population immunity because large numbers of measles-susceptible persons acquire immunity naturally following infection during the outbreak. However, in the present study, measles seroprevalence among adult pregnant women remained unchanged late in the measles outbreak (2010) compared with before the outbreak (2008), suggesting the outbreak did not affect population immunity substantially.

No effect of HIV status on measles seroprevalence was found. Past studies have shown a decreased serological response to measles vaccination among HIV-infected adults, waning immunity following vaccination in HIV-positive infants and children, and lower protective immunity to measles among infants born to HIV-infected mothers.^{25–28} Although HIV infection is associated with lower vaccine effectiveness²⁹ and an increased risk of measles outbreaks,³⁰ the contribution of the HIV pandemic to measles control and elimination in Sub-Saharan Africa appears to be minimal.^{31–33} The present findings mirror those of a Kenyan measles seroprevalence study in HIV-positive and negative adults, which also found no differences between these two populations.³⁴ It is likely that an association between HIV status and measles seroprevalence was not found because the study population received measles vaccination as children and acquired HIV as adults, with no loss of protective immunity.³⁴ Because of the severe course of measles in patients with advanced HIV infection, the WHO recommends that, in areas with a high incidence of both HIV and measles, the first dose of measles-containing vaccine be administered as early as 6 months of age, followed by two additional doses of measles vaccine according to the national

Table 7
Measles seroprevalence among pregnant women aged 15–44 years, by health district, from the 2008 and 2010 HIV sentinel surveys, Namibia

District	2008			2010		
	Unweighted, N	Weighted % negative (95% CI ^a)	Weighted % positive and equivocal (95% CI ^a)	Unweighted, N	Weighted % negative (95% CI ^a)	Weighted % positive and equivocal (95% CI ^a)
Andara	42	36 (23–50)	64 (49–77)	53	14 (7–26)	86 (74–93)
Aranos	24	12 (4–29)	88 (71–96)	16	8 (2–27)	92 (73–98)
Eenhana	77	11 (6–20)	89 (80–94)	67	22 (14–34)	77 (66–86)
Engela	70	6 (3–14)	94 (86–97)	72	17 (10–27)	83 (73–90)
Gobabis	35	7 (2–20)	93 (80–98)	66	6 (3–15)	94 (85–97)
Grootfontein	59	8 (3–18)	92 (82–97)	50	2 (0–10)	98 (91–100)
Oshakati	82	2 (0–7)	98 (93–100)	79	17 (10–26)	83 (74–90)
Karasburg	33	6 (2–18)	94 (82–98)	37	4 (1–16)	96 (84–99)
Katutura	68	4 (1–11)	96 (89–99)	76	5 (2–12)	95 (88–98)
Keetmanshoop	5 ^b			46	14 (6–26)	86 (74–93)
Khorixas	26	30 (15–49)	74 (51–85)	41	10 (3–24)	90 (76–97)
Katima Mulilo	76	19 (12–29)	81 (71–88)	91	16 (10–25)	84 (75–90)
Luderitz	27	9 (3–26)	91 (74–97)	74	6 (2–13)	94 (87–98)
Mariental	27	6 (2–22)	94 (79–98)	41	4 (1–14)	96 (86–99)
Nankudu	56	12 (6–22)	88 (78–94)	36	14 (6–28)	86 (72–94)
Nyangana	28	19 (9–37)	81 (63–91)	75	13 (7–22)	87 (78–93)
Okahao	74	11 (6–21)	89 (79–94)	103	14 (8–23)	86 (77–92)
Okahandja	84	9 (5–17)	91 (83–95)	54	18 (10–30)	82 (69–90)
Okakarara	41	10 (4–24)	90 (76–96)	48	30 (19–44)	70 (57–81)
Okongo	38	13 (5–28)	87 (72–95)	88	13 (7–23)	87 (77–93)
Omaruru	40	27 (16–42)	73 (58–84)	52	11 (5–24)	89 (76–95)
Onandjokwe	81	15 (9–25)	85 (75–91)	85	23 (16–34)	77 (66–85)
Opuwo	38	13 (6–26)	87 (74–94)	17	12 (3–38)	88 (62–97)
Oshikuku	49	3 (1–12)	97 (88–99)	70	6 (3–14)	94 (86–97)
Otjiwarongo	34	7 (2–21)	93 (79–98)	62	10 (4–20)	90 (80–96)
Outjo	42	15 (8–28)	85 (72–92)	60	30 (20–43)	69 (57–80)
Outapi	76	6 (2–14)	94 (86–98)	50	6 (2–16)	94 (84–98)
Rehoboth	52	13 (6–25)	87 (75–94)	26	10 (3–27)	90 (73–97)
Rundu	42	26 (15–40)	75 (60–85)	67	10 (5–19)	90 (81–95)
Swakopmund	50	16 (8–28)	84 (72–92)	56	5 (2–14)	95 (86–98)
Tsandi	48	27 (16–41)	73 (59–84)	87	14 (8–23)	86 (77–92)
Tsumeb	83	12 (6–20)	88 (80–94)	72	16 (9–26)	84 (74–91)
Usakos	26	25 (12–44)	75 (56–88)	22	16 (6–36)	84 (64–93)
Walvis Bay	36	21 (11–37)	79 (63–89)	71	16 (10–27)	84 (73–90)
Windhoek Central Hospital	39	11 (5–24)	89 (75–95)	31	13 (5–28)	87 (72–95)

CI, confidence interval.

^a Wilson score method.

^b Number too small to calculate meaningful statistics.

immunization schedule.²³ Measles vaccine should also be administered routinely to potentially susceptible, asymptomatic HIV-positive children and adults, and considered for those with symptomatic HIV infection if not severely immunosuppressed.²³

These findings should be considered in light of certain limitations. First, only pregnant women aged 15–44 years were examined in this study, and the ANC survey was not a random cross-section of the population of pregnant women. Therefore, the results might not be generalizable to all pregnant women or to other age groups and populations in Namibia. When feasible, prospective, population-based surveys could be considered to increase the generalizability of results and allow for the collection of additional information on variables of interest, such as immunization status; however, these studies are time- and resource-intensive, and utilizing specimens already collected and stored might allow for studies that would not otherwise be possible. Second, two cohorts of pregnant women who had specimens collected in 2008 and 2010 were tested, thus the same women might have been included by chance; however, because the specimens were de-identified and unlinked, it could not be determined whether this occurred. This limits inferences regarding differences in measles seropositivity between the two populations. Third, measles immunity was measured before the end of the outbreak; immunity might have been higher if immunity had been measured after the outbreak. However, the second survey was

conducted after 77% of measles cases had occurred in the outbreak, and it is believed that the additional cases that occurred during and after the 2010 survey would not have affected these findings substantially. Fourth, fewer HIV-positive specimens were available for testing compared with HIV-negative samples for the 2008 study year, and this could have biased the results. However, this difference in specimens was not seen in 2010, and similar findings were observed in both analysis years, making this bias less likely.

The cutoffs for the EIAs used to determine protective levels of antibody have varied considerably in measles seroprevalence studies depending on the methodology used, although there is a growing movement to standardize testing and report comparable outcomes. Persons with antibody titers in the equivocal and sometimes negative qualitative ranges, when retested by plaque reduction neutralization (PRN) test, have been found to have protective antibodies against measles.^{18,21} Additionally, persons who are vaccinated may have lower titers than those who are infected with wild-type virus.^{18,21,35} This may explain the differences by age group seen in the present study, with the highest percentage of equivocals in the youngest age groups (16–21% in 15–19-year-olds), as these youngest cohorts would have had the opportunity to receive measles vaccination through the routine immunization program which began in 1983. Unfortunately, this cannot be confirmed because the participants' vaccination histories were not available. Nonetheless, as seroprevalence

studies expand in settings where adults might have been vaccinated or exposed to wild-type virus but documentation of vaccination is not readily available, defining the appropriate cutoff for protection is critical for guiding programs and standardizing reporting across different settings.

In Namibia, the results from this study together with other data, including from surveillance showing a high age-specific incidence of measles in persons up to 39 years of age, is evidence of immunity gaps in adults beyond the usual SIA target groups. Additionally, since this study was conducted, measles outbreaks have continued in Namibia in 2013–2014, and cases continue to occur in older age groups.³⁶ Based on these recurrent outbreaks in adults and lower than expected seroprevalence, the MoHSS is considering implementing a nationwide SIA with measles–rubella vaccine among persons aged 9 months to 39 years, a target population of 1.8 million persons in 2016.³⁷ If high coverage can be achieved and sustained in both routine immunization services and SIAs, Namibia will be one step closer to achieving the goal of measles elimination.

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