

Steering Committee 27-28 November 2019 – Vientiane, Laos

# Vector Control Intervention in Schools to Measurably Reduce Transmission of DENV in the Community

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WP CAMBODIA



## ECOMORE-2, WP Cambodia



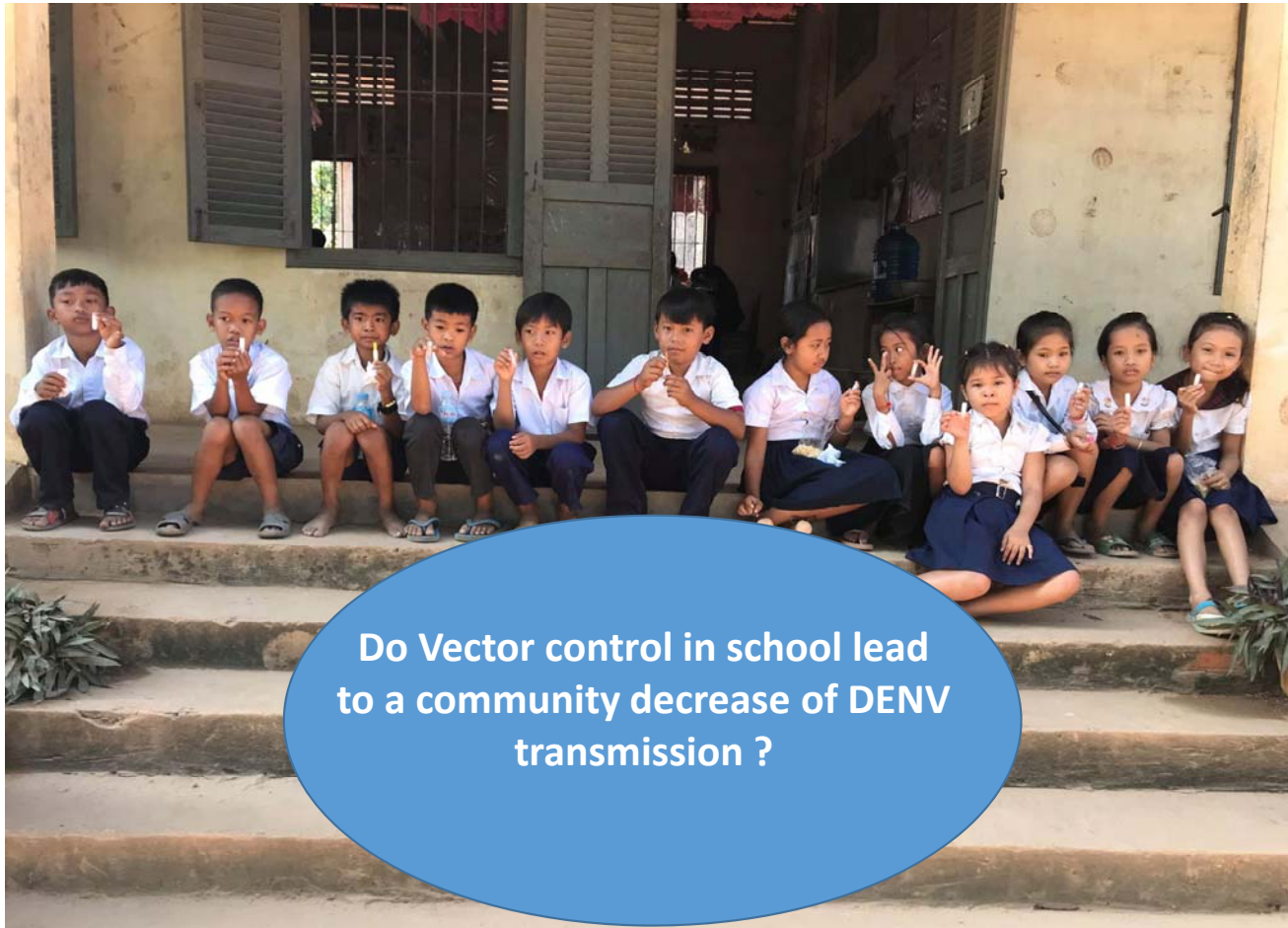
- Involvement of authorities
  - National Dengue Control Program, Ministry of Health
  - Ministry of Education, Youth and Sports
- Implementing the study by Institut Pasteur du Cambodge (IPC)
  - Entomology Unit
  - Virology Unit
  - Epidemiology Unit

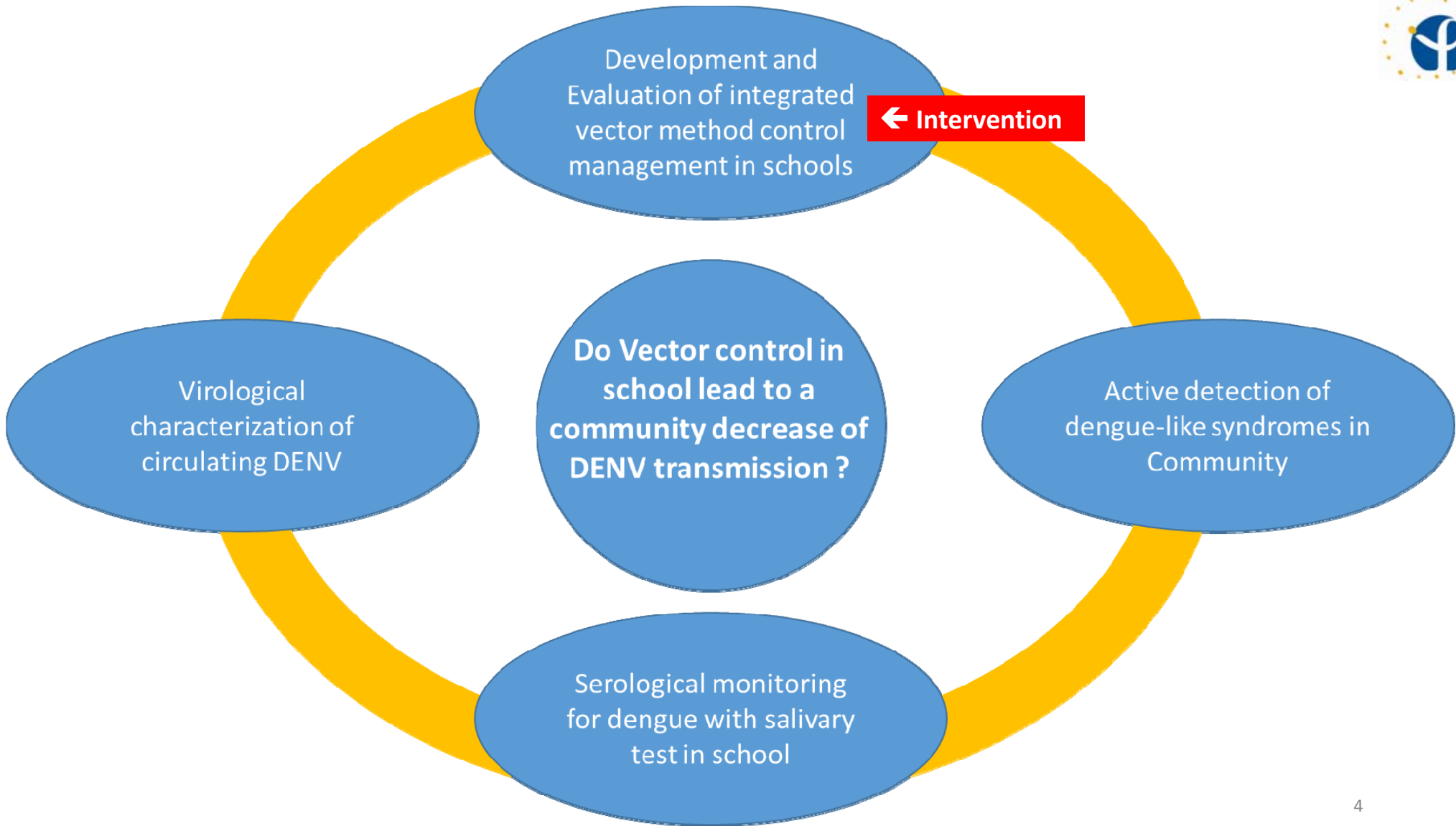




## ECOMORE-2, WP Cambodia

Schools could be hot spots for transmission of dengue among children in Cambodia

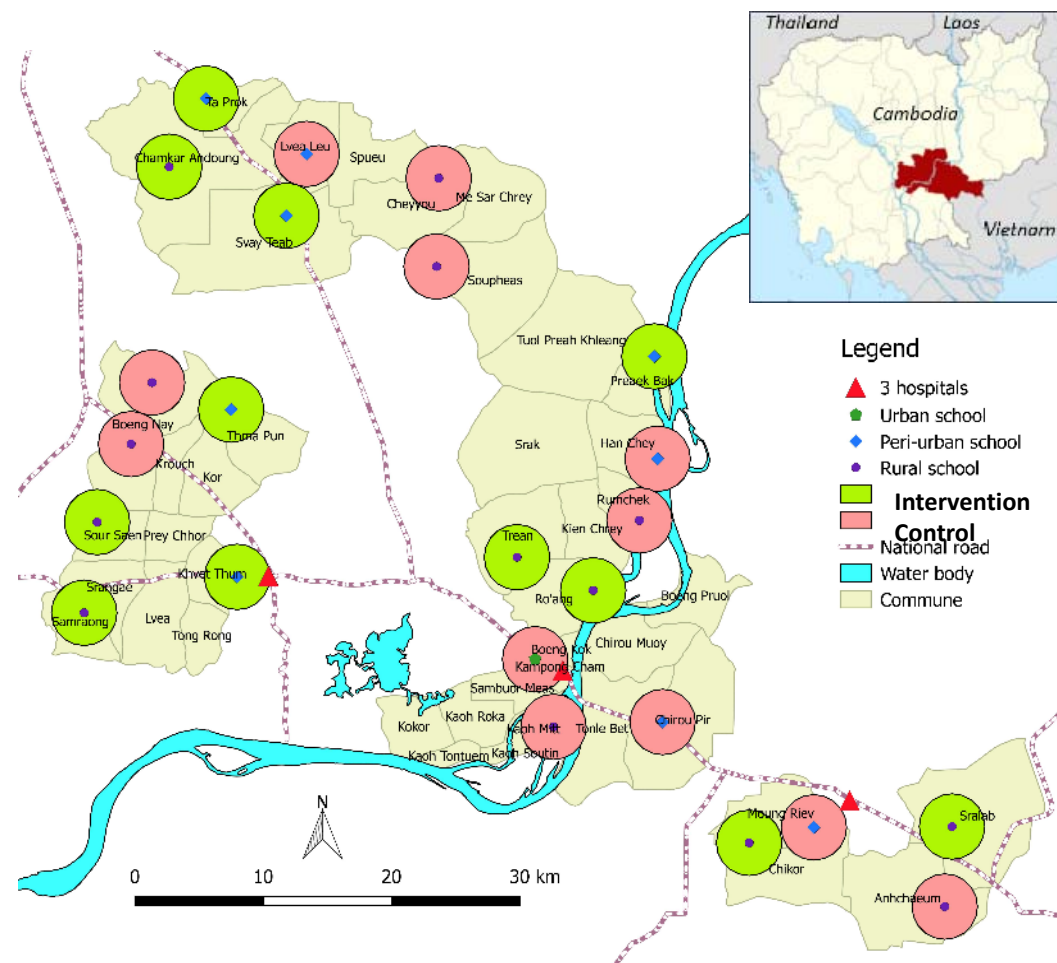




# Cluster Randomized Controlled Trial Study Kampong Cham & Tbong Khmum Provinces

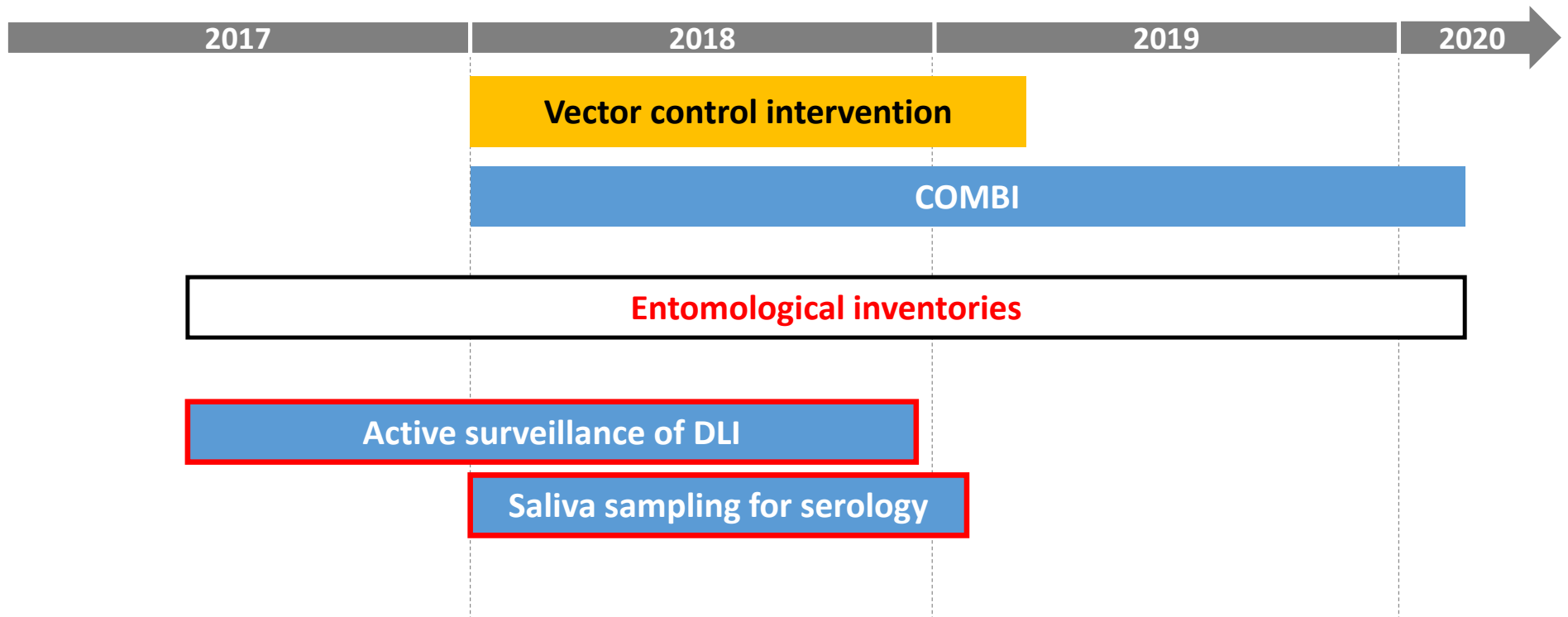


- 24 clusters in 5 districts
  - 71 villages (26 in urban/peri-urban)
  - 78,741 population
  - ~15,000 children aged 5-15 years old
- Cluster definition
  - One SCHOOL with primary grade
  - Several VILLAGES (300+ children aged 5-15 y.o.) surrounding and depending on that school
- Intervention arm (12 clusters)
  - Integrated vector control strategy

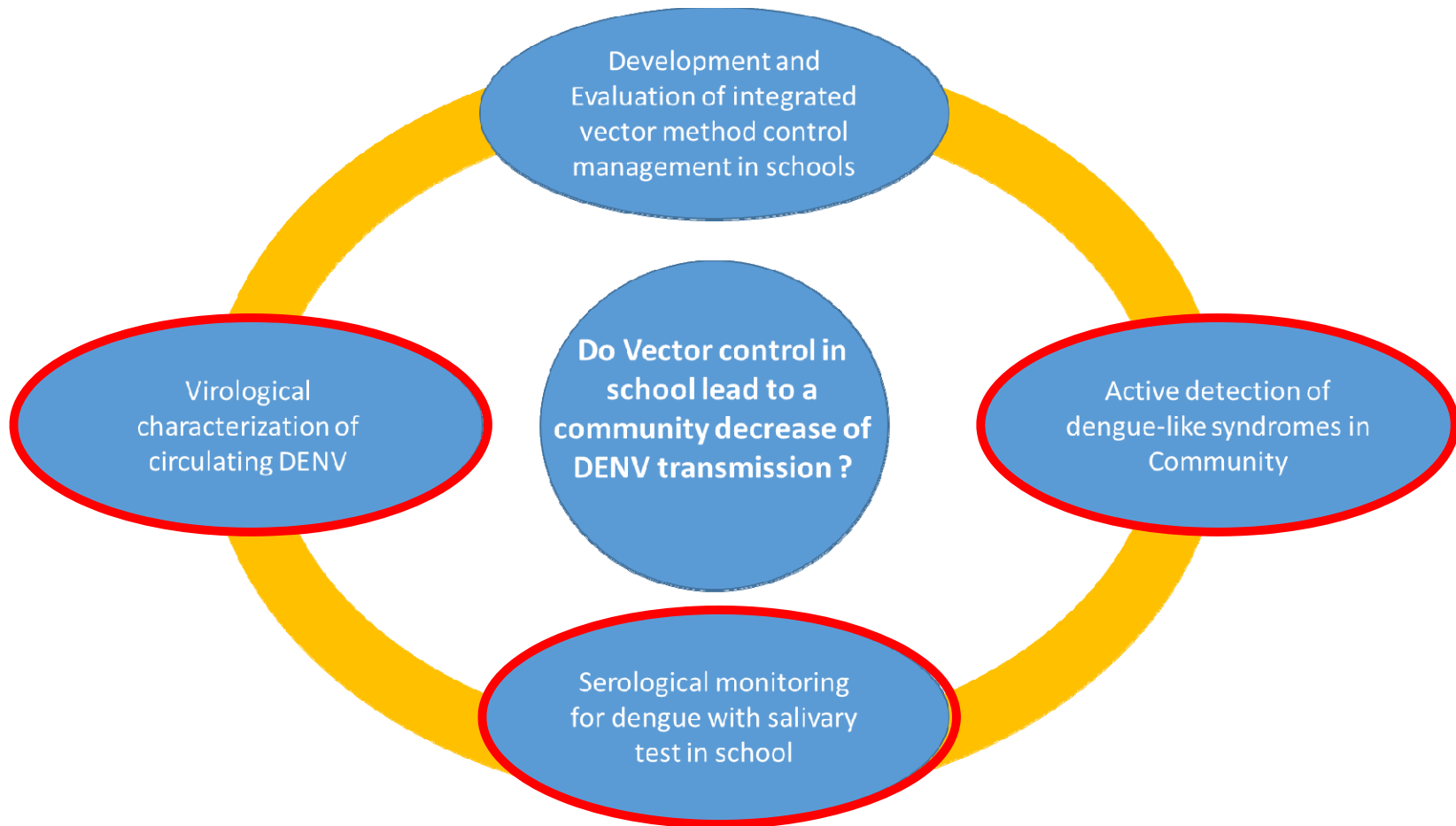




# Project Timeline



# Active Surveillance of Dengue-like Illness in Communities In Children Aged 5-15 Years Old



# Active Surveillance of Dengue-like Illness in Communities In Children Aged 5-15 Years Old



Epi Team at IPC (5 pple)



Nurses from  
Health Centers  
(42 pple)



Village Health Volunteers (90 pple)



Local Monitors  
Kg Cham (6 pple)





# Identification of Dengue-like Illness by Village Health Volunteers (VHV)

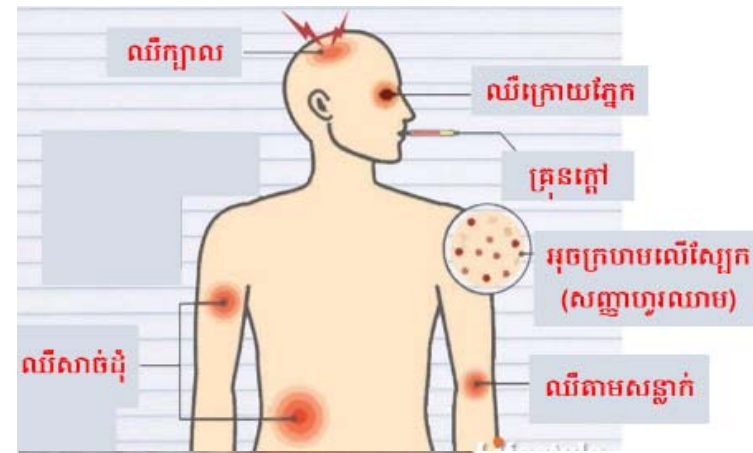


**Acute fever ( $T^\circ = \text{or} > 37.5^\circ\text{C}$ )**  
with at least 2 other signs below:

- Headache
- Retro orbital pain
- Muscle pain
- Joint pain
- Skin rash
- Bleeding sign at eyes
- Bleeding sign at nose
- Bleeding sign at gum
- Hematemesis
- Melena



Blood sampling for testing at IPC  
(acute and convalescence samples within 10-14 days)



អុតក្រហមលើស្បែក

## រោគសញ្ញាហូរឈាម



- ក្អិតមានឈាមឈាមក្រហម
- ដុះមានឈាមឈាមក្រហម ឬ ឈាមក្តៅ (ហូរឈាមក្នុង ពោះវៀន)

Training for local study teams



Office at study site



Weekly temperature follow-up





## Saliva Testing for Dengue in School Children Age 5-15 years old

Saliva samples - 3000 children, 5-15 years old  
(1500 non-treated area vs 1500 treated area)  
Lab testing by Indirect IgG ELISA / MAC-ELISA assays

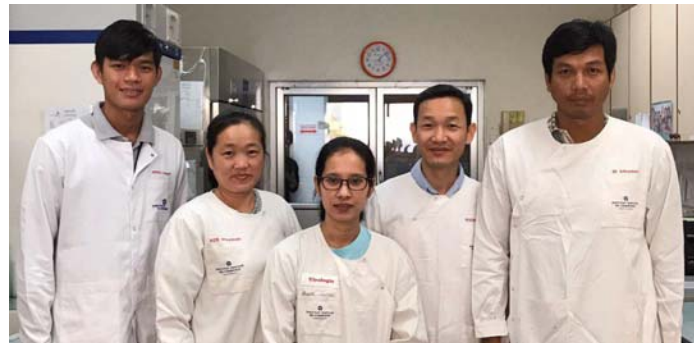
Saliva collection	Date of collection
Survey 1	May 2018
Survey 2	Jul 2018
Survey 3	Aug 2018
Survey 4	Nov 2018
Survey 5	Jan 2019



## Collecting saliva samples in school children



## Testing saliva samples at Virology Unit, IPC





## Statistical Data Analysis

- Descriptive analysis
- Effect of vector control intervention
  - On the incidence of DLI in study clusters
  - On the incidence of dengue in study clusters
  - On the dengue transmission in study schools
- Mixed Poisson model
- Mixed logistic model
- Take into account the cluster effects

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University of Bordeaux, France

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May-October 2019

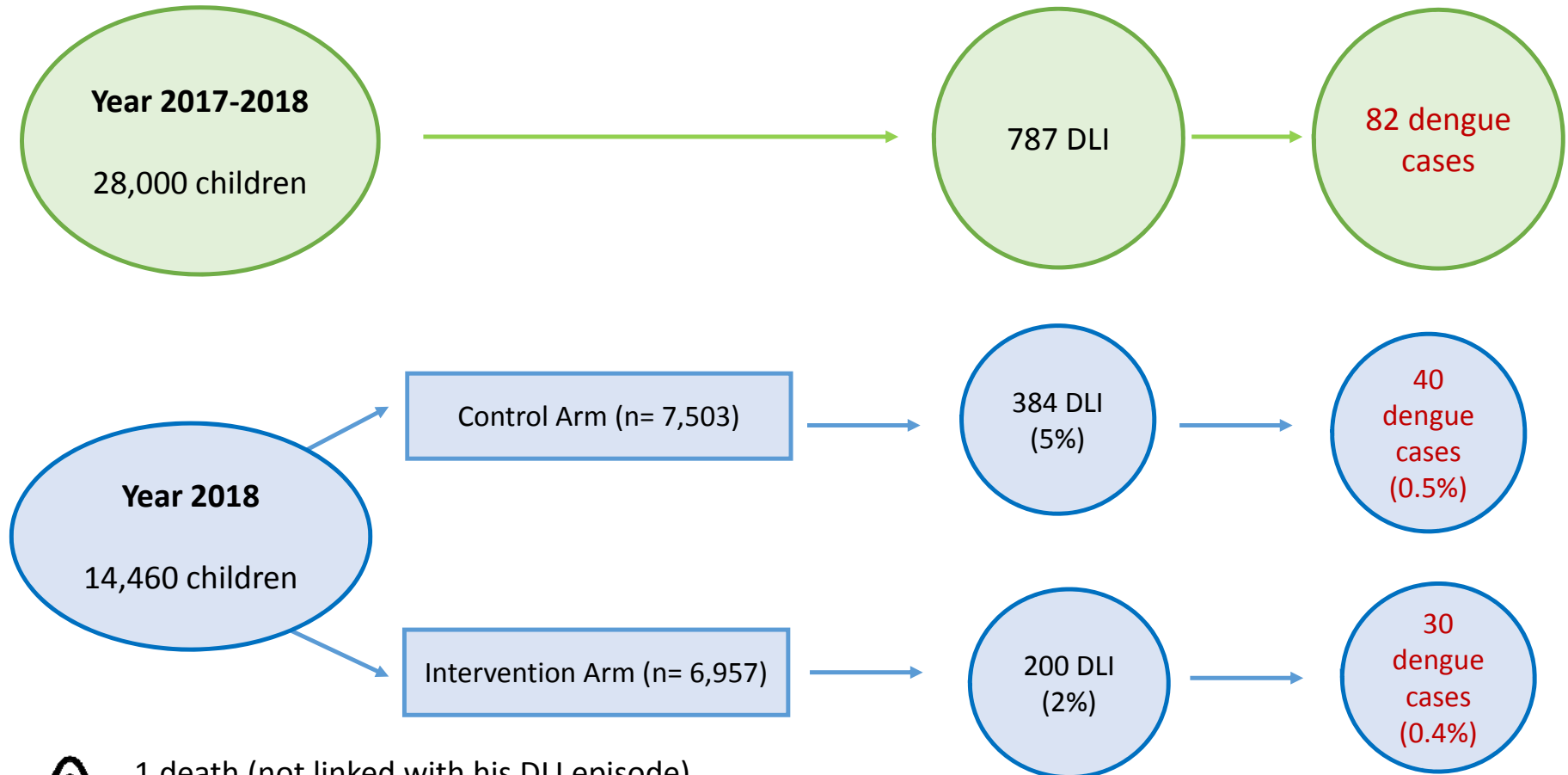
# Preliminary Results

## Active Surveillance of Dengue-like Illness in Community





# Active Surveillance of Dengue-like Illness in Community Children 5-15 years old

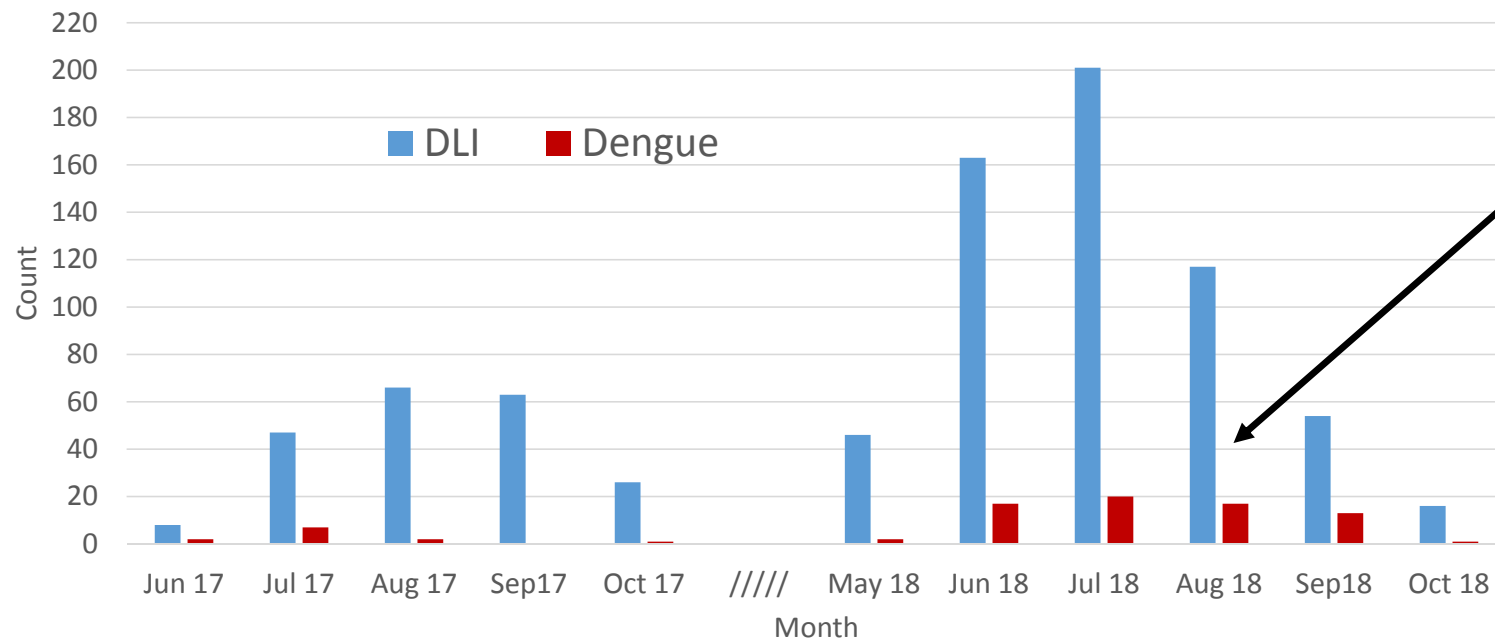


1 death (not linked with his DLI episode)  
3 children with sequels (no details)



# Active Surveillance of Dengue-like Illness in Community

Dengue-like Illness (n=787) and Dengue Positive (n=82)  
Active Surveillance, 2017 and 2018



2 clusters affected by flooding during August 2018





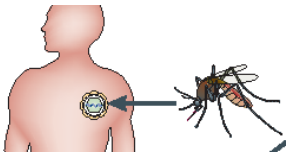
## Baseline Characteristics : Before any Intervention (2017)

Among children with DLI



56% of children declared previous vaccination against Japanese Encephalitis

- Mass vaccination campaign in Cambodia, 2016
- 85-90% children aged 9 months to 15 years vaccinated



16% declared previous dengue in the past

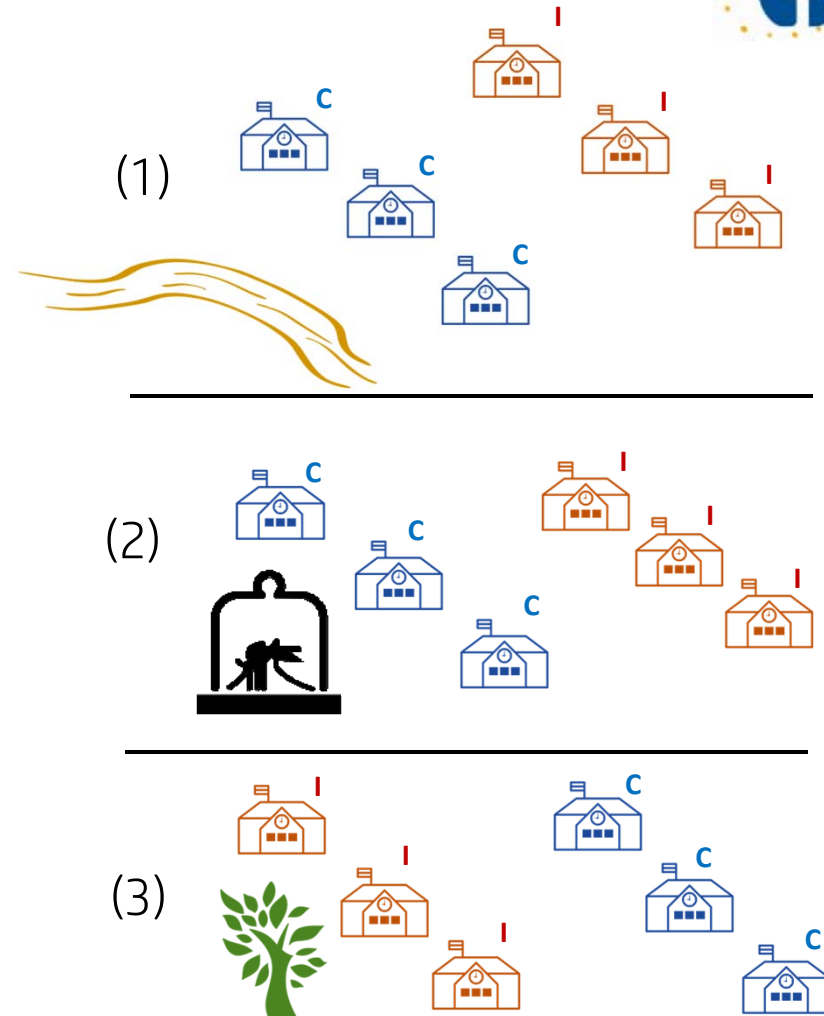


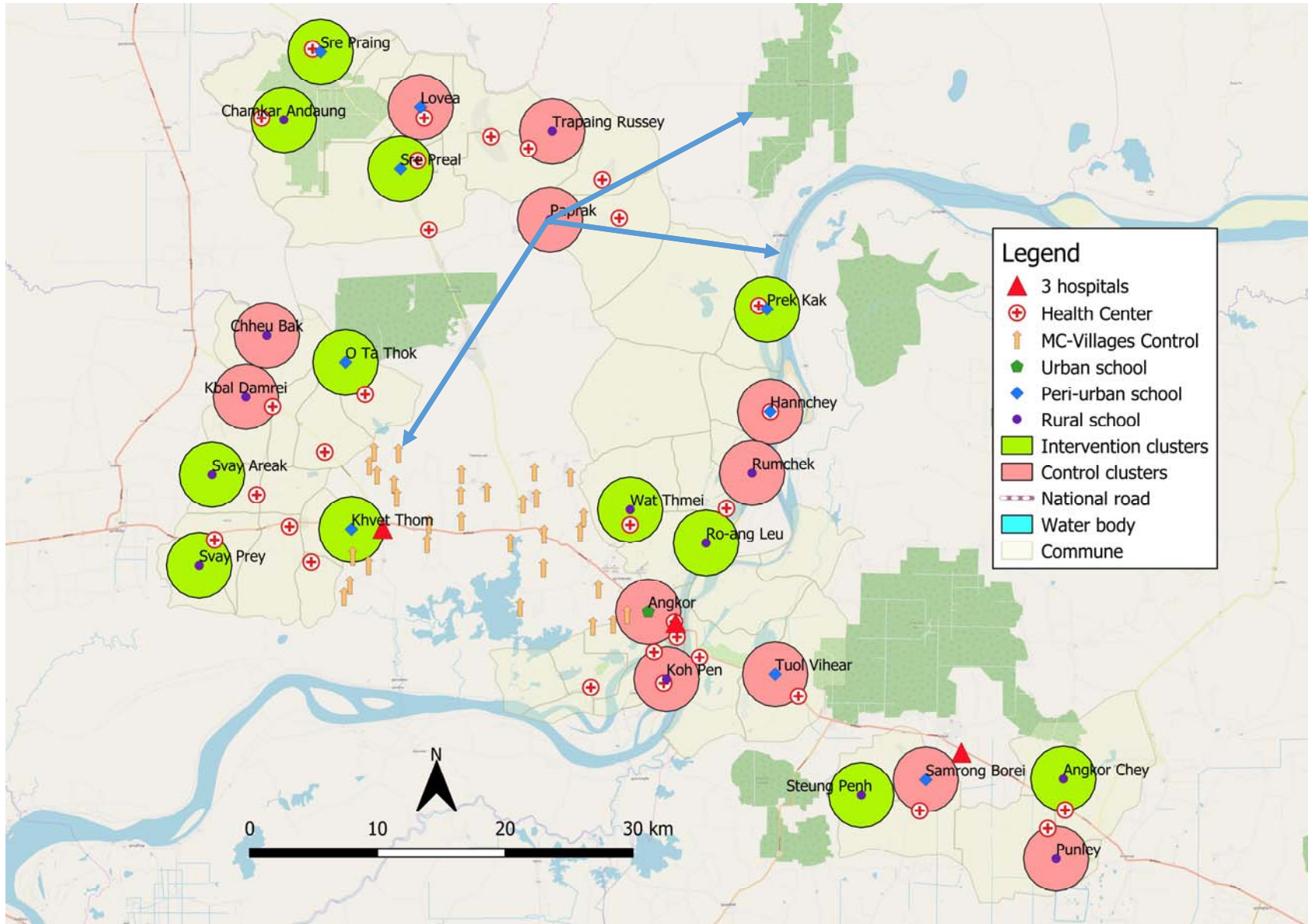
## Baseline Characteristics (2017)

Compared to « Control » clusters,

the « Intervention » clusters :

- Are further away from
  - The Mekong River (1)
  - Malair Consortium (MC) interventions (2)
- Are closer to
  - Rubber plantations (3)







# Active Surveillance of Dengue-like Illness in Community

In both 2017 and 2018

For 82 acute dengue episodes (PCR +) :

23 (28%) DENV-1

**46 (56%) DENV-2**

0 DENV-3

13 (16%) DENV-4

8 recent dengue episodes (PCR – / IgM dengue +)

5 flavivirus infections (PCR- and IgM of other arboviruses +)

Among dengue cases

14% of primary infections

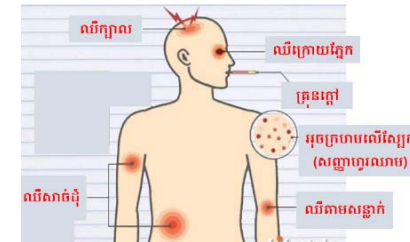
76% of secondary infections

10% of unclassified status



## Univariate Analysis

# Influence of Variables on the Probability of Developing DLI

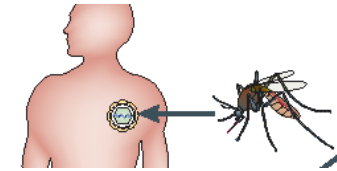


- Mixed Poisson models
- No intervention effect on the probability of developing DLI  
(OR [95%CI]= 0.7 [0.39 – 1.26] ; p= 0.24)
- Older children (10-15 YO compared to 5-10YO) are 50% less likely to develop a DLI episode  
(OR [95%CI]= 0.50 [0.42 - 0.61] ; p<0.001)



## Univariate Analysis

# Influence of Variables on the Probability of Developing Dengue



- Mixed logistic models
- **No intervention effect** on the probability of developing dengue in intervention clusters  
(OR [95%CI]= 0.85 [0.36 - 2.77] ; p= 0.79)
- Older children (10-15 YO compared to 5-10YO) are 50% less likely to develop dengue  
(OR [95%CI]= 0.54 [0.33 - 0.89] ; p= 0.01)
- Being close to the Mekong seems to increase 3 fold the risk of developing dengue  
(OR [95%CI]= 0.27 [0.09 - 0.81], p= 0.02)



# Multivariate Analysis

Mixed Poisson and logistic models

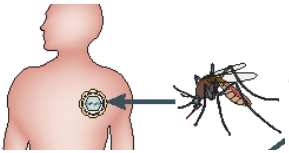
Variables included :

- Distances from Malaria Consortium interventions
- Distances from the Mekong River
- Distances from rubber plantations
- Children age (<10 YO ; >10 YO)

**Results : No intervention effect again (OR [95%CI]= 0.67 [0.38 - 1.18] ; p= 0.17)**

- Being in the age group of 11-15 compared to 5-10 decrease by 2 fold the risk of developing **DLI**  
(OR [95%CI]= 0.52 [0.44 - 0.61] ; p<0.001)

- Being close to the Mekong seems to increase by 3 fold the risk of developing **dengue**  
(OR [95%CI]= 0.17 [0.05 – 0.55], p< 0.01)
- Being in the age group of 11-15 compared to 5-10 decrease by 2 fold the risk of developing **dengue**  
(OR [95%CI]= 0.54 [0.32-0.89], p=0.02)



## Results

### Saliva Testing for Dengue in School Children





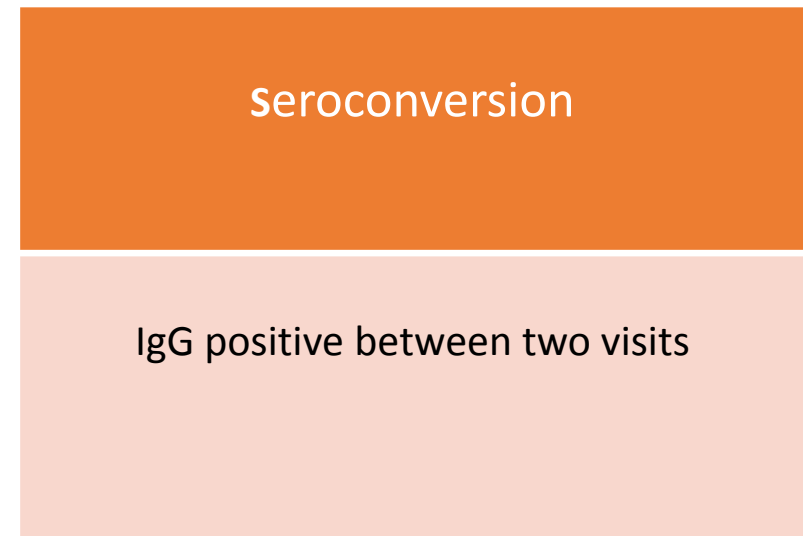
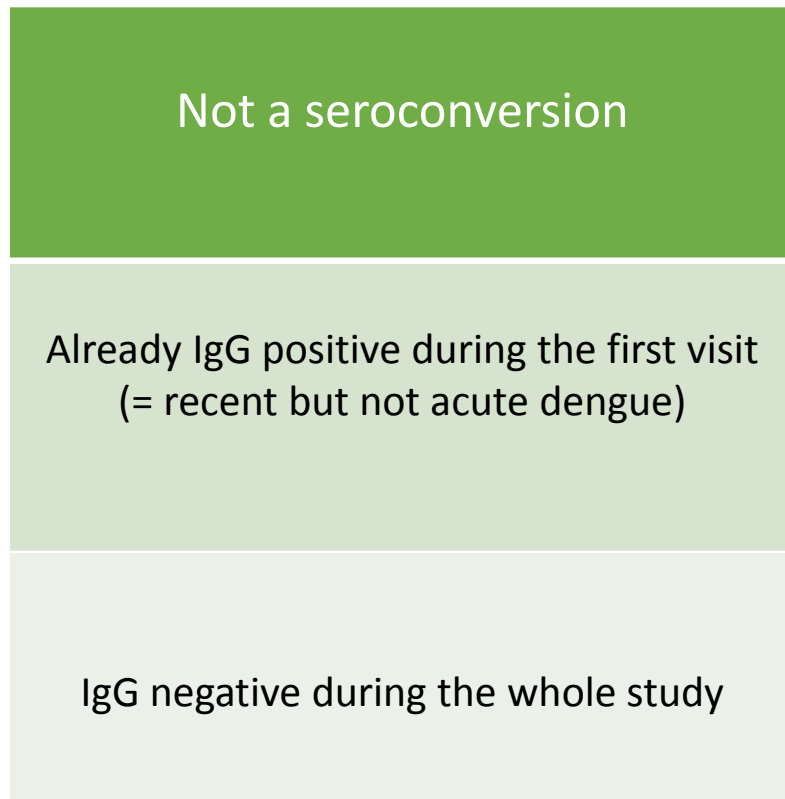


## Saliva Testing in School Children Age 5-15 Years Old

Saliva collection	Nb of saliva	Date of collection
Survey 1	3,003	23 -26 May & 13-23 June 2018
S2	2,973 (99.0% of S1)	10-20 July 2018
S3	2,801 (93.3% of S1)	22-31 August 2018
S4	2,556 (85.1% of S1)	12-18 November 2018
S5	2,530 (85.1% of S1)	14-21 January 2019



## What Is a Dengue Case in this Follow-up by Saliva Testing? New dengue infection = seroconversion based on IgG



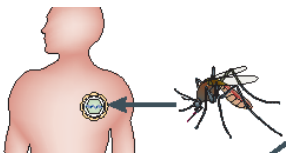
**234 seroconversions  
among 3,000 children  
from 1<sup>st</sup> to 5<sup>th</sup> visit (sampling)**



## Saliva Testing in School Children Baseline Characteristics



89% declared they had been vaccinated against JE  
→ From number of vaccinated children in 2016  
(mass campaign)



3% had dengue recently (IgG positive at baseline)  
1/3rd declared they had dengue at least once  
1/6th declared they already had been hospitalized  
for a dengue episode

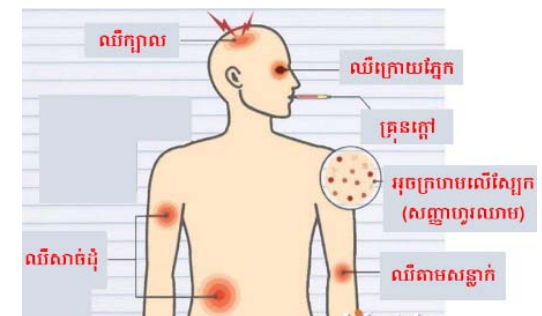


## Saliva Testing in School Children Clinical Form of Dengue Cases

Among 234 children with seroconversion

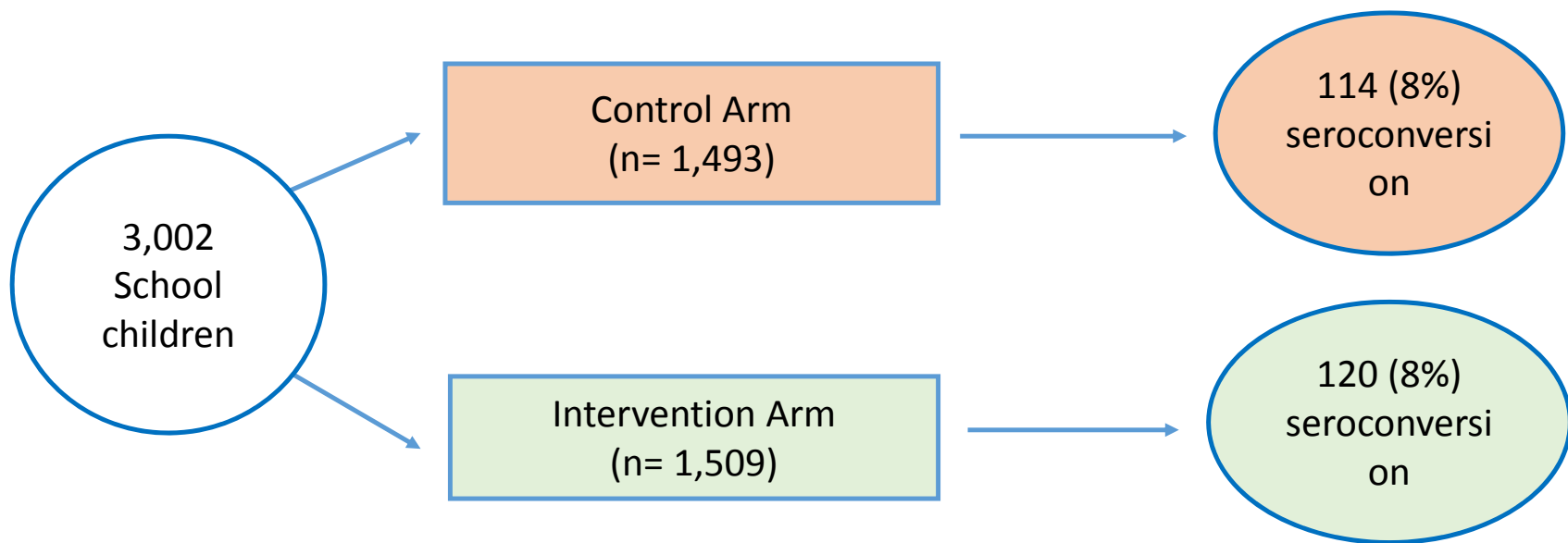
- 31 (13.2%) asymptomatic dengue cases according to our DLI criteria

- 113 (48.3%) dengue infections with symptoms





## Saliva Testing in School Children Number of Dengue Cases in 2018





## Saliva Testing in School Children

- Mixed logistic models
- Univariate analysis :
  - Models for all visits : **there is no intervention effect** on the probability of developing dengue  
(OR [95%CI]= 1.01 [0.65 – 1.57]; p= 0.95)
  - Models by visit are not significant neither
- Multivariate analysis :
  - **There is no intervention effect** on the probability of developing dengue  
(OR [95%CI]= 1.10 [0.49 – 3.83] ; p= 0.70)

## Discussion



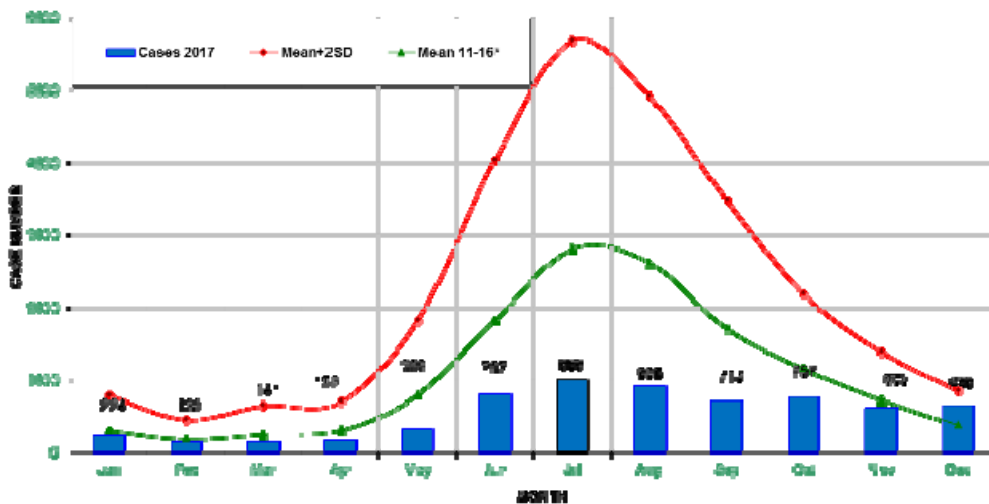
- Intervention in school doesn't seem to decrease dengue transmission among children in community
  - Short school daytime along with part of the study period overlapping with summer holidays : children could had dengue elsewhere
- Being close to the Mekong and being aged from 5 to 10 years old was significantly increasing the probability of developing DLI and dengue respectively
  - Children could had dengue younger (<5 years old)
- More secondary dengue infection than primary infection in active surveillance of DLI
  - First episodes could more often be asymptomatic infections



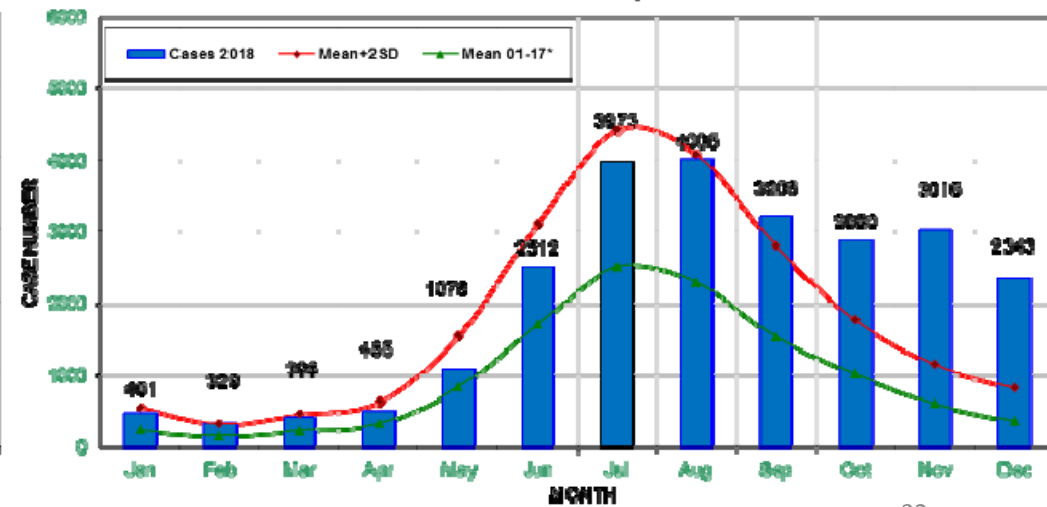
# Syndromic Hospital Surveillance, National Dengue Control Program, Cambodia, 2017-2018

- Low circulation of Dengue in 2017

**CUMULATIVE CASES OF DENGUE-REPORTED BY MONTH, 2017  
COMPARED WITH BASELINE OF 2011-2016 (\* excluding 2012), CAMBODIA.**



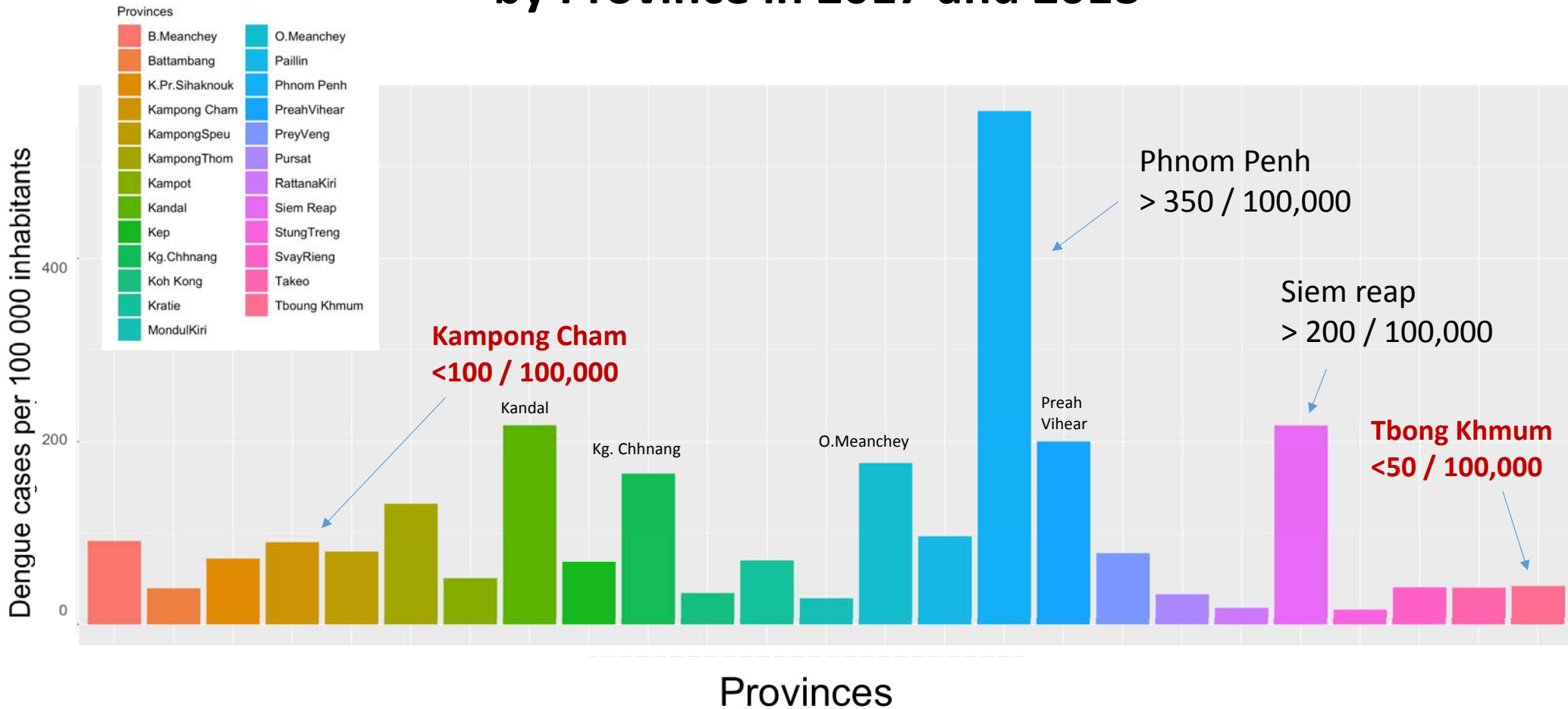
**CUMULATIVE CASES OF DENGUE-REPORTED BY MONTH COMPARE WITH BASELINE OF  
2011-2017\* (Excluded 2007 and 2012), CAMBODIA, 2018**







# Dengue Incidence Rates per 100,000 Inhabitants by Province in 2017 and 2018



# Conclusion



Milestonename / Short description	1st SC	2nd SC	3rd SC
Senior entomologist PhD deployment			
Study sites identification & selection			
Achievement of field visits to present the project to community and health authorities			
Design of the Cluster Randomized Trial Study			
Initial inventory of breeding sites in schools and destruction with participation of scholar			
Result of insecticide sensitivity and selection of products for the control of vectors			
Implementation of adult mosquitoes control			
Installation of auto-dissemination system around schools			
Kits for COMBI ready to be distributed			
Achievement of training of VHV involved in the active surveillance in villages			
Initial supply of saliva tests			
Collection and testing of saliva			
Data of active surveillance collected for statistical analysis			
Issue of recommendations for health authorities			

## Acknowledgements

- Nurses from local health centers
- Village health volunteers (VHV)
- School teachers in saliva collection
- Field monitoring teams
- Laboratory team, Virology Unit, IPC
- Team at Epidemiology and Public Health Unit, IPC
  - Amber KUNKEL for advices in data analyses
- Parents of children participants



Saliva tubes



Field team



Preparing for survey



Meeting with VHV



Interview



Interview parents



Teachers collecting children's saliva

# THANK YOU FOR YOUR ATTENTION !

