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How frequent are snakebites in Champone district, Savannakhet province in Laos? A cross-sectional survey

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Submitted by:

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Preface:

I came to Laos for the first time in 2005. Employed by Lux-Development S.A. at that time, I was in charge of teaching Lao medical doctors in internal medicine at Maria Teresa Hospital, the provincial hospital in Vientiane province, approximately 80 km north of the capital city Vientiane. During this assignment we also had to deal with snakebite patients, although our knowledge about assessment and treatment of snakebite patients was very limited at the beginning. Snake antivenom the only effective treatment of envenoming was not available in the hospital. The diagnosis on the admission sheet was simply “snakebite” without any further specification whether that might have been a bite from a venomous snake species with possibly serious effects of snake venom or a harmless bite from a non-venomous snake. The patients got supportive treatment and were admitted to the ward for further observation. The first patient I saw at the hospital was bitten in the hand while planting rice and had only minor local symptoms with little swelling at the bite site. She recovered uneventfully and went home after 1 day in the hospital. The second patient was bitten by a Malayan pit viper and developed a severe coagulation disorder with extensive subcutaneous bleedings and severe swelling, blistering and necrosis at the bite site. The initially normal value of haemoglobin slowly decreased and he needed 8 units of blood transfusion over 10 days until the blood coagulation disorder eventually resolved. Specific Malayan pit viper antivenom, which would have solved the problem of venom induced coagulation disorder within a few hours, was not available at that time. However, the patient survived with symptomatic treatment, the local tissue damage fully resolved and he went home after 10 days of hospitalization.

There were only these 2 patients in 2005 and snakebites looked like a rare event ranking far below the frequency of other diseases. However we purchased antivenom from the Thai Red Cross Society in Thailand to be better prepared for the next patient with severe envenoming and the availability was announced to the district hospitals throughout the province. During the following 18 months 21 snakebite patients were treated at Maria Teresa Hospital and 6 patients received antivenom. Together with my Lao colleagues this case series was published in the South East Asian Journal of Tropical Medicine and Public Health in 2010.

Further inquiries disclosed that the vast majority of snakebite victims don’t come to the

hospital and chose instead a traditional healer in their village or self-treatment with traditional medicine. This was not surprising, because treatment options for snakebite patients in the provincial and district hospitals were limited and the use of traditional medicine a reasonable choice. I went to interview one traditional healer and he told me that he was treating 1 or 2 snakebite patients per month. The snakebite problem seemed to be much bigger than I assumed after the first year at Maria Teresa Hospital.

Since this time I took more and more interest in this obviously neglected condition. There are no epidemiological data on the frequency of snakebites in Laos so far and antivenom, the only effective treatment is not available in most of the hospitals in the country.
The topic of my master thesis presented here evolved from the experience at Maria Teresa Hospital during the years 2005 to 2008. The thesis focuses on snakebite incidence in Champone district, Savannakhet province in Laos in order to estimate the magnitude of this neglected public health problem.

Dr. med. Jörg Blessmann April 2014
Savannakhet, Lao PDR

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Furthermore I would like to thank the medical and administrative staff of Champone district hospital and the staff of the Primary Health Care centers for providing data and their valuable participation during the tough work in the villages.
Last but not least, I am particularly grateful to Else Kröner-Fresenius-Stiftung for financial support for this survey within our project "Epidemiology and management of snakebites in Lao PDR".

Abbreviations:

CI	Confidence Interval
GBD	Global Burden of Disease
GDP	Gross Domestic Product
GNI	Gross National Income
HDI	Human Development Index
ICD	International Classification of Diseases
KAP	Knowledge, Attitude and Practice
NECHR	National Ethics Committee for Health Research
NIOPH	National Institute of Public Health
NTD	Neglected Tropical Disease
PHD	Provincial Health Department
PPP	Purchasing Power Parity
RR	Relative Risk
USD	United States Dollar
WHO	World Health Organization

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Abstract

How frequent are snakebites in Champone district, Savannakhet province in Laos? A cross-sectional survey.

Background

The incidence of snakebites is high in countries with warm climate and where agricultural activities are the main source of income. These characteristics apply to Laos, a landlocked country in Southeast Asia. There are no data on the incidence of snakebites in Laos so far, and this survey aims for providing data on the frequency of snakebites in a district of the southern province Savannakhet.

Methodology

A cross-sectional study was performed in Champone district, Savannakhet province to estimate the snakebite incidence in this region. Multistage cluster random sampling was applied. In the first stage 61 out of the total of 162 villages in Champone district were randomly selected. In the second stage one third of all households in each of the 61 villages were randomly chosen. One adult household member of each household was asked, whether a family member was bitten by a snake in the last 12 months.

Results

Thirty-five of 9856 interviewees reported a snakebite in the last 12 months. The estimated incidence of snakebites is 355/100,000 person per year (95% CI 254-495). The incidence is significantly higher in villages located in forested areas than in agricultural areas, 683/100,000 (95% CI 458 – 1012) and 161/100,000 (95% CI 83 - 301) respectively, with a Risk Ratio of 4.2 (95% CI 2.0 – 8.8). All snakebite victims were treated by traditional healers or by self-treatment at home. Nobody went for treatment to a hospital. In contrast to the result of the household survey in Champone district, the district hospital statistics reported only 1 snakebite patient treated in the hospital in 2012.

Conclusions

Incidence of snakebites is high in the rural district Champone, particularly in forested areas. There is a huge gap between the number of snakebites found during the community survey and the number of snakebites documented in Champone district hospital statistics, because the majority of snakebite victims are treated by traditional

healers or by self-treatment in their village. This is a reasonable choice because treatment options in the provincial and district hospitals are limited and snake antivenom is not available so far. There is an urgent need to train hospital staff in assessment and treatment of venomous snakebites and to make antivenom available in provincial and district hospitals in order to tackle this underestimated and neglected public health problem.

Introduction

Morbidity and mortality from snakebites are an important though neglected and underestimated public health problem in tropical and subtropical countries. Incidence of snakebites is particularly high in low-income countries with warm climate, a rich snake fauna and where activities in agriculture and forestry are the main source of income (Kasturiratne A. et al. 2008). Laos, a landlocked country in Southeast Asia match these characteristics. It is located at a latitude of 14° to 23° north and a longitude of 100° to 108° east, with a more subtropical climate in the northern part and tropical climate in the south (Figure 1). Laos shares borders with China and Myanmar in the north, Thailand in the west, Cambodia in the south and Vietnam in the east. The country stretches 1700 km from north to south, with an east-west width of over 500 km at its widest and only 140 km at the narrowest point. Mountains that average 1500 m above sea level dominate the northern provinces. Phou Bia in Xieng Khouang province is the highest peak with 2800 meter. The central and southern provinces comprise large and small plains along the Mekong river. The largest of these plains are the Vientiane plain in the central region of the capital Vientiane and the Savannakhet and Champassak plains in the southern region. The Annamite chain ranges along the border to Vietnam from northeast to southeast with mountains that average 1000 meter above sea level. It has three high plateaus, the Phouan plateau in the northern Xieng Khouang province, the Nakai plateau in the central Khammouane province and the Bolaven plateau in the southern Champassak province. The total surface area of Laos is 236,800 km^2, with a total population of 6,646,000 in 2012 and a population density of 28 inhabitants per km^2 (World Bank 2012).

Being a tropical country Laos has two seasons, a rainy season from May to October and a dry season from November to April. The annual rainfall is about 1000 – 2000 mm in the northern provinces and the Mekong plains and it can be more than 3000 mm in the Annamite mountain chain. The atmospheric humidity is usually 70 – 80% and 75-90% of the precipitation is recorded in the rainy season.

Laos belongs to the list of 49 least developed countries of the world with a Human Development Index (HDI) of 0.543 in 2013 (average HDI in the world 0.694). The Gross National Income (GNI) per capita is 2690 $ (PPP international $ in 2012). Life expectancy at birth is 66 and 69 for men and women respectively. The total expenditure on health per capita per year is 78 USD, which was only 2.8% of the GDP

in 2011. Approximately 70% of the population in Laos is living in rural and 30% in urban area and 25% of the population is still living under the poverty line, defined as living on an income of less than 2 USD per day (World Health Organization 2011, World Bank 2012).

Due to the subtropical and tropical climate, Laos has a rich snake fauna with 124 snake species described to date and 23 species are venomous (Teynié A. and David P, 2010 and personal communication with Alexandre Teynié). According to surveys in Thailand and preliminary experience in Laos, six snakes within the latter 23 species are responsible for the vast majority of venomous snakebites (Viravan C. et al. 1992, Blessmann J. et al. 2010). They are considered as medically important venomous snakes and snake antivenom is available for these 6 species ((Pochanugool C. et al. 1998, Chanhome L. et al. 1998). Envenoming caused by each of these six snakes results in significant morbidity and mortality (Reid et al. 1963, Wongtongkam N. et al. 2005 a, b, Chippaux JP, 2002, Warrell DA, 2010). Two snakes are pit vipers of the *Viperidae* family and four are snakes of the *Elapidae* family. The Malayan pit viper (*Calloselasma rhodostoma*) and the green pit viper (*Trimeresurus albolabris*) can cause severe local cytotoxic damage with swelling, blistering and necrosis, which sometimes need several weeks of wound treatment. Procoagulant enzymes in the venom of these vipers are responsible for systemic envenoming with severe coagulation disorder, which can cause bleeding at different sites of the body and without treatment, can be fatal. Sepsis from local wound infection due to inappropriate wound management is another cause of potentially life-threatening complication after viper bites. Amputation of the affected limb may be necessary in rare cases resulting in severe disability. The four snakes of the *Elapidae* family are the monocled cobra (*Naja kaouthia*), the king cobra (*Ophiophagus hannah*) the Malayan krait (*Bungarus candidus*) and banded krait (*Bungarus fasciatus*). Both cobras can cause extensive local cytotoxic damage with necrosis of the skin and subcutaneous tissue (Reid HA, 1964, Wongtong N. et al. 2005b). In contrast krait bites don’t cause any local signs at the bite site. Pre- and postsynaptic neurotoxins in the venom of all 4 elapid snakes are responsible for muscle paralysis in case of systemic envenoming. Death from respiratory failure may occur, if appropriate medical care is not available. Beside neurotoxic effects, cardiotoxins contribute to morbidity and mortality by causing cardiac

arrhythmia, arterial hyper- and hypotension and heart failure (Chippaux JP, 2002, Mackessy S, 2010, Wongtong N. et al. 2005b).

A literature search identified three major publications, released in the last 60 years on the worldwide incidence, morbidity and mortality of snakebites.
In 1954 Swaroop & Grab published a summary on worldwide snakebite mortality in the Bulletin of the World Health Organization (Swaroop S. and Grab B, 1954). Data were obtained from hospital mortality statistics and from public health reports of different countries in the world. He estimated the number of deaths from snakebite between 30,000 and 40,000 deaths per year excluding China, USSR and Central Europe. The highest number was found in Asia with 25,000– 35,000 deaths per year. In India 10,000 – 15,000 deaths were recorded, which corresponds to the highest mortality rate in the region at that time with 5.4 deaths per 100,000 persons per year. He acknowledged that the registration of deaths from various causes was incomplete in many areas of the world at the time these data were collected. Particularly snakebites generally occur in developing countries and in remote areas where access to healthcare service is difficult or impossible and no registration is done. Therefore the figures must be regarded as underestimates. Another difficulty in ascertaining the numbers of snakebite deaths was the classification in the manual of the International Statistical Classification of Diseases (ICD). Snakebites were not classified separately, but under all death from bites and stings by venomous animals and insects. It included death from centipede, bees, scorpions, venomous snakes etc and this would overestimate the number of snakebite deaths. However, the vast majority of deaths in this group were most likely caused by venomous snakes as death from scorpions and bees are rare events.
Jean-Philippe Chippaux published an appraisal on the worldwide incidence, envenomings and mortality of snakebites in 1998 (Chippaux JP, 1998). He evaluated and included scientific publications and reports to assess the magnitude of snakebite incidence as only very few countries in the world possess a reliable reporting system on the number of snakebites. He acknowledged that data from scientific publications are generally rather precise, but cover only limited geographical areas and estimations of broader regions are fairly vague. However, with a world population of 5.84 billion in 1998 the numbers of snakebite were estimated to be 5,400,000, with 2,680,000 envenomings and approximately 125,000 deaths. The calculated worldwide incidence

of snakebites was 92.5 snakebites per 100,000 persons with a mortality rate of 2.1/100,000 inhabitants. In Asia the incidence of snakebites was calculated to be 114 bites per 100,000 persons with a mortality rate of 2.9 deaths per 100,000.

Anuradhani Kasturiratne published the third paper on this issue recently (Kasturiratne A. et al. 2008). He applied three main strategies to obtain primary data for an estimation of the global burden of snakebite incidence, envenoming and mortality: (i) searching for publications on snakebite frequency and mortality, (ii) extraction of relevant country-specific mortality data from the WHO mortality database, and (iii) identification of grey literature by discussion with key informants. Countries were grouped into 21 distinct geographic regions that are epidemiologically homogeneous in line with the Global Burden of Disease (GBD) 2005 study. Incidence rates for envenomings were extracted from publications and used to estimate the number of envenomings in individual countries. If there were no data available for a particular country, the lowest incidence within a neighboring country in the same region was used. The authors estimate the worldwide yearly number of envenomings between 421,000 and 1,841,000, with 20,000 to 94,000 deaths from snakebite per year. The total number of snakebites, non-venomous and venomous bites was estimated to be between 1.2 and 5.5 million bites annually. The highest burden from snakebites is found in South Asia, Southeast Asia and Sub Saharan Africa. The number of envenomings in South Asia is 121,000 – 463,000 and for Southeast Asia 111,000 – 498,000 and the number of deaths are estimated to be 14,000 – 34,000 for South Asia and 790 – 19,000 for Southeast Asia. For South Asia with a total population of 1.6 Billion people these numbers correspond to an incidence of envenomings of 8 – 29/100,000 persons and a mortality rate of 0.9 – 2.1/100,000. For Southeast Asia with 620 Millions inhabitants the incidence of envenomings is 18 – 80/100,000 persons with a mortality rate of 0.1 – 3.1/100,000. He acknowledged that numbers of snakebites vary seasonally and geographically within countries, which makes estimations difficult with data obtained from limited geographical areas within a country. Furthermore mortality data from the WHO mortality database most likely underestimates mortality from snakebites, particularly in low- and middle-income countries, where health seeking behavior, health beliefs and access to health care are not optimal and a significant number of deaths from snakebite won’t be recorded.

Data on incidence and mortality of snakebites provided in these 3 reviews appears to be flawed. The authors have used either data from mortality statistics of hospitals or other public health institutions or data from community based surveys covering only limited geographical areas. Data from hospital statistics are prone to underestimate the real incidence and mortality of snakebites particularly in low and middle-income countries. Community based surveys of snakebite incidence are much more precise, but if they cover only limited geographical areas, extrapolation is inaccurate, because of significant geographical variations of snakebite incidence.
Properly designed nation wide community-based epidemiological studies are the most reliable way to assess the true rates of morbidity and mortality caused by snakebites, but they are more laborious, costly and time-consuming.
A recently published nation wide household survey from Bangladesh estimated an incidence of 623 snakebites per 100,000 persons (Rahman R. et al. 2010).
A national survey on snakebite mortality in India was conducted by Bijayeeni Mohaparta and his team (Mohapatra B. et al. 2011). This survey is part of the Million Deaths Study (MDS) in India, which seeks to assign causes to all deaths in randomly selected areas within India for the period from 2001 to 2014. Data were obtained by interviewing household members about the cause of death of a family member in randomly selected communities across India. The survey found, that 562 (0.47%) out of 123,000 evaluated deaths were caused by snakebites. This proportion represents 45,900 annual snakebite deaths nationally corresponding to a mortality rate of 4.1 deaths/100,000 persons in India.
In contrast, government of India reported only 1,364 snakebite deaths in 2008 according to hospital statistics, corresponding to a mortality rate of only 0.1/100,000 persons (Government of India, Central Bureau of Health Intelligence, National Health Profile 2008).

Numerous epidemiological surveys indicate, that snakebite morbidity and mortality is high in low-resourced countries with a high percentage of people living in poverty (Sharma SK et al. 2003, Hati HK et al. 1992). Robert Harrison and David Lalloo pointed out the link between poverty and snakebite (Harrison RA. et al. 2009). Maps depicting countries with a high level of poverty, defined as living on an income of less than 2 USD per day, show a remarkably similar profile as a snakebite mortality map does. The authors demonstrated a strong negative correlation between snakebite

mortality and Human Development Index (HDI), GDP/capita and the per capita government expenditure on health. Developed countries like Australia, which is habitat of some of the most venomous snakes in the world, has a very low mortality rate of approximately 0.01/100,000 persons, whereas India has a mortality rate of 4.1/100,000 (Mohapatra B. et al 2011, Kasturiratne A. et al. 2008).

The World Health Organization added snakebite to the list of neglected tropical diseases (NTD) in 2009 (World Health Organization 2007 and 2013). This also acknowledges the link of snakebites to poverty, a major distinctive characteristic of all NTDs, which are globally associated with poverty. However, in contrast to other NTDs like dengue fever, venomous snakebites remain largely invisible and unheard by the global public health community, although the estimated mortality rate caused by venomous snakebites is much higher than the mortality rate attributed to several presently recognized NTDs, including dengue haemorrhagic fever, leishmaniasis, schistosomiasis, Japanese encephalitis and Chagas' disease (Williams DJ. 2010).

Laos is one of the least developed countries in the world with an estimated 25% of the population living in poverty. It is habitat of some highly venomous snakes and the majority of the population earns their living from agricultural activities. Under these circumstances incidence of snakebites is expected to be high, but no data are available so far.
The cross-sectional, community-based survey presented here will provide epidemiological data on snakebite incidence in Champone district in Savannakhet province in Laos to estimate the magnitude of this public health problem in the region.

Methodology

Ethical approval:

The study was approved by the National Ethics Committee for Health Research (NECHR) at the National Institute of Public Health (NIOPH) in Vientiane capital, Lao PDR.

Informed consent for the interviews was obtained from the head or an adult member of each selected household.

Study site and study population:

From May to August 2013 a cross-sectional, community-based survey was carried out to estimate the frequency of snakebites in Champone district, in Savannakhet province in southern Laos (Figure 2 and 3).

Savannakhet province is located in the southern part of Laos at a latitude of 16° to 17° north. It is the largest province in Laos with a surface of approximately 21,800 km^2, a population of 920,000 and a population density of 42 inhabitants per square kilometer. The Mekong river plain covers approximately two third of the province surface area in the west and the Annamite mountains form the border to Vietnam in the east (Figure 1, 2 and 3).

Champone district is located 50 km west of the provincial capital Savannakhet in the lowland Mekong river plain. The district's surface is 1030 km^2 with a population density of 105 inhabitants per km^2. This is considerably higher than the average population density in Laos of 28 per km^2. The vast majority of the population is working in agriculture. Approximately 333 km^2 (32%) of the surface is covered with forest and 697 km^2 (68%) is predominantly used for rice cultivation (Figure 4). The district has 162 villages with approximately 17,600 households and 108,000 inhabitants. The average number of households per village is 109, with an average of 6.1 members per household (information from ministry of agriculture and forestry in Savannakhet).

Estimation of the population sample size:

The sample size for the survey was calculated with four variables, *Z* for confidence level, *P* for expected proportion of snakebite victims, *d* for precision and *deff* for design effect.

The number of snakebite incidents *P* per year was estimated to be 300 snakebites per

100,000 persons. (P = 0.3% = 0.003). This estimation is based on published data from other Asian countries, as there are neither data on snakebite incidence from Laos nor from the neighboring countries Vietnam and Cambodia, which are similar according to the socioeconomic situation (Williams DJ et al. 2009). Jean-Philippe Chippaux estimated the incidence of snakebites in Asia to be 114 bites per 100,000 persons. For Malaysia the estimate was 400-450/100,000, for Myanmar 35-200/100,000, for Papua New Guinea 215 – 526/100,000 and for India 66-163/100,000 (Chippaux JP. 1998). More recently Rahman estimated 623 snakebites per 100,000 persons in a nation wide household survey in Bangladesh (Rahman R. et al. 2010). The climate and socioeconomic situation in Bangladesh shares some similarities with Laos. It has a tropical climate with a rich snake fauna, the HDI is 0.515, the GDP per capita is 2083 USD (PPP) and the majority of Bangladeshi is working in agriculture.
Considering the estimates from these publications, an incidence of 300 snakebites per 100,000 persons was assumed for Champone district, well in the middle between the lowest estimate of 35/100,000 found in Myanmar, the rough estimate of Chippaux for the whole of Asia of 114/100,000 and the more recent number from Bangladesh with 623/100,000.
Precision *d* is recommended to be 50% of the expected proportion *P*, if *P* is expected to be less than 10%. Thus precision d is determined at d = 0.0015 (Naing L. et al. 2006).
Cluster random sampling instead of simple random sampling is applied for this survey. Therefore deff of 2 is recommended and set in for the sample size calculation in this survey.
The confidence level is defined at 95% with a value for Z of 1.96.
The calculation was performed at Openepi website (OpenEPI Open source epidemiologic statistics for Public Health, Version 3.01 updated 2013/04/06 www.openepi.com/v37/Menu/OE_Menu.htm).
The following numerical values were applied:

Z = 1.96 (for confidence level of 95%)
P = 0.003
d = 0.0015
deff = 2

The sample size is then 9753 with 95% confidence level (Annex 3, sample size calculation, PDF outprint from OpenEPI Open source epidemiologic statistics for public health).

Random selection of the study population to achieve the sample size:
A two-stage cluster random sampling was applied to select the participants of the survey.
In a first step sixty-one villages out of all162 villages in Champone district were randomly selected. In a second step 33% of all households in each of these 61 villages were randomly chosen. The average number of households per village in Champone district is 109, with 6.1 members per household. The expected sample size is then calculated to be 13,507 interviewees: 61 villages x 36.3 households x 6.1 household members = 13,507 interviewees. This number oversamples the calculated necessary number of interviewees of 9753 by approximately 28% in anticipation of 10% non-responders and 15 - 20% migration of the district population to the neighboring country Thailand or other provinces within Laos. This rather high percentage of migration predominantly for job seeking is well known for the western districts of Savannakhet province.
Random selection of 61 villages out of 162 villages and 33% of households in each village has been done at the website http://www.randomizer.org (Research randomizer, http://www.randomizer.org/form.htm).

Household and snakebite victim questionnaires:
The survey team visited 1794 households between May and August 2013. All household members actually living in each household during the last year were listed with age and gender. After informed consent had been obtained from the chief of household or if not present from another adult household member, interviewees were asked about an incident of snakebite regardless whether it was a bite from a venomous and non-venomous snake. Events like Lao New Year in mid of April or start of Buddhist lent in July were used to make sure that the reported snakebite happened within the last 12 months (Annex 1: Questionnaire for household survey). Those household-members, who were bitten by a snake in the last 12 months were asked additional questions about circumstances of the snakebite, snake species, what kind of

treatment has been done after the bite, in which month of the year the bite happened and the outcome. (Annex 2: Questionnaire for snakebite victims).

Allocation of villages into forest and agriculture villages coded with F and A:
All 61 randomly selected villages were allocated to one group of villages in or near forested areas (code F) and a second group of villages in agricultural areas (code A), according to the map of Champone district designed by the World Health Organization in 2003 (Figure 4). Twenty-nine villages were classified as forest villages and 32 villages as agricultural villages. Forest villages are located in the east and west part of the district stretching from north to south and agriculture villages in the central stretch (Figure 4). The location of the villages was confirmed again during the visit as the map has been designed already 10 years ago.

Estimation of snakebite incidence from hospital statistics:
For a second approach to estimate the incidence of snakebites per year, hospital administration offices of all 14 district hospitals, including Champone district hospital and the provincial hospital in Savannakhet were asked to provide data on the number of snakebite patients admitted and treated in their hospital in 2012.

Statistical analysis:
The snakebite incidence was calculated as the number of snakebites per 100,000 persons per year, using the number of snakebite incidents found during the survey as nominator and the number of interviewees as denominator.
A two by two table with Chi Square statistic was applied to compare the risk for snakebite for people living in forest or agriculture villages. Living in or nearby the forest is the positive exposure and the incidence of snakebite the positive outcome.
The calculated sample size of 9753 is sufficient to demonstrate an annual incidence of 300 per 100,000 persons with 95% Confidence interval (OpenEPI Open source epidemiologic statistics for Public Health, Version 3.01 updated 2013/04/06 www.openepi.com/v37/Menu/OE_Menu.htm).

Results

The age and gender distribution of the study population:

A total of 9856 individuals, 5025 females and 4831 males were interviewed and included in the survey. Comparison of age distribution in the study population and the Lao population in 2012 reveals significant fewer children less than 10 years, fewer young adults between 20 – 29 years and more people over 40 years in the study population. This is most likely due to the high percentage of migration of younger people with their children to Thailand.

The age and gender distribution of the study population and the Lao population in 2012 is outlined in table 2.

The incidence of snakebites in Champone district:

In 61 villages with 6006 households, 1986 households (33.1%) were randomly selected. One hundred ninety two households (9.7% of 1986 households) could not be interviewed, because they were either not at home (77 households) or the whole family moved to Thailand or another province within Laos (115 households). The field team visited 1794 households with 12218 officially listed members, but only 9856 were actually living in the households and were interviewed. The remaining 2362 household members (19.5%) moved out to work in Thailand or in another province in Laos. This high percentage of migration was already previewed.

Thirty-five out of 9856 interviewees reported an incident of snakebite in the last 12 months. The calculated incidence of snakebite in Champone district is then 355 snakebite incidents per 100,000 persons per year (95% CI 254 – 495).

Detailed information about all 61 randomly selected villages is outlined in table 1 and calculation of incidence and confidence interval in Annex 4.

Snakebite incidence in forested and agriculture areas:

There were 3659 interviewees in 703 households from villages in forested areas and 6197 interviewees in 1091 households in agricultural areas located in the central part of Champone district. Twenty-five individuals from the forest villages and 10 individuals from the agriculture villages reported an incident of snakebite in the last year. This results in an incidence of 683/100,000 persons per year (95% CI 458 - 1012) in forested areas and 161/100,000 persons per year (95% CI 83 - 301) in agriculture

areas. The Two by Two table evaluation shows, that the risk for snakebite is significantly higher for people living in a forest village with Risk Ratio of 4.2 (95% CI 2.0 – 8.8).

2 x 2 table for RR calculation:

	Snakebite (+)	Snakebite (-)	
Forest villagers	25	3634	3659
Agriculture villagers	10	6187	6197
All villagers	35	9821	9856

The calculation of the 2 x 2 table is outlined in Annex 4. (PDF outprint 2 x 2 table statistics from OpenEpi Open Source epidemiologic statistics for public health, www.openepi.com/v37/Menu/OE_Menu.htm)

Age and gender distribution of the snakebite victims, circumstances of the snakebite, symptoms and treatment seeking behavior:

Nine females (25%) and 26 males (75%) reported an incident of snakebite in the last 12 months. The median age of females is 28 years (range 13 – 70) and for males 32 years (range 7 – 60) (Table 2). Twenty-five snakebite victims were farmers, 9 students and 1 policeman. Twenty snakebites happened in the paddy fields, 7 in the forest, 6 in the river and 2 in the garden. Thirteen snakebites happened during work in the field or garden, 11 during hunting and searching for frogs, snakes or other kind of food like insects, 6 during fishing and 5 during walking.

All 35 snakebite victims reported self-treatment or treatment by a traditional healer in their village and nobody went to the hospital. The outcome was favorable in all but one man, who lost the mobility of his right index finger after a cobra bite. No death from snakebite was encountered in the study population.

Nine out of 35 snakebite victims (26%) reported a bite from a venomous snake species. Five interviewees reported Malayan pit viper bites, 1 green pit viper bite and 3 cobra bites. Twenty-four (68%) reported a bite from a non-venomous snake and 2 interviewees (6%) couldn’t identify the snake.

Five interviewees developed symptoms indicating envenoming. One cobra bite in the right index finger caused severe swelling of the whole arm and 2 villagers reported cobra spitting incidents with eye irritation, but without permanent eye damage. One

interviewee reported swelling of the leg after Malayan pit viper bite, indicating envenoming and one person described swelling after the bite, but he could not identify the snake.

All reported snakebites but one happened during the rainy season between May and October.
A list of all 35 snakebite victims with age and gender, the circumstances of the bite, symptoms and treatment seeking behavior is summarized in Table 3.

Evaluation of Hospital statistics in Champone district and Savannakhet province:
All 14 district hospitals of Savannakhet province and the provincial hospital administration were asked to report about the number of snakebites treated in their hospitals in 2012. The results are outlined in table 4.
Only one snakebite patient was treated in Champone district hospital in 2012. This results in an incidence of just 1 case per 100,000 persons per year.
Twenty-five snakebites were treated in the 13 remaining district hospitals and the provincial hospital in 2012. The annual incidence in Savannakhet province with a population of approximately 920,000 is then 3 snakebites per 100,000 persons per year.

Discussion

The household survey in Champone district, Savannakhet province in Laos, interviewed 9856 villagers in 1754 randomly selected households from 61 villages. Thirty-five individuals reported a snakebite in the past 12 months, which results in an incidence of 355 snakebites per 100,000 persons per year.
In contrast the Champone hospital statistics registered only 1 case of snakebite treated in the hospital in 2012, resulting in an incidence of just 1 per 100,000 persons. In the other 13 district hospitals and the provincial hospital of Savannakhet the number of snakebite patients were just as low, with a calculated incidence of 3 per 100,000 in the whole province. The questionnaire for snakebite victims gave the explanation for this huge difference. All 35 snakebite victims interviewed during the survey were treated in their village with traditional medicine and nobody went to the hospital. What are the reasons for this treatment seeking behavior? First of all the health financing in Laos is mostly a fee-for-service system and patients have to cover costs for transport to the hospital, treatment, accommodation and food. One or two family members have to accompany the patient and take care of him or her while staying in the hospital. This is a direct financial burden for the family and a particular burden in the rice-planting season, when all family members are needed to work in the field. The strong belief in the value and benefit of traditional treatment also contributes to this behavior. A KAP-survey performed in Champone district in 2013 confirmed that almost 90% believe in the effectiveness of traditional medicine for snakebite (Khamphanthong S, 2013). This is not surprising because Lao people rely on traditional medicine since decades and in case of snakebite traditional treatment appears to be effective in the majority of patients with snakebite, because only 10 - 15% of all snakebite victims need specific treatment with antivenom. However, all snakebite victims should have professional medical assessment after the bite (Wongtongkam N. et al. 2005 a, b).
Fee-for-service health financing system and strong believe in traditional medicine are definitely two strong reasons for the treatment seeking behavior. A third even more compelling reason is the fact, that snakebite patients with systemic envenoming won't get effective treatment in the local health facilities, because knowledge about treatment of venomous snakebites of health care staff in district and provincial hospitals is not sufficient and antivenom the only effective treatment of systemic envenoming is not available. At present time there is no better alternative to traditional medicine available

and treatment by traditional healers is a reasonable and good choice under these circumstances, though associated with considerable expenses for the services as well. The different results of the community-based survey in Champone and the hospital records of the district hospital indicate that hospital statistics on number of snakebites in Laos are extremely misleading and actually useless at the present level of health care system development. They profoundly underestimate snakebite morbidity and this is common in many middle and low-income countries where health seeking behavior, health beliefs, access to health care and quality of health care are not optimal. Studies from rural Nigeria and Kenya have reported similar health care seeking behavior and only 8.5% and 27% of snakebite victims, respectively, sought hospital treatment (Pugh RN. et al. 1980, Snow RW. et al. 1994). A survey in Sri Lanka highlights the underestimation of snakebite mortality by hospital statistics in Monaragala district and a field survey in the district of Burdwan, West Bengal in India found that only 22% of snakebite victims received hospital treatment (Fox S. et al. 2006, Hati HK et al. 1992). The community based mortality survey in India revealed 45,900 annual snakebite deaths compared to only 1364 deaths reported by Government of India in 2008 based on hospital statistics (Mohapatra B. et al. 2011, Government of India, Central Bureau of Health Intelligence, National Health Profile 2008).
Australia, a developed country with a rich snake fauna and some highly venomous snakes has the policy that all patients with suspected snakebite should be admitted to a hospital for assessment and treatment. In such a developed health system with well-trained health staff, treatment guidelines, availability of antivenom, and a universal coverage health financing system, hospital statistics are likely to reflect the real number of snakebite incidents in the country.

Approximately one third of Champone district is covered with forest and two thirds are mainly agricultural area with paddy fields. A district map created by the World Health Organization illustrates the two areas with predominantly farmland in the center and two strips of woodland located in the western and eastern part of the trapezoid-shaped district (figure 4). Villages were classified as agricultural and forest villages before the start of the survey according to this WHO map. The separate calculation of snakebite incidence revealed a much higher incidence in forested areas with 683 snakebites per 100,000 persons, compared to 161/100,000 for villagers living in agriculture areas. The Two by Two table evaluation confirms the significantly higher risk of snakebite for

people living in a forest village RR 4.2 (95% CI 2.0 – 8.8). It is well known that snakebite incidence is high in rural tropical areas compared to urban areas. This survey confirms the high incidence of snakebites in a rural region in Laos and it shows that there are also significant differences of snakebite incidence within the rural area. The survey and particularly the questionnaire for snakebite victims don't give an explanation for this observation. Villagers in forest villages may enter the forest regularly to collect wood, bamboo, fruits, and herbs and to hunt animals. These activities in the forest put people at a higher risk for snakebite.
Robert Harrison and David Lalloo illustrated a strong association between snakebite induced mortality and poverty (Harrison RA. et al. 2009). Forest products are for free and poor people will enter the forest regularly to collect forest products free of charge for their living. More affluent people buy the products at the local market, which is more expensive, but much more convenient and has a much lower risk for a snakebite incident. The survey doesn't provide socioeconomic data of the interviewees in the different areas and therefore the interrelations are speculative assumptions, but rather plausible and further surveys are necessary to prove the idea.

All 35 snakebites but one happened between May and October, which is the rainy season in this region. The concentration of snakebites during this time is not surprising, because this is the rice-planting season and most of the villagers are working in the fields and they go fishing in numerous ponds and water pools and hunting frogs in the paddy fields and forest. These outdoor activities put people at risk for a snakebite incident. The higher number of snakebites in the monsoon season is also observed in many other countries in Asia (Wongtongkam N. et al. 2005 a, b, Sharma SK et al. 2003). In the present survey young males with a medium age of 32 years are predominantly affected and the male/female ratio is 3:1, which is a common finding in other Asian countries and may reflect the fact that younger men are more involved in outdoor activity and work (Sharma SK. et al. 2004, Alirol E. et al. 2010). The interviewees reported 9 bites (26%) from venomous species, 24 bites (68%) from non-venomous species and in 2 incidents (6%) the snake could not be identified. One Cobra bite and the two spitting cobra incidents can be classified as venomous snake incidents with good evidence, but the reported viper bites must be considered with caution, as snake identification by layman is unreliable and confusion with non-venomous snakes cannot be excluded (Viravan C. et al. 1992). However there were in

total 5 incidents (14%) with local symptoms after the bite, which usually doesn't occur after a bite of a non-venomous snake and the rate of venomous snakebites can be assumed within the range of 14 – 26%. Kasturiratne estimated a similar rate with a relation of non-venomous/venomous snakebites of 3:1 (Kasturiratne A. et al. 2008). The interviewees reported bites from three different venomous snake species, the cobra, Malayan pit viper and green pit viper. There are no data on the proportional frequency of bites from the different venomous snakes in Laos. Data from Thailand reveals that approximately 70% of all venomous snakebites are from the two pit vipers and another 15% are from cobras (Viravan C. et al. 1992). Kraits are night active snakes and bites are rare and king cobras unlike common cobras are rarely found close to human settlements and bites are very rare. Preliminary observations in Vientiane and Savannakhet province confirm the predominance viper and cobra bites (Blessmann J. et al. 2010). However prospective hospital-based surveys with reliable snake identification are needed to describe the relative frequency of snake species involved in venomous snakebites in the region.

The outcome of all but one snakebite victims was favorable. One man lost the mobility of his index finger after a cobra bite. Death after snakebite was not reported in our survey.
Kasturiratne estimated a mortality of 0.1 – 3.2 per 100,000 in the Southeast Asian region (Kasturiratne A. et al. 2008). In India the mortality rate of snakebites was estimated to be 4.1 per 100,000 (Mahapatra B. et al. 2011). The estimated mortality rate in Laos would be expected in the range of 1 to 4 per 100,000 and therefore a significant statement on mortality of snakebites in the present survey is not possible, because the number of 9856 interviewees is to small.
It also appears that the number of severe life-threatening incidents and snakebites with permanent disability is relatively low, as only one snakebite victim developed disability and the remaining 34 fully recovered without professional help.
It confirms the fact that only a minority of patients develops life-threatening symptoms after a venomous snakebite and needs specific medical intervention to avoid death and disability. Respiratory failure develops in approximately 30% of patients after cobra bite and coagulation disorder after viper bites in 50% of cases. Life-threatening bleeding occurs even less frequent (Wongtongkam N. et al. 2005 a, b). These data are from Thailand, but they most likely apply to Laos as well.

This survey has been performed in Champone district in Savannakhet province. It is a limited geographical area in the Mekong river plain with two thirds of agricultural lowland and one third of woodland. The population density of the district is significantly higher compared to the average density in Laos. There are also differences in the age distribution of the study population compared to the Lao population most likely due to the high percentage of migration. Champone district was not identified as a poor district by the National Statistic center (NSC) in Vientiane in 2003 (Epprecht M. et al. 2008). At that time 72 out of 142 districts in Laos were identified as poor districts. These characteristics may influence the results of the present survey and incidence of snakebites may be even higher in other districts of the province and in other provinces in the country, particularly in regions with predominantly woodland and in communities with a higher level of poverty.

What kind of intervention will tackle this public health problem and reduce morbidity and mortality caused by snakebites?

There are many prevention measures to avoid snakebites. Appropriate footwear while working in the fields would protect farmers against snakebite at the foot (Tun Pe et al. 1998). Particularly farmers working in rice fields and workers on rubber, sugar cane and banana plantations should wear protective boots. A torch should be used while walking at nighttime. The area around the house should be free of high grass, scrub or stack of wood, where snakes like to hide. Granary and livestock should be kept away from the house. Food should be properly stored not to attract rodents, which would then attract snakes to hunt them. People should never put their hands in holes in order to find food. Sleeping on the ground should be avoided and bed nets should always be used, which protects not only against mosquitoes, but also against other biting insects, centipedes, scorpions and snakes, entering the house (Chappuis F. et al. 2007, Warrell DA. 2010a).

Clearing vegetation, collecting firewood, herbs or bamboo is a real danger and particular caution is important.

All these prevention measures are important and community members and plantation workers should know about them. They will most likely reduce the incidence of this environmental and occupational hazard.

Once a venomous snakebite has happened, only fast and good quality professional health care can reduce morbidity and mortality caused by local and systemic envenoming (Sharma SK et al. 2013). In a well-developed health care system like in Australia, mortality rate for snakebites is approximately 0.01/100,000, which accounts for 2 deaths caused by snakebites in a population of 20 million people (Kasturiratne A. et al. 2008).

Professional treatment for venomous snakebites and antivenom is not available in provincial or district hospitals in Laos so far and snakebite victims have to rely on the help from traditional healers in their village. A training program for health care staff in provincial and district hospitals is urgently needed together with the supply of antivenom for the hospitals in order to ensure professional help for patients with venomous snakebites.

Sophisticated medical equipment is not necessary to treat snakebite patients, but good knowledge about venomous snakes of the region, the effects of their venom and the use and availability of snake antivenom, the essential drug (Warrell DA, 2010a). Treatment costs are moderate. One vial of monovalent and polyvalent antivenom costs 40 and 60 US Dollar respectively and for a severe systemic envenoming approximately 4 vials are needed. Together with hospital costs it will add up to 250 – 350 USD total costs to treat a case of snakebite. Although a sizeable number of people in Laos cannot afford that sum, the costs are rather low, if we consider that we save a life or avoid disability of a young adult, which are most frequently affected.

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