

Frequency of occurrence of HIV-1 superinfection in MSM

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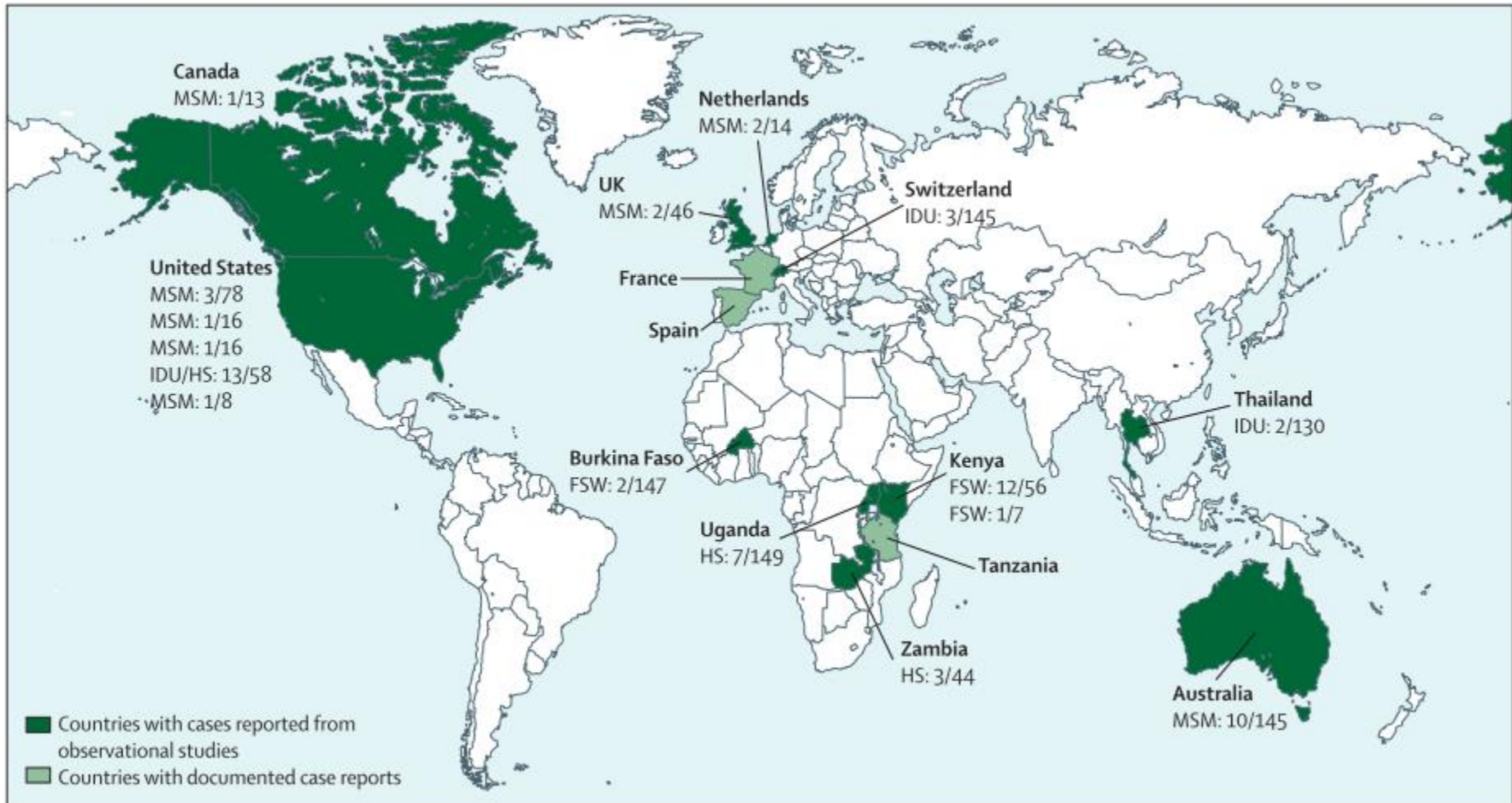


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Introduction

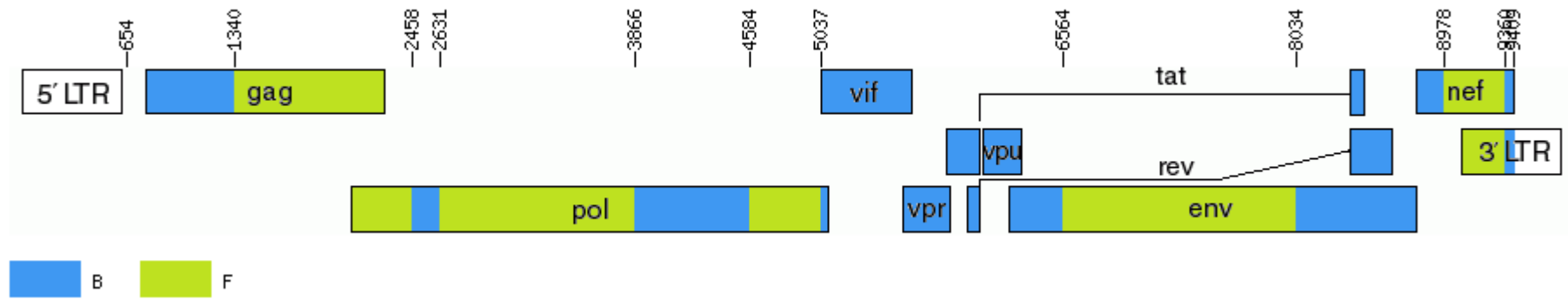
- HIV-1 superinfection
 - Re-infection after initial infection
- Challenges
 - Methodology
 - Temporary observation
 - Intrasubtype >< Intersubtype

- Incidence rate of HIV-1 superinfection: 0-7%
 - ~ Population studied & detection method

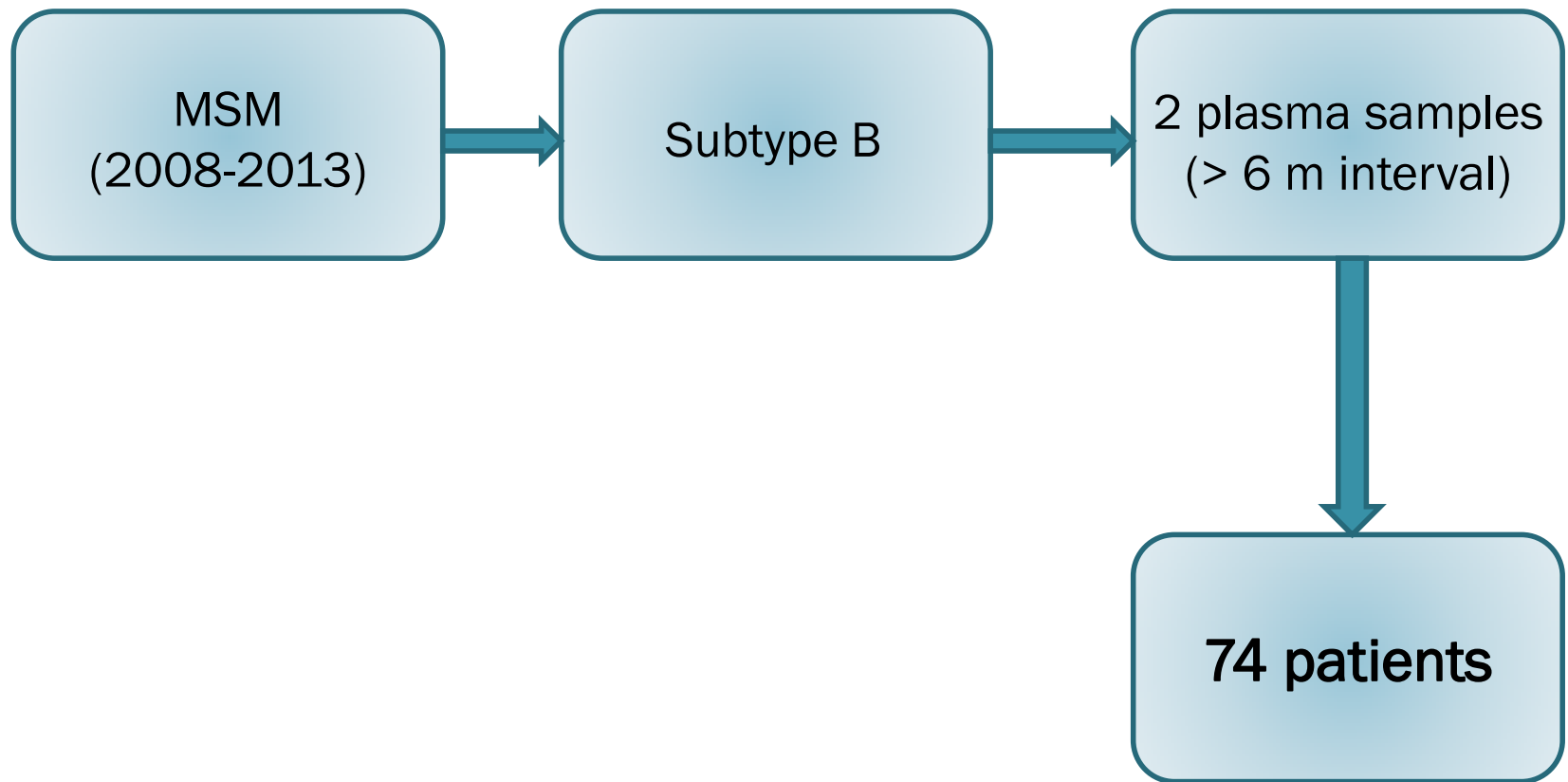


Study of HIV-1 superinfection

- Importance
 - Frequency of occurrence
 - In vivo model to study the host immune system
 - Viral immune escape
 - Recombination
 - CRF (88)



Patient selection



120 130 140 150 160
 TGGTATACAAACAGGAGCCATAATAGGAGATATAAGACAAGCACATTGTAAC
 TGGTATACAAACAGGAGCCATAATAGGAGATATAAGACAAGCACATTGTAAC
 TGGTATACAAACAGGAGCCATAATAGGAGATATAAGACAAGCACATTGTAAC
 TGGTATACAAACAGGAGAAGTGATAGGAAATCCAGAAAAGCACATTGTAAC
 TGGTATACAAACAGGAGAAGTGATAGGAAATCCAGAAAAGCACATTGTAAC
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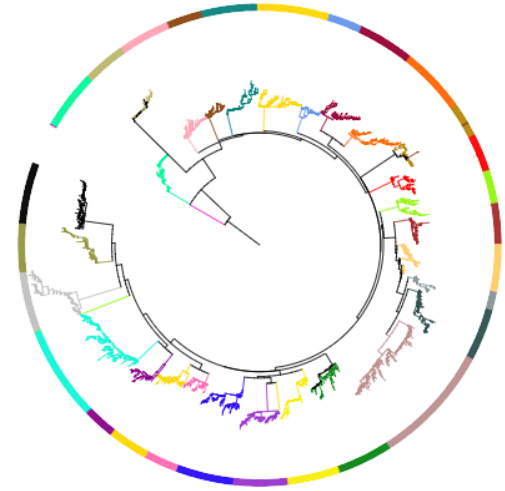
Methods

170 180 190 200 210
 ATTAGTGGAAACACAATGGAATAACCTTTAAAAACAGATAGTTAGGAAAT
 ATTAGTGGAAACACAATGGAATAACCTTTAAAAACAGATAGTTAGGAAAT
 ATTAGTGGAAACACAATGGAATAACCTTTAAAAACAGATAGTTAGGAAAT
 CTTTCAAGGACAACCTGGAGTAATCTTTAAAGCAGGTAGCTATGAAGT
 CTTTCAAGGACAACCTGGAGTAATCTTTAAAGCAGGTAGCTATGAAGT
 CTTTCAAGGACAACCTGGAGTAATCTTTAAAGCAGGTAGCTATGAAGT
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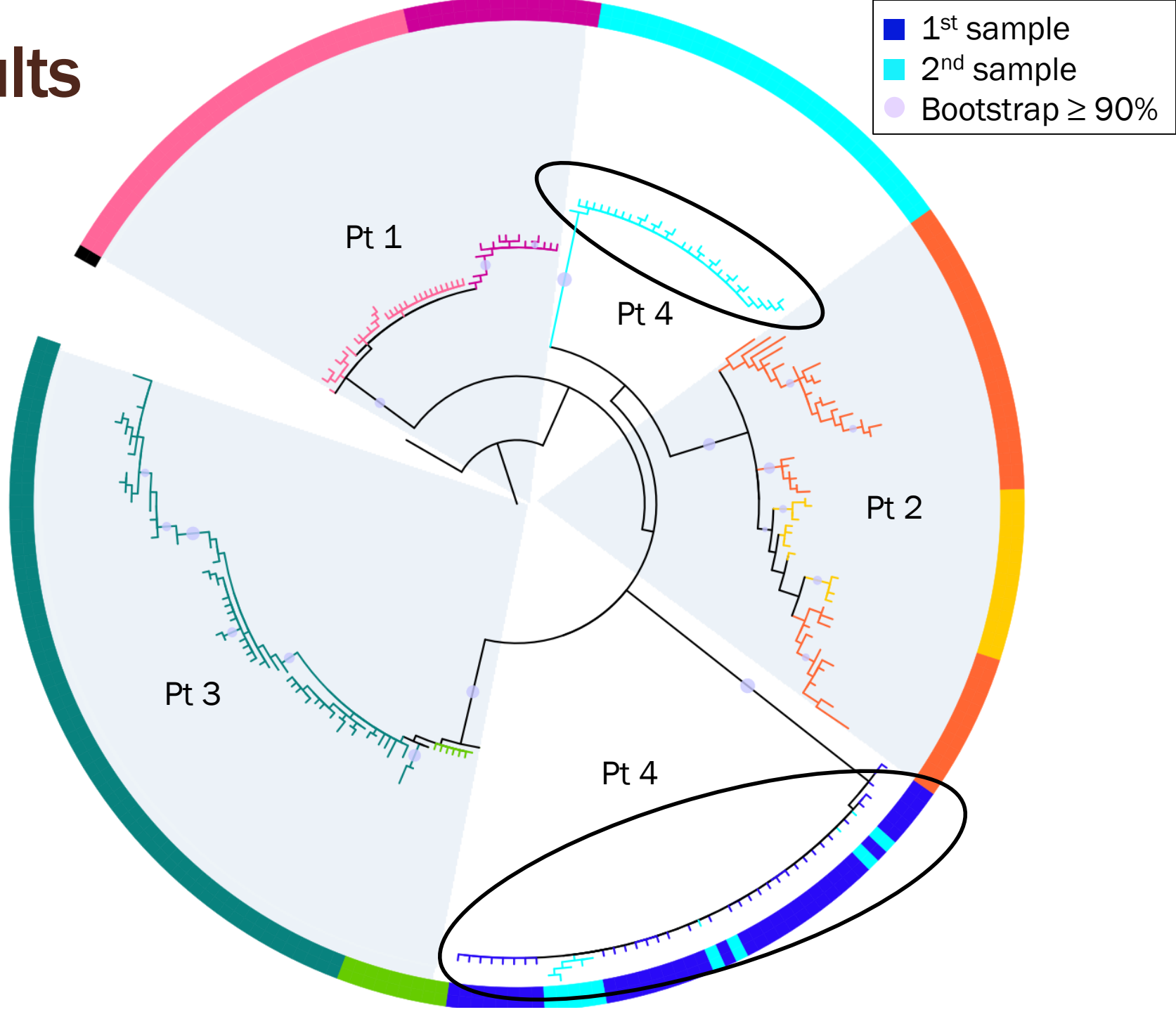
- Roche 454 deep sequencing
 - *env* V3 region (228 nucleotides/76 amino acids)
 - 2 samples from each patient
 - 34 samples pooled per run
- Manual data cleaning, editing and aligning
 - BioEdit + in-house software
- Maximum Likelihood phylogenetic trees construction (PhyML)

Identification of Superinfection

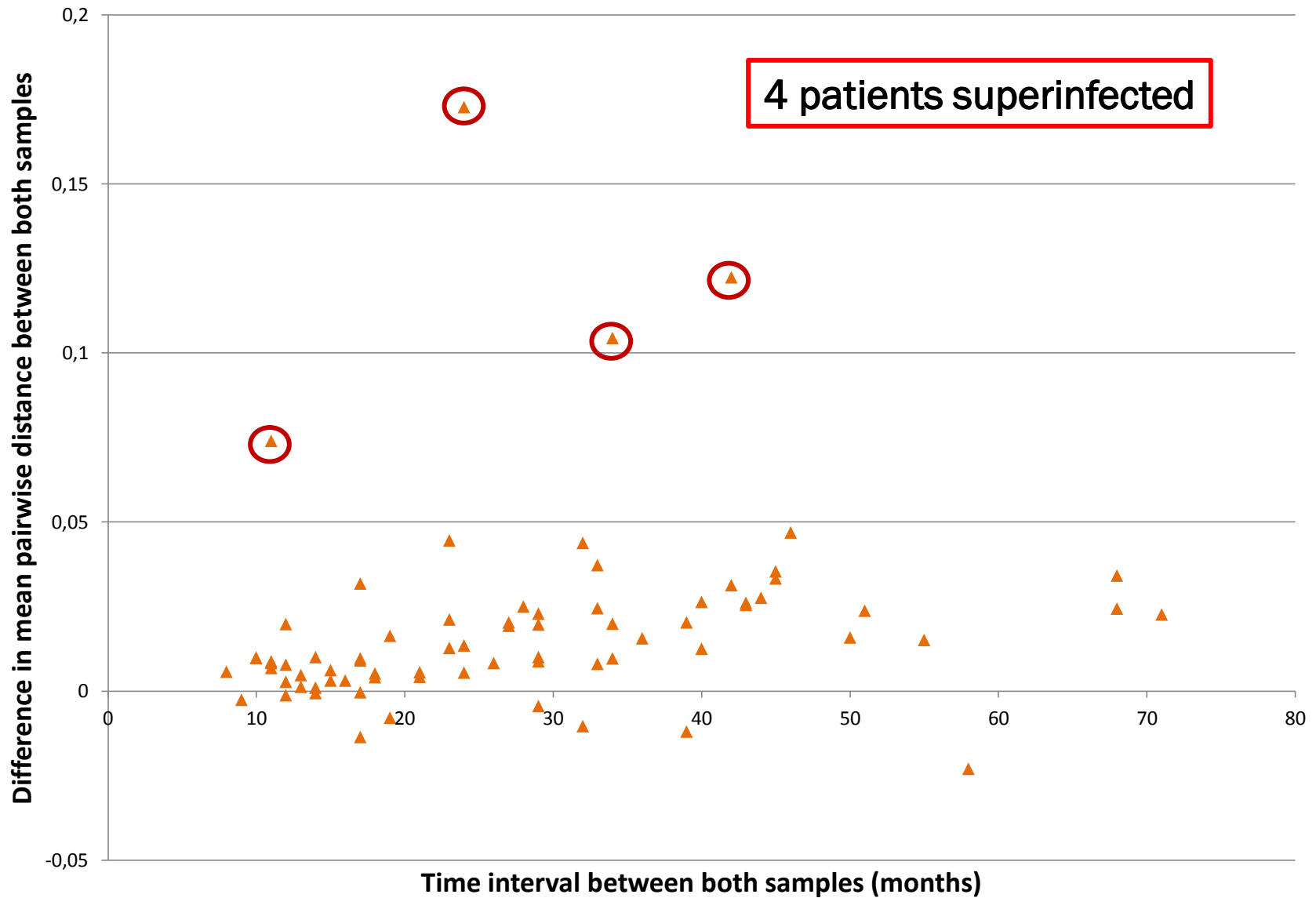
- Tree visualisation in iTol
- Superinfected patient
 - At least 1 of the 2 samples
 - 2 or more monophyletic clusters
 - Bootstrap value $\geq 90\%$
 - Separated by sequences of ≥ 1 patient



Results



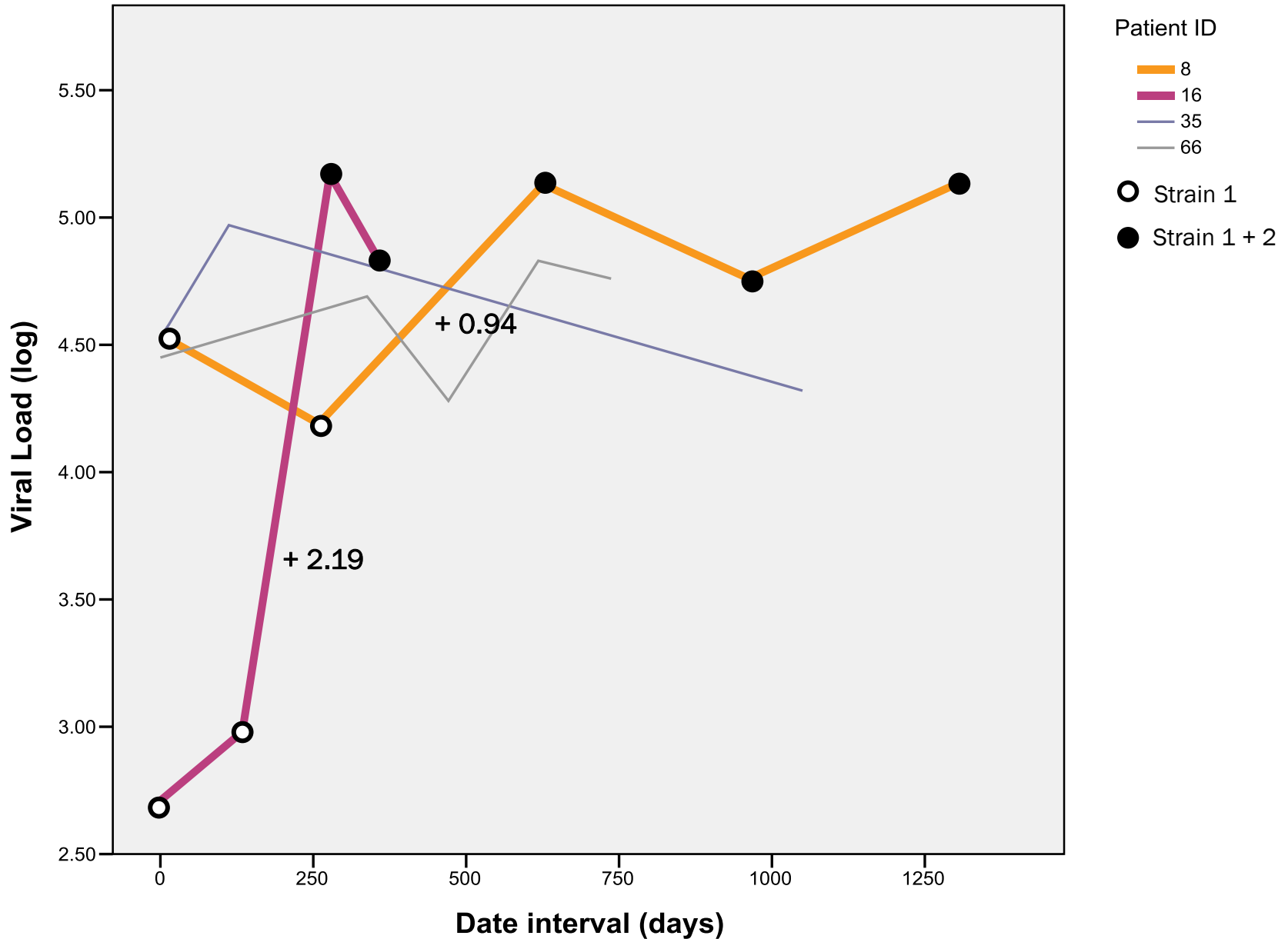
Difference in mean pairwise genetic distance between both samples



Confirmation of superinfection with longitudinal samples

Patient ID	Sample dates	Date interval (days)	Virus population	% strain 2
08	6/06/2008	0	strain 1	0
	20/02/2009	259	strain 1	0
	22/02/2010	626	strain 1 + 2	42%
	24/01/2011	962	strain 1 + 2	11%
	19/12/2011	1291	strain 1 + 2	79%
16	26/01/2009	0	strain 1	0%
	9/06/2009	134	strain 1 + 2	35%
	30/10/2009	277	strain 1 + 2	62%
	19/01/2010	358	strain 1 + 2	74%
35	24/02/2010	0	strain 1	0%
	10/03/2010	14	strain 1	0%
	16/06/2010	112	strain 1 + 2	4%
	9/01/2013	1050	strain 1 + 2	23%
66	19/03/2012	0	strain 1	0%
	20/02/2013	338	strain 1 + 2	23%
	3/07/2013	471	strain 1 + 2	6%
	27/11/2013	618	strain 1 + 2	19%
	26/03/2014	737	strain 1 + 2	39%

Viral load evolution in superinfected patients



Conclusions

- Frequency of occurrence of HIV-1 superinfection (intrasubtype)
 - 4/74 patients = 5.4%
 - Likely an underestimation
- Clinical consequences
 - Viral load increase
- Baseline drug resistance analysis
 - Sanger sequencing
 - Missing one of the variants
 - Deep sequencing (in high risk populations)

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