ARTICLE IN PRESS

Vaccine xxx (2018) xxx-xxx



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Factors associated with routine immunization coverage of children under one year old in Lao People's Democratic Republic

Bounfeng Phoummalaysith ^{a,b}, Eiko Yamamoto ^{a,*}, Anonh Xeuatvongsa ^c, Viengsakhone Louangpradith ^{a,d}, Bounxou Keohavong ^{a,e}, Yu Mon Saw ^a, Nobuyuki Hamajima ^a

- ^a Department of Healthcare Administration, Nagoya University Graduate School of Medicine, Nagoya, Japan
- ^b National Health Insurance Bureau, Ministry of Health, Vientiane, Lao Democratic People's Republic
- ^c National Immunization Program, Maternal and Child Health Center, Ministry of Health, Vientiane, Lao Democratic People's Republic
- ^d Administration and Planning Department, Mittaphab Hospital, Vientiane, Lao Democratic People's Republic
- ^e Food and Drug Department, Ministry of Health, Vientiane, Lao Democratic People's Republic

ARTICLE INFO

Article history: Received 13 November 2017 Received in revised form 16 February 2018 Accepted 19 March 2018 Available online xxxx

Keywords:
District
Immunization coverage
Lao People's Democratic Republic
Province
Routine immunization

ABSTRACT

Background: Routine vaccination is administered free of charge to all children under one year old in Lao People's Democratic Republic (Lao PDR) and the national goal is to achieve at least 95% coverage with all vaccines included in the national immunization program by 2025. In this study, factors related to the immunization system and characteristics of provinces and districts in Lao PDR were examined to evaluate the association with routine immunization coverage.

Methods: Coverage rates for Bacillus Calmette-Guerin (BCG), Diphtheria-Tetanus-Pertussis-Hepatitis B (DTP-HepB), DTP-HepB-Hib (Haemophilus influenzae type B), polio (OPV), and measles (MCV1) vaccines from 2002 to 2014 collected through regular reporting system, were used to identify the immunization coverage trends in Lao PDR. Correlation analysis was performed using immunization coverage, characteristics of provinces or districts (population, population density, and proportion of poor villages and highrisk villages), and factors related to immunization service (including the proportions of the following: villages served by health facility levels, vaccine session types, and presence of well-functioning cold chain equipment). To determine factors associated with low coverage, provinces were categorized based on 80% of DTP-HepB-Hib3 coverage (<80% = low group; >80% = high group).

Results: Coverages of BCG, DTP-HepB3, OPV3 and MCV1 increased gradually from 2007 to 2014 (82.2–88.3% in 2014). However, BCG coverage showed the least improvement from 2002 to 2014. The coverage of each vaccine correlated with the coverage of the other vaccines and DTP-HepB-Hib dropout rate in provinces as well as districts. The provinces with low immunization coverage were correlated with higher proportions of poor villages.

Conclusions: Routine immunization coverage has been improving in the last 13 years, but the national goal is not yet reached in Lao PDR. The results of this study suggest that BCG coverage and poor villages should be targeted to improve nationwide coverage.

© 2018 Elsevier Ltd. All rights reserved.

1. Introduction

The Expanded Program on Immunization (EPI) was established by the World Health Organization (WHO) in 1974 [1], and was introduced in Lao People's Democratic Republic (Lao PDR) in 1979 [2]. The National Immunization Program was launched with the introduction of six vaccines (Bacillus Calmette-Guerin [BCG],

E-mail address: yamaeiko@med.nagoya-u.ac.jp (E. Yamamoto).

https://doi.org/10.1016/j.vaccine.2018.03.051

0264-410X/© 2018 Elsevier Ltd. All rights reserved.

Diphtheria, Tetanus, Pertussis, Polio, and Measles [MCV1]) in 1984, in two provinces. The program was gradually extended to all provinces by 1994. Hepatitis B vaccine (HepB) was introduced in 2001 as part of the tetravalent diphtheria-tetanus-pertussis-he patitis B (DTP-HepB), followed by DTP-HepB-Hib (*Haemophilus influenzae* type B) vaccine in 2009. Table 1 shows the immunization schedule in Lao PDR [3,4]. However, the policy on BCG vaccination is at any time before one year old, not only at birth, because most newborns are delivered at home. Although vaccination is performed free of charge for all children under one year old in Lao PDR, it can be applied to children up to five years old if they have not been vaccinated.

Please cite this article in press as: Phounmalaysith B et al. Factors associated with routine immunization coverage of children under one year old in Lao People's Democratic Republic. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.03.051

^{*} Corresponding author at: Department of Healthcare Administration, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550. Japan.

Table 1Vaccine schedule in the Expanded Programme on Immunization in Lao PDR.

Vaccine	Age
Hepatitis B	Birth
BCG	Birth
DTP-HepB-Hib	6, 10, and 14 weeks
OPV	6, 10, and 14 weeks
Measles	9 months

BCG, Bacillus Calmette-Guérin vaccine; DTP-HepB-Hib, diphtheria-tetanus-pertussis-hepatitis B-*Haemophilus influenzae* type B vaccine; OPV, oral polio vaccine.

Vaccination coverage is a key indicator of vaccination program performance, and achieving very high vaccination coverage of routine vaccines is necessary for eliminating vaccine preventable diseases. In Lao PDR, the goal for vaccination coverage was at least 90% in 2015 and is at least 95% in 2025 [5,6]. It is reported that routine vaccination coverage remains low in many areas in Lao PDR and that there have been measles, diphtheria, and vaccinederived poliovirus outbreaks [7–10]. Previous studies which were conducted in some districts or provinces suggested that factors related to low immunization coverage were, poor knowledge among child caretakers, difficulties in access, ethnic minority, lack of advice on vaccine, lack of vaccine supply, difficulty in maintaining the cold chain, and lack of availability and competence among healthcare workers [4,7,11]. To address these issues, the National Immunization Program (NIP) and the government have taken many actions, such as, using materials translated in the local languages to educate the community, training on vaccine management and cold chain maintenance, and the development of a vaccine supply system.

To improve routine immunization coverage nationally, factors affecting coverage in provinces or districts with low coverage should be identified. In Lao PDR, vaccination activities are mostly carried out by mobile teams due to unavailability of cold chain systems as well as distance to health facilities. Vaccination by mobile teams is provided quarterly and health centers have to deliver a notice to the chief of the village and health volunteers, to ensure that villagers with children in the targeted population are notified to attend the immunization sessions, and to gather the targeted children. The aim of this study was to identify factors associated with immunization coverage among children under one year old at provincial and district levels.

2. Materials and methods

2.1. Reporting system of immunization data in Lao PDR

The regular reporting system of immunization data in Lao PDR is well established. Health centers report the number of children who were vaccinated to the district health offices every month. The compiled data are then reported to provincial health departments, and finally to NIP. NIP aggregates, analyzes the data, and reports to the Ministry of Health annually.

For this analysis, national data from the immunization system based on the coverage of BCG, 3 doses of OPV (OPV3) and MCV1 from 2002 to 2014, 3 doses of DTP-HepB (DTP-HepB3) from 2002 to 2008, and 3 doses of DTP-HepB-Hib (DTP-HepB-Hib3) from 2009 to 2014 in all districts and provinces collected through the regular reporting system, were used. The data of immunization coverage before 2002 were incomplete. The Ministry of Health defines immunization coverage as the number of children who received vaccination by age of one year divided by the estimated

number of children surviving to their first birthday. Dropout rate of DTP-HepB-Hib was derived as the difference between DTP-HepB-Hib1 and DTP-HepB-Hib3 coverage in 2014.

2.2. Characteristics of provinces

The National Statistics Bureau of Laos and the Poverty Reduction Office are responsible for collecting data on population, poor districts, poor villages, and high-risk villages. A family was rated as poor when the family's monthly income per person was lower than the poverty criteria; under 192,000 Kip (24 USD) nationally, under 180,000 Kip (22.5 USD) in rural areas and under 240,000 Kip (30 USD) in urban areas (Prime Minister's Decree No. 309 issued on November 14, 2013). Poor villages are defined meeting all the following five criteria: (1) over 50% of the total families are poor families, (2) no primary school, or has a school in the nearest village by walking over an hour, (3) no village drug kit or health center or when the nearest health center or district hospital can only be reached by walking for more than two hours, (4) no access to clean water, or (5) no road access or has road access only in dry season. The criterion for poor districts is that over 51% of total villages in the district are poor villages. High-risk villages are defined as villages in rural remote or border areas with migrant workers, refugees, and ethnic minority groups.

2.3. Categories of villages by vaccine providing session types

There are three vaccine-providing session types to each village: fixed site, outreach, and overnight. Fixed site villages are located approximately within 10 km from the health facility but require 30 min or less for the target population to reach either by walking or by using any kind of vehicle. Outreach villages are located around 5–10 km from the health facility but require more than one hour to reach. Overnight villages have difficulty in access, communication or service delivery due to the socio-economic, cultural, or traditional beliefs. The health workers drive to outreach and overnight villages but cannot return to the facility on the same day after the completion of the vaccination session in overnight villages. Although there were 148 districts, the data on session type were only available for 145 districts.

2.4. Cold chain equipment

Cold chain equipment are refrigerators and freezers which are used to keep vaccines at the health centers or used in carrying vaccines to villages. Depending on the conditions of all cold chain equipment at health centers, three categories are identified: well-functioning, functional but in need of repairs, and not functional as a result of breakages. Each health center reports to the EPI unit of the province through the district. The data on cold chain equipment in 2015 were used for this study because the data in 2014 were incomplete.

2.5. Statistical analyses

Data collected in 2014 were used in this study except for the data on cold chain. Correlation analysis was performed to measure the relationship between factors related to the immunization system, vaccine coverage, and characteristics of provinces or districts. Comparisons of continuous variables between two groups were performed using *t*-test. SPSS version 24.0 (IBM Corp., Armonk, New York) was used for all data analysis. A *P-value* of <0.05 was regarded as significant.

B. Phoummalaysith et al./Vaccine xxx (2018) xxx-xxx

3. Results

3.1. Immunization coverage of BCG, DTP-HepB3, OPV3 and MCV1 from 2002 to 2014 in Lao PDR

We first investigated the trend in the immunization coverage of BCG, DTP-HepB3 (DTP-HepB-Hib3), OPV3, and MCV1 among children in Lao PDR from 2002 to 2014 (Fig. 1). In 2002, BCG coverage was the highest (67%) while MCV1 coverage was the lowest (46%). Coverage of all vaccinations increased gradually from 2007 to a final peak of 82.2–88.3% in 2014. The gap in the reported immunization coverage for four vaccines became narrower towards 2014 compared to the wider gaps in 2002 (Fig. 1). Among all vaccines, BCG coverage was the highest until 2008, however, by 2014, it had become the lowest.

3.2. Immunization coverage in provinces from 2002 to 2014

Coverages for four vaccinations in each province in 2002 and 2014 are shown in Table 2. The coverage of each vaccination increased from 2002 to 2014 in most provinces. Vientiane Capital, Phongsaly, Luangprabang, and Huaphanh Provinces showed a great increase with all vaccines. The coverage of all vaccinations except BCG in Vientiane, Savannakhet and Champasak Provinces were better than the others in 2002, and although these improved, however, none reached up to 100%. Only Vientiane Capital showed coverage greater than 95% in all vaccinations in 2014, with BCG coverage reaching 100%. Dropout rates of DTP-HepB-Hib in provinces ranged from 0.2% (Bokeo) to 12.7% (Savannakhet) while the nationwide rate was 6.1%. Xiengkhuang and Savannakhet Provinces showed higher rates (11.7–12.7%) than 10%.

3.3. Characteristics of provinces

The demographic characteristics of each province are shown in Table 3. Although the overall population (all ages and <1-year old) was highest in Savannakhet Province, the density (both for overall population and <1-year old) was highest in Vientiane Capital. Population density for children < 1-year old ranged from 0.29 (Phongsaly) to 3.10/km² (Vientiane Capital) for all provinces while the national average was 0.69/km². The proportion of poor districts and poor villages nationwide were 20.3% and 23.1%, respectively.

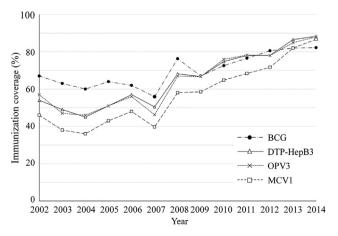


Fig. 1. Immunization coverage of BCG, DTP-HepB3, OPV3 and MCV1 in Lao PDR from 2002 to 2014. Coverage of BCG, DTP-HepB3 (DTP-HepB-Hib3), OPV3 and MCV1 improved from 67% to 82.2%, 54% to 88.3%, 57% to 88.0%, and 46% to 86.7%, respectively. DTP-HepB vaccine was used until 2008 and DTP-HepB-Hib vaccine was introduced in 2009. BCG, Bacillus Calmette–Guérin vaccine; DTP-HepB3, three doses of diphtheria-tetanus-pertussis-hepatitis B vaccine; OPV3, three doses of oral polio vaccine; MCV1, one dose of measles vaccine.

However, the proportions in each province varied, with Phongsaly and Huaphanh Provinces showing that more than half of the villages were poor. Sekong and Huaphanh Provinces had the highest and second highest proportions of high-risk villages, respectively.

The characteristics related to vaccine service in each province are shown in Table 4. Most villages in all provinces were covered by health centers. The major nationwide vaccine-providing session types were outreach (40.2%) and overnight (32.1%). Fixed site was predominant in Vientiane Capital (59%) and Khammouane Province (61%) only. The total number of cold chain equipment at health centers was 1279; however, nationwide, 79 health centers did not have refrigerators. The proportion of well-functioning equipment was 71.6–98.9%, and the best and the worst equipment were observed in Vientiane Capital and Saravanh Province, respectively.

3.4. Correlation analysis between immunization coverage and characteristics of provinces

The immunization coverage varied by vaccine antigen or province. To identify factors correlated with immunization coverage in provinces, a correlation analysis was performed using the characteristics of provinces. Results showed that the coverage of each vaccine was correlated with that of others (Table 5). Dropout rate was negatively correlated with the coverage of all vaccines significantly, except BCG. BCG coverage was correlated with population density of all ages and <1-year old. However, there was no correlation between immunization coverage and the proportion of session type or the presence of well-functioning cold chain equipment.

3.5. Correlation analysis between immunization coverage and characteristics of districts

Since the data on districts may better reflect factors correlated with immunization coverage compared to the data on provinces, we performed correlation analysis between immunization coverage and district characteristics. Results showed that coverage of each vaccine in districts was correlated with the province to which the district belonged (Table 5). Coverages of all vaccines in districts were correlated with each other and the dropout rate was significantly correlated with the coverage of DTP-HepB-Hib3 and OPV3. However, there was no correlation between coverage and session type. These results were consistent with the results of analysis based on the data on provinces.

3.6. Comparing two groups of provinces categorized by DTP-HepB-Hib3 coverage

In the Global Vaccine Action Plan endorsed by the World Health Assembly in 2012, the coverage of target populations should reach the goal of at least 80% vaccination coverage in every district [12]. DTP3 coverage is a key indicator for the performance of routine immunization services. To improve the coverage nationwide, provinces with coverage lower than 80% should be targeted and factors related to lower coverage should be identified. We made two groups of provinces based on DTP-HepB-Hib3 coverage: lower than 80% or not (provinces with DTP-HepB-Hib3 coverage <80% (low group) and >80% (high group)). Phongsaly, Xiengkhuang, Sekong and Saysomboune Provinces were in the low group. The total population of all ages and <1-year old in the low group was 9.7% and 11.8% of the whole population, respectively. We compared provincial characteristics in the two groups (Table 6). Population density of all ages and <1-year old were more likely to be higher in the high group than the low group. The proportion of high-risk villages was higher in the low group compared to the high group. The low group had more overnight while the high

Table 2 Immunization coverage in 2002 and 2014 in all provinces.

	Province	BCG 2002	BCG 2014	DTP-HepB3 2002	DTP-HepB-Hib3 2014	OPV3 2002	OPV3 2014	MCV1 2002	MCV1 2014	Dropout rate of DTP-HepB-Hib 2014
1	Vientiane C	44.0	100.4	28.0	96.1	54.0	96.2	45.2	97.0	5.7
2	Phongsaly	54.4	73.8	42.8	77.0	55.2	77.0	32.8	81.3	9.8
3	Luangnamtha	71.5	87.7	62.9	93.5	66.6	85.2	40.9	95.6	6.2
4	Oudomxay	70.6	74.0	70.3	87.2	69.8	87.7	56.4	91.7	1.5
5	Bokeo	56.9	74.0	50.8	94.4	54.5	94.4	31.0	98.8	0.2
6	Luangprabang	35.2	84.4	19.7	90.9	20.3	89.2	12.8	88.5	4.3
7	Huaphanh	45.5	94.6	22.0	95.2	22.8	96.5	25.2	89.3	7.6
8	Xayabuly	68.3	83.5	74.4	89.2	74.7	89.0	51.7	90.9	3.2
9	Xiengkhuang	58.0	59.4	41.8	66.7	46.2	66.7	49.0	61.6	11.7
10	Vientiane P	90.1	82.1	80.0	84.4	81.0	84.4	62.0	84.6	2.3
11	Borikhamxay	58.4	70.0	44.0	80.6	49.5	80.5	39.6	81.2	5.3
12	Khammouane	75.5	75.9	63.0	85.4	65.2	85.0	46.9	78.2	7.6
13	Savannakhet	80.8	92.1	74.2	90.2	74.2	90.3	62.5	91.8	12.7
14	Saravanh	73.8	73.0	41.9	85.5	43.1	84.5	30.0	76.9	3.8
15	Sekong	81.7	71.1	44.2	77.0	44.3	79.0	45.6	68.1	8.0
16	Champasak	90.2	72.3	71.0	86.5	72.7	86.5	60.2	83.9	1.7
17	Attapeu	62.8	78.2	54.5	88.3	54.6	85.9	49.3	84.3	6.2
18	Saysomboune ^b	_	61.7	_	66.2	_	66.2	_	61.5	9.3
	Total	67.0	82.2	54.0	88.3	57.0	88.0	46.0	86.7	6.1

Vientiane C, Vientiane Capital; Vientiane P, Vientiane Province; BCG, Bacillus Calmette-Guérin vaccine; DTP-HepB3, three doses of diphtheria-tetanus-pertussis-hepatitis B vaccine; DTP-HepB-Hib3, three doses of diphtheria-tetanus-pertussis-hepatitis B- *Haemophilus influenzae* type B vaccine; OPV3, three doses of oral polio vaccine; MCV1, Measles vaccine.

Table 3 Demographic characteristics of provinces.

	Province	nce Population		Populat density		N of districts	N of villages	Poor districts (%)	Poor villages (%)	High-risk villages (%)
		All	<1 Y	All	<1 Y					
1	Vientiane C	838,769	12,133	214.0	3.10	9	521	0.0	0	4.2
2	Phongsaly	174,090	4702	10.7	0.29	7	561	71.4	57.9	20.5
3	Luangnamtha	177,421	4182	19.0	0.45	5	462	40.0	32.2	23.6
4	Oudomxay	234,503	6794	15.3	0.44	7	410	28.6	46.0	16.8
5	Bokeo	172,049	3968	27.8	0.64	5	261	60.0	28.6	21.5
6	Luangprabang	446,075	11,063	26.4	0.66	12	916	25.0	24.1	21.3
7	Huaphanh	232,012	6278	14.1	0.38	10	640	60.0	55.8	37.5
8	Xayabuly	371,850	7348	22.7	0.45	11	459	9.1	3.5	27.9
9	Xiengkhuang	250,741	7106	15.8	0.45	7	662	14.3	22.8	20.1
10	Vientiane P	428,502	10,558	26.9	0.66	11	465	0.0	4.2	21.7
11	Borikhamxay	278,212	6618	18.7	0.45	7	311	14.3	11.1	22.3
12	Khammouane	374,614	10,903	23.0	0.67	10	914	0.0	2.6	0.0
13	Savannakhet	1,004,649	26,289	46.1	1.21	15	1814	6.7	21.2	22.1
14	Saravanh	393,604	12,642	24.0	0.77	8	926	25.0	19.1	34.1
15	Sekong	109,668	4756	14.3	0.62	4	291	50.0	46.5	53.3
16	Champasak	728,639	22,257	47.3	1.44	10	986	0.0	4.0	25.9
17	Attapeu	136,991	3807	13.3	0.37	5	200	0.0	19.1	11.0
18	Saysomboune	93,429	2888	11.3	0.35	5	103	20.0	31.3	17.5
Total	-	6,445,818	164,294	27.2	0.69	148	10,902	20.3	23.1	21.8

Vientiane C, Vientiane Capital; Vientiane P, Vientiane Province; <1 Y, under one year old.

group had more fixed. However, these differences were not significant. The proportion of poor villages was significantly higher in the low group compared with the high group (39.6% vs 19.4%, P = 0.049).

4. Discussion

This study showed that routine immunization coverage improved from 2002 to 2014 in Lao PDR. However, BCG coverage showed poorest improvement and the BCG coverage was also the lowest among the four vaccines in 2014. One of the reasons for the low BCG coverage might be due to the use of one vial of BCG that contains 20 doses; therefore, fixed sites provide service once a week at health centers to prevent BCG vaccine wastage although

other vaccines are provided 5 days a week. The average vaccine wastage over the last four years was estimated at 80% for BCG, the highest among all vaccines [13]. Another reason for the low BCG coverage might be due to the low rate of skilled birth attendance (SBA) and institutional delivery rate (IDR). The SBA rate and IDR in 2014 were 50.5% and 38.9%, respectively [14]. IDR was 29.2% in rural areas and 11.6% in rural areas with no roads; these values are much lower than those of urban areas (74.2%) [15]. Previous studies showed that HepB birth dose coverage was correlated with IDR and SBA rates worldwide and in South-East Asia [16], and that the lack of advice on vaccination at birth was an independent risk factor of non-vaccination status in Lao PDR [7]. These suggest that the low SBA and IDR might have affected the low BCG coverage.

Please cite this article in press as: Phoummalaysith B et al. Factors associated with routine immunization coverage of children under one year old in Lao People's Democratic Republic. Vaccine (2018), https://doi.org/10.1016/j.vaccine.2018.03.051

^a Dropout rate is the difference between coverage of DTP-HepB-Hib1 and DTP-HepB-Hib3.

^b Saysomboune Province was established from the special zone in 2006.

B. Phoummalaysith et al./Vaccine xxx (2018) xxx-xxx

Table 4Characteristics related to vaccine service in provinces.

	Province	N of HC	Villages se	erved directly (%)	Session type ^a (%)			Well-functioning cold	
				By DH	By PH	Fixed	Outreach	Overnight	chain equipment (%)	
1	Vientiane C	41	57.2	42.8	0	59	41	0	98.9	
2	Phongsaly	31	51.7	48.3	0	17	18	65	86.2	
3	Luangnamtha	39	68.4	25.1	6.5	22	37	40	92.2	
4	Oudomxay	46	63.2	36.8	0	18	26	56	92.3	
5	Bokeo	36	67.4	30.7	1.9	18	54	28	83.7	
6	Luangprabang	88	72.1	27.9	0	20	28	53	87.5	
7	Huaphanh	50	69.7	30.3	0	15	34	51	87.8	
8	Xayabuly	75	74.7	25.3	0	32	31	37	93.9	
9	Xiengkhuang	50	67.5	32.5	0	13	61	26	89.5	
10	Vientiane P	41	60.4	39.6	0	28	60	11	97.0	
11	Borikhamxay	29	76.7	23.3	0	20	68	12	79.7	
12	Khammouane	81	79.2	20.8	0	61	28	11	80.0	
13	Savannakhet	141	75.0	25.0	0	22	52	26	96.0	
14	Saravanh	63	77.1	22.4	0.5	22	31	47	71.6	
15	Sekong	23	69.1	30.9	0	23	36	41	93.2	
16	Champasak	65	67.4	33.6	0	18	64	18	95.6	
17	Attapeu	31	72.5	27.5	0	32	32	37	97.5	
18	Saysomboune	17	63.1	36.9	0	30	42	28	83.9	
	Total	947	69.1	32.8	0.4	25.9	42.0	32.1	90.1	

HC, health center; DH, district hospital; PH, provincial hospital.

 Table 5

 Correlation analysis between immunization coverage and characteristics of provinces and districts.

		Coverage of	f BCG	Coverage of DTP-HepB-		Coverage of OPV3		Coverage of MCV1	
		r	P	r	P	r	P	r	P
Provinces									
Population densi	ity	0.556	0.017°	0.383	0.117	0.418	0.084	0.372	0.128
Population densi	ity < 1 Y	0.516	0.028	0.381	0.119	0.427	0.077	0.339	0.169
Session type	Fixed	0.324	0.189	0.197	0.433	0.204	0.418	0.097	0.702
	Outreach	-0.213	0.397	-0.168	0.506	-0.142	0.574	-0.106	0.676
	Overnight	-0.068	0.790	-0.008	0.975	-0.032	0.899	0.014	0.957
Well-functioning equipment	g cold chain	0.434	0.072	0.241	0.335	0.240	0.337	0.318	0.199
Coverage of BCG		_	_	0.829	<0.001***	0.813	<0.001***	0.762	<0.001***
Coverage of DTP-HepB-Hib3		_	_	_	_	0.970	<0.001***	0.925	<0.001***
Coverage of OPV	3	_	_	_	_	_	_	0.836	<0.001***
Dropout rate of	DTP-HepB-Hib	-0.054	0.830	-0.470	0.049*	-0.475	0.046*	-0.487	0.041*
Districts									
Province		-0.219	0.008**	-0.189	0.021*	-0.164	0.047*	-0.369	<0.001***
Session type	Fixed	0.108	0.196	0.142	0.089	0.135	0.104	0.073	0.384
• •	Outreach	0.004	0.966	-0.022	0.791	0.000	0.999	0.006	0.944
	Overnight	-0.077	0.354	-0.089	0.287	-0.104	0.214	-0.066	0.431
Coverage of BCG	-	_	_	0.750	<0.001***	0.742	<0.001***	0.543	<0.001***
Coverage of DTP	-HepB-Hib3	_	_	_	-	0.976	<0.001***	0.707	<0.001***
Coverage of OPV	3	_	_	_	_	_	_	0.677	<0.001***
Dropout rate of l	DTP-HepB-Hib	-0.024	0.772	-0.177	0.031*	-0.171	0.037*	-0.157	0.061

Data of immunization coverage were from 148 districts and data of village served by session type were from 145 districts.

The coverage of not only BCG but also other vaccines in 2014 was lower than in neighboring countries, such as Cambodia, Myanmar, and Vietnam [17–19]. IDR and SBA rates were lower in Lao PDR than for these three countries. Inappropriate estimation of the number of target children due to migration and a lack of systematic population registration might also have affected the low coverage in Lao PDR.

We also showed that the coverage of each vaccine correlated with others including the dropout rates in provinces and districts. These results are consistent with the results from the global data analysis indicating that OPV3 and MCV1 coverage showed similar trends as DTP3 coverage [20]. This is understandable because mothers tend to know the schedule for the next vaccine and the

importance of vaccines once their children have initiated the vaccination schedule. Therefore, BCG vaccine seems the most important target to improve routine immunization coverage since it is scheduled to be given at birth.

Further, the proportions of poor villages were significantly higher in provinces with DTP-HepB-Hib3 coverage <80% (low group) compared with those \geq 80% (high group). Nationwide, the two major reasons for the low coverage in poor villages were road accessibility (51.5%) and the presence of poor family (26.7%). Distance and time to health facilities or the residence area have been reported as factors associated with vaccination status [4,7,11,21], and this concurs with our findings. Previous studies reported that children from the poorest households were more likely to be unim-

^a Session type of 122 villages were unknown.

<1 Y, under one year old; BCG, Bacillus Calmette-Guérin vaccine; DTP-HepB-Hib3, three doses of diphtheria-tetanus-pertussis-hepatitis B-Haemophilus influenzae type B vaccine; OPV3, three doses of oral polio vaccine; MCV1, Measles vaccine; r, correlation coefficient. *P < 0.05, **P < 0.01, ***P < 0.001.</p>

Table 6Comparing two groups of provinces according to DTP-HepB-Hib3 coverage.

_	Low group (<80%) (N = 4)	High group (≥80%) (N = 14)	P
	Mean ± SD	Mean ± SD	
Population density (/km²)	13.0 ± 2.4	38.5 ± 51.6	0.349
Population density <1Y (/km ²)	0.43 ± 0.15	0.83 ± 0.72	0.287
Proportion of poor village (%)	39.6 ± 15.6	19.4 ± 17.0	0.049*
Proportion of high-risk village (%)	27.6 ± 17.1	20.2 ± 10.3	0.287
Villages by HC (%)	62.2 ± 7.4	68.4 ± 7.6	0.169
Village served by session type			
Fixed (%)	20.8 ± 7.4	27.6 ± 14.7	0.386
Outreach (%)	39.3 ± 17.7	41.9 ± 14.7	0.766
Overnight (%)	40.0 ± 17.9	30.5 ± 18.0	0.366
Well-functioning cold chain equipment (%)	88.2 ± 4.0	89.6 ± 8.2	0.757

<1 Y, under one year old; HC, health center; SD, standard deviation. *P < 0.05.

munized than those from the richest households, not only in Lao PDR, but also in other developing countries [22,23]. It was reported that high coverage of measles vaccine was associated with high income [11] and that the difference in DTP3 coverage in the richest and poorest household wealth quintiles was very high in Lao PDR [23]. Although routine immunization is provided free of charge, the travelling cost and the loss of one day of work are financial barriers for poor families [7]. There might be other factors related to the poor, such as, low levels of education and the level of the knowledge of parents, which might affect people's attitudes toward health and health behavior. A poverty eradication policy has continued since 1996; and aim to achieve a gross national income (GNI) of more than 2500 USD by 2020. Under this policy, many interventions were undertaken by all sectors and poverty is thus, gradually reducing. The GNI was increased from 360 USD in 2002 to 2150 USD in 2016, and the proportion of poor families decreased from 36% in 2002 to 17% in 2016.

Lao PDR has a high rate of tuberculosis (TB) and the estimated prevalence in 2011 was 540/100,000 population [24]. According to the WHO, BCG vaccine should be given to all infants as soon as possible after birth and before 6th week [25]. BCG is currently the only available vaccine for TB and has been saving many lives by protecting them from TB meningitis and the dissemination of TB among infants and young children. In Lao PDR, mobile teams sometimes use one vial of BCG vaccine on just one child when they find very few unimmunized children in villages. NIP allocates more budgets to mobile teams to ensure six rounds per year when the BCG coverage is low, or includes the BCG vaccine during OPV or DTP-HepB-Hib campaigns. However, having to carry additional vaccines is difficult; moreover, the teams must focus on the need to increase OPV or DTP-HepB-Hib coverage. BCG vaccination is important as a standard TB control method in Lao PDR and a vial of one dose of BCG will be one of the solutions to low coverage. The use of mobile phones was reported to be effective in increasing of coverage of HepB birth dose in 2014 [26]. There is a pilot project of using mobile phones to report baby births at home which is being conducted in 2 districts of 2 provinces in the middle part of the country. This reporting system may be effective in providing BCG vaccine at birth to more babies who are born at home.

In this study, factors related to the immunization system and characteristics of provinces and districts were examined. However, no significant association was found with coverage and immunization system factors. The results suggest that the microplanning for immunization sessions made by the health centers and the district health offices, as well as the activities of mobile teams, were

successful in providing routine immunization, although, three quarters (74.1%) of villages were provided immunization services by mobile teams. These results were consistent with those of a previous study conducted to examine the factors of full vaccination status among children aged 12–35 months in 143 districts in 10 provinces of Lao PDR [4]. Distance from the health center was a factor, which was independently associated with non-vaccination against diphtheria in Huanphan Province [7].

There are some limitations to this study. First, we used a limited number of factors to determine the association with immunization coverage. This is because we used the national data collected from all provinces and districts. The characteristics of ethnic groups are reported as associated factors of immunization coverage [4]. In fact, it was reported that up to 80% of measles cases between 2011 and 2014 were from Mong and Akha ethnic communities [13]. Moreover, Sekong Province, with Akha as the major ethnic group and Xiengkhuang Province, with a lot of ethnic groups. showed lower coverages of DTP-HepB-Hib3. However, it is difficult to analyze ethnic groups as characteristics of provinces or districts. Secondly, proportions of poor villages were associated with lower coverage of DTP-HepB-Hib3. However, this study did not reveal which of the five categories (income, access to school, healthcare facility and clean water, and road accessibility) of poor villages was the most important factor for immunization coverage. Many factors are involved in immunization coverage and these results suggest that not only being poor but also education, concern about health, and road accessibility might be associated with immunization status. Thirdly, this study used the administrative data, which, as suggested, were overestimated by 10-20% compared to the survey data. However, no systematic survey has been conducted and the administrative data could be used to determine the trend in vaccine coverage. To collect more reliable data, NIP started a selfassessment data quality system in collaboration with the WHO and the United Nations Children's Fund (UNICEF) in 2015. The Lao government, the United States Centers for Disease Control and Prevention (US-CDC) and the WHO have initiated a project of data quality improvement for EPI and surveillance. The EPI reporting system has been improved to minimize errors in data manipulation introduced by a computerized system.

In conclusion, this study found that routine immunization coverage started increasing gradually from 2007. However, as of 2014, the national goal of >95% coverage with all vaccines included in the national immunization program had not been met in Lao PDR. BCG coverage showed the least improvement from 2002 to 2014 and was the lowest among all vaccines in 2014. The coverage of each vaccine correlated with other factors including the dropout rate of DTP-HepB-Hib in the provincial as well as districts-levels. The proportions of poor villages were significantly higher in the group with DTP-HepB-Hib3 <80% compared with the group ≥80%. These results suggest that BCG coverage and poor villages should be targeted to improve the routine immunization coverage nationwide.

Disclosure statement

The authors have nothing to disclose.

Acknowledgements

We thank Mr. Sisouveth Norasing and Dr. Bounthavy Detbandith for their technical assistance in facilitating and providing the immunization information. We would like to express our heartfelt thanks to Dr. Siddhartha Sankar Datta (World Health Organization Regional Office for Europe) for his invaluable advice on writing the manuscript.

B. Phoummalaysith et al./Vaccine xxx (2018) xxx-xxx

References

- Resolution WHA 27.57. WHO Expanded Programme on Immunization. Twenty-seven World Health Assembly, Geneva, 1974 WHA27/1974/REC/1. Geneva: World Health Organization; 1974.
- [2] World Health Organization. International review of the expanded programme on immunizationin the Lao People's Democratic Republic. Geneva: World Health Organization; 2012.
- [3] World Health Organization. WHO vaccine-preventable diseases: monitoring system. 2017 global summary. World Health Organization; 2017.
- [4] Xeuatvongsa A, Hachiya M, Miyano S, Mizoue T, Kitamura T. Determination of factors affecting the vaccination status of children aged 12–35 months in Lao People's Democratic Republic. Heliyon 2017;3:e00265.
- [5] Ministry of Planning and Investment. The Seventh Five-year National Socio-Economic Development Plan (2011–2015); 2011.
- [6] Ministry of Health, Lao People's Democratic Republic. National strategy and action plan for integrated services on reproductive, maternal, newborn and child health 2016–2020, 2016.
- [7] Nanthavong N, Black AP, Nouanthong P, Souvannaso C, Vilivong K, Muller CP, et al. Diphtheria in Lao PDR: insufficient coverage or ineffective vaccine? PLoS One 2015;10:e0121749.
- [8] Sein C, Tiwari T, Macneil A, Wannemuehler K, Soulaphy C, Souliphone P, et al. Diphtheria outbreak in Lao People's Democratic Republic, 2012–2013. Vaccine 2016; 34:4321–6
- [9] UNICEF. UNICEF Annual Report 2014, Lao People's Democratic Republic; 2014.
- [10] UNICEF. UNICEF Annual Report 2015, Lao People's Democratic Republic; 2015.
- [11] Phimmasane M, Douangmala S, Koffi P, Reinharz D, Buisson Y. Factors affecting compliance with measles vaccination in Lao PDR. Vaccine 2010:28:6723–9.
- [12] World Health Organization. Global Vaccine Action Plan 2011–2020.
- [13] National Immunization Program MoH, Lao People's Democratic Republic. Comprehensive multi-year plan for immunization, 2016–2020; 2016.
- [14] Ministry of Health, Lao People's Democratic Republic. National Health Statistics Reports – 2014–2015; 2015. p. 26.
- [15] Boudreaux C, Chanthala P, Lindelow M. Assessing the elimination of user fees for delivery services in Laos. PLoS One 2014;9:e89784.

- [16] Allison RD, Patel MK, Tohme RA. Hepatitis B vaccine birth dose coverage correlates worldwide with rates of institutional deliveries and skilled attendance at birth. Vaccine 2017;35:4094–8.
- [17] UNICEF. WHO and UNICEF estimates of national immunization coverage: Cambodia; 2016 version. [accessed 08. 02. 2018] http://www.who.int/ immunization/monitoring_surveillance/data/khm.pdf
- [18] UNICEF. WHO and UNICEF estimates of national immunization coverage: Myanmar; 2016 version. [accessed 08. 02. 2018] http://www.who.int/immunization/monitoring_surveillance/data/mmr.pdf.
- [19] UNICEF. WHO and UNICEF estimates of national immunization coverage: Viet Nam; 2016 version. [accessed 08. 02. 2018] http://www.who.int/ immunization/monitoring_surveillance/data/vnm.pdf.
- [20] Wallace AS, Ryman TK, Dietz V. Overview of global, regional, and national routine vaccination coverage trends and growth patterns from 1980 to 2009: implications for vaccine-preventable disease eradication and elimination initiatives. J Infect Dis 2014;210(Suppl 1):S514–22.
- [21] Maekawa M, Douangmala S, Sakisaka K, Takahashi K, Phathammavong O, Xeuatvongsa A, et al. Factors affecting routine immunization coverage among children aged 12–59 months in Lao PDR after regional polio eradication in western Pacific region. Biosci Trends 2007;1:43–51.
- [22] Wiysonge CS, Uthman OA, Ndumbe PM, Hussey GD. Individual and contextual factors associated with low childhood immunisation coverage in sub-Saharan Africa: a multilevel analysis. PLoS One 2012;7:e37905.
- [23] Hosseinpoor AR, Bergen N, Schlotheuber A, Gacic-Dobo M, Hansen PM, Senouci K, et al. State of inequality in diphtheria-tetanus-pertussis immunisation coverage in low-income and middle-income countries: a multicountry study of household health surveys. Lancet Glob Health 2016;4:e617–26.
- [24] Law I, Sylavanh P, Bounmala S, Nzabintwali F, Paboriboune P, Iem V, et al. The first national tuberculosis prevalence survey of Lao PDR (2010–2011). Trop Med Int Health 2015;20:1146–54.
- [25] World Health Organization. Weekly Epidemiol Rec 2004;4:25-40.
- [26] Xeuatvongsa A, Datta SS, Moturi E, Wannemuehler K, Philakong P, Vongxay V, et al. Improving hepatitis B birth dose in rural Lao People's Democratic Republic through the use of mobile phones to facilitate communication. Vaccine 2016;34:5777–84.