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Progress towards achieving hepatitis B control in the Cook Islands, Niue, Tokelau, and Kiribati

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Abstract

Background: Hepatitis B virus (HBV) is highly endemic in many of the Pacific Island countries. Four island countries—Cook Islands, Kiribati, Niue, and Tokelau—sought to evaluate the success of their hepatitis B vaccination programs by conducting nationally representative serosurveys among children born post-vaccine introduction.

Methods: Cook Islands, Niue, and Tokelau conducted school-based census serosurveys because of small populations. The Cook Islands tested children in second grade; Niue tested children in early childhood education through sixth grade; and Tokelau tested children in first through sixth grades. Because Kiribati has a much larger birth cohort, it conducted a one-stage stratified serosurvey among first grade students. All four countries tested children using the Alere Determine™ rapid point of care hepatitis B surface antigen (HBsAg) test.

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Conflicts of interest

No authors have any conflicts of interest.

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Results: In the three smaller countries, no children were seropositive for HBsAg (0/245 Cook Island students, 0/183 Niuean students, 0/171 Tokelau students). In Kiribati, 39 (3.3%, 95% confidence interval 2.4–4.6%) of 1249 students were HBsAg positive. Vaccination data collected in the Cook Islands and Tokelau showed high vaccination coverage in both countries with $\geq 95\%$ birth dose coverage and 100% 3-dose coverage.

Conclusions: The Cook Islands, Niue, and Tokelau have made remarkable progress in establishing strong vaccination programs and towards decreasing the burden of hepatitis B among children. Kiribati still needs to improve vaccination coverage to achieve the $<1\%$ HBsAg target established by the World Health Organization Western Pacific Region.

Keywords

Hepatitis B; Vaccination; Cook Islands; Niue; Tokelau; Kiribati

1. Introduction

Globally, an estimated 240 million people have chronic hepatitis B virus (HBV) infection and an estimated 600,000 die from the consequences of this infection yearly [1,2]. The burden of disease is greatest among those living in the World Health Organization (WHO) Western Pacific Region (WPR), most of whom are infected by perinatal or horizontal transmission during the first five years of life [3,4]. To help combat this public health problem, the WPR member states committed to controlling chronic HBV infection, defined as a hepatitis B surface antigen (HBsAg) seroprevalence $<1\%$ among children aged ≥ 5 years, by 2017 [5].

People living in the Pacific Island Countries (PICs) have some of the highest rates of chronic HBV infection in the world, with HBsAg seroprevalence ranging from 3% to 29% in the general population [6]. Recently, four PICs—Cook Islands, Kiribati, Niue, and Tokelau—sought to evaluate their hepatitis B vaccination programs and the progress they have made towards the 2017 WPR control goal. The pre-vaccine prevalence of HBsAg in three of these countries has been described in the literature; there are no published data describing the burden in Tokelau. In the Cook Islands, two convenience sample surveys from the 1970s to 1980s showed an HBsAg seroprevalence of 4.8% and 14% [7,8]. In Kiribati, HBsAg prevalence ranged from 3.8% among children aged 12–24 months in 1998 to 27–32% among older individuals in studies done in 1985–1986 and in 1998 [9,10]. In Niue, a census survey of adults in 1980 found 11.9% HBsAg prevalence, while a survey of children in 1983 found a prevalence of 3.4% among infants and of 10.3–11% among children and adolescents aged 1–19 years [11–13]. All four countries introduced hepatitis B-containing vaccine more than 20 years ago, and they have largely achieved and maintained the Global Vaccine Action Plan target of $\geq 90\%$ coverage with three doses of hepatitis B vaccine since 2011 (Table 1, Fig. 1). Hepatitis B vaccine birth dose (HepB-BD) coverage has been nearly universal in the Cook Islands and Niue. However, HepB-BD coverage has been below the targeted level in the two other countries, ranging from 66–84% in Kiribati and 33–100% in Tokelau since 2011 (Fig. 1).

To assess the progress of the national immunization programs in reaching the 2017 WPR HBV control goal, we undertook serosurveys in the four countries to ascertain HBsAg seroprevalence among children born after the nationwide implementation of the hepatitis B vaccination program. A secondary objective of the surveys was to assess hepatitis B vaccination coverage in the studied population, if possible.

2. Methods

During 2012–2015, we conducted nationwide, cross-sectional, school-based serosurveys among children in the four countries. Primary school enrollment was estimated to be >95% in all countries.

2.1. Sample size, sampling, and study design

Table 2 summarizes the key characteristics of the hepatitis B serosurveys conducted in the four countries. In the Cook Islands, a census survey of all children in second grade was conducted. Due to logistical challenges, 12 children living on the remote islands of Penrhyn, Palmerston, and Nassau were excluded. In Niue, a census survey of all children enrolled in early childhood education through sixth grade was conducted. In Tokelau, a census survey of all children enrolled in the first through sixth grades was conducted.

In Kiribati, a cluster survey was conducted because of the larger number of students and access challenges. In 2014, there were 3343 first grade 1 students in Kiribati. Assuming a seroprevalence of 1% with a precision of $\pm 0.5\%$, a design effect of 1.1, 2-sided 95% confidence interval (CI), $\alpha = 0.05$, and accounting for the finite population, a minimum sample size of 1116 children was needed. Factoring a 15% non-response due to refusals/absentee, 1313 children were targeted for enrollment. A stratified single-stage cluster survey approach was used. To help ensure selection of some outer islands, where population sizes were smaller, two strata were defined. The inner island strata included all public and private schools in North and South Tarawa. The outer island strata included all public and private schools on all the other islands, except two schools in Kanton and Banaba Islands that are small in population ($n = 20$ students) and extremely difficult to access. Most schools were classified as their own primary sampling unit (PSU). However, in order to create more consistent cluster sizes, geographically close islands with small cohorts of children were clustered together to create PSUs of approximately 30–40 children; this was done for the islands of Aranuka, Maiana, Nikanau, and Onotoa. In the first stage, 13 PSUs in the inner island strata and 20 PSUs in the outer island strata were chosen by systematic random sampling, with the goal of targeting the 1313 sample size requirement. All first grade children in the selected schools were eligible for participation.

2.2. Data collection

Consent was requested from parents/caregivers prior to participation in the serosurvey. To describe possible biases that might have resulted from refusal of children to participate in the serosurvey, data were collected on key demographic characteristics and vaccination data among eligible children using a standard form irrespective of consent when possible. Vaccination data for the survey were obtained from public health vaccination records.

2.3. Specimen collection and HBsAg testing

Approximately 50 µL of blood were collected from each consented child by finger prick and tested at the school using the Alere Determine™ HBsAg point-of-care test strip (reported sensitivity: 95–100%; reported specificity: 96–100%) [14–16]. The test reports either a positive or negative result. If no control line appears, the test is considered invalid.

2.4. Data management/analysis

Data were collected using a standardized data collection form, entered into an Excel spreadsheet (Seattle, WA, USA), and analyzed using SAS v9.3 (Cary, NC, USA) and SUDAAN v10 (Research Triangle Park, NC, USA). Participants were defined as those who had consent for HBsAg testing; nonparticipants were those without consent for HBsAg testing. HepB-BD was considered to have been given within 24 h of birth if the date of administration was on the day of birth or the day after birth. Any HepB-BD was defined as a dose given before day 42 of life (first day of eligibility for a multiple-antigen vaccine) if date of administration was noted. If date of HepB-BD administration was unavailable, it was assumed that an annotation in the birth dose column of the vaccination card was valid as ‘any HepB-BD’. For the Cook Islands, Niue, and Tokelau, no confidence intervals are presented since these were census surveys. For Kiribati, estimates and Logit 95% CI for population characteristics were calculated using Taylor series variance estimation methods and accounting for the survey design, the finite population, and weights (SUDAAN v10). For Kiribati, weights were used for population characteristics, seroprevalence estimates were adjusted for non-response, and weighted proportions are presented. For this evaluation, we decided that if <25% of children in each of the countries had vaccination data for review, the results would not be representative of the population, and they are not presented.

2.5. Human subjects’ rights and ethics

Informed consent was obtained from parents/caregivers before testing. The study protocol was approved by the Ethics Review Committee at the WHO Regional Office for the Western Pacific since none of the four countries had their own ethics committee. CDC determined the activity to be human subject research in Niue, but CDC involvement did not constitute direct engagement in human subject research; therefore, it did not require CDC Institutional Review Board (IRB) review. In Kiribati, Cook Islands, and Tokelau, CDC determined the activity to be program evaluation and did not require CDC IRB review.

3. Results

3.1. Cook Islands

There were 314 eligible children in second grade (mean age 6.5 ± 0.5 years) in the Cook Islands; 45 (14%) were not present or did not have consent to participate in the serosurvey (Table 3). Nonparticipants were more likely to be non-Maori (32% of nonparticipants versus 2% of participants), and were more likely born outside of the Cook Islands (30% of nonparticipants versus 9% of participants). Among participants, 258 (96%) of 269 children had vaccination data for review. Of these 258 children, 245 (95%) received a HepB-BD ≤ 24 h, 249 (97%) received any HepB-BD, and 258 (100%) received three doses of hepatitis B

vaccine. Among the 45 nonparticipants, 35 (78%) had vaccination data available for review in the electronic registry. Of these 35 children, 33 (94%) received a HepB-BD ≤ 24 h, 34 (97%) received any HepB-BD, and all received three doses of hepatitis B vaccine. No participants were found to be HBsAg positive.

3.2. Niue

There were 216 eligible children in early childhood education through sixth grade in Niue; 183 (85%) had consent to participate in the survey (Table 3). Participation rates ranged from 73–100% by grade. Information on nonparticipants was not available for review. Only 17 (9%) children, all participants, had documented age and vaccination data available for review; given the small proportion, these data were not reviewed. Of the 183 participants tested, no children were found to be HBsAg positive.

3.3. Tokelau

There were 171 eligible children in first through sixth grades, including one age-appropriate home-schooled child who was enrolled in the survey. All children had consent to participate (Table 3). The mean age of participants was 8.2 ± 1.8 years. Only 59 (35%) children were born in Tokelau; most of the rest were born in New Zealand. All children had vaccination data available for review. Of the 171 participants, 162 (95%) had documentation of receiving any HepB-BD, although date of administration was not documented for 76 children. Of the 95 participants with documented dates of vaccination, 73 (77%) received a HepB-BD ≤ 24 h. Of the 59 participants born in Tokelau, all had documented dates of vaccination: 45 (76%) received a HepB-BD ≤ 24 h, 52 (88%) received a HepB-BD ≤ 7 days, and 55 (93%) received any HepB-BD. Of the 112 children born outside of Tokelau, 108 (96%) received a HepB-BD, though only 36 had the exact date of vaccination documented. Among these 36 children, 28 (78%) received a HepB-BD ≤ 24 h, 31 (86%) received a HepB-BD ≤ 7 days, and 32 (89%) received any HepB-BD. All children received three doses of hepatitis B vaccine. No children were found to be HBsAg positive.

3.4. Kiribati

There were 1293 eligible first grade children (mean age 6.4 ± 0.7 years) in the selected schools; 1253 had parental consent for participation, but four children refused on the day of the testing. Thus, 44 (4%) did not participate in the serosurvey (Table 3). Participants and nonparticipants were similar with respect to sex, current residence (inner or outer island strata) and birth in Kiribati. Vaccination data were available for review from 104 (9%) participants and from none of the nonparticipants and thus were not analyzed. Of the 1249 participants, 39 (3.3% (2.4–4.6%)) were found to be HBsAg positive. There were no seropositive children in Abemama (0/22), Aranuka (0/30), Arorae (0/19), Makin (0/40), or South Tabiteuea (0/11) islands. Seroprevalence in the other islands varied: 5.3% (4/76) in Abaiang, 10.4% (9/87) in Butaritari, 3.8% (5/131) in Kirimati, 4.5% in (1/22) Nonouti, 3.2% (2/62) in North Tabiteuea, 0.6% (1/156) in North Tarawa, 2.8% (16/576) in South Tarawa, and 5.9% (1/17) in Onotoa.

4. Discussion

The Cook Islands, Kiribati, Niue, and Tokelau have made remarkable progress towards achieving hepatitis B control through vaccination. The Cook Islands, Niue, and Tokelau had no children among the target population with evidence of chronic HBV infection, documenting that they have achieved the 2017 WPR goal of <1% chronic HBV infection rate among children at least five years old. The three countries that have achieved the goal have done so through strong HBV control programs including prenatal screening, hepatitis B immunoglobulin (HBIG) administration to high risk newborns, and high vaccination coverage with HepB-BD and subsequent doses. Despite its progress, Kiribati has not achieved the target and will need to make improvements in its vaccination program to ensure further progress is made.

The Cook Islands, Niue, and Tokelau all have reported nearly 100% 3-dose hepatitis B vaccine coverage yearly for the past ten years (Fig. 1). Vaccination data reviewed in the Cook Islands and Tokelau for their surveys corroborated the 3-dose reported coverage estimates. In addition, 95–97% of children residing in the Cook Islands and Tokelau at the time of their surveys received any HepB-BD. In contrast to reported 3-dose and any HepB-BD coverage, however, reported HepB-BD ≤ 24 h coverage has sometimes fluctuated dramatically in these three small countries, since some births occurred in neighboring countries such as Australia and New Zealand. In the Cook Islands, 94–95% of both nonparticipants and participants received their HepB-BD ≤ 24 h, showing that a strong perinatal prevention program exists, facilitated by the fact that there is only one maternity hospital which has a protocol for HepB-BD provision to all newborns. In Tokelau, however, only 76–78% of children born in Tokelau and 78% of children born outside of Tokelau received a HepB-BD ≤ 24 h. Reasons for failing to receive a HepB-BD ≤ 24 h are unknown. Even though no cases of hepatitis B were found in this survey, Tokelau needs to strengthen timely HepB-BD administration so as not to miss a prevention opportunity. In Niue, reported vaccination data cannot be corroborated in this survey since very few vaccination data were available for review. However, it is known that the reported decrease in the 2010 HepB-BD ≤ 24 h coverage was due to an obstetrician not being available in country, and all women were flown to New Zealand to deliver there. These children who are born in another country might or might not receive the HepB-BD and do not get counted towards the number of doses administered in country, yet these births are counted in the denominator of eligible children. Given the small numbers of births in Niue as well as in the other islands, small changes in the numerator can have a large impact on the percentage of children vaccinated. The failure of another country to provide a HepB-BD should not be seen as a failure of the country's vaccination program. Because of the inability to verify the vaccination coverage in the studied cohorts, Niue should conduct a chart review to ensure that timely HepB-BD is provided to every newborn.

In Kiribati, the best estimate for pre-vaccine HBsAg prevalence was 29%. The reduction in seroprevalence to 3.3% in its serosurvey, an 89% decrease, is remarkable and is the result, in large part, of the vaccination program. The failure to achieve the <1% control goal is probably due to some remaining challenges in the vaccination program, although we were unable to assess vaccination coverage in this cohort to substantiate this. Delivery

of vaccination in Kiribati is challenging largely because a larger birth cohort lives on 21 inhabited islands/atolls spread over 3.4 million kilometers of ocean. However, 90% of children are reportedly born with skilled birth attendants (SBAs), and thus coverage with a HepB-BD ≤ 24 h should be high, although reported coverage in 2014 was only 66% (Fig. 1). One challenge is that vaccine is not readily available for all SBAs because of insufficient cold chain for vaccine storage [17]. Kiribati has a national policy to use hepatitis B monovalent vaccine outside the cold chain, but this policy has not been implemented [17]. One priority is to ensure those SBAs working without adequate access to cold chain are trained in using hepatitis B vaccine outside the cold chain. Additionally, health facilities that have adequate cold chain should be systematically evaluated to identify barriers to administration. Birth dose is vitally important to reducing chronic HBV infection prevalence in Kiribati, where one study found 48% of mothers with chronic HBV infection had evidence of hepatitis B e antigen, indicating a greater risk for perinatal transmission [9]. Finally, the immunization program will need to strengthen routine immunization services, since reported 3-dose coverage in 2014 was only 75%.

These four serosurveys have some limitations. First, participation was only 86% in the Cook Islands and 85% in Niue. However, characteristics of nonparticipants and participants in these two countries were similar. Additionally, in the Cook Islands, vaccination coverage was similar among participants and nonparticipants, suggesting that nonparticipants probably also had minimal, if any, chronic HBV infection given the high vaccine effectiveness ($>95\%$ for 3 doses) [18]. Second, some remote locations were excluded in the Cook Islands and Kiribati. This could bias our findings towards a lower HBsAg prevalence, since children living in more remote locations might be less likely to be vaccinated than those living on closer island, but the numbers and proportion of target population children residing in those remote islands were small (4% for the Cook Islands; 0.6% for Kiribati). Third, Kiribati also has only 95% school enrollment by first grade; therefore, children out of school were not represented in its survey; these children might have less access to vaccination services and a higher burden of chronic HBV infection than children attending school. Fourth, documented vaccination data were not available for most children in Niue and Kiribati, limiting our ability to make data-driven programmatic recommendations. In Tokelau, dates of HepB-BD vaccination were not well documented, limiting statements about timeliness of receipt of HepB-BD. In Kiribati and Niue, the lack of vaccination data prevented calculation of vaccine effectiveness; in Niue, Tokelau, and the Cook Islands, a lack of children with chronic HBV infection prevented calculation of vaccine effectiveness, although zero cases of chronic HBV infection compared to baseline rates in the setting of high vaccination rates suggest the vaccine is highly effective. Another limitation is that we did not test children for hepatitis B antibody to core antigen making it difficult to say if children had a resolved infection. Finally, prenatal screening and administration of HBIG to high-risk newborns occurs in the Cook Islands, Niue, and Tokelau; we are unable to account for which children were born to HBsAg positive mothers and received HBIG due to lack of documentation in the vaccination records.

These four countries have made remarkable progress towards achieving control of chronic HBV infections in children. The Cook Islands, Niue, and Tokelau need to sustain their high performing vaccination programs by continuing to ensure that every child born on the island

receives a HepB-BD ≤ 24 h. Kiribati needs to improve both timely birth dose and 3-dose coverage in order to achieve the $<1\%$ goal. Other countries in the region that have not assessed the impact of their hepatitis B vaccination program should conduct a serosurvey to understand progress towards the goal and identify areas that need improvement.

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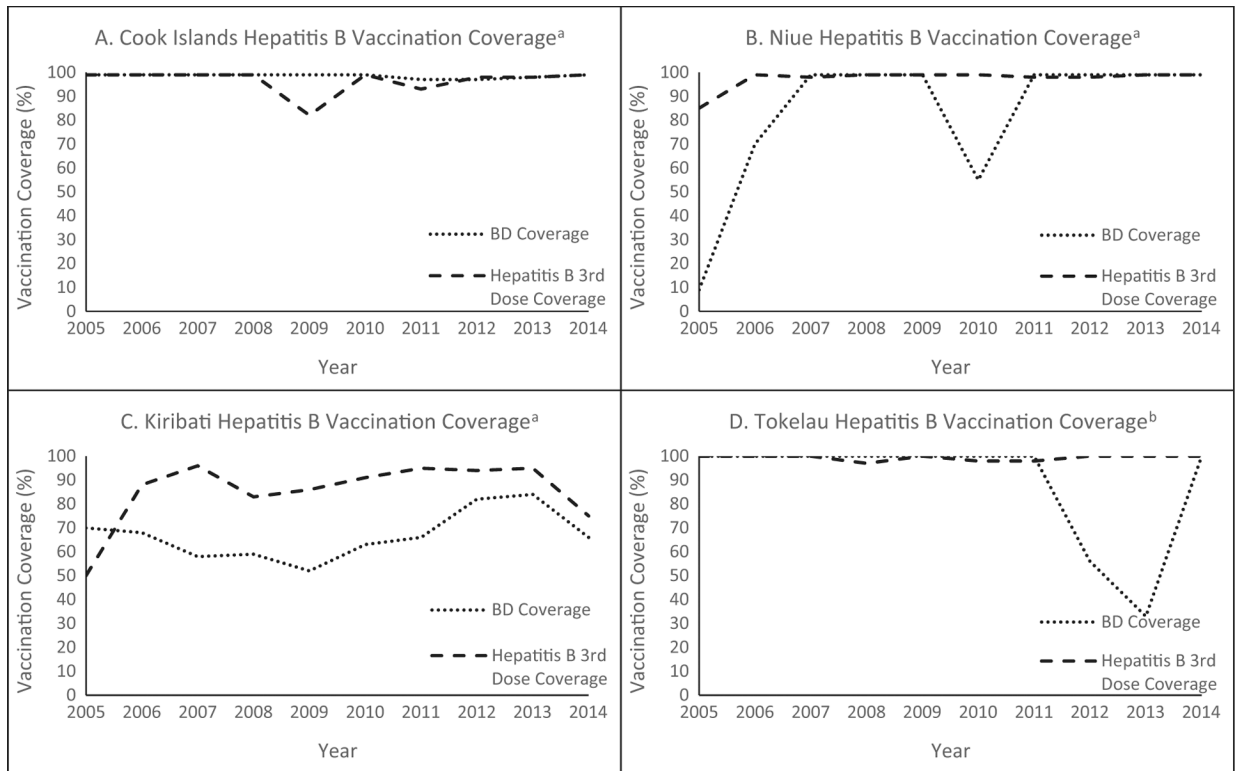


Fig. 1. Hepatitis B birth dose (HepB-BD) and 3rd dose vaccination coverage for Cook Islands (A), Niue (B), Kiribati (C), and Tokelau (D), 2005–2014.^aData Source: WHO-UNICEF Estimates [19]. ^bData Source: Official Country Estimates [20].

Table 1
 Characteristics of hepatitis B control programs through vaccination in the Cook Islands, Kiribati, Niue, and Tokelau.

	Cook Islands	Kiribati	Niue	Tokelau
Estimated hepatitis B surface antigen seroprevalence in the general population (%) ^a	10	29	8	Not available
Year hepatitis B vaccine introduced into national immunization schedule	1989	1995	1986	1990
Current hepatitis B vaccination schedule	<24 h, 6 weeks, 3 months, 5 months	<24 h, 6 weeks, 10 weeks, 14 weeks	<24 h, 6 weeks, 3 months, 5 months	<24 h, 6 weeks, 10 weeks, 14 weeks
Vaccine formulation-birth dose	Monovalent	Monovalent	Monovalent	Monovalent
Vaccine formulation-infant series	DTP-Hib-HepB	DTP-Hib-HepB	DTap-Hib-HepB-IPV	DTP-Hib-HepB
Prenatal hepatitis B surface antigen screening	Yes	No	Yes	Yes
Hepatitis B immunoglobulin provided to high-risk newborns	Yes	No	Yes	Yes
% of deliveries assisted by a skilled birth attendant (SBA) ^b	100%	90%	100%	100%
Primary school enrollment ^c	100%	>95%	100%	100%

^aWestern pacific regional plan for hepatitis B control through immunization.[6]

^bWestern pacific country health information profiles: 2011 revision.[21]

^cAs reported by country.

Table 2

Key characteristics of hepatitis B serosurveys conducted in Cook Islands, Kiribati, Niue, and Tokelau.

	Cook Islands, 2012	Kiribati, 2014	Niue, 2015	Tokelau, 2014
Time period of survey	May-June 2012	August 2014	February 2015	August-September 2014
Study design	Census of grade 2 students	One stage cluster survey of grade 1 students	Census of ECE ^a -grade 6 students	Census of grade 1-6 students
Total population in selected grade(s)	326	3343	216	171
Exclusionary criteria	3 remote islands (students excluded $n = 12$)	2 remote islands (students excluded $n = 20$)	None	None
Number of eligible children for survey	314	1293	216	171

^aECE: Early Childhood Education.

Table 3

Characteristics of hepatitis B serosurvey participants in the Cook Islands, Kiribati, Niue, and Tokelau.

	Cook Islands, 2012			Kiribati, 2014			Niue, 2015			Tokelau, 2014		
	n	N	%	n	N	%	n	N	%	n	N	%
Participation	269	314	86	1249	1293	96 (94–99)	183	216	85	171	171	100
Grade ^a												
Early Childhood Education (ECE)												
1				1249	1249	100	22	30	73			
2	269	269	100				24	30	80	22	22	100
3							29	34	85	27	27	100
4							28	32	88	30	30	100
5							30	30	100	23	23	100
6							22	29	76	39	39	100
Male	149	269	55	664	1288	51 (48–54)	28	31	90	29	29	100
Born in country	241	265	91	1285	1293	99 (99–100)				98	171	57
Ethnicity										59	171	35
Maori/Polynesian	252	257	98							163	171	95
Caucasian	5	257	2									
Melanesian	0	257	0							1	171	1
Mixed										7	171	4
Vaccination data available for review	258	269	96	104	1293	9 (3–16)	17	183	9	171	171	100
Any Birth Dose (HepB-BD) ^b	249	258	97							162	171	95
Received HepB-BD ≤24 h	245	258	95							73	95	77
Received 3+ doses of hepatitis B	258	258	100							171	171	100
HBsAg+	0	269	0	39	1249	3.3 (2.4–4.6)	0	183	0	0	171	0

^aTokelau: 1 child home schooled but included in survey.

^bAny birth dose is defined as a dose within 41 days of life (Cook Islands) or marked on vaccination card as ‘birth dose’ but no date provided (Tokelau).