Evolving VDPV2 Epidemiology - 2019

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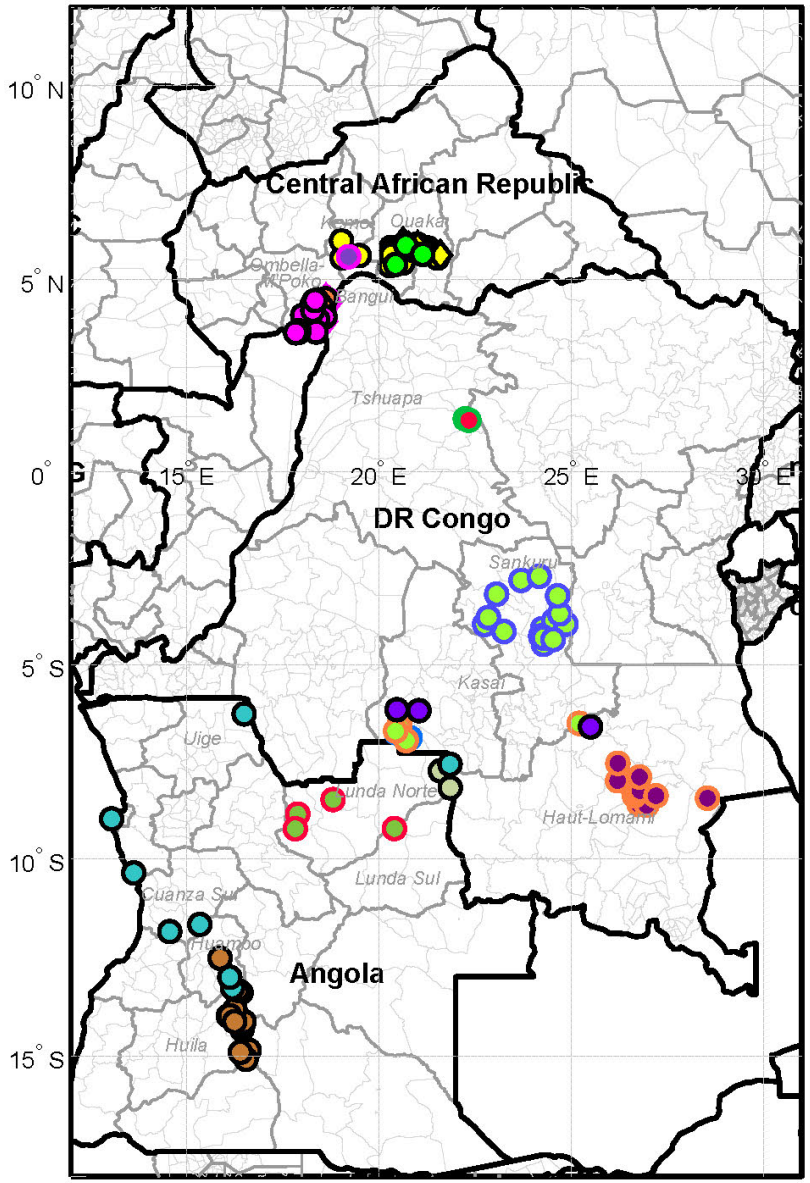
cVPDV2 in 2019

- **Dramatic increase in the number of new emergences (>40 in 2019 alone), disproportionately in Central Africa**
- **New emergences without obvious source**
  - Pakistan: Multiple VDPV2 emergences that are cVDPV2 or unclassified
    - Several genetically linked SL2 viruses with as few as 2 nt changes from Sabin 2, despite no recent OPV2 use

cVDPV2 in Central Africa

2019 PV2 Serotype Central Africa cVDPV



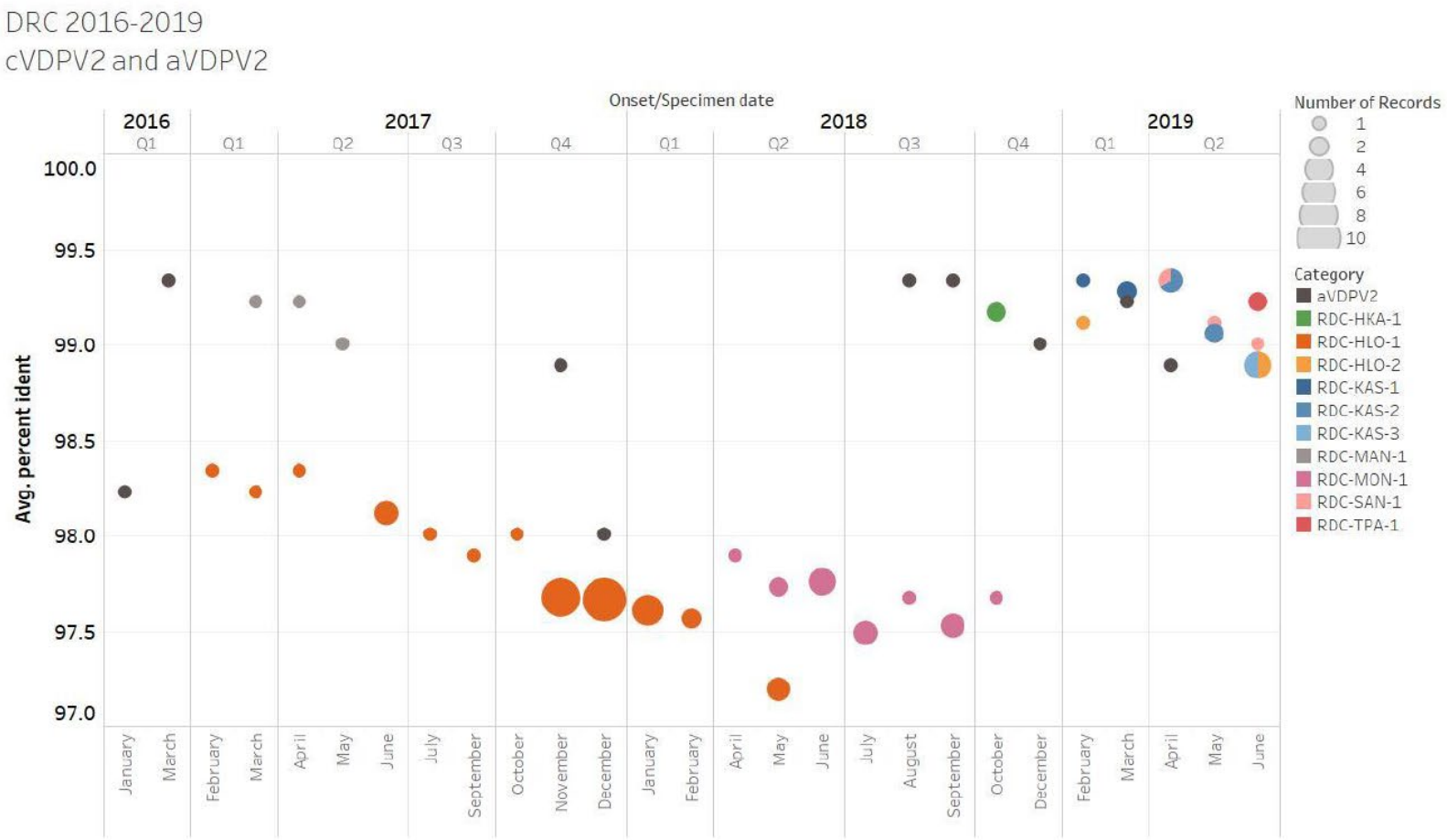
AFP cases, Contacts, Community Contacts, and ENV Specimens

Emergence Name

- ANG-HUI-1 (latest: contact 5019-06-04)
- ANG-LNO-1 (latest: contact 2019-05-14)
- ANG-LNO-2 (latest: contact 2019-08-01)
- CAF-BAM-1 (latest: case 2019-09-07)
- CAF-BAM-1-ENV (latest: collection 2019-07-22)
- CAF-BAM-2 (latest: contact 2019-05-27)
- CAF-BIM-1 (latest: case 2019-09-08)
- CAF-BIM-1-ENV (latest: collection 2019-09-05)
- CAF-BIM-2 (latest: contact 2019-06-28)
- CAF-BIM-2-ENV (latest: collection 2019-09-11)
- CAF-BIM-3 (latest: contact 2019-08-23)
- RDC-HLO-2 (latest: case 2019-09-02)
- RDC-KAS-1 (latest: contact 2019-03-17)
- RDC-KAS-2 (latest: case 2019-06-07)
- RDC-KAS-3 (latest: case 2019-06-30)
- RDC-SAN-1 (latest: case 2019-08-29)
- RDC-TPA-1 (latest: contact 2019-06-27)
- cVDPV2 (latest: case 2019-08-15)

1. Dots random within LGA
2. Created:10/24/2019
3. Last case dates are onset dates.
4. Last contact dates are specimen dates.
5. Last ENV dates are collection dates.

Changing frequency of emergences



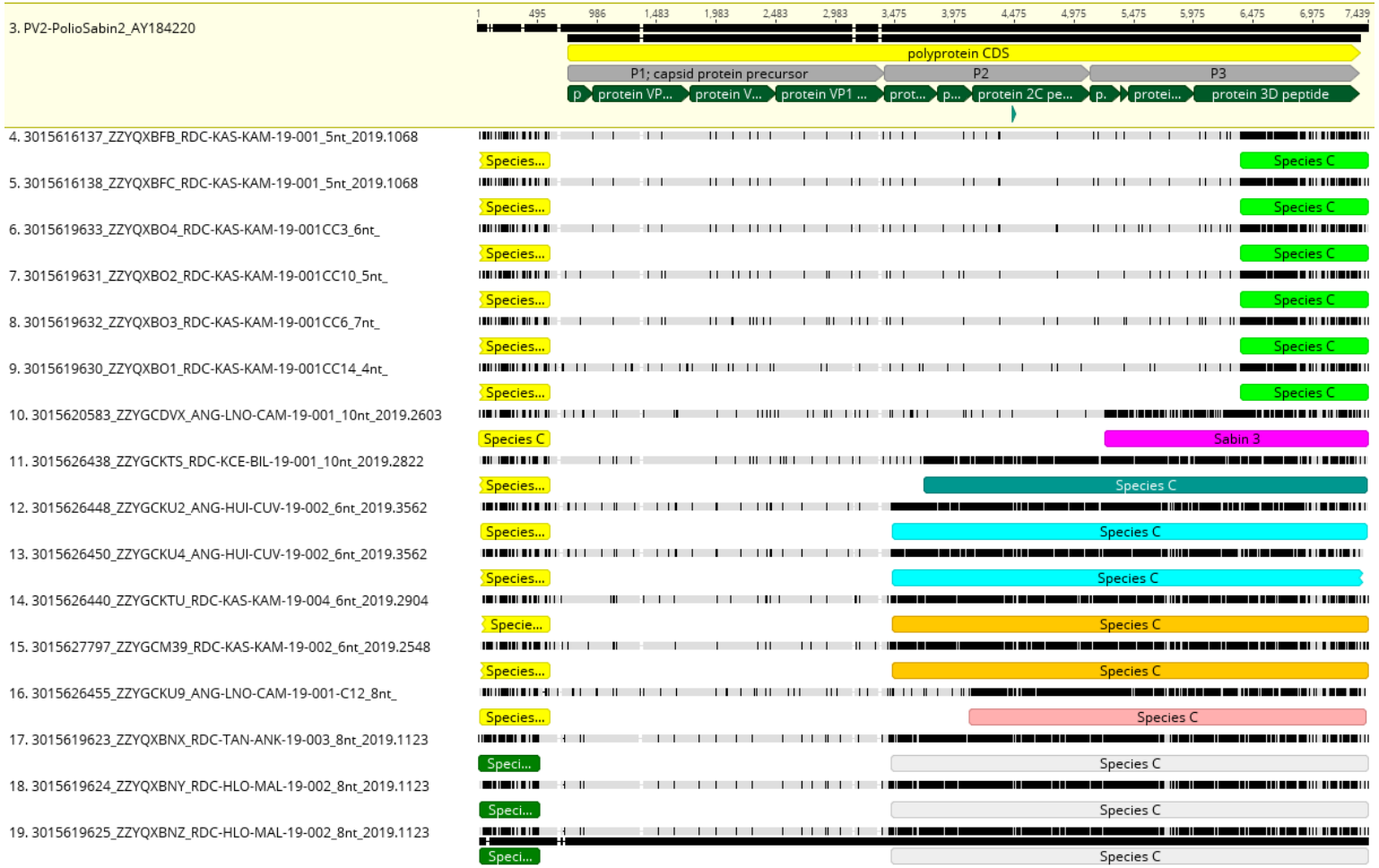
Investigation - Sequencing

Virus Genetics – Challenges of interpretation

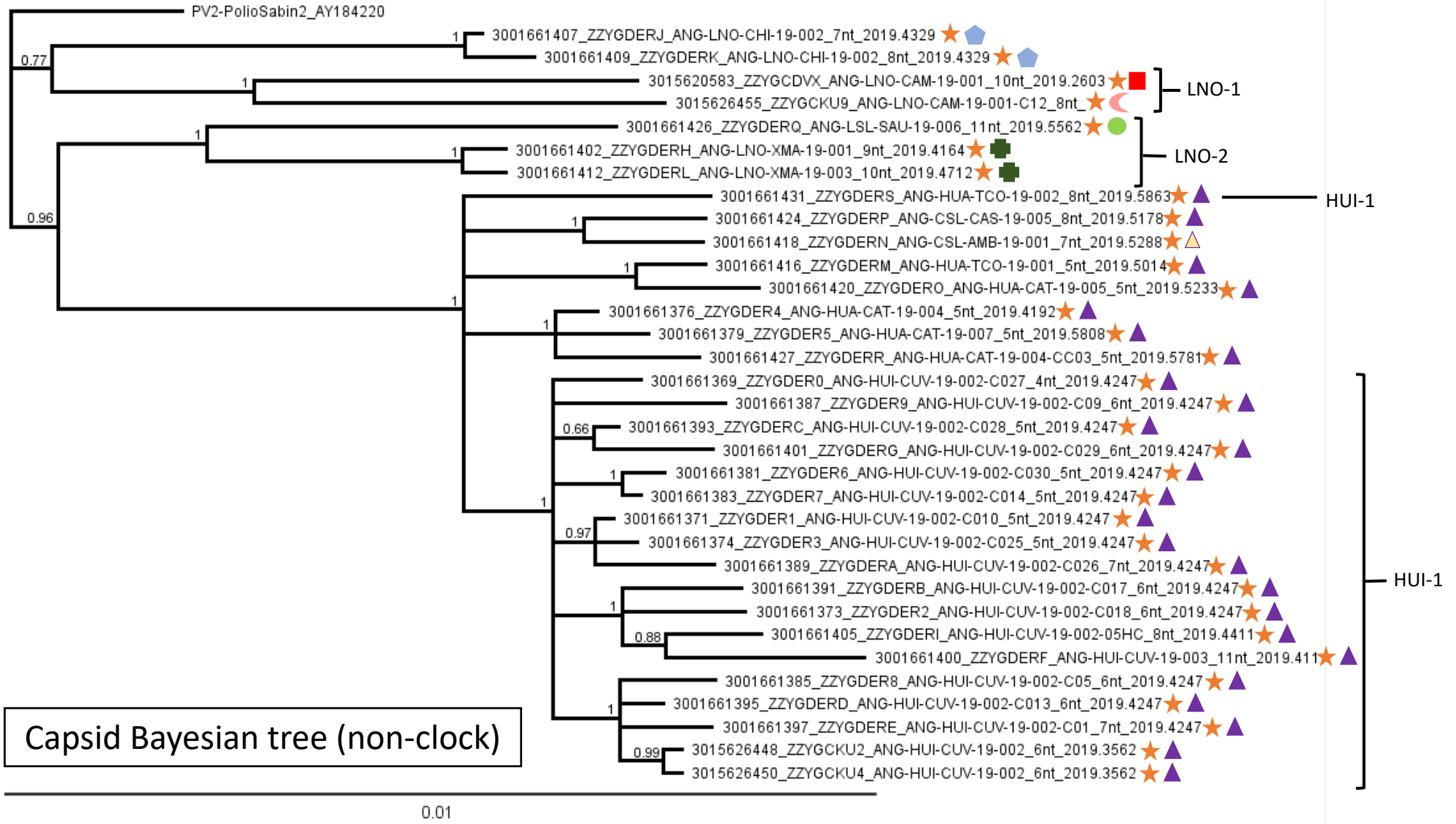
- Because of low divergence it has been challenging to establish unambiguous genetic linkages or independence among an increasing number of events.
- However, a unique mutation in the Kasai and Angola viruses allows for a unique opportunity to analyze the question of linkage and independence.
- This is being addressed by complete genome sequencing of all VDPV2 viruses in Central Africa (DRC, ANG, CAR).
- This is being expanded to other emergences sequentially (e.g., PAK is also in progress)

ANG, RDC/KAS, RDC/KCE whole genome analysis

- **VDPVs from ANG, RDC/ Kasai & Kasai Centrale all share 5’UTR**
  - Different from RDC/HLO and RDC/TAN
- **Multiple recombination partners in P2 and P3**
- **Suggests linkage**
- **Sequencing and analyses still ongoing**



Angola, 2019



Capsid Bayesian tree (non-clock)

Species C 5’ UTR: 97.6-100% identity

Species C P2/P3: 100% identity

Sabin 3 P3

Species C P2/P3

Species C P3 (matches RDC-KAS)

Species C P2/P3 99.8% identity

Species C P3 (P2 matches) ▲

Species C P2/P3 99-100% identity

Summary of genetic inference

- The viruses in Kasai/DRC and Angola are all descended from a single ‘source’ that is already genetically distinct (2nt different from Sabin in VP1)
- Complete genome sequencing of multiple viruses in 2019 from this geography confirm additional genetic traits (mutation and recombination) that are consistent with a single ‘source’ virus.
- Viruses with minimal Sabin divergence from this source have emerged in multiple geographies from February to September, which has never been observed previously
- After emergence, spread and accumulation of genetic mutations occurred just like typical of cVDPVs

Possible scenarios for an explanation

- 1) The ‘source’ is a single child whose virus spread to multiple geographies without accumulating genetic changes inconsistent with the prior 19 years experience
- 2) The ‘source’ is a single child whose virus was highly transmissible prior to becoming a VDPV, also never observed
- 3) The ‘source’ is a common source that is highly distributed in the defined geography leading to multiple independent emergences of cVDPV2 (e.g., vaccines)

Summary

- Changing epidemiology of VDPV2 emergence, primarily in Central Africa
- Increasing ambiguity of linkage/independence because of low divergent cVDPV2
- Common related source but divergent from Sabin as measured by unique genetic mutations and recombination may provide insight into explanation to changing epidemiology
- Immediate change to understand these 2019 emergence events will include whole genome sequencing on all emergent VDPV2
- Uncertainty whether this will be generalizable to other Central African geographies of explanations for cVDPV2 in areas without known mOPV2 use

Thank you