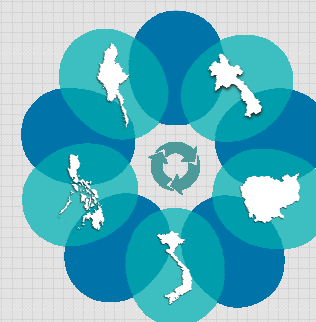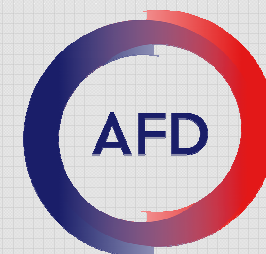# STEERING COMMITTEE 27-28 NOVEMBER 2019 - VIENTIANE

ECOMORE 2 PROJECT

COMPONENT IN LAO PDR

VIROLOGY

Somphavanh SOMLOR- Elodie CALVEZ- Virginie POMMELET
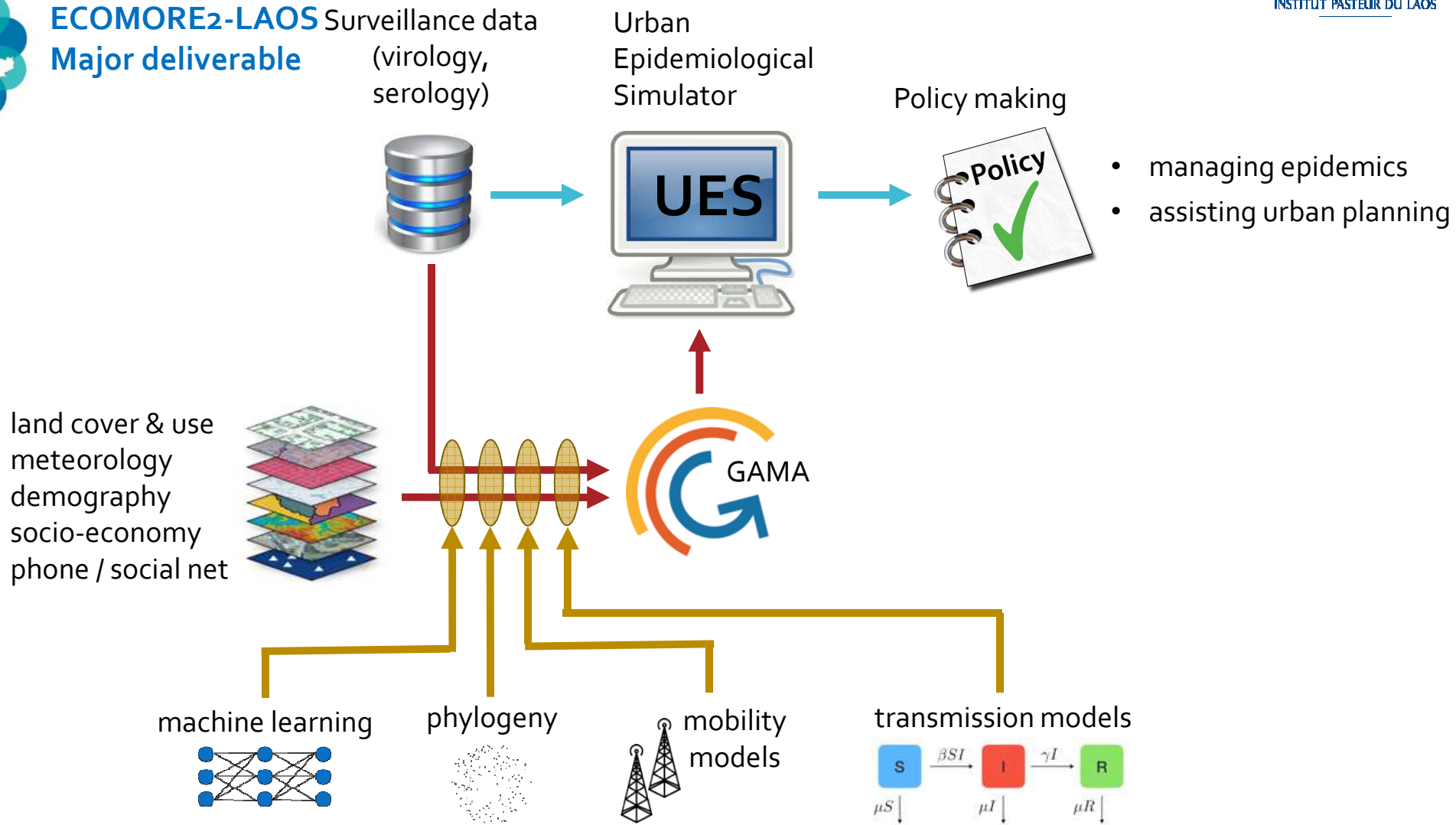**Marc GRANDADAM**

ECOMORE II

AFD

WP LAOS

Institut Pasteur

international network
Institut Pasteur

ສະຖາບັນ ປັດສະເຕີ ລາວ
INSTITUT PASTEUR DU LAOS

ECOMORE2-LAOS Major deliverable

Surveillance data (virology, serology)

Urban Epidemiological Simulator

UES

Policy making

Policy ✓

- managing epidemics
- assisting urban planning

land cover & use
meteorology
demography
socio-economy
phone / social net

GAMA

machine learning

phylogeny

mobility models

transmission models

S — $\beta S I$ → I — γI → R

μS μI μR

INSTITUT PASTEUR DU LAOS

Why in Vientiane?

- **Vientiane: general features**
  - ➢ 4.000 km²; 820.000 souls (Laos: 240.000 km², 7 millions people)
  - ➢ Fast urbanization (5% / year)
  - ➢ Sustainability of urban extension
  - ➢ Main entry door for immigration and tourism

- **Lab surveillance background since 2012**
  - ➢ High and rising dengue incidence
  - ➢ High heterogeneities in space and time
  - ➢ Availability of different data sources

  (entomology; meteorology; socio-economic; environmental…)

- **GOAL : A system for health**
  - ➢ Combine A.I. technology and field survey to improve understanding and prevent dengue transmission
  - ➢ System transposable (other cities; disease) and scalable (city ➔ country)

ECOMORE II

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PERSPECTIVES 2019 – HIGH RISK YEAR

➢ **Inoculum already exists with > 50% dengue confirmation among suspected cases**

   (Vientiane Capital; December 2018; January 2019)

➢ **Shift of serotype predominance DENV-4 ➜ DENV-2 (Vientiane Cal; Attapeu; Salavan);**

➢ **Co-circulation of 3 serotypes: DENV-2 > DENV-4 > DENV-1**

➢ **Major insecticide resistance (*Aedes* larvae / adults) may hamper vector control strategies**

➢ ***El Nino* southern oscillation (low magnitude);**

➢ **Impact DENV transmission ?**

National syndromic surveillance - 2019

Update 25/11/2019

38.371 cases / 74 deaths

NUMBER OF CASES

DISTRIBUTE BY DAYS AND MONTHS
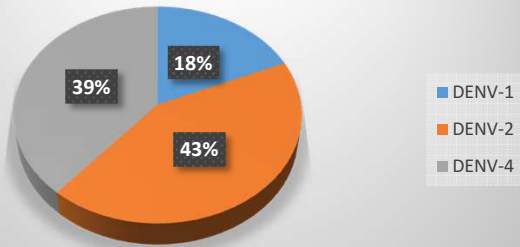
ຈຳນວນຜູ້ປ່ວຍ(CASES)
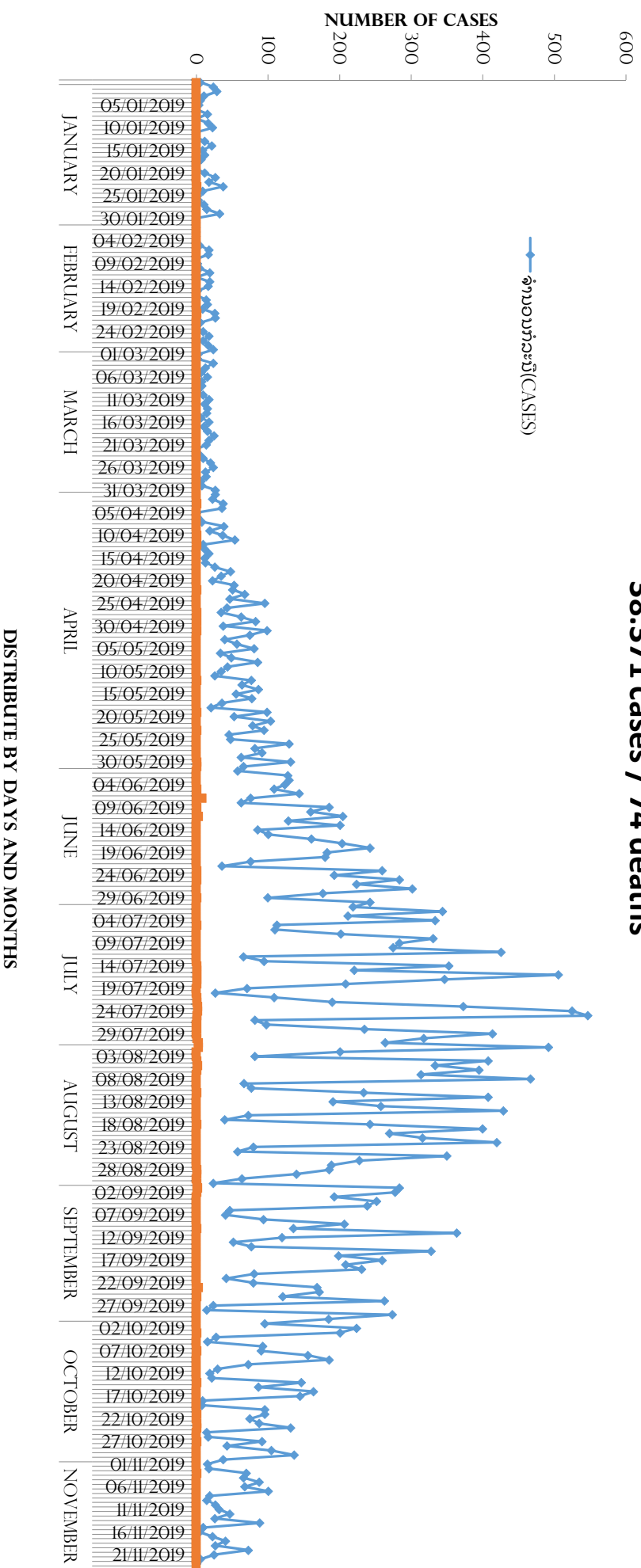
(source: NCLE, daily report)

➢ **DENGUE: 4971 susp. cases tested - week 47 - (2337 in 2013)**

➢ **Chikungunya: 2 cases (ex. Indonesia; ex. Myanmar)**

➢ **Screening Zika: RT-PCR on urine of dengue suspected cases negative for direct diagnostic markers (32 samples)**

➢ **Leptospirosis: PCR on plasma of suspected cases negative for dengue direct diagnosis (LOMWRU):**
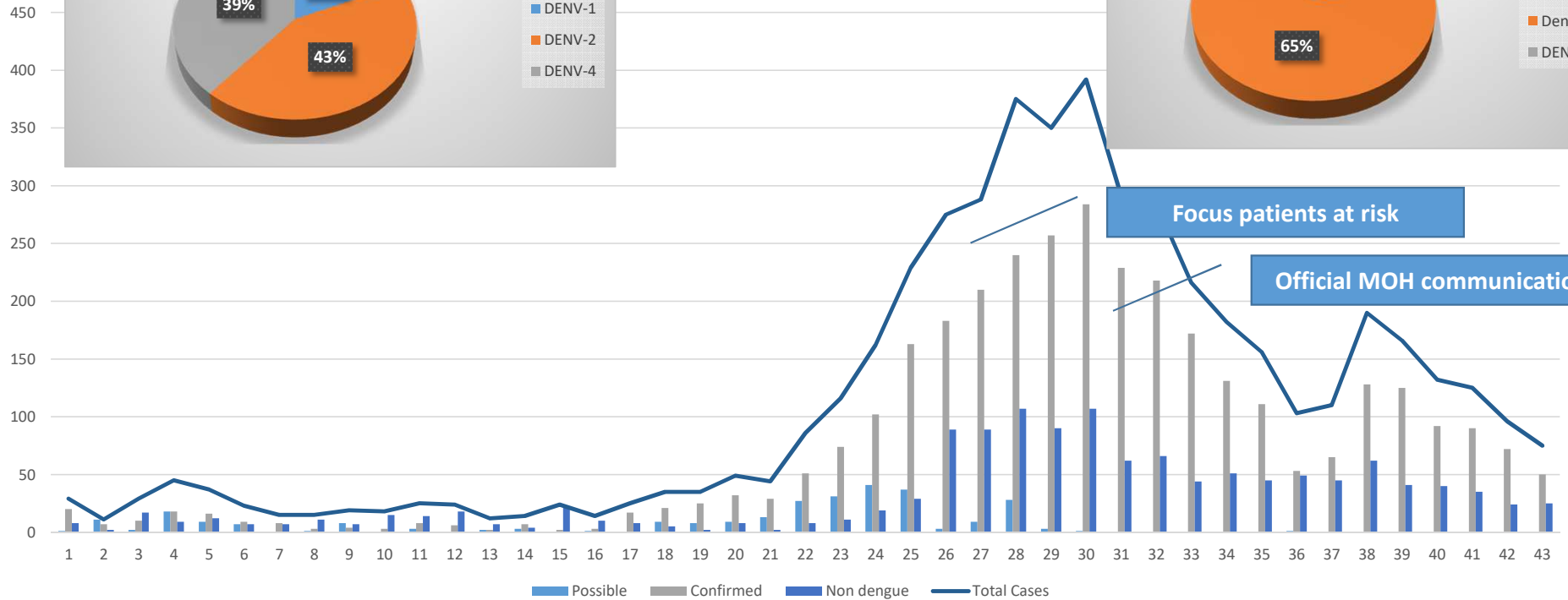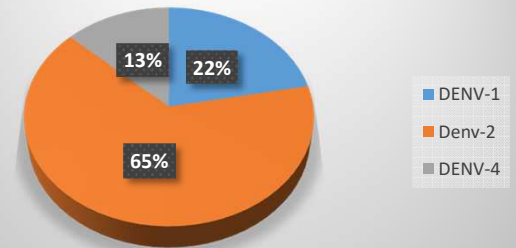
✓ **2018: 8/457 (1.81%)**

✓ **2019: 9/882 (1.02%)**

LABORATORY SURVEILLANCE – VIENTIANE Cal 2019

4941 cases / 9 provinces / 20-80% conf.
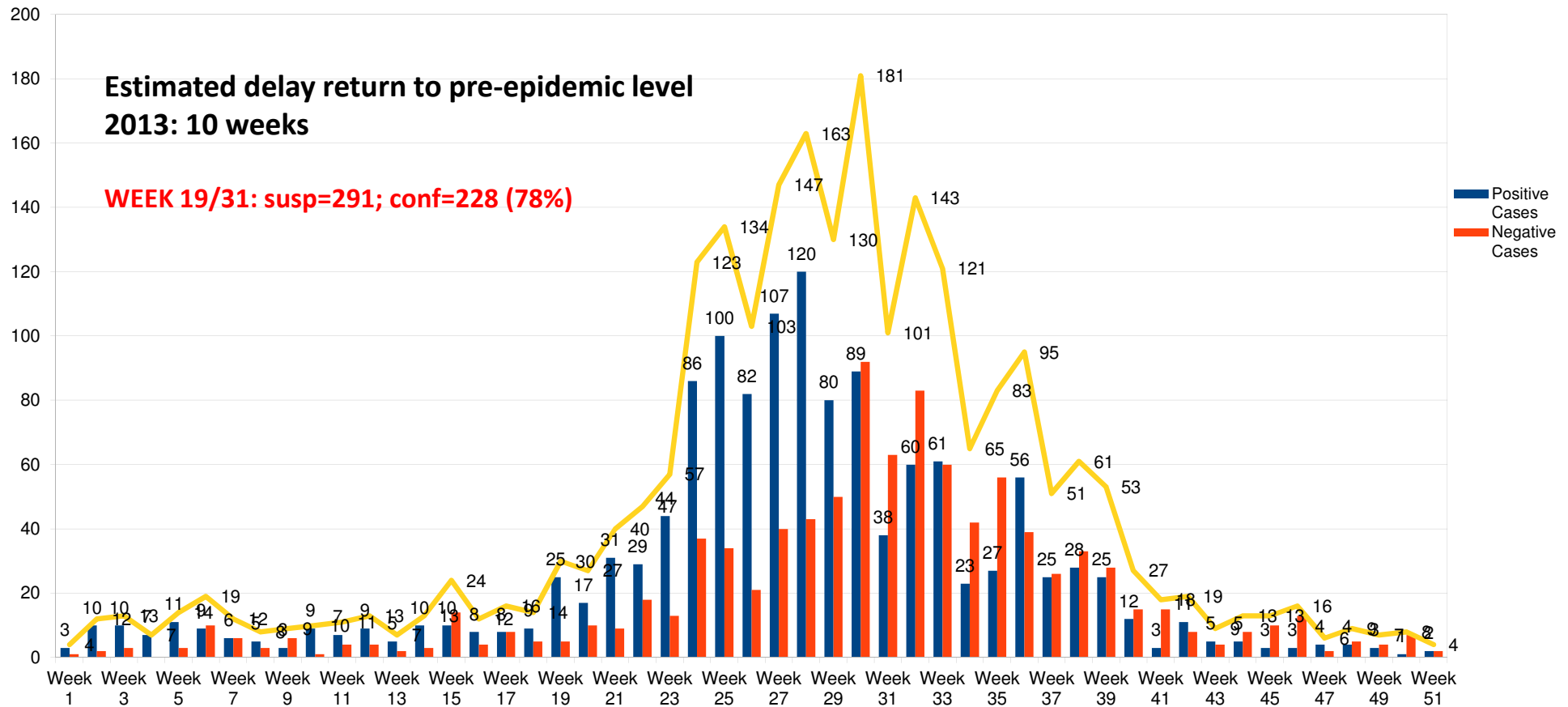
Dec. 2018 - 266 tests (1046 cs)

DENV-1 18%
DENV-2 43%
DENV-4 39%

2019 - 1149 tests (4103 cs)

DENV-1 22%
Denv-2 65%
DENV-4 13%

Focus patients at risk

Official MOH communication

Possible   Confirmed   Non dengue   Total Cases

IPL-WHO meeting 07/08/19

Estimated delay return to pre-epidemic level 2013: 10 weeks

WEEK 19/31: susp=291; conf=228 (78%)

Estimated delay return to pre-epidemic level
2013: 10 weeks

WEEK 19/31: susp=291; conf=228 (78%)
High hypothesis: >20 weeks
Low hypothesis: 20 weeks

DENV-2 PHYLO-GEOGRAPHY

Calvez *et al*, under soumission
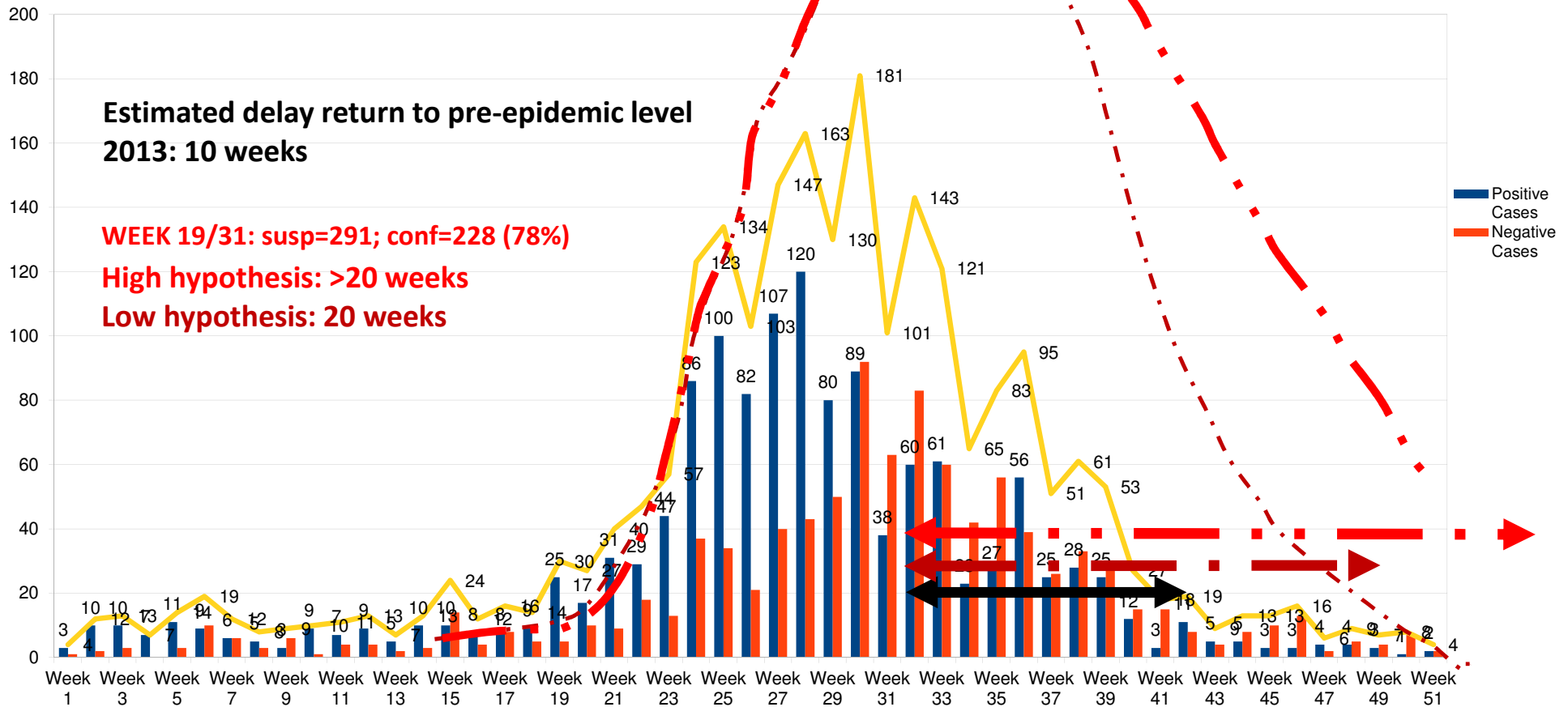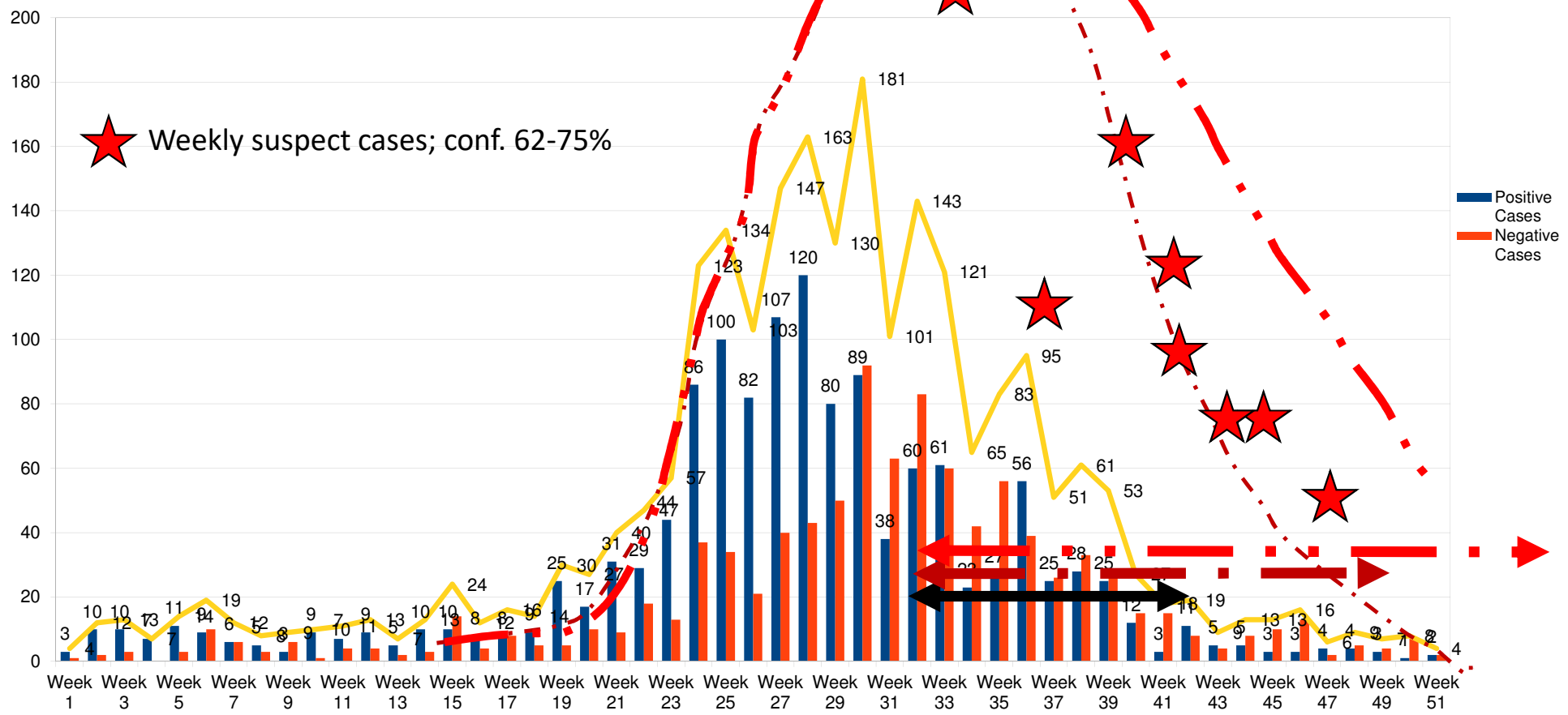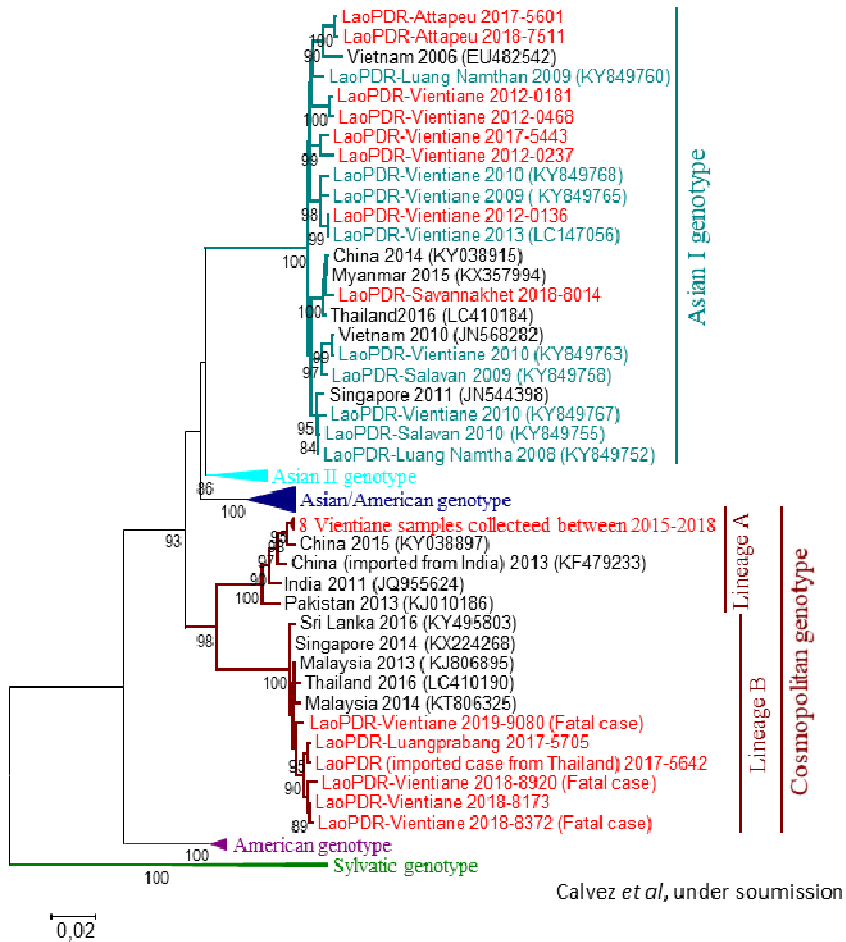
- Envelope protein sequencing

- Co-circulation of 2 genotypes

  - Asian I (at least since 2008)
    - Several clusters
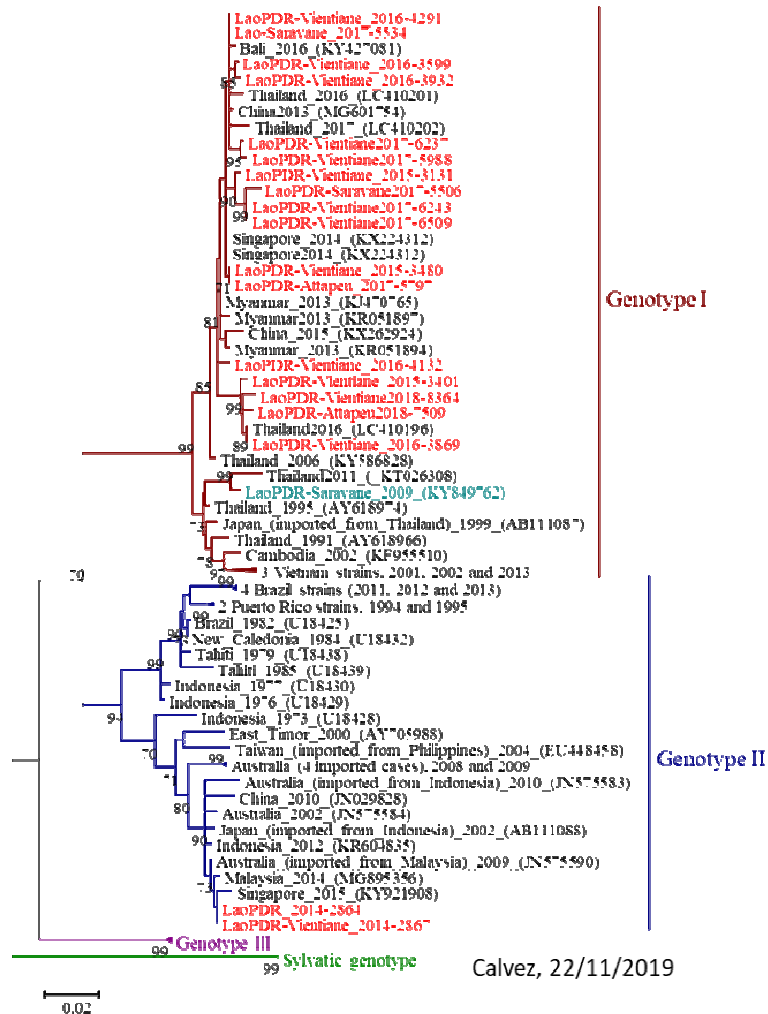   - Detected at the country level
    - Clustered with samples from South East Asia

  - Cosmopolitan (at least since 2015)
    - **Lineage A**
      - One cluster
      - Detected in Vientiane Capital, Vientiane Province and Luangprabang
      - Clustered with samples from China and India
    - **Lineage B**
      - (several clusters)
      - Detected at the country level
      - Clustered with samples from Malaysia, Thailand, Sri Lanka and Singapore

DENV-4 PHYLO-GEOGRAPHY

- **Preliminary results: Partial envelope protein sequencing**

- **Detection of 2 genotypes**

  - **Genotype I (at least since 2015)**
    - several clusters
    - Detected at the country level
  - Clustered with samples from Asia

  - **Genotype II**
    - Detected only in 2014 in Vientiane
    - Imported ex Malaysia
    - Clustered with samples from South East Asia

Calvez, 22/11/2019

DENV-1 PHYLO-GEOGRAPHY
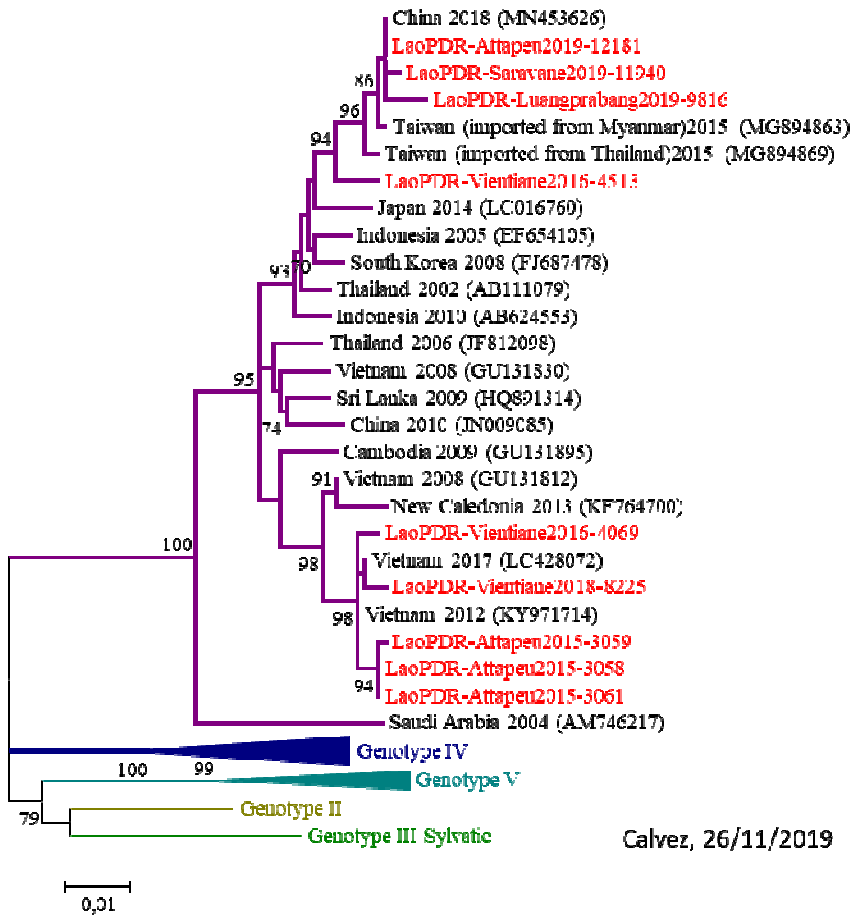
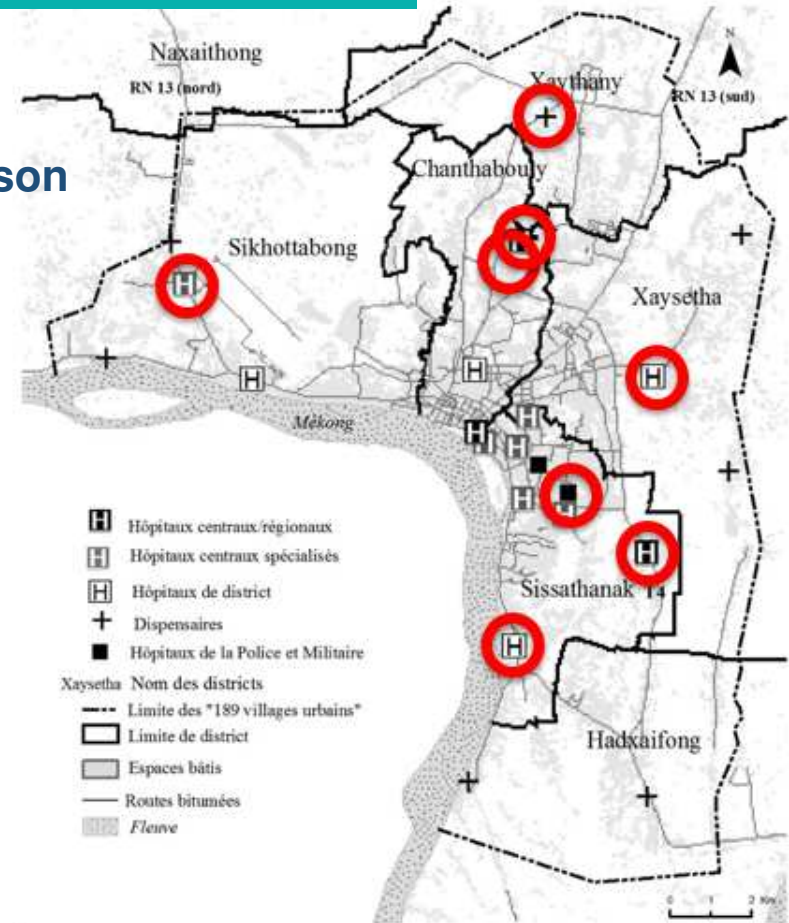- **Preliminary results: Partial envelope protein sequencing**

- **Genotype I (Asian genotype)**
  - **At least since 2015**
  - **Detected at the country level**
  - **Clustered with strains from South East Asia**

Calvez, 26/11/2019

➢ **9 hospitals (central / district; public & private)**

➢ **In / Out patients presenting at hospital for any reason**

➢ **Target: 2500 (8 class of age)**

➢ **Enrolled: 1312 samples / questionnaires**

➢ **Coverage: all city; general population**

➢ **Screening DELTAa assay**

Legend	
H	Hôpitaux centraux/régionaux
H	Hôpitaux centraux spécialisés
H	Hôpitaux de district
+	Dispensaires
■	Hôpitaux de la Police et Militaire
Xaysetha	Nom des districts
-·-·-	Limite des "189 villages urbains"
▭	Limite de district
▨	Espaces bâtis
—	Routes bitumées
░░	Fleuve

DELTAa
Discriminant ELISA for Typing Arbovirus antibodies

TMB → Blue = **OD1**

TMB → Blue = **OD2**

Anti-IgG/HRP conjugate

**Sample Atb**

Viral antigen

PBS

PBS + denat agent
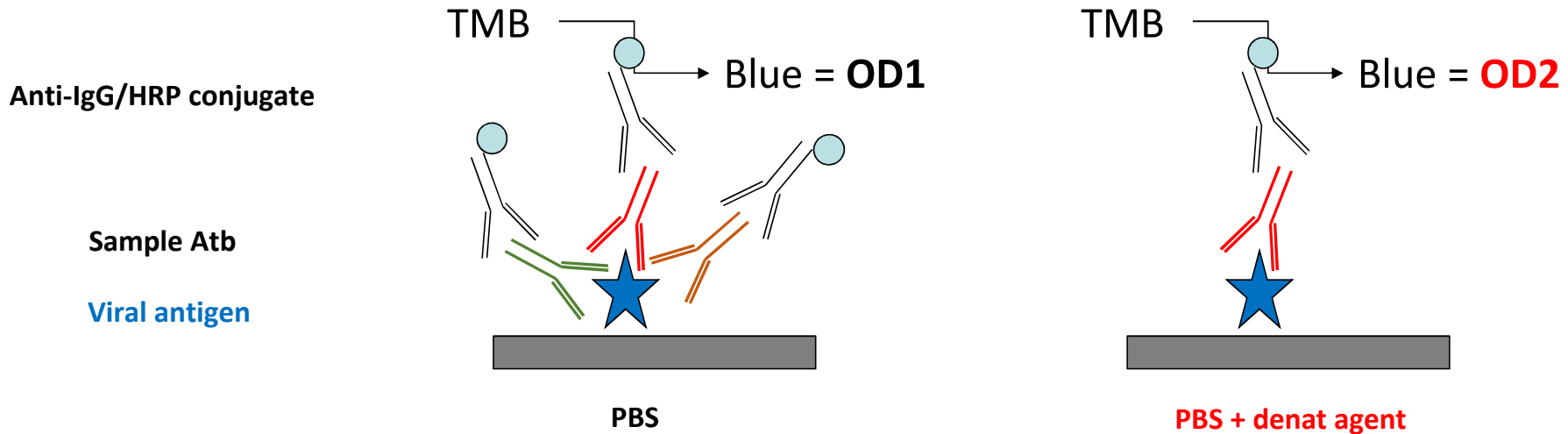
Interpretation:

✓ **OD2** = OD1 ➜ presence of HIGH affinity / avidity antibodies

✓ **OD2** < OD1 ➜ presence of LOW affinity / avidity antibodies

✓ Antigenic complex discrimination: A.I. ≥ 60%

✓ Serotype discrimination: A.I. ≥ 80%

DENGUE SEROPREVALENCE

Indirect standard ELISA vs DELTAa assay

- IgG DENV ELISA: **66.3% (95%CI 63.8-68.9**)

- IgG DENV DElTAa: **21.8% (95%CI 19.6-24.0)**

- ed
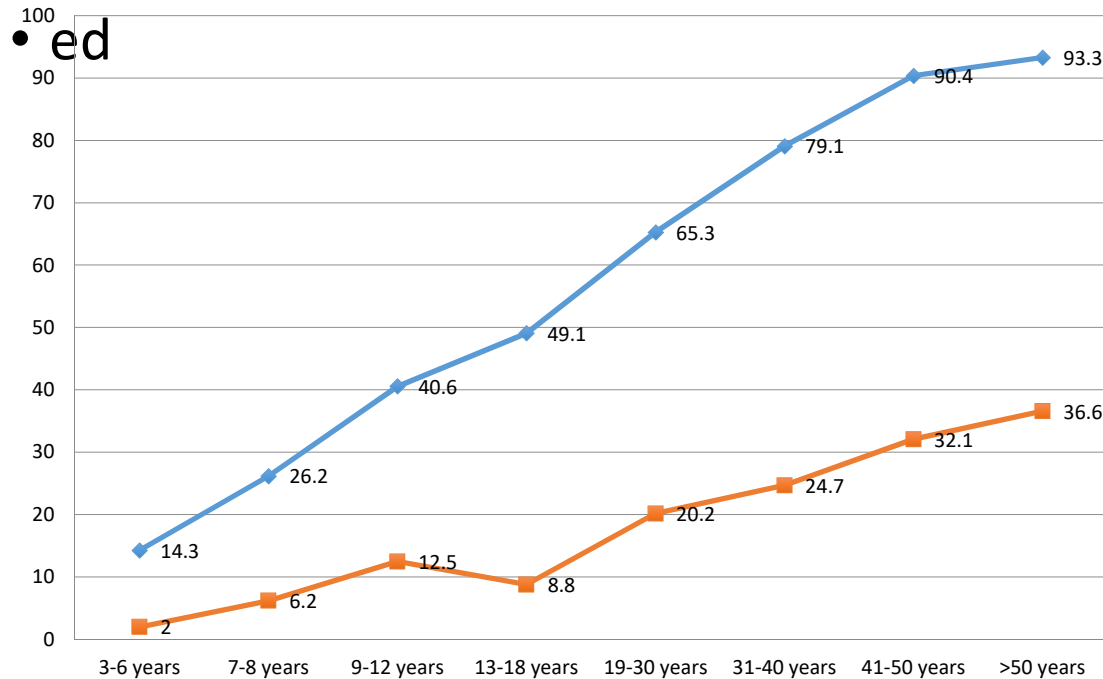
➢ **Seroprevalence increases with age**

➢ **Above 50 ys, 93% displayed anti-flavi ATBs**

➢ **But only 37% have anti-DENV IgG of high affinity**

➢ **Identify cross-reactive flavivirus?**

SEROTYPES' SPECIFIC SEROPREVALENCE

(DELTAa preliminary results)

DENV-1*	DENV-2*	DENV-3*	DENV-4*	Freq	%	Cumul. Freq.
0	0	0	0	26	9.39	9.39
0	0	0	1	38	13.72	23.10
0	0	1	0	1	0.36	23.47
0	0	1	1	4	1.44	24.91
0	1	0	0	3	1.08	25.99
0	1	0	1	2	0.72	26.71
0	1	1	0	1	0.36	27.08
0	1	1	1	1	0.36	27.44
1	0	0	1	12	4.33	31.77
1	0	1	0	2	0.72	32.49
1	0	1	1	49	17.69	50.18
1	1	0	1	13	4.69	54.87
1	1	1	0	1	0.36	55.23
1	1	1	1	124	44.77	100.00
				277	100.00	

(*) AI ≥ 80

➢ **Predominance of multiple exposure profiles (4 serotypes)**

JAPANESE ENCEPHALITIS
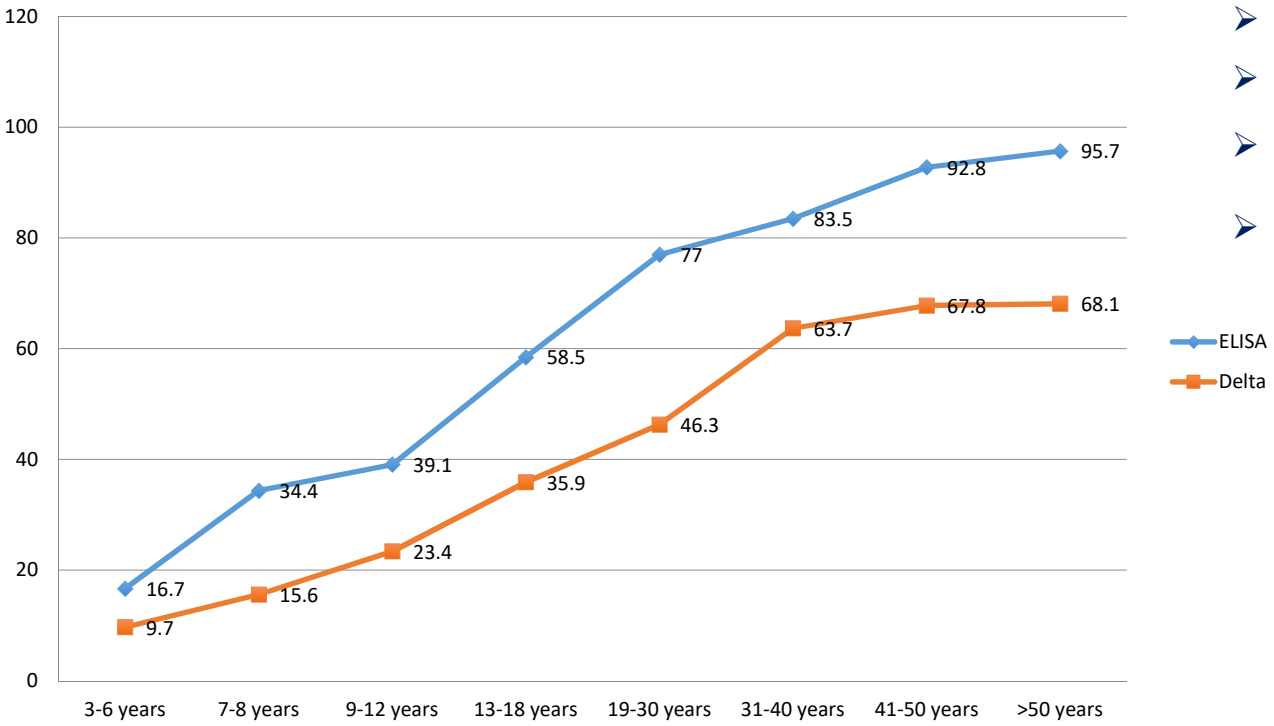
- IgG JEV ELISA: **71.9** (95% CI **69.4-74.3**)
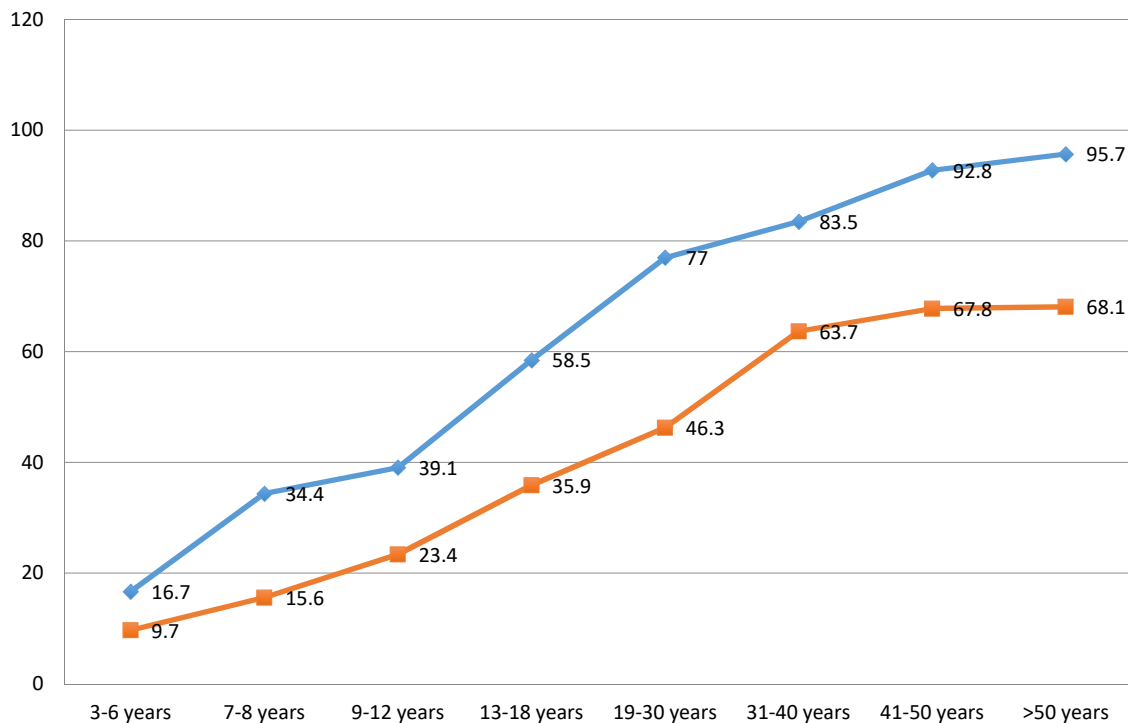- IgG JEV Delta: **48.8** (95% CI **46.0-51.5)**

➢ **Seroprevalence increases with age**

➢ **Above 50 ys, 96% displayed anti-flavi ATBs**

➢ **68% have anti-JEV IgG of high affinity**

➢ **Cross-reactive flavivirus: What else?**

JAPANESE ENCEPHALITIS

- IgG JEV ELISA: **71.9** (95% CI **69.4-74.3**)
- IgG JEV Delta: **48.8** (95% CI **46.0-51.5)**

➢ **Seroprevalence increases with age**

➢ **Above 50 ys, 96% displayed anti-flavi ATBs**

➢ **68% have anti-JEV cx IgG of high affinity**

➢ **JEV *vs* other JEV cx members**

➢ **Cross-reactive flavivirus: What else?**

SPONDWENI cx - ZIKA

Characteristics	Tested	Zik seropositive n	Zik seropositive (%)	95% CI	Zik-Delta seropositive n	Zik-Delta seropositive (%)	95% CI
Age							
3-6 years	55	4	7.3	0.3-14.2	4	7.3	0.3-14.2
7-8 years	26	1	3.9	_3.7-11.4	1	3.9	_3.7-11.4
9-12 years	27	3	11.1	_0.9-23.2	2	7.4	_2.6-17.5
13-18 years	23	9	39.1	18.7-59.6	3	13.0	_1.0-27.1
19-30 years	148	63	42.6	34.6-50.6	24	16.2	10.2-22.2
31-40 years	108	50	46.3	36.8-55.8	22	20.4	12.7-28.0
41-50 years	76	45	59.2	48.1-70.4	17	22.4	12.9-31.8
>50 years	112	79	70.5	62.0-79.0	27	24.1	16.1-32.1
Total	**575**	**254**	**44.2**	**40.1-48.2**	**100**	**17.4**	**14.2-20.5**

➤ **Seroprevalence increases with age**

➤ **Above 50 ys, 70% displayed anti-flavi ATBs**

➤ **17% have anti-SPONDV cx IgG of high affinity; only 20-24% after 30 ys (close rate recorded in blood donors)**

➤ **Zika PRNT**

SEROPREVALENCE STUDIES – NEXT STEPS

➢ **Round 2: fill the gap 6 - 18 years (addendum ethical clearance pending)**

➢ **Serotypes' specific seroprevalence**

➢ **DELTAa *versus* PRNT**

➢ **Data analysis: KAP; mobility; risks of exposure**

➢ **Mapping / data modeling**