# Factors associated with hepatitis B vaccination in Laos: findings from the multiple indicator cluster surveys in 2011/12 and 2017

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## Summary

**Background** Within Laos, the vaccination coverage rates with the monovalent hepatitis B birth dose vaccine and hepatitis B antigen-containing combination vaccines remain stagnant with 75% and 64%, respectively, in 2021. In this study, we used data from the Multiple Indicator Cluster Surveys to identify possible factors that represent barriers for receiving these childhood vaccinations.

**Methods** Data from the Multiple Indicator Cluster Surveys in 2011/12 and 2017 were analysed to examine factors associated with receiving the hepatitis B-containing vaccines using regression modelling. Data analyses were conducted in R.

**Findings** In 2011/12, the weight-adjusted coverage rate for receiving the hepatitis B birth dose was 48%, while the coverage with the hepatitis B antigen-containing combination vaccine was 55.1% based on both vaccination documents and recall; compared to 69.3% and 59.4% respectively in 2017. Ethno-linguistic group, maternal education, healthcare utilization and wealth were associated with receiving the vaccinations against hepatitis B.

**Interpretation** National estimates of vaccination coverage rates can conceal country-specific regional or socio-economic variations. Children from Hmong-Mien households, from less wealthier households and whose mothers were less educated and were not able to or did not utilize healthcare were identified as being less likely to receive the vaccinations. These findings indicate the need for improving access to healthcare, in particular for minority groups.

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**Keywords:** Laos; Child health; Hepatitis B; Vaccination coverage; Routine immunisation; Household surveys

## Introduction

Vaccination is one of the most powerful and cost-effective public health interventions. Between 1990 and 2017, deaths due to vaccine-preventable diseases declined from 5.1 to 1.8 million per year in children under 5.[1]

In Laos, vaccine-preventable diseases still represent a substantial public health threat. In recent years, outbreaks of vaccine-preventable diseases have been reported.[2–5] Hepatitis B is endemic in Laos and the prevalence of the hepatitis B surface antigen (HBsAg; used as a marker for chronic infection) in the general population is estimated to be 5–6%, based on a recent study published in 2022.[6] Although several studies reported on HBsAg prevalence rates in blood donors,

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## Research in context

### Evidence before this study

The WHO's global hepatitis strategy aims to reduce new hepatitis infections by 90% and hepatitis-related deaths by 65% between 2016 and 2030. However, in the context of Laos, there are several challenges to overcome. Hepatitis B is endemic in Laos and, due to the age-dependent risk of developing chronic hepatitis B infection, infants are particularly at risk. Vaccination at birth is recognized to be the most important tool for disease prevention, yet, in Laos, the vaccination coverage with hepatitis B antigen-containing vaccines remains suboptimal. Studies investigating hepatitis B infection or hepatitis B vaccination coverage rates in Laos differ widely in design, settings and target populations, making it difficult to draw nation-wide conclusions regarding hepatitis B epidemiology in the country.

### Added value of this study

This study uses data from the most recent multiple indicator cluster survey (MICS) which is designed to provide comprehensive data on child and maternal health. The data is nationally representative. We provide relevant information regarding hepatitis B vaccination coverage rates in Laos in children under two years of age and investigated demographic and socio-economic factors that affect hepatitis B vaccination coverage rates.

### Implications of all the available evidence

This is the first study utilizing MICS data to investigate vaccination-related research questions in Laos, complementing data provided by previous studies. We identified important factors that negatively affect the vaccination coverage and formulated suggestions to address these factors. In addition, the publication of the accompanying code may encourage others to exploit the large amount of publicly available data in future studies in an open and transparent manner, improving research quality overall.

women and children in the past years, it is difficult to understand hepatitis B epidemiology in Laos due to large differences in study populations, study designs and study sites.

The risk of chronic infection with hepatitis B is strongly related to the age at infection: infection in early childhood results in chronic infection in 95% of cases, while infection as an adult only leads to 5% of chronic infection.[7,8] The hepatitis B birth dose is of special relevance for preventing chronic hepatitis B infection as mother-to-child transmission is one of the main transmission routes in endemic countries.[7] Delaying the hepatitis B birth dose results in an increased risk of infection for children born to hepatitis B infected mothers; however, even a delayed vaccination can still have a preventative effect. Recognizing the importance of vaccination at birth, the WHO recommends vaccination preferably within 24 h or, if that is not feasible, up to the time point of the next dose in the vaccination schedule.[8]

Since 2001, hepatitis B vaccination at 6, 10 and 14 weeks of age combined with a diphtheria-tetanus-pertussis vaccine, was included in the vaccination schedule in Laos, followed by introduction of the hepatitis B birth dose with monovalent vaccine in 2003. At present, hepatitis B vaccination is part of the pentavalent diphtheria-tetanus-pertussis-hepatitis B-*Haemophilus influenzae* type b vaccine (DTPw-HepB-Hib).[9] Childhood immunization services are offered directly at the healthcare facility or during outreach activities in the villages.

Vaccination coverage data are routinely used to assess the performance of vaccination programmes. Despite improvements made in the health sector in Laos in recent years, the vaccination coverage for the third dose of the pentavalent vaccine and the hepatitis B birth dose in 2021 remains low at 75% and 64%.[10]

It is crucial for the success of vaccination programmes to maintain high vaccination coverage not just overall in the population but also in hard-to-reach settings and underserved population groups. Therefore, it is important to identify possible socio-economic factors that represent barriers for receiving childhood vaccinations.

The Multiple Indicator Cluster Surveys (MICS) were designed to collect internationally comparable household survey data.[11] The survey includes information on households, women/men, children aged 5–17 years and children under 5 years.

In this study, we examine the MICS data from 2011/2012 and 2017 to identify factors associated with the vaccination coverage with the monovalent hepatitis B birth dose vaccine and hepatitis B antigen-containing combination vaccines in Laos.

## Methods

### Data

Data from the MICS in 2011/12 and from the MICS in 2017 were obtained on the MICS website (https://mics.unicef.org/surveys). In the study, villages were selected as primary sampling units (PSU) and households were selected at the second stage. In this study, we used the datasets containing information of children <5 years of age and women between 15 and 45 years of age. The final sample weights are provided in each dataset. A detailed description of the methods can be found in the technical appendices of the reports from 2012 to 2017 that are available online and on the MICS website.

The vaccination histories were only available for children from 0 to 2 years in the 2017 survey. Therefore, only this age range was selected in both survey rounds (Figure S1). Only those children were selected whose mothers gave information regarding antenatal care (ANC) for the last live birth in the past two years. For the analysis of factors associated with the hepatitis B birth dose, the data of 4846 children were available in the survey from 2011/12 and 4958 in the survey from 2017. For the analysis of factors associated with vaccination with hepatitis B antigen-containing combination vaccines, only children aged 1–2 years were selected, to account for vaccination delay as younger children may not have completed the full round of vaccinations, resulting in 2678 children from 2011/12 and 2758 from 2017 included in the analyses.

### Variables

If the vaccination cards or other documents were not available, the mother's/caretaker's recall was used. The main outcome variables in this study were binary and indicated whether a child had received a specific vaccination or not. The dependent variables were defined as described in Table 1.

Variables deemed important according to the literature and country-specific knowledge were selected from the dataset as independent factors: sex, region (central, north, south), area (urban vs rural), ethno-linguistic group of household, wealth index quintile of household, the mother's education, ANC history of mother and assistance at delivery.[12–14] The questions regarding ANC history of mother and assistance at delivery were part of the questionnaire for women aged 15–45 years. The data from the women's questionnaire was merged with the children's questionnaire using the key variables according to the instructions provided online (https://mics.unicef.org/tools). Only women who had a live birth during the past two years were asked questions regarding ANC and the delivery for the last live birth; thus, the information is not child-specific, but mother-specific. However, ANC and delivery practices were believed to be an important indicator for hepatitis B vaccination at birth and therefore those variables were retained in the analyses, based on the assumption that ANC behaviour and delivery practices do not change for the individual woman.

### Data analysis

A detailed description of the data analyses can be found in the Supplementary Material. All code used in the analysis is available at GitHub.

Data analyses were conducted using R software[15] and a significance level of 0.05 was used. We applied an unconditional subpopulation analysis approach[16] and performed weighted multiple regression analyses to identify factors associated with having been vaccinated. Adjusted odds ratios with their 95% confidence interval were reported. As a sensitivity analysis, we also performed unweighted multilevel modelling including households as a random factor. The latter allows taking into account the dependency among the observations, resulting from the fact that children may come from the same household and is presented in the Supplementary Material (Tables S5, S7, S9 and S11). In addition, we performed sensitivity analyses to assess the impact of restricting the inclusion criteria to either children with a vaccination card or without a vaccination card (Tables S6, S8, S10 and S12). Analyses were not adjusted for multiplicity and are therefore exploratory.

### Role of the funding source

The funders had no role in study design, data collection, data analysis, interpretation, writing of the report.

## Results

### Population characteristics in 2011/12

Descriptive analysis showed that both subsets of data (children aged 0–2 years and children aged 1–2 years) were very similar in their socio-economic characteristics (Table S1). In 2012, most children aged 0–2 years were from households in rural areas with road access (68.7%), 9.7% were from households in rural areas without road access and 21.6% belonged to households in urban areas (Table S1). About half of the children belonged to Lao-Tai households (53.6%), 28.9% belonged to Mon-Khmer households and 13.9% to Hmong-Mien households. 29% of the households belonged to the poorest wealth index quintile and 14.9% to the richest. Overall, more children were born at home than in a hospital (60.4% vs 32%).

Participant characteristics strongly depended on their location: most households belonging to the richest

| Dependent variable | Survey 2011/12 | Survey 2017 |
|---|---|---|
| Having received hepatitis B vaccination at birth (yes/no) | Based on either vaccination documents or recall, independently of the timing of the vaccination. | Based on either vaccination documents or recall, independently of the timing of the vaccination. |
| Having received at least three doses of hepatitis B antigen-containing combination vaccine (yes/no) | Based on either vaccination documents or recall, independently of the timing of the vaccination.[a] | Based on either vaccination documents or recall, independently of the timing of the vaccination. |

[a]Among participants whose vaccination history was based on the mother's or caretaker's recall, stating to have received the Diphtheria-Tetanus-Pertussis (DTP) vaccine was also counted as having received the hepatitis B vaccine (since the hepatitis B vaccination was given as a tetravalent DTP-HepB vaccine from 2001 until 2009, when it was replaced by the DTPw-HepB-Hib vaccine).

*Table 1:* **Definition of dependent variables.**

wealth index quintile were located in urban areas, while most poor households were in rural areas without road access (Fig. 1a). In urban areas, Lao-Tai households made up the majority, while the distribution of ethnolinguistic groups was more varied in rural areas (Fig. 1b). The majority of births in rural areas were home births, contrary to urban settings (Fig. 1c).

Vaccination documents were available for about half (47.0%) of the children aged 0–2 years. From those children with vaccination documents, 63.5% had received the hepatitis B birth dose as compared to 34.2% of those children whose vaccination documents were not available. In total, 48% of the children with or without vaccination documents had received the hepatitis B birth dose (Table S2).

Vaccination documents were available for 44.5% of the children aged 1–2 years and among those, 81.1% of the children had received three doses of the hepatitis B antigen-containing combination vaccine. Among children whose vaccination history was based on the caretaker's/mother's recall, 34.2% had received three doses of the hepatitis B antigen-containing combination

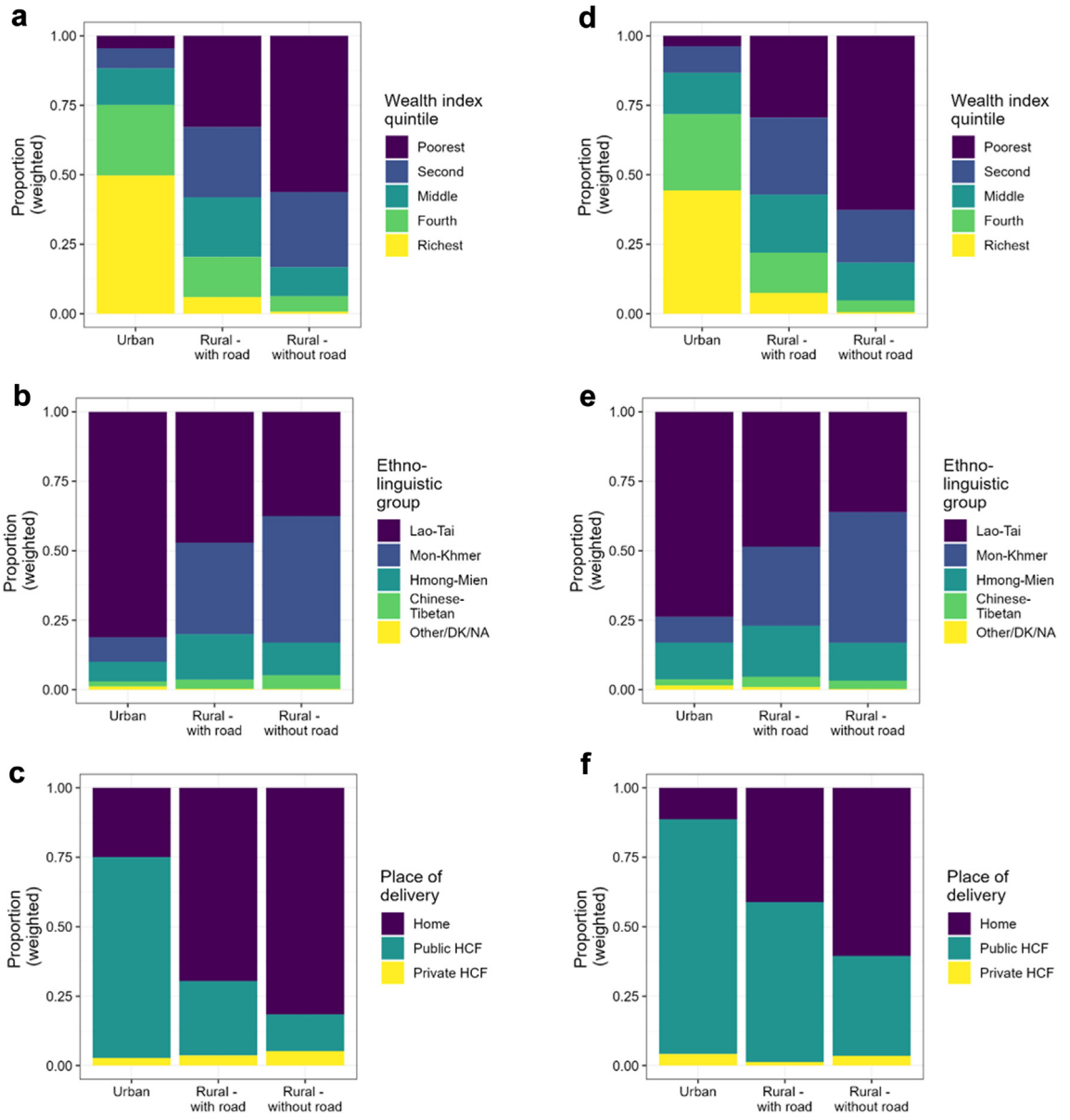



*Fig. 1:* Characteristics of the participants in the multiple indicator cluster surveys in 2011/12 (N = 4774.3; weighted estimates) and 2017 (N = 4848.5; weighted estimates). DK = don't know; NA = not available; HCF = healthcare facility.

vaccine. In total, 65.5% of the children had received three vaccinations with the hepatitis B antigen-containing combination vaccine (Table S2).

The estimated vaccination coverage with the hepatitis B birth dose varied extensively between provinces: while up to 74.5% of the children in Vientiane Capital were vaccinated, the coverage in Huaphan province reached only 15% (Fig. 2). The coverage with three doses of the hepatitis B antigen-containing combination vaccine varied from 23.1% in Phongsaly to 88.2% in Xayabouli (Fig. 2).

### Factors associated with receiving the hepatitis B birth dose in 2011/12

Participants who were from a Mon-Khmer or Hmong-Mien background were significantly less likely to have received the hepatitis B birth dose as compared to the Lao-Tai (Mon-Khmer: aOR = 0.74; 95% CI 0.56–0.97; p = 0.034; Hmong-Mien: aOR = 0.44; 95% CI 0.30–0.65; p = 0.00017). Children whose mothers gave birth in a hospital were more likely to be vaccinated (aOR = 2.7; 95% CI 2.03–3.65; p < 0.00001) as were those having a mother who attended ANC visits during her pregnancy (≤3 visits: aOR = 1.56; 95% CI 1.33–1.85; p = 0.0001; >3 visits; aOR = 2.26; 95% CI 1.71–2.98; p < 0.0001). Children from households belonging to the second to richest wealth index quintile were more likely to be vaccinated as compared to children from the poorest households (aOR = 1.19, 95% CI = 1.02–1.39; p = 0.036). Older children were also more likely to be vaccinated as compared to children under 1 year (1 year: aOR = 1.55; 95% CI = 1.25–1.92; p = 0.00034; 2 years: aOR = 2.94; 95% CI = 2.08–4.16; p < 0.0001) (Table 2).

When using a multilevel modelling approach without weights, all variables (excluding sex of child and level of mother's education) were associated with being vaccinated (Table S5). Looking at children without vaccination cards separately, children who came from the South, who were female, whose mothers received education and attended ANC visits were more likely to be vaccinated while children from Hmong-Mien or Mon-Khmer households were less likely to be vaccinated (Table S6). In the subset of children with vaccination cards, children who were living in rural areas were less likely to be vaccinated and children who were born at a hospital were more likely to be vaccinated (Table S6).

### Factors associated with receiving the hepatitis B antigen-containing combination vaccine in 2011/12

Logistic regression showed that children living in Hmong-Mien households were less likely to have received the hepatitis B antigen-containing combination vaccine (Hmong-Mien: aOR = 0.35; 95% CI 0.21–0.60; p = 0.00047) (Table 2). Children whose mothers received formal education were 1.92 times more likely to have been vaccinated as compared to those whose mothers stated not to have received any education (95% CI 1.46–2.53; p < 0.0001). Having a mother who went to ANC visits was also positively associated with having received the hepatitis B antigen-containing combination vaccine (less than three times: aOR = 1.56; 95% CI 1.28–1.92; p = 0.00012; more than three times: aOR = 2.61; 95% CI 1.81–3.77; p = 0.02).

In the multilevel model, the same factors were identified but in addition, the variable indicating the area was also found to be significant (Table S7). Children from rural areas without road access were found to be less likely to be vaccinated as compared to children from urban areas (aOR = 0.63; 95% CI 0.42–0.93; p = 0.02).

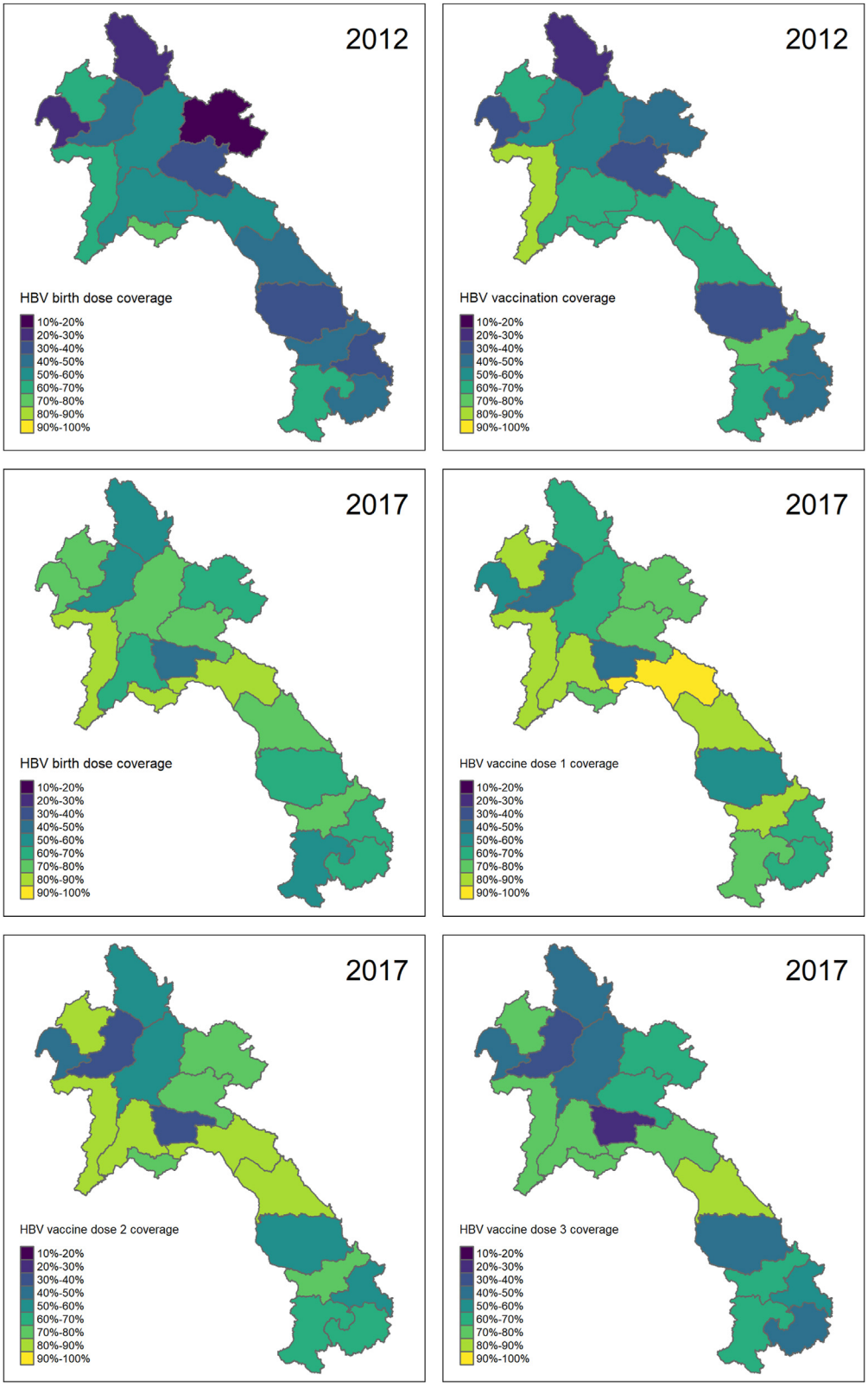
When looking at children with both vaccination card and without vaccination card individually, in both subset analyses, children from Hmong-Mien or Chinese-Tibetan households were less likely to be vaccinated and children whose mothers attended ANC visits were more likely to be vaccinated (Table S8).

### Population characteristics in the 2017 survey

In 2017, 60.3% of the 0–2 year old children belonged to households in rural areas with road access, 13.6% belonged to households in rural areas without road access and 26.2% were from urban areas (Table S1). Similar to the 2011/12 survey data, about half of the households were of Lao-Tai ethnicity (53.5%), 25.9% belonged to the Mon-Khmer group and 16.4% to Hmong-Mien households. 27.2% of the households belonged to the poorest wealth index quintile while 16.2% belonged to the richest. In contrast to 2011/12 survey data, more mothers stated to have delivered their last live birth in hospitals as compared to at home (46.7% vs 35.6%) and more children had mothers with more than 3 ANC consultations (62.7% vs 36%). In 2017, 19.4% of the participants had mothers who stated not to have received any education as compared to 30.7% in 2011/12.

Similar to the 2011/12 survey data, participant characteristics strongly depended on the location: in rural areas without road access, the majority of households belonged to Mon-Khmer, Hmong-Mien or other ethnic groups (Fig. 1e), home births were more prevalent in rural areas (Fig. 1f) and households belonging to the richer wealth index quintiles were primarily located in urban areas (Fig. 1d).

Vaccination documents were available for 60.4% of the children aged 0–2 years. Among those with vaccination documents, 79.9% of the children received the hepatitis B birth dose as compared to 53.2% according to caretaker's recall. Overall, 69.3% of the children received the birth dose. Among the 1–2 year olds, vaccination documents were available for 51.6% of the children and among those, 79.9% had received the full course of hepatitis B antigen-containing combination vaccine. Among those children whose vaccination


2012
HBV birth dose coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%
2012
HBV vaccination coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%
2017
HBV birth dose coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%
2017
HBV vaccine dose 1 coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%
2017
HBV vaccine dose 2 coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%
2017
HBV vaccine dose 3 coverage
10%-20%
20%-30%
30%-40%
40%-50%
50%-60%
60%-70%
70%-80%
80%-90%
90%-100%

history was based on recall, 37.5% had received the hepatitis B antigen-containing combination vaccinations. In total, 59.4% of all children with or without vaccination documents were vaccinated (Table S2).

The vaccination coverage with the hepatitis B birth dose varied between provinces from the lowest estimate at 48.6% in Xaysomboun to estimates between 82.7% and 89.2% in Vientiane Capital, Bolikhamxay and Xayabouly (Fig. 2). When comparing the birth dose vaccination coverage to the estimates from 2012, an overall increase in all but one province can be observed (Figure S4a). The differences in vaccination coverage between the survey years vary extensively as well (8.2%–47.2%).

The coverage with the first dose of the hepatitis B antigen-containing combination vaccine ranged from 40.5% in Oudomxay to 94.3% in Bolikhamxay compared to 27.1% in Xaysomboun to 80.0% in Khammouane for dose 3 (Fig. 2). In contrast to the vaccination coverage with the birth dose, five provinces seem to show a decline, while the rest experience a positive increase. The range of differences is notably varied, underscoring the heterogeneity in vaccination trends observed among the regions during this period (Figure S4b).

### Factors associated with receiving the hepatitis B birth dose in 2017

In the logistic regression model, children belonging to Hmong-Mien households were less likely to be vaccinated with the hepatitis B birth dose as compared to households of Lao-Tai ethnicity (aOR = 0.5; 95% CI 0.36–0.70; p = 0.00027). Children from households belonging to the second to richest wealth index quintile (aOR = 1.34, 95% CI 1.03–1.75; p = 0.036) and those whose mothers delivered their last live born child in a public health center (aOR = 4.63, 95% CI 3.51–6.11; p < 0.0001) or hospital (aOR = 6.17; 95% CI 4.74–8.02; p < 0.0001) were more likely to be vaccinated (Table 3).

The multilevel model identified the same variables as important factors for receiving the hepatitis B birth dose and in addition, the variable indicating ANC behavior was also significant (Table S9).

Children from wealthier households, whose mothers delivered their last live born child in a health-care facility and who attended ANC visits were also identified in the subset of children without vaccination documentation more likely to be vaccinated (Table S10).

### Factors associated with receiving the hepatitis B antigen-containing combination vaccine in 2017

Belonging to a Mon-Khmer or Hmong-Mien household was negatively associated with receiving the hepatitis B antigen-containing vaccination (Mon-Khmer: aOR = 0.62, 95% CI 0.48–0.80; p = 0.00093; Hmong-Mien: aOR = 0.47; 95% CI 0.29–0.77; p = 0.0045). Having a mother who attended up to 3 ANC visits (aOR = 1.34; 95% CI 1.04–1.82; p = 0.028) or more than three ANC visits (aOR = 1.94, 95% CI 1.34–2.94; p = 0.0022) was positively associated with vaccination. Children from wealthier households were 1.4 times more likely to have received the hepatitis B antigen-containing combination vaccine (95% CI 1.03–1.77; p = 0.038) (Table 3).

In the multilevel model, the same variables were identified as important for receiving the hepatitis B antigen-containing combination vaccine. In addition, participants from households located in rural regions and in the North were less likely to have been vaccinated (Table S11). Looking at each subset individually, children with and without vaccination cards were less likely to be vaccinated if they were not from a Lao-Tai household (Table S12).

## Discussion

Between the two survey rounds in 2012 and 2017, the vaccination coverage with the hepatitis B vaccinations rose considerably from 48% to 69.3% for the birth dose and from 55.1% to 59.4% for the following three vaccinations. We identified important predictors for receiving hepatitis B vaccinations, and by extension, for other vaccinations that are part of the combination vaccines in Laos. From 2001 to 2009, the hepatitis B vaccinations were given as a tetravalent Diphtheria-Tetanus-Pertussis (DTP)-HepB vaccine until it was replaced by the DTPw-HepB-Hib vaccine.

In both the 2011/12 and 2017 surveys, children from Hmong-Mien households were less likely to have received the hepatitis B vaccinations compared to children from Lao-Tai households. The distribution of ethno-linguistic groups in Laos correlates partially with the separation of the provinces into “Northern”, “Central” and “Southern” regions of the country. The population groups belonging to the Lao-Tai language family accounts for the largest share of the population with 53.2%, while the Mon-Khmer and Hmong-Mien

***Fig. 2:*** Estimated hepatitis B vaccination coverage in Laos (weighted proportions) among children. For the combination vaccines in 2011/12, we did not distinguish between the numbers of doses received. The map was created in R (see supplement information). The shapefiles containing the administrative boundaries of Lao PDR from 2012 were obtained from the International Steering Committee for Global Mapping (retrieved from https://maps.princeton.edu/catalog/stanford-cp768st2071). The shapefiles containing the administrative boundaries of the Laos in 2017 were obtained from the Humanitarian Data Exchange website (https://data.humdata.org/dataset/lao-admin-boundaries, dataset provided by the National Geographic Department of Lao PDR, 2019). Projection used: EPSG 4326 –WGS 84.

| Variables | Categories | Receiving hepatitis B birth dose vaccination[a] | | Receiving hepatitis B surface antigen-containing combination vaccine[b] | |
|---|---|---|---|---|---|
| | | Adj. OR | [95% CI], p value | Adj. OR | [95% CI], p value |
| Area | Urban | ref | | ref | |
| | Rural–with road | 0.71 | [0.46, 1.10], 0.13 | 1.17 | [0.64, 2.12], 0.62 |
| | Rural–without road | 0.58 | [0.24, 1.40], 0.23 | 0.69 | [0.34, 1.38], 0.302 |
| Wealth index quintile | Poorest (1st quintile) | ref | | ref | |
| | Second to richest (2nd, 3rd, 4th and 5th quintiles) | 1.19 | [1.02, 1.39], 0.036 | 1.27 | [1.03,1.55], 0.03 |
| Sex | Male | ref | | | |
| | Female | 1.13 | [0.99, 1.29], 0.076 | 1.12 | [0.92, 1.36], 0.25 |
| Ethno-linguistic group of household | Lao-Tai | ref | | ref | |
| | Mon-Khmer | 0.74 | [0.56, 0.97], 0.034 | 0.89 | [0.61, 1.30], 0.55 |
| | Hmong-Mien | 0.44 | [0.30, 0.65], 0.00017 | 0.35 | [0.21, 0.60], 0.00047 |
| | Chinese-Tibetan & other, don't know, missing | 0.69 | [0.40, 1.19], 0.19 | 0.48 | [0.24, 0.97], 0.047 |
| Mother's education level | None | ref | | ref | |
| | Primary, lower/upper/post-secondary, non-tertiary, higher | 1.37 | [1.06, 1.77], 0.023 | 1.92 | [1.46, 2.53], 0.00004 |
| Place of delivery (last live birth of mother in the last two years) | Home | *ref* | | *Excluded due to multicollinearity; correlation with "ANC visits"* | |
| | Public health center | 1.66 | [0.94, 2.93], 0.09 | | |
| | Public hospital, private hospital, private clinic, other | 2.72 | [2.03, 3.65], p < 0.0001 | | |
| ANC visits (last live birth of mother in the last two years) | No visit | ref | | ref | |
| | Yes, 3 visits or less | 1.56 | [1.33, 1.85], p < 0.0001 | 1.56 | [1.28, 1.92], 0.00012 |
| | Yes, more than 3 | 2.26 | [1.71, 2.98], p < 0.0001 | 2.61 | [1.81, 3.77], p < 0.00001 |
| Age (years) of child | 0 years | ref | | NA | |
| | 1 year | 1.55 | [1.25, 1.92], 0.00034 | ref | |
| | 2 years | 2.94 | [2.08, 4.16], p < 0.0001 | 1.40 | [1.07, 1.84], 0.020 |

Adj. = adjusted; OR = odds ratio; CI = confidence interval; ref = reference level. [a]Complete case analysis excludes 55 participants due to missing data. [b]Complete case analysis excludes 50 participants due to missing data.

***Table 2:*** **Multivariable logistic regression analysis with survey weights: Hepatitis B vaccination coverage and associated factors in Laos in the 2011/12 survey.**

account for 11% and 9.2%, respectively. While the Hmong-Mien groups reside mainly in Northern regions, the Mon-Khmer groups predominantly reside in Southern areas close to the border to Vietnam, but are also found in Northern areas. The majority of the Lao-Tai live along the Mekong.[17] Minority groups in Laos experience poverty at a higher rate than the Lao-Tai and face disadvantages in education, access to healthcare and access to clean water and sanitation. Limited access to healthcare for minority groups who tend to live in more remote areas and a historical distrust between the Hmong-Mien and the national authorities could explain the observed discrepancies in vaccine coverage rates between the Hmong-Mien in comparison to the Lao-Tai.[17–20] Differences in the hepatitis B birth dose coverage between ethnic groups were also observed in a study based on MICS data from Vietnam with children from the ethnic majority being more likely to have received the hepatitis B birth dose within 24 h of birth.[21] Further investigations are needed to understand if the main obstacles for vaccinations derive from difficulties to access healthcare services or from ethnographic boundaries. Outreach programmes specifically tailored to the needs of the minority communities may identify and overcome obstacles that hinder the provision of or access to immunization activities.

The regional or ethno-linguistic disparities observed in this study seemed more strongly associated with the hepatitis B vaccination than the classification of the households into "rural" and "urban". Only in the mixed models for the 2012 data, children from rural areas were less likely to have received the hepatitis B birth dose. Ensuring road connectivity throughout the country is important for health infrastructure, as vaccination coverage rates rely on vaccine supply chains. In Laos, vaccines are distributed from the central storage in Vientiane to provinces and then to districts and health centers. Vaccination services are offered either at the facility or through outreach campaigns in villages.[22–24] In the past three decades, the road network in Laos has been undergoing major changes and now comprises more than 50,000 km.[25,26] These investments in infrastructure, alongside improvements in the healthcare system Laos[22] may have resulted in an overall improvement of access to healthcare in rural and remote areas. Our findings suggest that cultural barriers between

| Variables | Categories | Receiving hepatitis B birth dose vaccination | | Receiving hepatitis B surface antigen-containing combination vaccine | |
|---|---|---|---|---|---|
| | | Adj. OR | [95% CI], p value | Adj. OR | [95% CI], p value |
| Area | Urban | ref | | ref | |
| | Rural–with road | 0.90 | [0.61, 1.33], 0.60 | 1.29 | [0.88, 1.89], 0.20 |
| | Rural–without road | 0.75 | [0.46, 1.21], 0.25 | 1.25 | [0.71, 2.20], 0.44 |
| Region | Central | *Excluded due to multicollinearity; correlation with "ANC visits"* | | ref | |
| | North | | | 0.79 | [0.47, 1.31], 0.37 |
| | South | | | 0.97 | [0.57, 1.65], 0.91 |
| Wealth index quintile | Poorest (1st quintile) | ref | | ref | |
| | Second to richest (2nd, 3rd, 4th and 5th quintiles) | 1.34 | [1.03, 1.75], 0.036 | 1.35 | [1.03, 1.77], 0.038 |
| Sex | Male | ref | | ref | |
| | Female | 0.95 | [0.82, 1.09], 0.44 | 1.03 | [0.89, 1.19], 0.70 |
| Ethno-linguistic group of household | Lao-Tai | ref | | ref | |
| | Mon-Khmer | 0.86 | [0.65, 1.14], 0.30 | 0.62 | [0.48, 0.80], 0.00093 |
| | Hmong-Mien | 0.50 | [0.36, 0.70], 0.00027 | 0.47 | [0.29, 0.77], 0.0045 |
| | Chinese-Tibetan & other, don't know, missing | 0.78 | [0.54, 1.12], 0.19 | 0.86 | [0.47, 1.59], 0.64 |
| Mother's education level | None | ref | | ref | |
| | Primary, lower/upper/post-secondary, non-tertiary, higher | 1.21 | [0.97, 1.50], 0.096 | 1.40 | [1.00, 1.95], 0.059 |
| Place of delivery (last live birth of mother in the last two years) | Home | ref | | ref | |
| | Public health center | 4.63 | [3.51, 6.11], <0.0001 | 1.29 | [0.95, 1.75], 0.11 |
| | Public hospital, private hospital, private clinic, other | 6.17 | [4.74, 8.02], <0.0001 | 1.24 | [0.94, 1.63], 0.13 |
| ANC visits (last live birth of mother in the last two years) | No visit | ref | | ref | |
| | Yes, 3 visits or less | 1.17 | [0.85, 1.61], 0.35 | 1.34 | [1.04, 1.72], 0.028 |
| | Yes, more than 3 | 1.36 | [0.97, 1.91], 0.081 | 1.94 | [1.31, 2.87], 0.002 |
| Age (years) of child | 0 years | ref | | NA | |
| | 1 year | 1.34 | [1.12, 1.60], 0.0034 | ref | |
| | 2 years | 1.30 | [0.99, 1.70], 0.063 | 0.92 | [0.71, 1.19], 0.53 |

Adj. = adjusted; OR = odds ratio; CI = confidence interval; ref = reference level.

***Table 3:*** **Multivariable logistic regression analysis with survey weights: Hepatitis B vaccination coverage and associated factors in Laos in the 2017 survey.**

ethno-linguistic groups have a greater impact on vaccination coverage rates as compared to geographic areas.

In this study, children from wealthier households were more likely to have been vaccinated as compared to the poorest population wealth quintile. Although vaccination services for children are free of charge, the lack of money may still represent a barrier for healthcare access as parents may not have the means for transportation or cannot afford to take time from work. The wealth index also relates to the geographic and ethno-linguistic differences in the country as particularly ethnic minorities belong to the poorest wealth index and live in rural areas.

Between the two surveys, home birth decreased considerably from 60% to 40%.[27,28] Nevertheless, the place of delivery still represents an important indicator for hepatitis B birth dose vaccination: children whose mothers stated that they delivered their last live birth in the past 2 years at a hospital were more likely to be vaccinated with the hepatitis B birth dose in both surveys as compared to mothers who delivered at home. In case of home births, health care facilities in villages may offer assistance and provide vaccinations at birth as part of their service.[29] Due to their correlated nature, it is not possible to distinguish completely between the variables "place of delivery" and "assistance at delivery". However, as previously shown, the availability of the vaccine and the knowledge of healthcare workers are both important predictors for the receipt of the vaccination: In a study assessing knowledge and practices concerning the hepatitis B birth dose, healthcare facility-based vaccination coverage with the birth dose was 74%. The report detailed that the vaccine was out of stock at about half of the facilities that were visited and that misunderstandings of vaccine contraindications and rare assistance of medical staff with home births added to missed opportunities to vaccinate.[29] Vaccination with the birth dose within 24 h of birth is an especially important issue as mother-to-child transmission is one of the main transmission routes in endemic countries.[7] Whenever hepatitis B birth dose vaccines are not in stock or the medical personnel are lacking the relevant

knowledge, missed vaccinations at delivery will also occur in healthcare facilities. Home births represent an additional challenge, as vaccines may need to be delivered in remote areas and the birth assistants—if present—need to be adequately trained. Improving the coverage with the hepatitis B birth dose requires a multi-level approach including training of medical staff and improving vaccine supply chains.

In the 2011/12 survey, children whose mothers attended ANC visits during the pregnancy with their last live born child were more likely to have been vaccinated with the hepatitis B birth dose; this was not observed in the 2017 survey. A possible explanation could be the increased number of births at a healthcare facility. ANC behaviour also played a role for further hepatitis B vaccinations: children of women who stated to have had ANC visits were more likely to be vaccinated. The utilization of maternal healthcare services is important to ensure the well-being of mother and child and for raising awareness of the mothers regarding the importance of post-natal care including vaccinations. However, a study based on MICS data from 2000 to 2012 from Laos also reported socio-economic disparities in the utilization of maternal healthcare services: women from minority ethnic groups used maternal healthcare services less than Lao-Tai women.[30]

The mothers' educational levels were associated with hepatitis B vaccination in the 2011/12 survey: children whose mothers had received some education were more likely to be vaccinated as compared to mothers with no education. Even though it is unclear to what extend the mother's education played a role, the finding that the mother's education and ANC are strong indicators for hepatitis B vaccinations underlines the importance of raising awareness for immunization benefits and activities in Laos and providing information to pregnant women.

Utilizing the MICS data has certain limitations inherent to the datasets. First, the ANC questions relate to the last live birth in the past two years and not necessarily to the particular child in the children's questionnaire. In the 2011/12 survey, two variables denote ethnicity or language group, while in the 2017 survey, it is only one variable. We chose the variable for "language group of the household head" in the 2011/12 survey since the categories match the ones in the 2017 survey. Another limitation of our study lies in the possibility of subgroup overrepresentation, particularly for socioeconomic factors like the wealth index quintile, which may introduce bias into our findings. Lastly, we cannot exclude the possibility that there were biases in household selection.

In addition, we acknowledge certain limitations that arose from the decisions made during the data analyses: The variable selection was hypothesis-driven and may not include all the variables that may influence vaccination coverage. However, the selection of variables was based on literature research and we consider the risk of missing variables low. The estimation of the proportion of children who received vaccinations was based on both the vaccination card and the recall of the caregiver. Information based on recall is considered less reliable; however, since the proportion of children for which vaccination documents were available ranged from 40 to 60%, we would have lost a considerable portion of the dataset, resulting in a greater bias. The socio-economic characteristics between children with and without vaccination cards differ extensively (Tables S3 and S4). We conducted sensitivity analyses to investigate whether including only children with a vaccination card in the analysis, as opposed to including those without as well. These subset analyses yielded significantly different results; however, certain variables like the ethnolinguistic group of the household remained widely associated with the vaccination outcome. These results should be interpreted with caution, as the dividing of the data in subsets results in different population sizes and multicollinearity issues, which complicates a direct comparison between the individual analyses and the data analyses shown in the result section considerably.

The timing of the hepatitis B birth dose was not considered in this analysis for simplicity reasons, but further data analyses regarding vaccination timeliness are planned. In the 2011/12 survey, we used the recall question of the diphtheria-tetanus-pertussis vaccination as proxy for receiving the hepatitis B vaccinations at 6, 10 and 14 weeks of age, since the hepatitis B vaccination was given as a tetravalent DTP-HepB vaccine from 2001 until 2009, when it was replaced by the DTPw-HepB-Hib vaccine.

## Conclusion

Our study represents the first assessment of hepatitis B vaccination coverage according to socioeconomic factors using national representative survey data in Laos. We identified children from Hmong-Mien households, from households with poor socio-economic status, with less educated mothers and with mothers who did not deliver at a hospital or who did not receive sufficient ANC as particularly vulnerable for missed vaccinations.

Our findings suggest that there is a need for the detailed assessment of barriers that prevent the access of ethnic minority groups to healthcare. Further improvements could be made in health infrastructure; for example investing in the training of medical staff at health center level. Emphasis should be placed on outreach and awareness activities regarding mother and child health for women of reproductive ages.

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#### Data sharing statement

The data from the Multiple Indicator Cluster Surveys are publicly available (https://mics.unicef.org/surveys). A detailed description of the data analyses can be found in the Supplementary Material. All code used in the analysis is available at https://github.com/lhefele/lao-h-076_mics-hepB_public.

#### Editor note

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#### Declaration of interests

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101059.

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