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Substantial decline in hepatitis B virus infections following vaccine introduction in Tajikistan

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Abstract

Background—Tajikistan, considered highly endemic area for hepatitis B virus (HBV) in a pre-vaccine era, introduced hepatitis B vaccine in 2002 and reported 80% coverage with three doses of hepatitis B vaccine (HepB3) since 2004. However, the impact of vaccine introduction has not been assessed.

Methods—We tested residual serum specimens from a 2010 national serosurvey for vaccine-preventable diseases in Tajikistan and assessed the prevalence of HBV infection across groups defined based on the birth cohorts' routine infant hepatitis B vaccination program implementation and HepB3 coverage achieved (80% versus <80%). Serosurvey participants were selected through stratified multi-stage cluster sampling among residents of all regions of Tajikistan aged 1–24 years. All specimens were tested for antibodies against HBV core antigen (anti-HBc) and those found positive were tested for HBV surface antigen (HBsAg). Seroprevalence and 95% confidence intervals were calculated and compared across subgroups using Satterthwaite-adjusted chi-square tests, accounting for the survey design and sampling weights.

Results—A total of 2188 samples were tested. Prevalence of HBV infection markers was lowest among cohorts with 80% HepB3 coverage (ages, 1–6 years): 2.1% (95% confidence interval, 1.1–4.3%) for anti-HBc, 0.4% (0.1–1.3%) for HBsAg, followed by 7.2% (4.1–12.4%) for anti-HBc and 2.1% (0.7–6.1%) for HBsAg among cohorts with <80% HepB3 coverage (ages, 7–8 years), by 12.0% (8.7–16.3%) for anti-HBc and 3.5% (2.2–5.6%) for HBsAg among children's cohorts not targeted for vaccination (ages, 9–14 years), and 28.9% (24.5–33.8%) for anti-HBc and

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Disclaimers

The findings and conclusions in this report are those of the author(s) and co-authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). Some of the co-authors are staff members of the World Health Organization (WHO). The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy, or views of the WHO.

6.8% (4.5–10.1%) for HBsAg among unvaccinated adult cohorts (ages, 15–24 years). Differences across groups were significant ($p < 0.001$, chi-square) for both markers.

Conclusions—The present study demonstrates substantial impact of hepatitis B vaccine introduction on reducing HBV infections in Tajikistan. To achieve further progress in hepatitis B control, Tajikistan should maintain high routine coverage with hepatitis B vaccine, including birth dose.

Keywords

Hepatitis B immunization; Hepatitis B vaccine impact; Hepatitis B virus infections; Prevalence of HBsAg; WHO European Region; Tajikistan

1. Background

Hepatitis B virus (HBV) is a major cause of acute hepatitis and chronic liver disease globally. In the pre-vaccine era, approximately 2 billion persons were infected with HBV, including 350 million with chronic infection, and approximately 620,000 died each year from chronic liver disease [1–3]. Increasing availability of affordable hepatitis B vaccine and implementation of effective prevention and control strategies since the 1990s have made it possible to substantially reduce HBV-associated disease [1,4,5].

The WHO position paper on hepatitis vaccines strongly recommends that all regions develop hepatitis B control goals [6]. In 2005, the World Health Organization (WHO) Western Pacific Region, which has the world's highest HBV burden [3,7], set the goal to achieve <2% prevalence of chronic HBV infection among children aged <5 years by 2012, as an interim milestone toward a regional goal of <1% prevalence [3,7,8]. The 2012 goal has been met by the region as a whole and by at least 30 of 37 countries [9]. In 2009, the WHO Eastern Mediterranean Region endorsed a regional target of achieving <1% prevalence of chronic hepatitis B virus infection among children aged <5 years by 2015 [10].

In the European Region, the WHO European Health 21—Health for All Policy Framework of 1999 stated that “by 2010 or earlier all countries should have ... new hepatitis B virus carrier incidence reduced by at least 80% through integration of hepatitis B vaccine in the child immunization programme” [11] although the progress toward achieving this target has not been systematically monitored or assessed. However, the recently developed European Vaccine Action Plan for 2015–2020 [12] adopted in endemicity for September 2014 states that the WHO Regional Office for Europe commits itself to prepare a program and action plan for the control of HBV infection and identify targets for 2020.

In the WHO European Region, the impact of vaccination on HBV infection prevalence in the member states with high HBV endemicity, such as Tajikistan, has not been systematically assessed. Tajikistan, a low-income former USSR country in Central Asia (population, 7.6 million, 2010) [13], is considered a high endemicity area for HBV endemicity area with an estimated 8% overall pre-vaccine prevalence of HBV surface antigen (HBsAg) [1,3]. This estimate is based on the extrapolation of the data from neighboring countries with comparable epidemiologic conditions [3,14,15] as data to directly assess pre-vaccine population prevalence of HBsAg in Tajikistan were unavailable.

In the 1980s, a study using less sensitive laboratory methods available at the time reported 7.2% overall HBsAg prevalence with the highest prevalence (13.9%) among children aged 1–4 years in Tajikistan [16]. In the mid-1990s, a high prevalence of HBsAg (15.7%) was found among adults who immigrated to Israel from Tajikistan and Uzbekistan [17]. During the Soviet period, Tajikistan, along with other Central Asian republics, had the highest incidence of acute hepatitis B in the USSR [18]. Numbers of acute hepatitis B cases reported during 1980–1989 (1983–4859 cases annually) were much higher than those since 1996² (217–962 cases annually during 1996–2012) [14] (Ministry of Health of Tajikistan, unpublished data). However, the quality of surveillance and availability of laboratory confirmation have been inconsistent over time and interpreting temporal trends in hepatitis B incidence in Tajikistan is difficult. A recent study found HBsAg in 40.4% of patients with chronic hepatitis and in 42.5% of patients with cirrhosis and/or hepatocellular carcinoma, confirming that HBV remains a major cause of chronic liver disease in Tajikistan [19].

Hepatitis B vaccine was introduced into the routine infant immunization program of Tajikistan in 2002 with the support from Gavi, the Vaccine Alliance. Initially, the immunization schedule consisted of vaccine doses given at birth, 2 and 4 months of age. Since 2008, with the introduction of the pentavalent combination vaccine,³ standalone hepatitis B vaccine is given at birth, and the pentavalent vaccine is administered at age 2, 3, and 4 months. Various sources of coverage data for three doses of hepatitis B vaccine (HepB3) indicate levels 80% since 2004, as well as generally high coverage with the birth dose (Table 1).

A nationwide serosurvey for vaccine-preventable diseases implemented in Tajikistan in response to the major poliomyelitis outbreak in 2010 [23,24] provided a unique opportunity to conduct an assessment of the impact of hepatitis B vaccine introduction. We analyzed specimens remaining after the initial testing was completed, for markers of HBV infection, and compared prevalence across groups defined by the vaccination history of birth cohorts.

2. Methods

2.1. Serosurvey design

The detailed description of the serosurvey design and sampling procedures has been published previously [23,24]. In brief, the sampling frame for the serosurvey included residents of all regions of Tajikistan aged 1–24 years (age groups sampled: 1–4, 5–9, 10–14, 15–19, 20–24 years). The age groups and sample sizes were determined by the primary objective of the serosurvey assessment of population immunity against polioviruses by the age group [23]. Participants were selected through stratified multi-stage cluster sampling and were identified from registries maintained at government health care facilities which serve practically entire population of Tajikistan. The basic demographic information and blood sample (3–5 ml, in serum separation tubes) were obtained following verbal informed consent by participants or their guardians. The information on participants' vaccination

²During 1990–1995, reporting was interrupted because of the civil war; resumed in 1996.

³Pentavalent vaccine used in Tajikistan contains diphtheria and tetanus toxoids, whole-cell pertussis, Hib and hepatitis B vaccines.

history was unavailable. Overall, 2459 specimens were collected for the original serosurvey and all available residual specimens were included in the present assessment.

2.2. Laboratory testing

Serum was split into three aliquots and stored at -20°C until testing. Residual aliquots retained at the Virology Laboratory of the Institute of Prophylactic Medicine, Tajikistan Ministry of Health, Dushanbe, which performed measles and rubella antibody testing, and at the Centers for Disease Control and Prevention (CDC), Atlanta, which performed polio antibody testing, were tested for markers of HBV infection.

In accordance with WHO guidance [25], all specimens were tested for total antibodies against HBV core antigen (anti-HBc), a marker of HBV infection (current or resolved), and positive specimens were tested for HBsAg, a marker of active (including chronic) HBV infection. In addition, HBsAg-positive specimens were tested for HBV e-antigen (HBeAg), a marker of high replication associated with a high likelihood of transmitting HBV, and for antibodies against hepatitis delta virus (anti-HDV), a marker of co- or super-infection with HDV, associated with severe outcomes of HBV infection [1,25].

Testing for anti-HBc and HBsAg was conducted at the laboratory in Dushanbe. Prior to testing the survey specimens, the laboratory successfully passed proficiency testing conducted for quality assurance purposes by the Assay Development and Diagnostic Reference Laboratory (ADDRL), Division of Viral Hepatitis, CDC. All specimens from participants with positive anti-HBc results as well as 12.5% of specimens with negative results of in-country testing underwent subsequent testing for anti-HBc and HBsAg at the ADDRL using aliquots stored at CDC. Testing for HBeAg and anti-HDV was performed at CDC on HBsAg-positive specimens.

Laboratory testing methods included enzyme-linked immunosorbent assays and chemiluminescence assays for anti-HBc, HBsAg (with confirmatory testing), HBeAg, and anti-HDV performed in accordance with the manufacturer's instructions using the test kits listed in Table 2. In cases of discordant results between in-country and CDC test results for a given specimen, an additional round of testing was performed at CDC and the final determination was made based on its outcome. For specimens not tested at CDC, the results of in-country testing were accepted. Participants, for whom the testing could not be completed due to insufficient volume or poor quality of specimens, were excluded from analysis.

2.3. Data analysis

The laboratory testing results were merged with the data set containing participants' demographic and geographic information. In the analysis, the birth cohorts were grouped according to the status of implementation of hepatitis B vaccination and national HepB3 coverage. The following subgroups were defined:

- Children targeted by vaccination when the program was fully implemented—HepB3 coverage 80%, aged 1–6 years (birth years, 2004–2009)

- Children targeted by vaccination at the initial stage of vaccine introduction when the program was partially implemented—HepB3 coverage <80%, aged 7–8 years (birth years, 2002–2003)
- Children not targeted by vaccination—aged 9–14 years (birth years, 1996–2001)
- Adults not targeted by vaccination—aged 15–24 years (birth years, 1986–1995).

Standard WHO guidance for assessing hepatitis B vaccine impact [25] is based on comparison of HBsAg prevalence between the vaccinated cohorts with 80% coverage and aged 5 years at the time of the serosurvey, and the cohorts not targeted for vaccination which have not yet reached 15 years of age.⁴ For the purpose of this comparison, we defined an additional subgroup of 5–6 year olds (birth years, 2004–2005)—the only cohorts in our survey which met the required coverage and age criteria. The HBV infection status of participants was classified as shown in Table 3.

In the analysis, we calculated the seroprevalence and 95% confidence intervals (CI) for markers of HBV infection overall and within sub-populations. Satterthwaite-adjusted Chi-square tests were used to compare seroprevalence among various sub-populations. These sub-populations included categorizations of age (by cohorts vaccination history and by age group as sampled), sex, birth setting (home versus health-care facility), ethnicity (Tajik versus other), and parental education level (high school or less versus more than high school). All analyses accounted for the survey design and sampling weights, including non-response due to inadequate sample volume to test, using SAS-callable SUDAAN v10.01.

2.4. Human subject issues

The serosurvey protocol was reviewed by CDC and determined to be a program evaluation and therefore exempt from institutional review board approval. The protocol was approved by the Tajikistan Ministry of Health.

3. Results

Of the 2459 participants enrolled in the initial serosurvey, samples from 2206 were available for HBV-related testing. However, for 18 samples, testing could not be completed due to their poor quality or insufficient volume, resulting in 2188 specimens included in the analysis.

The distribution of participants tested for HBV markers by age group is given in Table 4. Males accounted for 43.6% ($n = 953$); 84.1% (1808 of 2149 with available information) were ethnic Tajik, and 19.0% (406/2137) were born at home. Education level was more than high school for fathers of 38.5% (828/2148) and mothers of 15.5% (337/2175) of participants.

⁴To determine the impact of vaccination and verify achieving the HBV control goals, WHO recommends assessing prevalence in birth cohorts that had 80% HepB3 coverage and had already reached 5 years of age (i.e., are past the period of the highest risk of developing chronic HBV infection; in Tajikistan in 2010, only 5–6-year-olds met these criteria), and if the pre-vaccine prevalence data are not available, including unvaccinated cohorts aged <15 years (in this case, 9–14-year-olds) as the comparison group with baseline prevalence. The upper limit of 15 years was selected because after this age, major modes of HBV transmission are different from those among children and factors such as sexual transmission, and health-care- or injecting drug use-associated unsafe injections become increasingly important, which limits comparability to younger age groups in terms of exposures to hepatitis B virus [25].

Overall, 341 (15.9%; 95% CI, 13.5–18.6%) participants tested positive for anti-HBc. The prevalence of anti-HBc differed significantly ($p < 0.001$) across age cohorts defined by their hepatitis B vaccine program history and was lowest (2.1%; 95% CI, 1.1–4.3%) among cohorts with 80% HepB3 coverage, increasing to 28.7% (95% CI, 24.5–33.8%) among adults not targeted for vaccination (Table 4). In the latter group, the prevalence of anti-HBc increased from 20.2% (95% CI, 16.6–24.3%) among 15–19-year-olds to 38.7% (95% CI, 32.7–45.0%) among 20–24-year-olds. The 5–6-year-old age group ($n = 197$), a standard WHO-recommended subgroup for program assessment, had significantly lower prevalence of anti-HBc (2.4%; 95% CI, 0.9–6.4%) than 9–14-year-olds (12.0%; 95% CI, 8.7–16.3%; $p < 0.001$). The overall prevalence of anti-HBc did not differ significantly by sex (Table 4). In the analysis of the association of potential risk factors with HBV infection (as determined by the presence of anti-HBc), no significant associations were revealed for birth setting, ethnicity, or parental education level (data not shown).

The prevalence of HBsAg followed the same trends as anti-HBc. Overall, 79 (3.9%; 95% CI, 2.9–5.3%) specimens tested positive for HBsAg. The prevalence of HBsAg differed significantly ($p < 0.001$) across study groups defined by their hepatitis B vaccine program history and was lowest (0.4%; 95% CI, 0.1–1.3%) among cohorts with 80% HepB3 coverage, increasing to 6.8% (95% CI, 4.5–10.1%) among adults not targeted for vaccination (Table 4). In the latter group, the prevalence of HBsAg increased from 4.7% (95% CI, 2.8–7.9%) among 15–19-year-olds to 9.2% (95% CI, 5.9–13.9%) among 20–24-year-olds. The standard WHO assessment subgroup, children aged 5–6 years ($n = 197$), had significantly lower prevalence of HBsAg (0.5%; 95% CI, 0.1–2.4%) compared to 9–14-year-olds (3.5%; 95% CI, 2.2–5.6%; $p = 0.002$). The overall prevalence of HBsAg did not differ significantly by sex (Table 4).

Sufficient volumes of specimens from 73 of 79 HBsAg-positive participants were available for testing for HBeAg and anti-HDV. HBeAg was detected in 17 (23.3%, unweighted percent) specimens and all 73 specimens tested negative for anti-HDV.

4. Discussion

Throughout the world, hepatitis B vaccination has been shown to greatly reduce the prevalence of chronic HBV infection and the associated disease burden, including deaths from cirrhosis and liver cancer [1,6,26]. Although comprehensive strategies for HBV infection control include several other aspects as well (e.g., blood safety, injection safety, prevention of health care- and drug-associated infections or sexually transmitted infections), immunization remains the most effective means of preventing HBV infections during early childhood, the period when the virus is commonly acquired and the risk of developing chronic infection is highest [1,4].

The dramatic decline in HBV infections in Tajikistan, demonstrated by significantly lower prevalence of anti-HBc and HBsAg among cohorts with HepB3 coverage 80% versus age cohorts with lower coverage or not targeted for vaccination, suggests substantial positive impact of the national hepatitis B immunization program. Differences in chronic HBV infection prevalence were remarkable, although small number of HBsAg-positive persons

led to relatively wide confidence intervals in some subgroups. The standard WHO-recommended comparison [25] demonstrated a 7-fold lower prevalence of HBsAg in the birth cohorts aged 5 years with 80% HepB3 coverage (0.5%) compared with the baseline among unvaccinated cohorts aged 9–14 years (3.5%) despite the small sample size in the cohorts aged 5 years.

Prior to vaccine introduction, Tajikistan, similar to its neighboring countries, was a high prevalence area with most chronic HBV infections likely acquired before 5 years of age [1,15,16]. Therefore, the dramatic reduction in the prevalence of chronic HBV infection in vaccinated cohorts of children demonstrated by this study suggests that a large proportion of a future burden of chronic HBV-associated severe disease and deaths in Tajikistan has been averted.

Anti-HBc prevalence in this study increased in unvaccinated cohorts from 12.3% among persons aged 10–14 years to 38.7% among persons aged 20–24 years, suggesting a high burden of HBV infection among older children and young adults. Similar to other countries of Central Asia, in addition to early childhood transmission, cumulative exposure over time to risk factors such as medical or non-medical unsafe injections (e.g., injection drug use) as well as sexual transmission likely contributed to high HBV infection prevalence among young adults in Tajikistan [27–34]. Existing surveillance for acute hepatitis B in Tajikistan reports only aggregate case numbers among children aged <15 years and adults without further demographic, geographic or risk factor breakdown. Therefore, it does not provide sufficient data to determine the relative contribution of currently present risk factors versus prior unsafe practices to the age-related increase in HBV infection prevalence among adults. Almost one-fourth of the chronically infected persons were positive for HBeAg, the marker of high risk of HBV transmission. Together with high HBsAg prevalence among young adults in Tajikistan, this creates a substantial risk of mother-to-child transmission, emphasizing the importance of maintaining high vaccination coverage with the birth dose of hepatitis B vaccine. In addition, a time-limited catch-up hepatitis B immunization campaign among remaining unvaccinated cohorts of children could help prevent further HBV infections among them and accelerate overall reduction of HBV prevalence in Tajikistan [5]. To help monitor the remaining burden of acute hepatitis B and to better characterize risk groups, surveillance for acute hepatitis in Tajikistan should be improved by reporting detailed demographic, immunization, and risk factor data and strengthening laboratory capacity.

The present study provides evidence of the success in reducing HBV infections following introduction of routine hepatitis B immunization in the challenging setting of a high-endemicity subregion of Central Asia. These results are particularly encouraging, taking into account that Tajikistan is the poorest country of the WHO European Region with a recent history of civil war and continued economic problems. These factors have led to disruptions of the health-care system, including serious challenges with implementation of the immunization program that contributed to the spread of imported wild poliovirus in 2010 [23]. To sustain this accomplishment and achieve further progress in controlling HBV, Tajikistan will need to increase further and maintain high routine coverage of infants with hepatitis B vaccine, including the birth dose.

Current prevalence of HBV infection in the WHO European Region varies widely across member states. A recent review estimated overall region-wide HBsAg prevalence as 1.8%, with 13.3 million people chronically infected with HBV, predominantly in eastern and southern parts of the Region [35,36]. Countries of the WHO European Region have begun introducing hepatitis B vaccine in the early 1990s [37] and by 2014, 47 countries had hepatitis B vaccination included in their routine immunization schedules (universal vaccination of newborns, infants, or children/teenagers). Six countries,⁵ all with very low endemicity, have selective hepatitis B immunization programs for high-risk groups combined with screening of pregnant women [38,39].

In light of the positive experience of the Western Pacific Region toward achieving its hepatitis B control goals, and availability of standardized protocols for measuring progress and documenting vaccination impact [4,6,8,21,40], WHO Regional Office for Europe should pursue setting a new regional goal for hepatitis B control and developing the requirements for verifying that the goal has been met. The results of this study can aid the WHO Regional Office with determining the regional hepatitis B control goal as Tajikistan may serve as an indicator of the Region's capacity to reduce chronic hepatitis B infection prevalence among children through routine immunization even under the most difficult conditions. Establishing the renewed regional goal will help sustain low levels of HBV transmission in countries with current low HBV prevalence and focus efforts on further reducing HBV burden in countries where the prevalence of chronic HBV infection is still substantial.

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Table 1

Coverage with hepatitis B vaccine in Tajikistan, 2002–2012 [20–22].

Year	Age in 2010 (years) ^a	Birth dose administrative coverage (%)	3-dose coverage (%)	
			Administrative	WHO/UNICEF estimate
2002	8	80	39	39
2003	7	77	60	58
2004 ^b	6	90	85	81
2005	5	98	93	81
2006	4	94	94	88
2007	3	83	84	84
2008	2	85	86	86
2009	1	97	93	93
2010		96	93	93
2011 ^c		98	96	96
2012		98	94	94

^a Applicable only to birth cohorts included in the serosurvey (2002–2009).

^b Coverage for 2004 birth cohort in 2005 Multiple Indicator Cluster Survey (MICS): HepB1—85%, HepB2—77%, HepB3—69%.

^c Coverage for 2011 birth cohort in 2012 Demographic and Health Survey (DHS): birth dose—93%, Penta1—98%, Penta2—96%, Penta3—93%.

Table 2

Laboratory methods and test kits used for testing specimens for hepatitis B virus (HBV) infection markers.

Marker	Method	Test kit
Testing at the Virology Laboratory of the Institute of Prophylactic Medicine, Dushanbe, Tajikistan		
Anti-HBc	Enzyme-linked immunosorbent assay (ELISA)	Murex Anti-HBc (total), DiaSorin S.p.P., Dartford DA1 5LR, UK
HBsAg with confirmatory testing	ELISA	Murex HBsAg v.3; Murex HBsAg confirmatory v.3, DiaSorin S.p.P., Dartford DA1 5LR, UK
Testing at the Assay Development and Diagnostic Reference Laboratory (ADDRL), Division of Viral Hepatitis, CDC, Atlanta		
Anti-HBc	Chemiluminescent immunoassay (CIA)	VITROS Immunodiagnostic aHBc, Ortho-Clinical Diagnostics, Inc.; Rochester, NY
HBsAg with confirmatory testing	CIA	VITROS Immunodiagnostic HBsAg, Ortho-Clinical Diagnostics, Inc.; Rochester, NY
	CIA	Architect HBsAg, Abbott Diagnostics, Abbott Park, IL
HBeAg	ELISA	ETI-EBK-PLUS, DiaSorin, Inc., Stillwater, MN
Anti-HDV	ELISA	ETI AB-DELTAK-2, DiaSorin, Inc., Stillwater, MN

Table 3

Classification of hepatitis B virus (HBV) infection status based on the laboratory testing results.

HBV infection status	Antibodies against HBV core antigen (anti-HBc)	HBV surface antigen (HBsAg)
Uninfected	Negative	N/A
Past infection (infection cleared)	Positive	Negative
Chronic infection	Positive	Positive

N/A, not applicable. When calculating HBsAg prevalence, Anti-HBc Ab-negative participants were assumed to be HBsAg-negative.

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Table 4

Prevalence of antibody to hepatitis B virus core antigen (anti-HBc) and hepatitis B virus surface antigen (HBsAg), population-based serosurvey, Tajikistan, 2010; estimates adjusted to account for sampling weights and survey design.

Variables	Tested, No.			Anti-HBc seropositive			HBsAg seropositive		
	No.	%	95% CI	P value, chi square	No.	%	95% CI	P value, chi square	
Overall	2188	341	15.9	13.5–18.6	79	3.9	2.9–5.3	0.000	
Status of birth cohort's routine infant hepatitis B vaccination program implementation				0.000					
Fully implemented (aged 1–6 years, HepB3 coverage 80%)	579	14	2.1	1.1–4.3	3	0.4	0.1–1.3		
Partially implemented (aged 7–8 years, HepB3 coverage <80%)	179	12	7.2	4.1–12.4	3	2.1	0.7–6.1		
Not implemented—children targeted for vaccination (aged 9–14 years)	575	68	12.0	8.7–16.3	17	3.5	2.2–5.6		
Not implemented—adults not targeted for vaccination (aged 15–24 years)	855	247	28.7	24.5–33.8	56	6.8	4.5–10.1		
Age groups sampled for the serosurvey				0.000				0.000	
1–4 years	382	9	2.0	0.8–4.7	1	0.3	0.0–2.2		
5–9 years	456	27	5.5	4.0–7.7	7	1.4	0.6–3.2		
10–14 years	495	58	12.3	8.9–16.8	15	3.8	2.2–6.3		
15–19 years	448	91	20.2	16.6–24.3	20	4.7	2.8–7.9		
20–24 years	407	156	38.7	32.7–45.0	36	9.2	5.9–13.9		
Sex				0.676				0.249	
Male	953	145	15.5	12.9–18.5	41	4.5	3.2–6.2		
Female	1235	196	16.2	13.1–19.9	38	3.4	2.2–5.4		

Anti-HBc, antibodies against core antigen of hepatitis B virus (HBV); HBsAg, surface antigen of HBV; CI, confidence interval; HepB3, national coverage with 3 doses of hepatitis B vaccine.