HCV DIVERSITY AND TREATMENT OUTCOMES FOLLOWING DIRECT-ACTING ANTIVIRAL (DAA) THERAPY IN BENIN

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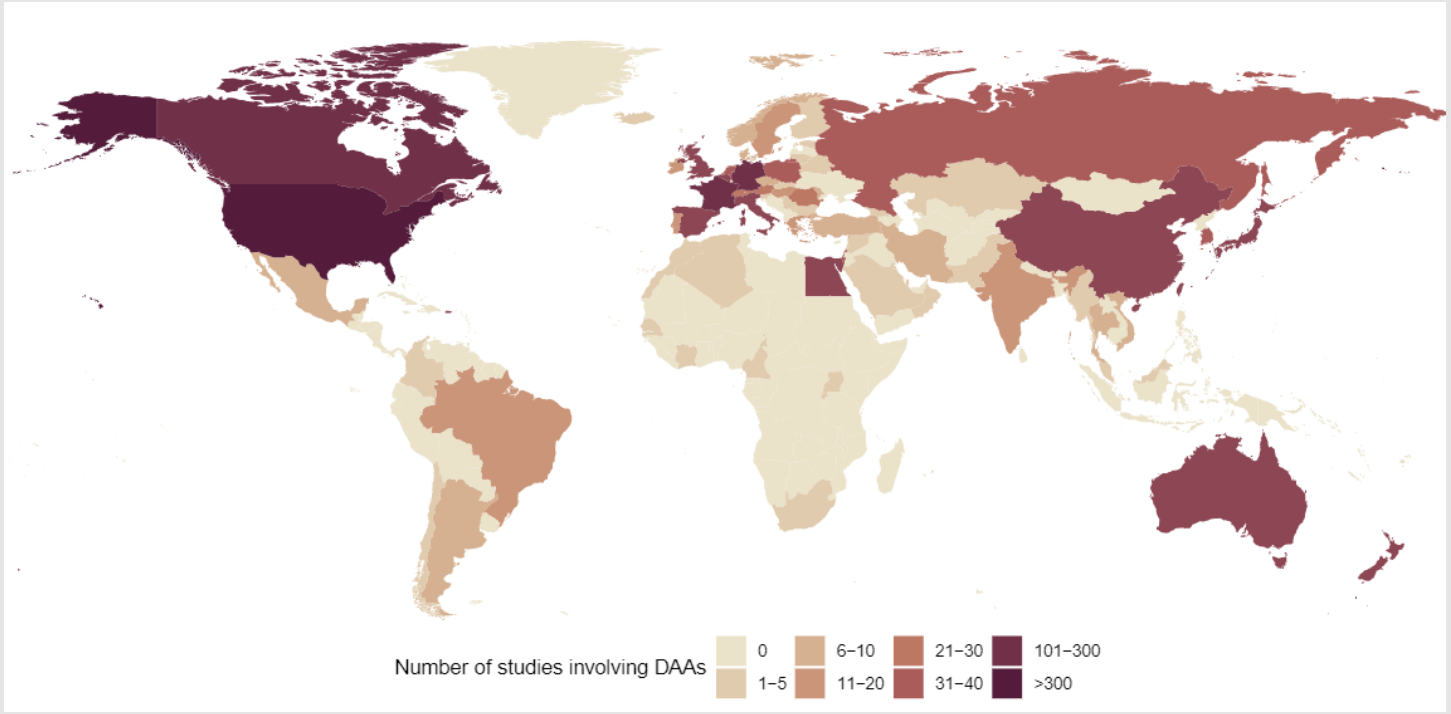
on behalf of the HCV SSA network

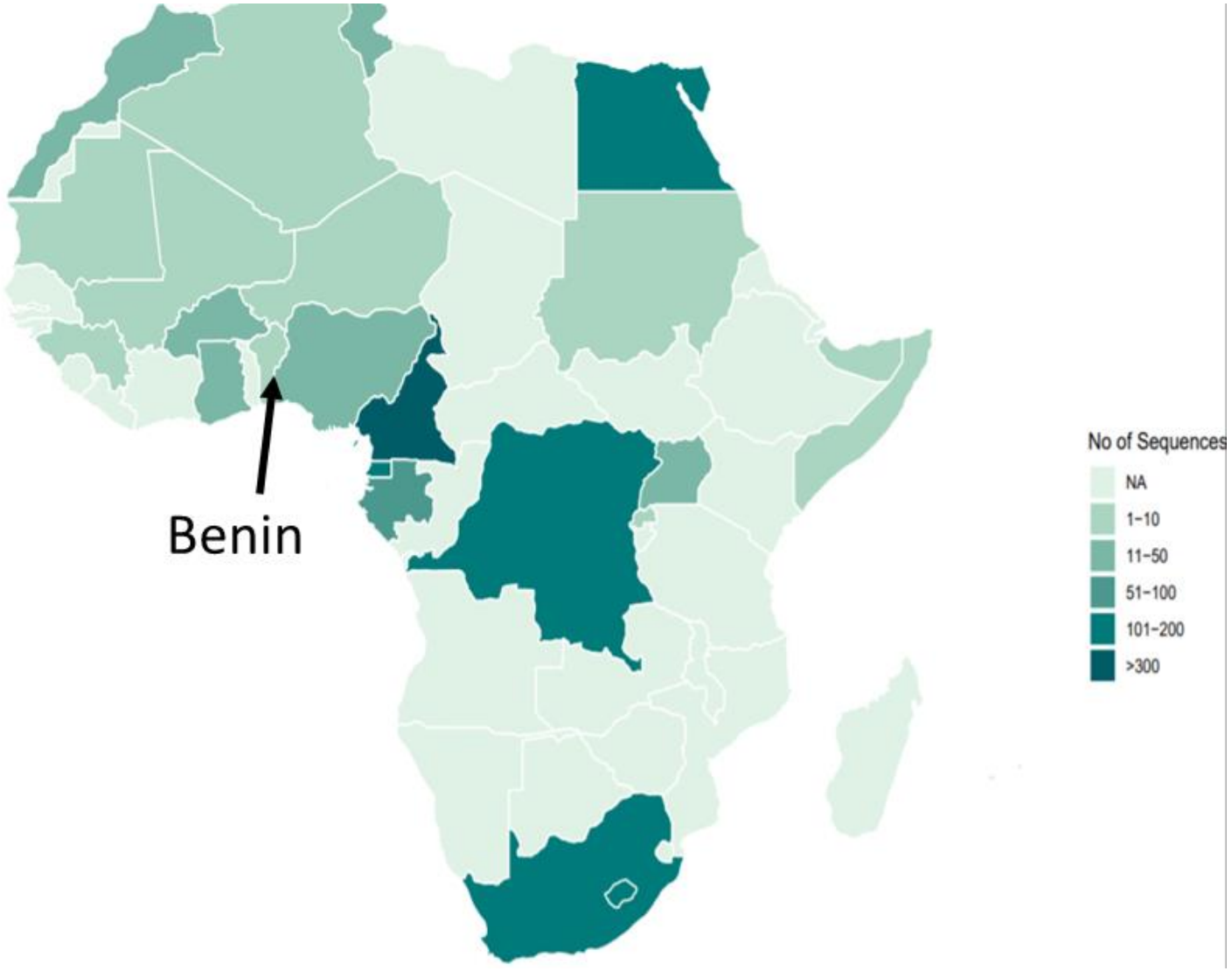
INHSU 2021

Background



- 71 million HCV infected, 10 million in SSA (Mohd et al. 2013)
- Global seroprevalence: 3.8% in Benin (Polaris study, 2015)
- Yearly deaths: 400,000 (WHO 2016)
- 8 different genotypes and 90 subtypes (ICTV)
- Very few clinical studies of DAA efficacy in SSA

Shah R, Ahovegbe L, Niebel M, Shepherd J, Thomson EC, Non-epidemic HCV genotypes in low- and middle-income countries and the risk of resistance to current direct-acting antiviral regimens, *Journal of Hepatology* (2021)



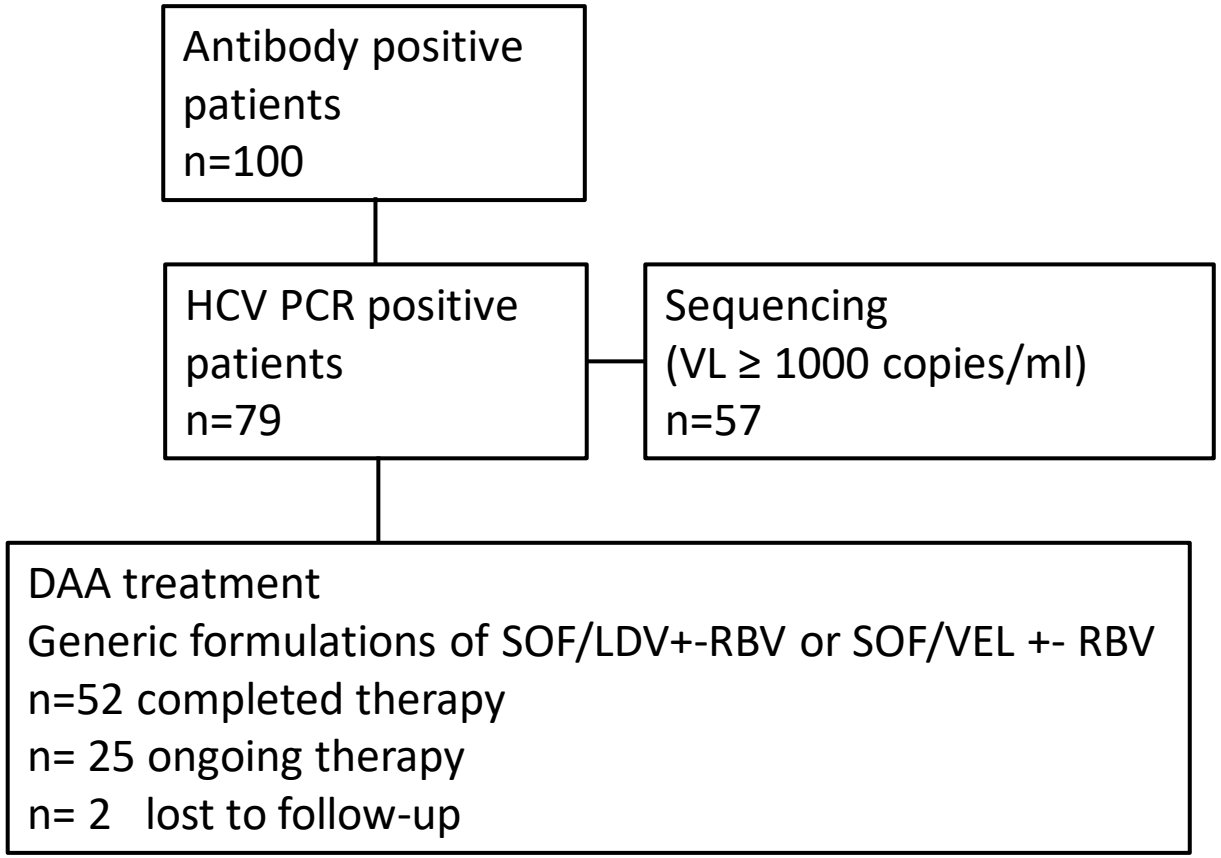
The genetic diversity of HCV in sub-Saharan Africa is very poorly characterized.

Shah R, Ahovegbe L, Niebel M, Shepherd J, Thomson EC, Non-epidemic HCV genotypes in low- and middle-income countries and the risk of resistance to current direct-acting antiviral regimens, *Journal of Hepatology* (2021)

Aims and study design

1. To characterise circulating HCV genotypes in Benin

2. To measure sustained virological response (SVR) to DAA treatment in Benin



Bioinformatic Analysis

De novo assembly

Assembly
- Clean/trimming raw fastq files
- Assembled using idba, spades, dipspades

Get Contigs
- Combined contigs from SPADES, IDBA, DIPSPADES assemblers using GARM

Confirm sequence identity
- BLASTn and phylogeny using maximum likelihood analysis

Reference based assembly

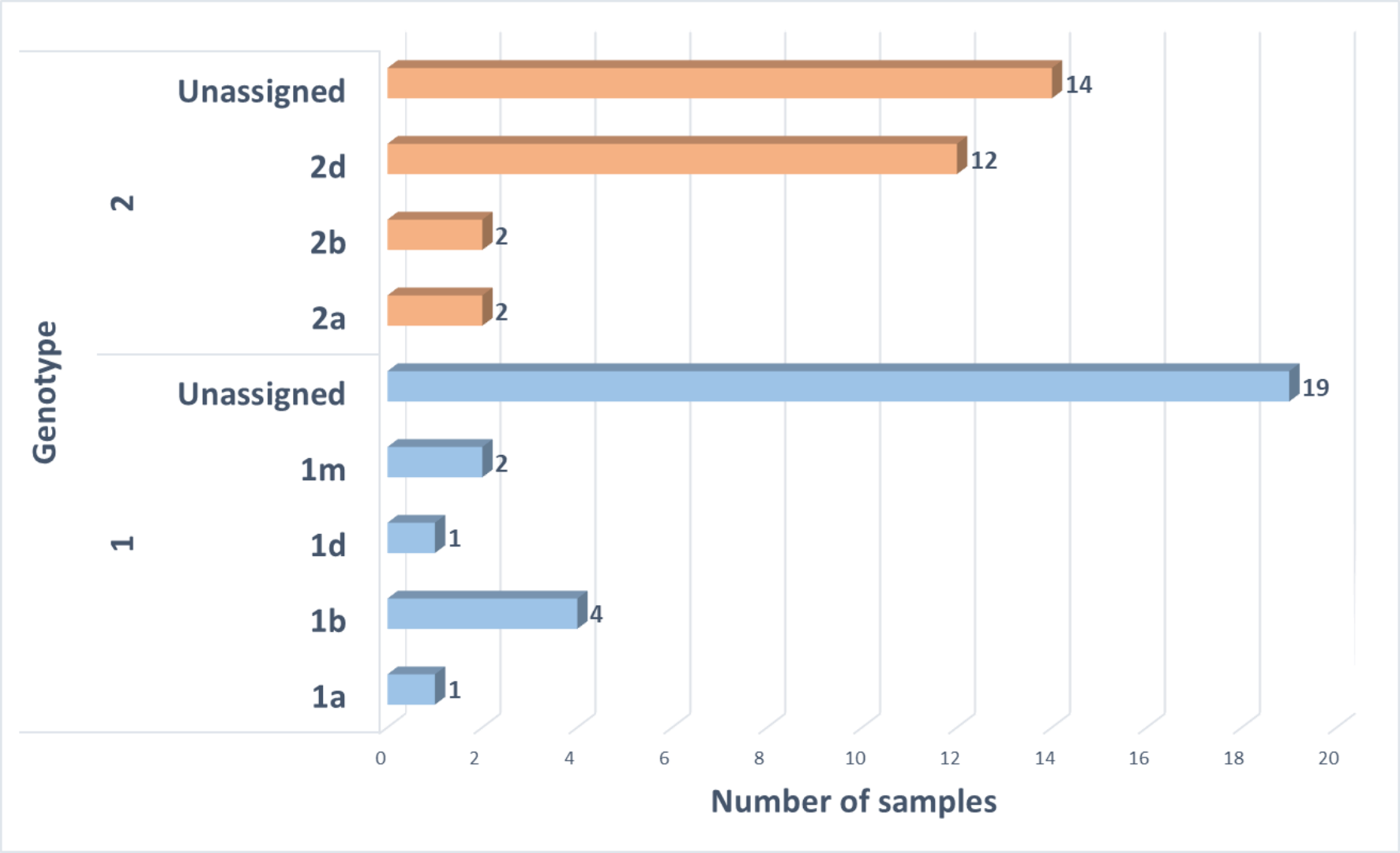
FIND BEST GENOME
- GENOTYPING using CREATE-KMERS
- Map reads using Tanoti
- Select best genome

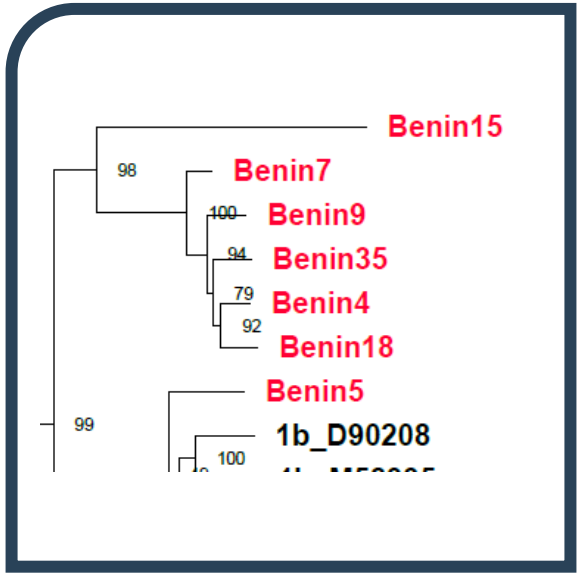
CREATE CONSENSUS SEQUENCES
- Select best reference or *de novo*
- Check mapping quality-SAM_STATS

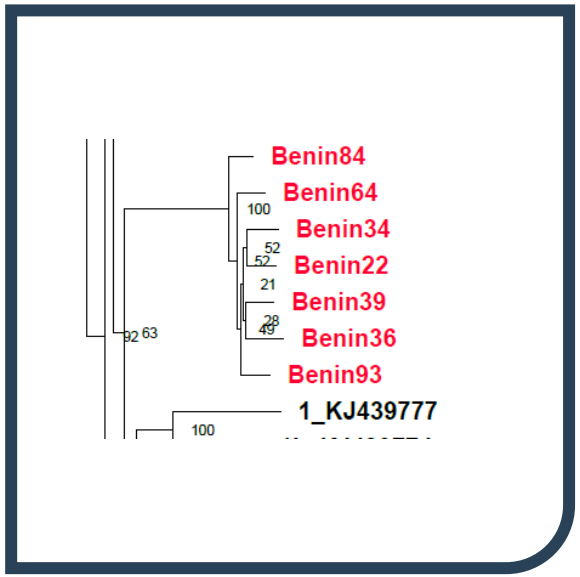
PHYLOGENETIC ANALYSIS
- Align consensus to references-MAFFT
- Construct phylogenetic tree, RaxML

Sreenu Vattipally https://github.com/vbsreenu/Tanoti/blob/master/src/README.md

Previously unassigned g1 and g2 subtypes occurred most frequently in the Benin cohort







Genotype 1

New subgenotype requires
-genetic distance >15% over the complete coding region
-minimum 3 in cluster (ICTV)

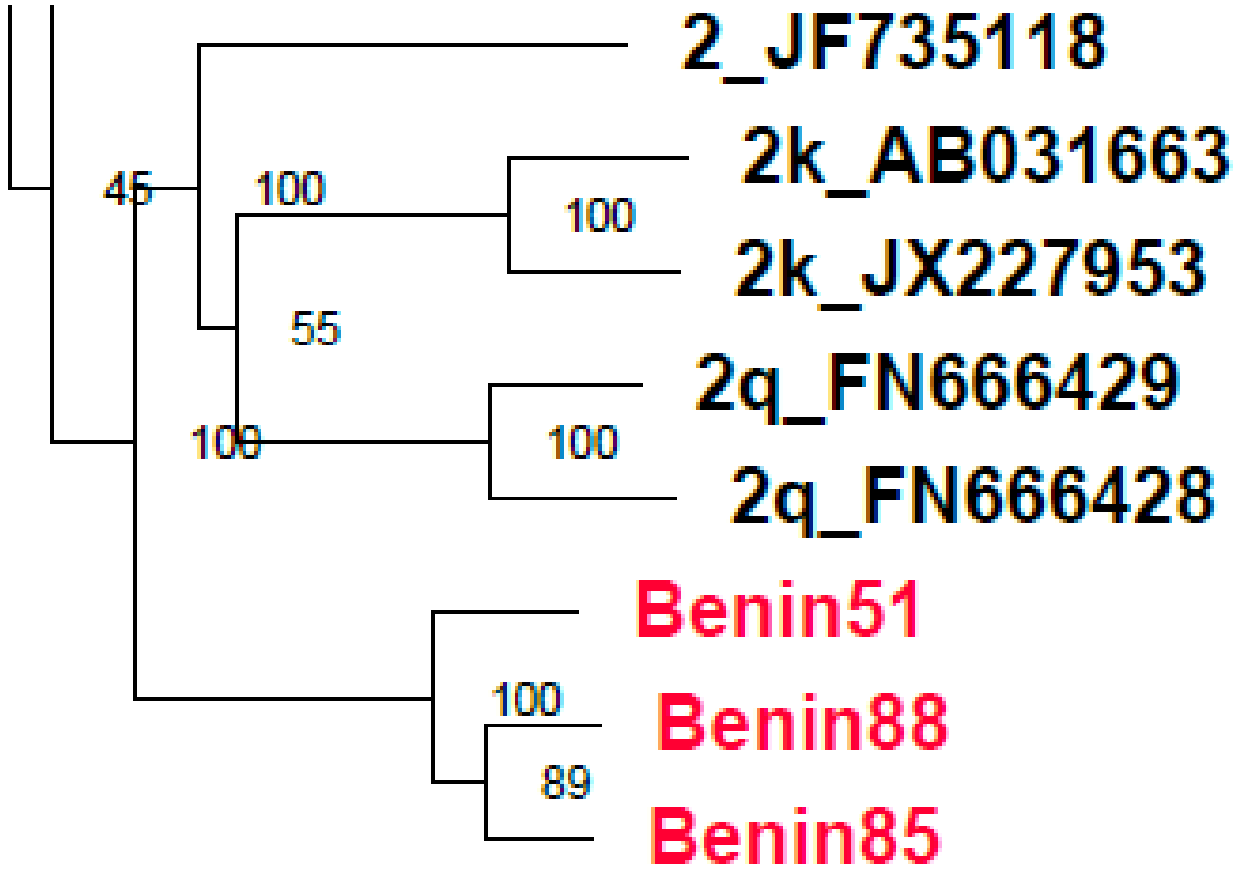
Two new subtypes of HCV genotype 1 identified

Multiple unassigned genotype 1 sequences (*)

Genotype 2

One new subtypes of HCV genotype 2 identified

Multiple unassigned genotype 2 sequences (*)



Sustained virological response at 12 weeks (SVR12)

Characteristic	SVR12 n (%)
Genotype/Subtype (n=36)	
1a	1/1 (100%)
1b	4/4 (100%)
1d	1/1 (100%)
1m	1/1 (100%)
1* (new subtypes)	12/12 (100%)
2b	**1/2 (50%)**
2d	**10/12 (83%)**
2* (new subtype)	3/3 (100%)
Treatment (n=52)	
Sofosbuvir + Ledipasvir (used for genotype 1 only)	12/12 (100%)
Sofosbuvir + Ledipasvir + Ribavirin (used for genotype 1 only)	1/1 (100%)
Sofosbuvir + Velpatasvir (used for genotypes 1 + 2)	**33/35 (94%)**
Sofosbuvir + Velpatasvir + Ribavirin (used for genotypes 1 + 2)	**3/4 (75%)**
Liver Status (n=52)	
Non-cirrhotic	22/22 (100)
Cirrhotic	**9/11 (82%)**
Unknown	**18/19 (95%)**

Baseline resistance associated polymorphisms in genotype 2

NS5A			
Positions	**RAS**	**Failure (%), N=3**	**SVR12(%), N=15**
24	K/Q24K	0	7,1
	S/T24S	**67,2**	**80,12**
28	**F/L28F,**	**67,2**	**87,14**
	L28L	33,1	0
	L/M28M	0	7,1
30	Q/R30Q	0	7,1
31	**L/M31M**	**67,2**	**53,8**
37	F/L/V37I	0	7,1

Treatment failure occurred in patients with genotype 2b (1/2) and 2d (10/12)

Key polymorphisms associated with treatment failure were at positions 24 (24S), 28 (28F) and 31 (31M).

GLUE: A flexible software system for virus sequence data. Joshua B Singer, Emma C Thomson, John McLauchlan, Joseph Hughes and Robert J Gifford, *BMC Bioinformatics* 2018 19:532

Conclusions

HCV genetic diversity and response to treatment in West Africa is very poorly characterized

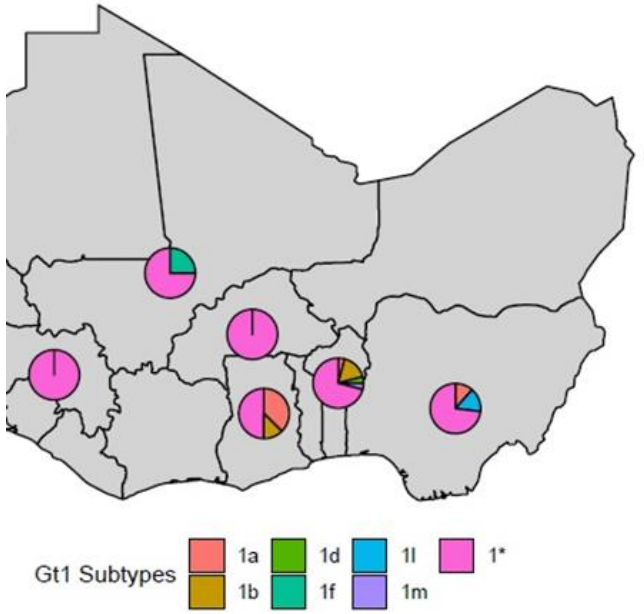
Previously uncharacterised genotype 1 and 2 subgenotypes were the most prevalent subtypes in Benin

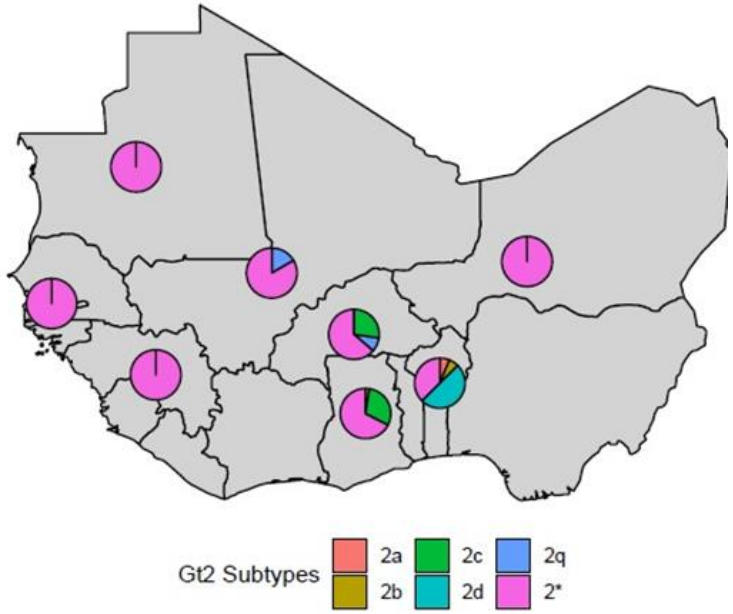
Genotype 2d was the most prevalent previously identified genotype

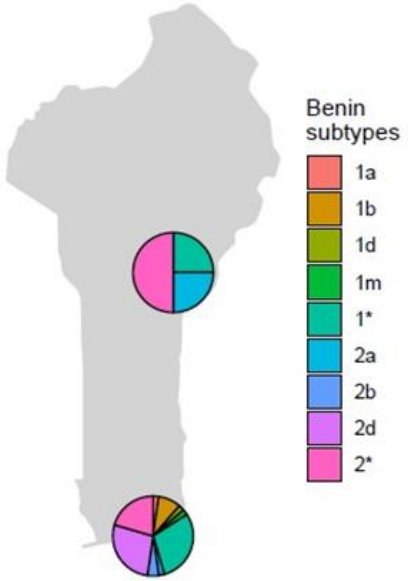
Two new subtypes-genotype1(1q, 1r) and new subtype-genotype 2 (2v) were identified

DAA efficacy was excellent and 94% had an SVR to treatment

Genotypes 2b and 2d may be associated with a slightly lower SVR in association with mutations at positions 24,28 and 31 of NS5A







Acknowledgements

HCV-SSA network

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