



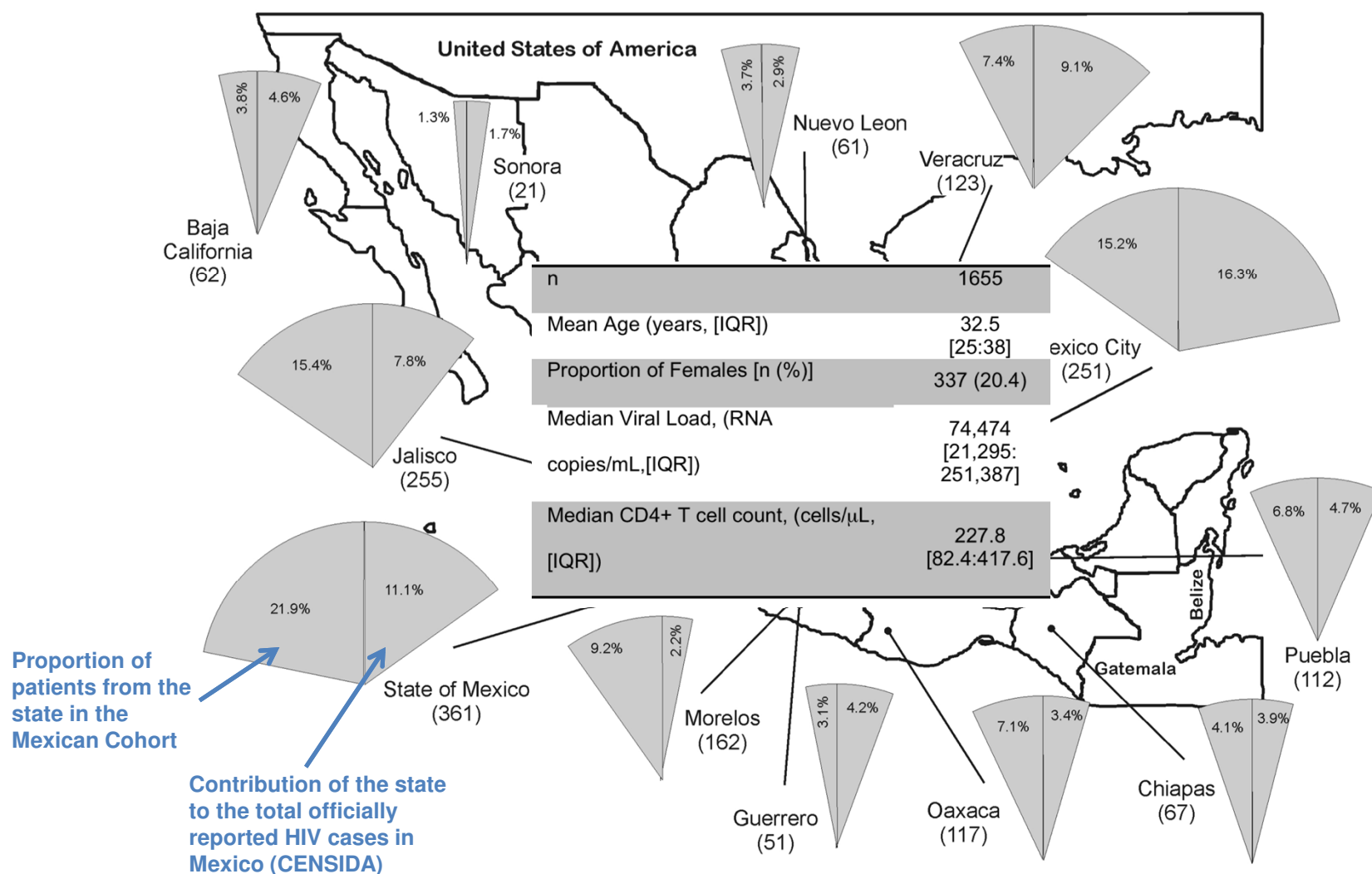
**WHO Meeting on HIV drug resistance
surveillance in Latin America and the Caribbean**

TDR surveillance in Mexico

Brasilia, March 2013

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The Mexican HIV TDR study: 1655 ART-naïve patients from 12 Mexican states enrolled from 2005 to 2010.



Avila-Ríos, et al., 2011 PLoS One

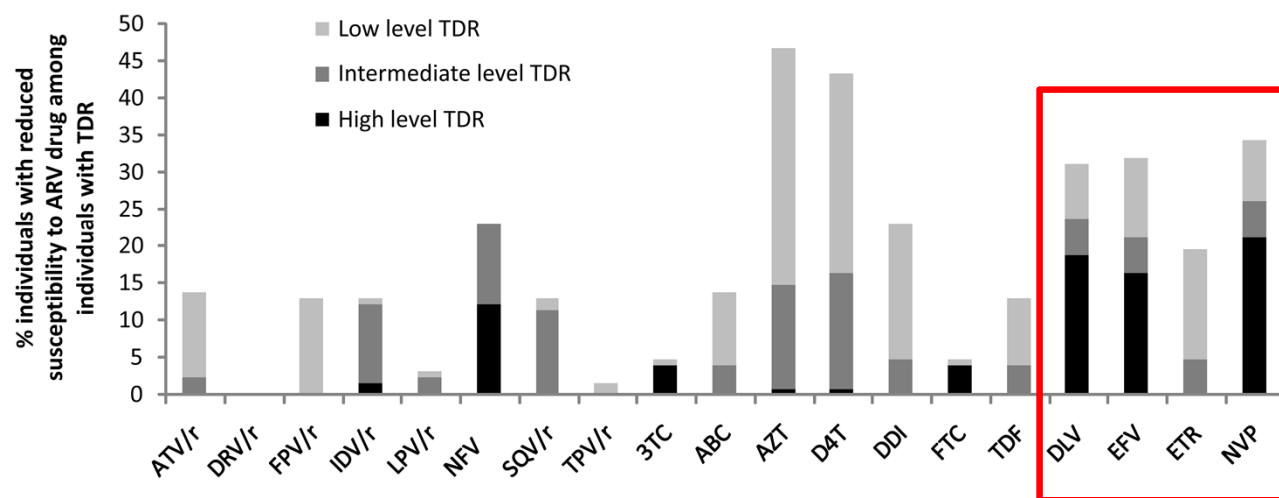
A global TDR level of 7.4% for any ARV drug was observed at the national level

Drug Class	TDR Level [n (% , 95% confidence interval)] ^a				
	SS $\geq$ 10	SS $\geq$ 15	SS $\geq$ 30	SS $\geq$ 60	WHO
Any ARV Drug	228 (13.8, 12.2:15.6)	122 (7.4, 6.2:8.8)	78 (4.7, 3.8:5.9)	41 (2.5, 1.8:3.4)	113 (6.8, 5.7:8.2)
NRTI	80 (4.8, 3.9:6.0)	69 (4.2, 3.3:5.3)	26 (1.6, 1.0:2.3)	6 (0.4, 0.1:0.8)	69 (4.2, 3.3:5.3)
PI	51 (3.1, 2.3:4.1)	28 (1.7, 1.1:2.5)	28 (1.7, 1.1:2.5)	14 (0.8, 0.5:1.5)	29 (1.8, 1.2:2.5)
NNRTI	118 (7.1, 6.0:8.5)	42 (2.5, 1.9:3.4)	32 (1.9, 1.3:2.8)	26 (1.6, 1.0:2.3)	31 (1.9, 1.3:2.7)

- TDR for NRTI was the highest (4.2%), followed by NNRTI (2.5%) and PI (1.7%).
 - NRTI: 70.4% of TDR cases explained by one or more TAMs. Type 1 mutation pathway more prevalent (70.6%).
 - NNRTI: K103NS explained 70% of high-level TDR cases. Low-level TDR cases explained by the combination of mainly K101QE, K103R, V179D.
 - PI: 64.3% TDR cases showed more than one mutation (range 2 to 6). All high-level PI TDR cases explained by L90M. Most of intermediate-level cases explained by M46IL.
- WHO TDR threshold at the moderate level (5-15%) for 2008 and 2009.

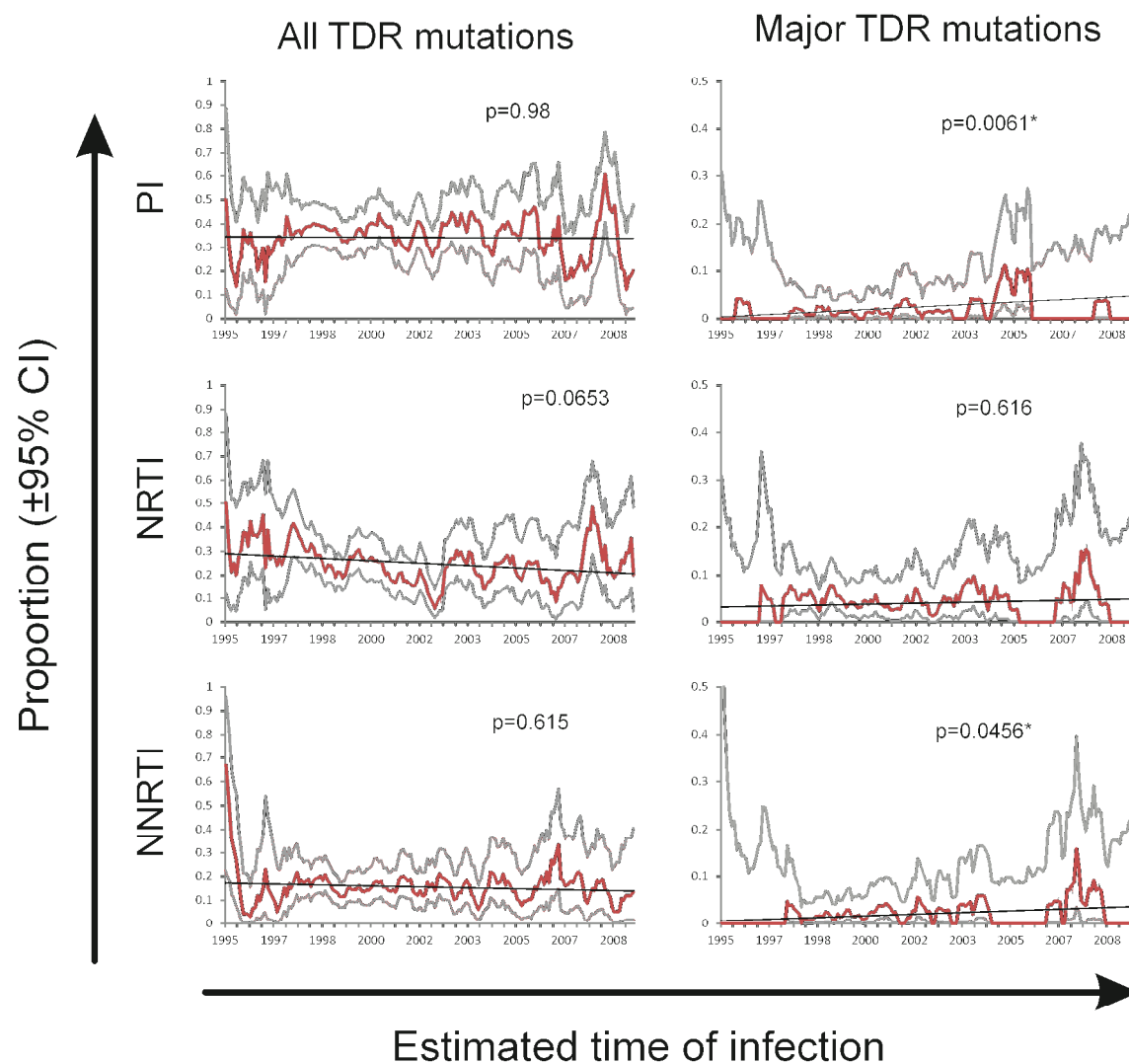
Avila-Ríos, et al., 2011 PLoS One

High level TDR was observed more frequently in NNRTIs



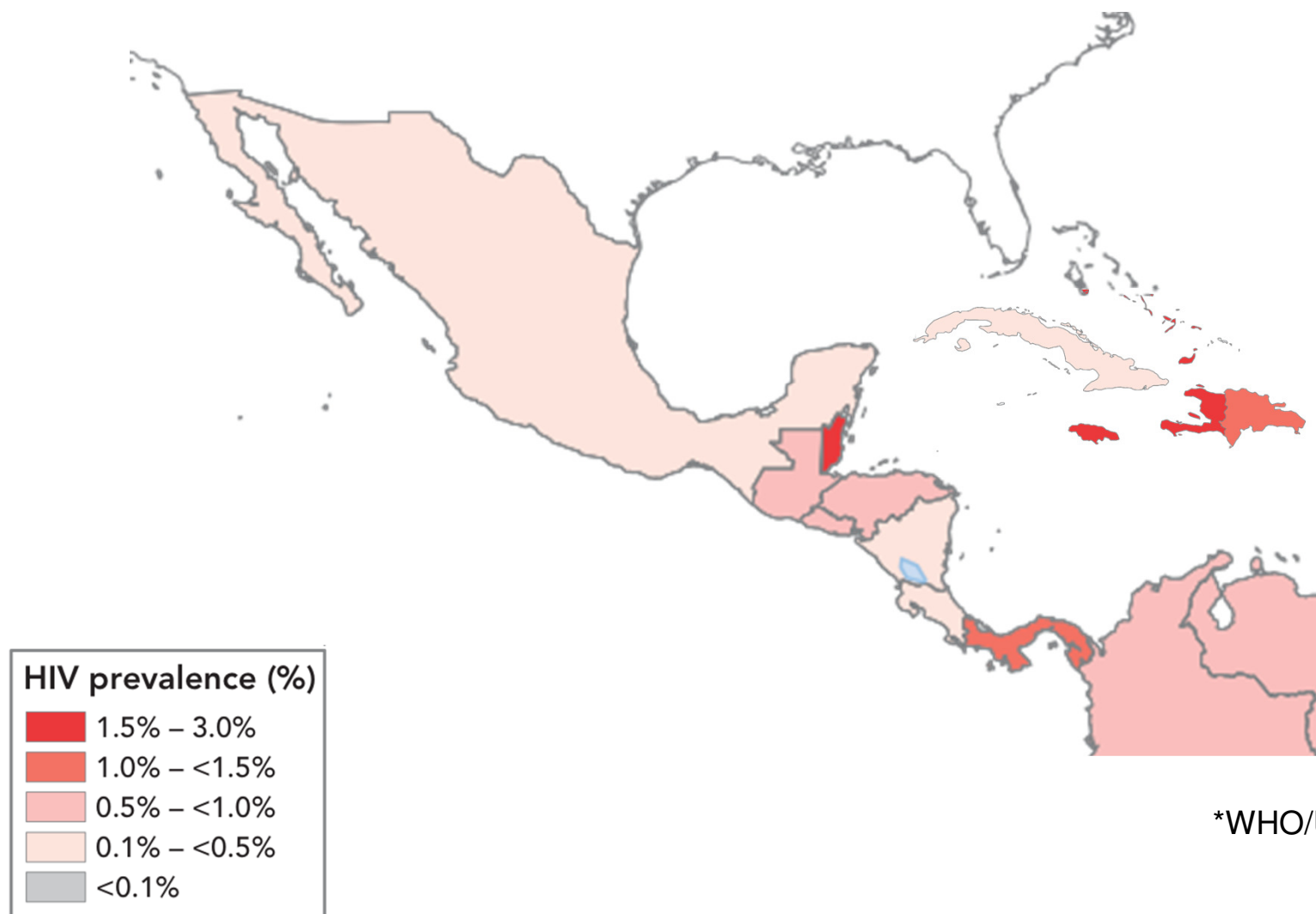
Avila-Ríos, et al., 2011 PLoS One

Significant increasing trends for NNRTI and PI TDR mutation frequencies in Mexico



Avila-Ríos, et al., 2011 PLoS One

Extending HIV TDR surveillance: The Mesoamerican Project



*WHO/UNAIDS, 2008.

A large cohort of HIV-infected, ART-naïve individuals is being formed in order to assess TDR prevalence and patterns in the Mesoamerican Region

Individuals included	Country	Number of individuals living with HIV*	HIV prevalence (%)*	Total number of individuals to be enrolled**
32 →	Belize	3,600	2.1	641
42 →	El Salvador	35,000	0.8	693
898 →	Guatemala	59,000	0.8	699
5 →	Honduras	28,000	0.7	690
121 →	Nicaragua	7,700	0.2	650
125 →	Panamá	20,000	1.0	684
840 →	Mexico	200,000	0.3	700
			Total	4,757

*WHO/UNAIDS.

**n by country with a 95% confidence level and a 2% confidence margin estimating a TDR prevalence of 8%

Clinical and demographic characteristics of the study cohorts

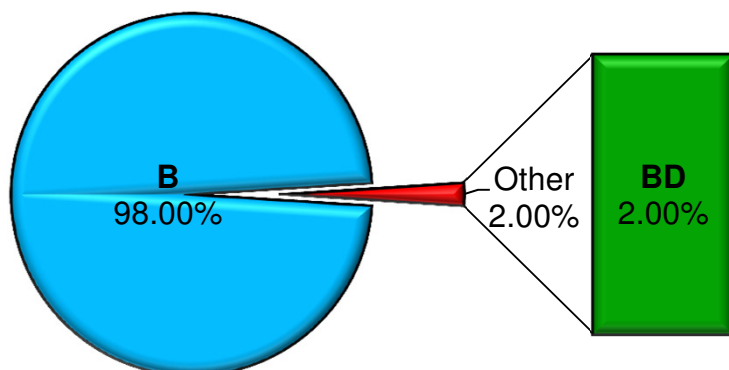


Demographic/Clinical Variable	Guatemala	Panama	Nicaragua	Mexico 2005-2010	Mexico 2011-2012
n	831	122	100	1720	721
Mean Age (years)	36.4	35.2	34.7	32.5	32.2
Men (%)	59.6	72.9	80.0	79.8	81.1
Median Viral Load, (RNA copies/ml)	61,624	25,659	61,366	74,400	67,369
Mean CD4+ T cell count, (cells/ml)	264	430	367	283	271
HIV transmission risk factor (%)					
Heterosexual	84.5	50.0	63.2	NA	33.9
MSM	11.0	40.7	32.2	NA	42.6
IDU	0.5	0.0	2.3	NA	2.7
Other/Unknown	2.5	8.3	1.2	NA	5.6

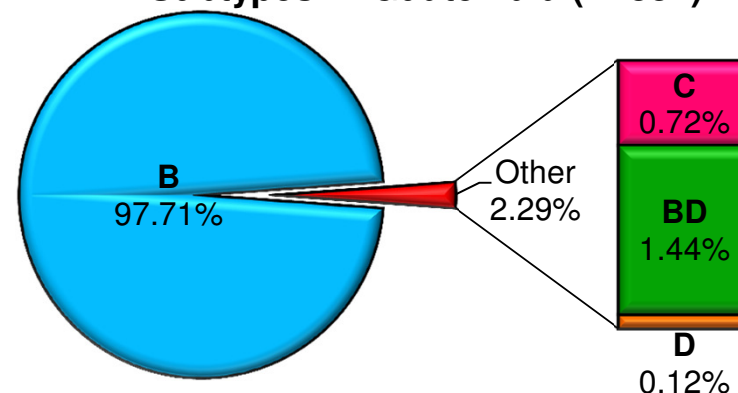
NA, Not Available

High prevalence of HIV subtype B in the region, but non-B subtypes also observed

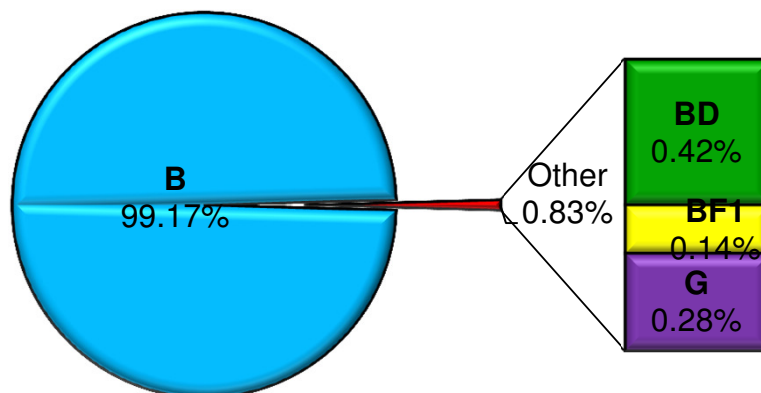
HIV Subtypes in Nicaragua (n=100)



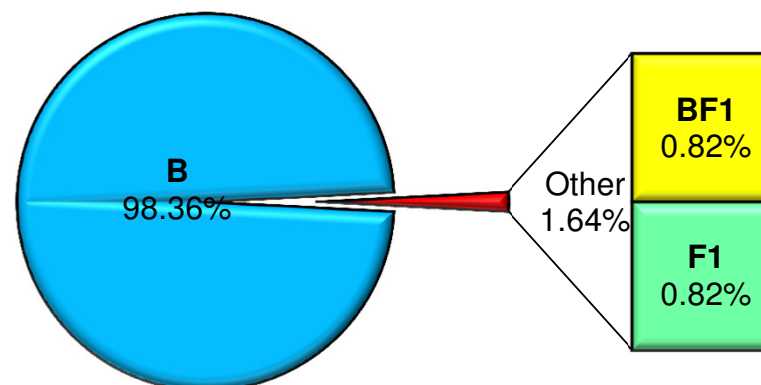
HIV Subtypes in Guatemala (n=831)



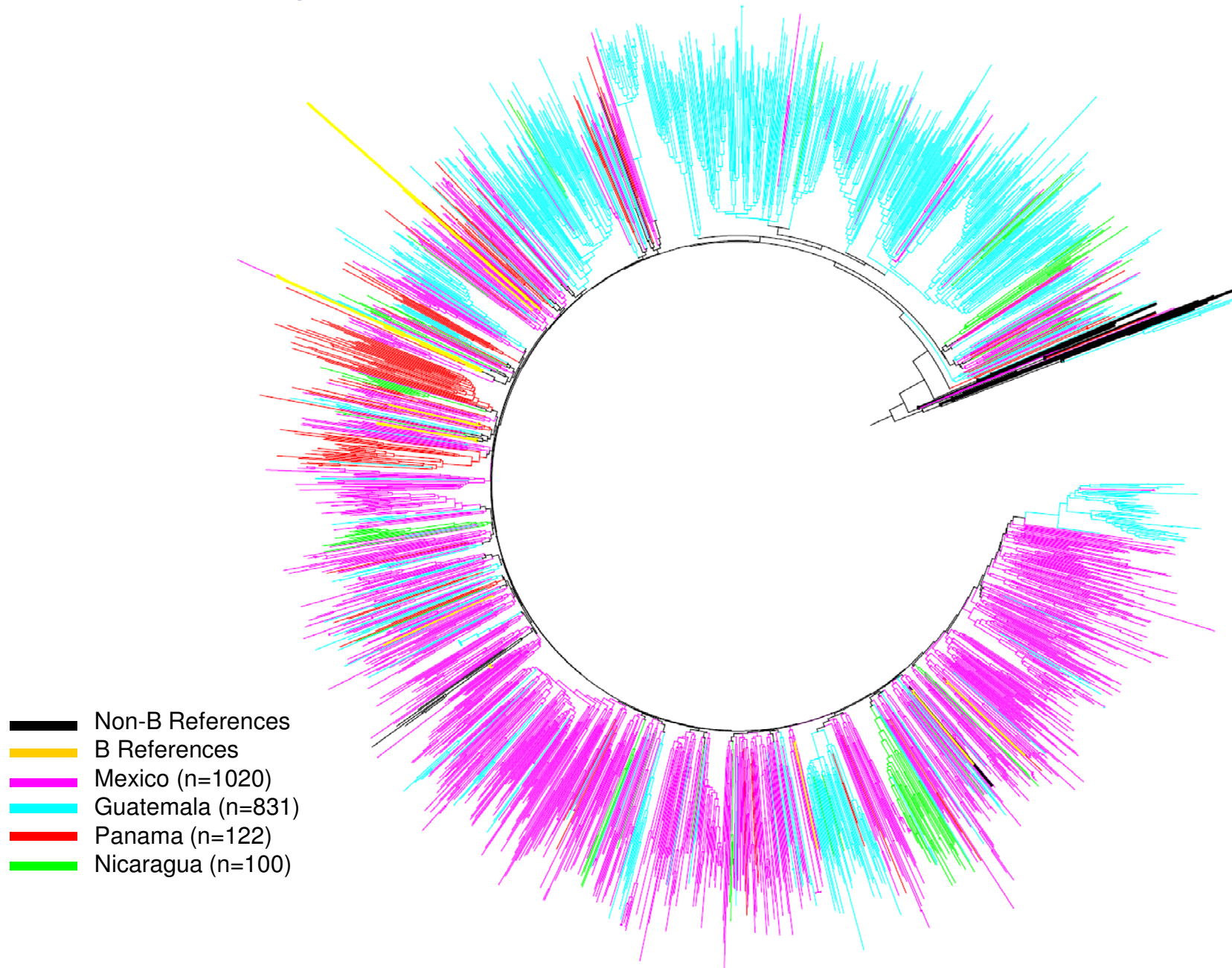
HIV Subtypes in Mexico 2011-2012 (n=721)



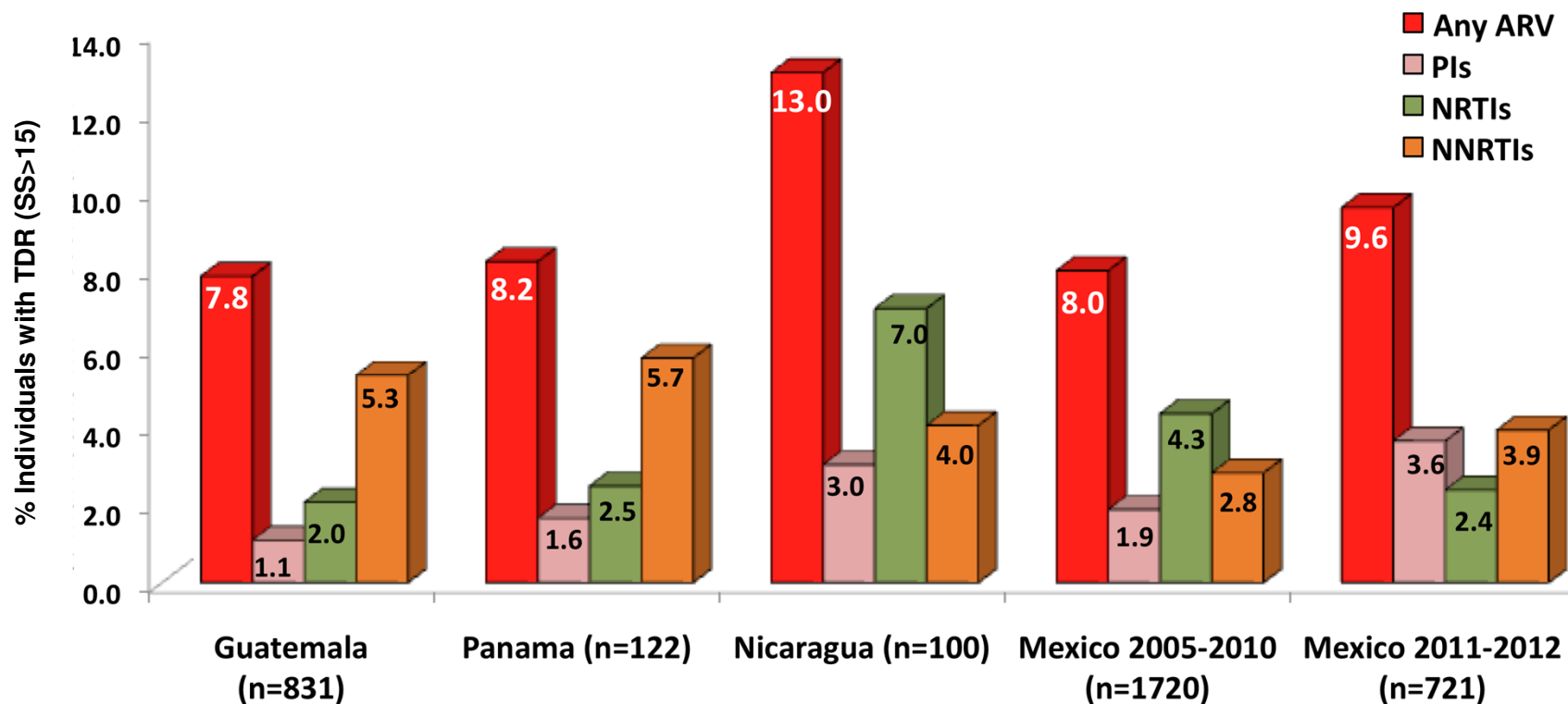
HIV Subtypes in Panama (n=122)



Remarkable geographic clustering of circulating HIV in Mexico, Guatemala, Nicaragua and Panama



Similar prevalence, but different TDR patterns in four countries of the Mesoamerican Region

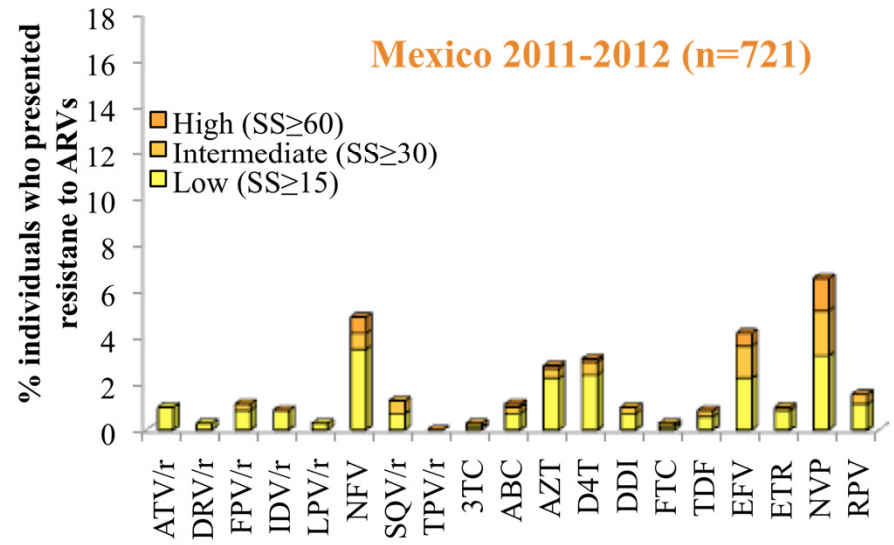
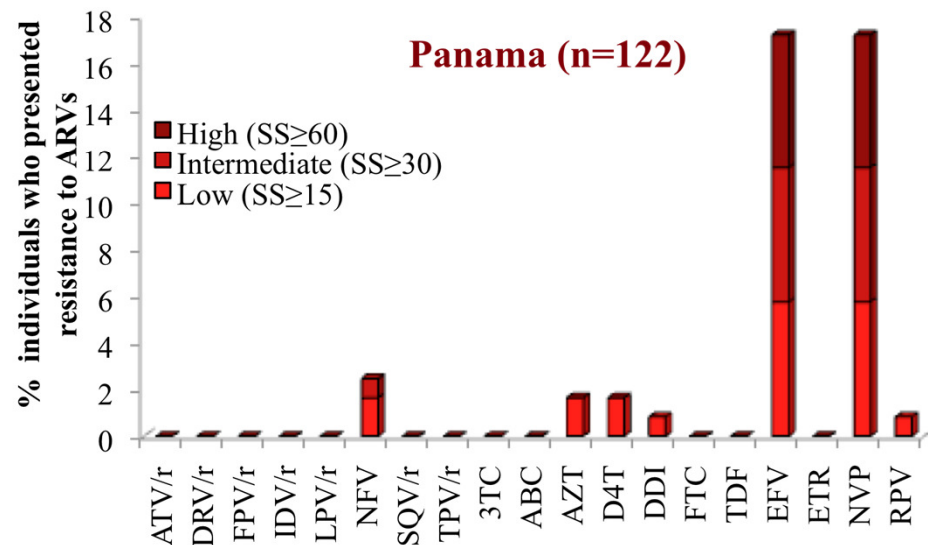
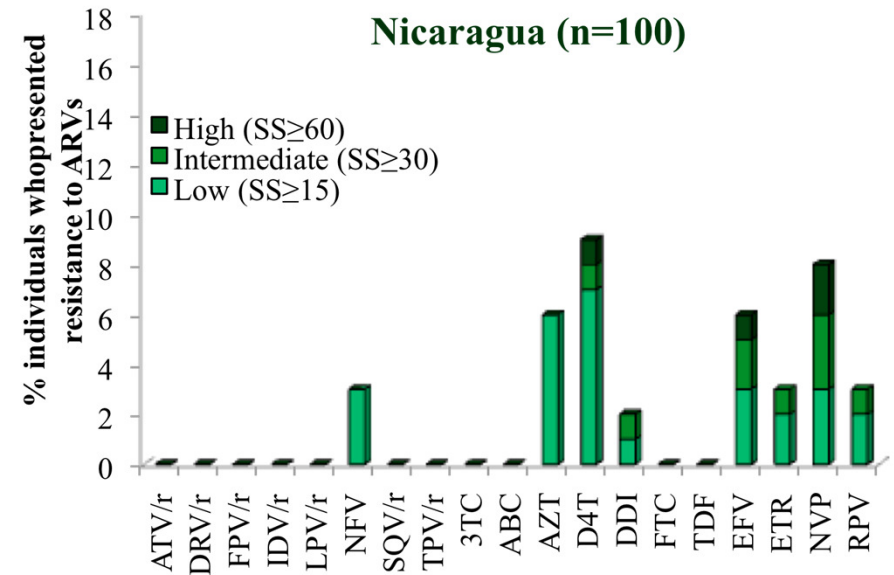
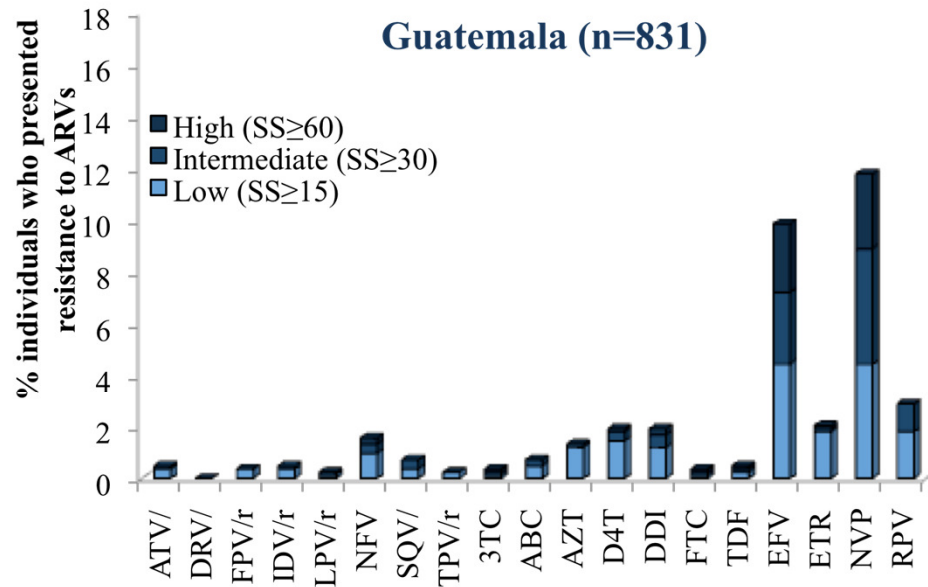


PI, Protease Inhibitors
NRTI, Nucleoside RT Inhibitors
NNRTI, Non-Nucleoside RT Inhibitors

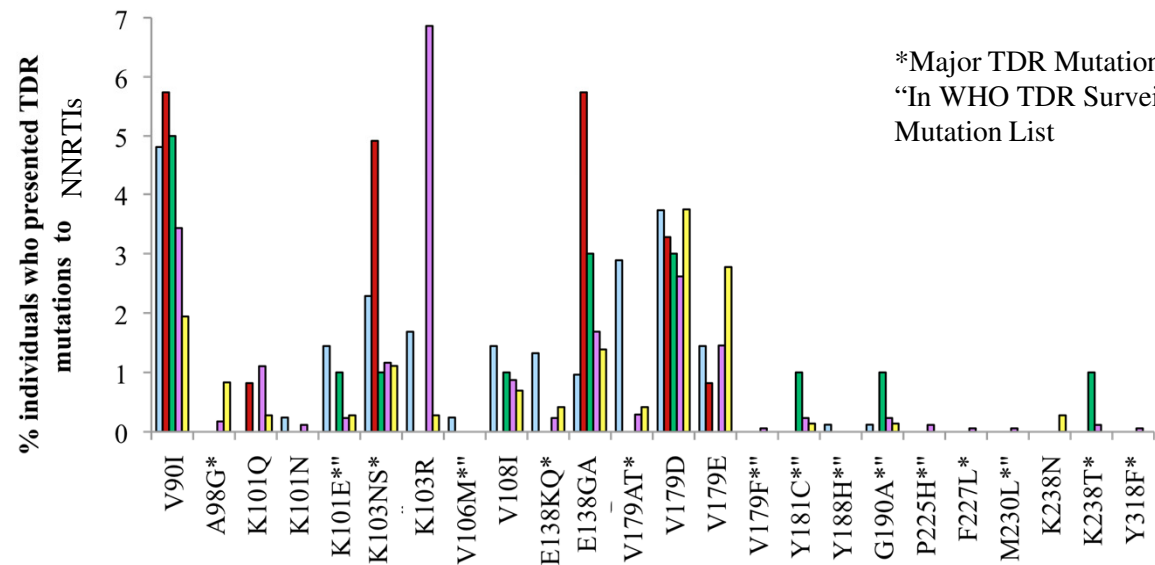
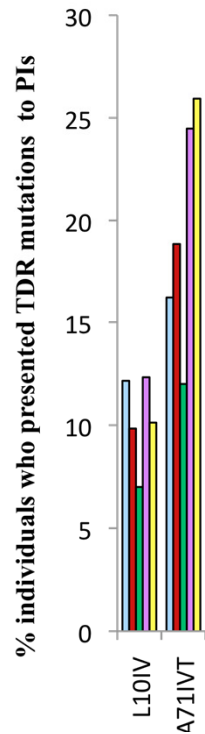
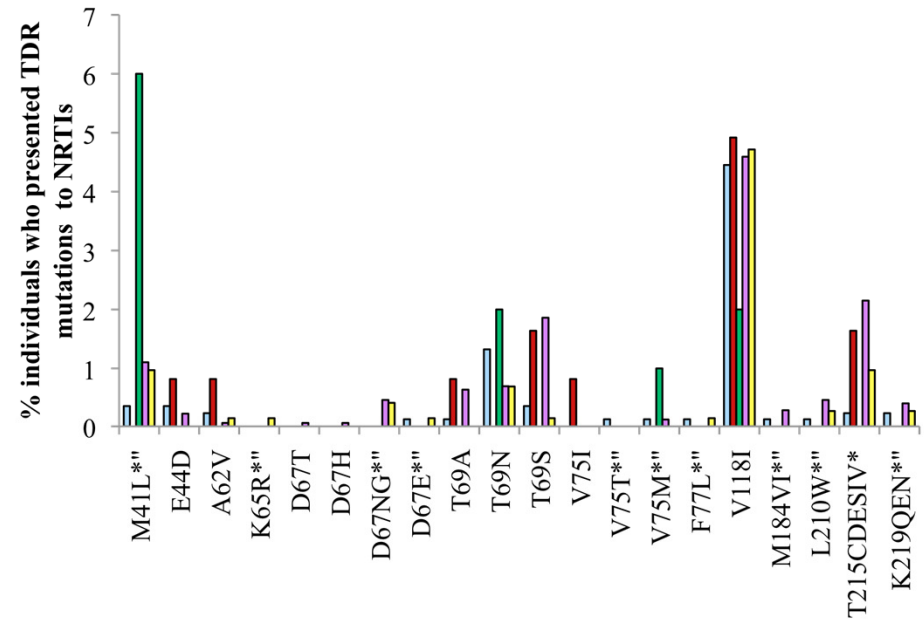
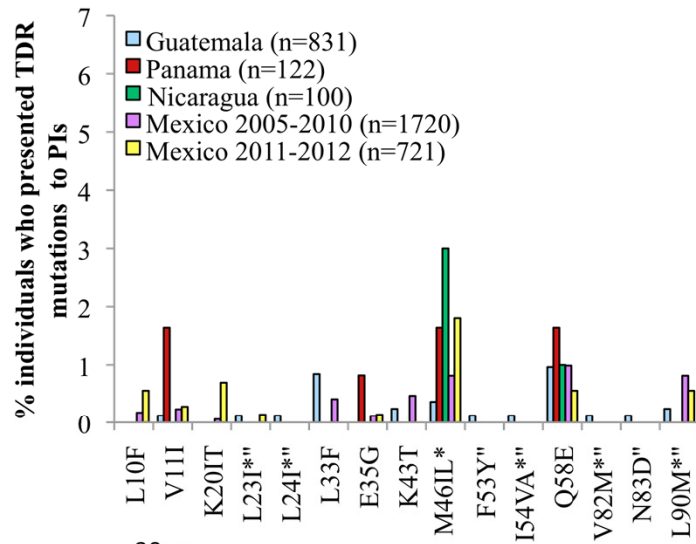
Using WHO TDR definitions...

	n	Any ARV	PIs	NRTIs	NNRTIs
Guatemala					
TDR (complete cohort)	831	7.8	1.1	2.0	5.3
TDR (≥ 500 CD4+ Tc/uL and ≤ 25 years)	31	3.2	0.0	0.0	3.2
Pre-Treatment Drug Resistance (≤ 350 CD4+ Tc/uL)	582	6.9	1.2	2.6	3.8
Mexico 2011-2012					
TDR (complete cohort)	721	9.6	3.6	2.4	3.9
TDR (≥ 500 CD4+ Tc/uL and ≤ 25 years)	58	19.0	12.1	5.2	1.7
Pre-Treatment Drug Resistance (≤ 350 CD4+ Tc/uL)	437	6.6	1.8	1.6	3.2

High resistance levels were more frequently observed for older NNRTIs both in Guatemala and Panama

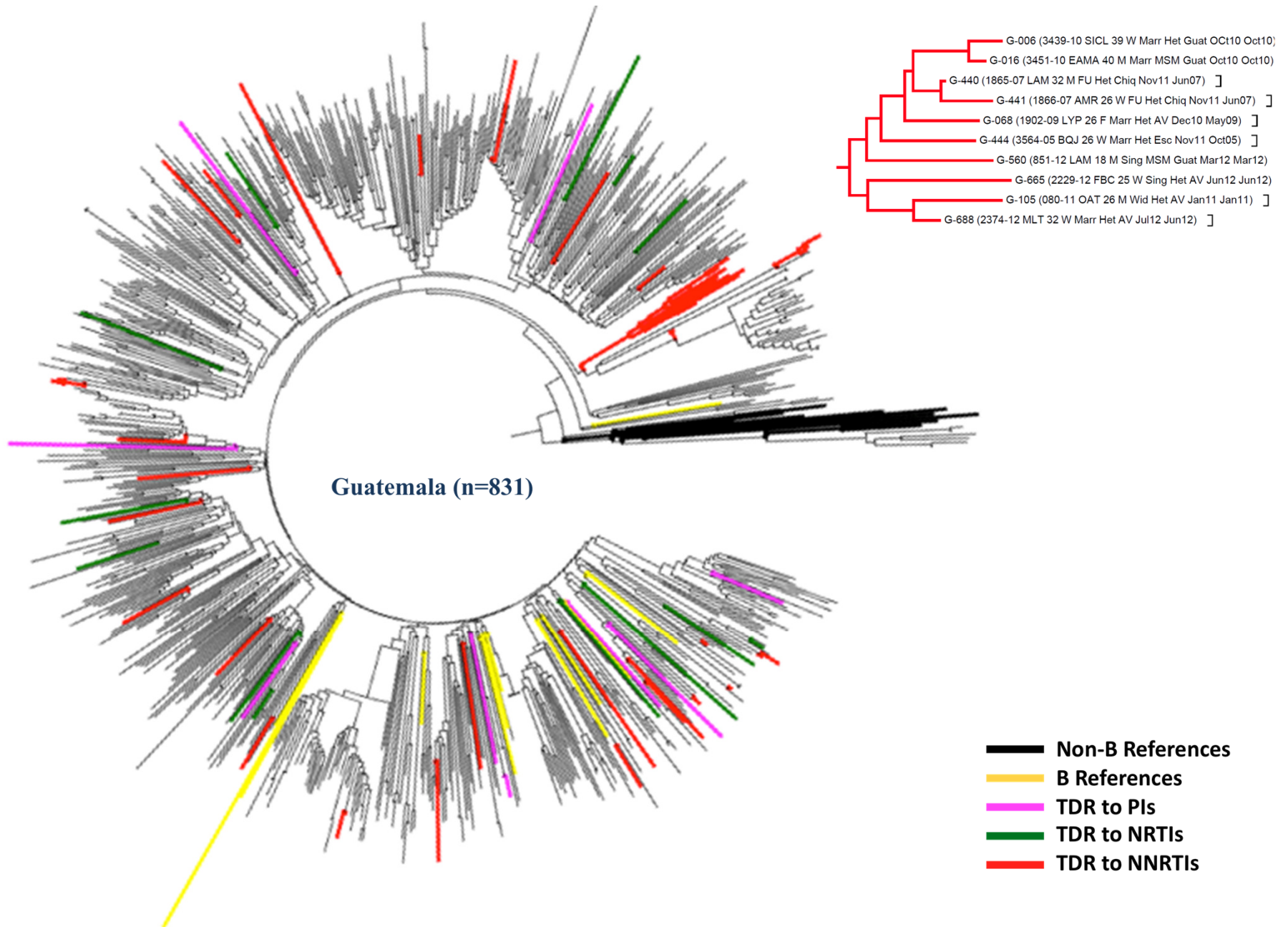


Different TDR mutation distributions/patterns in Mexico, Guatemala, Nicaragua and Panama

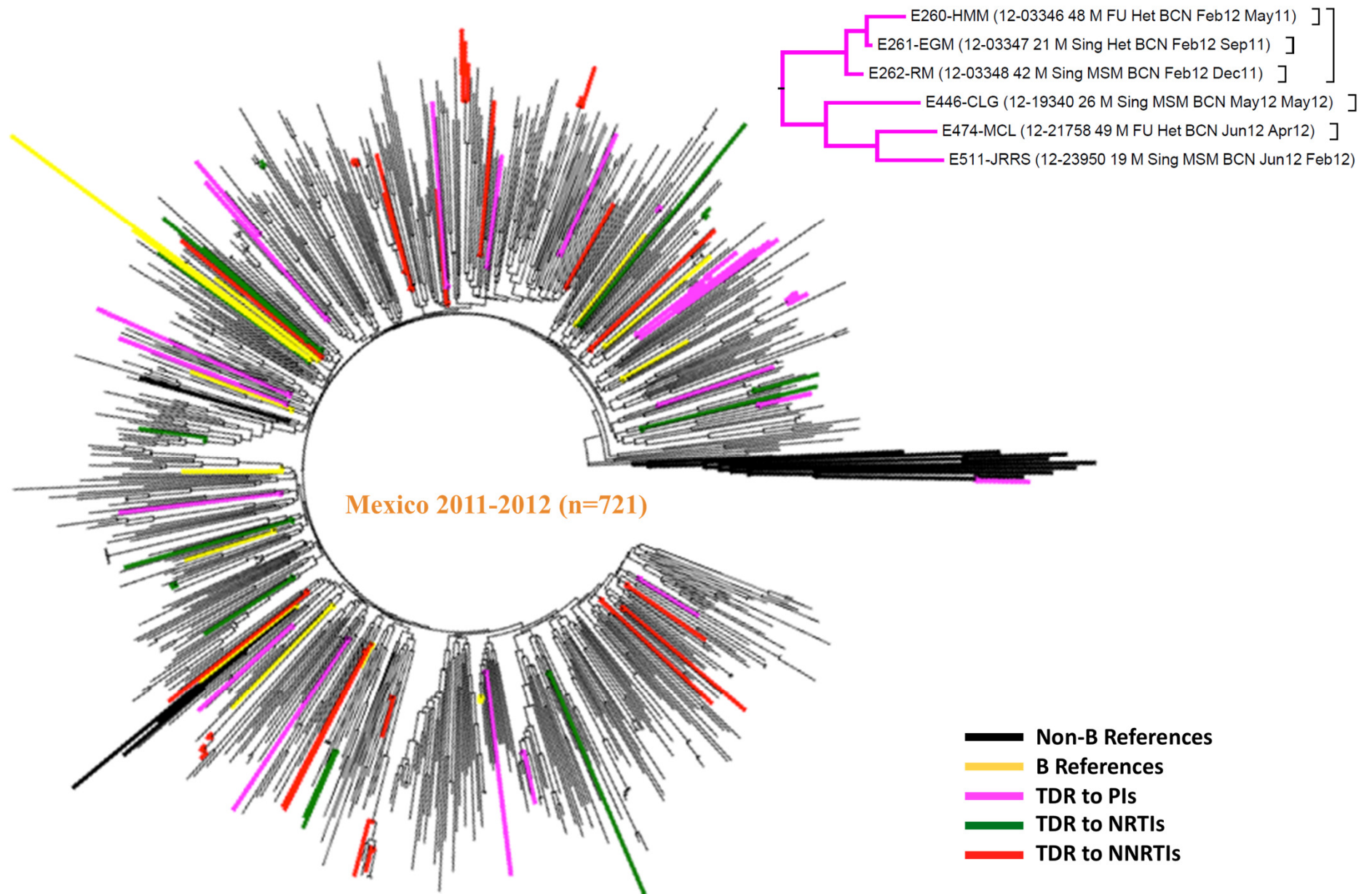


*Major TDR Mutation
 "In WHO TDR Surveillance
 Mutation List

Clustering of viruses with TDR to NNRTIs observed in Guatemala



Clustering of viruses with TDR to NNRTIs and PIs observed in Mexico



Conclusions

- ❖ TDR in Mexico at the intermediate level (2005-2012).
- ❖ Evidence of increasing trends in TDR to NNRTIs and PIs in Mexico (2005-2012).
 - WHO TDR threshold method suggests high levels of TDR in Mexico (any ARV drug) at the national level for 2011-2012.
 - Change of TDR patterns observed.
- ❖ Possible geographical differences in TDR levels within Mexico.
- ❖ TDR in Guatemala, Panama and Nicaragua remains at intermediate levels; however, characteristic TDR patterns were evident in each country.
 - Higher TDR to NNRTIs in Panama and Guatemala.
 - Higher TDR to NRTIs in Nicaragua.
- ❖ Possible transmission clusters of drug-resistant HIV in Mexico and Guatemala.
- ❖ Strong geographical HIV clustering suggests relatively closed transmission networks in each country.
- ❖ Ongoing work to assess HIV molecular epidemiology and TDR trends in the Mesoamerican Region.

Aknowledgements

Physicians, CIENI, INER

Akio Murakami
Daniela de la Rosa
María Gómez-Palacio
Karla Romero

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Christopher Ormsby
Ana Paola Carranco
Aarón Lecanda

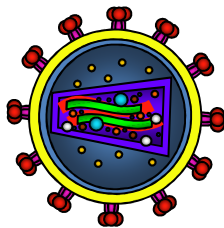
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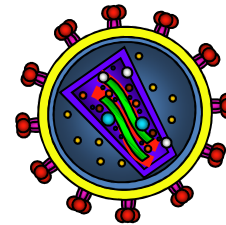
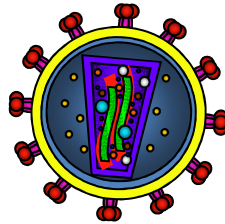
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Pamela González
Pedro Márquez
Verónica Quiroz
Margarita Matías



Funding

Comisión de Equidad y Género, Cámara de Diputados
Fundación México Vivo
ICyTDF
UC Mexus - CONACyT

Hospital Roosevelt, Guatemala, Guatemala

Carlos Mejía Villatoro
Ricardo Mendizábal
Amalia Girón
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National Ministry of Health, Belize

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Johani Lizama